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Evaluation of Enrollees' Perspectives on the Operations of the National Health Insurance Scheme in Nigeria

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Abstract

Background: The National Health Insurance Scheme (NHIS) was established in 2005 to act as an alternative source of funding for health care services but marred with operational problems. **Objective:** The study examined the mode of operation of the NHIS and assessed its adequacy to achieve set objectives in the face of contending factors from the point of view of enrollees. **Methods:** A descriptive cross-sectional survey of 300 enrollees in three tertiary health facilities in Southwestern Nigeria was undertaken between August and October, 2019. Participants were selected using a combination of quota and simple random sampling methods. Primary data were obtained using semi-structured questionnaires and focus group discussions. Frequency, percentages, weighted means and relative importance indices were used to analyse data at $p < 0.05$ level of significance. **Results:** Response rate for both focus groups and questionnaires was 100%. Mean age of respondents was 43.11 years while that of focus groups discussants was 40.81 years. Enrollees understood the objectives of the NHIS and its components especially its focus on improving service efficiency (85%). However, they posit that the mode of operations was inadequate to accomplish those goals. Factors identified as responsible for this include capacity limitations in terms of infrastructure (89%), human resources (84%), and financial resources (66%); corruption (65%) as well as poor responsiveness by service providers (44%). **Conclusion:** Enrollees in the NHIS in Nigeria understand the goals of the scheme even though more enlightenment is needed to drive home the philosophy. The mode of operations is inadequate to achieve the objectives of the scheme. Reforms are needed to address inadequacies in infrastructure, capacities and management of services.

Keywords: National Health Insurance Scheme; Healthcare Services, Nigeria

Introduction

The National Health Insurance Scheme (NHIS) in Nigeria was established in 2005 to provide universal coverage to Nigerians via social health insurance by providing a sustainable alternative source of funding for health care services. Nigeria is a federation of 36 semi-autonomous States with a federal capital territory in Abuja. There are 774 local government areas. Health is a joint responsibility of the federal, state, and local governments. The Federal government owns and manages the public-sector tertiary health care facilities; the states are responsible for secondary health facilities while the local governments are responsible for the primary health care centres across the country. The federal government sets the health agenda and gives policy directives to guide the health sector in Nigeria (Federal Ministry of Health Nigeria. 2014). The NHIS is one such policy initiative.

The NHIS is a social safety arrangement that provides financial security to the populace against unanticipated ill health. The formal sector workers, informal sector workers as well as the vulnerable groups are covered by the scheme programmes (NHIS, 2012; Mohammed, 2015). Contributions for NHIS are earnings-related. The employer pays 10% while the employee pays 5%, representing 15% of the employee's basic salary. However, the employer may choose to pay the whole contribution. The employee, a spouse and four biological children under the age of 18 years are covered by the healthcare benefits from the contributions. More children or dependents exceeding the age of 18 years on NHIS principal beneficiary could be covered on the payment of extra contributions by the principal beneficiary. The package is comprehensively planned to cover most of the health care needs of Nigerians (Odeyemi & Nixon. 2013).

There are five major stakeholders in the scheme; namely Employer, Employee, Health Care Provider (Primary and Secondary), Health Maintenance Organization (HMO) (the operators of the scheme) and the Government Agency -NHIS (Ministry of Health 2013). Employees of the federal civil service are automatically entitled to healthcare under the NHIS. However, to participate in the scheme, contributors will first register with an NHIS-approved HMO and thereafter register with a primary health care provider of their choice from an approved list of providers registered by their HMO. The contributor and his/her dependents are issued identification (ID) card at registration. In the event of sickness, the ID card entitles the insured person; his/her spouse and four children under the age of 18 years to full health benefits (Ministry of Health 2013).

Health care providers under the scheme are rewarded either by capitation or fee-for service rendered. Capitation is the payment to a primary health care provider by the Health Maintenance Organisations (HMOs) on behalf of a contributor. This is done monthly whether or not the services are accessed. Fee-for service is made by HMOs to non-capitation receiving health care providers who deliver services on referral from other health care providers (Adekola 2015). When a registered beneficiary (enrollee) in a health facility uses some form of health care, such person does not require cash to access the necessary treatment, except the 10% co-payment for the cost of drugs. In this manner, it prevents the normal practice of exchanging properties to cash for payment of health care services (catastrophic health expenditure). A 2013 report indicated that Nigeria had the highest out-of-pocket payment and the worst health indicators in the world (Gustafsson-Wright & Schellekens 2013). Reversing this trend must first address a number of challenges- from inadequate and poorly equipped health facilities, poor nutritional status inadequate access to affordable health care services, insufficient distribution of health care amenities, scarcity of drugs, poor thoughts of health workers, the huge cost of health services mostly out of the reach of the poor, poor infrastructure and improper health education approach (Olonade, et al.2019; Sparkes, et al. 2019).

As at February 2009, records indicate that the scheme had registered over 4 million Federal civil servants and their dependents (Agba, Ushie, & Osuchuchwu 2010). However, the services have been bedeviled with long waiting times, persistent out-of-pocket expenditures for out-of-stock medicines and supplies, corruption in the management of the scheme, poor attitudes of service providers, and inefficiencies at health care facilities, among others (Edeh & Udoikah 2015). Enrollees have been severally reported to express significant dissatisfaction with the scope, quality and management of services they receive under the NHIS, with some calling for the outright scrapping of the scheme (Edeh & Udoikah 2015; Eboh 2008; Azuogu, et al. 2016; Dutta & Charles 2013). Widespread discontent with the NHIS among consumers of healthcare seem to be justified considering that as of

2012, seven years after the commencement of the scheme, only an estimated 3% of the population of Nigeria had been covered by the scheme (Federal Government of Nigeria 1999).

From the foregoing, it seems inevitable that the NHIS must be reformed if it is to remain relevant in the quest for universal health coverage in Nigeria. Even though several stakeholders are involved in the scheme, all other participants (outside the enrollees/beneficiaries) contribute inputs and processes. The current study examined the perspectives of consumers of the health services as their opinions will provide an important calibration of the outputs of the collective efforts of all the input variables in the NHIS. The study considered enrollees' understanding of the objectives and mode of operation of the NHIS vis-a-vis the expected outcomes of the scheme.

Material and Methods

A descriptive cross-sectional study was undertaken using mixed data collection method. The study was carried out in three tertiary healthcare facilities, one from each of the States of Lagos, Ogun and Oyo in Southwestern Nigeria. These states were chosen because they are home to majority of the Health Maintenance Organisations (HMOs) with the highest registered principal enrollees or beneficiaries of the NHIS services in the country (NHIS. 2012). The Southwest zonal headquarters of NHIS is located in Ibadan, Oyo State with Lagos existing alone administratively. The study population comprised the NHIS Principal Enrollees/Beneficiaries in the three selected tertiary health facilities, namely Federal Medical Centre (FMC), Abeokuta, Ogun State; Federal Medical Centre (FMC), Ebute- Meta, Lagos State; and University College Hospital (UCH), Ibadan, Oyo State. Preliminary findings put the total population of enrollees at about 900.

In order to meet the objectives of the study, a combination of non-probabilistic and probabilistic sampling techniques was employed. First, quota sampling technique was used to select equal number of respondents (enrollees) from each tertiary healthcare facility. Sample size of 100 per facility was chosen. Simple random sampling technique was subsequently adopted to select the actual participants among the enrollees in the NHIS scheme. Seven (7) enrollees were randomly selected per facility to participate in the three Focus Group Discussions, one FGD per facility.

The study recruited enrollees who have been accessing health care services for at least one month and have visited for more than once. Beneficiaries/enrollees/patients who were 18 years old and above were included. These conditions were imposed to do away with the possibility of inability to recall and to ensure that individuals have sufficient knowledge about the services accessible under the NHIS scheme.

The study excluded individuals who were visiting for the first time, have not been accessing health care services under the NHIS or have not accessed services within the previous one month. Beneficiaries/enrollees who were below 18 years of age were excluded.

Research Instruments

Primary data were obtained using semi-structured questionnaires. Items on the instrument were developed from the policy document of the National Health Insurance Scheme (Federal Government of Nigeria 1999). The objectives of NHIS as stated in the policy document were examined. A 5-point agreement scale (strongly agree (5), agree (4), disagree (3), strongly disagree (2) and undecided (1)) was employed to assess level of awareness and satisfaction with mode of operation of NHIS by respondents. Data from questionnaires were augmented with Focus group discussions (FGDs) using an interview guide.

The questionnaires were subjected to the expert scrutiny of two senior faculty members (including the principal investigator) who had expertise in social health insurance. Their comments and corrections were used to ensure face and construct validity of the instruments. To ensure reliability of the instrument, a test-retest measurement was employed using forty (40) respondents from the Obafemi Awolowo University Teaching Hospital Ile-Ife, Osun State. The reliability analysis gave a Cronbach Alpha reliability coefficient of 0.87. (This indicated that the questionnaire was reliable as it measured the study constructs consistently).

Ethical approval (HREC No: IPHOAU/11/1024) was obtained from the Health Research Ethic Committee (HREC) of the Institute of Public Health, Obafemi Awolowo University, Ile-Ife Nigeria.

Eighteen (18) research assistants were carefully recruited and trained on data collection. They were assigned in three teams of six (6) to each of the three tertiary health facilities for the purpose of questionnaire administration and collection between August 1 to October 31, 2019. An overage of 30% (that is, additional 30) was added to number of questionnaires distributed per facility to ensure 100 useable responses were collected. The researchers personally conducted the focus group discussions with selected respondents within the same time period. A dual-moderator strategy was adopted with one researcher ensuring the discussions proceeded smoothly while the second ensured all relevant topics were covered (Ogunbameru & Ogunbameru 2018). A research assistant took notes. The discussions were tape-recorded and transcribed verbatim for data analysis. All respondents gave their informed consents in writing.

Data obtained from the instruments was carefully sorted, coded, and cross-checked for data management using Excel spreadsheet. It was then exported to Statistical Package for Social Sciences (SPSS) version 22.0 for Windows software for analysis at $p < 0.5$. Analytical tools employed include descriptive statistics (means and frequencies), Bar Charts, Multiple Comparison, Range tests and Relative Importance Index (RII).

For a critical examination of the objectives of NHIS, the study identified the major goals stated in the NHIS policy statement and examined the extent to which the enrollees (beneficiaries/patients) agreed that the operations of the scheme actually addressed these goals. Ten statements were drawn up for examination as follows:

- Every Nigerian now has access to good health care services.
- The NHIS scheme has protected every Nigerian family from the financial hardship of huge medical bills;
- It has limited the rise in the cost of health care services in Nigeria;
- It has ensured an equitable distribution of health care costs among different income groups in Nigeria;
- The scheme has ensured the maintenance of high standard of health care delivery services;
- It has also ensured efficiency in health care services;
- The scheme has improved and harnessed private sector participation in the provision of health care services;
- It has ensured adequate distribution of health facilities within the Federation;
- The NHIS has ensured equitable patronage of all levels of health care; and
- The scheme has ensured the availability of funds to the health sector for improved services.

Responses from the ten statements were measured using a Likert Scale (Strongly Agreed, Agreed, Undecided, Disagreed, Strongly Disagreed) and were coded 5, 4, 3, 2, 1 respectively. These codes were used as weighting factors for the computation of weighted totals. These totals were divided by the respective sample sizes to obtain weighted average, also referred to as relative importance indices (RII), for each of the statements. The RII was used in ranking the statements and to generate the corresponding significant values.

$$\text{Weighted Total} = \sum f \dots\dots\dots (i)$$

$$\text{Relative Importance Index } (\bar{X}) = \sum f/n \dots\dots\dots (ii)$$

Enrollees' perspective on the operations of the scheme was examined alongside factors affecting the effectiveness of the programme.

Results

Sociodemographic characteristics of respondents showed that for every male enrollee in NHIS, there were about two females (31%: 69%). The age distribution revealed that the largest proportion of enrollees (55%) ranged between 30 and 49 years. Majority (75%) of the respondents were married. In terms of education, the largest group (70%) had basic tertiary education (between Advanced Levels and first degrees) while the smallest group (6.3%) had Masters Degrees or PhDs. Most of the respondents may be considered as sufficiently knowledgeable in social health insurance as over half (55%) had 6-10 years' experience with NHIS while another 22% had been receiving services for over a decade (Table 1). The mode of operations of the NHIS revealed that the most prominent point

of agreement among beneficiaries (85% agreed or strongly agreed) was that the scheme has ensured efficiency in healthcare services (Table 2). Most enrollees (76%) were of the opinion that NHIS ensured adequate distribution of healthcare facilities. Enrollees (73%) were generally satisfied with the NHIS strategy of pulling of funds/investments to drive the scheme. Majority (71%) either agreed or strongly agreed that the scheme has protected Nigerian families from catastrophic financial burdens of huge medical bills. These data need to be weighed against the finding that while 42% of enrollees were aware of the components of the NHIS, another 42% was unaware (Table 3). As high as 34% of enrollees were unsure whether NHIS has improved access to quality health care services as 65% could not access care at the nearest accredited facilities for medical emergencies (Table 4). In terms of the driving philosophy of the scheme, 66% of enrollees did not know that NHIS was meant to be private sector driven (Table 3) while 56% were unsure of whether the scheme has mobilized private sector participation in the provision of health care services. Most clients reported a significant level of satisfaction with the range and quality of services they received under the scheme. Only 28% felt the inadequacy of services was a serious factor while 39% felt otherwise (Table 5). Social health insurance as a healthcare financing mechanism requires a robust infrastructure backbone. Most enrollees (89.4%) identified poor infrastructure/equipment as the major bane of the NHIS (Table 5). Closely following the infrastructure deficit is the dearth of skilled manpower (83.7%) and poor manpower development programme (64.3%). Even though the enrollees were satisfied with the fund pooling strategy of NHIS, 66% of them still were of the opinion that poor funding exerts serious or very serious effects on the scheme. In Nigeria, the healthcare system is notorious for frequent industrial unrest and 66% of enrollees believe this exerts serious negative effects on the effectiveness of NHIS. A significant number of the enrollees thought that poor responsiveness by healthcare providers seriously affects the effectiveness of the NHIS. While 44.3% experience delays in issuance of identification and registration numbers, 57.3% had delays in issuance of their referral codes. About 60% rated the organisation of work by healthcare service providers as poor but only 26% saw the overall quality of care as low. Evidence from Focus Group Discussions revealed that certain trends were common among the three focus groups. The enrollees expressed that they were being faced with delay in the issuance of registration cards and referral codes, poor response and empathy of the workers. An excerpt from the responses given by the enrollees went thus;

“We must say NHIS has really been helpful. But the workers are not helping most times. After a very slow registration process, to even get referral code is like war. On two occasions, I had to keep calling the worker that would issue referral codes to me. I called up to 5 times before he could send it to me ... another problem with the scheme is the incessant out-of-stock syndrome. After drug prescriptions, the NHIS pharmacy is used to giving cheap drugs and telling us that the other drugs have finished ... apart from this, they need to add more services, especially laboratory tests, to the coverage of the scheme.”

One enrollee from FMC Abeokuta said

“It seems the scheme is faced with funding inadequacy. We experience delays in obtaining referral codes for emergencies. I hear there are delays and/or irregular payment of capitation fee and fee-for-service claims to the service providers. Aside all these, you can see there are significant shortages of personnel. Some of their equipment and infrastructure are dilapidated. We are also being faced with referral issues, out-of-pocket payment, registration delays, out-of-stock syndrome and exclusion of some services. If the NHIS handlers can help look into these, there will be less operational issues to contend with”

Discussants were asked, whether in their opinion, they thought that all the stakeholders were sufficiently carried along in the operations of the scheme? Their unanimous response across the three health facilities indicated that they were not sufficiently consulted and considered in the design, implementation and assessment of the NHIS.

Table 1: Socio-demographic Characteristics of the Respondents

Variables	FMC Abeokuta		FMC Ebute Metta		UCH Ibadan		Total N (%)
	n	%	n	%	n	%	
Gender							
Male	32	32.0	28	28.0	33	33.0	93 (31.0)
Female	68	68.0	72	72.0	67	67.0	207 (69.0)
Age Groups							

Below 20	0	0.0	5	5.0	5	5.0	10 (3.3)
20 – 29	4	4.0	24	24.0	15	15.0	43 (14.3)
30 – 39	21	21.0	33	33.0	24	24.0	78 (26.0)
40 – 49	38	38.0	16	16.0	33	33.0	87 (29.0)
50 – 59	23	23.0	12	12.0	20	20.0	55 (18.3)
60 and above	14	14.0	10	10.0	3	3.0	27 (9.0)
Marital Status							
Single	29	29.0	10	10.0	24	24.0	63 (21.0)
Married	68	68.0	88	88.0	69	69.0	225 (75.0)
Others	3	3.0	2	2.0	7	7.0	12 (4.0)
Education							
Grade II	17	17.0	27	27.0	27	27.0	71 (23.7)
Cert/SSE/GCE							
O'Level							
A'Level/NCE/OND	48	48.0	39	39.0	28	28.0	115 (38.3)
D							
HND/Degree	32	32.0	28	28.0	35	35.0	95 (31.7)
Master/Ph.D.	3	3.0	6	6.0	10	10.0	19 (6.3)
Length of experience¹							
≤ 5 years	35	35.0	21	21.0	14	14.0	70 (23.3)
6 – 10 years	46	46.0	56	56.0	62	62.0	164 (54.7)
11 -15 years	14	14.0	12	12.0	20	20.0	46 (15.3)
≥ 15 years	5	5.0	11	11.0	4	4.0	20 (6.7)
<i>Total</i>	100	100	100	100	100	100	300 (100.0)

Abbreviations: FMC-Federal Medical Centre; UCH – University College Hospital; OND Ordinary National Diploma; HND- Higher National Diploma

Table 2: Enrollees' Assessment of the Objectives of NHIS (N=300)

<i>To what extent do you agree with the following statements about the objectives of NHIS?</i>	SA (f ₅)	A (f ₄)	UD (f ₃)	D (f ₂)	SD (f ₁)	Sig.	Σ	\bar{X}	Rank
Ensured efficiency in health care services	199 (66.3)	56 (18.7)	21 (7.0)	11 (3.7)	13 (4.3)	0.00	1317	4.39	1 st
Ensured adequate distribution of health facilities within the Federation	63 (21.0)	166 (55.3)	29 (9.7)	29 (9.7)	13 (4.3)	0.01	1137	3.79	2 nd
Protected every Nigerian family from the financial hardship of huge medical bills	78 (26.0)	135 (45.0)	18 (6.0)	55 (18.3)	14 (4.7)	0.01	1108	3.69	3 rd
Maintenance of high standard of health care delivery services	101 (33.7)	52 (17.3)	69 (23.0)	28 (9.3)	50 (16.7)	0.01	1026	3.42	4 th
Ensured the availability of funds to the health sector for improved services	91 (30.3)	29 (9.7)	89 (29.7)	35 (11.7)	56 (18.7)	0.02	964	3.21	5 th

Ensured an equitable distribution of health care costs among different income groups in Nigeria	37 (12.3)	121 (40.3)	29 (9.7)	88 (29.3)	25 (8.3)	0.02	957	3.19	6 th
Ensured equitable patronage of all levels of health care	55 (18.3)	87 (29.0)	36 (12.0)	100 (33.3)	22 (7.3)	0.02	953	3.18	7 th
Improved and harnessed private sector participation in the provision of health care services	23 (7.7)	56 (18.7)	169 (56.3)	19 (6.3)	33 (11.0)	0.03	917	3.06	8 th
Limited the rise in the cost of health care services in Nigeria	74 (24.7)	52 (17.3)	69 (23.0)	15 (5.0)	90 (30.0)	0.03	905	3.02	9 th
Every Nigerian now has access to good health care services	28 (9.3)	69 (23.0)	101 (33.7)	39 (13.0)	63 (21.0)	0.04	860	2.87	10 th
SA - Strongly Agree; A – Agree; UD - Undecided; D - Disagree; SD - Strongly Disagree; Σ - Weighted Total; \bar{X} – Weighted Mean; Significant at $p < 0.05$ level									

Table 3: Enrollees' Awareness of the Components of the NHIS ($N=300$)

<i>Awareness of Components of NHIS</i>	SA	A	D	SD	UD	Sig.
I am aware of the NHIS and its contents	53 (17.7)	74 (24.7)	47 (15.7)	25 (8.3)	101 (33.7)	0.00
The philosophy on which the NHIS is pivoted is private-sector driven	11 (3.7)	25 (8.3)	67 (22.3)	158 (52.7)	39 (13.0)	0.11
Government's position of administrator-regulator instead of owner-operator is considered appropriate for successful implementation	89 (29.7)	94 (31.3)	16 (5.3)	41 (13.7)	60 (20.0)	0.06
The objectives contained in the scheme are clearly spelt out and adequate for growth and development of the health sector	29 (9.7)	138 (46.0)	41 (13.7)	60 (20.0)	32 (10.7)	0.02
The focus on accessing, sensitization, processing, funding, utilization and marketing of health insurance in the scheme is quite in order	63 (21.0)	101 (33.7)	63 (21.0)	21 (7.0)	52 (17.3)	0.01
The emphasis on human resources development and capacity building as contained in the scheme is very crucial to successful implementation	169 (56.3)	17 (5.7)	52 (17.3)	32 (10.7)	30 (10.0)	0.03
Attention drawn on government's provision of adequate infrastructural facilities will guarantee smooth operations in the health sector	94 (31.3)	59 (19.7)	42 (14.0)	32 (10.7)	73 (24.3)	0.01

Emphasis placed on funding/investment in the health sector as contained in the scheme is a welcome development	203 (67.7)	17 (5.7)	35 (11.7)	41 (13.7)	4 (1.3)	0.00
Appropriate emphasis placed on research and development will guarantee successful implementation	72 (24.0)	63 (21.0)	101 (33.7)	25 (8.3)	39 (13.0)	0.02
The procedure for constant review of the scheme needs to be specified in the policy document	214 (71.3)	32 (10.7)	19 (6.3)	19 (6.3)	16 (5.3)	0.07

SA - Strongly Agreed; A – Agreed; UD - Undecided; D - Disagreed; SD - Strongly Disagreed; p <0.05

Table 4: Enrollees' Perspectives on Mode of Operations of HMOs regarding the Rights and Privileges of Beneficiaries/Enrollees (N=300)

<i>To what extent is an enrollee allowed to:</i>	SA	A	UN	D	SD	Sig.
Freely choose his/her accredited primary health care facility (ies)	63 (21.0)	28 (9.3)	178 (59.3)	12 (4.0)	19 (6.3)	0.00
Change primary health care facility after six (6) months with the present primary health care facility if he/she so desires?	79 (26.3)	84 (28.0)	67 (22.3)	41 (13.7)	29 (9.7)	0.01
Access care once the name is on the current NHIS enrollee register after proper identification?	81 (27.0)	127 (42.3)	63 (21.0)	9 (3.0)	20 (6.7)	0.00
Access treatment at the nearest NHIS accredited health care facilities on emergency presentations?	18 (6.0)	32 (10.7)	56 (18.7)	100 (33.3)	94 (31.3)	0.00
Add or remove dependant (s) subject to approval by NHIS?	114 (38.0)	59 (19.7)	67 (22.3)	12 (4.0)	48 (16.0)	0.01
Allowed to add extra dependant (s) on payment of a fee?	97 (32.3)	111 (37.0)	70 (23.3)	12 (4.0)	10 (3.3)	0.00

SA - Strongly Agreed; A – Agreed; UD - Undecided; D - Disagreed; SD - Strongly Disagreed; Σ - Weighted Total; \bar{X} – Weighted Mean; p <0.05

Table 5: Enrollees' Perspectives on Factors Affecting NHIS operations (N=300)

<i>To what extent do the under listed factors affect the effectiveness of NHIS operations?</i>	No Effect	Very Little Effect	Moderate Effect	High Effect	Very High Effect
Delayed issuance of NHIS identity card and registration number to enrollees	4 (1.3)	74 (24.7)	89 (29.7)	100 (33.3)	33 (11.0)
Delayed issuance of referral codes to beneficiaries by HMOs	2 (1.0)	55 (18.3)	71 (23.7)	141 (47.0)	31 (10.3)
Industrial and social unrest	1 (0.0)	6 (2.0)	95 (31.7)	139 (46.3)	59 (19.7)
Poor/Inadequate funding	0 (0.0)	4 (1.3)	98 (32.7)	189 (63.0)	9 (3.0)
Lack of proper enlightenment of the enrollees at the point of registration on what services are covered (or not covered)	54 (18.0)	87 (29.0)	120 (40.0)	20 (6.7)	19 (6.3)

Inadequate level of infrastructural facilities, materials and equipment	4 (1.3)	9 (3.0)	19 (6.3)	206 (68.7)	62 (20.7)
Inadequate manpower (staffing)	0 (0.0)	2 (1.0)	47 (15.7)	219 (73.0)	32 (10.7)
Inadequate human capacity development (i.e. training and re-training of HCPs, HMO and NHIS staff members)	25 (8.3)	19 (6.3)	63 (21.0)	174 (58.0)	19 (6.3)
Out-of-pocket spending by enrollees due to non-availability of services or tests or procedures at the HCF level	11 (3.7)	32 (10.7)	124 (41.3)	62 (20.7)	71 (23.7)
Lack of access by enrollees to care outside their primary care provider even in cases of emergency?	10 (3.3)	26 (8.7)	147 (49.0)	69 (23.0)	48 (16.0)
Inefficient dispute resolution mechanisms among stakeholders (NHIS, HMOs, HCFs and enrollees) gone in resolving some of the challenges?	151 (50.3)	29 (9.7)	87 (29.0)	11 (3.7)	22 (7.3)
Inadequate protection of enrollees from abuse and avoidable harm (i.e. Safety)	84 (28.0)	36 (12.0)	47 (15.7)	58 (19.3)	75 (25.0)
Inadequate patients care, treatment and support services (i.e. Effectiveness and efficiency)	48 (16.0)	69 (23.0)	99 (33.0)	62 (20.7)	22 (7.3)
Poor staff involvement and treatment of patients with compassion, kindness, dignity and respect (i.e. poor attitude to care)	75 (25.0)	62 (20.7)	94 (31.3)	19 (6.3)	50 (16.7)
Poor organization of services so that they do not meet patient's needs (i.e. poor responsiveness)	22 (7.3)	39 (13.0)	58 (19.3)	105 (35.0)	76 (25.3)
Low Quality of care and services	58 (19.3)	101 (33.7)	63 (21.0)	19 (6.3)	59 (19.7)
Lack of transparency and accountability (i.e. Corruption)	0 (0.0)	21 (7.0)	84 (28.0)	113 (37.7)	82 (27.3)
Inadequate financial protection for enrollees	14 (4.7)	25 (8.3)	179 (59.7)	34 (11.3)	48 (16.0)
Lack of patient satisfaction with the services delivered	28 (9.3)	187 (62.3)	24 (8.0)	19 (6.3)	42 (14.0)

NHIS-National Health Insurance Scheme; HMO-Health Maintenance Organisations; HCF- Health care facilities

Discussion

The male to female ratio was about 1:2. Even though there has not been any similar previous evidence, this finding may be a reflection of the health-seeking behaviour of the different gender in Nigeria. The age distribution of the respondents fell between 20-59years. This is understandable given that a greater part of those currently employed in the formal public sector lie within that age bracket. Most of the respondents were of the opinion that NHIS Scheme was of immense benefit to them. This is in apparent agreement previous evidence that the NHIS has succeeded in saving many Nigerians from finance-related barriers in accessing quality health care (Onwujekwe, et al. 2019). However, 35% disagreed or strongly disagreed that the scheme has slowed down the rise in healthcare cost which affirms the claim by HMOs that limiting the rise in cost of healthcare represents the least achieved goal of the NHIS, a fact which has previously been attributed to low health insurance penetration (Adekola 2015). Some authors have expressed strong opinion that for the NHIS to achieve its objective of universal access to quality health care there would be urgent need for expansionary drive and more funding to establish more NHIS offices in health care facilities (Hao 2015). A survey of some service providers in Lagos State examined the

objectives of the NHIS and reported that the scheme had improved and harnessed private sector participation in the provision of health care services and ensured adequate distribution of health facilities within the federation (Adeniyi & Onajole 2010). It was also reported that the NHIS has harnessed private sector participation in the provision of health care services and many more corporate bodies were interested in partnering with the scheme (Mohammed 2015). Findings from this study show that enrollees cannot be said to agree with these claims. There seems to be a significant disconnect between the HMOs and enrollees on the mode of operation of the scheme as 22% of beneficiaries were unsure whether they could add or remove dependents subject to NHIS approval while only 30% knew they were allowed to freely choose accredited health care facilities (Table 4). As earlier reported by Ibe, et al. 2017; poor orientation and the attendant misinformation about NHIS left enrollees ignorant of the service coverage of the NHIS, which in turn affected their perception of the scheme. This contradicts the finding of this study, that 56% of enrollees agree or strongly agree that the objectives of NHIS are clearly spelt out and adequate for the growth and development of the health sector. The study showed that the mode of operations of the NHIS did not allow enrollees to access treatment at the nearest NHIS accredited health care facilities on emergency presentations. This has implications for avoiding complications in cases of emergencies. Over half of respondents (57.7%) reported they were free to add or remove dependents in consonance with earlier evidence which reported the flexibility in the modes of NHIS operations in that enrollees were allowed to add or remove dependents, subject to approval by the NHIS (Agba, Ushie, & Osuchuchwu 2010). The addition of such enrollees required extra payment though; the amount to be paid would be less than the amount hitherto paid by the original beneficiary. A related study underscored the need to allow the addition of enrollees (Odeyemi & Nixon 2013). For example, when a single (unmarried) NHIS beneficiary gets married, there is need for the spouse to be added. A newly married wife needs to be immediately added as NHIS beneficiary so that her antenatal, delivery and post-natal care could be adequately covered under the scheme. The need to allow the addition of one's spouse and children upon the payment of a specified extra amount of money has been well published (Odeyemi & Nixon 2013; Onyedibe, Goyit, & Nnadi, 2012). This confers same benefits on the original beneficiary and the new additions. An earlier report showed that sexual and reproductive health services were the most sought services among female enrollees of the NHIS in a health facility based assessment of the utilization of NHIS services by specific population groups (Odeyemi & Nixon 2013). Focus group discussants (enrollees) in the present study also acknowledged that they were provided with health and family planning education and choices. Family planning education was considered important in that it helps prevent unwanted pregnancy/births and by extension, helps prevent or reduce strain on health care facilities. The finding from this study on factors affecting operations of NHIS re-enforces previous evidence that inadequate human capacity development (i.e. training and re-training programmes for health care professionals, HMO and NHIS staff members) was partly responsible for the apparent ineffectiveness of the NHIS (Gustafsson-Wright & Schellekens 2013). Doctor-patient ratio in the sampled health care facilities was so high that patients reportedly had to wait for long hours before they could be attended to. The inadequate manpower in Nigerian health facilities have been previously discussed by various researchers (Olonade, et al.2019; Sparkes, et al. 2019; Adesina, 2019). The organisation of the healthcare services as well as the quality of services were identified by this study as poor. This finding is consistent with the view expressed in a similar study which identified sharp disparities on the perception of quality of care reported by the patients and the care givers (Adekola 2015). However, health system experts caution that though patients who were the beneficiaries of the services were likely to be honest, they would also possibly under-report effectiveness on the belief that they could be better served (Stuckler, et al. 2010). Healthcare facilities often experience out-of-stock syndrome for many essential medicines and supplies leading to avoidable out-of-pocket expenditures for 44.4% of enrollees who have to source these necessities elsewhere. Ordinarily, the NHIS operational guidelines entitle enrollees to drugs and equipment with only 10% of the cost payable by enrollees for full treatment until recovery (Ministry of Health 2013). Moreover, the inability to access care outside the primary healthcare providers, even after proper identification, was considered a serious setback by 39% of enrollees. Findings from the Focus Group Discussions were in agreement with previous evidence on patients' perceptions of the quality of service in general and the effectiveness of health insurance in particular (Odeyemi & Nixon 2013; Abiola, et al. 2019). However, discussants appreciated the importance of certain services they received under the scheme, including health and family planning education and choices, diagnostic tests as contained in the NHIS Diagnostic Test Lists, and certain consultation within the area of dental care and specific surgical operations. Earlier evidence reported that prescribed drugs and pharmaceutical care as contained in the NHIS Drugs List, in addition to preventive care including immunization (as applied in the National Programme on Immunisation) were made available to NHIS

enrollees (Osungbade, et al. 2014). These findings were supported by discussants. Further on the modes of operations of the NHIS, discussants acknowledged that in emergency cases, referral notifications were received within 48 hours as stipulated in the scheme. However, this finding falls short of best practices as seen when compared to the mode of operation of the health insurance in the United States where there were real time instant referral notifications of all referral operations (Odeyemi & Nixon 2013). In the United States and the United Kingdom, authorisation codes remained active until the patients were certified to have fully stabilized and completed all treatments (Onoka, et al. 2013).

Conclusion

National Health Insurance Scheme (NHIS) activities were fairly understood by enrollees (patients), especially as it relates to ensuring equitable distribution of health care costs among different income groups in Nigeria. However, the mode of operation of the scheme was inadequate due to capacity limitations in terms of infrastructure, financial and human resources, inefficient management and poor responsiveness by service providers. Therefore, an urgent policy is needed to reform the NHIS in order to address these identified constraints.

References

- Abiola, A.O., Ladi-Akinyemi, T.W., Oyeleye, O.A., Oyeleke, G.K., Olowoselu, O.I., & Abdulkareem, A.T. (2019). Knowledge and utilisation of National Health Insurance Scheme among adult patients attending a tertiary health facility in Lagos State, South-Western Nigeria. *African Journal of Primary Healthcare and Family Medicine*, 11(1), 2018. doi: [10.4102/phcfm.v11i1.2018](https://doi.org/10.4102/phcfm.v11i1.2018)
- Adekola, L. (2015). Health Insurance: The Theoretical Basis of Administration. Available at <http://www.medicalworldnigeria.com/2015/01/health-insurance-the-theoretical-basis-by-dr-lawumi-adekola#.VL9oC2Mpe00>. Retrieved February 20, 2020.
- Adeniyi, A.A., & Onajole, A. T. (2010). The National Health Insurance Scheme (NHIS): A Survey of Knowledge and Opinions of Nigerian Dentists' in Lagos. *African Journal of Medicine and Medical Sciences*, 39(1), pp 29-35.
- Adesina, D. (2019). The National Health Insurance Scheme: The Nigerian Doctor Available at <http://www.thenigeriandoctor.com.?news.php?extend.85D> Retrieved Dec.15, 2020.
- Agba, A.M.O, Ushie, E.M., & Osuchuchwu, N.C. (2010). National Health Insurance Scheme and Employee's Access to Health Services in Cross River State. *Global Journal of Human Social Science*, 10 (7), pp 9-16.
- Azuogu, B.N., Madubueze, U.C., Alo, C, Ogbonnaya, L.U. & Ajayi, N.A. (2016). Level of awareness, and factors associated with willingness to participate in the National Health Insurance Scheme among traders' in Abakaliki main market, Ebonyi State, Nigeria; *African Journal of Medical and Health Sciences*, 15 (1), pp18-23. doi: 10.4103/2384-5589.183887
- Dutta, A & Charles, H. (2013). Scaling up National Health Insurance in Nigeria: Learning from Case Studies of India, Colombia, and Thailand. Washington, DC: Futures Group, Health Policy Project. Available at <https://www.healthpolicyproject.com/index.cfm?ID=publications&get=pubID&pubID=96>; Retrieved May 21, 2019
- Eboh, D. (2008). National Health Insurance Scheme: Just a Name or a Model for Realistic Change in Health Care Delivery in Nigeria. Available at <http://www.mebodomanagement> Retrieved Sep 12, 2019.
- Edeh, J.N. & Udoikah, J.M. (2015). National Health Insurance Scheme and Administration in Nigeria: An Assessment. *International Journal of Science and Research*, 6 (4), pp 1-12.
- Federal Government of Nigeria. (1999). The National Health Insurance Act 1999. Available at <http://www.nhis.gov.ng/home>. Retrieved Sep 10, 2019
- Federal Ministry of Health Nigeria. (2014). Harmonized Country Plan of Priority Interventions 2014-2015. Abuja: Federal Ministry of Health. Available from: <http://www.health.gov.ng/doc/HCPofP%20I.pdf>. Accessed June 2, 2020
- Gustafsson-Wright E, & Schellekens O. (2013). Achieving Universal Health Coverage in Nigeria One State at a Time: A Public-Private Partnership Community-Based Health Insurance Model. Brookings, Washington DC, USA. Available at <https://+Achieving+universal+health+coverage+in+Nigeria+one+state+at+a+time%3A+a+public-private+partnership+community-based+health+insurance+model.&btnG>; Retrieved Aug 12, 2019.

- Hao, Y. (2015). Universal Health Insurance Coverage for 1.3 Billion People: What Accounts for China's Success? *Health Policy*, 119 (9), pp 1145–1152.
- Ibe, O., Honda, A., Etiaba, E., Ezumah, N., Hanson, K. & Onwujekwe, O. (2017). Do beneficiaries' views matter in health care purchasing decisions? Experiences from the Nigerian tax-funded health system and the formal sector social health insurance program of the national health insurance scheme. *International Journal of Equity in Health*, 16:216. <https://doi.org/10.1186/s12939-017-0711-y>.
- Ministry of Health. (2013). Federal Republic of Nigeria National Health Insurance Scheme Handbook. Operational Guidelines on National Health Insurance Scheme 2006. National Health Insurance Scheme. *Nigeria Medical Practice*, 43(2): p 2.
- Mohammed, D. (2015) Expanding Health Insurance Coverage in Nigeria. Available at <http://www.gamji.com/article9000/news9562.html>. Retrieved Sep 10, 2019.
- NHIS. (2012) National Health Insurance Scheme. Operational Guidelines. Available at <http://www.nhis.gov.ng/home/> Retrieved Sep 5, 2019.
- Odeyemi IAO, & Nixon J. (2013). Assessing Equity in Healthcare through the National Health Insurance Schemes of Nigeria and Ghana: A Review-Based Comparative Analysis. *International Journal for Equity in Health*, 2: 9. DOI <http://doi.org/10.1186/1475-9276-129>
- Ogunbameru, O.A., & Ogunbameru, B.O. (2018). The Dynamics of Social Science Research; Penthouse Publications, Ibadan Nigeria, pp 134-9
- Olonade O, Olawande, T.I., Alabi, O.J. & Imhonopi, D. (2019). Maternal mortality and maternal health care in Nigeria: Implications for socioeconomic development. *Open Access Macedonian Journal of Medical Sciences*, 7(5), pp 849–855. doi:10.3889/oamjms.2019.041
- Onoka, C.A., Onwujekwe, O.E., Uzochukwu, B.S., & Ezumah, N.N. (2013). Promoting universal financial protection: Constraints and enabling factors in scaling-up coverage with social health insurance in Nigeria. *Health Research and Policy Systems*, pp 11:20.
- Onwujekwe, O., Ezumah, N., Mbachu, C., Obi, F., Ichoku, H., Uzochukwu, B. & Wang, H. (2019). Exploring effectiveness of different health financing mechanisms in Nigeria; what needs to change and how can it happen? *BMC Health Services Research*, 19, 661. <https://doi.org/10.1186/s12913-019-4512-4>
- Onyedibe, K.I., Goyit, M.G. & Nnadi, N.E. (2012). An Evaluation of the Health Insurance Scheme (NHIS) in Jos; a North-Central Nigerian City. *Global Advanced Research Journal of Microbiology*, 1(1), pp 5-12.
- Osungbade, K.O., Obembe, T.A. & Oludoyi, A. (2014). User's satisfaction with services provided under National Health Insurance Scheme in South Western Nigeria. *International Journal of Tropical Diseases and Health*. 4(5), pp 595–607. doi:10.9734/IJTDDH/2014/7280
- Sparkes, S.P., Bump, J.B., Özçelik, E.A., Kutzin, J. & Reich, M.R. (2019). Political Economy Analysis for Health Financing Reform, *Health Systems and Reforms* 5(3), pp183-194, doi: 10.1080/23288604.2019.1633874
- Stuckler, D., Feigl, A.B., Basu, S. & McKee, M. (2010). The Political Economy of Universal Health Coverage: Background Paper for the First Global Symposium on Health Systems Research. Technical Report. WHO, Geneva. Available at <https://researchonline.lshtm.ac.uk/id/eprint/2157>; Retrieved January 26, 2020



Effect of Egg Consumption on Serum Protein Levels of Some Secondary School Students in Ibadan, Nigeria

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Abstract

Background: Eggs are sources of protein, fats and micronutrients that play an important role in basic nutrition. **Objectives:** This study was designed to assess the effect of egg consumption on serum protein levels of some secondary school students of two local Government areas in Ibadan. **Method:** This study involved 154 students selected using random selection sampling method, aged between 13 and 23 years. Teachers were exempted from the study. Protein Level was measured using standard methods in all the subjects at baseline and two weekly for eight weeks. Test group of subjects were given one boiled averaged sized egg to eat daily and the control group was given 100mls of water to drink daily for one month. All measurements were recorded in the recording book. Data was analyzed using descriptive statistic. **Results & Interpretations:** The ages 16 to 19 years constituted the highest age group. There were 49(63.64%) male subject and 50(64.4%) female. The mean BMI of test group \pm was 23.06kg/m² \pm 0.32 and 23.15kg/m² \pm 0.33for control. Moreover, in the male test group there was progressive significant increase in mean TP from baseline with 6.94g/dl \pm 0.08 to 7.57g/dl \pm 0.07 at 8 weeks of study period ($p < 0.05$). The mean Albumin increased progressively and significantly from 4.01g/dl \pm 0.03 to 5.29g/dl \pm 0.04 after 8 weeks of study period ($p < 0.05$). **Conclusions:** There is increase in total Protein and Albumin levels in the subjects who ingested egg and the increase is higher in females than males. Egg consumption improved Protein level.

Keywords: Egg, Total Protein, Albumin, Water

INTRODUCTION

Eggs are sources of protein, fats and micronutrients that play an important role in basic nutrition. However, eggs are traditionally associated with adverse factors in human health, mainly due to their cholesterol content. Nowadays, however, it is known that the response of cholesterol in human serum levels to dietary cholesterol consumption depends on several factors, such as ethnicity, genetic makeup, hormonal factors and the nutritional status of the consumer.

There is also scientific evidence that eggs contain other biologically active compounds that may have a role in the therapy and prevention of chronic and infectious diseases. The presence of compounds with antimicrobial, immunomodulator, antioxidant, anti-cancer or anti-hypertensive properties have been reported in eggs

(Abeyrathne et al, 2013). Lysozyme, ovomucoid, ovomucoprotein and cystatin are biologically active proteins in egg albumen, and their activity prolongs the shelf life of table egg (Rakonjac et al, 2014). Some of these protective substances are isolated and produced on an industrial scale as lysozymes and avidin. Additionally, eggs are an important source of lecithin and are one of the few food sources that contain high concentrations of choline (Herron and Fernandez, 2004, Zeisel et al, 2003). Lecithin, as a polyunsaturated phosphatidylcholine, is a functional and structural component of all biological membranes, which acts in the rate-limiting step of the activation of membrane enzymes such as superoxide dismutase. It has been suggested that ineffective activation of these antioxidant enzymes would lead to increased damage of membranes by reactive oxygen species. In addition, lecithin increases the secretion of bile, preventing stagnation in the bladder and, consequently, decreases the lithogenicity (Herron and Fernandez, 2004).

However, as a component of egg lecithin, choline has numerous important physiologic functions, which include the synthesis of phospholipids, the metabolism of methyl and cholinergic neurotransmission, and it is a required nutrient that is essential for the normal development of the brain (Jung et al, 2012).

Another important nutritional component from eggs is phosvitin, a phosphoglycoprotein present in egg yolk and represents about 7% of yolk proteins. It has a specific amino-acid composition, comprised of 50% serine, and 90% of which are phosphorylated. This specific structure makes phosvitin a strong metal chelator and, by this mechanism, it acts as an important melanogenesis inhibitor to control excessive melanin synthesis in the melanocytes of animal and human skin (Jung et al, 2012). It was suggested that egg-yolk phosvitin has the potential to be used as a natural bioactive compound as a hyper-pigmentation inhibitor for human skin (Jung et al, 2012).

Other interesting egg components from the nutritional point of view are the carotenoids. Carotenoids are natural pigments in hen egg yolks that confer its yellow color, which can range from very pale yellow to dark brilliant orange. Egg carotenoids represent less than 1% of yolk lipids, and are mainly composed of carotene and xanthophylls (lutein, cryptoxanthin and zeaxanthin) (Kassis et al, 2010, Skrivan and Englamaierova, 2014, Rakonjac et al, 2014).

The total concentration of lutein and zeaxanthin is 10 times greater than of cryptoxanthin and carotene, combined, (Rakonjac et al, 2014) and are not endogenously synthesized by the human body and tissue levels therefore depend on dietary intake. These natural compounds found in the bodies of animals, and in dietary animal products, are ultimately derived from plant sources in the diet, mainly from dark green leafy plants (Kelly et al, 2014). Lutein and zeaxanthin content of eggs depends on different factors, such as the feed given to laying hens, or the husbandry system. Thus, variable contents of these carotenoids in non-enriched eggs were recently reported, varying about 167–216 µg/yolk for lutein and about 85–185 µg/yolk for zeaxanthin (Skrivan and Englamaierova, 2014, Kelly et al, 2014). Additionally, a greater serum response to lutein was reported following the consumption of eggs compared with the consumption of dietary lutein supplements or vegetables (Skrivan and Englamaierova, 2014, Kelly et al, 2014). This could be related with the fact that carotenoids depend on a lipophilic environment for optimal gastrointestinal uptake (Kelly et al, 2014). Consequently, eggs are a very important food source of these carotenoids, especially in the case of people that consume low amounts of vegetables with a high content of these substances (as occurs in western developed countries).

These carotenoids are, perhaps, best known for their function in the neural retina, where they are found in high concentration and, along with their isomer meso-zeaxanthin, are termed macular pigment (Bovier et al, 2014). Lutein and zeaxanthin are known to serve light-absorbing and blue-filtering optical functions, as well as antioxidant and anti-inflammatory functions, and thereby, is considered to play a role reducing immune-mediated macular degeneration and age-related cataract formation (Rakonjac et al, 2014, Kelly et al, 2014 Bovier et al, 2014).

There is little of knowledge on egg consumption with relationship to protein levels and gender difference in this environment. Many previous studies obtained from literature search are from the Western world and none were from this region. Our eating habits and culture differ from the western world, coupled with the variant degree of malnutrition we observe in Ibadan.

The aim of this study is to determine the effect of egg consumption on serum Total Protein measurements among secondary school students and gender differences if any. This will serve as a basis for advice against the development of protein energy malnutrition in the nearest future.

MATERIALS AND METHODS

This study involved cross-sectional selection of 154 secondary students living in Ibadan, an urban city in Oyo state, South-West, Nigeria, aged between 12 and 23 years. They were from four secondary schools in Ibadan North and South Local Government areas. Teachers in the schools were exempted from this study because they were not part of the study groups.

The weight of subjects were recorded in kilograms (to the nearest 1.0 kg) without them wearing any heavy clothing like a coat, jacket, shoes or agbada, using a calibrated bathroom scale (Soehnle Waagen GmbH and Co. KG,D 71540 Murrhardt/Germany) positioned on a firm horizontal surface.

Height in meters of subjects were measured (to the nearest 0.1m) using a stadiometer. Subjects stood erect, without shoes and headgears, on a flat surface with the heels and occiput in contact with the stadiometer(Prestige HM0016D) (India) and to the nearest 0.1 meter.

The body mass index (B.M.I) was subsequently calculated using the formula: weigh (kg)/ height² (metres²). There were two groups of students (control and test group). Each test subject was given one average sized egg daily for 30 days. The control group was given one cup of water (100ml) daily for 30 days. 5mls of blood was taken from each subject into a plain bottle after an overnight fasting. Estimation of serum protein levels were done in each of the subject as described below:

Total Protein was estimated according to the method described by Bradford (1976)

Principle: 100 mg Coomassie Brilliant Blue G-250 was dissolved in 50 mL 95% ethanol (C₂H₅OH). Thereafter, 100 mL of 85% phosphoric acid (H₃PO₄) was carefully added under stirring, before H₂O was added to a total volume of 1 L. The solution was filtered and kept at 4 °C. For the measurements, 100 µL extract and 5 mL Bradford solution were mixed and incubated for 5 min and absorbance was read at 595 nm (Siro et al, 2008).

Serum Albumin was estimated by Dye- binding Method.

Principle: Albumin at pH 4.2 sufficiently cationic to bind the anionic dye bromocresol green (BCG) to form a blue-green colored complex. At pH 4.2 Albumin + BCG BCG complex. The intensity of the blue-green color is directly proportional to albumin concentration in the specimen. It was determined by measuring the increase in absorbance at 620 - 630 nm.

Ethical Approval and Informed Consent

Ethical clearance for the study was obtained from the Health Research Ethics Committee (HREC) University College Hospital (UCH), Ibadan. All participants (154) of this study signed an informed consent form, in accordance to the committee regulations, before answering the questionnaire and taking their anthropometric measurements. Data was recorded on a proforma.

Statistical analysis: The data obtained was analyzed using the computer statistical programme package SPSS version 25.0. Student t test was used to compare variability between male and female. Probability value of **P** less than 0.05 was considered statistically significant.

Results:

The study involved 154 students randomly selected with their age group between 13 and 23 years. There were 77 students in each of the control and test groups. The age group 16 to 19 years constituted the highest age group. There were 49(63.64%) male subjects and 50(64.4%) female in this age group (table1). The mean BMI of test group was $23.06\text{kg}/\text{m}^2 \pm 0.32$ and for the control group was $23.15\text{kg}/\text{m}^2 \pm 0.33$ (tables 1 and 2).

Moreover, in the male test group there was progressive significant increase in mean TP at baseline with $6.94\text{g}/\text{dl} \pm 0.08$ to $7.57\text{g}/\text{dl} \pm 0.07$ at 8 weeks of study period ($p < 0.05$). The mean Albumin increased progressively and significantly from $4.01\text{g}/\text{dl} \pm 0.03$ to $5.29\text{g}/\text{dl} \pm 0.04$ after 8 weeks of study period ($p < 0.05$) while in the female test group there was progressive and significant increase in mean TP at baseline with $7.08\text{g}/\text{dl} \pm 0.09$ to $7.59\text{g}/\text{dl} \pm 0.07$ at 8 weeks of study period ($p < 0.05$). The mean Albumin increased progressively and significantly from $4.04\text{g}/\text{dl} \pm 0.04$ to $5.32\text{g}/\text{dl} \pm 0.06$ after 8 weeks of study period ($p < 0.05$). (tables 3).

It was also observed in the control male group that there was negligible increase of TP from baseline with $7.04\text{g}/\text{dl} \pm 0.07$ to $7.11\text{g}/\text{dl} \pm 0.05$ at 8 weeks of egg study period. The mean Albumin was nearly the same value at $4.02\text{g}/\text{dl} \pm 0.04$ and $4.01\text{g}/\text{dl} \pm 0.03$ after 8 weeks of study period while in the female control group. There was no increase in mean TP at baseline with $7.00\text{g}/\text{dl} \pm 0.07$ to $7.07\text{g}/\text{dl} \pm 0.04$ at 8 weeks of study period. The mean Albumin is the same value at baseline $4.03\text{g}/\text{dl} \pm 0.04$ and $4.03\text{g}/\text{dl} \pm 0.14$ after 8 weeks of the study period (table 4).

Table1: Showing demographic characteristics of the participants.

Variable	Total (n=154)	Test (n=77)	Control (n=77)
Age			
12-15 years	34 (22.1)	18 (23.4)	16 (20.8)
16-19 years	99 (64.3)	49 (63.6)	50 (64.9)
20-23 years	21 (13.6)	10 (13.0)	11 (14.3)
Gender			
Male	75 (48.7)	40 (51.9)	35 (45.5)
Female	79 (51.3)	37 (48.1)	42 (54.5)

Table 2: Comparison of baseline characteristics in participants with variability of the Protein levels.

Variable	Test	Control	T	P
Weight	60.44 ± 1.29	60.34 ± 1.25	0.059	0.953
BMI	23.06 ± 0.32	23.15 ± 0.33	-0.198	0.843
TP	7.10 ± 0.06	7.12 ± 0.05	-0.154	0.878
Albumin	4.02 ± 0.03	4.03 ± 0.04	-0.172	0.857

Table 3: Male and female participants of control group with variability in Protein levels over the study period.

Variables	Baseline	2wks	4wks	6wks	8wks	F	P
Weight female	58.38 ± 1.64	62.04 ± 1.86	60.51 ± 1.84	61.92 ± 1.89	60.11 ± 1.41	0.749	0.545
Weight male	62.69 ± 1.88	61.17 ± 1.53	61.33 ± 1.72	63.47 ± 2.00	63.32 ± 2.18	0.232	0.908
BMI female	24.12 ± 0.47	26.39 ± 1.21	25.85 ± 1.26	26.03 ± 1.01	25.49 ± 1.00	1.292	0.278
BMI male	21.99 ± 0.40	22.09 ± 0.99	22.20 ± 1.11	22.46 ± 0.99	22.91 ± 1.13	0.262	0.890
TP female	7.00 ± 0.07	7.12 ± 0.06	7.19 ± 0.10	6.91 ± 0.08	7.07 ± 0.04	0.782	0.432
TP male	7.04 ± 0.07	7.12 ± 0.07	6.71 ± 1.10	7.05 ± 0.07	7.11 ± 0.05	1.349	0.262
Albumin female	4.03 ± 0.04	4.06 ± 0.05	4.00 ± 0.03	4.01 ± 0.04	4.03 ± 0.04	0.724	0.422
Albumin male	4.02 ± 0.04	4.04 ± 0.05	4.00 ± 0.04	4.00 ± 0.04	4.01 ± 0.03	0.831	0.489

Table 4: Male and female participants of test group with variability in Protein levels over the study period.

Variables	Baseline	2wks	4wks	6wks	8wks	F	P
Weight female	58.46+1.77	59.32+1.75	60.35+1.72	61.81+1.72	62.03+1.69	153.924	0.000*
Weight male	62.28+1.84	64.03+1.80	64.70+1.85	65.20+1.79	65.85+1.78	105.381	0.000*
BMI female	24.11+0.48	24.90+0.49	25.39+0.54	29.00+0.55	26.51+0.53	108.689	0.000*
BMI male	22.09+0.37	22.74+0.37	23.16+0.40	23.55+0.40	24.13+0.37	114.199	0.000*
TP female	7.08+0.09	7.21+0.08	7.32+0.08	7.45+0.07	7.59+0.07	121.242	0.000*
TP male	6.94+0.08	7.12+0.08	7.23+0.07	7.37+0.07	7.57+0.07	196.989	0.000*
Albumin female	4.04+0.04	4.15+0.05	4.53+0.05	5.14+0.06	5.32+0.006	152.185	0.000*
Albumin male	4.01+0.03	4.10+0.04	4.50+0.04	5.08+0.03	5.29+0.04	166.481	0.000*

DISCUSSIONS

In this study, we found that there was progressive increase in Total Protein level and Albumin. This is in agreement with the study done by Herron and Fernandez in 2004 on egg consumption. The increased serum protein also showed that egg eating is beneficial to health (Eilat-Adar et al, 2013). The slight level change in control group signified physiological variations in protein level over time (Natoli et al, 2007).

The increase in TP in female which was slightly higher than male in the study group suggests that female may be less active than males, hence, according to Phillips et al,1993, male displayed an increased estimate of whole-body protein anabolism in their study. Testosterone plus Growth Hormone also increase absolute fat free-mass¹⁴. This is in contrast to the study done by Mauras et al,2003 who affirmed the preponderance in TP higher in male subjects which they claimed may be due to physical activity level and leucine oxidation during aerobic exercise (Mauras et al,2003). Anabolic stimuli like feeding and exercise turnover between male and female, however, making the rate of burning fat higher in males than female subjects (Mauras et al,2003).

Despite their above mentioned nutritional benefits, egg consumption was traditionally associated with adverse factors for human health and nutrition. In this sense, egg whites contain anti-nutritional factors, among which are proteins such as ovomucoid that can inhibit trypsin.

Taking into account the presence of all these components, eggs can be considered a nutritious inclusion in the diet for people of all ages and at different stages of life, but they may play a particularly useful role in the diets of those at risk of low-nutrient intakes (Natoli et al, 2007). Owing to their high nutritional value, eggs are also an important food that should be included in the planning of diets for patients, and are especially valuable in feeding people with gout, because it is a source of protein that does not add purines. Additionally, for people in sports training, egg proteins may have a profound effect on the training results, because, by its inclusion in the diet, it could be possible to enhance skeletal muscles synthesis (Herron and Fernandez, 2004). It is well established that essential amino acids stimulate skeletal muscle protein synthesis in animal and human models, and the protein in egg has the highest biological value (Glynn et al, 2010). Fifteen grams of egg white protein contain about 1300 mg of leucine (the third most common amino acid in egg, after glutamic and aspartic acids), and is also an abundant source of branched amino acids and aromatic amino acids. Recent data showed that leucine induces a maximal skeletal muscle protein anabolic response in young people, which suggests that egg white protein intake might have an important effect on body mass accretion (Hida et al, 2012). Specifically, leucine stimulates skeletal muscle synthesis independently of all other amino acids in animal models and is a potent stimulator of the cell hypertrophy mammalian target of rapamycin complex pathway. Additionally, leucine decreases muscle protein breakdown and breakdown-associated cellular signaling and mRNA expression (Glynn et al, 2010).

The increasing demand for functional foods during recent decades can be explained by the increasing cost of healthcare, the steady increase in life expectancy and the desire for an improved quality of life in later years. Functional foods may improve the general condition of the body, decrease the risk of some diseases and may

even be used to cure some illnesses. Taking into account the progressive aging of the population of developed countries, functional foods are a good alternative for controlling health costs, because medical services for the aging population are rather expensive (Siro et al, 2008).

Limitations of the study:

Prospective study over years and inability to measure TP over long period of time and the other underlying health challenges in the subjects which were not identified at the time of study may be confounding variables. This is an interesting issue for future investigations. However, continuous research is needed to validate our findings.

CONCLUSION

There is increase in Protein levels in the subjects who ingested egg and the increase is higher in female subjects than males. There is preponderance increase Albumin level in female subjects compared to male subjects. Egg consumption, however improved Protein levels in the study group.

The research has proven that egg consumption improves TP and has a beneficial role on general health. Based on the outcome of this research, Government should introduce egg into the meals of secondary students to improve the wellbeing of the youth in the country at large.

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Conflict of Interest

No conflict of interest.

Source of Funding

Self

References

- Abeyrathne E.D.N.S., Lee H.Y., Ahn D.U.(2013) Egg white proteins and their potential use in food processing or as nutraceutical and pharmaceutical agents—A review. *Poult. Sci.*;92:3292–3299.
- Rakonjac S., Bogosavljevic-Boskovic S., Pavlovski Z., Skrbic Z., Doskovic V., Petrovic M.D., Petricevic V. (2014) Laying hen rearing systems: A review of major production results and egg quality traits. *World Poult. Sci. J.*;70:93–104.
- Herron K.L., Fernandez M.L.(2004) Are the current dietary guidelines regarding egg consumption appropriate? *J. Nutr.*;134:187–190.
- Zeisel S.H., Mar M.H., Howe J.C., Holden J.M. (2003) Concentrations of choline-containing compounds and betaine in common foods. *J. Nutr.*;133:1302–1307.
- Jung S., Kim D.H., Son J.H., Nam K., Dong D.U., Jo C.(2012) The functional property of egg yolk phosvitin as a melanogenesis inhibitor. *Food Chem.*;135:993–998.
- Kassis N., Drake S.R., Beamer S.K., Matak K.E., Jaczynski J.(2010) Development of nutraceutical egg products with omega-3-rich oils. *LWT-Food Sci. Technol.*;43:777–783.
- Skrivan M., Englamaierová M.(2014) The deposition of carotenoids and α -tocopherol in hen eggs produced under a combination of sequential feeding and grazing. *Anim. Feed Sci. Technol.*;190:79–86.
- Rakonjac S., Bogosavljevic-Boskovic S., Pavlovski Z., Skrbic Z., Doskovic V., Petrovic M.D., Petricevic V.(2014) Laying hen rearing Systems: A review of Chemicals composition and hygienic conditions of eggs. *World Poult. Sci. J.* ;70:151–163.
- Kelly E.R., Plat J., Haenen G.R.M.M., Kijlstra A., Berendschot T.T.J.M (2014). The effect of modified eggs and egg-yolk based bevegare on serum lutein and zeaxanthin concentrations and macular pigment optical density: Results from a randomized trial. *PLoS One*.9:e92659

- Bovier E.R., Renzi L.M., Hammond B.R.(2014) A double-blind, placebo-controlled study on the effects of lutein and zeaxanthin on neural processing speed and efficiency. *PLoS One.*;9:e108178.
- Bradford M.M.(1976) Rapid and sensitive method for quantitation of microgram quantities of protein utilizing principle of protein-dye binding. *Anal. Biochem.*;72:248–254.
- Eilat-Adar S., Sinai T., Yosefy C., Henkin Y. (2013) Nutritional recommendations for cardiovascular disease prevention. *Nutrients.*;5:3646–3683.
- Natoli S., Markovic T., Lim D., Noakes M., Kostner K.(2007) Unscrambling the research: Eggs, serum cholesterol and coronary heart disease. *Nutr. Diet.*;64:105–111.
- Phillips SM, Atkinson SA, Tarnopolsky MA, MacDougall JD. (1993) Gender differences in leucine kinetics and nitrogen balance in endurance athletes. *Journal of Applied Physiology.* ;75(5):2134-41.
- Mauras N, Rini A, Welch S, Sager B, Murphy SP. (2003) Synergistic effects of testosterone and growth hormone on protein metabolism and body composition in prepubertal boys. *Metabolism.*;52(8):964-9.
- Glynn E.L., Fry C.S., Drummond M.J., Timmerman K.L., Dhanani S., Volpi E., Rasmussen B.R. (2010) Excess leucine intake enhances muscle anabolic signaling but not net protein anabolism in young men and women. *J. Nutr.* ;140:1970–1976.
- Hida A., Hasegawa Y., Mekata Y., Usuda M., Masuda Y., Kawano H., Kawano Y. (2012) Effects of egg white protein supplementation on muscle strength and serum free amino acid concentrations. *Nutrients.*;4:1504–1517.
- Siró I., Kápolna E., Kápolna B., Lugasi A. (2008) Functional food. Product development, marketing and consumer acceptance-A review. *Appetite.*;51:456–467.



The Determinants of Developing Tuberculosis at Specialized Hospital

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Abstract

Introduction: Tuberculosis (TB) infection is caused by Mycobacterium sp which can spread through the lymph nodes and bloodstream to all parts of the body. **Objective:** To identify the determinants of the developing TB at Khartoum locality in Al-shaab hospital. **Methodology:** A cases control study included 50 cases with diagnosis TB and 50 non TB controls from Al-shaab hospital in Sudan, cluster random sample technique used, designed questionnaire used to collect information, BMI was calculated. **Results:** The study showed that 72% from the positive participants were male found significant relationship between gender and TB infection (p value 0.004), 52% of them were between 30-40 years, significant relation found between the TB infection and age (p value 0.001), 60% lived inside of Khartoum, 70 % from the participant drink alcohol and smokers, with strong relationship (p value 0.000). **Conclusion:** The knowledge and raising awareness about factors that lead to infection, and improving socio-economic status can reduce the incidence of TB in the community, availability of direct observed therapy services can help.

Keywords: Tuberculosis, Determinant factors, Case Control Study, Al Shaab Hospital

Introduction

Tuberculosis (TB) infection is caused by a bacterium that, Mycobacterium sp can spread through the lymph nodes and bloodstream to all parts of the body. The germ is transmitted through the air is infectious disease. Tuberculosis is an infectious bacterial disease caused by bacillus tuberculosis and lead to damage to the lung tissue or other body organs (WHO, 2006). The disease was discovered on March 24, 1882 by German scientist Robert Koch. It was in ancient times called the deadly disease. The researchers found the discovery of appropriate treatment for these bacteria from antibiotics 40 years ago after caused the death of millions of people (Crofter et al., 1995). The most at risk to the disease are children and AIDS patients due to weakened immune systems. The WHO expect that during the next twenty years from the beginning of this century the number of tuberculosis (TB) patient will be billion people, or about one-sixth of the world's population now (WHO,1993). Tuberculosis is one of the most prevalent disease in the of Sudan, Although WHO, the Sudanese and health authorities are observing standard

ways of providing free treatment, but the problem still exists. Pulmonary tuberculosis or (TB) is a contagious bacterial infection caused by *Mycobacterium tuberculosis*. The lungs are primarily involved, but the infection can spread to other organs. Pulmonary tuberculosis can developed after inhaling droplets sprayed into the air from a cough or sneeze by someone infection by, *Mycobacterium tuberculosis*. The disease is characterized by the development of granular tumors in the infected tissues. One third of the world's population 2220 million people is estimated to be infected with *Mycobacterium tuberculosis* .However, the incidence of infection is not the same for males and females, estimated to be infected with the *Mycobacterium tuberculosis* (Dwainet .al.,1998).

Tuberculosis is a health problem among the Sudanese population. This was confirmed by surveys carried out by WHO in 1963. Changes in life style of Sudanese people, due to gross economical transformation, inflation, affliction towards nutritional habits, and traditional mining are factors that may enhance tuberculosis spread (Bayoumi,1979).T uberculosis is a classic example of disease that disproportionately affect the under privileged and witch,because of the social and economical burden, it imposes on individual, make access to cure a distant dream for a large majority(WHO,2012).

1.2 Problems statement

There are currently 16 million of people living with TB in the world each year, 2 million of them died, including of poor and developing country, this health indicators cannot be overlooked or dropped from our calculation because we are not immunized against the disease so as not to be quorum one person can affect 10-15 people per ear, in view of his statistic TB has caused the death of 200million people since 1882 until today, TB infection at least 1 person every 10 seconds TB infection count for 1% of the world population annually, TB still killed between 2-3 million people per year, which exceeds the total number of victims, AIDS, malaria, and disease of hot areas combined, it is expected that 30 million of people will die in the next decade. (Robert et al., 2003).

1.3 Justification

Global situation and trends: in 2015, there were an estimated 10, 4million new (incident) TB cases worldwide, of which 5, 9 million (56%) were among men, 3, 5 million (34%) among women and 1,0 million (10%) among children. people living with HIV accounted for 1,2 million (11%) of all new TB cases. There were an estimated 480 000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100 000 people with rifampici – resistant TB (RR-TB) who were also newly eligible for MDR-TB treatment. There were an estimated 1,4 million TB death, and an additional 0,4 million deaths resulting from TB disease among people living with HIV. Although the number of TB deaths fell by 22% between 2000 and 2015, TB remained one of the top 10 causes of death worldwide in 2015.

1.3 OBJECTIVES

1.3.1 General objective:

To identify the determinants' of the developing TB at Khartoum locality in al-shaab hospital

1.3.2 Specific objective:

1. To determine the gender and age group of the disease
2. To identify which types of tuberculosis more spread among the patients
3. To identify the determinants factor that lead to tuberculosis (socio demographic factor, behavioral, nutritional).

Methodology

2.1 study design:

This study was descriptive analytical study by using case control approach to assess the determinants of developing tuberculosis among the patients in al-shaab hospital at Khartoum locality, April 2017.

2.2 Study area:

Al- Shaab hospital is located in the heart of Khartoum. It was founded in 1959 and was opened on November 17 of the same year by Ibrahim Aboud as an alternative to Al-Nahr hospital, called Al-Thwart hospital for thoracic diseases. Then the section of general surgery, heart, brain and neurology were opened. of which the total area of the hospital is 2500 square meters. The public network is a groundwater well and distinguished by a hospital medical department under supervision of the general medical director in the department of operations. Nursing, medical engineering, statistic, diagnostic laboratories. The accidents and department of the physiotherapy and the department of health the administrative section under the supervision of the secretary general contains the administrative observer, workers, general system, a public relation, accounts, engineering workshop, preparation of students, cleanliness and personnel affairs. Dr. Mohieddin Mahdi first director of the hospital, Suleiman Abu Saleh the first director of the school of nursing people the first nursing in Sudan, celebrities died of tuberculosis Tijani Yusuf Basher.

2.3 Study population:

There were two populations in this study which includes; cases population and controls population. Cases population were participants affected by the diseases (Tuberculosis inpatients), and control population were participants free from tuberculosis (Tuberculosis outpatients) attending the Tuberculosis clinic in Al-Shaab hospital, Khartoum locality, 2017

2.4 Sampling techniques:

The sampling techniques in this study were total coverage patients attending TB unit in Al-Shaab hospital at Khartoum, 2017

$$n = N / (1 + N(e)^2)$$

n = sample size

N = number of all participation

e = precision level = 0.05

l = constant

2.5 study sample size:

The sample size obtained was (100) patients (inpatients and out patients), male were 57 while female 43 patients attending the Tuberculosis unit in Al-Shaab hospital at Khartoum locality, April 2017

2.6 Data collection techniques:

Primary data (record in Al-Shaab hospital). Secondary data was collected by using questionnaire which included information about socio-demographic, socio economic and environmental factors and statistical information

2.7 Data analysis:

The collected data from study units has been entered into the Statistical package of social science 20 (SPSS version 20).

2.8 Ethical consideration:

The study was ethically approved by Faculty of Public and Environmental Health and Al-Shaab hospital Administration as well as all patients included in the study were agreed to respond after being informed about the purpose of study and the reasons behind sampling.

Results

Table (1) The distribution of participants according to the gender, in al Shaab hospital, Khartoum, April 2017, n =100

Gender	TB DISEASE				p value
	CASES		CONTROL		
	n	%	n	%	
Male	36	72.0	21	42.0	0.004
Female	14	28.0	29	58.0	
Total	50	100.0	50	100.0	

Table (1) shown that the majority cases group in this study was male (72%) of cases, and (42%) in control group, and female was(28%) in cases group and (58%) in control group, there is significant different between cases and control groups (p value 0.004). Tuberculosis associated with gender in this study.

Table (2) distribution of participants according to the Age groups in al Saab hospital, Khartoum locality, April 2017, n =100

Age	TB DISEASE				P value
	CASES		CONTROL		
	N	%	N	%	
10-20 years	6	12.0	7	14.0	0.001
20-30 years	8	16.0	26	52.0	
30-40 years	26	52.0	15	30.0	
More than 40	10	20.0	2	4.0	
Total	50	100	50	100	

Table (2) describe that majority of cases were 30-40 years, (52%) and the majority in control group was 20-30 (52%), chi square test shown the significant relation between the ages and disease, there was significant different between cases and control (p value 0.001)

Table (3) the distribution of level of education among the participants, in al-shaab hospital, Khartoum locality, April 2017, n=100

Level of education	TB DISEASE				P value
	CASES		CONTROL		
	N	%	N	%	
Uneducated	4	8.0	2	4.0	.010
Primary	6	12.0	1	2.0	
Secondary	5	30.0	10	20.0	
University	25	50.0	35	70.0	
Postgraduate	0	0.0	2	4.0	
Total	50	100	50	100	

Table (3) explain the majority of level of education in cases group was university (50%), and the majority in control was (70%) also university. There was different between cases and control groups (p value 0.10)

Table (4) the distribution of drinking alcohol or smoking among the participants, in al- shaab hospital, Khartoum locality, April 2017, n=100

Drunk alcohol or smoking	CASES		CONTROL		P value
	N	%	N	%	
Yes	35	70.0	8	16.0	.000
No	15	30.0	42	84.0	
Total	50	100	50	100	

Table (4) show that majority of cases group drink alcohol or smoke (70%) while who didn't drink (30%), and in control group the majority don't drink alcohol or smoking (84%) while who drink or smoke (16%), chi square is strong relationship (p value 0.000)

Table (5) the distribution of if the participants suffer from any other viral disease, al-shaab hospital, Khartoum locality, April 2017, n=100

Suffer from other viral disease	TB DISEASE				P value
	CASES		CONTROL		
	n	%	N	%	
Yes	39	78.0	0	0.0	.000
No	11	22.0	50	100.0	
Total	50	100	50	100	

Table (5) shown the majority of TB patient have other viral disease (78%) in cases group and (22%) there haven't while in control group all of them they haven't viral disease (100), chi square is strong relationship (p value 0.000)

Table (6) the distribution of if anyone from the participants families also has TB, Al-Shabab, hospital, Khartoum locality, April 2017, n=100

Family history TB disease	TB DISEASE				P value
	CASES		CONTROL		
	N	%	N	%	
Yes	28	56.0	6	12.0	.000
No	22	44.0	44	88.0	
Total	50	100	50	100	

Table (6) show that the majority of TB patient in cases group their family also suffered from the TB (56%) while who no one in their family suffered from TB(44%), and in control group the majority their family haven't TB (88%) and who their family was have (12%), chi square there is strong relationship (p value 0.000)

Table (7) the distribution of the type of TB among participants, al-shaab hospital Khartoum locality, April 2017, n=100

Type of TB	TB DISEASE				P value
	CASES		CONTROL		
	n	%	n	%	
Pulmonary	47	94.0	34	68.0	.006
Extra pulmonary	3	6.0	16	32.0	
Total	50	100	50	100	

Table(7) shown that the majority type of TB among the patient in cases group was pulmonary (94%) and extra pulmonary (6%), while in control group the pulmonary is (68%) and extra pulmonary (32%), chi square there is significant different between cases and control groups (p value .006)

Table (8) the distribution of the TB treatment among participants, Al-shaab hospital, Khartoum locality, April 2017, n=100

Type of treatment	TB DISEASE				P value
	CASES		CONTROL		
	N	%	N	%	
Al-aizoniazid	14	28.0	12	24.0	0.004
Reframing	33	66.0	24	48.0	
Al-aithanbotol	3	6.0	14	28.0	
Total	50	100	50	100	

Table (8) shown that the majority treatment the TB patient received is reframing (66%) in cases group, while in control group also the majority treatment is reframing (48%), chi square there is significant different between cases and control groups (p value 0.004)

Table (9) the distribution if the participants commit the treatment describe by the doctors Al-shaab hospital, Khartoum locality, April 2017,n=100

Commit the treatment describe by the doctor?	TB DISEASE				P value
	CASES		CONTROL		
	N	%	n	%	
yes	43	86.0	47.0	94.0	.009
No	7	14.0	3.0	6.0	
total	50	100	50	100	

Table (10) explain the majority TB patient in cases group was commit by the treatment describe by the doctors (86%) while (14%) don't commit by treatment describe by the doctor, in control group the majority commit by doctors treatment (94%) and (6%) don't commit, chi square there is significant different between cases and control groups (p value 0.009).

Table (10) the distribution if the participants who don't commit by the doctor's treatment ,that cause their health deteriorate , Al- shaab hospital, Khartoum, April 2017 ,n=100

If your answer is no, causehealth deteriorate?	TB DISEASE				P value
	CASES		CONTROL		
	N	%	N	%	
Yes	7	100.0	3	100.0	.000
Total	50	100	50	100	

Table (11) describe the majority of TB patient in cases group don't commit by doctor's treatment their health deteriorate (100%), and in control group also (100%), there is strong relationship between cases and control groups (p value 0.000)

Discussion

The study aimed to identify the determinants and risk factors of developing tuberculosis among the target groups to identify the age group, gender and other factors that facilitate tuberculosis spread.

The study revealed the majority (72.0%) of cases subjects is male and the female is 28% that mean the male is more exposure to infection by TB disease. there was association between the gender and the disease TB. There

was association between the gender and infection of TB. Previous study shown that the male is more affected by TB than female. the study agree with (park, 2015) which clarified that prevalence is higher among males.

The study revealed 52%of TB patient ages between {30-40 year}, 20% more than 40 year, and then 16% their age {20-30 year}, and the last age group {10-20year} is 12%, the finding indicate that the age {30-40year} is more exposure to TB infection than other age groups.

There was association between the age and infection of TB, ,previous study showed that the age group (30-40 years) is more affected by TB than other groups.

The study revealed that 70%of TB patient drink alcohol or smoke and 30% of them don't drink alcohol or smoke, the finding indicate that drinking alcohol or smoking lead to exposure of TB.

There was association between the gender and infection of TB. Previous studies showed that the percipients who drink alcohol or smoke is more affected by TB than other people. The study agrees with (WHO, 2015), the possible biological mechanisms for the association between tobacco smoke and TB are that tobacco smoke results in; - impaired clearance of mucosal secretions in the trachea bronchial tree. This allows the M TB to reach the alveoli. - impaired functioning of the pulmonary alveolar macrophages, resulting in lower levels of cytokines being secreted. - Decreased intracellular tumor necrosis factor- α production leading to impaired intracellular killing MTB.

The study revealed 78%of TB patient have other viral disease indicating that other viral disease may accompany TB. There was association between the people suffer from viral disease and infection of TB.

The study revealed that 56%of TB patient found someone in their family also have TB and 44% of them haven't TB in their family, the finding indicate that the TB is easy to transmitted between the family members, There was association between the family history and infection of TB, Previous study showed that the persons with family history(heredity) is more affected by TB than others. study disagree with (Mhfn, 2008) concluded that Tuberculosis is not a heredity disease however; twin studies indicate that inherited susceptibility is an important risk factor.

The study revealed 94% of TB patient the TB type they have is pulmonary and 6% have extra pulmonary, the finding indicate that the more type of TB spread is pulmonary.

Previous studies showed that the pulmonary is more effective than other types of TB, study agree (Hussein et al, 2003) which concluded that this type is the most frequent common type that affects the lung and leads to interweave damages.

The study revealed 82% of TB patient doesn't receive the BCG vaccine There was association between receiving the BCG vaccine and infection of TB,. Previous study showed that who didn't receive the BCG vaccine earlier is the more affected by TB than others, study agreed with Grigg et.al. 1958.

Conclusion

- ❖ The study concluded that the majority of TB patients are male 72%.
- ❖ The result show that 52% from TB patients ranging in the age group from (30-40year).
- ❖ 94% from the TB patients have pulmonary tuberculosis.
- ❖ 67% of TB patients have HIV.
- ❖ The majority of TB patients (82%) don't receive the BCG vaccine earlier.
- ❖ 28% from TB patient's loss their appetite and weigh less aloes 28% have cough more than three weeks.
- ❖ The majority of TB patients drink alcohol and smoke, 66% of patients have recently contact with other have tuberculosis.

Recommendations:

According to the above results here are recommendations:

- Minimize alcohol consumption in the country by legislations and awareness raising on the serious health risks associated with it.
- TB patients to be quarantined to stop transmission from patients to well people.
- Health authorities should ensure that all children had been vaccinated against Tuberculosis.
- Awareness raising campaigns among community on TB.
- Encourage patients for direct observed therapy.
- More researches are requested on TB determinants and risk factors.

References

- APC infectious disease, 2008. James. Tan, second edition.
- Cigarette smoking in patients with schizophrenic vs. mood disorders, October 1998, Apama Diwan, DOI: 10.1016/S090-9964(98)00045-0
- Communicable disease control and health protection, Jeremy Hawker, 2012
- Communicable disease 2006 Erik Nordberg, revise, African medical and research foundation in Nairobi, Kenya.
- Communicable disease 2006, manual for health workers in Saharan Africa, third edition.
- E.R. Grigg, „The arcane of tuberculosis with a brief epidemiologic history of the disease in the U.S.A., *Am. Rev. Tubercle.* 78 (1958), 151-72.
- Gatt and crafting, published in Scottish affairs, no 12, 1995, pp. 73-86, by Osbert Lancaster and Alastair McIntosh.
- Health and wellness program, 2009
- John M. G and Alimaddinzumla tuberculosis. Manson tropical disease edition, 2009, 22 editions.
- K. PARK 2009
- Preventive and social medicine M^{rs} Banarsidas Bhanot, 2013
- Park, S. Textbook of prevention and social medicine, 2013, Banarsidas Bhanot, 5th or later edition.
- Singla N, Sharma PP, Singla R, Jain RC. Survey of knowledge, attitudes and practices for tuberculosis among general practitioners in Delhi, India. *Int J Tubercle Lung Dis.* 1998; 2(5): 384-9.
- Wood, W., Jacinto, A., Grose, R., Woolner, S., Gale, J., Wilson, C., Martin, P. (2002). Wound healing recapitulates morphogenesis in *Drosophila* embryos. *Nat. Cell Biol.* 4 (11): 907-912. (Export to RIS)
- World Health Organization. History of Tuberculosis disease, 2006.
- World Health Organization, report 2015
- World Health Organization. Recommendations for investigating contacts of persons with infectious Tuberculosis in low- and middle-income countries. Geneva: World Health Organization, 2012. WHO/HTM/TB/2012.9.



Qualitative Analysis of Strengths, Weaknesses, Opportunities and Threats of Professional Services by Community Pharmacies in Nigeria

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Abstract

Background: Professional services hold important promises for community pharmacy which remain under-exploited. Objective: To analyse strengths, weaknesses, opportunities and threats of professional services and propose strategic options for their management in community pharmacies in Nigeria. Method: A mixed method was used. Two focus groups were conducted with nine pharmacists who own retail outlets and seven superintendent pharmacists respectively. Validated, semi-structured questionnaires were administered on 321 randomly-selected community pharmacists and 642 pharmacy clients. Data collected were subjected to appropriate descriptive and inferential analysis at $p < 0.05$. Results: The strongest strengths of the community pharmacists were easy accessibility (MWA 3.69) and good managerial skills (3.63). Inability to quantify services and get paid for them (3.39); and time constraints (3.36) were the most prominent weaknesses identified. The Pharm.D programme with attendant improvements in clinical skills (3.52); and digital technologies (3.51) presented the greatest opportunities; while unhealthy competition (3.50) and increasing recognition for patent and proprietary medicines vendors (3.50) were the greatest threats. Higher educational qualifications and location of practice did not improve service management scores but length of practice experience did ($p = 0.00$). Exploiting opportunities had strongest relationship with service quality ($r = 0.129$, $p = 0.02$) while weaknesses influenced opportunities the most ($r^2 = 0.35$, $t = 12.98$, $p = 0.001$). Conclusion: Strategic planning for professional services was inadequate. The community pharmacists exhibited marginal capacity to exploit opportunities and mitigate threats. Weaknesses and threats were major factors limiting service outcomes. There is need to strengthen strategic planning to optimize professional pharmacy services.

Keywords: Community Pharmacy, Professional Services, SWOT Analysis, Strategic Planning, Nigeria

1. INTRODUCTION

Community pharmacy has always been a service market and the medicines and other health commodities offered by community pharmacists have always been accompanied by professional services meant to maximize therapeutic outcomes (Marcrom, Hoton & Shephard, 1992). Professional pharmacy services (PPS) comprise the set of traditional and emerging services delivered by pharmacists or those under their supervision. In doing this, they deploy specialized skills, directed at clients, members of the community, or other health professionals, with the goal of improving quality of care and overall health delivery outcomes (Moulin, Sabater-Hernandez, Fernandez-Llimos & Benrimoi, 2013). There seems to be an increasing demand for these services given the rising incidence of chronic non-communicable diseases (NCDs), increasing comorbidities with attendant polypharmacy and higher risks of adverse drug reactions, increasing antimicrobial resistance, disparities in health literacy, inequities in access to quality health care; unpredictable outbreaks of epidemics, among other demand-side factors (Mcintosh et al, 2018; Zgarrick, Moczygamba, Alston & Desselle, 2016). Community pharmacists' response may be seen in the evolution of an array of value-added services ranging from advocacy for vaccine uptake and actual vaccine administration, pharmacy-based disease parameter screening, medication therapy management (MTM), smoking cessation counselling, healthy living and well-being services, among other supply-side initiatives (Smalls, Broughton, Hylick 2015; Queeno, 2017; Alsabbagh et al., 2018; APhA, 2019).

To explore new service ideas and evaluate risks and likelihood of success before actually investing organisational resources, certain questions must be addressed. Some of these questions are:

Should the pharmacy be in the “prescriptions business” or “professional services business”?

What professional services should be offered?

Which customer groups should be targeted?

How much money and other organizational resources should be invested?

How can the services be managed to ensure their profitability and sustainability (Feletto, Wilson, Roberts & Benrimoj, 2010)?

Providing answers to these and similar questions in a fast-changing practice ecosystem requires strategic planning and appropriate management action (Desselle, Moczygamba, Coe, Hess & Zgarrick, 2019). Strategic planning adopts a long-term view encompassing the organization's vision, mission, and values; analyzes internal capabilities and external developments; and throws up strategic options for management to identify priority services (George, Walker & Monster, 2019). In Nigeria, literature on strategic planning in community pharmacy is under-developed and reporting is uncommon.

SWOT-analysis is a popular tool that may be deployed to evaluate the interplay of internal capabilities (strengths(S) and weaknesses (W)) with external variables (opportunities (O) and threats (T)) and to formulate strategic plans for effective management of professional pharmacy services (Gebremariam & Mekuria, 2019). It is a realistic, fact-based, data-driven approach to planning based on real-life contexts. Strength factors refer to beneficial variables, internal to the pharmacy organisation, which facilitate the success of the service programmes and confer competitive advantage on the pharmacy. Weaknesses are features of the pharmacy or team which hinder progress towards service goals and place the organisation at a disadvantage in the competitive arena. Opportunities include features/developments in the external environment that provide incentives for success of the service programme, and offer competitive edge to the pharmacy. Threats are uncontrollable variables/developments in the external practice environment that have the capacity to complicate the weaknesses of the pharmacy organisation and stop progress towards service goals (Harrison, 2005; Zgarrick et al., 2016). An understanding of the SWOT factors associated with each PPS is necessary to convince stakeholders (payers, business owners, investors, administrators etc.) of the prospects of the service and demonstrate how it advances the strategic priorities of the organisation. However, evolution of professional pharmacy services in Nigeria is still nascent, and there is significant lack of objective evidence of the SWOT elements associated with the services.

Extant literature does not offer a consensus on how to carry out SWOT analysis. However, most authors identified factors in the external environment that present opportunities and threats; as well as factors in the internal environment that represent strengths and weaknesses; and then confronted the strengths and weaknesses with the

opportunities and threats in order to generate strategic options for management (van Wijngaarden, Scholten & van Wijk, 2012; Zgarrick et al, 2016; Wang & Wang, 2020). Hence the present study adopted this same approach in relation to professional pharmacy services with particular emphasis on the unique contexts of Nigeria community pharmacy.

METHODS

A mixed-method design was used in this study. An initial exploratory phase employed an ethnographic approach using focus group discussions (FGDs) - with two homogenous groups of community pharmacists in Southwestern Nigeria. The first group comprised nine (9) pharmacy owners who were leaders in the Association of Community Pharmacists of Nigeria. The second group had seven (7) superintendent pharmacists drawn from Fellows of West African postgraduate college of pharmacists. Information from the FGDs were combined with those from in-depth review of literature to prepare semi-structured questionnaires which were administered on 321 community pharmacists. A separate questionnaire was designed and administered on 642 clients of the pharmacies.

The study was carried out in community pharmacies across the six Southwestern States of Nigeria, namely Lagos, Ogun, Oyo, Osun, Ondo and Ekiti between June and August 2019. About 60% of all registered pharmacists in Nigeria are in community practice, and about half of all the community pharmacists in Nigeria are located in the Southwest. Moreover, above 60% of the drug manufacturing and importation outfits from where community pharmacists source their products are also located in the Southwest (Oseni, 2017; PCN, 2019).

Only retail pharmacies were included in this study. Although pharmaceutical wholesalers are classified as community pharmacists in Nigeria, they were excluded from the study because the range of their environment does not include the provision of professional pharmacy services. Community pharmacists with less than one year of practice experience were excluded as they were deemed to possess inadequate experience to assess PPSs.

The size of participants in focus group discussions were in line with conventional practice (usually 6-12) (Bernard, 2000). Cochran (1977) formula at 5% error rate was used to calculate sample size for the questionnaire-driven surveys from the population of 1941 community pharmacists in the register of Pharmacists Council of Nigeria as at 31st December, 2018 (Cochran, 1977). Two clients were sampled from each selected community pharmacy.

Purposive sampling technique was used to select participants in the focus group discussions. Discussants were pharmacist owners of retail pharmacies and superintendents who worked in the pharmacies. Simple random sampling technique was used to select pharmacist respondents to the questionnaires while accidental sampling technique was used to select clients based on whoever was available and consenting at the time data collectors were present at the pharmacy.

A strategy of triangulation of data source/collection was used. First a detailed review of relevant literature was undertaken to identify general SWOT factors of importance (Harrison, 2005; McIntosh et al, 2018; Gebremariam & Mekuria, 2019).Then two FGDs were conducted using an interview guide. From the brainstorming sessions, each of which lasted about 90 minutes, key issues in the Nigeria practice environment were identified. Findings from these activities were used to develop a draft questionnaire, which was subjected to the informed scrutiny of four senior faculty members who are experts in different sub-specialties in pharmacy administration. Corrections and suggestions from faculty members were applied to refine questionnaire items and ensure face and construct validity. Items in the questionnaire for clients were adapted from the standard SERVQUAL instrument (Butt & Cyril de Run, 2010), and was named Client Assessment of Service Quality (CASQUAL). The CASQUAL instrument was translated to the local language (Yoruba), for the benefit of clients who could not communicate effectively in English.

Forty (40) community pharmacists from outside the study area were randomly selected for a pilot survey. The CASQUAL instrument was administered on two clients per pharmacy, selected by accidental sampling technique. Data from the pilot study was used to determine the reliability coefficient of the instruments. The sample size of 40 was considered appropriate being more than 10% of sample size for the main study.²³ The Cronbach's alpha coefficients showed internal consistency above the minimum cut off ≥ 0.7 for all sections of the questionnaires

(Israel, 2013; Ararat, 2016). Pharmacists and clients spent an average of 15 and 10 minutes respectively in filling the questionnaires.

Ethical approval (HREC No: IPHOAU/12/1437) was obtained from the Health Research Ethic Committee (HREC) of the Institute of Public Health, Obafemi Awolowo University, Ile-Ife Nigeria for the study.

Ten (10) research assistants who were proficient in oral and written English and Yoruba language were recruited and trained to collect data. Dual moderator focus group strategy was adopted with the two researchers moderating both sessions held August 2nd and 9th 2019 respectively, following established guidelines (Krueger & Casey, 2014). While one moderator ensured the sessions progressed smoothly, the other ensured all relevant topics were covered. The sessions were tape-recorded and transcribed verbatim, alongside handwritten notes taken by a research assistant. Questionnaires were administered on respondents from 16th to 31st August 2019 across the six states. Online versions of the questionnaires were sent as google forms via emails and WhatsApp addresses of selected pharmacists to complement the efforts of research assistants. All respondents gave their informed consents in writing.

Transcripts of the focus groups were analysed based on the grounded theory approach. In-vivo coding, using actual phrases from discussants, were used to identify emerging themes and analytical categories applying inductive reasoning. Notice was taken of how many times each phrase was repeated by discussants across the two focus groups and the possible relationships among emerging themes. This information was synthesized to construct SWOT items for the questionnaires subject to scrutiny by senior faculty members.

Data from the questionnaires were sorted, coded, and cross-checked for data management using Excel spreadsheet. It was then exported to Statistical Package for Social Sciences (SPSS) version 21 for Windows software for analysis at $p < 0.05$. Demographic data of respondents were summarized and presented as frequency, percentages and median scores. Weighted Mean \pm SD (standard deviation) were used to analyze the SWOT items. Analysis of variance and t-test were applied to test relationships of SWOT domains with demographic variables of respondents. Pearson correlation coefficient was used to examine impacts of SWOT domains on professional pharmacy service quality. The interplay of internal capabilities of the community pharmacies (SW) with external developments (OT) was evaluated using linear regression analysis.

RESULTS

Response rate for the two focus groups was 100%. The first group had 6 males (66.7%) and 3 females (33.3%), median age 44.25 years, and drawn from the six States as follows: Lagos-3, Ogun-2, Oyo/Osun/Ondo/Ekiti-1 each. The second focus group had 2 males (28.6%) and 5 females (71.4%), median age 40.18 years, and drawn from the six States as follows: Lagos-2, Ogun/Oyo/Osun/Ondo/Ekiti- 1 each. For the questionnaire surveys (Table 1), response rates for pharmacists and clients were 74.7% and 100%; their mean ages 39.41 and 51.20 years respectively. For client responses, 605 (94.2%) were in English while 37 (5.8%) were in Yoruba language. Male to female ratio for community pharmacists was 210:111 or 2:1. Possession of higher academic degrees was used as proxy measure of specialization; and only 27% of the pharmacists had higher degrees in addition to the basic Bachelor of Pharmacy degree. Hence specialization may be said to be yet in infancy.

About 50% of Nigerians live in rural communities (World Bank, 2018), but the study found only 18% of the community pharmacists located in rural areas while 82% were in urban centres.. This finding reinforces previous evidence (Alenoghena, Aigbiremolen, Abejegah & Eboime, 2014), and presents significant challenges for universal health coverage in Nigeria.

Among the community pharmacies, 84% had no company handbooks; 68% had no vision statements; 72% without mission statements; and 73% had no organisational structures. This shows there was no formal approach to organisational management, as is common among small and medium scale enterprises in Nigeria (Fatai, 2011). There were significant associations between age and practice experience ($r = 0.714$, $p = .001$); age and marital status ($\chi^2 = 0.624$, $p = .002$), and location and average daily customer count ($\chi^2 = 1.146$, $p = 0.002$).

Table 1: Demographic Data of Respondents (N=321)

Variables	Freq.	(%)
Gender		
Male	210	65.4
Female	111	34.6
Level of Education		
B.Pharm./B.Sc.(Pharm.) only	235	73.2
M.B.A./M.Sc. and Other Higher Degrees	86	26.8
Marital Status		
Married	228	71.0
Single	73	22.7
Others	20	6.3
Age (Years)		
20-40	178	55.4
41-Above	143	44.6
Years of Community Pharmacy Practice Experience		
1-10	198	61.7
11-20	89	27.7
Above 20	34	10.6
Location of Practice		
Rural	57	17.8
Urban	264	82.2
Average Daily Customer Count		
1-50	86	26.8
51-100	149	46.4
Above 100	86	26.8
Do you have		
a. Company Handbook?		
Yes	51	15.9
No	270	84.1
b. Vision Statement?		
Yes	103	32.1
No	218	67.9
c. Mission Statement?		
Yes	91	28.4
No	230	71.6
d. Organisational Structure?		
Yes	87	27.1
No	234	72.9

Table 2: Item Performance of SWOT Factors

S/N	SWOT Factors	Mean	SD
	Strengths		
1	Easy accessibility of Community Pharmacist	3.69	.50
2	Possess clinical skills to provide care and support for patients	3.51	.54
3	Possess Managerial skills	3.63	.52
4	Provide Expert Advice	3.48	.54
5	Positive reputation in the community	3.59	.51
6	Strong relationships with Family Physicians in the community	3.46	.55
	Total	3.44	.43
	Weaknesses		
7	Poor documentation skills	3.32	.71
8	Inadequate time for service delivery	3.36	.72
9	Unsure how to quantify and get patients pay for non-drug services	3.39	.76
10	My pharmacy looks like a shop and not a health care facility	3.04	.84
11	Inadequate clinical skills to offer quality patient care services	3.19	.89

16-20yrs	3.33	.34			3.45	.41		
20yrs+	3.18	.72			2.96	.62		
Age of Comm. Pharmacy								
1-5yrs	3.07	.67	4.96	0.01*	2.91	.76	2.12	0.12
6-10yrs	2.98	1.03			2.73	.83		
11yrs+	3.31	.54			2.95	.71		

CP- Community Pharmacy; Independent t-test for Educational Qualification and Location of Practice; ANOVA for Length of active community pharmacy experience and Age of the community pharmacy organisation; Significance at $p < 0.05$

Table 4: Relationship of SWOT Domains with Service Quality (CASQUAL)

SWOT Domains	Pearson (r)	Correlation	P value	rank
Opportunities		0.129	0.021	1
Threats		0.099	0.078	2
Weaknesses		-0.01	0.86	3
Strengths		-0.019	0.74	4

Table 5: Regression of Internal Capabilities against External Developments

	r	r ²	F	F _p	β	t	t _p
Strengths against Opportunities "SO"	0.409	0.168	64.25	0.001*	0.581 ^a	8.016	0.001*
Strength against Threats "ST"	0.275	0.076	26.18	0.001*	0.424 ^a	12.981	0.001*
Weaknesses against Opportunities "WO"	0.588	0.346	168.5	0.001*	0.466 ^b	12.981	0.001*
Weaknesses against Threats "WT"	0.440	0.194	76.68	0.194	0.379 ^b	8.757	0.001*

* Significant at 0.01 level; a - strength is the predictor; b- weakness is the predictor

DISCUSSION

Focus groups was considered appropriate method for the initial exploratory phase of data collection because of its ability to generate rich, complex, nuanced and even contradictory accounts of how a homogenous group of people ascribe meaning to and interpret their experiences (FIP, 2015; Goundrey-Smith, 2018). The gender mix and ages of discussants in focus groups were not reflective of those of the population of community pharmacists in Southwestern Nigeria. However effort was made to have representatives from all the States. The 100% response rate of clients was reported because only those pharmacist responses with corresponding two (2) useable client responses available were considered for data analysis.

Strength Analysis

Easy accessibility (3.69) was shown to be a major strength of the community pharmacists in line with global trends (Table 2).²⁹ Clients do not generally need prior appointments to see their community pharmacists, neither do they pay consultation fees. Leveraging the positive reputation within their communities (3.59), strong relationships with family physicians (3.46), as well as their wide geographical spread, there are significant prospects for community pharmacists to deploy their clinical (3.51) and managerial skills (3.63) to bridge the gaps in access to

quality care both in terms of accessibility, availability, acceptability, and affordability in order to attain universal health coverage (WHO, 2017; Goundrey-Smith, 2018).

Weakness Analysis

To explore a new professional service idea, community pharmacists must justify its profit potential (Feletto, Wilson, Roberts & Benrimoj, 2010). The study found that a major weakness was lack of capacity to quantify a PPS and get customers to pay for it (3.39). This is understandable given that health insurance penetration in Nigeria stands below 7% and majority of clients have to pay out of pocket for medicines and professional services (Aregbesola, 2016; Chizoba, Okekeze, Asiegbu & Nwanna-Nzewunwa, 2018) while the pricing of medicines remains unregulated (Onoka, Onwujekwe, Uzochukwu & Ezumah, 2013). Most community pharmacies in Nigeria are independent retailers with sizes of small and medium-scale enterprises (Fatai, 2011). With obvious capacity constraints, community pharmacists are saddled with human resource management, inventory management, financial management, relating with sales representatives, among others. This leaves them insufficient time to implement quality professional services (3.36) even though a recent study in South-South Nigeria found that time constraint was actually of insignificant consequence (Agbo, Esienmoh, Inah, Eko, & Nwachukwu, 2019). There is also the important challenge of attracting and retaining skilled workforce leading to high staff attrition rates (3.28) as already highlighted by previous evidence (Ekpenyong, Udoh, Kpokiri, & Bates, 2018). Lack of integration with the primary health care architecture and absence of interoperable health information system may be blamed, at least in part, for the failure of community pharmacists to evolve a robust, uniform documentation framework for their services (3.32) (Awaisu, Mohammed & Yakubu, 2016). While possession of clinical skills is an important strength factor, lack of it remains a significant weakness (3.19). Given the poor regulatory environment, many community pharmacists seem compelled by competitive forces to lean more on business practices (as shops) than on professional services (as health care facilities), and this shows in the physical evidence of their premises (3.04) (Page, 2015).

Opportunities Analysis

Recently, there was a nation-wide review in pharmacy education curriculum making the Doctor of Pharmacy (Pharm.D) the minimum entry point to practice (Mohammed, 2020). This paradigm shift placed a major emphasis on clinical skills and presents an important opportunity for community pharmacists to evolve relevant professional services (3.52). The expected capacity enhancement will be made more sustainable by the current unbundling of the mandatory continuing professional development (MCPD) framework which gives every pharmacist the freedom to access additional educational materials relevant to their needs via online content (3.43) (PCN, 2013). With increasing penetration of digital technologies (3.51) and absence of red-tape as in the public sector (3.50), community pharmacists are free to host services relevant to the needs of their communities. Digital technologies also present underutilized opportunities for pharmacy-based disease parameter screening services, particularly in the management of chronic non-communicable diseases (3.38).

Threat Analysis

WHO data show that Nigeria has less than 5 pharmacists per 10,000 population (WHO, 2019). This shortage in workforce, coupled with poor regulatory environment creates room for many poorly-trained non-professionals to enter the medicines supply value chain. A local study estimated that for every community pharmacist, there were over thirteen patent and proprietary medicine vendors (Durowade, Bolarinwa, Fenenga, & Akande, 2018). With increasing pressure on government to achieve universal health coverage, there is increasing recognition and engagement of these medicine sellers. This has engendered unhealthy competition with many people unsure of the roles of pharmacists and showing apathy to value-added services offered by community pharmacists. This scenario becomes worse in communities where there is inadequate collaboration between community pharmacists and family physicians leaving community pharmacists to operate as isolated “silos”, outnumbered by competitors. Moreover, easy access to specialized medicines information via modern technologies continues to erode the asymmetry of information between the pharmacist and lay clients. Hence, advancements in digital and health care technologies present existential threat to community pharmacists as they now have to evolve professional services of such finesse as to earn the right to be patronized as professionals.

Association of Demographic variables with SWOT Factors

The internal capabilities of the pharmacies (strength and weakness SW) were not significantly influenced by additional educational qualifications and location of practice (Table 3). However, length of practice experience had significant positive influence on both (strength, $p = 0.002$; weakness, $p = 0.00$), while age of the pharmacy firm significantly improved their strength ($p = 0.01$). Higher educational qualification had significant negative influence on opportunities ($p = 0.00$). This runs contrary to existing evidence as higher education (specialization) was expected to impart higher knowledge and better capacity to maximize opportunities (Adeyeye, 2009). Length of practice experience had significant positive influence on opportunities ($p = 0.00$) and threats ($p = 0.00$). Moreover, the longer the community pharmacy were in practice, the better they seemed capable of maximizing service opportunities ($p = 0.01$).

Clientele Perspectives of Professional Pharmacy Services

Professional pharmacy services (PPS) have both technical and functional components (Moulin et al., 2013). The average client may not have the expertise to assess the technical aspects of a PPS (such as accuracy of interpretation of prescriptions and medicines information) but they make judgements about the functional components such as facility layout, stock levels, and responsiveness of staff, among others. The correlation of SWOT domains with service quality (Table 4) showed that developments in external environment (OT) ranked higher (1 and 2) than internal capabilities (WS, ranked 3 and 4) in shaping customer perceptions of service quality. The implication of this finding is that community pharmacists need the break out of the “silos” effect and pay more attention to variables in the external environment if their professional services are to make the right impact on society.

Interplay of Internal Capabilities with External Factors (SW vs OT)

SO: From the β values (Table 5), there was a 0.581 or 58% chance for the community pharmacists to leverage their strengths in order to identify and maximize opportunities for professional services. The strengths had a significantly positive impact on the opportunities ($r^2 = 0.168$, $p = 0.001$)

WO: The weaknesses have the capacity to limit the capacity of community pharmacists to identify and maximize opportunities in professional services by as much as 0.466 or 47%. Compared to strengths, the weaknesses had an even greater impact on opportunities ($r^2 = 0.346$, $p = 0.001$). With $F = 168.52$ and associated $p = 0.001$, it can be affirmed that the weaknesses most reliably predict the behavior of opportunities.

The difference between 58% success rate and 47% failure rate is 11% and this is considered marginal particularly in view of the unfair competitive and regulatory environments.

ST: The β values show there was a 0.424 or 42% chance for the community pharmacists to leverage their strengths in order to identify and mitigate threats to professional services. The strengths had a relatively smaller impact on the threats ($r^2 = 0.076$, $p = 0.001$).

WT: There was a 0.379 or 38% chance that the weaknesses will worsen the impact of threats to professional pharmacy services. The difference between 42% success rate and 38% failure rate being 4% is considered marginal.

Implications of the Findings

For community pharmacists to make the desired impact in professional pharmacy services, there is need for policy development and practice shift with priority given to addressing identified weaknesses in the internal environment while closer attention should be given to threats in the external environment.

Limitations of the Study

The study was limited to Southwestern Nigeria. Findings may not represent the true state of affairs for the whole country. Time frame for the study is considered insufficient, being a cross-sectional study. Cross sectional studies tend to be froth with bias.

CONCLUSION

There is inadequate strategic planning for professional services by community pharmacists in Nigeria. The community pharmacists exhibited marginal capacity to exploit opportunities and mitigate threats. Weaknesses and threat factors are most prominent in limiting service outcomes and must be given priority attention.

Suggestions for Further Studies

A longitudinal implementation study covering the entire country is recommended with a goal to address identified weaknesses and test how this will impact professional practice outcomes.

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References

- Adeyeye, J.O. (2009). An evaluation of human resource management practices in Nigerian Universities; the impact of size. *The Social Science Year*, 2009; 4(5): 494-498
- Agbo, B.B., Esienmoh, E., Inah, S.A., Eko, J.E., & Nwachukwu, E.J. (2019). Challenges in Providing Immunization Services amongst Community Pharmacists in South-south, Nigeria: A Cross-sectional Study. *J. Adv. Med. & Pharm. Sci.* 21(3), 1-8. <https://doi.org/10.9734/jamps/2019/v21i330133>
- Alenoghena, I., Aigbiremolen, A., Abejegah, C., & Eboreime, E. (2014). Primary health Care in Nigeria: strategies and constraints in implementation. *Int. J. Comm. Res.* 3(3):74–9.
- Alsabbagh, M.W., Wenger, L., Raman-Wilms, L., Schneider, E., Church, D., Waite, N. (2018). Pharmacists as immunizers, their pharmacies and immunization services: A survey of Ontario community pharmacists; *Can. Pharm. J. (Ott)*. 151(4):263-273. doi: 10.1177/1715163518779095.
- American Pharmacists Association (APhA) (2019). Pharmacist Scope of Services.; Available online: <https://www.pharmacist.com/sites/default/files/files/APhA%20-%20PAPCC%20Scope%20of%20Services.pdf>; Accessed June 4, 2019
- Ararat, S.M. (2016). Psychometric validation of the Bangla version of the patient-doctor relationship questionnaire, *Psychiatry Journal*, Article ID 9385364, 4 pages, doi: 10.1155/2016/9385364
- Aregbesola, B.S. (2016). Out-of-pocket payment in Nigeria. *The Lancet*, June 2016, 387(10037): 2506. doi: [10.1016/S0140-6736\(16\)30798-X](https://doi.org/10.1016/S0140-6736(16)30798-X)
- Awaisu A., Mohammed, S., & Yakubu, R. (2016). Chapter 17 - pharmacy practice in Nigeria. In: Ibrahim MIM, Wertheimer AI, editors. Pharmacy practice in developing countries [internet]. Boston: Academic Press; p. 343–70. Available from: <http://www.sciencedirect.com/science/article/pii/B9780128017142000174>.
- Bernard, H.R.(2000). Social Research Methods: Qualitative and Quantitative Approaches; Sage Publications Inc. Thousand Oaks California USA.
- Butt, M.M., & Cyril de Run, E. (2010). Private Healthcare Quality: Applying a SERVQUAL model. *Int. J. Healthcare Qual. Assur.*, 23(7): 658-673
- Chizoba, A.F., Okekeze, C., Asiegbu, C.J., & Nwanna-Nzewunwa, O. (2018). Accessibility of medications by chronically-ill older patients: a cross-sectional assessment of universal health coverage in Nigeria. *The Lancet*, March 2018. Available at [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(18\)30164-5/fu](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30164-5/fu); Accessed June 3, 2020
- Cochran, W.G. (1977). Sampling Techniques 3rd Ed. New York: John Wiley & Sons Inc.
- Desselle, S.P., Moczygemba, L.R., Coe, A.B., Hess, K, & Zgarrick, D.P. (2019). Applying contemporary management principles to implementing and evaluating value-added pharmacy services. *Pharmacy (Basel)* 7(3): 99 doi: [10.3390/pharmacy7030099](https://doi.org/10.3390/pharmacy7030099)
- Durowade, K.A., Bolarinwa, O.A., Fenenga, C.J., & Akande, T.M. (2018). Operations and Roles of Patent and Proprietary Medicines Vendors in Selected Rural Communities in Edu Local Government Area of Kwara State, North-Central Nigeria. *J. of Community Medicine and Primary Health Care*.2018; 30 (2) 75-89
- Ekpenyong, A., Udoh, A., Kpokiri, E., & Bates, I. (2018). An analysis of pharmacy workforce capacity in Nigeria. *J. Pharm. Pol. & Pract.* 11 (20): 21-36
- Fatai, A. (2011). Small and Medium Scale Enterprises in Nigeria: The Problems and Prospects, *The Collegiate Journal of Economics*, 5(6):1-22

- Feletto, E., Wilson, L.K., Roberts, A.S., & Benrimoj, S.I. (2010). Building capacity to implement cognitive pharmaceutical services: Quantifying the needs of community pharmacies. *Res. Soc. Adm. Pharm.* 6:163–173. doi: 10.1016/j.sapharm.2009.08.003.
- FIP. (2015). Vision of a Community-based Pharmacist: Community Pharmacy Section. International Pharmaceutical Federation; available at www.fip.org/community_pharmacy. Accessed 28th September, 2019.
- Gebremariam, E.T., & Mekuria, B. (2019). A qualitative review of strengths, weaknesses, opportunities, and threats of clinical pharmacy services provided by Tirunesh Beijing General Hospital. *J. Pharma. Care Health Sys.* 6: 206. doi:10.35248/2376-0419.19.6.206
- George, B., Walker, R.M., & Monster, J. (2019). Does strategic planning improve organisational performance? A meta-analysis. *Pub. Admin. Rev.* 2019; <https://doi.org/10.1111/puar.13104>
- Goundrey-Smith, S. (2018). The connected community pharmacy: Benefits for healthcare and implications for health policy. *Frontiers in Pharmacology*, 9: 1352. doi: [10.3389/fphar.2018.01352](https://doi.org/10.3389/fphar.2018.01352)
- Harrison, D.L.(2005). Strategic planning by independent community pharmacies. *J. Am. Pharm. Assoc.*, 45:726-733
- Israel, G.D. (2013). Determining Sample Size. Program Evaluation and Organizational Development, IFAS, University of Florida. PEOD-6. .Available at <http://edis.ifas.ufl.edu>. Accessed 10th September, 201
- Krueger, R.A., & Casey, M.A. (2014). Focus Groups: A Practical Guide for Applied Research 5th Ed. SAGE Publications Inc. USA.
- Marcrom, R.E., Horton, R.M., & Shepherd, M.D. (1992). Creating value-added services to meet patient needs: Use these practical suggestions to help tailor your services to various market segments and expand your practice. *J. Am. Pharm. Assoc.* 32:48–57.
- Mcintosh, J., Alonso, A., MacLure, K., Stewart, D., Kmpen, T., Mair, A., et al. (2018). A case study of polypharmacy management in nine European countries: Implications for change management and implementation. *PLoS ONE*, 13(4): e0195232. <https://doi.org/10.1371/journal.pone.0195232>
- Mohammed, N.A.E. (2020). Why Nigeria Universities delay in starting Pharm,D Programme. Available online at <https://psnnational.org/index.php/2020/02/02/why-nigeria-varsities-delay-in-starting-pharm-d-degree-pcn-registrar/>, Accessed 20th June 2020
- Moulin, J.C., Sabater-Hernandez, D., Fernandez-Llimos, F., & Benrimoi, S.I. (2013.) Defining professional services in community pharmacy. *Res. Soc. Adm. Pharm.* 9(6):989-995.
- Onoka, C.A., Onwujekwe, O.E., Uzochukwu, B.S., & Ezumah, N.N. (2013). Promoting universal financial protection: constraints and enabling factors in scaling-up coverage with social health insurance in Nigeria. *Health Res Policy Syst.* 11:20.
- Oseni, Y.O. (2017). Pharmacists Distribution in Nigeria; Implications in the Provision of Safe Medicines and Pharmaceutical Care, *Int. J. Pharm. and Pharm. Sci.*, 9(10): 49-54
- Page, E. (2015). Five tips to change your pharmacy from a “shop” to a “healthcare business” The Pharmaceutical Journal, 24th February, 2015. Accessed 3th August 2019.
- Pharmacists Council of Nigeria (PCN) (2013). Mandatory Continuing Professional Development (MCPD) Programme for the Re-Certification of Pharmacists in Nigeria. Available at http://www.pcn.gov.ng/files/MCPD_brochure.pdf; Accessed 10th September, 2019
- Pharmacists Council of Nigeria, (PCN) (2019). List of Registered Community Pharmacies in Nigeria. Available at <http://www.pcn.gov.ng> accessed 10th August, 2019.
- Queeno , B.V. (2017). Evaluation of inpatient influenza and pneumococcal vaccination acceptance rates with pharmacist education. *J. Pharm. Pract.* 30:202–208. doi: 10.1177/0897190016628963.
- Smalls, T.D., Broughton, A.D., Hylick, E.V., & Woodard, T.J. (2015). Providing medication therapy management for smoking cessation patients. *J. Pharm. Pract.* 28:21–25. doi: 10.1177/0897190014562381.
- Van Wijngaarden, J.D.H., Scholten, G.R.M., & van Wijk, K.P. (2012). Strategic analysis for healthcare organisations: the suitability of the SWOT-analysis; *Int. J. Health Plann. Magt.*, 27: 34-49.doi: 10.1002/hpm.1032
- Wang J., & Wang, Z. (2020). Strengths, Weaknesses, Opportunities, and Threats (SWOT) analysis of China’s prevention and control strategy for Covid-19 epidemic. *Int. J. Environ. Res. Public Health*; 17(7), 2235; <https://doi.org/10.3390/ijerph17072235>
- World Bank. Rural population (% of total population) estimates based on the United Nations Population Division’s World Urbanization Prospects 2018 Revision. www.data.worldbank.org/indicator/SP.RUR.TOTL.ZS. Accessed December 14, 2019
- World Health Organisation (2017). Indicators of Access to Medicines; developed by the World Health Organization; available at <http://www.un.org/esa/policy/mdggap/appendix.pdf>. Accessed 10th July, 2019

World Health Organisation (2019). World Health Data Platform/Global health observatory/Indicators - Pharmacists (per 10, 000 population). Available at [https://www.who.int/data/gho/data/indicators/indicator-details/GHO/pharmacists-\(per-10-000-population\)](https://www.who.int/data/gho/data/indicators/indicator-details/GHO/pharmacists-(per-10-000-population)); Accessed 10th September, 2019

Zgarrick, D.P., Moczygemba, L.R., Alston, G.L., Desselle, S.P. (2016). Pharmacy Management: Essentials for All Practice Settings. 4th ed. McGraw-Hill; New York, NY, USA.



Effects of Different Sintering Times on The Adaptation of Monolithic Zirconia Crowns

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Abstract

Changes to heat and time during the sintering process, which is one of the most critical stages in the production of monolithic zirconia crown restoration, can affect the physical properties of the material. The study was examined the effect of change in sintering time on the adaptation of monolithic zirconia crowns. Sixty monolithic crowns in upper first molar tooth form were produced from Y-TZP semi-sintered different blocks. Samples were divided into three groups according to brands and two subgroups according to sintering time (n=10). Marginal and internal gaps were photographed with a video microscope at x 180 magnification. The two-way ANOVA test was used for the effect of brand, and sintering time on adaptations were examined. There was no statistically significant difference in the overall gap values between the groups according to the long sintering times ($p > 0.05$). In crowns produced from zirCAD and Lava blocks, marginal gap values were not affected statistically significantly from sintering time ($p > 0.05$). In crowns produced from katana blocks, shortening of sintering time caused a statistically significant increase in marginal and occlusal gap values ($p < 0.05$). It can be said that the sintering time and temperature are an important factor in the biocompatibility of monolithic crowns.

Keywords: Ytria Stabilized Tetragonal Zirconia, Marginal Gap, Biological Adaptation, Dental Crown, Time

1. Introduction

Zirconium is a material with high biocompatibility and has no local or systemic side effects (Griffin, 2013). They also reduce the risk of pulp irritation that may occur due to their low thermal conductivity (Pereira et al., 2016). Since they are in opaque white colour, they are used as infrastructure material by veneering with feldspathic porcelains (Denry & Kelly, 2008). The biggest problem we encounter in these crowns and the reasons for being short-lived are cohesive breaks, especially in veneer porcelain (Suttor et al., 2001). For this, monolithic crowns produced with only one material, which are produced with CAD/CAM systems, do not need veneer porcelain, have been developed. Recently, the clinical indication of monolithic zirconium (MZ) has been expanding due to its superior mechanical properties (Marchack et al., 2011).

The term monolithic comes from the Greek words "mono: single" and "lithos: stone." It means that the materials have a regular feature throughout. Monolithic materials are two or more phases as microstructures. They still have fixed properties. MZ is partially stabilized with yttrium (0.01%). This process gives high bending resistance (1570 MPa) and high heat resistance (up to 2600 °C). This resistance to heat, in particular, ensures that it is a material with high dimensional stability (Zhang et al., 2013). The atoms in the structure of these blocks, also called solid or translucent, are intertwined without any organic binder (Laboratories G. Bruxzir Solid Zirconia., n.d.). Moreover, their abrasion resistance is very close to the natural tooth. While the microstructure of the porcelain used as veneer ceramics causes abrasions and aging in the opposite natural tooth over time, MZ crowns do not have such an abrasion disadvantage (Batson et al., 2014). Their high resistance to breakage provides the advantage of use in cases where the interocclusal distance is insufficient. Even with an occlusal thickness of 0.5 mm, they can show sufficient resistance and durability, allowing them to be used in posterior restorations (Vafae et al., 2017).

MZ restorations are prepared with CAD/CAM systems. For this reason, an appropriate closing relationship is obtained with the opposite teeth or restorations. Batson et al., in their study comparing the clinical properties of metal-ceramic, lithium disilicate, and MZ; They reported that crowns produced with CAD/CAM have acceptable high clinical properties. However, they reported that MZ showed no occlusal incompatibility with the antagonist region at 80%. Also; They reported that the gingival margin fit of MZ crowns is sufficient when evaluated according to the US health service criteria (Laboratories G. Bruxzir Solid Zirconia., n.d.).

One of the most important factors in long-term successful clinical results of the restorations is marginal fitting. Marginal misfit can cause plaque retention and bacterial microleakage, damaging both dental and supporting periodontal tissues (Kohorst et al., 2009). There is no definite consensus on the clinically acceptable full maximum range value in the scientific literature. Christensen proposed 34 to 119 μm as an acceptable, marginal range (Christensen, 1966). Currently, most authors use the criterion specified by McLean as 120 μm as the maximum acceptable, marginal gap for long-term success. (McLean & von, 1971) Besides marginal misfit, the restoration sits. Another factor affecting retention and survival is internal misfitting. Anadioti et al. The 25 μm thick cement spacer has shown to increase the casting seat and fit (Anadioti et al., 2015). Besides, an internal misfit can reduce the fracture resistance of all-ceramic restorations (Badran et al., 2019).

The most popular way to produce zirconia restorations now is to use the sintered zirconia blocks, which facilitates a smoother grinding process of the planned prosthesis. A specific sintering protocol is applied in order to reach the final density and maximum strength of the milled zirconia restoration, but together, the final sintering process is accompanied by a high shrinkage (about 20-30%) (Lankford et al., 1988). For compensate this shrinkage, the milled framework dimensions are enlarged by a single predefined percentage for all (Lankford et al., 1988).

High marginal fitting is an important factor for the clinical success of fixed restorations. Poor marginal adaptation causes the development of secondary caries and periodontal diseases (Felton et al., 1991). On the other hand, adjusting the prosthesis to ensure proper fit creates stress concentrations that can trigger the tetragonal to monoclinic ($t \rightarrow m$) phase transformation of zirconium, which could potentially lead to disaster for the survival of the prosthesis (Piconi & Maccauro, 1999).

The sintering time and temperature change the grain size of the zirconia. The longer the sintering time and the higher the temperature, the larger the resulting grain size, which can lead to an increase in zirconia creep deformation and can, therefore, lead to distortion of the last crowns. As the particle size increases $>1\mu\text{m}$, zirconia becomes less stable and more prone to higher phase transformation (tetragonal to monoclinic phase). On the other hand, a smaller grain size $<0.2\mu\text{m}$ can be achieved fracture toughness (Stawarczyk et al., 2013). The most common sintering method for zirconia uses conventional furnaces at temperatures between 1350⁰ and 1600⁰ C and waiting times of 2 to 4 hours. An alternative sintering protocol proposed by manufacturers is a rapid sintering protocol that is claimed to save time and be more economical. The manufacturers 'in-house' testing claims similar compatibility, translucency, and colour stability of zirconia restorations with standard or rapid protocols. However, actual test data to support the claim are lacking. Several recent in vitro studies have shown that a combination of high sintering temperatures with short sintering times increases the flexural strength of the zirconia (Ersoy et al., 2015) and

increases its optical properties (Ebeid et al., 2014). Also, a recent in vitro study has shown that changing sintering times does not affect marginal adaptation of zirconia copings (Khaledi et al., 2019).

2. Method

Acrylic right maxillary first molar was prepared according to the preparation rules for the full ceramic crown. The master resin die was doubled with silicone. Sixty resin die samples were fabricated. The samples obtained were randomly divided into three groups of twenty. A total of 60 monolithic zirconia crowns were produced, including twenty full ceramic restorations from three different zirconia blocks. Each group was divided into two subgroups, and one group was sintered in a short time, and the other group was sintered in a long time.

Three different monolithic zirconia materials were used in this study (Table 1). Digital designs of MZ crowns were made in Exocad Valetta 2.2 programs (exocad GmbH, Darmstadt, Germany) (Figure 1). After the design process on the computer, Y-TZP blocks were subjected to milling with five-axis machine. Yenadent D40 (Yenadent Ltd., Istanbul, Turkey) unit was used.

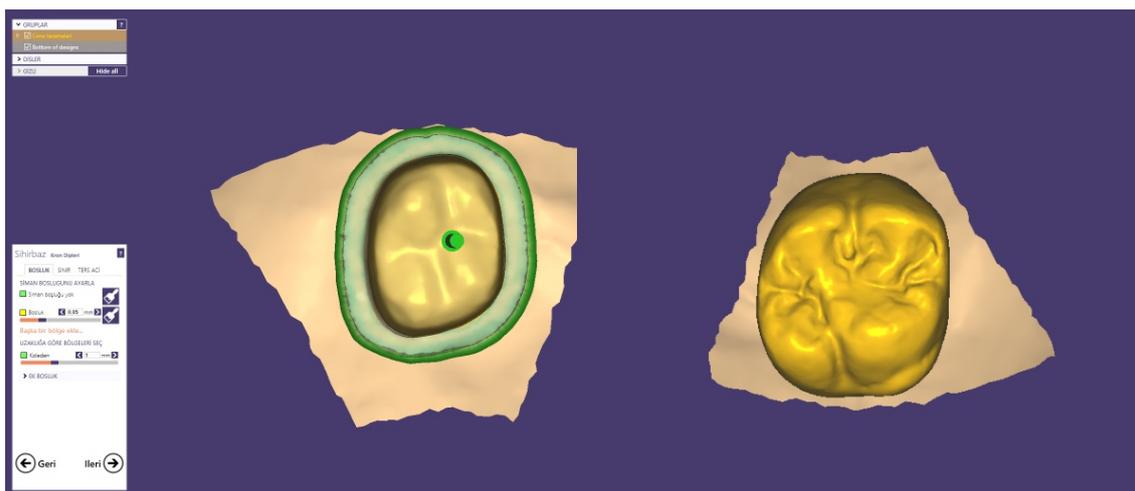


Figure 1. Digital desing on Exocad software

Table 1. Used blocks

Trade Name	Manufacturer
Lava™ Plus High Translucency Zirconia	3M, United Kingdom
IPS e.max ZirCAD Prime	Ivoclar Vivadent AG, Liechtenstein
KATANA™ HT	Kuraray Europe GmbH, Germany

Short and long sintering processes were applied to the samples in the ‘Sirona inFire HTC speed’ oven (Sirona Dental Systems GmbH, Bensheim, Germany). Time/temperature charts of short and long sintering processes are shown in Table 2.

Table 2. Sintering Processes

	Short-term			Long-term		
	Heat rise °C/min.	Heat °C	Waiting time Min.	Heat rise °C/min.	Heat °C	Waiting time Min.
Stage 1	10	0	0	12	0	0
Stage 2	10	0	0	70	1540	30
Stage 3	12	1540	120	70	1100	0
Stage 4	12	300	0	70	750	0

The silicone replica method was used to evaluate the compatibility of MZ crowns with resin abutments. Liquid petroleum jelly onto the resin die (Vazelin Blanc, Kalimed Medikal, Ankara, Turkey) was applied (Figure 2a,b). The polyvinylsiloxane material to be applied afterwards was prevented from deforming during detachment. The polyvinyl siloxane impression material (Xantopen VL Plus, Kulzer GmbH, Hanau, Germany) was squeezed into

the inner surface of the samples with the help of a silicone dispenser gun and placed on the supports with 50 N load pressure. (Figure 2c) This load pressure was continued until the polymerization of the silicone material was completed.

After completing the polymerization of the silicon material, the samples were carefully removed from the resin dies. A different colour silicone material (president, Xtra light body, Coltène, West Sussex, UK.) was placed in the samples to support the thin silicon layer. After completing the polymerization of the silicone impression material applied for the support, the silicone replicates obtained were delicately separated from the supports. The presence of deformation on the surfaces of the separated silicone replicas was examined under the dental loop, and the same procedures were repeated for samples that did not preserve their integrity.

Silicon replica samples were cut with a scalpel to pass through the central occlusal groove in the mesiodistal direction. Markings were made on the silicone parts for the standardization of the measuring points. The adaptation of the copings was observed with at x 180 magnification with a video microscope (Lapsun Video Microscope, Lapsun, Hong Kong, China). (Figure 3c). All sample photos were taken for calibration using a precision micrometre with an interval of 0.01 mm. In twelve points determined by Holmes and et., the marginal and internal gap values were repeated five times for each point and averaged. Thus, 60 measurements were performed for each sample. All measurements were made with IC Measure software (The Imaging Source Europe GmbH, Bremen, Germany).

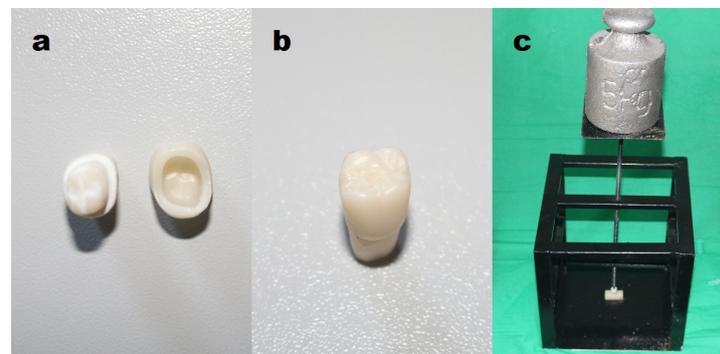


Figure 2. a: resin die, b: monolithic crown, c: applied light body silicon with 50 N force

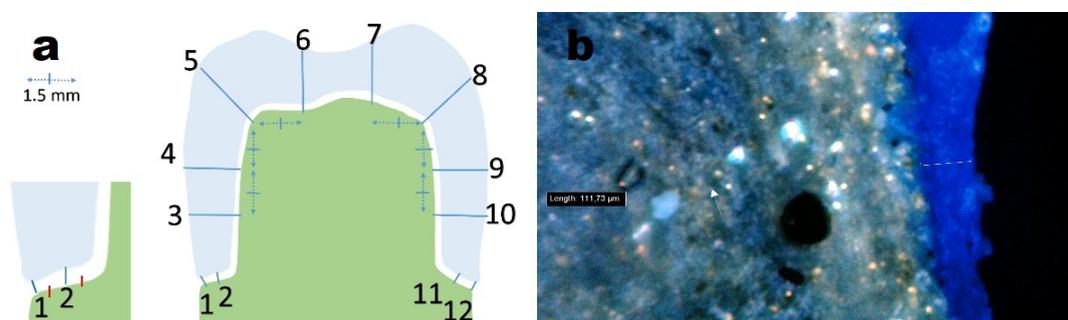


Figure 2. a.: marginal points (1,2,11,12), axial points (3,4,5,8,9,10); occlusal points (6,7) internal points (3,4,5,6,7,8,9,10), b: microscopic measurement image

Data analyzed with SPSS 22 program (SPSS Inc). The two-way ANOVA statistical analysis was used since the effects of brand and sintering time on the marginal and internal intervals were examined at the same time. The Leneve test was performed for control of the homogeneity of the group variances. The variations of the comparison groups were found to be similar. Due to the variance homogeneity, F statistics obtained as a result of the ANOVA test were accepted as reliable. Marginal, axial, and occlusal values were examined separately, and the results were evaluated within themselves. The presence/absence of statistically significant significance among the values obtained was evaluated with "T-test."

3. Results

There is no statistically significant difference between the marginal interval values of MZ crowns with long and short sintering times produced using Lava blocks ($p>0.05$). While average marginal interval values of samples sintered with zirCAD blocks in a long time were determined as $35.80\pm 8.08\ \mu\text{m}$; Average marginal interval values of samples sintered with zirCAD blocks in a short time were found to be $32.20\pm 10.92\ \mu\text{m}$. As a result, there is no statistically significant difference between the marginal interval values of MZ crowns with long and short sintering times produced using zirCAD blocks. While the average marginal interval values of the samples sintered with Katana blocks in a long time were determined as $39.20\pm 15.72\ \mu\text{m}$; Average marginal interval values of samples sintered with Katana blocks in a short time were found to be $78.65\pm 11.23\ \mu\text{m}$. The change in sintering time affected the marginal interval values of MZ crowns produced using Katana blocks. Marginal interval values in samples produced with long sintering time were found to be statistically significantly lower than in samples with short sintering time ($p<0.05$). As a result, there is no significant difference between the marginal interval values of samples produced with zirCAD and Lava type materials with short and long sintering times. However, in Katana blocks, a statistically significant difference was detected between the groups that were sintered in a long and short time ($p<0.05$).

In Lava and Katana type materials, there is no significant difference between the axial gap values of the samples produced with short and long sintering times. However, in zirCAD blocks, a statistically significant difference was detected between groups that were sintered in a long and short time ($p<0.05$). When the differences between the groups are evaluated, no difference between the groups can be detected in the samples produced by sintering in a long time; in samples produced by sintering in a short time between Lava blocks and zirCAD blocks ($p>0.05$); Statistically significant differences were found between Katana blocks and zirCAD blocks ($p>0.05$).

In Lava groups, no significant difference can be detected between the occlusal interval values of the samples produced with short and long sintering times. In contrast, in zirCAD and Katana blocks, there was a statistically significant difference between the groups that were sintered in a long and short time. There was no difference in overall internal interval values between the groups for long-term sintering. For the short term, the zirCAD group had the lowest internal interval value and was statistically different from the Katana group.

For Lava type materials, there is no significant difference between the cement range average values for all measurement points of samples produced with short and long sintering times. However, in zirCAD and Katana blocks, a statistically significant difference was detected between the groups that were sintered in a long and short time.

Table 3. Overall gap values

Groups	Sintering process	Marginal gap		Axial gap		Occlusal gap		General average gap		Overall Internal gap	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Lava™ Plus	Long	59.35	14.01	45.00	9.92	126.55	16.33	64.67	30.51	67.98	35.48
	Short	69.05	17.30	50.85	13.29	136.80	15.75	70.74	33.87	72.00	39.99
IPS e.max ZirCAD	Long	35.80	8.08	50.40	11.26	125.90	30.72	60.61	36.03	73.55	37.69
	Short	32.20	10.92	44.00	13.26	99.05	14.99	47.86	26.33	55.25	28.72
KATANA™ HT	Long	39.20	15.72	52.18	13.57	125.50	28.03	61.00	34.08	68.46	38.11
	Short	78.65	11.23	44.85	13.91	188.25	23.83	81.14	52.28	82.48	63.45

4. Discussion

Three different blocks and two different sintering times were evaluated in this study. The null hypothesis of the study was determined as "changes in sintering time do not affect the marginal and internal adaptation of MZ

restorations. When the total cement film thickness evaluated, this hypothesis was accepted for Lava Plus group, while the hypothesis was rejected for Katana and zirCAD groups.

The marginal gap values of all the samples in this study remained within limits accepted in the literature (McLean & von, 1971). Crowns produced in a short period using the highest marginal range value with $78.65 \pm 11.23 \mu\text{m}$, in Katana group. Crowns produced with the lowest marginal range value with $32.20 \pm 10.92 \mu\text{m}$ in zirCAD group. When the marginal interval values of crowns produced by sintering in a long time were examined, a statistically significant difference was found between the groups. Accordingly, zirCAD $35.80 \pm 8.08 \mu\text{m}$, Katana $39.20 \pm 15.72 \mu\text{m}$ and Lava $59.01 \pm 14.01 \mu\text{m}$ marginal interval values were measured. This result contradicts the results of the study of three different zircon infrastructures conducted by Karataşlı et al. (Karataşlı et al., 2011). In this study, the mean marginal interval value for Lava was reported as $24.6 \pm 14.0 \mu\text{m}$, and the lowest marginal interval value was obtained in Lava infrastructures. However, unlike this study, they produced a non-anatomical infrastructure, not MZ crowns. Lee KH et al. reported the highest values for Lava ($87.2 \pm 22.8 \mu\text{m}$) in their studies evaluating the marginal compatibility of all-ceramic crowns (Lee et al., 2015).

Literature studies are showing that sintering time affects the mechanical properties of zirconia restorations. The sintering temperature and duration are thought to affect the particle size of the material. Increased grain size; "T-m" reduces the stability and strength of the material by stimulating the phase transformation. Studies are showing that high sintering temperature and long sintering time increase the particle size. For a natural "t-m" phase transformation, very fine particles are required (Lee et al., 2015). Lazar et al. stated that the presence of thick particles in the microstructure of zirconia ceramics stabilized by yttrium is an indication of the presence of the monoclinic form (Lazar et al., 2008). This contrasts with the results of Hjerppe et al.'s work on zirconia discs sintered at different times. In this study, there was no difference between samples in terms of micro strength. The reason for this is; It may be related to the length of the sintering time. In the study, discs produced by short sintering were applied for 1 hour 40 minutes increase and 1 hour waiting time. Although it was not statistically significant in the same study, it was observed that the particle size of the discs produced by short sintering decreased (Hjerppe et al., 2009).

Beuer et al. emphasized that milling is done mostly before sintering, and therefore, sintering may affect the compatibility of zirconia restorations (Beuer et al., 2008). In this study, shortening the sintering time did not cause a statistically significant difference in the marginal interval values of the samples produced with zirCAD and Lava brand blocks. In contrast, the samples produced with Katana brand blocks increased statistically significantly with the reduction of the sintering time ($p < 0.05$). Although acceptable values ($< 120 \mu\text{m}$) for the marginal range are defined in the literature, there is no consensus on what the ideal internal range value is (Tsirogiannis et al., 2016). Wettstein et al. reported that the axial pitch values of the restorations were between 9 microns and 38.3 microns (Wettstein et al., 2008). In a study performed on full ceramic restorations, it was shown that smaller spaces in the axial wall and marginal area were better against compressive forces (Badran et al., 2019). The optimal internal range value was determined as $73 \mu\text{m}$ against the compressive forces, and there was no significant difference in the compatibility of the restorations at the range values up to $122 \mu\text{m}$; however, it is stated that there is a decrease in their durability. Internal range values; The cementation stage, the underlying material used, the magnification device used to make measurements, measurement points and numbers can be affected by many factors (Beschnidt & Strub, 1999).

The internal gap values of MZ produced by two different CAD/CAM systems (Zirkonzahn and Ceramill) were compared, and the internal gap values varied according to the areas measured. The highest internal range values were determined in the occlusal areas ($213.40 \pm 19.57 \mu\text{m}$) of the samples produced with the Ceramill system, and the lowest internal range values ($42.90 \pm 6.84 \mu\text{m}$) in the lingual axial walls (Ha & Cho, 2016).

The highest values were recorded in the occlusal range measurements ($99.05 \pm 14.99 \mu\text{m}$ and $188.25 \pm 23.45 \mu\text{m}$) in this study. Luthard et al. reported that the occlusal spacing values of the restorations produced using CAD/CAM systems might cause a higher resolution of the scanning device. In the same study, it was reported that the inability of the scanner to read the sharp edges thoroughly and the small details that could not be copied by the scraping unit might result in high occlusal spacing values (Kelvin Khng et al., 2016).

In MZ restorations, the cement spacing is set up during digital design. There are literature studies on the ideal cement range (Contrepolis et al., 2013). In this study, the samples were not cemented, but they were designed with the cement spacing in mind. The cement gap value is set to 50 μm . Since cementation of zirconia restorations is not required to use an adhesive based cement, 50 μm cement interval value may be sufficient. Al-Rabab et al. examined the effect of cement spacing values on marginal spacing in restoration designs in CAD/CAM systems and showed that marginal compatibility is better than designs produced with 100 μm cement spacing values in designs produced with a 50 μm cement spacing value (Contrepolis et al., 2013).

Weaver et al. placed the restorations on the abutments with a non-standard press and said that the finger pressure was an average of 78.5 N. They also reported that pressure differences did not make a statistically significant difference on the silicone layer (Weaver et al., 1991), but standard pressure used in this study.

Conclusions

Within the limitations of this study, the following results were obtained:

1. No statistically significant difference was observed between the systems used in the study in terms of total cement film thickness values by the long sintering times.
2. In crowns produced from zirCAD and Lava blocks, marginal gap values were not statistically significantly affected by the sintering time.
3. The shortening of sintering time in crowns produced from Katana blocks caused a statistically significant increase in marginal and occlusal gap values.

The sintering times recommended by the manufacturer of the materials used in the production of monolithic crowns must be complied with.

References

- Anadioti, E., Aquilino, S. A., Gratton, D. G., Holloway, J. A., Denry, I. L., Thomas, G. W., & Qian, F. (2015). Internal fit of pressed and computer-aided design/computer-aided manufacturing ceramic crowns made from digital and conventional impressions. *Journal of Prosthetic Dentistry*, 113(4), 304–309. <https://doi.org/10.1016/j.prosdent.2014.09.015>
- Badran, N., Abdel Kader, S., & Alabbassy, F. (2019). Effect of incisal porcelain veneering thickness on the fracture resistance of CAD/CAM zirconia all-ceramic anterior crowns. *International Journal of Dentistry*, 2019. <https://doi.org/10.1155/2019/6548519>
- Batson, E. R., Cooper, L. F., Duqum, I., & Mendonça, G. (2014). Clinical outcomes of three different crown systems with CAD/CAM technology. *Journal of Prosthetic Dentistry*, 112(4), 770–777. <https://doi.org/10.1016/j.prosdent.2014.05.002>
- Beschmidt, S. M., & Strub, J. R. (1999). Evaluation of the marginal accuracy of different all-ceramic crown systems after simulation in the artificial mouth. *Journal of Oral Rehabilitation*, 26(7), 582–593. <https://doi.org/10.1046/j.1365-2842.1999.00449.x>
- Beuer, F., Schweiger, J., & Edelhoff, D. (2008). Digital dentistry: An overview of recent developments for CAD/CAM generated restorations. *British Dental Journal*, 204(9), 505–511. <https://doi.org/10.1038/sj.bdj.2008.350>
- Christensen, G. J. (1966). Marginal fit of gold inlay castings. *The Journal of Prosthetic Dentistry*, 16(2), 297–305. [https://doi.org/10.1016/0022-3913\(66\)90082-5](https://doi.org/10.1016/0022-3913(66)90082-5)
- Contrepolis, M., Soenen, A., Bartala, M., & Laviolle, O. (2013). Marginal adaptation of ceramic crowns: A systematic review. *Journal of Prosthetic Dentistry*, 110(6), 447–454.e10. <https://doi.org/10.1016/j.prosdent.2013.08.003>
- Denry, I., & Kelly, J. R. (2008). State of the art of zirconia for dental applications. *Dental Materials*, 24(3). <https://doi.org/10.1016/j.dental.2007.05.007>
- Ebeid, K., Wille, S., Hamdy, A., Salah, T., El-Etreby, A., & Kern, M. (2014). Effect of changes in sintering parameters on monolithic translucent zirconia. *Dental Materials*, 30(12). <https://doi.org/10.1016/j.dental.2014.09.003>
- Ersoy, N. M., Aydoğdu, H. M., Değirmenci, B. Ü., Çökük, N., & Sevimay, M. (2015). The effects of sintering temperature and duration on the flexural strength and grain size of zirconia. *Acta Biomaterialia Odontologica Scandinavica*, 1(2–4). <https://doi.org/10.3109/23337931.2015.1068126>
- Felton, D. A., Kanoy, B. E., Bayne, S. C., & Wirthman, G. P. (1991). Effect of in vivo crown margin discrepancies on periodontal health. *The Journal of Prosthetic Dentistry*, 65(3). [https://doi.org/10.1016/0022-3913\(91\)90225-L](https://doi.org/10.1016/0022-3913(91)90225-L)

- Griffin, J. D. (2013). Combining monolithic zirconia crowns, digital impressing, and regenerative cement for a predictable restorative alternative to PFM. In *Compendium of continuing education in dentistry (Jamesburg, N.J. : 1995)* (Vol. 34, Issue 3).
- Ha, S. J., & Cho, J. H. (2016). Comparison of the fit accuracy of zirconia-based prostheses generated by two CAD/CAM systems. *Journal of Advanced Prosthodontics*, 8(6), 439–448. <https://doi.org/10.4047/jap.2016.8.6.439>
- Hjerpe, J., Vallittu, P. K., Fröberg, K., & Lassila, L. V. J. (2009). Effect of sintering time on biaxial strength of zirconium dioxide. *Dental Materials*, 25(2). <https://doi.org/10.1016/j.dental.2008.05.011>
- Karataşlı, Ö., Kursoglu, P., Çapa, N., & Kazazoglu, E. (2011). Comparison of the marginal fit of different coping materials and designs produced by computer aided manufacturing systems. *Dental Materials Journal*, 30(1). <https://doi.org/10.4012/dmj.2010-063>
- Kelvin Khng, K. Y., Ettinger, R. L., Armstrong, S. R., Lindquist, T., Gratton, D. G., & Qian, F. (2016). In vitro evaluation of the marginal integrity of CAD/CAM interim crowns. *Journal of Prosthetic Dentistry*, 115(5). <https://doi.org/10.1016/j.prosdent.2015.10.002>
- Khaledi, A. A. R., Vojdani, M., Farzin, M., Pirouzi, S., & Orandi, S. (2019). The Effect of Sintering Time on the Marginal Fit of Zirconia Copings. *Journal of Prosthodontics*, 28(1). <https://doi.org/10.1111/jopr.12731>
- Kohorst, P., Brinkmann, H., Li, J., Borchers, L., & Marginal, S. M. (2009). Marginal accuracy of four-unit zirconia fixed dental prostheses fabricated using different computer-aided design/computer-aided manufacturing systems. *European Journal of Oral Sciences*, 2, 319–325.
- Laboratories G. Bruxzir Solid Zirconia. (n.d.). *You just get more with Over 14 million restorations delivered through the*. <http://bruxzir.com/wp-content/uploads/2018/02/scientific-clinical-compendium-english.pdf>
- Lankford, J., Page, R. A., & Rabenberg, L. (1988). Deformation mechanisms in yttria-stabilized zirconia. *Journal of Materials Science*, 23(11). <https://doi.org/10.1007/BF01106850>
- Lazar, D. R. R., Bottino, M. C., Özcan, M., Valandro, L. F., Amaral, R., Ussui, V., & Bressiani, A. H. A. (2008). Y-TZP ceramic processing from coprecipitated powders: A comparative study with three commercial dental ceramics. *Dental Materials*, 24(12). <https://doi.org/10.1016/j.dental.2008.04.002>
- Lee, K. H., Yeo, I. S., Wu, B. M., Yang, J. H., Han, J. S., Kim, S. H., Yi, Y. J., & Kwon, T. K. (2015). Effects of Computer-Aided Manufacturing Technology on Precision of Clinical Metal-Free Restorations. *BioMed Research International*, 2015. <https://doi.org/10.1155/2015/619027>
- Marchack, B. W., Sato, S., Marchack, C. B., & White, S. N. (2011). Complete and partial contour zirconia designs for crowns and fixed dental prostheses: A clinical report. *Journal of Prosthetic Dentistry*, 106(3). [https://doi.org/10.1016/S0022-3913\(11\)60112-1](https://doi.org/10.1016/S0022-3913(11)60112-1)
- McLean, J. W., & von, F. (1971). The estimation of cement film thickness by an in vivo technique. *British Dental Journal*, 131(3), 107–111. <https://doi.org/10.1038/sj.bdj.4802708>
- Pereira, G. K. R., Venturini, A. B., Silvestri, T., Dapieve, K. S., Montagner, A. F., Soares, F. Z. M., & Valandro, L. F. (2016). Low-temperature degradation of Y-TZP ceramics: A systematic review and meta-analysis. In *Journal of the Mechanical Behavior of Biomedical Materials* (Vol. 55). <https://doi.org/10.1016/j.jmbbm.2015.10.017>
- Piconi, C., & Maccauro, G. (1999). Zirconia as a ceramic biomaterial. In *Biomaterials* (Vol. 20, Issue 1). [https://doi.org/10.1016/S0142-9612\(98\)00010-6](https://doi.org/10.1016/S0142-9612(98)00010-6)
- Stawarczyk, B., Özcan, M., Hallmann, L., Ender, A., Mehl, A., & Hämmerle, C. H. F. (2013). The effect of zirconia sintering temperature on flexural strength, grain size, and contrast ratio. *Clinical Oral Investigations*, 17(1). <https://doi.org/10.1007/s00784-012-0692-6>
- Suttor, D., Bunke, K., Hoescheler, S., Hauptmann, H., & Hertlein, G. (2001). LAVA--the system for all-ceramic ZrO₂ crown and bridge frameworks. *International Journal of Computerized Dentistry*, 4(3).
- Tsirogiannis, P., Reissmann, D. R., & Heydecke, G. (2016). Evaluation of the marginal fit of single-unit, complete-coverage ceramic restorations fabricated after digital and conventional impressions: A systematic review and meta-analysis. *Journal of Prosthetic Dentistry*, 116(3), 328–335.e2. <https://doi.org/10.1016/j.prosdent.2016.01.028>
- Vafae, F., Firouz, F., Khoshhal, M., Hooshyarfard, A., Shahbazi, A., & Roshanaei, G. (2017). Fatigue Fracture Strength of Implant-Supported Full Contour Zirconia and Metal Ceramic Fixed Partial Dentures. *Journal of Dentistry (Tehran, Iran)*, 14(3), 165–172. <http://www.ncbi.nlm.nih.gov/pubmed/29167689> <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5694850>
- Weaver, J. D., Johnson, G. H., & Bales, D. J. (1991). Marginal adaptation of castable ceramic crowns. *The Journal of Prosthetic Dentistry*, 66(6), 747–753. [https://doi.org/10.1016/0022-3913\(91\)90408-O](https://doi.org/10.1016/0022-3913(91)90408-O)
- Wettstein, F., Sailer, I., Roos, M., & Hämmerle, C. H. F. (2008). Clinical study of the internal gaps of zirconia and metal frameworks for fixed partial dentures. *European Journal of Oral Sciences*, 116(3). <https://doi.org/10.1111/j.1600-0722.2008.00527.x>
- Zhang, Y., Lee, J. J. W., Srikanth, R., & Lawn, B. R. (2013). Edge chipping and flexural resistance of monolithic ceramics. *Dental Materials*, 29(12), 1201–1208. <https://doi.org/10.1016/j.dental.2013.09.004>

International Medical Graduate (IMG) Mentoring When it Matters: Basic Sciences to Clinical Rotations and What to Know

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Abstract

One-fourth of the medical doctors in the United States come from international medical schools; they are known as International Medical Graduates, IMGs. Future medical doctors need a guide and specific information which could come by way of a mentoring relationship in order to transition from the Basic Sciences to Clinical Rotations. Now, more than ever the conversations among medical doctors and incoming IMGs need to be happening in order to navigate the transition successfully. IMGs find mentors within their own ranks, from external sources and from medical doctors too.

Keywords: International Medical Graduates, Mentoring, Clinical Rotations

1. Introduction

With the shortage of medical doctors and health care providers in a certain crisis, the United States continues to rely on International Medical Graduates (IMGs) to fill the dire need for medical doctors (American Academy of Pediatrics, 2020) The traditional road to earning a medical degree consists of completing two years of Basic Sciences and moving forward with two more years of Clinical rotations. The purpose of this paper is to provide a voice for the current medical students moving from the Basic Sciences into Clinical rotations. As this paper was developed, the pandemic came to fruition and the need to finalize these ideas became even more pertinent. In order for future medical doctors to successfully complete the lengthy journey, mentors and a measure of guidance are needed to provide support for future doctors. International Medical Graduates (IMGs) make up 25% of the medical doctors in the United States; these future medical doctors come equipped with highly needed skills with the fast-changing population in the United States. At the same time, these hopeful medical students remain in need of mentorship and support.

There are numerous resources available online and hard copy text that provide vetted and unvetted information about the *right* way to be a successful medical student and hopefully a successful physician. Suffice to say, when medical students are bombarded with so much information, it is difficult to know how to determine the most relevant and accurate information. In addition to this, at first glance, some of the information is compiled by persons that have not had the unique experience of being an international medical school graduate. This article intends to be a voice from the field, the voice of international medical students headed to the United States, who have had the unique experience of being an IMG. IMGs need some measure of guidelines since no medical school experience abroad is the same. Most importantly for medical students, little has been written to provide guidance or to lend voice to those IMGs.

2. International Medical Graduates (IMG)s in the U.S. physician workforce

Based on the American Medical Association's (AMA) 2019 Physician Masterfile, IMGs represent 23.6% of the total active U.S. physician workforce, and 22.1% of residents. The *Top 10 IMG Friendly Specialties* as of 2019-2020 NRMP Data include:

1. Internal Medicine
2. Family Medicine
3. Pediatrics (categorical)
4. Psychiatry
5. Pathology
6. Surgery (prelim)
7. Neurology
8. Surgery (categorical)
9. Emergency Medicine
10. Anesthesiology.

IMGs constitute approximately 26% of the U.S. pediatric workforce, and approximately 41% of practicing IMGs are in primary care disciplines (American Academy of Pediatrics, 2020; "International Medical Graduate" n.d.). Most of these primary care settings are either in rural areas or in urban, underserved communities. For this reason, IMGs play a vital role in the care of vulnerable populations in both rural and urban underserved areas. For instance, Dr. Rana Chakraborty, who studied medicine in Antigua and went on to pursue a career in pediatric medicine, readily advocates for IMGs interested in pediatrics. He was the Chair of the American Academy of Pediatrics Section on the International Medical Graduates Executive Committee, and worked diligently to guide up-and-coming IMGs through the challenging process that comes with being an IMG in the United States.

Recently, the United States Medical Licensure Exam (USMLE) changed the way in which Step 1 scores will be assessed. Starting in 2022, all results for the USMLE Step 1 will be pass or fail. Whether this is a good change or not is uncertain; however, one thing to keep in mind is how important it will be to take on a holistic approach and to be sure to be viewed as a well-rounded person and not just as an exam score. For IMG students, the word moving is an understatement; thus, the need for a mentor is even more important. IMG students relocate to another country and acquire a set of invaluable skills which include: cultural competence and adaptability. We know that 25% of all medical doctors in the United States studied in an international setting, and the skills acquired during this experience are much needed during an age of an ever-changing demographic and in the era of the pandemic.

3. Why Mentorship is critical to Future Doctors

Mentorship was first developed in the United States in the 1970s to significantly enhance professional development in the early stages of a career (Garmel, 2004; Kram, 1983). The wellbeing (emotional, physical and professional) of doctors is crucial, both for the individuals themselves and their ability to deliver the best patient care. With increased pressures on healthcare to serve a diverse population, support mechanisms that attend to junior doctors' preparation to serve this population require greater emphasis in medical schools. There is a wealth of research that explores the mentor and mentee interaction in mentoring structures with roles, functions, benefits and challenges highlighted (Connor et al., 2000; Driessen et al., 2011; Overeem et al., 2010; Steven, 2008). The focus of this research is also primarily on professional aspects, such as career progression, career success and career choice (Kalen et al., 2010; Stamm & Buddeberg-Fischer, 2011). Transitioning from medical student to working effectively as a junior doctor might be one of the biggest challenges that a new medical school graduate will face. Having a medical mentorship program can be an effective conduit to supporting the transfer of learning to practicum, increase the student's confidence and allow them to reflect on their professional development. Within the literature there is an acknowledged performance gap that students experience when transitioning from academia to practice (Cervantes et al., 2014; Frei et al., 2010; Kramer, 1974). The early professional years of development can present the following struggles for junior doctors- struggling with increased responsibilities, such

as time management, prescribing, clinical procedures, reporting risks to patient safety, coping in emergency situations, resilience, professionalism and complex communication tasks.

Mentorship becomes critical to future doctors when we begin to address the large diversity gap in medicine and the sciences. Researchers feel this gap prevents our society from experiencing the benefits of a diverse physician workforce and a culturally competent health care system. Underrepresented minorities make up a small percentage of the physician workforce. One way to increase the slow pace representation of minorities and even the decrease in the number of medical school student enrollment from 1997 to 2000 (Fang et al., 2000) could be through a well developed and implemented mentorship program. The lack of diversity in the healthcare system can have ripple effects in other areas, less diversity in medical students means that there is a lack of representation when it comes to senior faculty which in turns affects the agenda for health care policy, bringing often neglected research topics to the forefront, and in the training of future physicians.

New doctors assume their responsibilities gradually over several months while completing their practicum. This gradual release of responsibility is ideal to give new doctors access to professionals that can support them, answer their questions, and provide needed guidance. Creating a mentoring program is critical, especially in a fast-paced working environment in which the development of future doctors that can have a wide range of talents, such as the ability to innovate new services and products, develop visionary strategic skills and provide future leadership capabilities, is essential for their hospitals to sustain themselves (Entezami et al., 2012). Well designed and well managed mentoring programs can also have a significant impact on the financial bottom line of hospitals, this will pave the way to be able to improve their ranking and attract high caliber professionals (Parise & Forret, 2008; Swenson & Shanafelt, 2017).

Understanding mentoring from the perspective of a diverse group of individuals who are embarking on their preparation will ensure that we are able to gather a range of viewpoints. Research from DeCastro et al. (2013) found that there is an improbability of finding a single person who can fulfill the diverse mentoring needs of future doctors and that there is an importance to developing those mentor networks. Mentorship is a vital/critical component for development in academic and clinical medicine. In medicine the term mentor can be used to describe an experienced and knowledgeable person that has the ability to advise his/her mentee in the right path in order for their mentee to attain academic and professional excellence. Initially one of the main goals of mentoring could serve to help the mentee develop an interest in a particular specialty. With quality and committed mentoring a mentee should be gaining a good amount of knowledge in order to be able to choose a professional trajectory that is fulfilling on a personal level that can impact satisfaction with their career choice in the field of medicine.

As with other fields, mentoring is becoming a necessity for minority medical students in order for them to achieve maximum career success (Bronson & Ellison, 2015).

Medical students need insight which can serve as a guide for the transitioning phase from the Basic Sciences to clinical rotations. IMGs may need the additional perspective which they may lose while they are occupied working hard to move through their medical education. IMGs need information as they look ahead and consider future residencies. The assumption is that graduate students know how to behave in a professional manner, but the truth is that in today's era of instant communication, a good reminder is needed. IMGs needed to know about beneficial resources that could help in planning for STEP 1. Students who are spending 10 to 12 hours a day studying may not consider the need to attend conferences, to build networks, and to stay up to date in their medical field of interest. In addition, all of this information must be shared to support future medical doctors who are in a medical school during an unprecedented global pandemic.

3.1 Relationships

Mentoring highlights the value of encouraging and enabling good communication and ensuring effective relationships both inside and outside of the work environment.⁷ Improved relationships and communication provide 'social capital' which promotes a doctors' mental health, wellbeing and engagement (Steven et al., 2008). In a study by Steven et al. (2008), interviewees suggested mentoring activities enhanced professional practice and

collegiality in both mentees and mentors, through facilitation of improved working relationships and teamwork. The authors suggest this collegial approach fosters peer support, which protects against feelings of isolation and adds to workplace satisfaction, an important component of wellbeing.

3.2 Physical and Psychological Health

A well designed and implemented mentorship program will promote the importance of a safe working environment, and healthy behaviors, to ensure better physical and psychological health. The components could include stress, anxiety, satisfaction, accomplishment, optimism, confidence, control, empowerment and safety (Dodge et al., 2012).

3.3 Better Work Environment

Mentorship programs also need to ensure the working environment is engaging and supportive and that it gives the junior doctors a voice. Better work is further ensured by managerial styles and organizational cultures which facilitate mutual trust and respect (Wilson et al., 2017).

4. Looking for a Mentor

Every medical student can think of that one person who provided guidance towards a brighter future or provided inspiration to dream big. Or is this a cliché? According to Pisani (2018), women in medicine say they never had a mentor during their training. In 2020 and especially during this pandemic, this notion seems unacceptable. Mentors play such a critical role in a person's life and even more so in that of a medical student. The impact a seasoned mentor has on a future doctor can change the course of a life. Generations to come should take the time to reflect at those moments when the challenges and obstacles were so great that the only question left to ask is, "What would this journey have been better with a mentor?" If the answer is a resounding yes, then the immediate response and call to action for all generations should be to serve as a mentor for someone who needs one.

Medical students are in need of mentorship and guidance from seasoned individuals with experience. In medical school in particular, a supportive environment must exist and be created as opposed to a competitive one. The idea is for the medical profession to be thinking in terms of long-term goals that encourage future residents who will be practicing physicians in the age of a pandemic. After all, the ideal setting consists of one which all medical students and medical doctors look forward to.

Nina Madjer, a University of Medicine and Health Sciences- St. Kitts (UMHS) medical student in her first clinical rotation in Internal Medicine at Weiss Memorial Hospital in Chicago, hopes to be a resource to any and all students who are going through the same steps she went through in her previous semester in the Basic Sciences. In thinking of ways to share advice or tips about upcoming semesters, she began to share ideas through an online professional learning community using Edmodo ("Edmodo" n.d.). The need to share information about topics ranging from housing to the process of transitioning fueled the desire to support her classmates.

5. Professionalism Communication Mentorship

How medical students demonstrate the highest form of professionalism? Well, as a graduate student it should be intuitive and it should go without saying, but unfortunately, there are more instances of students, residents, and attendings who may not be aware that they are in fact being unprofessional. Clear expectations and qualities of professionalism include: demonstrating respect, compassion, and integrity, respecting patients' values, religious beliefs, and backgrounds, having compassion for the existing situation, and respecting colleagues regardless of their job title or description. Confidentiality is part of this effective professional communication. In order to provide the best patient care, future medical doctors need to demonstrate a commitment to ethical principles as they pertain to clinical care, i.e. confidentiality of patient information and informed consent. The doctor-patient relationship implies trust. Part of the job includes protecting that trust. Professionalism can be reflected in the way medical students dress consistent with that of a medical professional. Wearing attire that is clean, pressed, and reflects a sense of confidence matters.

6. Transitional Housing

Every medical student understands the experience of moving in order to start the medical school experience before the pandemic and during the pandemic. However, one of the most cathartic and symbolic physical and geographical moves includes the moment when medical students go from finishing up the Basic Sciences and beginning the transition to Clinical Rotations. Even though every university provides guidance and plenty of useful information, at the end of the day, medical students rely on each other for recent information.

The first question which a medical student might have is whether or not to get a roommate? What are the benefits of literally living with another person during one of the most stressful times in the life of a medical student? For starters, sharing the rent with someone makes it more financially viable. Additionally, medical students know that this type of housing is consistently very short-term. The best resources to begin this search include university databases and university staff.

University staff understands student needs, and they consider all factors. They have updated information, and they also have a very good understanding of local rental properties and rates based on existing rental markets. For all of those medical students burning the midnight oil and leaving the hospital late at night, university staff can provide critical guidance regarding safe locations to live and within reasonable distances from required locations for clinical rotations. Additionally, every semester varies in medical schools. As class sizes grow or are reduced, options for reasonable rental properties vary, and in this case, the best source for useful information will always be the university faculty and staff.

Is it all right to talk to fellow classmates and colleagues about transitional housing? The answer is always yes. However, keep in mind that this information will vary like anything you might find on a social media review forum unlike popular reviews available on Yelp. More than likely, each university will host a student social media page which will allow existing and former students to post useful information related to experiences with different locations and rental properties.

In many ways, these social media forums provide informal mentoring. The voices of previous students provide a snapshot view of existing and previous experiences. Through this type of informal feedback and sharing of information, medical students provide intentional and somewhat unintentional mentoring. The primary usefulness of mentorship is that the information is just that, useful. Because students have a shared experience, they can authenticate and verify a slew of information, like prices, affordability and rates.

In today's era of social media and technology, the veracity of information is easy to challenge by simply speaking to a peer or a university staff or faculty member. Every medical student understands that every penny counts; therefore, in order to confidently put down a deposit on a rental property, the dialogue or informal conversation with a mentor during this phase of medical school is fundamental.

7. Organization and Planning Ahead

Another way which medical students need mentorship is in the area of organization. The abundance of information and the delivery of too much information can be very overwhelming for a person who is in transition. What are the vital things a pre-clinical rotation student would want to know? For starters, it can be invaluable to narrow down the scope of what resources to use. Also, the creation of a schedule can be life-changing because an organized schedule which focuses on time management can help students hold themselves accountable.

Here are the top two things that can make all of the difference, in terms of getting organized when studying for important licensure exams: **Cram Fighter**: This is an online algorithm created for students in medicine (Cram Fighter, 2017). This program includes all of the available and relevant study resources, from First Aid to Sketchy and even more. Therefore, choosing what to rely on in order to study, CramFighter can create a daily schedule which dictates the amount of time it should take to complete all of the tasks which are looming.

Nearly every medical student will find value in using this program, and each of those students will also wonder what the experience would have been like without it. This program is a saving grace in order to prepare for Step. The **Erin Condren Planner** website has planners for all occasions, from student academic planners, to meal prep planners and even budgeting planners; this site is a must-have for all medical students (Erin Condren, 2020).

The truth is that every second of a medical student's life has to be planned and organized. Academic planners are useful to prepare specific study plans. Notebooks are needed for Internal Medicine notes, and smaller notebooks for "on rounds" notes that the attending mentions while with patients are invaluable. Smaller and portable notebooks are convenient enough that they can just be tucked easily into any white coat. With so much responsibility and so much at stake, any small tip to keep on top of things makes a world of difference.

8. Networking

One simple way to receive informal mentoring is by attending or presenting at conferences, preferably national ones. After the crucial step of passing the USMLE Step 1 is passed, one good recommendation for all medical students entering into clinical rotations is to consider attending conferences which focus on specialties. Here are a few considerations to discuss with a mentor:

- American College of Physicians Meeting (Internal Medicine)
- American Academy of Pediatrics Meeting:
- American Academy of Family Physicians Meeting (Family Medicine):
- American College of Surgeons Meeting
- American College of Obstetricians and Gynecologists

Many others exist, but these are a few to start thinking about during the transitional period.

It is important to get to know the program directors, to know a little about the hospitals they are from, and to have some knowledge of their programs so it is easier to start up a conversation. Of course, it is a good idea to have a curriculum vitae handy. A mentor can also give objective feedback to a CV and give a fresh perspective regarding what to include and what to highlight.

9. Residency Searching

The mentoring relationship is long-term and continuous as each phase of a career in medicine is completed. Before clinical rotations are completed and before all examinations are taken, medical students may want to be researching potential residencies. Some considerations could include elective rotations. It is possible to potentially schedule an elective rotation well in advance. One useful resource to discuss with a mentor is FREIDA <https://freida.ama-assn.org/Freida/> This website is a great resource for looking up different specialties in specific regions of the country and which programs are more "IMG friendly", which becomes very pertinent for IMGs.

As per the new change in USMLE Step 1 being pass/fail, it becomes more important than before that an IMG highlights his /her strengths in residency match application. A mentor can provide assistance to an IMG in terms of publications, participation in professional meetings and conferences or additional training which might boost the residency application.

10. Staying Active During a Pandemic

Professional Development courses demonstrate a desire to continue to learn and to be productive when options are limited. Oftentimes, mentoring relationships, ideally, include a one on one sit down and a conversation with someone who can provide sound advice and concrete examples about how to move forward. However, informal mentoring can also occur through continuing education courses and by learning from experts in different fields. Here are some examples of on-going courses which can offer great insight into different fields:

- Sex and Gender Health Specific Learning Modules → Texas Tech University Health Sciences Center
- Mechanical Ventilation for COVID-19→ Harvard University
- IMG Roadmappers course→ Created by Dr. Nina Lum
- Chicovidsitters → volunteering to support frontline workers

Other ideas include reviewing for the next clinical rotation. Read a medicine-related book, or find a virtual annual specialty conference to attend.

11. Medical Podcasts

Medical students born in the age of technology now rely on podcasts and innovative ideas to receive updates and research. Medical podcasts allow for opportunities to listen and to learn while on the go. They offer interesting and informative perspectives for IMG candidates who may be living abroad. They are fun to listen to while in transition or while waiting for exam results. These podcasts provide yet another chance to hear from medical professionals in the absence of a formal mentor. Some examples include:

- Reconciling Medicine→ Dr. Renee Paro & Dr. John Paro
- As A Woman: Dr. Natalie Crawford
- The IMG Roadmap→ Dr. Nina Lum
- The Undifferentiated Medical Student Nutrition Rounds → Dr. Danielle Belardo
- Surviving Medicine→ Dr. Frank Cusimano
- More Than A Pretty Face→ Dr. Azideh Shirazi Curbsiders

12. Burn Out

Some of life's highs and lows can be expected and managed, but it can be easy for medical students to feel alone and helpless even more so during this pandemic. These emotions can be triggered by many factors, which can include: studying for hours a day, for weeks on end, and without achieving the desired results. It is common for medical students to be overcome by self-doubt and worry. Because of these shared experiences, IMGs need to know they can lean on friends, family and mentors. The support of a mentor and of the relationships can make all of the difference in the life of an IMG.

13. Recent Changes in Testing

The recent pandemic has brought on a series of new challenges for all medical students. Existing Certification requirements include the following:

1. Your medical school must be listed in the World Directory of Medical Schools
2. Completed ECFMG certification application
3. Completed/passed USMLE Step 1 and Step 2 CK
4. Completed/passed USMLE Step 2 CS (Temporarily not required; see adjusted requirements in place on their website)
Currently the Step 2 CSK has been replaced by the OET for IMGs.
5. Medical School Diploma with date of graduation

14. Social and Emotional Wellness

Finally, every university has a school counselor on board who can provide support for maintaining a healthy mindset and to have a measure of emotional support during these tough transitions. After all, there is so much at stake. Medical students are consistently reminded of the need to be empathetic, but it would not be surprising to find out that these students feel isolated and sometimes misunderstood. Medical students need empathy and sympathy also. They are embarking on one of the most noble professions. They are worthy of help and of mentorship wherever they can find it. Therefore, even when one person cannot provide all of that is required to support one medical student, everyone can find one small way to mentor and to support a future medical doctor who may be caring for a loved one in the near future.

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References

- American Academy of Pediatrics. (2020). Section on International Medical Graduates (SOIMG). Retrieved September 13, 2020, from <https://services.aap.org/en/community/aap-sections/international-medical-graduates/>
- American Medical Association. (2020). The AMA Residency & Fellowship Database. Retrieved September 13, 2020, from <https://freida.ama-assn.org/>.
- Bronson, D., & Ellison, E. (2015). Crafting successful training programs for physician leaders. *Healthcare*. doi:10.1016/j.hjdsi.2015.08.010
- Cervantes, L., Chu, E., Nogar, C., Burden, M., Fischer, S., Valtierra, C., & Albert, R. K. (2014). A Hospitalist mentoring program to sustain interest in healthcare careers in under-represented minority undergraduates. *Journal of Hospital Medicine*, 9(9), 586-589. doi:10.1002/jhm.2218
- Connor, M., Bynoe, A., Redfern, N., Pokora, J., & Clarke, J. (2000). Developing senior doctors as mentors: A form of continuing professional development. Report of an initiative to develop a network of senior doctors as mentors: 1994-99. *Medical Education*, 34(9), 747-753. doi:10.1046/j.1365-2923.2000.00630.x
- Cram Fighter. (2017, April 20). *Create Your Step 1 Study Plan with Cram Fighter* [Video]. Youtube. <https://www.youtube.com/watch?v=jr7MgcTQ1fg>
- Decastro, R., Sambuco, D., Ubel, P. A., Stewart, A., & Jagsi, R. (2013). Mentor Networks in Academic Medicine. *Academic Medicine*, 88(4), 488-496. doi:10.1097/acm.0b013e318285d302
- Dodge, R., Daly, A., Huyton, J., & Sanders, L. (2012). The challenge of defining wellbeing. *International Journal of Wellbeing*, 2(3), 222-235. doi:10.5502/ijw.v2i3.4
- Driessen, E. W., Overeem, K., & CPM Van Der Vleuten. (2011). Get yourself a mentor. *Medical Education*, 45(5), 438-439. doi:10.1111/j.1365-2923.2011.03948.x
- Edmodo. (2020, August 11). In *Wikipedia*. Retrieved September 13, 2020, from <https://en.wikipedia.org/wiki/Edmodo>
- Entezami, P., Franzblau, L. E., & Chung, K. C. (2011). Mentorship in Surgical Training: A Systematic Review. *Hand*, 7(1), 30-36. doi:10.1007/s11552-011-9379-8
- Erin Condren. (2020, April 29). *Inside the new 2020-2021 Life Planner Collection* [Video]. Youtube. https://www.youtube.com/watch?v=MIsPC_Anh-c&feature=emb_logo
- Fang, D., Moy, E., & Colburn, L. (2000). Racial and Ethnic Disparities in Faculty Promotion in Academic Medicine. *Jama*, 284(9), 1085-1092. doi:10.1001/jama.284.9.1085
- Frei, E., Stamm, M., & Buddeberg-Fischer, B. (2010). Mentoring programs for medical students - a review of the PubMed literature 2000 - 2008. *BMC Medical Education*, 10(1), 1-14. doi:10.1186/1472-6920-10-32
- Garmel, G. M. (2004). Mentoring Medical Students in Academic Emergency Medicine. *Academic Emergency Medicine*, 11(12), 1351-1357. doi:10.1197/j.aem.2004.06.013
- International medical graduate. (2020, June 21). In *Wikipedia*. Retrieved September 13, 2020, from https://en.wikipedia.org/wiki/International_medical_graduate
- Kalén, S., Stenfors-Hayes, T., Hylin, U., Larm, M. F., Hindbeck, H., & Ponzer, S. (2010). Mentoring medical students during clinical courses: A way to enhance professional development. *Medical Teacher*, 32(8), E315-E321. doi:10.3109/01421591003695295
- Kram, K. E. (1983). Phases of the Mentor Relationship. *Academy of Management Journal*, 26(4), 608-625. doi:10.2307/255910
- Kram, K. E. (1985). *Mentoring at work development relationships in organizational life*. Glenview, IL: Scott, Foresman and.
- Kramer, M. (1975). REALITY SHOCK: Why Nurses Leave Nursing. *AJN, American Journal of Nursing*, 75(5), 891. doi:10.1097/00000446-197505000-00041
- Megginson, D., Cluerbuck, D., Gravey, B., Stokes, P., & Garret-Harris, R. (2006). *Mentoring in action: A practical guide* (2nd ed.). London: Kogan Page.
- Overeem, K., Driessen, E. W., Arah, O. A., Lombarts, K. J., Wollersheim, H. C., & Grol, R. P. (2010). Peer mentoring in doctor performance assessment: Strategies, obstacles and benefits. *Medical Education*, 44(2), 140-147. doi:10.1111/j.1365-2923.2009.03580.x
- Parise, M. R., & Forret, M. L. (2008). Formal mentoring programs: The relationship of program design and support to mentors' perceptions of benefits and costs. *Journal of Vocational Behavior*, 72(2), 225-240. doi:10.1016/j.jvb.2007.10.011
- Pisani, M., (2018, October 12). Women in Medicine Struggle with Mentorship and Sponsorship. [Blog Post]. Retrieved from https://opmed.doximity.com/articles/women-in-medicine-struggle-with-mentorship-and-sponsorship?csrf_attempted=yes
- Rhodes, J. E. (2002). *Stand by Me: The Risks and Rewards of Mentoring Today's Youth*. Cambridge, MA: Harvard University Press. doi:10.2307/j.ctvjz8142
- Sandberg, S., & Scovell, N. (2013). *Lean In: Women, Work, and the Will to Lead*. New York, NY: Knopf.

- Stamm, M., & Buddeberg-Fischer, B. (2011). The impact of mentoring during postgraduate training on doctors' career success. *Medical Education*, 45(5), 488-496. doi:10.1111/j.1365-2923.2010.03857.x
- Steven, A. (2008). *Mentoring Schemes for Psychiatrists in the North East: An Evaluation and Exploration* (Rep.). University of Newcastle Upon Tyne.
- Steven, A., Oxley, J., & Fleming, W. (2008). Mentoring for NHS doctors: Perceived benefits across the personal–professional interface. *Journal of the Royal Society of Medicine*, 101(11), 552-557. doi:10.1258/jrsm.2008.080153
- Swensen, S. J., & Shanafelt, T. (2017). An Organizational Framework to Reduce Professional Burnout and Bring Back Joy in Practice. *The Joint Commission Journal on Quality and Patient Safety*, 43(6), 308-313. doi:10.1016/j.jcjq.2017.01.007
- Thomas, D. A. (2001, April). The Truth about Mentoring Minorities: Race Matters. *Harvard Business Review*, 99-107.
- Vygotsky, L. S. (1978). *Mind in society: The development of higher psychological processes*. Cambridge, MA: Harvard University Press.
- Wanberg, C. R., Welsh, E. T., & Hezlett, S. A. (2003). Mentoring Research: A Review And Dynamic Process Model. *Research in Personnel and Human Resources Management*, 22, 39-124. doi:10.1016/s0742-7301(03)22002-8
- Wilson, G., Larkin, V., Redfern, N., Stewart, J., & Steven, A. (2017). Exploring the relationship between mentoring and doctors' health and wellbeing: A narrative review. *Journal of the Royal Society of Medicine*, 110(5), 188-197. doi:10.1177/0141076817700848



Health Conditions of Landfills Workers, Lagos State, Nigeria

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Abstract

This study investigated health conditions of landfills workers in Lagos State, Nigeria. The adverse effects of different management practices particularly from landfills are enormous with such concerns on health conditions of workers prompted the interest of this paper. The objective was to identify the causative agents associated with diseases occurring amongst landfill workers and to evaluate its potential health issues including psychological effects, diseases, and accidents of solid waste on humans while also identifying types of sicknesses amongst workers at Landfill Sites in Lagos State. The research design adopted was a survey descriptive method. Convenience sampling technique was employed to select 336 respondents using questionnaire which was structured on a 2-6-point Likert Scale. The Cronbach's alpha reliability coefficients for the constructs ranged between 0.727 and 0.930. The response rate was 75.5% and data were analyzed using descriptive and inferential statistics. Data gathered were analyzed with the aid of Statistical Package for the Social Sciences (SPSS) via Pearson Product Moment Correlation (PPMC). The result obtained indicate a significant and positive relationship between causative agents associated with diseases and landfill workers in Lagos State. Results also showed a positive correlation between potential health effects and landfill workers in Lagos State. It further showed that the levels of heavy metals in the soil were within acceptable limit relative to World Health Organization's standard. It is also noted that people living and doing business in the landfill were at risk from diseases. Microbial organisms such as *E. coli*, *Salmonella* Sp, *Klebsiella* Sp, *Staphylococcus aureus* and *Pseudomonas* Sp were also isolated. Provision of solid waste workers with Personal Protective Equipment (PPE), restriction of access to landfill sites, and review of existing laws to ensure compliance are strongly recommended.

Keywords: Health Conditions, Landfill Workers, Causative Agents, Solid Waste, Sickness/Disease

Introduction

The issue of health conditions of landfill workers is one that has been discussed by many authors and scholars with various perspectives on the subject, most coming at it from different sides than the others (Grant, 2013; Niekerk & Wegmann, 2019, Ojelowo & Wahab 2017). Health conditions of landfill workers are therefore a cause for concern globally. This concern is linked with man's struggling to meet his basic needs as the essence of existence

and development of human society (Singh, Chokhandre, Salve, & Rajak, 2020). To satisfy these needs, man exploits the natural environment in many ways, such as (i) agriculture, (ii) industrialization, (iii) energy generation, etc., and these have severe impact on the environment resulting in environmental degradation and attendant health effect on man.

Human population has increased significantly; this has led to tremendous generation of solid waste (International Labour Organization [ILO], 2019; Isemekhai, 2016). In developed countries, the amount of waste generated is very high compared to developing countries while the developed countries have better and efficient management systems, which may be resulted from awareness, enlightenment, more money, good legislature and technology to manage their wastes. However, developing countries does not have such capacity (Rotich, Zhao & Dong, 2005). The generation of waste, its collection, processing, transportation and disposal is of great importance for public health and environmental reasons. Waste is anything discarded by an individual, household or organization. Waste has no economic or physical value to the generator. As a result, waste is a complex mixture of different substances for example: plastic, metals, papers, food items, etc., (Oyeniyi, 2011). Landfill is a method of solid waste disposal and generally known for its common features for being exposed directly to the atmosphere or covered improperly with solid layer and without proper bottom line support (United Nations, 2014).

In Lagos State, the dumpsites are commonly used as disposal option to manage solid waste for long time. At the initial time of locating dumpsite in the Lagos metropolis, they were located far from residential areas, but due to accelerated population, urbanization and industrialization, people now live and work in landfill's vicinity. The open dumpsites are sources of environmental pollution and public health concern. The Lagos State since 1961 set up the Lagos State Waste Disposal Board, which it changed to the Lagos State Waste Management Authority (LAWMA) in 1992. It is observed that the waste disposal board suffered inefficiency, mal-administration, lack of funds and ineffective implementation of government policies.

Creating a better environment should not be left in the hands of the government alone. Communities should be involved in the process of formulation and implementation of proposals and policies of the physical development of their areas. This process involves the mobilization of both men and material resources to improve the quality of their environment. This process is described by Oyesiku (1998) as an active process, in which the person in question takes part in the contribution and implementation of decisions for the fact that the government alone cannot provide the needs of the people.

LAWMA is responsible to collect and manage solid waste from individual residents. The authority has designated staff to handle the waste management activities. Waste management therefore is the organized and systematic channeling of waste through pathways to ensure that they are disposed of with attention to acceptable public health and environmental safeguards (Niekerk & Wegmann, 2019; Oyeniyi, 2011). However, proper management cannot be achieved without a well-designed waste management plan.

Landfill is also prone to the activities of scavengers. Interestingly, an open landfill attracts flies, vermin and other insects that serve as disease vectors that considerably affect people's health. Individuals who stay close to the landfill vicinity especially waste workers, scavengers who often come in contact with dumped waste are prone to develop health disorders (Ojelowo & Wahab, 2017).

For individuals to live in an environment that is void of pollutant, that will cause health problems such as diarrhea, dysentery, pneumonia, eye irritation, malaria, cholera etc. we have to efficiently manage the waste generated in our environment. There is need for the environment to be healthy if we need a healthy population. Environmental health may be defined as the provision and control of all those factors in people's physical water supply, efficient and effective sanitary waste disposal, access to good housing; food hygiene, vector control and personal hygiene are necessary for a healthy environment. The immediate environment where people live and work, greatly affects their health (Environmental and Social Safeguards Audit, 2015). This study therefore examined health conditions of landfills workers, Lagos State, Nigeria.

Statement of the Problem

The amount of waste generated is in an increasing trend with time due to urbanization, industrialization and increase population. Population residing and particularly those working within the landfills are exposed to environmental health risks (Singh, *et al.*, 2020). This is due to emission of toxic gases and air pollutants (landfill gas containing methane, carbon dioxide, hydrogen sulphide and other contaminants including volatile organic compounds bioaerosols and particulate matter) or to contaminated soil and water (Singh, *et al.*, 2020). Across the cities, it is the urban poor that suffer most from the life-threatening conditions stemming from deficient solid waste management (Schenck, Blaauw, Viljoen, & Swart, 2019).

Wastes are disposed of to prevent or control hazardous consequences on the human environment. However, landfill workers are constantly in contact with waste from various collection points. These workers are therefore constantly at risk of contracting disease agents or pathogens. There is need to determine and know the health and environmental problems associated with solid waste management.

Nonetheless, quite a lot of studies have been carried out on the concept of “waste or its management”, for instance, Niekerk and Wegmann (2019), Ojolowo and Wahab (2017), Cole (2015), Oyeniyi (2011) and World Health Organization (2011) and etc. However, not much has been written on the issues relating to “and health conditions” (Singh, *et al.*, 20-2020; Ezirim & Agbo, 2018, Martine, 2010). In the same vein, extant literatures on landfill workers include Fielder, Poon, Palmer and Coleman, (2000), Longe and Balogun (2010) and Eludoyin and Oyeku (2010) etc. Notwithstanding, the findings of these scholars, and the problem associated with the subject matter areas has not been concretely addressed. This has created a gap-in-knowledge which this study intends to fill.

Objectives of the Study

The primary aim of this paper is to investigate health conditions of landfill workers in Lagos State, Nigeria. Other specific objectives include:

- (i) To investigate the causative agents associated with diseases occurring among landfill workers in Lagos State;
- (ii) Identify the types of sicknesses among landfill workers using soil and leachate samples.
- (iii) To evaluate the potential health issues on landfill workers in Lagos State.

Research Hypotheses

This paper tested the following null hypotheses.

- H₀₁:** There is no significant relationship between causative agents associated with diseases and landfill workers in Lagos State.
- H₀₂:** Soil and leachates samples do not determine types of sicknesses affecting workers at landfill site located at Isheri-LASU Road in Ikotun-Igando, Lagos State.
- H₀₃:** There is no significant relationship between potential health effects on landfill workers in Lagos State.

Literature Review

An extensive literature review is herein conducted to determine the status of academic thought on the subject-matter areas that are considered to be critical to this study. The review processes and corresponding findings are then reported and presented with regards to causative agents associated with diseases occurring among landfill workers; the potential health effects on landfill workers and types of sicknesses among landfill workers using soil samples.

The causative agents associated with diseases among landfill workers usually refers to the biological pathogen that also causes a disease including parasite, virus, fungus as well as bacterium (Wikipedia, 2020). This could also be described as a toxin or otherwise known as toxic chemical which causes illness. According to International Labour Organization (2019), the negative impacts of toxins found in waste are not just limited to workers, but can also

have detrimental impacts on human health in general (ILO, 2019). Humans are exposed via ingestion, inhalation or dermal contact. Workers working in the waste management sector are a particularly vulnerable group, as they are prone to absorbing toxic substances rapidly adults. The concentration of copper, lead, zinc and tin is almost higher in places like major markets in Lagos (including Oshodi market, Balogun market, Alaba International market amongst others) when compared to typical background levels. Since their bodies are still developing, some people are much more vulnerable to health risks and irreversible damage from exposure to hazardous materials. Some individuals' hand-to-mouth behaviour puts them at high risk in areas with soil and dust contaminated with lead. Exposure to lead could cause intellectual impairment (Osibanjo, 2015).

Waste generally poses a threat not just to workers involved in the waste value chain, but also to individuals living in cities very close to the landfill areas including Igando-Solous sites. A comparative study on the environmental and health impacts of waste in China and Nigeria observed significant DNA damage to populations that were exposed to the processing of waste (Alabi, 2012; Environmental Justice Atlas, 2017).

Specific health outcomes that have been examined in epidemiological studies of the health effects of landfill sites include as submitted by (a) congenital malformations, (b) birth weight, prematurity and child growth, (c) cancers, (d) symptoms of illness (Staines, Crowley, Bruen, & O'Connor, 2019). Most of the studies on human health close to landfill sites have used a very non-specific model of exposure. Usually proximity to the site has been used as a proxy for exposure, presumably working on a model of simple radial diffusion of unspecified contaminants from the site.

As the likely routes of exposure are more structured than this, such studies have fundamental weaknesses. There must be an exposure pathway from a source in order for an agent released into the environment to ultimately effect human health (Ezirim & Agbo, 2018). The potential exposure pathways are water, air, soil and locally produced food and so exposures to the local population could be ingestion, inhalation or through the skin (trans-dermal) (Zheng & Wang, 1999). Some exposure of the wider population might occur through eating food produced near the landfill site. A description of exposure for a particular route should include the concentration, and the duration of contact. For example, landfill leachate might enter local groundwater and surface water but people are only exposed if the waters are used for drinking, producing or preparing food or for recreational purposes.

Landfill operations, especially those of poorly run sites, can lead to the emission of unpleasant odours. The health effects of this do not seem to be well established. In the literature, odour for instance is commonly referred to as a 'nuisance', with the implication that it is not a serious issue, and hence, not a priority for betterment (Ogungbuyi, 2016). Noise from traffic from site operations is another potential health issue. A great deal of published work on airport noise exists, but like odour, this issue has not been well explored in the waste management and health literature. Emissions from landfills do not always lead to human exposure. Exposure can only arise if individuals come into contact with the harmful agents in emissions. Contact can be by breathing, skin contact or eating or drinking food or water contaminated with the substance. If there is no contact there can be no toxicity.

Landfill sites contain many different potentially toxic substances. Potential and actual hazardous emissions from these sites have caused concern to both local populations and regulatory bodies. This has resulted in numerous studies examining different potential adverse effects. These studies indicate that residence near certain specific sites is associated with risks to health.

Although a great number of studies have been carried out, evidence of a causal relationship between specific health outcomes and landfill exposures is still inconclusive. Methodological difficulties make determination of cause and effect very difficult. Difficulties in assessing and categorising exposure, and difficulties in controlling for other confounding factors, limit the ability of such studies to detect these adverse effects.

Many studies of symptoms conducted in communities living near landfill sites rely on self-reported symptoms. The knowledge of and concern about possible exposure to hazards present in the landfill may introduce some bias into the results of these studies. When compared to populations living further away from such sites, individuals in proximity to landfills may be more likely to recall minor complaints and symptoms, which they may attribute to landfill exposures.

Currently, there is unsatisfactory evidence to demonstrate a clear link between potential health effect, for example in the form of cancer and exposure to landfill. Excesses of bladder, lung, leukemia and stomach cancer have been reported in some studies and not in others (Schenck, Blaauw, Viljoen & Swart, 2019). The association between adverse birth outcomes such as low birth weight and birth defects is more compelling, but as yet cannot be described as causal. Further studies are required. In particular, examination of specific types of defects, which may be related to exposure to specific environmental agents may serve to clarify these questions (Staines, *et al.*, 2019). Reports of increased risk of respiratory, skin and gastrointestinal illnesses are based mainly on self-reported symptoms. Although this evidence must not be dismissed, consideration should be given to the strong possibility of bias and the influence of fears and worry related to the waste sites.

Much of the existing work relates to older landfills, which would have been managed poorly by modern standards, or specifically to hazardous waste landfills. It seems likely that the health effects of workers at landfills, run in strict accordance with standard operating procedures (Kumar, Bathma, Dixit & Parashau, 2020).

Materials and Methods

The paper employed the use of descriptive survey design to investigate health conditions of landfill workers, Lagos State, Nigeria. The study was conducted using Solus 2 and 3 in Lagos State. The landfill was opened by Lagos State Government to receive wastes from Alimosho and its environs. The site is located at Isheri-Lasu Road in Ikotun-Igando Local Government Development Area with a size of about 10.2 hectares. It lies approximately between longitude 3°13'30" E to 3°17'15" E and Latitude 6°28'N to 6°42'N.

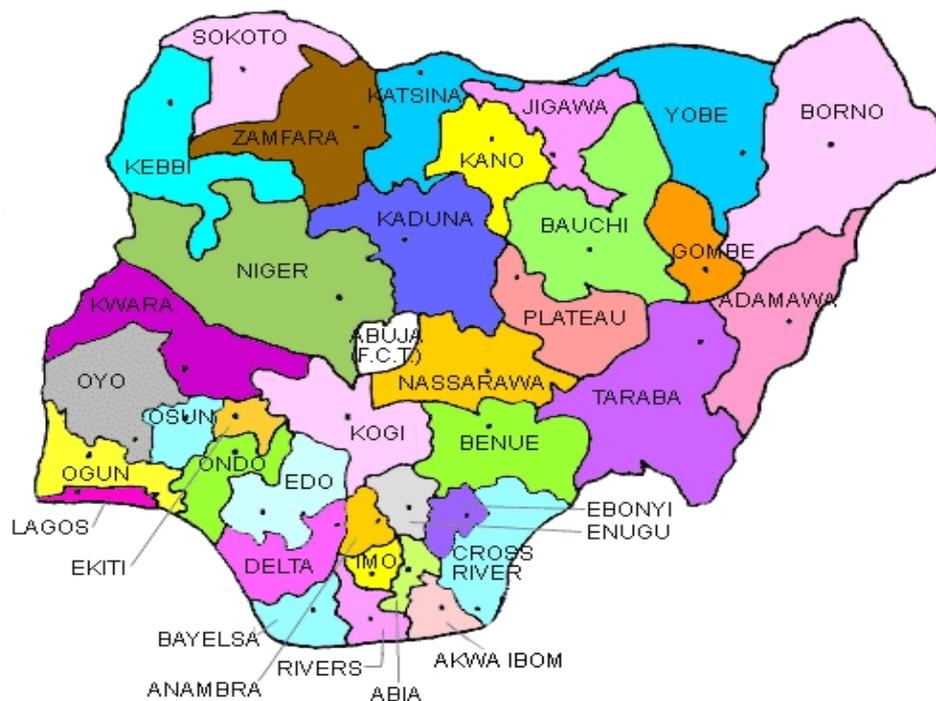


Figure 1: Map of Nigeria showing Lagos State and other States.



Figure 2: Map of Lagos State

The population of the study comprised of all landfill workers at Igando, Lagos State. These categories were targeted because they are in the best position to provide the required information on causative agents associated with diseases, prevention and controlling of diseases and accidents relating to landfill workers amongst others. Convenience sampling technique was used to select 336 out of 445 participants for the study based on availability, accessibility, convenience and willingness.

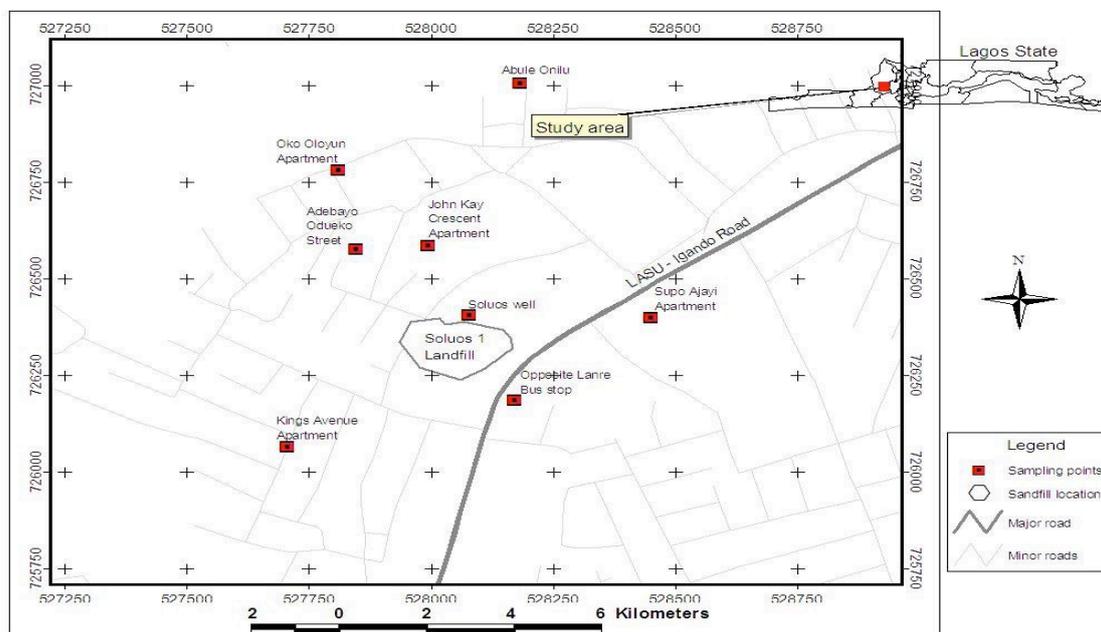


Figure 3: Map showing study area

The study was carried out by using both questionnaires and laboratory analysis of leachates and soil samples collected from the study landfill. The questionnaire was to obtain demographic and health information regarding landfill workers at the study site. The research instrument with the name “Health Condition and Landfill Workers Questionnaire” (HECOLAWQ) has three sections. Section A (personal information) has five items (including sex, position at work, age category, marital status, and level of education) and was used to collect general information about the participants’ demographic data. Section “B” has fourteen items, intended to elicit information on issues relating to health condition of landfill workers, while Section “C” requested the provision of any other related information that the respondents perceive to be relevant and useful on the subject. The items were structured on a 2-6-point Likert rating scale with response options. The instrument was subjected to face and content validity by

experts in Environmental Biology, Environment and Science Education, and Waste Management. They were to examine the instrument items for clarity and suitability for use in collecting data for the study. Observations and suggestions of these experts improved the instrument. The reliability test of the instrument was administered on 30 participants. Cronbach Alpha at 0.05 level of significance was computed for testing the internal reliability from the responses using Statistical Package for the Social Sciences (SPSS) and the reliability coefficient was 0.886 indicating that the instrument was reliable for the study. The result from the two tests showed some similarities thus attesting reliability of the instrument for this study. The instrument was administered during the visits to study areas, and 336 copies were retrieved from the initial 445 over a period of three weeks. This represented 75.5% return rate and were all found useful.

Also, soil samples were collected at two different locations in Solous 2 and 3 respectively. The soil samples were collected at 15cm deep with soil auger. The samples were labeled as follows: (a) Solous 2: S1 and S2; (b) Solous 3: S3 and S4.

Each sample was collected at 50m interval. The soil samples were sieved through 2mm sieve to remove stones and other coarse particles. 2g of the sieved soil was transferred to a conical flask of 100ml capacity and 20ml of conc. Hcl together with 20ml of conc. HNO₃ was added. The solution was heated at 120°C for 30 minutes. The solution was cooled to room temperature and diluted with deionized water to fill the flask. After settling overnight, samples were filtered through the Ashless filter paper into a 50ml volumetric flask. The digested sample was then analyzed for heavy metal by a flame type Atomic Absorption Spectrometer (AAS) model series (711047). This analysis was carried out with Lagos State Environment Protection Agency (LASEPA).

Leachate Samples: Leachate samples from 3 different locations in Solous 2 and 3 different locations in Solous 3, at a distance of 50 Metres apart were collected in a sterile bottle and taken to the laboratory. The samples were collected under sterile condition so as to minimize the possibility of introducing secondary bacteria contamination. The samples were labeled as follows:

Solous 2: First Extreme (E1), Second Extreme (E2). First Centre (C1).
Solous 3: Third Extreme (E3), Fourth Extreme (E4). Second Centre (C2).

The Leachate samples were flooded on MacConkey agar plate; duplicate of each plate was made. The plates were incubated at 37°C for 24 hours to 48 hours depending on the bacteria growth. Bacteria colonies were noted on different media and subcultures several times and a pure culture was obtained. Morphological and biological test for bacteria isolate were carried out to obtain the desired results.

Results

After careful and systematic analysis of the respondents' responses to the baseline research objectives, the following analyses are further carried out for the specific testing of the formulated research hypotheses and laboratory analysis. Pearson Correlation was used to test the first two hypotheses, while laboratory analysis was used to test the third hypothesis.

Hypothesis One:

H₀₁: There is no significant relationship between causative agents associated with diseases and landfill workers in Lagos State.

Table 1: Correlation analysis showing significant relationship between causative agents associated with diseases and landfill workers in Lagos State.

		Causative agents associated with diseases	Landfill workers in Lagos State
Causative agents associated with diseases	Pearson Correlation	1	.820**
	Sig. (2-tailed)		.000
	N	336	336
Landfill workers in Lagos State	Pearson Correlation	.820**	1
	Sig. (2-tailed)	.000	
	N	336	336

** . Correlation is significant at the 0.01 level (2-tailed).

Source: Computer SPSS version 23.0 Output, Field Survey, 2020.

From the Table 1 above, the Pearson correlation coefficient between the independent variable and dependent variable is 0.820, indicating a significant positive relationship between causative agents associated with diseases and landfill workers in Lagos State. Therefore, we reject the null hypothesis and accept the alternate hypothesis.

Hypothesis Two:

H0₂: Soil and leachate samples do not determine types of sicknesses affecting workers at landfill site located at Isheri-LASU Road in Ikotun-Igando, Lagos State.

The study shows that 5 microbial organisms were isolated from different Leachate samples collected in different locations within the study site. These microbial organisms are:

E Coli, Salmonella Sp, Klebsiella Sp, Staphylococcus Gurena and Pseudomona Sp. Among the organisms isolated, E coli had the highest occurrence (35.3%) while staphylococcus aureus and salmonella sp had the lowest occurrence of 11.8% each. The detail of this occurrence is presented in table 2i.

Table 2i: The Occurrence of Bacteria isolated from the Leachate

Bacteria Isolate	E1	E2	E3	E4	C1	C2	No. of Isolate	Percentage Occurrence
E. coli	+	+	+	+	+	+	6	35.3%
Salmonella sp	-	+	-	+	-	-	2	11.8%
Klebsiella sp	-	-	+	+	+	-	3	17.6%
Staphylococcus aureus	+	+	-	-	-	-	2	11.8%
Pseudomonas sp	+	+	+	-	-	+	4	23.5%

E₁ E₂ and C₁ leachate samples from Solous 2

E₃ E₄ and C₁ leachate samples from Solous 3

Table 2ii: Soil Analysis for Heavy/Trace Metals Associated with study site

Trace/Heavy Metals	S1	S2	S3	S4	WHO Standard
Zinc	0.0654	0.2619	0.0313	0.4174	<1
Iron	3.8185	4.0265	4.1286	4.4391	5mg/kg
Lead	0.0464	0.8017	0.0364	0.3339	5.0mg/kg
Chromium	0.0332	0.0494	0.0418	0.0590	5.0mg/kg
Potassium	0.3609		0.0674	0.8514	725mg

S1, S2 soil samples collected from Solous 2

S3, S4 soil samples collected from Solous 3

Hypothesis Three:

H₀₃: *There is no significant relationship between potential health issues and landfill workers in Lagos State.*

Table 3: Correlation analysis showing significant relationship between potential health issues and landfill workers in Lagos State.

		Potential health issues (psychological effects, diseases, accidents in terms of solid waste)	landfill workers in Lagos State
Potential health effects (psychological effects, diseases, accidents in terms of solid waste)	Pearson Correlation Sig. (2-tailed)	1	.819** .000
	N	336	336
Landfill workers in Lagos State	Pearson Correlation Sig. (2-tailed)	.819** .000	1
	N	336	336

** . Correlation is significant at the 0.01 level (2-tailed).

Source: Computer SPSS Version 23.0 Output, Field Survey, 2020.

From the Table 3 above, the Pearson correlation coefficient between health problems and productivity loss is 0.819, indicating a positive and strong correlation between potential health effects (psychological effects, diseases, accidents in terms of solid waste) and landfill workers in Lagos State. Therefore, we reject the null hypothesis and accept the alternate hypothesis.

Discussion of Findings

Overall, the following findings were made through this study:

There was a significant positive relationship between causative agents associated with diseases and landfill workers in Lagos State. This finding is supported with the submission of Ojolowo and Wahab (2017). The author is prone to the activities of scavengers. Interestingly, an open landfill attracts flies, vermin and other insects that serve as disease vectors that considerably affect people's health. Individuals who stay close to the landfill vicinity especially waste workers, scavengers who often come in contact with dumped waste are prone to develop health disorders.

Microbial infection is very common among people working in and around landfill sites. The high symptoms of disease expressed from the results shows that waste workers are highly prone to microbial infection. Symptoms such as diarrhea, headache, dizziness, fever, coughing and eye irritation are suggestive of pathogens. These symptoms correlate with the microbial organisms isolated, as recorded. For example: E. coli, pseudomonas, salmonella, spp, etc. This finding is in line with Eber (2000). In comparing the incidences of disease symptoms among waste workers and the incidence of disease symptoms among waste workers family. It is also suggestive that there could be link of disease transmission from the waste workers to their family members. It is also of great importance that waste workers are prone to various degrees of injuries. From this finding, it shows that waste workers are more prone to cuts due to injuries from glass, sharp objects such as metals, syringe, blade, scalpels; these could also create health hazard to waste workers, this find is in line with Ajadike (2001). The work of waste collectors involved considerable heave lifting as well as other normal handling of containers, increasing the risk of muscular skeletal problems such as sprain, dislocation and fracture, this is in tandem with Gustavsson (1989).

The soil analysis was carried out in order to determine the extent of contamination from the landfill, and verily, the associated hazardous substance such as heavy metals that could cause health and environmental problems to the waste workers. The quantity of trace/hazardous elements in Solous 2 and 3 are very close. When compared to standard, it is clear that the amount of trace elements in both landfills is within acceptable limit. The low level of hazardousness of the soil sample could also imply that the solid waste deposited on this landfill were not hazardous waste, this could be further subjected to future academic research. The low amount of hazardousness could also be traceable to leaching. The adverse potential impact of these heavy metal on the waste workers may be noticeable in the nearest future due to environmental persistence, bioaccumulation as reported by the U.S. Department for health and human services (1995).

It is also of importance that perception to wearing of protective gadgets is very low, 20.8% of the waste workers questioned uses one out of four protective equipment's. This could be attributed to low education or inability of employers to provide this equipment for them. The low usage of protective equipment by the waste workers agrees with Ajadike's assertion that the risk to solid waste workers in low income countries like Nigeria are expected to be much higher because workers protection is not required (Ajadike, 2001). Those that spend more time on the landfill are more prone to infection such as waste workers and scavengers.

There is was positive and strong correlation between potential health issues and landfill workers in Lagos State. No wonder existing literature is linked with man's struggling to meet his basic needs as the essence of existence and development of human society (Singh, Chokhandre, Salve, & Rajak, 2020). To satisfy these needs, man exploits the natural environment in many ways, such as (i) agriculture, (ii) industrialization, (iii) energy generation, etc., and these have severe impact on the environment resulting in environmental degradation and attendant health effect on man.

Conclusion

The purpose of this study was to investigate and present results relating to health conditions of landfill workers in Lagos State, Nigeria. In line with the statistical results obtained, it was concluded that a significant and positive relationship exist between causative agents associated with diseases and landfill workers in Lagos State. Results also showed a positive correlation between potential health issues and landfill workers in Lagos State, while leachate samples did determine types of bacteria affecting workers at landfill site in Lagos State. However, the levels of heavy metals in the soil were within acceptable limit relative to World Health Organization's standard.

There is need for the environment to be healthy and conducive if we need a healthy population. Human activities have had severe negative impact on the environment. Waste management involves the collection, transportation, storage, treatment of waste and the efficient management options of the final disposal sites; this has to take into consideration, activities that will minimize the health, environmental and aesthetic impact of solid waste. People working and doing businesses in the landfill sites are at great risk of contracting microbial organisms. Other negative health outcome such as cancers, infertility, etc. that results from trace elements would not be expected to occur until several years after exposure. It is therefore, clear that improved solid waste collection and disposal options would decrease the population exposed to risk.

Recommendations

Based on the finding of the study, the following recommendations were made:

- i. Educating and training on occupational and environmental health issues associated with solid waste management is key to safety of waste workers. Such training provision should include operational procedures for safe waste handling, accident response procedures, first aid and emergency evacuation procedures, hazardous material release response, fire control, self-hygienic tips, and emergency call numbers.
- ii. There is need of strict monitoring and control of hazardous waste coming to the landfill. Regular monitoring of the level of hazardous substances such as heavy metals should be done annually. This is important, in the sense that it will reduce and maintain the level of hazardous substances that would generate into environmental and health problems.

- iii. Vaccination of solid waste workers for hepatitis A and B, tetanus, diphtheria, polio, typhoid and rabies. A good medical surveillance, standard including baseline and follow-up medical examination. Routine survey of workers about job task performed and their physiological responses to their job task. Provision of clean drinking water and sanitation facilities. (a) Provision of solid waste workers with protective equipment: Protective equipment such as protective clothing, shoes/boots, gloves, eye glasses and helmets. This protective equipment will reduce the incidence of injuries and accidents also created with solid waste management; (b) Provision of data base of solid waste workers: This takes into consideration of record-keeping on incidents of diseases, injuries and death. It also includes the record keeping of personal data of waste workers; (c) Restriction of access to landfill sites: Such that only safety-trained personnel with protective gears are permitted. Animals, such as dogs, goats, pigs, rats, etc. should be restricted and controlled from getting into the landfills. This will reduce the incident of disease transmission; (d) Enabling Laws: The government should review and strengthen existing laws and regulations for efficient solid waste management and ensure strict compliance.

References

- Ajadike J. C. (2001). Urban solid waste: problems and management in Nigeria. In Ofomata, G. E. K. & Phil-Eze P. O. (Eds.) *Geographical perspectives on environmental problems and management in Nigeria*. Nigeria: James Ent. Pp.134-181.
- Alabi, O. A. (2012). Comparative evaluation of environmental contamination and DNA damage induced by electronic-waste in Nigeria and China. *Science of the Total Environment*, 423(6), 62-72.
- Cole, E. C. (2015). *Internal medical waste management*. Durham, North Carolina: Thompson Press.
- Ebere, N. (2000). Democratizing the planning process in Nigeria through public participation, a challenge to town planners in the 21st century. *Journal of the Nigeria Institute of Town Planners*, XIII (2), 1-11.
- Eludoyin, A. O. & Oyeku, O. T. (2010). Heavy metal contamination of groundwater 445 resources in a Nigerian urban settlement. *African Journal of Environmental 446 Science and Technology*, 4(4), 201-214.
- Environmental and Social Safeguards Audit (2015). *Environmental and social safeguards audit*. Abuja, Nigeria: National Agency for the Control of AIDS (NACA). Retrieved 30th March, 2020 from: <http://documents.worldbank.org/curated/en/>.
- Environmental Justice Atlas, (2017). *E-waste in Lagos, Nigeria*. Retrieved 30th March 2020 from: <https://www.ejatlus.org/conflict/e-waste>.
- Ezirim, I. & Agbo, F. (2018). Role of national policy in improving health care waste management in Nigeria. *Journal of Health & Pollution*, 8(19), 1-8.
- Fielder, H. M. P., Poon, K. C., Palmer, S. R., & Coleman, G. (2000). Assessment of the impact on health of residents living near the Nanty-Gwyddon Landfill site. *Journal of Environmental Management*, 8(3), 19-23.
- Grant, K. (2013). Health consequences of exposure to e-waste: A systematic review” in *Lancet Global Health*, 1(1), 350-361.
- Gustavsson P. (1989). Mortality among workers at a municipal waste incinerator. *American Journal of Industrial Medicine*, 15(2), 2002-2009.
- International Labour Organization [ILO], (2019). *From waste to jobs: Decent work challenges and opportunities in the management of e-waste in Nigeria*, International Labour Office, Sectoral Policies Department. Geneva: ILO.
- Isemekhai, K. A. (2016). *Environmental risk assessment for an informal e-waste recycling site in Lagos state, Nigeria*. Middlesex: Middlesex University.
- Kumar, S., Bathma, V., Dixit, A. K. & Parashau, L. (2020). Assessment of respiratory health of landfill workers and its correlation with their knowledge and use of personal protective equipment's. *National Journal of Community Medicine*, 11(1), 53-56.
- Longe, E. O. & Balogun, M. R. (2010). Groundwater quality assessment near a municipal landfill, Lagos, Nigeria. *Research Journal of Applied Sciences, Engineering and Technology*, 2(1), 39-44.
- Martine, V. (2010). Health effects of residence near hazardous waste landfill sites: A Review of Epidemiologic Literature. *Environmental Health Perspective*, 1(8), 101-463.
- Niekerk, S. & Wegmann, V. (2019). Municipal solid waste management services in Africa. *Working Paper*.
- Ogunbunyi, O. (2016). *E-waste country assessment Nigeria; e-Waste Africa project of the Secretariat of the Basel Convention*. The Secretariat of the Basel Convention and the Swiss Federal Laboratories for Materials Science and Technology - Empa. Retrieved 12th March, 2020 from: <http://www.basel.int/Portals/>.
- Ojolowo, S. & Wahab, B. (2017). *Municipal solid waste and flooding in Lagos metropolis, Nigeria: Deconstructing the evil nexus*. Retrieved 23rd March, 2020 from: <http://www.academicjournals.org/journal/JGRP/article-full-text>.

- Osibanjo, O. (2015). *Gender and e-waste management in Africa*. Nigeria: Basel Convention Coordinating Centre for the African Region.
- Oyeniya, B. A. (2011). Waste management in contemporary: The Abuja example. *International Journal of Politics and Goods Governance*, 2(2.2), 1-18.
- Oyesiku, R. (1998). *Citizen participation in environmental planning and management, in Nigeria*. Lagos: Pumark Publishers.
- Rotich, K. H., Zhao, Y., & Dong, T. (2005) *Municipal solid waste management challenges in developing countries*. China: College of Environment and Resources, Jilin University, China.
- Schenck, C. J., Blaauw, P. F., Viljoen, J. M. M. & Swart, E. C. (2019). Exploring the potential health risks faced by waste pickers on landfills in South Africa: A socio-ecological perspective. *International Journal of Environmental Research and Public Health*, 6(2), 818-822.
- Singh, S. K., Chokhandre, P., Salve, P. S. & Rajak, R. (2020). Open dumping site and health risks to proximate communities in Mumbai, India: A cross-sectional case-comparison study. *Clinical Epidemiology and Global Health*. Retrieved 11th February, 2020 from <https://doi.org/10.1016/j.cegh.2020.06.008>.
- Staines, A., Crowley, D., Bruen, M. & O'Connor, P. (2019). *Public health and landfill sites*. Dublin: Department of Public Health and Epidemiology.
- U.S. Department for Health and Human Services (1995).
- United Nations (2011). *United Nations University/ step initiative, 2011. One Global Definition of E-waste*. (Bonn, Solving the E-Waste problem White Paper).
- Wikipedia (2020). *Disease causative agent*. The Free Encyclopedia. Retrieved 30th March 2020 from www.google.org.
- World Health Organization. (2011). *Basic steps in the preparation of health care and waste management plans for health care establishments*. Geneva/Switzerland: WHO.
- Zheng, C. & Wang, P. (1999). *A modular three-dimensional multi-species transport model for simulation of advection, dispersion and chemical reactions of contaminants in groundwater systems: documentation and user's guide*. Vicksburg, Missouri, US Army Engineer Research and Development Center: p. 202.



Massage Using Frangipani Aromatherapy Oil to Speed up The Duration of Childbirth

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Abstract

Excessive anxiety during childbirth can cause changes in bodily functions. The impact is that the labor process takes longer, causing complications to both mother and baby. One of the non-pharmacological ways that can be done so that the labor process is gone naturally is by providing complementary massage therapy and frangipani aromatherapy. This research aims to determine the effect of back massage using frangipani aromatherapy oil in the first stage of labor on the duration of childbirth. The type of this research is Quasi-Experimental Design, posttest control group design. The sample is 80 people consisting of the control group of 40 people and the treatment group of 40 people. The sampling technique used is Consecutive Nonprobability Sampling. The data were recorded in the observation sheet. Also. The data analysis was done through univariate and bivariate "unpaired t-test". The results showed that the average duration of childbirth in the control group was 31.25 minutes, while the treatment group was 23.75 minutes. There is an effect of massage using frangipani aromatherapy oil in the first stage of labor on the duration of childbirth at a significance level of 0.01 ($p < 0.05$). In conclusion, there is the effect of massage using frangipani aromatherapy oil in the first stage of labor on the duration of childbirth. It is hoped that midwives will use complementary frangipani aromatherapy massage in providing midwifery care during the first stage of normal labor.

Keywords: Massage, Aromatherapy, Frangipani, Duration, Childbirth

1. Introduction

Childbirth or labor and delivery is a series of events that ends with the expulsion of the baby at term or nearly term, followed by removal of the placenta and fetal membranes from the mother's body. Physiological labor is accompanied by pain, which is caused by the opening of the cervix, hypoxia, and ischemia of the uterine muscles during contraction, and the stretching of the lower uterine segment and the nerve compression in the cervix (Byron & Brueggemann, 2009; Nilvér, Begley, & Berg, 2017).

Mothers who give birth normally, if they have begun the second stage of labor, will feel more frequent and stronger pain. This is often feared by mothers, so they choose to avoid spontaneous labor by performing a caesarean section or caesarean section on request as an effort to minimize the sensation of labor pain (Alipour, Services, & Lamyian, 2011; Weckesser et al., 2019; Belizán et al., 2018). During the process of childbirth, midwives have an important role in dealing with maternal pain or stress, as one of the efforts of the Mother Care Movement or Gerakan Sayang Ibu (GSI) (Hamnah, 2008). One of those that can be done independently by midwives is doing massage and aromatherapy (Barreto et al., 2013; Czech, Fuchs, Fuchs, Lorek, & Tobolska-lorek, 2018) (Smith, Collins, & Crowther, 2011; Dewi, Sukini, Thaariq, & Hidayati, 2017; Buckley, 2015).

The presence of pain that occurs during physiological labor can cause anxiety and fear for any pregnant woman. Fear and anxiety towards pain can cause acute stress, increasing the release of the adrenocorticotropin hormone (ACTH), cortisol, anti-diuretic hormone (ADH), steroids, and various activities that are mediated by autonomic nerves (Simkin & Hara, 2007). These hormones cause tension on smooth muscle and vascular vasoconstriction. This leads to a decrease in uterine contractions, disruption of uteroplacental circulation, decrement of the flow of blood and oxygen to the uterus, and uterine ischemia which makes the pain impulses multiply (Simkin & Hara, 2007).

The escalation of autonomic nerve activity in laboring mothers increases the release of catecholamines which results in the disruption of uterine contractions, the increase of peripheral resistance, as well as cardiac output and blood pressure (Bolbol-Haghighi, Masoumi, & Kazemi, 2016). The occurrence of hyperventilation can result in hypocalcemia, increase oxygen consumption, and even respiratory alkalosis. Hypocalcemia causes tetany, paraesthesia, and impaired orientation. Respiratory alkalosis that continues without a good body compensation mechanism can lead to a metabolic acidosis resulting in acidosis in the fetus. This situation stimulates an increase in catecholamines which can cause interference to the strength of uterine contractions, and vascular as well as smooth muscle vasoconstriction (Dixon, Skinner, & Foureur, 2013; Manuaba, 2010; Byron & Brueggemann, 2009).

Excessive anxiety during labor can also cause changes in bodily functions. This occurs due to an increase in adrenaline secretion, which causes the smooth muscle of the birth canal to become stiff and less relaxed, the prolongation of the labor process, thereby increasing complications for the mother and the fetus (Alipour et al., 2011; Dixon et al., 2013). The complications that occur in labor are in the form of prolongation of the labor process so that lead to the incidence of bleeding and infection, as well as complications in infants in the form of fetal distress, asphyxia, and infection (Kat et al., 2015). The prolongation during the process of childbirth will increase labor by vacuum extraction, forceps extraction, and Caesarean section (Koelewijn, Sluijs, & Vrijkotte, 2017; Dixon et al., 2013).

The World Health Organization (WHO) recommends that the rate of cesarean section in a country is 5% - 15% (World Health Organization (WHO), 2015). In Southeast Asia the average incidence of cesarean section is 27%, varies between 19% - 35% among the countries (Festin et al., 2009). Caesarean section labor and delivery in Indonesia continues to increase every year in both public and private hospitals. Research on the proportion of caesarean section in one private hospital and one public hospital in Jakarta during the period of 1 January to 31 December 2011 found 59.2% cesarean section (Andayasari et al., 2014; Suryati, 2010; M & Nasution, 2012). The representation of women who had cesarean section surgery; 75% were not at the age of high risk for normal delivery, 80% had no history of fetal death, and only 15.4% had signs of complications during pregnancy (Suryati, 2010). The results of the study at Sanglah Central General Hospital (RSUP Sanglah) Denpasar found that there had been an increase in the rate of cesarean section labor and delivery from 22.27% in 2001 to 34.56% in 2006 (Gondo & Sugiharta, 2010).

One of the efforts to help mothers so that they can go through the labor process naturally, without drugs, and with the independent authority of midwives is by using massage and aromatherapy techniques (Astuti et al., 2016; Gondo & Sugiharta, 2010; Simkin & Hara, 2007). Aromatherapy is a complementary therapy in midwifery practice using essential oils from the fragrant aroma of plants to improve physical and emotional conditions (Luo, Huang, Xia, & Zeng, 2015; Sumarni, Astuti, & Karmilah, 2019). Frangipani is aromatherapy that has the character and benefits of increasing concentration, enthusiasm, joy, self-confidence, relaxation, reducing fear, depression,

panic, relaxing muscles, and skin (Smith et al., 2011; Simkin & Hara, 2007). Empirical experience of giving frangipani aromatherapy has not been popularly used in midwifery services. Aromatherapy research that has been done a lot is lavender and roses (Lamadah & Nomani, 2016; Massomeh Kheirkhah, Valipour, Neisani, & Haghani, 2013; Masoomah Kheirkhah, Setayesh, Pour, Nisani, & Haghani, 2014). The research found there was an effect of massage using frangipani aromatherapy oil on labor pain intensity at a significance level of $p < 0.001$ (Gusti et al., 2019).

Researchers are interested in conducting a study on the aromatherapy of frangipani as in Bali there are many frangipanis or bunga Kamboja (in Balinese bunga Jepun) and are often used for ceremonial purposes. This flower is easy to obtain no matter what the season is, but has not been widely used in midwifery services so that its benefits need to be further explored. Also, this can change the image of frangipani which are identical to mystical flowers into flowers that are useful in midwifery services, as well as has an economic value to the Balinese. Therefore, according to the background aforesaid, the researchers are interested in examining the effect of massage using frangipani aromatherapy oil in the first stage of labor on the duration of childbirth. In general, this research aims to determine the effect of massage using frangipani aromatherapy oil in the first stage of labor on the duration of the childbirth.

2. Materials and Method

2.1 Study area and population:

This research is a Quasy Experimental Design, posttest control group design using a prospective approach. The sampling technique used is Consecutive Nonprobability Sampling. The research has received permission from the Research Ethics Commission of Udayana University and Sanglah Hospital Denpasar, conducted from June to October 2016. The research subjects were mothers who gave birth at PP Dauh Puri Denpasar and BPM Gusti Ayu Widiasih Gianyar.

2.2 Sample size:

The sample was 80 people, divided into treatment and control groups. The treatment group of 40 people performed back massage using frangipani aromatherapy oil on thoracic, and lumbar 1 during the labor process in the first active phase, while a control group of 40 people was given a massage using virgin coconut oil (VCO) without aromatherapy.

2.3 Sample collection and processing:

The inclusive criteria are: first-time labor, the active phase of labor, cooperative, attending antenatal classes during pregnancy, the position of the fetus behind the head, estimated fetal weight 2,500 grams to 4,000 grams, willing to be the respondents. Then the primary data were collected. The treatment and control groups were determined using a simple random system. After the respondents were given the treatment, then the second stage was carried out, namely from the opening of the uterine cervix completely until the baby was born, then recorded on the observation sheet. The data analysis techniques include univariate and bivariate analysis using the "unpaired t-test", and the hypothesis testing through concluding is based on the p-value at the 95% confidence level.

3. Results

The data collection was carried out after obtaining Ethical Clearance approval from the Research Ethics Commission of Udayana University and RSUP Sanglah Denpasar from June-October 2016 with the following results:

Table 1. Characteristics of Research Respondents: The Effect of Back Massage Using Frangipani Aromatherapy Oil in the First Stage of Labor on the Childbirth Duration

No	Characteristics	Control Group		Treatment Group	
		f	%	f	%
1.	Education				
	Primary	15	37,50	14	12,5
	Secondary	24	60,00	26	65,00
	Higher	1	2,50	0	0
	Total	40	100	40	100
2.	Age				
	< 20 years old / > 35 years old	2	5,00	1	2,50
	20-35 years old	38	95	39	97,5
	Total	40	100	40	100
3.	Occupation				
	At work	35	97,50	36	90,00
	Not at work	5	12,50	4	10,00
	Total	40	100	40	100

Table 1 showed that the distribution of respondents in each type of education and age between the control and treatment group is almost the same. Most respondents in both groups are secondary education, ranging in age from 20-35 years, and almost all respondents are at work.

Table 2. Data Normality Test of Childbirth Duration on Research: The Effect of Massage Using Frangipani Aromatherapy Oil in First Stage of Labor on the Duration of Childbirth

No	Variable	Standard Deviation	Statistic	<i>p</i>
1	Childbirth duration on the control group	11.234	Kolmogorov-Smirnov =0,094	0.200
2	Childbirth duration on the treatment group	7.150	Shapiro-Wilk =0,963	0.208

Table 2 showed that the two groups have a *p* value > 0.5, which means that the data for the two groups are normally distributed. Thus, a parametric analysis can be carried out using the unpaired *t* test.

Table 3. Analysis Result on the Effect of Massage Using Frangipani Aromatherapy Oil on Stage I Labor on the Duration of Baby Birth

Variable	Average	Standard Deviation	<i>t</i>	<i>p</i>
Childbirth duration Without aromatherapy (n=40)	31,25	11,234	-3,562	0,01
Frangipani aromatherapy (n=40)	23,75	23,75		

Table 3 showed the duration of childbirth in the group of women who gave birth using Frangipani aromatherapy oil in the first stage labor massage had an average duration of 23.75 minutes, faster than the group of women who did not use aromatherapy in the first stage labor massage (31.25 minutes). The result of the *t* test was -3.562 with a value of *p* = 0.01 (*p* < 0.05), indicating that there was an effect of massage using frangipani aromatherapy oil in the first stage of labor on the childbirth duration at a significance level of *p* < 0.05.

4. Discussion

Aromatherapy is a complementary therapy in midwifery practice using essential oils from the fragrance of plants to improve physical and emotional conditions (Silva et al., 2019). According to Regulation of the Minister of Health of Indonesia number 103 of 2014, the ingredients used in aromatherapy are active substances taken from aromatic plants (extracts from flowers, leaves, roots, stems/twigs, fruit, seeds, etc.) which provide stimulating or relaxing effects. Aromatherapy is a body care technique using or utilizing nutritious essential oils. Aromatherapy can be used by rubbing on the skin or to be more effective with a massage.

Frangipani, also known as plumeria or frangipani flower, plays a very important role in daily activities in Bali. It is used in religious ceremonies, as well as for beauty, massage, and body scrubs. It contains saponins, flavonoids, and polyphenols. Frangipani's *Simplicia* extract contains bioactive compounds in the form of tannins, total phenols, and vitamin C. Frangipani also contains several elements of triterpenoid and amyryl compounds which are relaxing. The relaxing characteristics given off by frangipani aromatherapy oil can help increase comfort (Amirudin, Harnany, & Widowati, 2020). Frangipani Aromatherapy is one type of traditional healing method which have been known thousands of years ago. Frangipani aromatherapy massage oil is made in the form of oil with the addition of olive oil or virgin coconut oil (VCO), so it is thicker than essential oils. Its use is by applying the massage oil to the body.

Based on the research findings on the characteristics of respondents, most of the mothers got secondary education, which means that from the point of view, the level of education has exceeded primary education. This allows mothers to be able to receive information related to childbirth properly. The level of education can influence their psychosocial condition towards the preparation, expectations and treatment that will be undertaken. Age of the respondents in the control and treatment groups is mostly at the age of 20 to 25 years. Age is one of the factors that influence a person's experience. Also, it is indirectly related to labor and delivery process because it affects a person's emotions and affects the mother's expectations of treatment during the labor.

The results showed that the childbirth duration in the group that was given a massage without frangipani aromatherapy is 11 minutes (the fastest) and 60 minutes (the longest), and in the group that was given massage with frangipani aromatherapy is 8 minutes (the fastest) and 37 minutes (the longest). This means that respondents who got massage using frangipani aromatherapy experienced a shorter duration of childbirth. This is in line with the mechanism of labor pain following a series of nerve fiber pathways in general, where the nociceptive process is grouped into 4 stages, namely transduction, transmission, modulation, and perception. The massage mechanism in the thoracic area 10,11,12, and lumbar 1 which is carried out in labor to relieve pain through gentle and slow massage, a source of innervation to the uterus and cervix, will activate the transmission of more A-beta sensory nerve fibers fast as a neurotransmitter. It will then reduce pain transmission through small diameter C and A-delta fibers as well as close the synapses for the transmission of pain impulses (Barreto et al., 2013). If pain transmission is blocked it will also block modulation and pain will not be perceived. Several studies have also found that massage during the first stage of labor reduces severe pain, and mothers who give birth do not feel pain or even the pain decreases and will feel calmer (Kat et al., 2015; Astuti et al., 2016).

Massage that is carried out on the thoracic region 10, 11, 12, and lumbar 1 stimulates ascending nerve receptors. Then, the stimulation is sent to the hypothalamus through the spinal cord, is transmitted to the pons, and continued to the gray part of the midbrain (periaqueductal). This received stimulus is delivered to Hypothalamus, from the hypothalamus through the descending nerve pathways, endorphin hormones are released into the blood vessels (Smith et al., 2011; Barreto et al., 2013; Gondo & Sugiharta, 2010; Bolbol-Haghighi et al., 2016; Dixon et al., 2013). This causes the mother to be calmer, there is relaxation of smooth muscles including those in the pelvic area, coordination of regular uterine contractions so that the process of expulsion of the fetus becomes faster (Smith et al., 2011; Bolbol-Haghighi et al., 2016; Simkin & Hara, 2007; Festin et al., 2009). The results of this study are in accordance with the research which found that massage therapy during childbirth accelerates the process of stage I and stage II and increases the APGAR Score for newborns (Bolbol-Haghighi et al., 2016; Kat et al., 2015). The labor process is influenced by power, passage, passenger, psychic and assistant (Manuaba, 2010). The results of this research indicate that massage using frangipani aromatherapy provides a good response to maternal psychology. The principle of using aromatherapy is based on the nose's function. The smell that is inhaled will

make a vibration in the nose. The olfactory nerves pick up on smells, then send them to the brain, affecting the limbic system, where memory centers, moods, and intellect, which then affect the work of the brain and nerves (Smith et al., 2011). Apart from the smell, aromatherapy oil is applied as a massage oil. When frangipani aromatherapy oil massage is absorbed by the skin and muscles, it will give a warm sensation that soothes the muscles, and the mother feels calm, relaxed. The application of aromatherapy in this research has a psychological effect through the limbic system and healing physical complaints through the endocrine and nervous system (Smith et al., 2011; Simkin & Hara, 2007; Ministry of Health of Indonesia, 2008).

This research showed that Massage using frangipani aromatherapy speeds up the childbirth duration on an average of 23.75 minutes. This is faster than massage without aromatherapy with an average of 31.25 minutes. The decrease in the feeling of pain and tension of the mother during giving birth, the peace of mind and mental health, and relaxation, make the mother stronger in facing labor (Smith et al., 2018). These will also have a positive impact on uterine contractions. The regular contraction of the uterus, the stronger it is, will lead to progress and decrease in the lowest part of the fetus, thereby accelerating the process of fetal birth (Bolbol-Haghighi et al., 2016).

An aromatherapy massage is a combination of massage and the use of essential fragrant oils, providing the benefits of deep relaxation, releasing muscle tension, reducing pain, and reducing stress. The psychic condition of the mother in labor who is calm, not stressed or afraid, makes muscle contraction and relaxation become better and increases its elasticity. The elastic pelvic muscles will make it easier to stretch as the fetus passes through the birth canal.

According to the Regulation of the Minister of Health number 103 of 2014, the ingredients used in aromatherapy are active substances taken from aromatic plants. One of the aromatherapy used is frangipani which is another name for bunga Kamboja. This flower grows a lot in Bali containing several elements of triterpenoid and amyryn compounds which are relaxing. Frangipani aromatherapy can be used for massage, meditation and provides a quiet atmosphere (Bolbol-Haghighi et al., 2016; Dixon et al., 2013). Research has proven that frangipani aromatherapy oil is used by mothers who are in menopause to increase comfort during sexual intercourse and reduce the intensity of labor pain.

The skills of the assistant (midwives) determine the length of the labor process. Labor can be led when the opening stage is complete and the fetus' head is already at the base of the pelvis (Ministry of Health of Indonesia, 2008). In this research, the level of education and work experience of assistant varied, however, the labor and delivery aid methods used were the same, namely referring to the standard steps in normal delivery care.

The childbirth duration in the group of women getting frangipani aromatherapy oil in the first stage labor massage had an average time faster (23.75 minutes) than the group of women who did not receive aromatherapy in the first stage labor massage (31,25 minute). The result of the "t" test was obtained -3.562 with a value of $p = 0.01$ ($p < 0.05$). This shows that there is an effect of massage using frangipani aromatherapy oil in the first stage of labor on the childbirth process.

The duration of the childbirth in primiparous is 1-2 hours (Manuaba, 2010). Giving frangipani aromatherapy which is rubbed during massage contains the mechanism of action in the human body which takes place through two physiological systems, namely the blood circulation and the olfactory. Aromatherapy can affect a person's psychological, memory, and emotional conditions. The olfactory organ is a natural means of communication in humans (Dixon et al., 2013). The odor is a molecule that evaporates into the air and enters the nasal cavity through inhalation. The vibrating hairs in the nasal cavity function as receptors to deliver electrochemical messages to a person's emotional and memory centers so that they are recorded by the brain as the olfactory process, then the smell is transmitted as a message to the olfactory center. In this place, various neuronal cell systems interpret the smell and deliver it to the limbic system which is then sent to the hypothalamus to process (Bolbol-Haghighi et al., 2016; Manuaba, 2010).

Frangipani aromatherapy can affect a person's psychological condition, memory, and emotions. The response delivery carried out by the hypothalamus, all the elements in the essential oil are delivered by the circulatory system and chemical agents in the organs of the body that are in need. The message that is delivered throughout

the body is converted into action with the release of neurochemical substances in the form of feelings of calm, pleasure, relaxation, contraction, and relaxation of the uterine muscles. This will affect the leveling and opening of the cervix and make the mother feel stronger against fear, stress, and anxiety during labor (Astuti et al., 2016). The results of this research indicate that massage in the thoracic area 10,11,12 and lumbar 1 using frangipani aromatherapy oil provides a good response to the pelvic floor muscles. In general, two factors influence the delivery process, namely physical and psychological factors. Massage in the thoracic area 10,11,12, and lumbar 1 inhibits the series of pain nerve fiber pathways, especially at the transmission, modulation, and perception stages, so that pain is not interpreted and perceived in the central nervous system (Barreto et al., 2013; Gondo & Sugiharta, 2010). The use of frangipani aromatherapy will stimulate the thalamus to secrete enkephalin which acts as a natural pain reliever and produces a feeling of calm. This condition will stimulate the raphe nucleus to release serotonin which induces sleep. The continued impact of massage on the thoracic area 10,11,12, and lumbar 1 causes the pelvic floor muscles to become more elastic supported by the effects of aromatherapy which causes a feeling of calm, relaxation, pain, and reduced muscle tension, thus making it easier to stretch when the fetus passes birth canal, thus the duration of the baby's birth becomes faster (Dixon et al., 2013).

5. Conclusion

Based on the research findings and discussions, the researcher concluded that the duration of the childbirth for mothers who are given a massage during the first stage of labor without using frangipani aromatherapy oil is the fastest 11 minutes and the longest is 60 minutes, and the average is 31.25 minutes. On the other hand, the mothers who give birth using frangipani aromatherapy oil massage is the fastest 8 minutes and the longest 37 minutes, with an average of 23.75 minutes. Thus, there is an effect of massage using frangipani aromatherapy oil in the first stage of labor on the childbirth duration at a significance level of $p < 0.05$.

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References

- Alipour, Z., Services, H., & Lamyian, M. (2011). The association between antenatal anxiety and fear of childbirth in nulliparous women: A prospective study. *Iran J Nurs Midwifery Res*, 16(2), 169–173.
- Amirudin, Z., Harnany, A. S., & Widowati, I. (2020). Effect of a Slow-stroke Back Massage Combination and Frangipani Essential Oils against the Comfort of Menopause Sexual Relationship. *Journal of Complementary and Alternative Medical Research*, 10(1), 37–44. <https://doi.org/10.9734/JOCAMR/2020/v10i130156>
- Andayasari, L., Muljati, S., Sihombing, M., Arlinda, D., Opitasari, C., Mogsa, D. F., & Widiyanto. (2014). Proporsi Seksio Sesarea dan Faktor yang Berhubungan dengan Seksio Sesarea di Jakarta. *Buletin Penelitian Kesehatan*, 43(2), 6–16.
- Astuti, I., Hamdah, N. M. N., Jend, S., Cimahi, A. Y., Terusan, J., Sudirman, J., ... Cimahi, K. (2016). The Influence of Massage Therapy to Reduce Pain Scale of Inpartu Woman in The Active Phase of The First Stage of Labour (A Case Study in Bandung City). *The Southeast Asian Journal of Midwifery*, 2(1), 1–8.
- Barreto, R., Gallo, S., Santana, L. S., Homs, C., Ferreira, J., Marcolin, C., ... Quintana, S. M. (2013). Massage reduced severity of pain during labour : a randomised trial. *Australian Journal of Physiotherapy*, 59(2), 109–116. [https://doi.org/10.1016/S1836-9553\(13\)70163-2](https://doi.org/10.1016/S1836-9553(13)70163-2)
- Belizán, J. M., Minckas, N., McClure, E. M., Saleem, S., Moore, J. L., Goudar, S. S., ... Goldenberg, R. L. (2018). Articles An approach to identify a minimum and rational proportion of caesarean sections in resource-poor settings : a global network study. *Lancet Glob Health*, 6, 894–901. [https://doi.org/10.1016/S2214-109X\(18\)30241-9](https://doi.org/10.1016/S2214-109X(18)30241-9)
- Bolbol-Haghighi, N., Masoumi, S. Z., & Kazemi, F. (2016). Effect of Massage Therapy on Duration of Labour : A Randomized Controlled Trial. *Journal of Clinical and Diagnostic Research*, 10(4), 10–13. <https://doi.org/10.7860/JCDR/2016/17447.7688>
- Buckley, S. J. (2015). Executive Summary of Hormonal Physiology of Childbearing : Evidence and Implications for Women , Babies , and Maternity Care. *The Journal of Perinatal Education*, 24(3), 145–153.

- Byron, K. L., & Brueggemann, L. I. (2009). Kenneth L. Byron and Liubov I. Brueggemann. *J Physiol*, 10, 2109–2110. <https://doi.org/10.1113/jphysiol.2009.173641>
- Czech, I., Fuchs, P., Fuchs, A., Lorek, M., & Tobolska-lorek, D. (2018). Pharmacological and Non-Pharmacological Methods of Labour Pain Relief — Establishment of Effectiveness and Comparison. *International Journal of Environmental Research and Public Health*, 15(2792), 1–11. <https://doi.org/10.3390/ijerph15122792>
- Dewi, M. M., Sukini, T., Thaariq, N. A. A. T., & Hidayati, N. W. (2017). Effectiveness of Endorphins Massage and Ice Packs to Relieve The First Stage of Labor Pain Among The Pregnant Woman in Candimulyo Health Center, Indonesia. In *International Conference on Applied Science and Health* (pp. 109–114).
- Dixon, L., Skinner, J., & Foureur, M. J. (2013). The emotional and hormonal pathways of labour and birth : integrating mind , body and behaviour. *New Zealand College of Midwives*, (December). <https://doi.org/10.12784/nzcomjnl48.2013.3.15-23>
- Festin, M. R., Laopaiboon, M., Pattanittum, P., Ewens, M. R., Henderson-smart, D. J., & Crowther, C. A. (2009). Caesarean section in four South East Asian countries : reasons for , rates , associated care practices and health outcomes. *BMC Pregnancy and Childbirth*, 11(9), 9–17. <https://doi.org/10.1186/1471-2393-9-17>
- Gondo, H., & Sugiharta, K. (2010). Profil Operasi Seksio Sesarea di SMF Obstetri dan Ginekologi RSUP Sanglah Denpasar Bali Tahun 2001 - 2006. *CDK*, 37(2), 97–101.
- Gusti, N., Sriasih, K., Kes, M., Hadi, M. C., Kes, M., Suindri, N. N., ... Keb, M. (2019). The Effect of Massage Therapy Using Frangipani Aromatherapy Oil to Reduce the Childbirth Pain Intensity. *International Journal of Therapeutic Massage and Bodywork*, 12(2), 18–24.
- Hamnah. (2008). *Ilmu Kebidanan*. Jakarta: Yayasan Keperawatan Bina.
- Kat, S. L., Berghella, V., Reddy, U. M., Sundaram, R., Lu, Z., & Hoffman, M. K. (2015). Neonatal and Maternal Outcomes With Prolonged Second Stage of Labor. *NIH Public Access*, 124(1), 57–67. <https://doi.org/10.1097/AOG.0000000000000278>. Neonatal
- Kheirkhah, M., Setayesh, N., Pour, V., Nisani, L., & Haghani, H. (2014). Comparing the Effects of Aromatherapy With Rose Oils and Warm Foot Bath on Anxiety in the First Stage of Labor in Nulliparous Women. *Iran Red Crescent Med J*, 16(9), 1–5. <https://doi.org/10.5812/ircmj.14455>
- Kheirkhah, M., Valipour, N. S., Neisani, L., & Haghani, H. (2013). A Controlled Trial of the Effect of Aromatherapy on Birth Outcomes Using " Rose Essential Oil " Inhalation and Foot Bath. *J Midwifery Reprod Health*, 1(2), 77–82.
- Koelewijn, J. M., Sluijs, A. M., & Vrijkotte, T. G. M. (2017). Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process : a prospective cohort study. *BMJ Open*, 7(e013413), 1–13. <https://doi.org/10.1136/bmjopen-2016-013413>
- Lamadah, S. M., & Nomani, I. (2016). The Effect of Aromatherapy Massage Using Lavender Oil on the Level of Pain and Anxiety During Labour Among Primigravida Women The Effect of Aromatherapy Massage Using Lavender Oil on the Level of Pain and Anxiety During Labour Among Primigravida Women. *American Journal of Nursing Science*, 5(2), 37–44. <https://doi.org/10.11648/j.ajns.20160502.11>
- Luo, T., Huang, M., Xia, H., & Zeng, Y. (2015). Aromatherapy for Laboring Women : A Meta-Analysis of Randomized Controlled Trials. *Open Journal of Nursing*, 4(May), 1–6. <https://doi.org/10.4236/ojn.2014.43021>
- M, I. S., & Nasution, S. S. (2012). Faktor Pemilihan Persalinan Sectio Caesarea Tanpa Indikasi Medis di RSU Bunda Thamrin Medan. *Jurnal Keperawatan Klinis*, 1(1), 7–12.
- Manuaba. (2010). *Ilmu Kebidanan Penyakit Kandungan dan Keluarga Berencana untuk Pendidikan Bidan*. Jakarta: EGC.
- Ministry of Health of Indonesia. (2008). *Maternal & Neonatal Care*. Ministry of Health Indonesia.
- Nilvér, H., Begley, C., & Berg, M. (2017). Measuring women ' s childbirth experiences : a systematic review for identification and analysis of validated instruments. *BMC Pregnancy and Childbirth*, 17(203), 1–19. <https://doi.org/10.1186/s12884-017-1356-y>
- Silva, M. A. da, Sombra, I. V. de S., Silva, J. S. J. da, César, J. B. da S., Dias, L. R. F. de M., Calado, R. S. F., ... Silva, G. A. de M. (2019). Aromatherapy for Pain Relief During Labor. *Journal of Nursing*, 13(2), 455–463.
- Simkin, P. P., & Hara, M. O. (2007). Nonpharmacologic relief of pain during labor : Systematic reviews of five methods. *Am J Obstet Gynecol*, 185(5), 131–159. <https://doi.org/10.1067/mob.2002.122382>
- Smith, C. A., Collins, C. T., & Crowther, C. A. (2011). Aromatherapy for pain management in labour (Review). *Cochrane Library*, 1–3. <https://doi.org/10.1002/14651858.CD009215>. Copyright
- Smith, C. A., Levett, K. M., Collins, C. T., Armour, M., Dahlen, H. G., & Sukanuma, M. (2018). Relaxation techniques for pain management in labour (Review). *Cochrane Database of Systematic Reviews*, (3). <https://doi.org/10.1002/14651858.CD009514.pub2>. www.cochranelibrary.com
- Sumarni, R., Astuti, I., & Karmilah, N. (2019). The Relations of Aromatherapy with The Intensity of Pain on Labor Women Stage I Active Phase PMB Cimahi City. *Third International Seminar on Global Health (3rd ISGH)*, 3(1), 21–26.

- Suryati, T. (2010). Percentage of Sectio Caesaria in Indonesia is Passad the Maximum Standard, is it in accordance to Medical Indication. *Buletin Penelitian Sistem Kesehatan*, 15(4), 331–338.
- Weckesser, A., Farmer, N., Dam, R., Wilson, A., Morton, V. H., & Morris, R. K. (2019). Women ' s perspectives on caesarean section recovery , infection and the PREPS trial : a qualitative pilot study. *BMC Pregnancy and Childbirth*, 8(245), 1–10.
- World Health Organization (WHO). (2015). Statement on caesarean section rates: Executive summary. Retrieved from http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/cs-statement



Schizophrenia: Epidemiology, Causes, Neurobiology, Pathophysiology, and Treatment

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Abstract

Schizophrenia is a severe mental illness that has devastating consequences for those who suffer from the disorder. The epidemiology of schizophrenia indicates that it occurs relatively often, in many different contexts, and in conjunction with other disorders, decreasing quality of life and causing premature death. There has been an enormous amount of research into the causes of schizophrenia and there is now have a much better understanding of the genetic, environmental, and psychological factors that contribute to the disease. While there are numerous ways to understand and conceptualize schizophrenia, a unified picture of the neurobiology, changes in brain structure, cognitive and social-cognitive impairments related to the disorder has yet to emerge. Convulsive therapies and psychosurgery were used unsuccessfully, indiscriminately and without scientific validation in the past to treat schizophrenia. Medical advances including advanced imaging technology have now provided the ability to perform specifically focused neuromodulation and psychosurgery in severe and treatment resistant cases of schizophrenia. While still at a preliminary stage, these approaches have the potential to yield effective treatments in the future. For the last 70 years antipsychotic medication has become the prevailing treatment for schizophrenia. However, many people suffering from the disorder have trouble with side-effects and adhering to a regimen of antipsychotic medication. Newer pharmacological agents are being developed and include not only novel antipsychotic drugs, but anti-inflammatory and immunomodulating agents as well. These new agents, used either alone or in combination, have the potential to improve outcomes for people suffering from schizophrenia. Nevertheless, conclusively better pharmacotherapies will likely not arise until there is better understanding of the pathophysiology underlying schizophrenia. After the development of antipsychotic medication, psychotherapeutic methods for treating schizophrenia fell out of favor, but there is currently some reversal of this trend. The use of newer psychotherapies and modified forms of older therapeutic treatments are not only targeting the symptoms of schizophrenia but are also now focusing on recovery from the disorder. These newer approaches as well as efforts at preventing schizophrenia show promise in reducing the suffering caused by this disease.

Keywords: Schizophrenia, Autoimmunity, Brain Structure, Antipsychotic Medication, Neuromodulation, Psychotherapy

1. Introduction

Schizophrenia is the term for a mental disorder in which thought and perception are severely impaired. People suffering from schizophrenia have delusional beliefs and, in many instances, these are accompanied by auditory or visual hallucinations. People with schizophrenia display disorganized thinking that can manifest as bizarre personality and behavioral changes that cause impairment in social functioning. The person suffering from schizophrenia demonstrates a marked loss of contact with reality.

The fifth edition of The Diagnostic and Statistical Manual of Mental Disorders (DSM V) now understands all psychoses as variants of schizophrenia (American Psychiatric Association, 2013). This schizophrenia spectrum includes schizophrenia, other psychotic disorders, as well as schizotypal disorder (which is generally diagnosed as a personality disorder). The DSM V lists the following schizophrenia spectrum disorders: *schizophrenia*, *schizophreniform disorder*, *schizoaffective disorder*, *delusional disorder*, *brief psychotic disorder*, *substance/medication induced psychotic disorder*, *psychotic disorder due to another medical condition*, *unspecified schizophrenia and other psychotic disorder* (pp. 87-160). When we examine these schizophrenia spectrum disorders, it becomes obvious that there are many similarities among the disorders and that they differ only in duration or emphasis on a particular symptom. For instance, schizophrenia, schizophreniform disorder, and brief psychotic disorder differ in terms of duration, while schizophrenia, delusional disorder, and schizoaffective disorder differ in symptomatic content¹. Psychotic disorder due to a general medical condition and substance-induced psychotic disorder are both related to psychoses that result from chemical or structural changes in the body. What is clear from all these descriptions is that schizophrenia encompasses all the psychotic characteristics of these disease entities. Another way of saying this is that all these disorders are easily understood as variations of schizophrenia. For that reason, our discussion will focus on schizophrenia.

Schizophrenia presents with symptoms that can be positive, negative, or mixed. Positive symptoms of schizophrenia include overt delusions, auditory, visual, and tactile hallucinations, thought disorder, and behavior that is bizarre when compared to normal behavior in the culture where it occurs. Negative schizophrenic symptoms include a flat affect, alogia, avolition, anhedonia, and impairment of attention. Cognition may also be impaired in those who have the disease with consequences for social functioning (Rossello et al., 2013). Mixed schizophrenic symptoms that include both positive and negative symptoms may also occur (Dion & Dellario, 1988).

2. Epidemiology of Schizophrenia

Schizophrenia typically has an onset in adolescence or young adulthood and most estimates are that approximately 1% of the population is affected (Castle & Morgan, 2008). A review of prevalence data from a large number of geographically diverse studies indicates lifetime prevalence ranging from around .2% to almost 1.5% (Simeone et al., 2015). Men are significantly more likely than women have the disorder (Grignon & Trottier, 2005). While it has commonly been held that prevalence rates for Schizophrenia are fairly stable around the world (Nixon & Doody, 2005), some studies are now questioning this dogma, demonstrating that sex, age, ethnicity, and geography are related to its incidence (McGrath et al., 2011; McGrath, 2006). Other studies have shown increasing general rates of schizophrenia (Boydell et al., 2003; Bray et al., 2006) while others have not (Nixon & Doody, 2005; Suvisaari et al., 1999).

There is some debate about whether schizophrenia represents a single disease or many different syndromes. This idea is supported by some studies that have found that different biological markers are associated with how well patients respond to antipsychotic drugs (Garver et al., 2000). The presence of these different biological markers gives support to the idea that schizophrenia may in fact be multiple syndromes rather than a single disease entity. Ross (2014; 2006) argues against the prevailing view schizophrenia is primarily an inherited biological disorder to be treated solely with medication. He goes on to make the case for viewing the positive symptoms of schizophrenia as being more representative of dissociative identity disorder and proposes a dissociative subtype

¹ Some researchers question whether or not schizoaffective disorder is really a separate disorder and not either a variation of schizophrenia or mood disorder (Cheniaux et al., 2008; Marneros, 2007). In fact, scientists and clinicians continue to debate just what constitutes a psychosis (Castle & Morgan, 2008).

of schizophrenia. Kroll (2007) after reviewing many cross-cultural studies of psychoses concludes that there are so many shared risk factors for psychosis and affective disorders that he questions whether or not there should be a categorical distinction between disorders.

3. Co-Morbidity and Mortality

People who suffer from schizophrenia often suffer from other mental health issues such as anxiety disorders, depression, and substance abuse, as well as from physical problems related to cardiovascular, oral, respiratory and endocrine pathology (Laursen, 2019; Laursen et al., 2012). People with schizophrenia may have more risk of contracting COVID-19 (Fonseca et al., 2020; Kozloff et al., 2020). Some of the problems stem from unhealthy behavior patterns related to smoking, eating, and sexual behaviors, which are preventable (Arnaiz et al., 2011; Chwastiak & Tek, 2009; Findlay, 2015; Trudeau et al., 2018). As might be expected, the presence of co-morbid conditions is associated with worse symptoms, treatment outcomes, and social functioning (Pratt, 2012; Sim, Chan, et al., 2006; Sim, Chua, et al., 2006). People who suffer from schizophrenia often have social dysfunction. They are more likely to be unemployed, poor, and homeless. Unfortunately, this leads to decreased life expectancy with some estimates as much as 10-12 years less than people who do not suffer from schizophrenia (S. Brown et al., 2000). Other studies have shown that on average individuals with schizophrenia live about 36 years after diagnosis and that this number is decreasing (Capasso et al., 2008; Sukanta Saha et al., 2007).

After reviewing more than forty thousand studies Leucht et. al. (2007) concluded that individuals suffering from schizophrenia in developed nations have increased rates of HIV, hepatitis, osteoporosis, sensitivity to pain, sexual dysfunction, obstetric complications, cardiovascular diseases, obesity, diabetes, dental problems, and polydipsia when compared to the general population. Interestingly, people suffering from schizophrenia were found to have lower rates of rheumatoid arthritis and cancer. The authors conclude that many of these medical problems may be related to the treatment delivered by health services as well as the social stigma attached to the disease.

Infection with *Toxoplasma gondii* (T. gondii), which has been suspected of contributing to the development of schizophrenia (see below), has also been associated with increased mortality among schizophrenia sufferers (Dickerson et al., 2007). Long-term use of antipsychotic medication is also suspected of decreasing life expectancy in people suffering from schizophrenia (Fors et al., 2007; Healy, 2006; Joukamaa et al., 2006). Antipsychotic medications may increase mortality among individuals suffering from schizophrenia by contributing to obesity, hyperglycemia, diabetes mellitus, and dyslipidemia (Casey et al., 2004; Robinson, 2008). One study reported that people suffering from schizophrenia who use antipsychotic medication were five times more likely to suffer from a heart attack than healthy controls (Enger et al., 2004). Suicide is found more often in people suffering from schizophrenia with males having higher rates of mortality (Lester, 2007). This finding is seen across cultures and may explain the higher prevalence of schizophrenia among females in some areas (Ran et al., 2007).

4. Causes of Schizophrenia

It is still not known what causes schizophrenia and how it develops. Yet researchers are cautiously optimistic that we will soon have some answers regarding the etiology of this disease (Schwab & Wildenauer, 2008). While generally thought to be a disease of the brain, studies suggest that genetics, early environment, psychological, and social processes are important contributory factors to its development (K. Dean et al., 2003; Gilmore, 2010). Indeed, there is recent support for the older idea of psychogenic causes or contributions to the development of the disease. As Lublin and Erbehard (2008) put it:

“Basic research into the mechanisms behind the disorder suggest that the possibility of psychogenesis still appears to have some validity, although we may never entirely come to understand the relationships and possible interactions between the environmental and genetic risks...We know that, like many other disorders, there are susceptible individuals who appear to have inherited a number of genetic traits, each of which is also present in the general population, but which, together, render that individual vulnerable to schizophrenia. These include neurodevelopmental genes — but they are by no means the whole story...there is still much work to do on our understanding of the contribution of early environmental ‘insults’ such as prenatal infections, maternal malnutrition, substance abuse, and obstetric complications...” (p. v)

Schizophrenia is thought to have a genetic component and having first degree relatives with the disorder greatly increases the risk of developing schizophrenia. Recent research indicates that mutations at genetic loci related to schizophrenia are heterogenous, with a relatively weak contribution on of any single mutation (Zhenxing et al., 2018).

Torrey et. al. (2012) report on a number of causative risk factors for schizophrenia. Having a mother with schizophrenia raises risk of the disorder about 9 times, while having a father or sibling with the disorder increases risk about 7 times. However, other risk factors abound. Being the offspring of an immigrant increases risk of schizophrenia 4.5 times while being an immigrant from or to certain countries increases the risk 2.7 times. *T. gondii* infection results in a 2.7 times greater risk. Being born or raised in an urban setting increases risk 2.2 – 2.8 times, while cannabis use, minor physical abnormalities, and having a father over 55 at time of birth results in around 2 times the risk. The authors found other risk factors to have minor impacts, increasing the risk of schizophrenia 1-1.7 times. These factors include traumatic brain injury, being sexual abused as a child, complications during birth, having a father 45 or older at birth, season of birth, having specific genetic variations, and maternal exposure to the flu. Some of these factors are discussed below.

5. Childhood Abuse, Trauma, and Schizophrenia

The association between childhood abuse and subsequent diagnosis of schizophrenia is complicated. There have been a number of studies that indicate a relationship between childhood abuse and schizophrenia. Read et. al. (2003) found that abuse as a child (sexual and physical) was significantly related to hallucinations, but not delusions, thought disorders, or negative symptoms among community mental health center clients. Child abuse and subsequent abuse as an adult, predicted hallucinations, delusions, and thought disorders.

Read et. al. (2005) in a systematic review of the literature found a strong causal association between child physical and sexual abuse, and schizophrenic symptoms, especially hallucinations. This review also supports the idea of a dosage effect with higher levels of abuse being associated with more severe psychotic symptoms. The authors conclude that many severe mental illnesses, including schizophrenia as well as post traumatic stress syndrome and other diagnoses related to dissociation (e.g. borderline personality disorder and dissociative disorders) can be understood as adaptive responses to early childhood trauma which are subsequently maladaptive in adults.

Janssen et. al. (2004) in a study of over 4000 subjects drawn from a general population found that people who had suffered abuse as a child were 7.3 times more likely to develop positive schizophrenic symptoms compared to those who had not been subjected to abuse as a child after adjustment for confounding. This study also demonstrated a dose-effect with those having experienced higher levels of abuse having more severe psychotic symptoms. Those subjects with the highest frequency of abuse as children were found to be 30 times more likely to have psychotic symptoms than those who were not abused.

While many studies show a strong association between childhood sexual and physical abuse and schizophrenia, other studies have found conflicting results. Spataro et. al. (2004) in a study of 1612 sexually abused children found significant rates of affective disorders, anxiety disorders, childhood mental disorders, and personality disorders, but not schizophrenia. It may be that the associations in many studies were related to schizophrenic symptoms but not the fully diagnosable disorder (Mullen, 2005).

Lysaker et. al. (2001, 2004, 2005) found that childhood sexual abuse victims who were later diagnosed with schizophrenia spectrum disorders reported higher levels of psychotic symptoms, as well as poorer psychosocial functioning and participation in vocational rehabilitation. The subjects who suffered from schizophrenia were also more likely to perform worse on tests of executive function and have higher levels of hallucinations and anxiety. A similar study by Gil et. al. (2009) found that adult patients diagnosed with schizophrenia (but not having an acute psychotic episode) had increased disability, functional impairment in overall behavior, social role performance, and global functioning (which was derived from a combination of the other measures). Higher emotional abuse was associated with impaired overall behavioral functioning and higher emotional neglect was

associated with a decrease in global functioning. Physical neglect was associated with the subjects' overall ability to function as adults. There was no association found between sexual and physical abuse and schizophrenia.

Schürhoff et. al. (2009) found a strong correlation between childhood trauma and positive schizotypal tendencies among unaffected first degree relatives of people suffering from schizophrenia. A correlation between childhood trauma and bi-polar tendencies was not found among the relatives of subjects with bi-polar disorder. Vogel et. al. (2011) compared non-psychotic subjects and adult subjects suffering from schizophrenia and found that childhood abuse was related to non-psychotic disorders while neglect was related to development of schizophrenia. It was thought that childhood abuse can cause different symptoms in adults with psychotic and non-psychotic disorders. Ashcroft et. al. (2012) in a study of patients suffering from schizophrenia found that those with persecutory delusions reported significantly more emotional abuse than those patients without these delusions. There was no difference in these two groups with regard to total trauma, physical abuse, physical neglect and sexual abuse. Leonhardt et. al. (2015) found that patients suffering from schizophrenia with increased awareness and concomitant increased distress were more likely to have experienced abuse as children. A study by Kelly et. al. (2016) found a positive relationship between men and women diagnosed with schizophrenic and schizoaffective disorders and childhood abuse. Women who were sexually abused as children were more likely to show significantly more psychotic and depressive symptoms compared to women without childhood trauma and men with and without childhood trauma. A study by Kim et al. (2018) examined the relationship between childhood trauma and delusions and hallucinations among 42 subjects diagnosed with schizophrenia. Delusions of reference, persecutory delusions, and delusions of being controlled were found to be related to childhood emotional abuse. Childhood abuse and neglect was not found to be related to hallucinations.

Rokita et. al. (2020) found that patients suffering from schizophrenia were significantly more likely to recall childhood trauma and scored lower on social-cognitive measures and measures of parental bonding. Physical neglect was the strongest predictor of impairment in the ability to recognize emotions in others. Good bonding with parents attenuated the impact of childhood trauma and impairment in emotional recognition.

Overall, the preponderance of the evidence is that there is a relationship between childhood abuse and schizophrenic symptoms. A dose-effect relationship has been demonstrated in many studies where an increase in child abuse leads to worse schizophrenic symptoms and negative effects of the disorder. Emotional abuse seems to show a relationship to schizophrenic symptoms in many studies, while the specific contributions of neglect and sexual abuse to the development of schizophrenia have been mixed. Likewise, the relationship between child abuse and the development of delusions and hallucinations is mixed with some studies reporting a positive association with these symptoms and others not. More research with large populations examining different types of specific types of child abuse and trauma with schizophrenia is in order. Given what is known, however, clinicians working with those suffering from schizophrenia would do well to consider the possibility and effects of child abuse among their clients.

6. Drug Abuse and Schizophrenia

While both schizophrenia and drug abuse typically have onset in adolescence or young adulthood the relationship between them is not clear. It may be that vulnerability to substance abuse disorders and schizophrenia involve a similar neurobiological substrate (Murray et al., 2003; Zullino et al., 2010). Some studies suggest that drug abuse may in fact be causally related to later development of schizophrenia. This is especially likely for dopaminergic substances such as amphetamines, cocaine, and cannabis (Tsapakis et al., 2003; Weiser et al., 2003). Other studies suggest that drug use among people suffering from schizophrenia may be related to emotional abuse and that they use drugs mainly for social reasons (Gearon et al., 2001). Genetically vulnerable individuals who have experienced high stress events, and who use drugs may be especially at risk for developing schizophrenia (P. Miller et al., 2001). Nevertheless, there is also evidence that substance abusers with schizophrenia do not suffer from increased neuropsychological impairments and exhibit fewer negative symptoms (Joyal et al., 2003).

Cannabis use has especially been linked to schizophrenia in a number of studies (Roser, 2019). Cannabis is thought to double the risk of developing schizophrenia in vulnerable people. Heavier dosage and early age of use are associated with increased risk (Ortiz-Medina et al., 2018). A large study of young adults aged 18-34 which looked

at risk factors for schizophrenia found that a diagnosis of schizophrenia was associated with a history of trauma, a family history of drug problems, bisexuality, use of cannabis, cigarettes and alcohol, as well as drug use before the age of 16. The majority of people who developed schizophrenia used both cannabis and cigarettes. The researchers concluded that there was little support for an association between cannabis use and the development of schizophrenia after adjusting for history of trauma, sexual orientation, use of other substances, and family history of substance use. Cigarette use in adolescence and other drug use was associated with schizophrenia. This study demonstrates the importance of including potentially confounding factors when researching the association between cannabis use and schizophrenia (Ryan et al., 2020). These results contradict a slightly earlier study which used a genetic approach to demonstrate a causal relationship between cannabis use and schizophrenia even when accounting for cigarette smoking (Vaucher et al., 2018). As more locations legalize cannabis use the need for research to clarify the causal association between cannabis use and schizophrenia becomes increasingly important. Until more is known it would remain prudent for clinicians to advise against the use of cannabis before or during adolescence and young adulthood, especially if other risk factors are present and there is a family history of schizophrenia. Some good news is that patients suffering a first episode of psychosis who then stopped using cannabis, were able to reverse the worsening of schizophrenic symptoms that could be attributed to cannabis use. This suggests that intervention efforts aimed at getting patients with first episode psychotic breaks, and perhaps individuals with more established schizophrenia, to stop using cannabis could reduce the severity of the disease (Setién-Suero et al., 2019).

7. The Role of Stress, Geography, and Birth Conditions

Stress may play a role in the development of schizophrenic disease (Gomes & Grace, 2018). Immigration and migration, which are highly stressful, are known to increase risk of schizophrenia (Dykxhoorn et al., 2019; Henssler et al., 2020). Elevated prevalence of schizophrenia has been demonstrated in both current and past immigrant populations (Fearon et al., 2006; Henssler et al., 2020; Leão et al., 2006; Shekunov, 2016). Second generation immigrants are also at increased risk for schizophrenia (Bhugra, 2000). A study of Holocaust survivors demonstrated that pre-natal and early life exposure to adversity resulted in a significantly greater risk of developing schizophrenia (Butler et al., 1994).

Researchers have shown a relationship between prevalence of schizophrenia and latitude (Saha et al., 2006). Although a difference in rates of schizophrenia has been noted between developed and developing nations (Bresnahan et al., 2003) and a higher incidence of schizophrenia has been associated with developed nations, economic status of a country by itself was not predictive of incidence of the disease (Saha et al., 2006). However, inequality among the most socio-economically deprived has been associated with an increased incidence of schizophrenia (Peltzer, 1999).

Some research has suggested that season of birth may be related to the development of schizophrenia later in life. This seasonality may be a proxy for stress as well as infection status, maternal hormone levels, sperm quality, etc. (Tochigi et al., 2004). Other research has shown that a mother's pregnancy and birth conditions themselves have a moderate association with the development of schizophrenia in her offspring. Lack of contact with health care professionals, premature birth, infection with influenza virus, preeclampsia, hemorrhage during birth, manual extraction of the baby during delivery, and maternal sepsis during childbirth and the puerperium, all increased the risk of subsequent development of schizophrenia in the offspring. Interestingly, the greatest risk shown in this study was from infection of the mother by the influenza virus (Byrne et al., 2007). Severe obstetric complications have been shown to be related to lower IQ and the development of schizophrenia. It is thought that obstetric complications should be considered as a neurodevelopmental risk factor for severe mental illness (Wortinger et al., 2020).

8. Infectious Disease as a Cause of Schizophrenia

A number of infectious agents have been theorized to cause or trigger the onset of schizophrenia. This theory gained some prominence in the 20th century, with physicians noting the increase in cases of psychosis after the influenza pandemic of 1918 (Hendrick, 1928). Around the turn of the century the so-called 'focal sepsis' theory of mental illness became popular in Europe and the United States. Psychiatrists were eager to identify and treat

(often through surgery) mental illness through the eradication of infection just as physicians were doing successfully in many other areas of medicine. The use of surgical eradication of bacteria to cure mental illness is documented by Scull in the book *Madhouse: A Tragic Tale of Megalomania and Modern Medicine* (2005). In the early 20th century Dr. Henry A. Cotton, a noted psychiatrist and director of a mental hospital in New Jersey, promoted the surgical removal of body parts in order to 'remove' the infection that he was certain caused psychosis and other mental illness in his patients. The organs Dr. Cotton ordered removed included the cervix, gall bladder, ovaries, sinuses, spleen, stomach, teeth, testicles, and tonsils. Dr. Cotton was especially worried about the colon and this organ was often the target of his infection elimination surgery. Many hundreds of patients underwent unnecessary and dangerous surgeries (in pre-anti-biotic times) because of Dr. Cotton's obsession about the infectious causation of severe mental disease. Dr. Cotton reported very high success rates; upwards of 85%. However, these rates were largely anecdotal, and he didn't mention the very high rates of morbidity from the surgeries, not to mention their debilitating effects among the survivors (ironically enough, most morbidity and mortality from the surgeries were due to postoperative infections which were common in the pre-antibiotic era). Dr. Cotton even had his sons' teeth removed in order to prevent them from being infected as a preventative measure to insure their mental health. He also subjected his youngest son to abdominal surgery as a prophylaxis against mental illness and eventually convinced his wife to have all her teeth removed. Dr. Cotton's positive results for treating mental disease through focal sepsis could not be replicated by other researchers. Two very damning reviews of his research and methods were completed, but never disseminated. While Dr. Cotton's work was investigated and prominent psychiatrists involved with the investigation knew the uselessness of his treatment methods, his career remained largely unaffected. He continued in his post until his retirement, after which there was a marked reduction at least in abdominal surgery. The removal of focal sepsis as a treatment for mental disease did not fall out of favor until other treatments such as lobotomy came on the scene (Scull, 2005).

Because of clinicians like Cotton, infection as a causative factor in schizophrenia and psychoses fell out of favor. However, using much more sensitive tools, medicine is turning again to this line of research. Researchers have now proposed that there may indeed be infectious agents that directly affect the development of schizophrenia or, trigger autoimmune reactions that may be related to the disorder (Potvin et al., 2008). Potential schizophrenic infectious agents include *cytomegalovirus*, *herpes simplex virus* (HSV 1 & 2) and *T. gondii* (a parasitic protozoa commonly found in house cats) as well as influenza viruses. Dickerson et. al. (2006) found a relationship between the presence of antibodies to cytomegalovirus and 'deficit' schizophrenia (i.e. schizophrenia with a preponderance of negative symptoms). She did not find any relationships between other viruses and schizophrenia.

T. gondii is a neurotropic protozoan parasite that infects over a billion people around the world. Most people do not notice any ill effects from the parasite although it can cause complications in pregnancy including miscarriage, premature labor, stillbirth, and fetal abnormalities (Rashno et al., 2019). There have been numerous studies showing a relationship between *T. gondii* infection and risk for schizophrenia (Dickerson et al., 2007; Xiao et al., 2018). Best estimates from numerous studies indicate that *T. gondii* infection results in an almost 2.7 times increase in risk for developing schizophrenia compared to non-infected people (Torrey et al., 2012). A genome wide association study found a number of genes associated with *T. gondii* infection were related to neurodevelopment and psychiatric disorders, especially schizophrenia (A.W. Wang et al., 2019). Niebuhr and colleagues (2008) found a significant positive association between *T. gondii* antibodies and diagnosis of schizophrenia among military personnel. Interestingly *T. gondii* infection has been shown to be related to a number of risk-taking behaviors ranging from dangerous driving, suicide attempts, and risky sexual pursuits (Flegr & Kuba, 2016; Sutterland et al., 2019). It may be that *T. gondii*-induced neuronal changes that can cause an escalation in risk-taking behavior may be related to an increased risk of developing schizophrenia.

Studies in Sweden found that viral infection of the central nervous system conferred a slight increased risk of developing schizophrenia and non-affective psychoses while bacterial infection did not. The later development of psychotic illness was specifically associated with the mumps or cytomegalovirus. The authors concluded that there was an association of severe viral central nervous system infection in childhood to viruses that can invade the actual brain tissue (Dalman et al., 2008; Khandaker et al., 2012). Some studies have suggested that the interaction of genes known to have variations related to schizophrenia and viral infection could increase the likelihood of schizophrenia (Beraki et al., 2005). Human respiratory coronaviruses are also known to infect the nervous system.

Therefore, it is possible that there could be a future increase in schizophrenia due to the COVID-19 pandemic (Cowan, 2020; Zandifar & Badrfam, 2020).

Prefrontal cortical structures in the brain have been found to be different among people with schizophrenia depending upon herpes simplex virus 1 (HSV-1) seropositivity (Prasad et al., 2007a). On first-diagnosis, patients suffering from schizophrenic and schizoaffective disorders who were exposed to HSV1 had decreased gray matter in the dorsolateral prefrontal cortex and anterior cingulate cortex when compared to patients suffering from schizophrenia who were not exposed to HSV1. Differences in brain structure that were related to HSV-1 exposure were not found among healthy control subjects. This suggests that HSV1 exposure may be related to changes in brain morphology commonly associated with schizophrenia, independent of medication use, co-morbid chronic illness, and substance abuse (Prasad et al., 2007b).

Animal models have demonstrated the theoretical possibility of pre-natal induced schizophrenia in offspring through a mimicked viral infection (Moreno et al., 2011). Studies in humans have suggested that pre-natal exposure to infectious agents appear to contribute more to subsequent development of schizophrenia than post-natal exposure. In humans, actual viral infection has not been definitively shown to directly cause schizophrenia in the offspring of infected mothers, but there is increasing evidence that it is a contributing factor. For instance, maternal exposure to HSV-2 has been theorized to cause schizophrenia and schizoaffective disorders. Yet, a study by Brown et. al (2006) did not find any support for a relationship between HSV-2 and subsequent schizophrenia and schizoaffective disorder in the offspring of infected mothers. On the other hand, a case-control study, did show a significant increased risk for the development of psychoses among offspring of mothers who had been exposed to HSV-2 (Buka et al., 2008). The risk was even greater if the mothers had high rates of sexual activity during their pregnancy. A study in mice suggests that a disruption of the balance of cytokines in mothers during gestation may lead to neurodevelopmental problems in their offspring (Meyer et al., 2008; Meyer et al., 2006, 2008). Another study with rats has shown that malnourishment in mothers is related to pro-inflammatory factors that may increase the risk of schizophrenia among their offspring (J. Xu et al., 2015). Fatemi et. al. (2008) examined the effects of maternal infection in mice with subsequent effects on brain structure and function in mice. They showed that infection near the end of the second trimester of pregnancy could lead to abnormal gene expression in the brain and subsequent structural defects that could be related to schizophrenia and autism. Mittal et. al. (2008) found that adolescents diagnosed with schizotypal personality disorder who had prenatal exposure to a viral teratogen were at increased risk for developing schizophrenia when compared to a similar group who did not have exposure. They conclude that the risk of psychosis is increased among the offspring of infected mothers. However, they note that mothers of high-risk children tended to over report exposure to infectious disease.

9. Autoimmune Hypothesis of Schizophrenia

In the 1980s, it was proposed that autoantibodies affected neurons in the limbic region of the brain, thereby causing schizophrenia (Knight, 1982). There is now an increasing amount of evidence that supports the idea that schizophrenia may be an autoimmune disease (Severance et al., 2016). A recent study found that the genes responsible for producing the cytokine Interleukin-8 (IL-8) were highly expressed in people suffering from schizophrenia causing greater production of the cytokine when compared to a control group. The results suggest that IL-8 could be responsible for pathophysiological changes in the brain that occur in people suffering from schizophrenia (L. Xu et al., 2018).

Lending credence to the autoimmune hypothesis of schizophrenia, another study found that the presence of many autoimmune diseases increased the risk of developing schizophrenia. Specifically, people suffering from systemic lupus erythematosus had 3.73 times more risk of developing schizophrenia. People suffering from rheumatoid arthritis had 2.89 times increase in risk and those with dermatomyositis had 5.85 times the risk of developing schizophrenia respectively. This contradicts reports that did not find an association between arthritis and schizophrenia (Cullen et al., 2019). Autoimmune vasculitis increased risk of developing schizophrenia by 2.44 times. This study also found that steroid use protected against developing schizophrenia (L-Y. Wang et al., 2018).

Other researchers conducted a meta-analysis of research on the relationship between non-neurological autoimmune (NNAI) disorders and psychoses. They found an overall positive relationship between NNAs and

psychoses. Those with NNAs were 1.26 times more likely to develop a psychosis. However, the specific disorders differed from the previous study cited above. People suffering from pernicious anemia and those with pemphigoid had 1.9 greater odds of becoming schizophrenic, while those with psoriasis, celiac disease, and Graves' disease had 1.7, 1.5 and 1.3 greater odds, respectively, of having schizophrenia. On the other hand, those suffering from ankylosing spondylitis and rheumatoid arthritis had about 0.7 decreased odds for developing the disorder. It is possible that inflammatory pathways, genetics, autoantibodies targeting brain proteins, and exposure to corticosteroids underlie the observed associations (Cullen et al., 2019).

A study of the connection between the genetics of autoimmune disorders and schizophrenia did not find genetic overlap in common single nucleotide polymorphisms which could explain co-morbidity in autoimmune disorders and schizophrenia (Hoeffding et al., 2017). The role of gastrointestinal disorders has been examined as a link between autoimmune disorders and schizophrenia (Severance et al., 2015). It is hypothesized that exposure to wheat gluten and bovine milk casein creates gut inflammation and humeral immunity to food antigens, which occurs early during the course of schizophrenia. The gut inflammation can increase gut permeability which allows gut bacteria to translocate into the circulatory system. This can trigger innate immunity including activation of CIq, which also functions in brain synapses. *T. gondii* infection is also known to initiate gut inflammation and could affect activation of immune responses in the brain in the same way. Immigrants, who are known to be at greater risk for schizophrenia, may be forced to modify their diets in a way which promotes gut inflammation and immune system activation affecting the brain. The authors conclude that an understanding of the disrupted microbiome can provide useful models of brain pathogenesis (Severance et al., 2016). A better understanding of the role of gut pathogens, the microbiome and their effects on the brain could lead to immunologic and microbial methods of prevention and treatment (Severance & Yolken, 2020).

10. Neurobiology of Schizophrenia

Much research is focused on the role of neurobiology in schizophrenia. However, the relationship of neurobiology to understanding the causes of the disease is still being debated (Brambilla & Tansella, 2007). While neurobiology is undoubtedly important, it is thought that the etiology of schizophrenia is multi-factorial (K. Dean et al., 2003).

The neurotransmitter dopamine has long been suspected as a key component of schizophrenic pathology. The so-called 'dopamine hypothesis' of schizophrenia grew from the observation that drugs that increase the activity of dopamine in the brain can also induce psychosis. Conversely drugs that block dopamine receptors were found to reduce psychotic symptoms (Baumeister & Francis, 2002). Briefly, the dopamine hypothesis asserts that in normal people the prefrontal dopamine system controls the limbic dopamine system through suppression. In individuals suffering from schizophrenia the activity of the dopaminergic neurons in the pre-frontal dopamine system is reduced causing overactivity of the limbic dopamine system. The reduced activity of the prefrontal dopamine neurons is responsible for the negative symptoms of schizophrenia while the overactivity of the limbic basal ganglia dopamine system is responsible for the positive symptoms of the disease. (Gründer & Cumming, 2016; Ohara, 2007).

Some studies have demonstrated increased dopaminergic activity in the mesolimbic pathway of the brain as well as abnormalities in cortical cholinergic transmission in people with schizophrenia (Masciotra et al., 2005; Sarter et al., 2005). Other neurotransmitters may work in concert with dopamine to form the basis of schizophrenic pathology. In normal people the action of dopamine is mediated by receptors on pyramidal and local circuit neurons that stabilize cortical representations of external and internal stimuli. In people with schizophrenia this mediation effect may be reduced, and along with dysfunction in gamma aminobutyric acid (GABA) and glutamate transmission, may contribute to cortical dysfunction (Winterer, 2006).

A number of studies suggest that dysfunction in the neurotransmitter GABA may be important in understanding schizophrenia. Abnormal GABA transmission in the brain may be related to cognitive, affective, sensory and motor problems in people with schizophrenia. A study assessing expression levels of GABA-related genes in the dorsolateral prefrontal cortex, anterior cingulate cortex (ACC), primary motor cortex, and primary visual cortex found reduced gene expression among subjects suffering from schizophrenia when compared to healthy controls. The authors concluded that since the areas studied represent major functional areas of the cortex, abnormality of

GABA transmission may be a contributing factor to a number of different schizophrenic symptoms (Hashimoto et al., 2008). An imaging study using proton magnetic resonance spectroscopy found lower levels of GABA in the ACC and frontal cortex of patients suffering from schizophrenia when compared to healthy control subjects. These differences were especially pronounced in first episode patients with schizophrenia (Kumar et al., 2020).

Some speculation related to the dopamine hypothesis suggests an important role for the N-methyl-D-aspartate (NMDA) receptor for the neurotransmitter glutamate, as these receptors regulate dopamine neurons in the cortex. Inhibition of the functioning of these receptors can bring about both the positive and negative symptoms of schizophrenia. This NMDA receptor hypofunction hypothesis of schizophrenia is supported by the observation that drugs like PCP, which reduce NMDA function, cause both negative and positive schizophrenic symptoms (Jentsch & Roth, 1999). Nevertheless, there are still issues to be worked out with this approach (Gilmour et al., 2012). There is some evidence that GABA-A receptors are disrupted in patients suffering from schizophrenia. There is some clinical evidence that when benzodiazepines, which act on GABA-A receptors, are administered with antipsychotic medications, better therapeutic outcomes are achieved than with antipsychotic medication alone (Włodarczyk et al., 2017).

There is an increasing amount of evidence that points to the role of limbic-cortico-striatal glutamate transmission pathology as an underlying basis for schizophrenia. A review of the literature by Szumlinski & Kippin (2008) lists six findings that support this theory: smaller cortical volumes, reduced glutamatergic unmyelinated neuronal processes, fewer dendritic spines, pyramidal cell disarray, expression alteration in glutamate receptor subtypes, and reduced expression of cortical synaptic proteins. They go on to explain that the mainstream view is that these glutamate abnormalities in schizophrenia cause hypofrontality, or a reduction in cortical activity and activation. The authors also note that there are other theories that hold the opposite view; i.e. that glutamate hyperactivation caused by a disinhibition of glutamate transmission underlies the psychotic and cognitive abnormalities present in schizophrenia.

Serotonin receptor pathology in the cortex has been hypothesized to be associated with schizophrenia and other illnesses such as bi-polar disorder. Alteration of serotonin receptors may be subtle and may differ according to gender (Gray et al., 2006). Studies examining the contribution of genetic variation of serotonin-related receptors to schizophrenia have indicated that certain alleles, as well as the synergy among different alleles, may increase susceptibility to schizophrenia (Lorenzo et al., 2006). Serotonin (5-HT) function, which is known to be related to aggressive behavior in general, may also be related to aggressiveness among people suffering from schizophrenia (Barkan et al., 2006).

Other serotonin receptors may play a role in schizophrenia. Dean and his colleagues have shown that decreased levels of serotonin-sub-7 receptors in Brodmann's area 9 may be related to schizophrenic pathology in a post-mortem study of patients suffering from schizophrenia and in rats. These results are supported by the fact that cortical serotonin-sub-7 and -sub(1D) receptors are affected by antipsychotic drugs among individuals suffering from schizophrenia (Barkan et al., 2006; B. Dean et al., 2001, 2006). Additional studies have found that variations in serotonin transport related genes may be associated with increased susceptibility to schizophrenia as well as suicidal behavior among individuals suffering from schizophrenia (De Luca et al., 2006; Fan & Sklar, 2005). Antipsychotic drugs which are partial agonists to serotonin-5-HT-sub(1A) receptors, have improved cognition, including attention, executive function, verbal learning, and memory in some studies with patients suffering from schizophrenia (Sumiyoshi et al., 2007). Other drugs targeting serotonin reuptake inhibition have not been definitively shown to be useful in treating the negative symptoms of schizophrenia. A meta-analysis examining well-designed studies found that the negative symptoms of schizophrenia did not improve when medication was augmented with serotonin reuptake inhibitors. While some studies have shown alterations in the 5HT-sub(1a) receptor binding parameters in schizophrenia patients at post-mortem, a study with living patients did not find any relationship between schizophrenic symptoms and 5HT-sub(1a) binding (Sepehry et al., 2007). Therefore, there is some question about the role of 5HT-sub(1a) receptors in the pathophysiology of schizophrenia (Frankle et al., 2006). Other studies have not found any association between 5-HT receptor polymorphism and schizophrenia (Kapelski et al., 2006).

11. Brain Structure and Schizophrenia

The ACC has been identified as a key area in the pathology of schizophrenia. Most studies of the ACC have focused on fairly simple measurements such as volume when comparing individuals suffering from schizophrenia to normal controls. One study using case control methodology and a novel scanning method was able to show reduced bilateral thickness in the paralimbic region of the ACC along with increased surface area in both the limbic and paralimbic ACC among subjects suffering from schizophrenia. No differences were found in grey matter volume, surface curvature, or central sulcus depth. This study illustrates the rapidly increasing sophistication of brain structure studies of schizophrenia (Fornito et al., 2008).

Limbic system pathology has become one of the focal areas of research in schizophrenia. Limbic areas of the brains in adults suffering from schizophrenia differ consistently from healthy people, but areas outside the limbic system also show differences. Children and adolescents with schizophrenia, however, tend to just have differences in the limbic system as opposed to the whole brain. This has led to the hypothesis that brain pathology associated with schizophrenia starts in the limbic system and then spreads over time. It also may be the case that the limbic pathology is just be part of a more global brain abnormality (White et al., 2008).

A number of studies have now shown that people suffering from schizophrenia have both anatomical and functional brain-wide connection dysfunction when compared to healthy people. These dysfunctions are thought to be the main mechanism for the pathophysiology of schizophrenia (Wotruba et al., 2014). One study found a decrease in the connections within and between limbic structures. There was also observed reduction in fibers connecting to the left fronto-temporal region in people suffering from schizophrenia when compared to healthy subjects. This is thought to be evidence for the fronto-temporal dysconnectivity hypotheses of the pathogenesis of schizophrenia (Ottet et al., 2013).

Research using functional magnetic resonance imaging (fMRI) has been used to compare resting state effective connectivity (rsEC) and resting state functional connectivity (rsFC) in people suffering from schizophrenia with healthy control subjects. Seventeen disruptions in rsEC were found in patients suffering from schizophrenia. These rsEC disruptions were associated with the thalamus and pathways from the limbic areas (including the hippocampus, parahippocampus, and cingulate cortex) to the thalamus. Among patients suffering from schizophrenia rsFC abnormality was found to be distributed throughout the whole brain. Since rsEC provides information about the directionality of connections in the brain, the idea that schizophrenia can be characterized by disruptions in the limbic areas that spread to the thalamus is not far-fetched. It should be possible to use rsEC and rsFC patterns in combination as diagnostic markers for schizophrenia (Hua et al., 2020).

A recent systematic review of the research literature by Gault et. al. (2018) provides much evidence that schizophrenia is caused by problems in the dopaminergic circuitry in the brain. The dopamine D receptor gene (DRD2) which exists in the highest quantities in the striatum, is part of the reward circuitry. Abnormalities related to the reward circuit have been associated with schizophrenia. Blockage of the DRD2 receptors by antipsychotic medication has been shown to normalize the reward circuitry and reduce schizophrenic symptoms. Because of the high concentrations of DRD2 in the striatum these areas of the brain could be targets for therapies that seek to normalize striatal dopaminergic circuitry. Also, abnormality in circuitry between the striatum and frontal and temporal lobes of the brain may contribute to negative and cognitive symptoms of schizophrenia. Structures that provide input to the striatum including the ventral tegmental area and hippocampus, as well as structures receiving signals from the striatum such as the basal ganglia, may also contribute to dopamine circuitry pathology. Based on the research literature, seven models of schizophrenia related dysfunction based on the above circuit abnormalities are hypothesized. These models suggest ~~that~~ intervention sites for new treatment technologies like deep brain stimulation (DBS).

12. Recent Findings Associated with Cognition and Schizophrenia

Cognitive impairment is key feature among people suffering from schizophrenia. In general, studies of cognition among people suffering from schizophrenia can be conceptualized into two areas, non-social and social cognition. Non-social cognition includes processing speed, verbal and visuospatial learning and memory, working memory,

attention/vigilance, and reasoning/problem solving. People suffering from schizophrenia demonstrate impairments in all of these cognitive domains as well as having impairments in perception. Studies of people with schizophrenia have shown that patterns of cognitive impairment in schizophrenia differ from other disorders such as dementia and bipolar disorders. The cognitive impairments that accompany schizophrenic illness have negative effects on how well people suffering from schizophrenia are able to function. Diminished functionality among people suffering from schizophrenia include the ability to take care of themselves, to work and hold down a job, and the ability to acquire important skills related to rehabilitation (Green et al., 2019). Antipsychotic medication is known to induce cognitive decline as well as other side effects related to greater morbidity and mortality (Agbeli, 2020). Moran et. al. (2020) compared cognitive performance among individuals with schizophrenia who were taking antipsychotic medication and not taking antipsychotic medication, with healthy subjects. Given the role of dopamine in reinforcement-based learning it was thought antipsychotic medication might be responsible for some cognitive deficit. The study found that both medicated and non-medicated subjects suffering from schizophrenia had pervasive cognitive deficits when compared to healthy subjects. Deficits were found in reinforcement learning, processing speed, cognitive control, working memory, verbal learning, and relational encoding and retrieval. This study demonstrates that cognitive deficits are attributable primarily to schizophrenic disease and not antipsychotic medication. However, another study by Albert et. al. (2019) found that patients suffering from schizophrenia who discontinued antipsychotic medication had better cognitive functioning than those who did not stop taking antipsychotic medication. Another study by Fu et. al. (2019) demonstrated that people suffering from schizophrenia who discontinued antipsychotic medication because of negative side effects had improved cognition. Many of these patients were then able to use active coping mechanisms to maintain their recovery. It may be that some patients suffering from schizophrenia have differing cognitive responses to antipsychotic medication depending on their genotype (Nelson et al., 2018).

It is likely that there are overlapping biological pathways in schizophrenia and normal cognitive ability. Genes associated with cognitive performance have been found to be related to genes associated with increased risk of schizophrenic disease. These genes play a role in neurotransmitter systems that are important to cognitive performance (Koch et al., 2020).

It may be the case that cognitive impairment in childhood can be predictive of later development of schizophrenic illness (Dickson et al., 2020). This is important because early identification of schizophrenic risk could help identify those who might benefit from interventions to improve cognitive abilities. Psychoeducational and therapeutic interventions have been shown to lessen the impact of cognitive impairment in people suffering from schizophrenia. It is not known if these interventions work on the social and functional impairments that result from cognitive impairment or whether the techniques work directly to improve cognitive impairment itself. Regardless, psychoeducational and therapeutic interventions have been shown to improve the quality of life for people suffering from schizophrenia (Maurel et al., 2011).

Sleep disorders are common among people who suffer from schizophrenia. Laskemoen et; al. (2020) found sleep disturbances among people with schizophrenia were related to cognitive impairment. Processing speed and inhibition, which are related to insomnia and hypersomnia, were associated with cognitive impairment in patients suffering from schizophrenia. This suggests that treating sleep disturbances may help cognitive functioning in people suffering from schizophrenia.

13. Social-Cognitive and Emotional Recognition Impairment in Schizophrenia

Burns (2007) in his book *The Decent of Madness*, presents an argument that schizophrenia is the by-product of the evolution of the human brain. The same genes that evolved to give humans a highly social brain are also responsible for the potential development of schizophrenia in our species. Enhanced social-cognitive skills gave early humans a huge fitness advantage and were therefore selected for during evolution even though, for a small percentage of the population, this genetic gift could go awry and cause schizophrenia. The ability to read emotional states in others is an important social-cognitive skill that has survival value for humans. Individuals suffering from schizophrenia are known to have difficulty in reading emotions in others, especially facial affect. A study by Gur, et. al. (2007) demonstrated that when patients diagnosed with schizophrenia performed an emotional identification task, they showed reduced activation of the limbic system compared to healthy controls. For healthy people correct

identification of threat-related facial expressions was associated with increased amygdala activation. Patients suffering from schizophrenia reacted just the opposite, showing decreased activation of the amygdala when confronted with threat expressions. When presented with fearful faces subjects suffering from schizophrenia responded with increased amygdala activation, but with a flat affect. The authors theorized this reaction might be related to overstimulation of the limbic system. They concluded that the abnormal activation of the amygdala in response to threat and fearful facial expression could lead to misidentification of emotions in others.

Another study examined subjects suffering from schizophrenia and normal subjects while they engaged in tasks involving intuitive and cognitive emotional conditions. When subjects suffering from schizophrenia performed the emotional recognition tasks the limbic areas of the brain related to processing of emotions failed to activate. Subjects suffering from schizophrenia showed reduced activation in areas of the brain related to holistic processing of facial features and instead showed increased activity in brain regions that analyze facial features. The results suggest that subjects suffering from schizophrenia lack the ability to intuitively read affect in others and compensate for this loss by using a more cognitive approach to identifying features related to emotions in others (Fakra et al., 2008). Another study examining gaze discrimination impairment found that subjects suffering from schizophrenia and healthy control subjects have similar gaze discrimination abilities. Yet the people suffering from schizophrenia showed reduced brain activity in areas related to executive, emotional and visual processing. When performing more difficult tasks, the healthy control subjects showed increased activation in the frontal and temporal regions of the brain. Increased activation was found in people suffering from schizophrenia when they were directly gazing at another face. The authors conclude that the results may be related to the problems people with schizophrenia have in interacting with other people (Kohler et al., 2008).

A study examining the disconnection of the autonomic arousal in the amygdala related to fear found individuals suffering from schizophrenia had abnormally increased arousal along with reductions in emotion-specific regions and the medial pre-frontal cortex. The authors concluded that when confronted with signals for danger the central and autonomic processing in people suffering from schizophrenia is disconnected. This type of dysfunction might be related to paranoid symptoms such as delusions (Williams et al., 2007). Some of this dysfunction could be related to suboptimal parental bonding in people suffering from schizophrenia. As mentioned above, people suffering from schizophrenia are more likely to have experienced childhood trauma and to have impairments in parental bonding and social cognitive skills. Physical neglect was found to be especially predictive of impairment in emotional recognition. However, optimal parental bonding attenuated the negative impact of childhood trauma on emotional recognition (Rokita et al., 2020).

14. Treatment of Schizophrenia

Historically, schizophrenia has been treated with a wide variety of modalities which were not especially effective. Trepanation, exorcism, beating, spinning, and hydrotherapy (immersion in both hot and cold water) were some of the early treatments for schizophrenia (Braslow, 1999; González de Chávez, 2009; Høyersten, 1996; Whitaker, 2002). Treatments such as immersion in water continued well into the modern era and could be brutal and dangerous².

Physical torment, especially in the form of beatings has dogged people suffering from schizophrenia throughout history (Whitaker, 2002). Like hydrotherapy, beating has only lately gone out of style even though it has long been outlawed. Beating was not so much a treatment but a form of patient management. Other forms of violence served as ways to manage patients into compliance while masquerading as treatments.

15. Neuromodulation

By the late 19th and early 20th centuries new treatments were being invented to treat schizophrenia and other severe mental illnesses. Primitive neuromodulation treatments in the form of convulsive therapies using insulin,

² My current position is at the site of a former mental hospital. When I first arrived, I was directed to go to an old hospital building which was being used as a warehouse where office furniture was being stored. There among the desks and chairs was a hydrotherapy apparatus that had been used with patients suffering from schizophrenia, presumably until the hospital had closed down in the late 1990s.

Cardiazol, Metrazol, and eventually electricity became routine for people suffering from schizophrenia. These forms of convulsive therapies were considered to reduce psychotic symptoms. Electroshock (ECT) became the preferred method because it was cheap and thought to be less dangerous than the other methods. ECT was thought to work by damaging the brain, causing the stripping away of the intellect. Psychotic symptoms were abated but this was short lived requiring further sessions and further damage to the brain. ECT could be especially dangerous when multiple sessions were administered over a short period of time. Strong muscle convulsions also caused bone breakage in up to 40% of patients (Whitaker, 2002).

While ECT is still used in psychiatry it has become much safer with the concurrent administration of muscle relaxants, lower current, and the use of ultra-brief pulsed stimulation which is not thought to cause permanent brain damage. Modern ECT is mostly used to treat pharmacoresistant mood disorders but has been used to treat schizophrenia as well. ECT is also used to treat schizophrenia in parts of the world where antipsychotics are not practical for financial reasons (Gazdag & Ungvari, 2019). There are positive anecdotal reports as to clinical effectiveness of treating schizophrenia with modern ECT though large studies are lacking (Rado & Hernandez, 2014). Research evidence is emerging for the effectiveness of modern ECT in treating pharmacoresistant schizophrenia. A small study by Thomann et. al. (2017) used modern ECT with pharmacoresistant patients suffering from schizophrenia and major depressive disorder (MDD) to research changes in brain structure and function. Right-sided unilateral ECT was found to change brain structure and function regardless of diagnosis. All patients in the study experienced improvement in their clinical symptoms. Seven patients suffering from MDD achieved remission and the other four experienced at least a 50% improvement. Four patients suffering from schizophrenia experienced at least a 50% improvement while the other five subjects experienced 25% improvement at minimum.

Other non-invasive methods of neuromodulation have been developed in recent years, but they are primarily used for treating mood disorders and are not thought to be as effective as modern ECT:

“Additional non-invasive therapies include magnetic seizure therapy, which focally induces the superficial cortex to produce seizures, repetitive transcranial magnetic stimulation, involving the pulse application of magnetic stimuli to alter cortical excitability, and vagal nerve stimulation, which sends electrical impulses to various brain regions via the solitary nucleus...The role for these alternative treatments remains unclear, as ECT is generally considered clinically superior.” (Staudt et al., 2019, p. 4)

Nevertheless, Poulet et. al. (2008) report that the use of transcranial magnetic stimulation (TMS) reduced resistant auditory hallucinations. A study by Fröhlich and Lustenberger (2020) speculates that non-invasive neuromodulation may be able to correct sleep abnormalities among people suffering from schizophrenia. Rado and Hernandez (2014) report that TMS combined with a small amount of electric current shows promise in treating schizophrenia.

16. Psychosurgery

Beside convulsive therapies, the other treatment that was widely used to treat schizophrenia was psychosurgery. Staudt et. al. (2019) have given an excellent review of the history of psychosurgery and the section below is mostly drawn from their work. Burckhardt first reported performing the excision of regions of the brain with six patients. After being inspired by research on the removal of the frontal lobes in primates, Portuguese physicians Edgar Moniz and neurosurgeon Almeida Lima developed a procedure for creating lesions in the frontal lobes called a leucotomy. This was used to treat depression, anxiety, and aggression. In the United States the neurologist-neurosurgeon team of Walther Freeman and James Watts refined Moniz' procedure and renamed it the prefrontal lobotomy. A minimal form of the procedure was used for patients with affective disorders while a more invasive radical form was used for people suffering from schizophrenia. Freeman later adopted the technique of transorbital lobotomy which was developed by Italian psychiatrist Amaro Fiamberti. This technique involved sedating the patient with ECT, inserting an “ice-pick” like instrument through the orbital socket, and performing sweeping motions to destroy areas of the frontal lobes of the brain. This operation could be done by minimally trained physicians without the need for a surgeon or anesthesiologist and without the need for a specialized operating theater. Freeman ambitiously advocated for the technique and it became quite popular. Transorbital lobotomies

were performed throughout America and Europe. It is estimated that Freeman himself performed over 3000 procedures from the 1930s through the 1960s, with tens of thousands performed around the world (Caruso & Sheehan, 2017). Freeman claimed almost miraculous results from transorbital lobotomies, but as in many of the early treatments what counted as success was highly questionable and biased by the lack of scientific study. Some of Freeman's patients claimed long term improvement but this was not the majority. It is likely that patients had a very different view about what was considered a cure or improvement than many mental health professionals. For the latter, a positive outcome was anything that made patients easier to manage. The book *One Flew Over the Cuckoo's Nest* (Kesey, 1963) and subsequent film (Forman, 1975), dramatically illustrates this.

Freeman performed his last transorbital lobotomy in 1967 on a patient that had twice previously had the procedure. Unfortunately, he nicked a blood vessel and the patient died. Shortly thereafter, Freeman retired from practice and drove around the country in his recreational vehicle interviewing former patients about their positive experience with the operation. It is interesting to note that over time Freeman relaxed the indications for the transorbital lobotomy. He increasingly saw it as a panacea and by the end of his career he was lobotomizing children. In one notable case he lobotomized a 12-year-old boy who was having problems adjusting to the death of his mother and getting along with his stepmother (Dully & Fleming, 2007). Many physicians were not enthusiasts about transorbital lobotomies and when the first antipsychotic medication, chlorpromazine (trade name Thorazine) became available (and marketed as a lobotomy in a bottle) it was enthusiastically adopted as the primary treatment for schizophrenia (López-Muñoz et al., 2005).

More precise forms of psychosurgery are still performed in very few cases but are mostly used to treat obsessive-compulsive disorder (Brakoulias et al., 2019). Nevertheless, the idea of using psychosurgery to treat schizophrenia has recently re-emerged, albeit in a far more subtle and less invasive forms. Deep brain stimulation (DBS) which involves placing an electrode which can deliver a small amount of current directly into the brain is now being proposed as a treatment for schizophrenia. In one study DBS was shown to prevent the emergence of sensorimotor gating, attentional selectivity, and executive functioning deficits in a rat model of schizophrenia (Hadar et al., 2018).

Gault et. al. (2018) review the growing interest in using neuromodulation via DBS to treat schizophrenia. As mentioned previously, they report on seven models of predominantly striatal dysregulation that provide possible therapeutic targets. The authors report that DBS could be used to correct dysregulation in these target circuits as well as treat areas of the brain related to tardive dyskinesia (a side effect from antipsychotic medication) and negative and cognitive symptoms of schizophrenia. Highlights of their research reports include the following studies:

In two reports where DBS was used in the ventral cortex and ventral striatum. The first report was a patient who suffered from OCD and residual schizophrenic symptoms. While the negative symptoms of schizophrenia did not change for this patient, their OCD symptoms and psychosocial functioning improved 25%-58%.

The second patient who suffered from schizophrenia was part of a clinical trial using DBS to alleviate symptoms in treatment-resistant schizophrenia. This study used a protocol with patients randomized to receive DBS at either the medial prefrontal cortex or nucleus accumbens. DBS stimulation would then remain on for three months, after which responsive patients would be crossed over to either a stimulation on or stimulation off group. This was a small trial of eight planned patients. The one patient to finish the trial demonstrated a 62% reduction in positive symptoms and a 33% improvement in negative symptoms. This patient initially received bi-lateral stimulation after adjusting to unilateral left sided stimulation. However, bilateral stimulation caused akathisia and the patient was returned to unilateral stimulation which resulted in a relapse of negative symptoms. Positive symptoms remained improved.

Another trial is slated to target the pars reticulata of the substantia nigra in order to modulate activity in the basal ganglia, as well as the medial dorsal and lateral prefrontal cortex. This may normalize medial dorsal activity and improve both cognitive and positive symptoms of schizophrenia. Lastly, a trial that was to use DBS targeting the ventral striatum and ventral tegmental area closed due to an inability to enroll patients.

A prospective, non-control group study treated schizophrenia with capsulotomy. This therapy, which has been used for severe cases of treatment-resistant OCD, involves the bi-lateral destruction of brain tissue in the internal capsule. The study reported improvement in 74% of patients suffering from schizophrenia.³

In their review Gault et. al. (2018) argue that people suffering from schizophrenia should have access to the possible benefits of DBS, but also caution that patients suffering from severe schizophrenia may not have the capacity to consent to such an invasive procedure.

17. Antipsychotic Medication

Since the 1950s schizophrenia has been generally treated with a variety of antipsychotic medications that alleviate the symptoms of the disease, but not the underlying pathology. Most of these drugs work by suppressing dopamine activity in the brain, and because of this, have many serious side effects such as tardive dyskinesia (Baumeister & Francis, 2002). While newer antipsychotic medications also affect the function of other neurotransmitters (B. Dean et al., 2006; Hagiwara et al., 2008), dopamine targets still play a key role in the newer drugs that treat schizophrenia (Seeman, 2000). The fact that newer second-generation antipsychotic drugs do not seem to be more effective than first generation antipsychotic drugs supports the importance of dopamine as a target for medication (Lewis & Lieberman, 2008; Lieberman et al., 2005). Unfortunately, second generation antipsychotic medications also retain many of the side effects of the first-generation drugs (Divac et al., 2014). Nevertheless, dopamine agonist antipsychotic medications have the best evidence for effectiveness in treating schizophrenia (Tandon et al., 2010).

While treatment with antipsychotic drugs has been in existence for almost 70 years, there are still many important unanswered questions related using them to treat individuals with schizophrenic and other psychotic disorders. Questions related to choice of drug, dosage, when and if another drug should be tried, monitoring the effects of the drug treatment, and whether drugs can halt or slow the progression of the illness remain without definitive answers. While medicine in general has been moving towards 'evidence based' treatment, the treatment of people suffering from schizophrenia largely remains precedent and experientially based – i.e. based on what an individual physician was taught and what they intuit to be best for a given patient (Davis & Leucht, 2008; Kane & Leucht, 2008).

Many people who suffer from schizophrenia may need to be hospitalized at some time in their lives. Hospitalization allows the patient to stabilize and receive regular doses of medication and is generally short in duration. However, when medication compliance is poor, patients suffering from schizophrenia may de-stabilize once they leave the inpatient setting and require re-hospitalization. This creates a 'revolving door' through the mental health system. A recent study supports this view, demonstrating that patients suffering from schizophrenia who take their antipsychotic medication on a regular basis have fewer and shorter incidences of hospitalization (dosReis et al., 2008).

Most currently available antipsychotic medications are primarily effective against the positive symptoms of schizophrenia. Negative and cognitive symptoms have been more difficult to treat. So-called second generation or atypical antipsychotic drugs have not proven themselves to be more effective than first generation antipsychotic medications in dealing with these symptoms (Lieberman et al., 2005). It may even be the case that first generation antipsychotic drugs are superior to second generation antipsychotics (Foussias & Remington, 2010).

A review by Krogmann, et. al. (2019) outlines a number of mono and add-on therapeutic agents are now being examined for their ability to treat schizophrenia. Some of these drugs are targeted towards positive and negative symptoms, negative symptoms alone, and residual and treatment-resistant positive symptoms. These drugs include dopamine receptor 1, 2 and 3 (D1, D2, D3) agonists, 5-hydroxytryptamine (serotonin) receptor (5HT) agonists and

³ Capsulotomy has been used for a number of years for people suffering with treatment resistant OCD. One study of 19 severe OCD patients receiving capsulotomy had 37% fully responded to the surgery (meaning their OCD scores improved by at least 35%), while 10% had a partial response (i.e. their OCD scores improved by 25%). Three patients achieved remission. More than half the patients did not respond. These patients had suffered severe OCD for a longer time. Capsulotomy is not without risk. Two patients in the study suffered permanent complications including paralysis and cognitive impairment (D'Astous et al., 2013). Given the success rate and risk of capsulotomy, DBS, which is thought to be just as effective, may be a more promising treatment.

inhibitors, a dopamine receptor 1-regulated NMDA (glutamate) receptor and α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (glutamate) receptor (AMPA) agonists, phosphodiesterase 10A enzyme (PDE10A) inhibitors, trace amine-associated receptor 1 (TAAR1) agonists, a nitric oxide donor, a sigma2 receptor (which is highly expressed in malignant cancer cells) antagonist, an alpha1-adrenergic (which is involved in norepinephrine and epinephrine signaling) antagonist, and a D-amino acid oxidase (DAAO - which produces ammonia and hydrogen peroxide that affect the brain) inhibitor. In addition, a number of existing antipsychotic drugs have been reformulated into long lasting and injectable formulations to improve adherence to antipsychotic medication regimens. Lastly a μ -opioid receptor antagonist is being tested to reduce Olanzapine-induced weight gain, associated cardiovascular issues, and (one assumes) constipation. The clinical trial results for these new therapeutic agents has been mixed. While progress has been made, challenges remain in finding a balance between side effects and adherence to the medication regimen for dopamine modulating medications. With regard to non-dopamine modulating novel drugs the authors state:

“These studies will need to prove that, in fact, such non-dopamine modulating agents can improve negative symptoms while maintaining positive symptom stability, despite the removal of the prior dopamine modulating antipsychotic agent that at one point was needed to reduce schizophrenia symptoms.” (p. 63)

They conclude that despite an urgent need for better pharmacological agents to treat schizophrenia, these will likely not be forthcoming until the pathophysiology of the disease is better understood.

18. Anti-Inflammatory and Immunomodulating Agents

As described above, immunity, autoimmunity, and inflammation may play a role in schizophrenia. The evidence linking autoimmune disorders and schizophrenia suggests that immunosuppressive therapies might be helpful in treating schizophrenia (Chaudhry et al., 2015; Knight et al., 2007). However, immunosuppressive therapies have had mixed results. It does seem that at least some cases of schizophrenia have an immunological component and that prevention of immune triggers may be helpful for high risk populations (Richard & Brahm, 2012). Evidence exists indicating there are abnormalities in cell-mediated processes, acute phase proteins, cytokines, and intracellular mediators among people suffering from schizophrenia. One study found that pro-inflammatory cytokines are increased in the blood of schizophrenic patients. Antipsychotic medication was not found to be a confounding factor (B. Miller et al., 2011). C-reactive protein (CRP) may be a marker for low-grade neuroinflammation which can become chronic, damaging the microvascular system in the brain and reducing cerebral blood flow (B & Tk, 2014).

Maternal immune activation can lead to prenatal exposure of pro-inflammatory cytokines, which can in turn cause both acute and long-term changes in neurobehavioral development. These present possible pre-natal targets for reducing susceptibility for developing schizophrenia. Treatment targets include neuroprotection and functional enhancement to prevent abnormal structural and functional changes in the brain, reduction of oxidative stress and toxicity, reduction of pro-inflammatory cytokines, increase in anti-inflammatory cytokines, modulation of microglia function, and reduction of environmental stressors (Hong & Bang, 2020).

New treatments based on immunosuppression, immunomodulation, and neuroinflammation are theoretically promising but have yet been proven. Medications or substances that have anti-inflammatory, immunomodulation or neuroprotective effects could be repurposed. These include davunetide (an eight amino acid peptide with neuroprotective qualities), IFN- γ -1b (an interferon used to treat multiple sclerosis), mesenchymal stem cells (which can change microglia from an activated to an anti-inflammatory state), minocycline (an antibiotic with anti-inflammatory effects), monoclonal antibodies (which have anti-inflammatory effects), non-steroidal anti-inflammatory drugs (NSAIDs), omega 3 fatty acids (which have anti-inflammatory effects) and statins (which have anti-inflammatory effects). Other substances could include antioxidant supplements like N-acetylcysteine (which may be neuroprotective), herbal substances such as cannabidiol (the anti-inflammatory non-THC component of the cannabis plant), and foods thought to reduce inflammation. It is possible these could be used in combination and in conjunction with standard pharmacotherapies. It is also possible that optimal use of

antipsychotic medication could help reduce inflammation.⁴ Also, targeting immune and anti-inflammatory therapies to specific bio-markers and specific clinical sub-groups could provide a more personalized, and hopefully, more effective approach to treating schizophrenia (Hong & Bang, 2020; Krogmann et al., 2019; Pandurangi & Buckley, 2020; Sommer et al., 2012).

The role of immunity in the development of schizophrenia continues to be a promising area of research not only for treating schizophrenia but also for its prevention (Dickerson et al., 2017). If a microbial trigger could be found for schizophrenia, it is possible that a vaccine could be developed against the trigger, thereby preventing the disease (Adams et al., 2012). Clearly, more research on the relationship between immunity, schizophrenia, and immunity-mediating treatments needs to be done.

19. Psychotherapeutic Approaches to Treating Schizophrenia

Supportive psychotherapy is sometimes offered to people with Schizophrenia; however, this is usually to help patients cope with the disease rather than treating the disease itself. A recent review found that supportive therapy was not any better than standard care and less helpful than a variety of psychotherapeutic approaches (Buckley & Pettit, 2007). However, supportive care in a group setting has been shown to be useful (Nightingale & McQueeney, 1996).

There is growing use of cognitive-behavioral therapy (CBT) with patients suffering from schizophrenia. This use of CBT is usually done in concert with the use of antipsychotic medication and has demonstrated a general reduction in symptoms with especially good results in reducing positive and residual symptoms and strengthening reality testing. Depression is also seen as amenable to treatment using CBT among people suffering from schizophrenia (Sudak, 2004; Turkington et al., 2003, 2004; Warman & Beck, 2003). CBT group therapy has also been tried with patients suffering from schizophrenia. Some studies have shown improvements in overcoming social phobia and depression, but the results are not definitive (Lawrence et al., 2006). Another study demonstrated a reduction in feelings of hopelessness and low self-esteem using CBT in a group setting with patients suffering from schizophrenia (Barrowclough et al., 2006). In a study of a single patient who suffered from schizophrenia and pathological gambling, CBT combined with medication awareness training was found to reduce the severity of psychotic and pathological gambling symptoms, as well as improve psychosocial functioning and dispositional mindfulness (Shonin et al., 2014). A study of 16 patients suffering from schizophrenia spectrum disorders examined the effects of a form of CBT that was manualized and adapted to psychotic patients. The researchers found a reduction of delusional symptoms as well as a decrease in depressive symptoms (Lamster et al., 2018). The effects of CBT tailored to treat insomnia was examined among patients suffering from schizophrenia and insomnia. This study examined three types of insomnia in patients suffering from schizophrenia; classic severe insomnia, insomnia with normal sleep duration, and insomnia with hypersomnia. Patients with classic severe insomnia showed marked improvement in total sleep time while patients suffering from schizophrenia with insomnia and hypersomnia showed reductions in total sleep time. Patients suffering from schizophrenia with insomnia but normal sleep duration had a blunted response to CBT (Chiu et al., 2018).

Jauhur et. al. (2014) conducted a meta-analysis of the effectiveness of CBT for people suffering from schizophrenia. This study pooled data from randomized trials, controlling for randomization, masking of outcomes, incompleteness of data, use of a control, and publication bias. Results demonstrated that the therapeutic effect of CBT is small. In a comment on this study Gold (2015) notes that the data do not show much relationship between positive therapeutic outcomes and the number of sessions. He even suggests that there may be an inverse relationship with better outcomes coming from fewer sessions. Meta-analytic studies are especially helpful because many CBT studies have small numbers and data pooled from multiple studies may provide better estimates of the effectiveness of CBT. In his book *CBT for schizophrenia: Evidence-based interventions and future directions* Steel (2013) gives an overview of CBT-based treatments that are likely to be helpful to people suffering

⁴ However, a potential problem is that antipsychotic medication can cause global immunosuppression. While this effect could enhance the therapeutic effect of the medication for schizophrenia, it could make subjects suffering from schizophrenia more susceptible to diseases and complications related to further immune suppression (May, 1968; Pang et al., 2017).

from schizophrenia. He also makes the case for using specialized CBT protocols that are tailored to specific symptoms such as command hallucinations, violent behavior and PTSD.

20. Psychodynamic Approaches to Treating Schizophrenia

Freud believed that psychoanalysis could not be successfully used with patients suffering from schizophrenia, but that has not stopped psychodynamic psychotherapists from trying work with patients suffering from this disorder over the years. There are many examples of psychodynamic treatments with patients suffering from schizophrenia with some important examples presented below.

Freud's most famous follower, until he broke off to form his own form of analysis, Carl Jung, began his career treating patients with schizophrenia and later made valuable efforts to understand the symbolism which appeared in psychotic symptoms (Jung, 1925). Other of Freud's followers also attempted to at least understand schizophrenia following Freud's principles (Ferenczi & Jones, 1916). Tidd (1937) reported the successful psychoanalytic treatment of a patient we might now label as schizotypal. He went on to report on the use of psychoanalytic treatment with patients suffering from schizophrenia that had undergone shock (convulsive) therapies (Tidd, 1938). Weininger (1938), recommended modification of psychoanalytic technique to be more active during acute psychosis. Fromm-Reichmann (1939) maintained that psychoanalysts could develop and maintain workable relationships with patients suffering from schizophrenia and that successful psychotherapy requires understanding a different kind of transference phenomena. Fairbairn (1941), who was one of the principle figures in the British Object Relations School of psychoanalysis, proposed revisions to Freud's original libido theory in terms of the development of object relations. He also modified psychoanalytic techniques when working with patients suffering from schizophrenia. In the 1950s French psychoanalyst Gisela Pankow developed a technique she called dynamic structuring which combined working with clay, psychoanalysis, and phenomenological therapy to help patients suffering from schizophrenia (Valon, 2020). More modern analytic-based therapies have built on Pankow's work (Bonnigal-Katz, 2019). By the 1970s Searles (1986) greatly contributed to the psychoanalytic understanding of schizophrenia. He proposed a more direct analytic approach to working with patients suffering from schizophrenia. More recently Downing and Mills (2018) have compiled evidence-based psychodynamic approaches to treatment for individuals suffering from schizophrenia in outpatient settings.

These are just some of the psychoanalytic clinicians who have worked with patients suffering from schizophrenia over the last 100 years. Psychodynamic approaches to treating schizophrenia have waxed and waned over time. An influential, but deeply flawed study demonstrating that antipsychotic medication had as good results as analytic treatment had a huge negative impact on the use of psychodynamic therapies with patients suffering from schizophrenia (May, 1968). However, the psychoanalytic treatment in the study was provided by very poorly trained resident physicians and was clearly not up to the level of a properly trained analyst or psychodynamic therapist. Nevertheless, after the study was published, interest in using psychodynamic-related treatment for schizophrenia dropped precipitously (Stone, 1999).

Other past reviews have suggested the negative effects of psychodynamic treatment of patients suffering from schizophrenia (Mueser & Berenbaum, 1990). Nevertheless, there are some modern psychodynamic therapists and analysts who have done psychotherapy or even a modified form of psychoanalysis with psychotic patients with good success (Gibbs, 2007; Giovachinni & Boyer, 1980; Gottdiener, 2006; Grotstein, 2001, 2003; Kortegaard, 1993; V. Volkan, 1995; 2012). Though not definitive, there is some positive evidence that a psychodynamic approach can be useful; even with long-term patients in an inpatient setting (Davenport et al., 2000). It is also thought that a psychodynamic understanding of schizophrenia can help improve treatment even when the treatment itself is not psychodynamic (Kline et al., 1992). Lucas (2003) suggests that psychodynamic approaches to treatment give clinicians a way in which to symbolically understand and communicate with their patients suffering from schizophrenia in a way that can help them make sense of their situation.

Most psychodynamic approaches to the treatment of schizophrenia assume that psychotic processes develop in early childhood and are related to either a withdrawal from the world or an inability to separate from being

psychically fused with a mother-figure (De Masi, 2020). This may be due to pathological neurobiology, structural changes in the brain, and/or pathogenic parenting (V. Volkan, 1995).

Eecke (2019) advocates using a Lacanian form of treatment with patients suffering from schizophrenia. This approach follows Lacan's idea that people with schizophrenia are unable to integrate a 'third' in their personalities. The person suffering from schizophrenia has a psychic structure that is a dyad between the infant and an omnipotent mother. An ego-structuring technique is used to let such people perceive themselves outside of this dyad and allow them to discover themselves as a separate individual.

V. Volkan has written about people with a psychotic self-organization (2012; 1995). In his chapter *Cat People Revisited* he presents a case of a person with this a psychotic self-organization and how this relates to the hoarding of cats. Volkan makes the case that such individuals have an undifferentiated core self-representation that is infused with 'bad' or aggressive emotions which he deems an infantile psychotic self (V. Volkan, 1995). This psychotic self can be enveloped by a healthier self-representation allowing the person to function relatively normally. However, they can become psychotic if the healthier self is overwhelmed by the infantile psychotic self. Psychoanalysis can be used to help the patient modify the infantile psychotic self and achieve separation-individuation (Akhtar & Volkan, 2005).

It is interesting to note from the studies cited above that much of the work using psychodynamic approaches to working with patients suffering from schizophrenia is being done outside of the United States. France in particular has been pioneering psychoanalytic based therapies for use with people suffering from schizophrenia (Kapsambelis, 2019).

21. Non-Western and Novel Treatments for Schizophrenia

In a review of a number of small studies traditional Indian Ayurvedic medicine showed promise for treating schizophrenia but was not as effective as chlorpromazine in acutely ill people (Agarwal et al., 2007). It has been speculated that Ayurvedic medicine, which has traditionally been used to treat immunologic disorders, may have a positive effect on schizophrenia by acting on the immune system (Juckel & Hoffmann, 2018). An ayurvedic polyherbal formulation called *brahmi vati* was found to have anticonvulsant and memory enhancement properties, and to counter amphetamine-induced schizophrenia in mice. Brahmi vati has been used since ancient times to treat seizures and schizophrenic symptoms in India (Mishra et al., 2018).

Research on Traditional Chinese medicine suggests that Chinese herbal medicine may work well in combination with antipsychotic drugs (Rathbone et al., 2007). Patients receiving electroacupuncture along with electroconvulsive therapies were shown to have fewer schizophrenic symptoms than controls. In addition, patients receiving electroacupuncture showed reduced weight as well as reduction in headaches, insomnia, dry mouth, and electrocardiographic abnormalities (Jia et al., 2019).

Some studies have indicated that the brains of people suffering from schizophrenia have reduced levels of Omega-3 fatty acids and some think that this may explain the reduced dopamine activity of the prefrontal cortex as well as suggesting Omega-3 fatty acid supplementation as a possible treatment (Ohara, 2007). It may be possible that a subset of patients suffering from schizophrenia can benefit from niacin augmentation (X. J. Xu & Jiang, 2015). Exercise has been shown to improve both positive and negative symptoms of schizophrenia, as well as quality of life, hippocampal function and volume, and cognition (Girdler et al., 2019; Mitsadali et al., 2020; Sabe et al., 2020; Shimada et al., 2019).

22. Recovery from Schizophrenia

Before the advent of antipsychotic medication most people suffering from schizophrenia in the Western world were relegated to living in institutions or some type of asylum. With the advent of antipsychotic medication, it became possible for people suffering from schizophrenia to exert some control over their psychotic symptoms. However, treatment goals for people suffering from schizophrenia have moved beyond control over symptoms to regaining social and cognitive function and a better quality of life (Silva & Restrepo, 2019).

Hope and self-esteem have been found to contribute to the subjective sense of recovery among people suffering from schizophrenia suggesting that these should be promoted during recovery (İpçi et al., 2020). One dimension of recovery from schizophrenia is the feeling of not being dominated by psychotic symptoms. This feeling was found to be associated with time spent in self-directed and sustained exercise (Gonzalez-Flores, 2020). In a qualitative study of people suffering from schizophrenia subjects describe facing considerable challenges in functioning but also describe a sense of well-being and satisfaction with their lives. This was described as being related to the presence of trusting relationships with healthcare providers and therapeutic conversations, as well as antipsychotic medication, and family support (Møllerhøj et al., 2019).

Early intervention is thought to be related to better recovery from schizophrenia, especially among those who are experiencing a first psychotic episode (Azrin et al., 2015). One study found that while early intervention defined as shorter duration of untreated psychotic symptoms, had a positive effect on recovery from schizophrenia, other factors were needed to predict complete recovery. These factors included including higher education level, a longer period of employment, and planned medication discontinuation within three years together (Chan et al., 2019).

Therapeutic intervention and support play an important role in recovery, which is defined as a personal process of establishing a fulfilling and meaningful life along with a positive sense of identity. Recovery has been found to be promoted by cognitive therapy among individuals suffering from schizophrenia (Vidal & Huguélet, 2019). This demonstrates that psychotherapy can move beyond dealing with specific aspects of schizophrenic disease, to the enhancement of a person's life. A systematic review of cognitive-behavioral and other types of therapy demonstrate they have a positive effect on recovery from schizophrenia (Rakitzki et al., 2020). There a good deal of evidence that psychodynamic therapy and psychoanalysis can be an effective approach to helping patients suffering from schizophrenia achieve full recovery as well as increasing their sense of meaning in their lives (Angyal, 1950; Downing & Mills, 2018; Garfield & Mackler, 2013; Gibbs, 2007; V. Volkan, 1995).

There is still a long way to go in fostering recovery from schizophrenia. Available data indicate that about one in seven people suffering from schizophrenia are able to achieve functional recovery (Silva & Restrepo, 2019). The addition of various types of support, including family support, educational attainment, and psychotherapies could change recovery rates for the better. More research needs to be done on the effectiveness of these modalities on the improvement of recovery.

23. Prevention of Schizophrenia

While prevention of schizophrenia appears to be far-fetched on the surface, many of the latest findings about the disorder provide evidence that preventative approaches may be useful. Environmentally mitigated risk factors related to migration and immigration that are known to increase risk for schizophrenia could be targeted. Exposure to various types of infection could be mitigated or treated. Nutritional risk factors can easily be prevented if adequate and high-quality food supplies are available. Psycho-social stressors, cannabis use, and advanced paternal age, all of which are associated with increased risk for schizophrenia, can be altered to reduce incidence of schizophrenia (A. S. Brown & McGrath, 2011).

There is some evidence that prenatal nutritional deficits increase the risk of schizophrenia. Vitamin D, folic acid, and iron are the three micronutrients that are possibly related to the subsequent development of schizophrenia. Therefore, pre-natal supplementation may be protective against the disease (McGrath et al., 2011).

Maternal influenza, toxoplasmosis, and genital/reproductive infections are known to be related to increased risk of schizophrenia in offspring. Prevention of these infections in mothers should be a relatively straightforward and effective prevention strategy (A. Brown & Patterson, 2011).

Possible immunological triggers of schizophrenia, including things that cause gut inflammation and degradation of the gut biome can be avoided, especially among people known to at higher risk, for example first degree relatives of patients suffering from schizophrenia (Severance & Yolken, 2020).

24. Conclusion

Schizophrenia is an intense, and widespread mental illness. It has a complex epidemiology with serious comorbidities and mortalities. The voluminous amount of research into the causes of schizophrenia has made tremendous progress in unraveling the disease. While we have a much more nuanced and detailed knowledge of the disorder, a definitive comprehensive understanding of schizophrenia has not emerged. Nevertheless, new knowledge about schizophrenia has begun to influence how the disorder is treated. In the past, convulsive therapies and psychosurgery were erroneously thought to be effective treatments for schizophrenia. These invasive and dangerous methods were used often and indiscriminately, causing a great deal of suffering. Recently, however, greater understanding of the brain, advances in medical technology, and the success of deep brain stimulation and psychosurgery for OCD, have sparked an interest in using these techniques to treat schizophrenia. Advanced imaging technology combined with precision surgery now allow for selective targeting of brain structures for neuromodulation via DBS or precise ablation of brain tissue in severe and treatment resistant cases of schizophrenia. These approaches, in an environment of ethical oversight, could lead to important insights about the control of schizophrenic symptoms, while providing treatment options in severe and intractable cases of schizophrenia. Nevertheless, for most people suffering from schizophrenia, dopamine modulating antipsychotic medications remain the predominant treatment modality. Both first- and second-generation antipsychotic medications, however, have a number of serious side effects and do not effectively treat the negative and cognitive symptoms associated with schizophrenia. As a result, novel antipsychotic medications and better medication delivery systems are being developed. Clinical trials have produced mixed results but there is some hope that some of these new approaches will prove as effective or better than previous antipsychotic drugs with fewer side effects. Nevertheless, definitively better antipsychotic pharmacological agents will likely not appear until the pathophysiology of schizophrenia is better understood. Another promising area of pharmacological treatment of schizophrenia is anti-inflammatory and immunomodulating agents. A number of these have been studied and there is promise that this approach alone or in conjunction with antipsychotic medication will provide a breakthrough in the treatment and understanding of schizophrenia. While pharmacology continues to be the primary mechanism for treating schizophrenia, psychotherapeutic treatments are showing promise in alleviating some of the debilitating effects of the disease. Newer psychotherapeutic techniques derived from cognitive-behavioral therapies are showing promise in improving the lives of people suffering from schizophrenia. Innovative formulations of psychodynamic therapies as well as more nuanced understanding of the developmental psychopathology of schizophrenia also show promise in helping to treat the disorder. Many psychotherapies have moved beyond the treatment of symptoms to a focus on recovery. Treatments derived from alternative medicine, as well methods of prevention are also being tried or are on the horizon. Even though recovery rates are still low, there is hope that newer therapies as well as the combination of different therapeutic approaches may allow more people suffering from schizophrenia to live happy and fulfilling lives.

References

- Adams, D. D., Knight, J. G., & Ebringer, A. (2012). The autoimmune model of schizophrenia. *ISRN Psychiatry*, 2012, 758072. <https://doi.org/10.5402/2012/758072>
- Agarwal, V., Abhijnhan, A., & Raviraj, P. (2007). Ayurvedic medicine for schizophrenia. *The Cochrane Database of Systematic Reviews*, 4, CD006867. <https://doi.org/10.1002/14651858.CD006867>
- Agbeli, M. O. (2020). *Reducing antipsychotic medication use in long-term care settings* (2020-04052-126; Issues 5-A). ProQuest Information & Learning.
- Akhtar, S., & Volkan, V. D. (2005). *Mental zoo: Animals in the human mind and its pathology*. International Universities Press.
- Albert, N., Randers, L., Allott, K., Jensen, H. D., Melau, M., Hjorthøj, C., & Nordentoft, M. (2019). Cognitive functioning following discontinuation of antipsychotic medication A naturalistic sub-group analysis from the OPUS II trial. *Psychological Medicine*, 49(7), 1138–1147. <https://doi.org/10.1017/S0033291718001836>
- American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5* (5 edition). American Psychiatric Publishing.
- Angyal, A. (1950). The psychodynamic process of illness and recovery in a case of catatonic schizophrenia. *Psychiatry: Journal for the Study of Interpersonal Processes*, 13, 149–165.

- Arnaiz, A., Zumárraga, M., Díez-Altuna, I., Uriarte, J. J., Moro, J., & Pérez-Ansorena, M. A. (2011). Oral health and the symptoms of schizophrenia. *Psychiatry Research*, *188*(1), 24–28. <https://doi.org/10.1016/j.psychres.2010.09.012>
- Ashcroft, K., Kingdon, D. G., & Chadwick, P. (2012). Persecutory delusions and childhood emotional abuse in people with a diagnosis of schizophrenia. *Psychosis: Psychological, Social and Integrative Approaches*, *4*(2), 168–171. <https://doi.org/10.1080/17522439.2011.619012>
- Azrin, S. T., Goldstein, A. B., & Heinessen, R. K. (2015). Early intervention for psychosis: The Recovery After an Initial Schizophrenia Episode project. *Psychiatric Annals*, *45*(11), 548–553. <https://doi.org/10.3928/00485713-20151103-05>
- B, S., & Tk, C. (2014). Role of C-reactive protein in schizophrenia: An overview. *Psychiatry Research*, *216*(2), 277–285. <https://doi.org/10.1016/j.psychres.2014.02.004>
- Barkan, T., Peled, A., Modai, I., Barak, P., Weizman, A., & Rehavi, M. (2006). Serotonin transporter characteristics in lymphocytes and platelets of male aggressive schizophrenia patients compared to non-aggressive schizophrenia patients. *European Neuropsychopharmacology*, *16*(8), 572–579. <https://doi.org/10.1016/j.euroneuro.2006.03.001>
- Barrowclough, C., Haddock, G., Lobban, F., Jones, S., Siddler, R., Roberts, C., & Gregg, L. (2006). Group cognitive-behavioural therapy for schizophrenia. *British Journal of Psychiatry*, *189*(6), 527–532. <https://doi.org/10.1192/bjp.bp.106.021386>
- Baumeister, A. A., & Francis, J. L. (2002). Historical development of the dopamine hypothesis of schizophrenia. *Journal of the History of the Neurosciences*, *11*(3), 265–277. <https://doi.org/10.1076/jhin.11.3.265.10391>
- Beraki, S., Aronsson, F., Karlsson, H., Ögren, S. O., & Kristensson, K. (2005). Influenza A virus infection causes alterations in expression of synaptic regulatory genes combined with changes in cognitive and emotional behaviors in mice. *Molecular Psychiatry*, *10*(3), 299–308. <https://doi.org/10.1038/sj.mp.4001545>
- Bhugra, D. (2000). Migration and schizophrenia. *Acta Psychiatrica Scandinavica*, *102*, 68–73. <https://doi.org/10.1034/j.1600-0447.2000.00015.x>
- Bonnigal-Katz, D. (2019). Psychosis Therapy Project: A psychoanalytic project in the community. *British Journal of Psychotherapy*, *35*(4), 586–589. <https://doi.org/10.1111/bjp.12466>
- Boydell, J., Van Os, J., Lambri, M., Castle, D., Allardyce, J., McCreddie, R. G., & Murray, R. M. (2003). Incidence of schizophrenia in south-east London between 1965 and 1997. *British Journal of Psychiatry*, *182*(1), 45–49. <https://doi.org/10.1192/bjp.182.1.45>
- Brakoulias, V., Starcevic, V., Albert, U., Arumugham, S. S., Bailey, B. E., Belloch, A., Borda, T., Dell’Osso, L., Elias, J. A., Falkenstein, M. J., Ferrao, Y. A., Fontenelle, L. F., Jelinek, L., Kalogeraki, L., Kay, B., Laurito, L. D., Lochner, C., Maina, G., Marazziti, D., ... Fineberg, N. A. (2019). Treatments used for obsessive-compulsive disorder-An international perspective. *Human Psychopharmacology*, *34*(1), e2686. <https://doi.org/10.1002/hup.2686>
- Brambilla, P., & Tansella, M. (2007). Can neuroimaging studies help us in understanding the biological causes of schizophrenia? *International Review of Psychiatry*, *19*(4), 313–314. <https://doi.org/10.1080/09540260701507954>
- Braslow, J. T. (1999). History and evidence-based medicine: Lessons from the history of somatic treatments from the 1900s to the 1950s. *Mental Health Services Research*, *1*(4), 231–240. <https://doi.org/10.1023/a:1022325508430>
- Bray, I., Waraich, P., Jones, W., Slater, S., Goldner, E. M., & Somers, J. (2006). Increase in schizophrenia incidence rates: Findings in a Canadian cohort born 1975–1985. *Social Psychiatry and Psychiatric Epidemiology*, *41*(8), 611–618. <https://doi.org/10.1007/s00127-006-0073-z>
- Bresnahan, M., Menezes, P., Varma, V., & Susser, E. (2003). Geographical variation in incidence, course and outcome of schizophrenia: A comparison of developing and developed countries. *The Epidemiology of Schizophrenia*, 18–33.
- Brown, A. S., & McGrath, J. J. (2011). The Prevention of Schizophrenia. *Schizophrenia Bulletin*, *37*(2), 257–261. <https://doi.org/10.1093/schbul/sbq122>
- Brown, A. S., & Patterson, P. H. (2011). Maternal Infection and Schizophrenia: Implications for Prevention. *Schizophrenia Bulletin*, *37*(2), 284–290. <https://doi.org/10.1093/schbul/sbq146>
- Brown, A. S., Schaefer, C. A., Quesenberry, C. P. Jr., Shen, L., & Susser, E. S. (2006). No evidence of relation between maternal exposure to herpes simplex virus type 2 and risk of schizophrenia? *American Journal of Psychiatry*, *163*(12), 2178–2180. <https://doi.org/10.1176/appi.ajp.163.12.2178>
- Brown, S., Inskip, H., & Barraclough, B. (2000). Causes of the excess mortality of schizophrenia. *British Journal of Psychiatry*, *177*, 212–217. <https://doi.org/10.1192/bjp.177.3.212>
- Buckley, L., & Pettit, T. (2007). Supportive therapy for schizophrenia. *Schizophrenia Bulletin*, *33*(4), 859–860. <https://doi.org/10.1093/schbul/sbm058>
- Buka, S. L., Cannon, T. D., Torrey, E. F., & Yolken, R. H. (2008). Maternal exposure to herpes simplex virus and risk of psychosis among adult offspring. *Biological Psychiatry*, *63*(8), 809–815.
- Burns, J. (2007). *The Descent of Madness: Evolutionary Origins of Psychosis and the Social Brain* (1 edition). Routledge.

- Butler, P. D., Susser, E. S., Brown, A. S., Kaufmann, C. A., & Gorman, J. M. (1994). Prenatal nutritional deprivation as a risk factor in schizophrenia: Preclinical evidence. *Neuropsychopharmacology*, *11*(4), 227–235. <https://doi.org/10.1038/sj.npp.1380109>
- Byrne, M., Agerbo, E., Bennedsen, B., Eaton, W. W., & Mortensen, P. B. (2007). Obstetric conditions and risk of first admission with schizophrenia: A Danish national register based study. *Schizophrenia Research*, *97*(1), 51–59. <https://doi.org/10.1016/j.schres.2007.07.018>
- Capasso, R. M., Lineberry, T. W., Bostwick, J. M., Decker, P. A., & St. Sauver, J. (2008). Mortality in schizophrenia and schizoaffective disorder: An Olmsted County, Minnesota cohort: 1950-2005. *Schizophrenia Research*, *98*(1), 287–294. <https://doi.org/10.1016/j.schres.2007.10.005>
- Caruso, J. P., & Sheehan, J. P. (2017). Psychosurgery, ethics, and media: A history of Walter Freeman and the lobotomy. *Neurosurgical Focus*, *43*(3), E6. <https://doi.org/10.3171/2017.6.FOCUS17257>
- Casey, D. E., Haupt, D. W., Newcomer, J. W., Henderson, D. C., Sernyak, M. J., Davidson, M., Lindenmayer, J.-P., Manoukian, S. V., Banerji, M. A., Lebovitz, H. E., & Hennekens, C. H. (2004). Antipsychotic-Induced Weight Gain and Metabolic Abnormalities: Implications for Increased Mortality in Patients with Schizophrenia. *Journal of Clinical Psychiatry*, *65*, 4–18.
- Castle, D. J., & Morgan, V. (2008). Epidemiology. *Clinical Handbook of Schizophrenia*, 14–24.
- Chan, S. K. W., Hui, C. L. M., Chang, W. C., Lee, E. H. M., & Chen, E. Y. H. (2019). Ten-year follow up of patients with first-episode schizophrenia spectrum disorder from an early intervention service: Predictors of clinical remission and functional recovery. *Schizophrenia Research*, *204*, 65–71. <https://doi.org/10.1016/j.schres.2018.08.022>
- Chaudhry, I. B., Husain, N., ur Rahman, R., Husain, M. O., Hamirani, M. M., Kazmi, A., Baig, S., Haddad, P. M., Buch, M. H., Qureshi, I., Mehmood, N., Kiran, T., Fu, B., Afsar, S., & Deakin, B. (2015). A randomised double-blind placebo-controlled 12-week feasibility trial of methotrexate added to treatment as usual in early schizophrenia: Study protocol for a randomised controlled trial. *Trials*, *16*, 9. <https://doi.org/10.1186/1745-6215-16-9>
- Cheniaux, E., Landeira-Fernandez, J., Telles, L. L., Lessa, J. L. M., Dias, A., Duncan, T., & Versiani, M. (2008). Does schizoaffective disorder really exist? A systematic review of the studies that compared schizoaffective disorder with schizophrenia or mood. *Journal of Affective Disorders*, *106*(3), 209–217. <https://doi.org/10.1016/j.jad.2007.07.009>
- Chiu, V. W., Ree, M., Janca, A., Iyyalol, R., Dragovic, M., & Waters, F. (2018). Sleep profiles and CBT-I response in schizophrenia and related psychoses. *Psychiatry Research*, *268*, 279–287. <https://doi.org/10.1016/j.psychres.2018.07.027>
- Chwastiak, L. A., & Tek, C. (2009). The unchanging mortality gap for people with schizophrenia. *The Lancet*, *374*(9690), 590–592. [https://doi.org/10.1016/S0140-6736\(09\)61072-2](https://doi.org/10.1016/S0140-6736(09)61072-2)
- Cowan, H. R. (2020). Is schizophrenia research relevant during the COVID-19 pandemic? *Schizophrenia Research*. <https://doi.org/10.1016/j.schres.2020.04.002>
- Cullen, A. E., Holmes, S., Pollak, T. A., Blackman, G., Joyce, D. W., Kempton, M. J., Murray, R. M., McGuire, P., & Mondelli, V. (2019). Associations Between Non-neurological Autoimmune Disorders and Psychosis: A Meta-analysis. *Biological Psychiatry*, *85*(1), 35–48. <https://doi.org/10.1016/j.biopsych.2018.06.016>
- Dalman, C., Allebeck, P., Gunnell, D., Harrison, G., Kristensson, K., Lewis, G., Lofving, S., Rasmussen, F., Wicks, S., & Karlsson, H. (2008). Infections in the CNS during childhood and the risk of subsequent psychotic illness: A cohort study of more than one million Swedish subjects. *American Journal of Psychiatry*, *165*(1), 59–65. <https://doi.org/10.1176/appi.ajp.2007.07050740>
- D'Astous, M., Cottin, S., Roy, M., Picard, C., & Cantin, L. (2013). Bilateral stereotactic anterior capsulotomy for obsessive-compulsive disorder: Long-term follow-up. *Journal of Neurology, Neurosurgery, and Psychiatry*, *84*(11), 1208–1213. <https://doi.org/10.1136/jnnp-2012-303826>
- Davenport, S., Hobson, R., & Margison, F. (2000). Treatment development in psychodynamic-interpersonal psychotherapy (Hobson's 'Conversational Model') for chronic treatment resistant schizophrenia: Two single case studies. *British Journal of Psychotherapy*, *16*(3), 287–302. <https://doi.org/10.1111/j.1752-0118.2000.tb00520.x>
- Davis, J. M., & Leucht, S. (2008). Has research informed us on the practical drug treatment of schizophrenia? *Schizophrenia Bulletin*, *34*(3), 403–405. <https://doi.org/10.1093/schbul/sbn011>
- De Luca, V., Zai, G., Tharmalingam, S., de Bartolomeis, A., Wong, G., & Kennedy, J. L. (2006). Association study between the novel functional polymorphism of the serotonin transporter gene and suicidal behaviour in schizophrenia. *European Neuropsychopharmacology*, *16*(4), 268–271. <https://doi.org/10.1016/j.euroneuro.2005.09.007>
- De Masi, F. (2020). Psychosis and analytic therapy: A complex relationship. *The International Journal of Psychoanalysis*, *101*(1), 152–168. <https://doi.org/10.1080/00207578.2020.1716626>
- Dean, B., Hussain, T., Scarr, E., Pavey, G., & Copolov, D. L. (2001). Extended treatment with typical and atypical antipsychotic drugs: Differential effects on the densities of dopamine D-sub-2-like and GABA-sub(A) receptors in rat striatum. *Life Sciences*, *69*(11), 1257–1268. [https://doi.org/10.1016/S0024-3205\(01\)01214-0](https://doi.org/10.1016/S0024-3205(01)01214-0)

- Dean, B., Pavey, G., Thomas, D., & Scarr, E. (2006). Cortical serotonin-sub(7, 1D) and -sub(1F) receptors: Effects of schizophrenia, suicide and antipsychotic drug treatment. *Schizophrenia Research*, 88(1), 265–274. <https://doi.org/10.1016/j.schres.2006.07.003>
- Dean, K., Bramon, E., & Murray, R. M. (2003). The causes of schizophrenia: Neurodevelopment and other risk factors. *Journal of Psychiatric Practice*, 9(6), 442–454. <https://doi.org/10.1097/00131746-200311000-00007>
- Dickerson, F., Boronow, J., Stallings, C., Origoni, A., & Yolken, R. (2007). Toxoplasma gondii in individuals with schizophrenia: Association with clinical and demographic factors and with mortality. *Schizophrenia Bulletin*, 33(3), 737–740. <https://doi.org/10.1093/schbul/sbm005>
- Dickerson, F., Kirkpatrick, B., Boronow, J., Stallings, C., Origoni, A., & Yolken, R. (2006). Deficit schizophrenia: Association with serum antibodies to cytomegalovirus. *Schizophrenia Bulletin*, 32(2), 396–400. <https://doi.org/10.1093/schbul/sbi054>
- Dickerson, F., Severance, E., & Yolken, R. (2017). The microbiome, immunity, and schizophrenia and bipolar disorder. *Brain, Behavior, and Immunity*, 62, 46–52. <https://doi.org/10.1016/j.bbi.2016.12.010>
- Dickson, H., Hedges, E. P., Ma, S. Y., Cullen, A. E., MacCabe, J. H., Kempton, M. J., Downs, J., & Laurens, K. R. (2020). Academic achievement and schizophrenia: A systematic meta-analysis. *Psychological Medicine*. <https://doi.org/10.1017/S0033291720002354>
- Dion, G. L., & Dellario, D. (1988). Symptom subtypes in persons institutionalized with schizophrenia: Comparison of demographics, outcome and functional skills. *Rehabilitation Psychology*, 33(2), 95–104. <https://doi.org/10.1037/h0091684>
- Divac, N., Prostran, M., Jakovceviski, I., & Cerovac, N. (2014). Second-generation antipsychotics and extrapyramidal adverse effects. *BioMed Research International*, 2014, 656370. <https://doi.org/10.1155/2014/656370>
- dosReis, S., Johnson, E., Steinwachs, D., Rohde, C., Skinner, E. A., Fahey, M., & Lehman, A. F. (2008). Antipsychotic treatment patterns and hospitalizations among adults with schizophrenia. *Schizophrenia Research*, 101(1), 304–311. <https://doi.org/10.1016/j.schres.2007.12.475>
- Downing, D. L., & Mills, J. (2018). *Outpatient Treatment of Psychosis: Psychodynamic Approaches to Evidence-Based Practice*. Routledge. <https://doi.org/10.4324/9780429478123>
- Dully, H., & Fleming, C. (2007). *My Lobotomy*. Crown.
- Dykxhoorn, J., Hollander, A.-C., Lewis, G., Magnusson, C., Dalman, C., & Kirkbride, J. B. (2019). Risk of schizophrenia, schizoaffective, and bipolar disorders by migrant status, region of origin, and age-at-migration: A national cohort study of 18 million people. *Psychological Medicine*, 49(14), 2354–2363. <https://doi.org/10.1017/S0033291718003227>
- Eecke, W. V. (2019). How Does Psychoanalysis Work with Persons Afflicted By Schizophrenia? *Journal of Psychology & Psychotherapy*, 9(5), 1–5. <https://doi.org/10.35248/2161-0487.19.9.367>
- Enger, C., Weatherby, L., Reynolds, R. F., Glasser, D. B., & Walker, A. M. (2004). Serious Cardiovascular Events and Mortality Among Patients with Schizophrenia. *Journal of Nervous and Mental Disease*, 192(1), 19–27. <https://doi.org/10.1097/01.nmd.0000105996.62105.07>
- Fairbairn, W. R. D. (1941). A revised psychopathology of the psychoses and psychoneuroses. *The International Journal of Psychoanalysis*, 22, 250–270.
- Fakra, E., Salgado-Pineda, P., Delaveau, P., Hariri, A. R., & Blin, O. (2008). Neural bases of different cognitive strategies for facial affect processing in schizophrenia. *Schizophrenia Research*, 100(1), 191–205. <https://doi.org/10.1016/j.schres.2007.11.040>
- Fan, J. B., & Sklar, P. (2005). Meta-analysis reveals association between serotonin transporter gene STin2 VNTR polymorphism and schizophrenia. *Molecular Psychiatry*, 10(10), 928–938. <https://doi.org/10.1038/sj.mp.4001690>
- Fatemi, S. H., Reutiman, T. J., Folsom, T. D., Huang, H., Oishi, K., Mori, S., Smee, D. F., Pearce, D. A., Winter, C., Sohr, R., & Juckel, G. (2008). Maternal infection leads to abnormal gene regulation and brain atrophy in mouse offspring: Implications for genesis of neurodevelopmental disorders. *Schizophrenia Research*, 99(1), 56–70. <https://doi.org/10.1016/j.schres.2007.11.018>
- Fearon, P., Kirkbride, J. B., Morgan, C., Dazzan, P., Morgan, K., Lloyd, T., Hutchinson, G., Tarrant, J., Fung, W. L. A., Holloway, J., Mallett, R., Harrison, G., Leff, J., Jones, P. B., & Murray, R. M. (2006). Incidence of schizophrenia and other psychoses in ethnic minority groups: Results from the MRC AESOP Study. *Psychological Medicine*, 36(11), 1541–1550. <https://doi.org/10.1017/S0033291706008774>
- Ferenczi, S., & Jones, E. (1916). Some Clinical Observations on Paranoia and Paraphrenia. In *Contributions to psycho-analysis*. (2006-03526-011; pp. 238–249). Richard G. Badger. <https://doi.org/10.1037/10925-011>
- Findlay, L. J. (2015). *Decision-making processes and health behaviors among adults diagnosed with schizophrenia* (2015-99060-062; Issues 9-B(E)). ProQuest Information & Learning.
- Flegr, J., & Kuba, R. (2016). The relation of Toxoplasma infection and sexual attraction to fear, danger, pain, and submissiveness. *Evolutionary Psychology*, 14(3). <https://doi.org/10.1177/1474704916659746>

- Fonseca, L., Diniz, E., Mendonça, G., Malinowski, F., Mari, J., Gadelha, A., Fonseca, L., Diniz, E., Mendonça, G., Malinowski, F., Mari, J., & Gadelha, A. (2020). Schizophrenia and COVID-19: Risks and recommendations. *Brazilian Journal of Psychiatry, AHEAD*. <https://doi.org/10.1590/1516-4446-2020-0010>
- Forman, M. (1975). *One Flew Over the Cuckoo's Nest*. Warner.
- Fornito, A., Yücel, M., Wood, S. J., Adamson, C., Velakoulis, D., Saling, M. M., McGorry, P. D., & Pantelis, C. (2008). Surface-based morphometry of the anterior cingulate cortex in first episode schizophrenia. *Human Brain Mapping, 29*(4), 478–489. <https://doi.org/10.1002/hbm.20412>
- Fors, B. M., Isacson, D., Bingeors, K., & Widerlöv, B. (2007). Mortality among persons with schizophrenia in Sweden: An epidemiological study. *Nordic Journal of Psychiatry, 61*(4), 252–259. <https://doi.org/10.1080/08039480701414932>
- Foussias, G., & Remington, G. (2010). Antipsychotics and schizophrenia: From efficacy and effectiveness to clinical decision-making. *Canadian Journal of Psychiatry. Revue Canadienne De Psychiatrie, 55*(3), 117–125. <https://doi.org/10.1177/070674371005500302>
- Frankle, W. G., Lombardo, I., Kegeles, L. S., Slifstein, M., Martin, J. H., Huang, Y., Hwang, D.-R., Reich, E., Cangianno, C., Gil, R., Laruelle, M., & Abi-Dargham, A. (2006). Serotonin 1A receptor availability in patients with schizophrenia and schizo-affective disorder: A positron emission tomography imaging study with [¹¹C] WAY 100635. *Psychopharmacology, 189*(2), 155–164. <https://doi.org/10.1007/s00213-006-0543-8>
- Fröhlich, F., & Lustenberger, C. (2020). Neuromodulation of sleep rhythms in schizophrenia: Towards the rational design of non-invasive brain stimulation. *Schizophrenia Research*. <https://doi.org/10.1016/j.schres.2020.04.003>
- Fromm-Reichmann, F. (1939). Transference problems in schizophrenics. *The Psychoanalytic Quarterly, 8*, 412–426.
- Fu, S., Czajkowski, N., & Torgalsbøen, A.-K. (2019). Cognitive, work, and social outcomes in fully recovered first-episode schizophrenia: On and off antipsychotic medication. *Psychiatry: Interpersonal and Biological Processes*. <https://doi.org/10.1080/00332747.2018.1550735>
- Garfield, D., & Mackler, D. (2013). *Beyond Medication: Therapeutic Engagement and the Recovery from Psychosis*. Routledge.
- Garver, D. L., Holcomb, J. A., & Christensen, J. D. (2000). Heterogeneity of response to antipsychotics from multiple disorders in the schizophrenia spectrum. *Journal of Clinical Psychiatry, 61*(12), 964–974.
- Gault, J. M., Davis, R., Cascella, N. G., Saks, E. R., Corripio-Collado, I., Anderson, W. S., Olincy, A., Thompson, J. A., Pomarol-Clotet, E., Sawa, A., Daskalakis, Z. J., Lipsman, N., & Abosch, A. (2018). Approaches to neuromodulation for schizophrenia. *Journal of Neurology, Neurosurgery & Psychiatry, 89*(7), 777–787. <https://doi.org/10.1136/jnnp-2017-316946>
- Gazdag, G., & Ungvari, G. S. (2019). Electroconvulsive therapy: 80 years old and still going strong. *World Journal of Psychiatry, 9*(1), 1–6. <https://doi.org/10.5498/wjp.v9.i1.1>
- Gearon, J. S., Bellack, A. S., Rachbeisel, J., & Dixon, L. (2001). Drug-use behavior and correlates in people with schizophrenia. *Addictive Behaviors, 26*(1), 51–61. [https://doi.org/10.1016/S0306-4603\(00\)00084-8](https://doi.org/10.1016/S0306-4603(00)00084-8)
- Gibbs, P. L. (2007). The primacy of psychoanalytic intervention in recovery from the psychoses and schizophrenias. *The Journal of the American Academy of Psychoanalysis and Dynamic Psychiatry, 35*(2), 287–312.
- Gil, A., Gama, C. S., de Jesus, D. R., Lobato, M. I., Zimmer, M., & Belmonte-de-Abreu, P. (2009). The association of child abuse and neglect with adult disability in schizophrenia and the prominent role of physical neglect. *Child Abuse & Neglect, 33*(9), 618–624. <https://doi.org/10.1016/j.chiabu.2009.02.006>
- Gilmore, J. H. (2010). Understanding what causes schizophrenia: A developmental perspective. *The American Journal of Psychiatry, 167*(1), 8–10. <https://doi.org/10.1176/appi.ajp.2009.09111588>
- Gilmour, G., Dix, S., Fellini, L., Gastambide, F., Plath, N., Steckler, T., Talpos, J., & Tricklebank, M. (2012). NMDA receptors, cognition and schizophrenia – testing the validity of the NMDA receptor hypofunction hypothesis. *Neuropharmacology, 62*(3), 1401–1412. <https://doi.org/10.1016/j.neuropharm.2011.03.015>
- Giovachinni, P., & Boyer, B. L. (1980). *Psychoanalytic Treatment of Schizophrenic Borderline and Characterological Disorders* (Enlarged 2nd Edition). Jason Aronson, Inc.
- Girdler, S. J., Confino, J. E., & Woesner, M. E. (2019). Exercise as a Treatment for Schizophrenia: A Review. *Psychopharmacology Bulletin, 49*(1), 56–69.
- Gold, C. (2015). Dose and effect in CBT for schizophrenia. *The British Journal of Psychiatry, 207*(3), 269–273. <https://doi.org/10.1192/bjp.207.3.269>
- González de Chávez, M. (2009). Treatment of psychoses before the twentieth century. In Y. O. Alanen, M. González de Chávez, A.-L. S. Silver, & B. Martindale (Eds.), *Psychotherapeutic approaches to schizophrenic psychoses: Past, present and future*. (2009-10328-002; pp. 10–22). Routledge/Taylor & Francis Group.
- Gonzalez-Flores, B. L. (2020). *Impact of independent exercise on recovery, well-being, and motivation among individuals with schizophrenia* (2020-28121-043; Issues 4-B). ProQuest Information & Learning.

- Gottdiener, W. H. (2006). Individual psychodynamic psychotherapy of schizophrenia: Empirical evidence for the practicing clinician. *Psychoanalytic Psychology*, 23(3), 583–589. <https://doi.org/10.1037/0736-9735.23.3.583>
- Gray, L., Scarr, E., & Dean, B. (2006). Serotonin 1a receptor and associated G-protein activation schizophrenia and bipolar disorder. *Psychiatry Research*, 143(2), 111–120. <https://doi.org/10.1016/j.psychres.2005.09.010>
- Green, M. F., Horan, W. P., & Lee, J. (2019). Nonsocial and social cognition in schizophrenia: Current evidence and future directions. *World Psychiatry*, 18(2), 146–161. <https://doi.org/10.1002/wps.20624>
- Grignon, S., & Trotter, M. (2005). Capgras Syndrome in the Modern Era: Self Misidentification on an ID Picture. *The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie*, 50(1), 74–75.
- Grotstein, J. S. (2001). A rationale for the psychoanalytically informed psychotherapy of schizophrenia and other psychoses: Towards the concept of “rehabilitative psychoanalysis.” *A Language for Psychosis: Psychoanalysis of Psychotic States.*, 9–26.
- Grotstein, J. S. (2003). Towards the concept of “rehabilitative psychoanalytic psychotherapy” in the treatment of schizophrenia. *Preventive Strategies for Schizophrenic Disorders: Basic Principles, Opportunities and Limits.*, 350–365.
- Gründer, G., & Cumming, P. (2016). The dopamine hypothesis of schizophrenia: Current status. In T. Abel & T. Nickl-Jockschat (Eds.), *The neurobiology of schizophrenia*. (2016-43112-007; pp. 109–124). Elsevier Academic Press. <https://doi.org/10.1016/B978-0-12-801829-3.00015-X>
- Gur, R. E., Loughhead, J., Kohler, C. G., Elliott, M. A., Lesko, K., Ruparel, K., Wolf, D. H., Bilker, W. B., & Gur, R. C. (2007). Limbic activation associated with misidentification of fearful faces and flat affect in schizophrenia. *Archives of General Psychiatry*, 64(12), 1356–1366. <https://doi.org/10.1001/archpsyc.64.12.1356>
- Hadar, R., Bikovski, L., Soto-Montenegro, M. L., Schimke, J., Maier, P., Ewing, S., Voget, M., Wieske, F., Götz, T., Desco, M., Hamani, C., Pascau, J., Weiner, I., & Winter, C. (2018). Early neuromodulation prevents the development of brain and behavioral abnormalities in a rodent model of schizophrenia. *Molecular Psychiatry*, 23(4), 943–951. <https://doi.org/10.1038/mp.2017.52>
- Hagiwara, H., Fujita, Y., Ishima, T., Kunitachi, S., Shirayama, Y., Iyo, M., & Hashimoto, K. (2008). Phencyclidine-induced cognitive deficits in mice are improved by subsequent subchronic administration of the antipsychotic drug perospirone: Role of serotonin 5-HT-sub(1A) receptors. *European Neuropsychopharmacology*, 18(6), 448–454. <https://doi.org/10.1016/j.euroneuro.2007.11.005>
- Hashimoto, T., Bazmi, H. H., Mirmics, K., Wu, Q., Sampson, A. R., & Lewis, D. A. (2008). Conserved regional patterns of GABA-related transcript expression in the neocortex of subjects with schizophrenia. *American Journal of Psychiatry*, 165(4), 479–489. <https://doi.org/10.1176/appi.ajp.2007.07081223>
- Healy, D. (2006). Neuroleptics and mortality: A 50-year cycle: Invited commentary on... schizophrenia, neuroleptic medication and mortality. *British Journal of Psychiatry*, 188(2), 128. <https://doi.org/10.1192/bjp.bp.105.018911>
- Hendrick, I. (1928). Encephalitis lethargica and the interpretation of mental disease. *American Journal of Psychiatry*, 7, 989–1014.
- Henssler, J., Brandt, L., Müller, M., Liu, S., Montag, C., Sterzer, P., & Heinz, A. (2020). Migration and schizophrenia: Meta-analysis and explanatory framework. *European Archives of Psychiatry and Clinical Neuroscience*, 270(3), 325–335. <https://doi.org/10.1007/s00406-019-01028-7>
- Hoeffding, L. K., Rosengren, A., Thygesen, J. H., Schmock, H., Werge, T., & Hansen, T. (2017). Evaluation of shared genetic susceptibility loci between autoimmune diseases and schizophrenia based on genome-wide association studies. *Nordic Journal of Psychiatry*, 71(1), 20–25. <https://doi.org/10.1080/08039488.2016.1198420>
- Hong, J., & Bang, M. (2020). Anti-inflammatory Strategies for Schizophrenia: A Review of Evidence for Therapeutic Applications and Drug Repurposing. *Clinical Psychopharmacology and Neuroscience*, 18(1), 10–24. <https://doi.org/10.9758/cpn.2020.18.1.10>
- Høyersten, J. G. (1996). [Possessed! Some historical, psychiatric and current moments of demonic possession]. *Tidsskrift for Den Norske Lægeforening: Tidsskrift for Praktisk Medicin, Ny Raekke*, 116(30), 3602–3606.
- Hua, M., Peng, Y., Zhou, Y., Qin, W., Yu, C., & Liang, M. (2020). Disrupted pathways from limbic areas to thalamus in schizophrenia highlighted by whole-brain resting-state effective connectivity analysis. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 99, 109837. <https://doi.org/10.1016/j.pnpbp.2019.109837>
- İpçi, K., Yildiz, M., İncedere, A., Kiras, F., Esen, D., & Gürcan, M. B. (2020). Subjective recovery in patients with schizophrenia and related factors. *Community Mental Health Journal*. <https://doi.org/10.1007/s10597-020-00616-5>
- Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., de Graaf, R., & van Os, J. (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica*, 109(1), 38–45. <https://doi.org/10.1046/j.0001-690X.2003.00217.x>

- Jauhar, S., McKenna, P. J., Radua, J., Fung, E., Salvador, R., & Laws, K. R. (2014). Cognitive-behavioural therapy for the symptoms of schizophrenia: Systematic review and meta-analysis with examination of potential bias. *The British Journal of Psychiatry*, 204(1), 20–29. <https://doi.org/10.1192/bjp.bp.112.116285>
- Jentsch, J. D., & Roth, R. H. (1999). The neuropsychopharmacology of phencyclidine: From NMDA receptor hypofunction to the dopamine hypothesis of schizophrenia. *Neuropsychopharmacology*, 20(3), 201–225. [https://doi.org/10.1016/S0893-133X\(98\)00060-8](https://doi.org/10.1016/S0893-133X(98)00060-8)
- Jia, J., Shen, J., Liu, F.-H., Wong, H. K., Yang, X.-J., Wu, Q.-J., Zhang, H., Wang, H.-N., Tan, Q.-R., & Zhang, Z.-J. (2019). Effectiveness of electroacupuncture and electroconvulsive therapy as additional treatment in hospitalized patients with schizophrenia: A retrospective controlled study. *Frontiers in Psychology*, 10. <https://doi.org/10.3389/fpsyg.2019.02306>
- Joukamaa, M., Heliövaara, M., Knekt, P., Aromaa, A., Raitasalo, R., & Lehtinen, V. (2006). Schizophrenia, neuroleptic medication and mortality. *British Journal of Psychiatry*, 188(2), 122–127. <https://doi.org/10.1192/bjp.188.2.122>
- Joyal, C. C., Hallé, P., Lapierre, D., & Hodgins, S. (2003). Drug abuse and/or dependence and better neuropsychological performance in patients with schizophrenia. *Schizophrenia Research*, 63(3), 297–299. [https://doi.org/10.1016/S0920-9964\(02\)00387-0](https://doi.org/10.1016/S0920-9964(02)00387-0)
- Juckel, G., & Hoffmann, K. (2018). [The Indian Ayurveda medicine-a meaningful supplement to psychiatric treatment?]. *Der Nervenarzt*, 89(9), 999–1008. <https://doi.org/10.1007/s00115-018-0538-9>
- Jung, C. G. (1925). The content of the psychoses. In J. S. Van Teslaar (Ed.), *An outline of psychoanalysis*. (2006-21557-012; pp. 255–271). Modern Library. <https://doi.org/10.1037/11350-012>
- Kane, J. M., & Leucht, S. (2008). Unanswered questions in schizophrenia clinical trials. *Schizophrenia Bulletin*, 34(2), 302–309. <https://doi.org/10.1093/schbul/sbm143>
- Kapelski, P., Hauser, J., Dmitrzak-Weglarz, M., Skibinska, M., Slopian, A., Kaczmarkiewicz-Fass, M., Rajewska, A., Gattner, K., & Czernski, P. M. (2006). Brak asocjacji pomiedzy polimorfizmem insercyjno-delecyjnym promotorowego odcinka genu transportera serotoniny a schizofrenia. *Psychiatria Polska*, 40(5), 925–935.
- Kapsambelis, V. (2019). Psychoanalytic approaches to psychotic disorders in a public mental health system. *British Journal of Psychotherapy*, 35(4), 577–585. <https://doi.org/10.1111/bjp.12482>
- Kelly, D. L., Rowland, L. M., Patchan, K. M., Sullivan, K., Earl, A., Raley, H., Liu, F., Feldman, S., & McMahon, R. P. (2016). Schizophrenia clinical symptom differences in women vs men with and without a history of childhood physical abuse. *Child and Adolescent Psychiatry and Mental Health*, 10. <https://doi.org/10.1186/s13034-016-0092-9>
- Kesey, K. (1963). *One Flew Over the Cuckoo's Nest*. Berkley.
- Khandaker, G. M., Zimbron, J., Dalman, C., Lewis, G., & Jones, P. B. (2012). Childhood infection and adult schizophrenia: A meta-analysis of population-based studies. *Schizophrenia Research*, 139(1–3), 161–168. <https://doi.org/10.1016/j.schres.2012.05.023>
- Kim, H., Kim, D., & Kim, S. H. (2018). Association of types of delusions and hallucinations with childhood abuse and neglect among inpatients with schizophrenia in South Korea: A preliminary study. *Psychosis: Psychological, Social and Integrative Approaches*, 10(3), 208–212. <https://doi.org/10.1080/17522439.2018.1472627>
- Kline, J., Becker, J., & Giese, C. (1992). Psychodynamic interventions revisited: Options for the treatment of schizophrenia. *Psychotherapy: Theory, Research, Practice, Training*, 29(3), 366–377. <https://doi.org/10.1037/h0088538>
- Knight, J. G. (1982). Dopamine-receptor-stimulating autoantibodies: A possible cause of schizophrenia. *Lancet (London, England)*, 2(8307), 1073–1076. [https://doi.org/10.1016/s0140-6736\(82\)90007-1](https://doi.org/10.1016/s0140-6736(82)90007-1)
- Knight, J. G., Menkes, D. B., Highton, J., & Adams, D. D. (2007). Rationale for a trial of immunosuppressive therapy in acute schizophrenia. *Molecular Psychiatry*, 12(5), 424–431.
- Koch, E., Rosenthal, B., Lundquist, A., Chen, C.-H., & Kauppi, K. (2020). Interactome overlap between schizophrenia and cognition. *Schizophrenia Research*, S0920996420303467. <https://doi.org/10.1016/j.schres.2020.06.002>
- Kohler, C. G., Loughead, J., Ruparel, K., Indersmitten, T., Barrett, F. S., Gur, R. E., & Gur, R. C. (2008). Brain activation during eye gaze discrimination in stable schizophrenia. *Schizophrenia Research*, 99(1), 286–293. <https://doi.org/10.1016/j.schres.2007.09.038>
- Kortegaard, H. M. (1993). Music therapy in the psychodynamic treatment of schizophrenia. *Music Therapy in Health and Education*, 55–65.
- Kozloff, N., Mulsant, B. H., Stergiopoulos, V., & Voineskos, A. N. (2020). The COVID-19 Global Pandemic: Implications for People with Schizophrenia and Related Disorders. *Schizophrenia Bulletin*. <https://doi.org/10.1093/schbul/sbaa051>
- Krogmann, A., Peters, L., von Hardenberg, L., Bödeker, K., Nöhles, V. B., & Correll, C. U. (2019). Keeping up with the therapeutic advances in schizophrenia: A review of novel and emerging pharmacological entities. *CNS Spectrums*, 24(S1), 38–69. <https://doi.org/10.1017/S109285291900124X>

- Kroll, J. L. (2007). New directions in the conceptualization of psychotic disorders. *Current Opinion in Psychiatry*, 20(6), 573–577.
- Kumar, V., Vajawat, B., & Rao, N. P. (2020). Frontal gaba in schizophrenia: A meta-analysis of 1h-mrs studies. *The World Journal of Biological Psychiatry*. <https://doi.org/10.1080/15622975.2020.1731925>
- Lamster, F., Kiener, J., Wagner, K., Rief, W., Görge, S. C., Iwaniuk, S., Leube, D., Falkenberg, I., Kluge, I., Kircher, T., & Mehl, S. (2018). Ist Wahn indirekt veränderbar? Ein stimmungsverbesserndes Konzept der kognitive Verhaltenstherapie für die stationäre Standardversorgung von Patienten mit schizophrenen Störungen = Are delusions indirectly alterable? A mood-stabilizing CBT-p concept for inpatients with schizophrenia. *Verhaltenstherapie*, 28(3), 138–146. <https://doi.org/10.1159/000486966>
- Laskemoen, J. F., Büchmann, C., Barrett, E. A., Collier-Høegh, M., Haatveit, B., Vedal, T. J., Ueland, T., Melle, I., Aas, M., & Simonsen, C. (2020). Do sleep disturbances contribute to cognitive impairments in schizophrenia spectrum and bipolar disorders? *European Archives of Psychiatry and Clinical Neuroscience*, 270(6), 749–759. <https://doi.org/10.1007/s00406-019-01075-0>
- Laursen, T. M. (2019). Causes of premature mortality in schizophrenia: A review of literature published in 2018. *Current Opinion in Psychiatry*, 32(5), 388–393. <https://doi.org/10.1097/YCO.0000000000000530>
- Laursen, T. M., Munk-Olsena, T., & Vestergaardb, M. (2012). Life expectancy and cardiovascular mortality in persons with schizophrenia. *Current Opinion in Psychiatry*, 25(2), 83–88. <https://doi.org/10.1097/YCO.0b013e32835035ca>
- Lawrence, R., Bradshaw, T., & Mairs, H. (2006). Group cognitive behavioural therapy for schizophrenia: A systematic review of the literature. *Journal of Psychiatric and Mental Health Nursing*, 13(6), 673–681. <https://doi.org/10.1111/j.1365-2850.2006.01014.x>
- Leão, T. S., Sundquist, J., Frank, G., Johansson, L.-M., Johansson, S.-E., & Sundquist, K. (2006). Incidence of schizophrenia or other psychoses in first-and second-generation immigrants: A national cohort study. *Journal of Nervous and Mental Disease*, 194(1), 27–33. <https://doi.org/10.1097/01.nmd.0000195312.81334.81>
- Leonhardt, B. L., Hamm, J. A., Belanger, E. A., & Lysaker, P. H. (2015). Childhood sexual abuse moderates the relationship of self-reflectivity with increased emotional distress in schizophrenia. *Psychosis: Psychological, Social and Integrative Approaches*, 7(3), 195–205. <https://doi.org/10.1080/17522439.2014.968858>
- Lester, D. (2007). Suicide mortality in schizophrenics. *Suicide in Schizophrenia*, 19–29.
- Leucht, S., Burkard, T., Henderson, J., Maj, M., & Sartorius, N. (2007). Physical illness and schizophrenia: A review of the literature. *Acta Psychiatrica Scandinavica*, 116(5), 317–333. <https://doi.org/10.1111/j.1600-0447.2007.01095.x>
- Lewis, S., & Lieberman, J. (2008). CATIE and CutLASS: Can we handle the truth? *British Journal of Psychiatry*, 192(3), 161–163. <https://doi.org/10.1192/bjp.bp.107.037218>
- Lieberman, J. A., Stroup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins, D. O., Keefe, R. S. E., Davis, S. M., Davis, C. E., Lebowitz, B. D., Severe, J., & Hsiao, John K. (2005). Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. *New England Journal of Medicine*, 353(12), 1209–1223. <https://doi.org/10.1056/NEJMoa051688>
- López-Muñoz, F., Alamo, C., Cuenca, E., Shen, W. W., Clervoy, P., & Rubio, G. (2005). History of the discovery and clinical introduction of chlorpromazine. *Annals of Clinical Psychiatry: Official Journal of the American Academy of Clinical Psychiatrists*, 17(3), 113–135. <https://doi.org/10.1080/10401230591002002>
- Lorenzo, C. V., Baca-Garcia, E., Diaz-Hernandez, M., Botillo-Martin, C., Perez-Rodriguez, M. M., Fernandez-Ramos, C., Saiz-Gonzalez, M. D., Quintero-Gutierrez, F. J., Saiz-Ruiz, J., Piqueras, J. F., de Rivera, J. L. G., & de Leon, J. (2006). Association between the T102C polymorphism of the serotonin-2A receptor gene and schizophrenia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 30(6), 1136–1138. <https://doi.org/10.1016/j.pnpbp.2006.04.027>
- Lublin, H., & Eberhard, J. (2008). Content versus delivery: Challenges and options in the treatment of schizophrenia. *European Neuropsychopharmacology*, 18(3), v–vi. <https://doi.org/10.1016/j.euroneuro.2008.04.001>
- Lucas, R. (2003). The relationship between psychoanalysis and schizophrenia. *International Journal of Psychoanalysis*, 84(1), 3–9. <https://doi.org/10.1516/00207570360509439>
- Lysaker, P. H., Beattie, N. L., Strasburger, A. M., & Davis, L. W. (2005). Reported history of child sexual abuse in schizophrenia: Associations with heightened symptom levels and poorer participation over four months in vocational rehabilitation. *Journal of Nervous and Mental Disease*, 193(12), 790–795. <https://doi.org/10.1097/01.nmd.0000188970.11916.76>
- Lysaker, P. H., Meyer, P. S., Evans, J. D., Clements, C. A., & Marks, K. A. (2001). Childhood Sexual Trauma and Psychosocial Functioning in Adults with Schizophrenia. *Psychiatric Services*, 52(11), 1485–1488. <https://doi.org/10.1176/appi.ps.52.11.1485>

- Lysaker, P. H., Nees, M. A., Lancaster, R. S., & Davis, L. W. (2004). Vocational function among persons with schizophrenia with and without history of childhood sexual trauma. *Journal of Traumatic Stress, 17*(5), 435–438. <https://doi.org/10.1023/B:JOTS.0000048957.70768.b9>
- Marneros, A. (2007). Do schizoaffective disorders exist at all? *Acta Psychiatrica Scandinavica, 115*(2), 162. <https://doi.org/10.1111/j.1600-0447.2006.00945.x>
- Masciotra, L., Landreau, F., Conesa, H. A., & Erausquin, G. A. de. (2005). Pathophysiology of Schizophrenia: A New Look at the Role of Dopamine. *Trends in Schizophrenia Research, 27–44*.
- Maurel, M., Belzeaux, R., Adida, M., Fakra, E., Cermolacce, M., Da Fonseca, D., & Azorin, J.-M. (2011). Schizophrénie, cognition et psycho-éducation = Schizophrenia, cognition and psychoeducation. *L'Encéphale: Revue de Psychiatrie Clinique Biologique et Thérapeutique, 37*(Suppl 2), S151–S154. [https://doi.org/10.1016/S0013-7006\(11\)70043-4](https://doi.org/10.1016/S0013-7006(11)70043-4)
- May, P. (1968). *Treatment of schizophrenia; A comparative study of five treatment methods* (First Edition edition). Science House.
- McGrath, J., Brown, A., & St Clair, D. (2011). Prevention and Schizophrenia—The Role of Dietary Factors. *Schizophrenia Bulletin, 37*(2), 272–283. <https://doi.org/10.1093/schbul/sbq121>
- McGrath, J. J. (2006). Variations in the incidence of schizophrenia: Data versus dogma. *Schizophrenia Bulletin, 32*(1), 195–197. <https://doi.org/10.1093/schbul/sbi052>
- Meyer, U., Murray, P. J., Urwyler, A., Yee, B. K., Schedlowski, M., & Feldon, J. (2008). Adult behavioral and pharmacological dysfunctions following disruption of the fetal brain balance between pro-inflammatory and IL-10-mediated anti-inflammatory signaling. *Molecular Psychiatry, 13*(2), 208–221. <https://doi.org/10.1038/sj.mp.4002042>
- Meyer, Urs, Feldon, J., Schedlowski, M., & Yee, B. K. (2006). Immunological stress at the maternal-foetal interface: A link between neurodevelopment and adult psychopathology. *Brain, Behavior, and Immunity, 20*(4), 378–388. <https://doi.org/10.1016/j.bbi.2005.11.003>
- Meyer, Urs, Nyffeler, M., Schwendener, S., Knuesel, I., Yee, B. K., & Feldon, J. (2008). Relative prenatal and postnatal maternal contributions to schizophrenia-related neurochemical dysfunction after in utero immune challenge. *Neuropsychopharmacology, 33*(2), 441–456. <https://doi.org/10.1038/sj.npp.1301413>
- Miller, B. J., Buckley, P., Seabolt, W., Mellor, A., & Kirkpatrick, B. (2011). Meta-Analysis of Cytokine Alterations in Schizophrenia: Clinical Status and Antipsychotic Effects. *Biological Psychiatry, 70*(7), 663–671. <https://doi.org/10.1016/j.biopsych.2011.04.013>
- Miller, P., Lawrie, S. M., Hodges, A., Clafferty, R., Cosway, R., & Johnstone, E. C. (2001). Genetic liability, illicit drug use, life stress and psychotic symptoms: Preliminary findings from the Edinburgh study of people at high risk for schizophrenia. *Social Psychiatry and Psychiatric Epidemiology, 36*(7), 338–342. <https://doi.org/10.1007/s001270170038>
- Mishra, A., Mishra, A. K., & Jha, S. (2018). Effect of traditional medicine brahmi vati and bacoside A-rich fraction of *Bacopa monnieri* on acute pentylenetetrazole-induced seizures, amphetamine-induced model of schizophrenia, and scopolamine-induced memory loss in laboratory animals. *Epilepsy & Behavior: E&B, 80*, 144–151. <https://doi.org/10.1016/j.yebeh.2017.12.040>
- Mitsadali, I., Grayson, B., Idris, N. F., Watson, L., Burgess, M., & Neill, J. (2020). Aerobic exercise improves memory and prevents cognitive deficits of relevance to schizophrenia in an animal model. *Journal of Psychopharmacology, 34*(7), 695–708. <https://doi.org/10.1177/0269881120922963>
- Mittal, V. A., Saczawa, M. E., Walker, E., Willhite, R., & Walder, D. (2008). Prenatal exposure to viral infection and conversion among adolescents at high-risk for psychotic disorders. *Schizophrenia Research, 99*(1), 375–376. <https://doi.org/10.1016/j.schres.2007.11.037>
- Møllerhøj, J., Os Stølan, L., Erdner, A., Hedberg, B., Stahl, K., Riise, J., Jedenius, E., & Rise, M. B. (2019). 'i live, I don't work, but I live a very normal life'—A qualitative interview study of scandinavian user experiences of schizophrenia, antipsychotic medication, and personal recovery processes. *Perspectives in Psychiatric Care*. <https://doi.org/10.1111/ppc.12444>
- Moran, E. K., Gold, J. M., Carter, C. S., MacDonald, A. W., Ragland, J. D., Silverstein, S. M., Luck, S. J., & Barch, D. M. (2020). Both unmedicated and medicated individuals with schizophrenia show impairments across a wide array of cognitive and reinforcement learning tasks. *Psychological Medicine*. <https://doi.org/10.1017/S003329172000286X>
- Moreno, J. L., Kurita, M., Holloway, T., López, J., Cadagan, R., Martínez-Sobrido, L., García-Sastre, A., & González-Maeso, J. (2011). Maternal influenza viral infection causes schizophrenia-like alterations of 5-HT_{2A} and mGlu₂ receptors in the adult offspring. *The Journal of Neuroscience, 31*(5), 1863–1872. <https://doi.org/10.1523/JNEUROSCI.4230-10.2011>
- Mueser, K. T., & Berenbaum, H. (1990). Psychodynamic treatment of schizophrenia: Is there a future? *Psychological Medicine, 20*(2), 253–262.
- Mullen, P. E. (2005). Child sexual abuse and schizophrenia: Author's reply. *The British Journal of Psychiatry, 186*(1), 76–76.

- Murray, R. M., Grech, A., Phillips, P., & Johnson, S. (2003). What is the relationship between substance abuse and schizophrenia? In R. M. Murray, P. B. Jones, E. Susser, J. van Os, & M. Cannon (Eds.), *The epidemiology of schizophrenia*. (2003-04863-016; pp. 317–342). Cambridge University Press.
- Nelson, C. L. M., Amsbaugh, H. M., Reilly, J. L., Rosen, C., Marvin, R. W., Ragozzino, M. E., Bishop, J. R., Sweeney, J. A., & Hill, S. K. (2018). Beneficial and adverse effects of antipsychotic medication on cognitive flexibility are related to COMT genotype in first episode psychosis. *Schizophrenia Research*, 202, 212–216. <https://doi.org/10.1016/j.schres.2018.06.029>
- Niebuhr, D. W., Millikan, A. M., Cowan, D. N., Yolken, R., Li, Y., & Weber, N. S. (2008). Selected infectious agents and risk of schizophrenia among U.S. Military personnel. *American Journal of Psychiatry*, 165(1), 99–106. <https://doi.org/10.1176/appi.ajp.2007.06081254>
- Nightingale, L. C., & McQueeney, D. A. (1996). Group therapy for schizophrenia: Combining and expanding the psychoeducational model with supportive psychotherapy. *International Journal of Group Psychotherapy*, 46(4), 517–533.
- Nixon, N. L., & Doody, G. A. (2005). Official psychiatric morbidity and the incidence of schizophrenia 1881–1994. *Psychological Medicine*, 35(8), 1145–1153. <https://doi.org/10.1017/S0033291705004939>
- Ohara, K. (2007). The n-3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 31(2), 469–474. <https://doi.org/10.1016/j.pnpbp.2006.11.013>
- Ortiz-Medina, M. B., Perea, M., Torales, J., Ventriglio, A., Vitrani, G., Aguilar, L., & Roncero, C. (2018). Cannabis consumption and psychosis or schizophrenia development. *International Journal of Social Psychiatry*, 64(7), 690–704. <https://doi.org/10.1177/0020764018801690>
- Ottet, M.-C., Schaer, M., Cammoun, L., Schneider, M., Debbané, M., Thiran, J.-P., & Eliez, S. (2013). Reduced fronto-temporal and limbic connectivity in the 22q11.2 deletion syndrome: Vulnerability markers for developing schizophrenia? *PLoS ONE*, 8(3). <https://doi.org/10.1371/journal.pone.0058429>
- Pandurangi, A. K., & Buckley, P. F. (2020). Inflammation, Antipsychotic Drugs, and Evidence for Effectiveness of Anti-inflammatory Agents in Schizophrenia. In G. M. Khandaker, U. Meyer, & P. B. Jones (Eds.), *Neuroinflammation and Schizophrenia* (pp. 227–244). Springer International Publishing. https://doi.org/10.1007/7854_2019_91
- Pang, N., Thrichelvam, N., & Naing, K. O. (2017). Olanzapine-induced Pancytopenia: A Rare but Worrying Complication. *East Asian Archives of Psychiatry: Official Journal of the Hong Kong College of Psychiatrists = Dong Ya Jing Shen Ke Xue Zhi: Xianggang Jing Shen Ke Yi Xue Yuan Qi Kan*, 27(1), 35–37.
- Peltzer, K. (1999). Faith Healing for Mental and Social Disorders in the Northern Province (South Africa). *Journal of Religion in Africa*, 29(3), 387–402.
- Potvin, S., Stip, E., Sepehry, A. A., Gendron, A., Bah, R., & Kouassi, E. (2008). Inflammatory cytokine alterations in schizophrenia: A systematic quantitative review. *Biological Psychiatry*, 63(8), 801–808.
- Poulet, E., Brunelin, J., Kallel, L., D'Amato, T., & Saoud, M. (2008). Maintenance treatment with transcranial magnetic stimulation in a patient with late-onset schizophrenia. *American Journal of Psychiatry*, 165(4), 537–538. <https://doi.org/10.1176/appi.ajp.2007.07060868>
- Prasad, K. M. R., Shirts, B. H., Yolken, R. H., Keshavan, M. S., & Nimgaonkar, V. L. (2007a). Brain morphological changes associated with exposure to HSV1 in first-episode schizophrenia. *Molecular Psychiatry*, 12(1), 105–113. <https://doi.org/10.1038/sj.mp.4001915>
- Prasad, K. M. R., Shirts, B. H., Yolken, R. H., Keshavan, M. S., & Nimgaonkar, V. L. (2007b). HSV1 exposure affects prefrontal cortical structure in schizophrenia patients. *Molecular Psychiatry*, 12(1), 1. <https://doi.org/10.1038/sj.mp.4001942>
- Pratt, L. A. (2012). Characteristics of adults with serious mental illness in the United States household population in 2007. *Psychiatric Services*, 63(10), 1042–1046. <https://doi.org/10.1176/appi.ps.201100442>
- Rado, J. T., & Hernandez, E. I. (2014). Therapeutic neuromodulation for treatment of schizophrenia. In P. G. Janicak, S. R. Marder, R. Tandon, & M. Goldman (Eds.), *Schizophrenia: Recent advances in diagnosis and treatment*. (2014-26994-008; pp. 139–160). Springer Science + Business Media.
- Rakitzis, S., Georgila, P., & Becker-Woitag, A. P. (2020). The recovery process for individuals with schizophrenia in the context of evidence-based psychotherapy and rehabilitation: A systematic review. *European Psychologist*. <https://doi.org/10.1027/1016-9040/a000400>
- Ran, M.-S., Chen, E. Y.-H., Conwell, Y., Lai-Wan Chan, C., Yip, P. S. F., Xiang, M.-Z., & Caine, E. D. (2007). Mortality in people with schizophrenia in rural China: 10-year cohort study. *British Journal of Psychiatry*, 190(3), 237–242. <https://doi.org/10.1192/bjp.bp.106.025155>
- Rashno, M. M., Fallahi, S., Arab-Mazar, Z., & Dana, H. (2019). Seromolecular assess of Toxoplasma gondii infection in pregnant women and neonatal umbilical cord blood. *EXCLI Journal*, 18, 1–7.
- Rathbone, J., Zhang, L., Zhang, M., Xia, J., Liu, X., Yang, Y., & Adams, C. E. (2007). Chinese herbal medicine for schizophrenia: Cochrane systematic review of randomised trials. *The British Journal of Psychiatry*, 190, 379–384. <https://doi.org/10.1192/bjp.bp.106.026880>

- Read, J., van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and schizophrenia: A literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica*, *112*(5), 330–350. <https://doi.org/10.1111/j.1600-0447.2005.00634.x>
- Read, John, Agar, K., Argyle, N., & Aderhold, V. (2003). Sexual and physical abuse during childhood and adulthood as predictors of hallucinations, delusions and thought disorder. *Psychology and Psychotherapy: Theory, Research and Practice*, *76*(1), 1–22. <https://doi.org/10.1348/14760830260569210>
- Richard, M. D., & Brahm, N. C. (2012). Schizophrenia and the immune system: Pathophysiology, prevention, and treatment. *American Journal of Health-System Pharmacy: AJHP: Official Journal of the American Society of Health-System Pharmacists*, *69*(9), 757–766. <https://doi.org/10.2146/ajhp110271>
- Robinson, D. S. (2008). Mortality risks and antipsychotics. *Primary Psychiatry*, *15*(4), 21–23.
- Rokita, K. I., Dauvermann, M. R., Mothersill, D., Holleran, L., Holland, J., Costello, L., Cullen, C., Kane, R., McKernan, D., Morris, D. W., Kelly, J., Gill, M., Corvin, A., Hallahan, B., McDonald, C., & Donohoe, G. (2020). Childhood trauma, parental bonding, and social cognition in patients with schizophrenia and healthy adults. *Journal of Clinical Psychology*. <https://doi.org/10.1002/jclp.23023>
- Roser, P. (2019). Cannabis und Schizophrenie—Risikofaktoren, diagnostische Einordnung und Auswirkungen auf Verlauf und Prognose = Cannabis and schizophrenia—Risk factors, diagnostic classification and effects on course and outcome. *Forensische Psychiatrie, Psychologie, Kriminologie*, *13*(3), 225–232. <https://doi.org/10.1007/s11757-019-00543-6>
- Ross, C. (2014). Dissociation in classical texts on schizophrenia. *Psychosis: Psychological, Social and Integrative Approaches*, *6*(4), 342–354. <https://doi.org/10.1080/17522439.2013.806570>
- Ross, C. A. (2006). Dissociation and psychosis: The need for integration of theory and practice. *Evolving Psychosis.*, 238–254.
- Rossello, J.-J., Gaillard, G., & Neuilly, M.-T. (2013). Une institution en quête de limites. Le mythe de Tom Sawyer: Un objet transitionnel collectif. = An institution seeking limits. The myth of Tom Sawyer : A collective transitional object. *Revue de Psychothérapie Psychanalytique de Groupe*, *60*, 141–152. <https://doi.org/10.3917/rppg.060.0141>
- Ryan, J. E., Veliz, P., McCabe, S. E., Stoddard, S. A., & Boyd, C. J. (2020). Association of early onset of cannabis, cigarette, other drug use and schizophrenia or psychosis. *Schizophrenia Research*, *215*, 482–484. <https://doi.org/10.1016/j.schres.2019.10.002>
- Sabe, M., Kaiser, S., & Sentissi, O. (2020). Physical exercise for negative symptoms of schizophrenia: Systematic review of randomized controlled trials and meta-analysis. *General Hospital Psychiatry*, *62*, 13–20. <https://doi.org/10.1016/j.genhosppsych.2019.11.002>
- Saha, S., Chant, D. C., Welham, J. L., & McGrath, J. J. (2006). The incidence and prevalence of schizophrenia varies with latitude. *Acta Psychiatrica Scandinavica*, *114*(1), 36–39. <https://doi.org/10.1111/j.1600-0447.2005.00742.x>
- Saha, S., Chant, D., & McGrath, J. (2007). A systematic review of mortality in schizophrenia: Is the differential mortality gap worsening over time? *Archives of General Psychiatry*, *64*(10), 1123–1131. <https://doi.org/10.1001/archpsyc.64.10.1123>
- Saha, S., Welham, J., Chant, D., & McGrath, J. (2006). Incidence of schizophrenia does not vary with economic status of the country: Evidence from a systematic review. *Social Psychiatry and Psychiatric Epidemiology*, *41*(5), 338–340. <https://doi.org/10.1007/s00127-006-0041-7>
- Sarter, M., Nelson, C. L., & Bruno, J. P. (2005). Cortical Cholinergic Transmission and Cortical Information Processing in Schizophrenia. *Schizophrenia Bulletin*, *31*(1), 117–138. <https://doi.org/10.1093/schbul/sbi006>
- Schürhoff, F., Laguerre, A., Fisher, H., Etain, B., Méary, A., Soussy, C., Szöke, A., & Leboyer, M. (2009). Self-reported childhood trauma correlates with schizotypal measures in schizophrenia but not bipolar pedigrees. *Psychological Medicine*, *39*(3), 365–370. <https://doi.org/10.1017/S0033291708003905>
- Schwab, S. G., & Wildenauer, D. B. (2008). Research on causes for schizophrenia: Are we close? *Schizophrenia Research*, *102*(1), 29–30. <https://doi.org/10.1016/j.schres.2008.04.005>
- Scull, A. (2005). *Madhouse: A Tragic Tale of Megalomania and Modern Medicine* (1st ed.). Yale University Press.
- Searles, H. F. (1986). *Collected Papers on Schizophrenia and Related Subjects* (1 edition). Routledge.
- Seeman, P. (2000). Antipsychotic drugs, dopamine D2 receptors, and schizophrenia. *Neurotransmitter Receptors in Actions of Antipsychotic Medications.*, 43–63.
- Sepehry, A. A., Potvin, S., Élie, R., & Stip, E. (2007). Selective serotonin reuptake inhibitor (SSRI) add-on therapy for the negative symptoms of schizophrenia: A meta-analysis. *Journal of Clinical Psychiatry*, *68*(4), 604–610.
- Setién-Suero, E., Neergaard, K., Ortiz-García de la Foz, V., Suárez-Pinilla, P., Martínez-García, O., Crespo-Facorro, B., & Ayesa-Arriola, R. (2019). Stopping cannabis use benefits outcome in psychosis: Findings from 10-year follow-up study in the PAFIP-cohort. *Acta Psychiatrica Scandinavica*, *140*(4), 349–359. <https://doi.org/10.1111/acps.13081>

- Severance, E. G., Prandovszky, E., Castiglione, J., & Yolken, R. H. (2015). Gastroenterology issues in schizophrenia: Why the gut matters. *Current Psychiatry Reports, 17*(5), 27. <https://doi.org/10.1007/s11920-015-0574-0>
- Severance, E. G., & Yolken, R. H. (2020). From Infection to the Microbiome: An Evolving Role of Microbes in Schizophrenia. *Current Topics in Behavioral Neurosciences, 44*, 67–84. https://doi.org/10.1007/7854_2018_84
- Severance, E. G., Yolken, R. H., & Eaton, W. W. (2016). Autoimmune diseases, gastrointestinal disorders and the microbiome in schizophrenia: More than a gut feeling. *Schizophrenia Research, 176*(1), 23–35. <https://doi.org/10.1016/j.schres.2014.06.027>
- Shekunov, J. (2016). Immigration and Risk of Psychiatric Disorders: A Review of Existing Literature. *American Journal of Psychiatry Residents' Journal, 11*(2), 3–5. <https://doi.org/10.1176/appi.ajp-rj.2016.110202>
- Shimada, T., Ito, S., Makabe, A., Yamanushi, A., Takenaka, A., & Kobayashi, M. (2019). Aerobic exercise and cognitive functioning in schizophrenia: A pilot randomized controlled trial. *Psychiatry Research, 282*. <https://doi.org/10.1016/j.psychres.2019.112638>
- Shonin, E., Van Gordon, W., & Griffiths, M. D. (2014). Cognitive behavioral therapy (CBT) and Meditation Awareness Training (MAT) for the treatment of co-occurring schizophrenia and pathological gambling: A case study. *International Journal of Mental Health and Addiction, 12*(2), 181–196. <https://doi.org/10.1007/s11469-013-9460-3>
- Silva, M. A., & Restrepo, D. (2019). Recuperación funcional en la esquizofrenia = Functional recovery in schizophrenia. *Revista Colombiana de Psiquiatría, 48*(4), 252–260. <https://doi.org/10.1016/j.rcp.2017.08.004>
- Sim, K., Chan, Y. H., Chua, T. H., Mahendran, R., Chong, S. A., & McGorry, P. (2006). Physical comorbidity, insight, quality of life and global functioning in first episode schizophrenia: A 24-month, longitudinal outcome study. *Schizophrenia Research, 88*(1), 82–89. <https://doi.org/10.1016/j.schres.2006.07.004>
- Sim, K., Chua, T. H., Chan, Y. H., Mahendran, R., & Chong, S. A. (2006). Psychiatric comorbidity in first episode schizophrenia: A 2 year, longitudinal outcome study. *Journal of Psychiatric Research, 40*(7), 656–663. <https://doi.org/10.1016/j.jpsychires.2006.06.008>
- Simeone, J. C., Ward, A. J., Rotella, P., Collins, J., & Windisch, R. (2015). An evaluation of variation in published estimates of schizophrenia prevalence from 1990-2013: A systematic literature review. *BMC Psychiatry, 15*(1), 1–14. <https://doi.org/10.1186/s12888-015-0578-7>
- Sommer, I. E., de Witte, L., Begemann, M., & Kahn, R. S. (2012). Nonsteroidal anti-inflammatory drugs in schizophrenia: Ready for practice or a good start? A meta-analysis. *The Journal of Clinical Psychiatry, 73*(4), 414–419. <https://doi.org/10.4088/JCP.10r06823>
- Spataro, J., Mullen, P. E., Burgess, P. M., Wells, D. L., & Moss, S. A. (2004). Impact of child sexual abuse on mental health: Prospective study in males and females. *The British Journal of Psychiatry, 184*(5), 416–421. <https://doi.org/10.1192/bjp.184.5.416>
- Staudt, M. D., Herring, E. Z., Gao, K., Miller, J. P., & Sweet, J. A. (2019). Evolution in the Treatment of Psychiatric Disorders: From Psychosurgery to Psychopharmacology to Neuromodulation. *Frontiers in Neuroscience, 13*. <https://doi.org/10.3389/fnins.2019.00108>
- Steel, C. (2013). *CBT for schizophrenia: Evidence-based interventions and future directions* (C. Steel, Ed.; 2013-04591-000). Wiley Blackwell. <https://doi.org/10.1002/9781118330029>
- Stone, M. H. (1999). The History of the Psychoanalytic Treatment of Schizophrenia. *J. Amer. Acad. Psychoanal., 583–601*.
- Sudak, D. M. (2004). Cognitive-behavioral therapy for schizophrenia. *Journal of Psychiatric Practice, 10*(5), 331–333. <https://doi.org/10.1097/00131746-200409000-00007>
- Sumiyoshi, T., Park, S., Jayathilake, K., Roy, A., Ertugrul, A., & Meltzer, H. Y. (2007). Effect of buspirone, a serotonin-sub(1A) partial agonist, on cognitive function in schizophrenia: A randomized, double-blind, placebo-controlled study. *Schizophrenia Research, 95*(1), 158–168. <https://doi.org/10.1016/j.schres.2007.06.008>
- Sutterland, A. L., Kuin, A., Kuiper, B., van Gool, T., Leboyer, M., Fond, G., & de Haan, L. (2019). Driving us mad: The association of *Toxoplasma gondii* with suicide attempts and traffic accidents—A systematic review and meta-analysis. *Psychological Medicine, 49*(10), 1608–1623. <https://doi.org/10.1017/S0033291719000813>
- Suvisaari, J. M., Haukka, J. K., Tanskanen, A. J., & Lönnqvist, J. K. (1999). Decline in the incidence of schizophrenia in Finnish cohorts born from 1954 to 1965. *Archives of General Psychiatry, 56*(8), 733–740. <https://doi.org/10.1001/archpsyc.56.8.733>
- Szumliński, K. K., & Kippin, T. E. (2008). Homer: A genetic factor in schizophrenia? *Cortical Deficits in Schizophrenia: From Genes to Function., 29–72*.
- Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2010). Schizophrenia, “Just the Facts” 5. Treatment and prevention Past, present, and future. *Schizophrenia Research, 122*(1), 1–23. <https://doi.org/10.1016/j.schres.2010.05.025>

- Thomann, P. A., Wolf, R. C., Nolte, H. M., Hirjak, D., Hofer, S., Seidl, U., Depping, M. S., Stieltjes, B., Maier-Hein, K., Sambataro, F., & Wüstenberg, T. (2017). Neuromodulation in response to electroconvulsive therapy in schizophrenia and major depression. *Brain Stimulation, 10*(3), 637–644. <https://doi.org/10.1016/j.brs.2017.01.578>
- Tidd, C. W. (1937). Increasing reality acceptance by a schizoid personality during analysis. *Bulletin of the Menninger Clinic, 1*, 176–183.
- Tidd, C. W. (1938). A note on the treatment of schizophrenia. *Bulletin of the Menninger Clinic, 2*, 89–93.
- Tochigi, M., Okazaki, Y., Kato, N., & Sasaki, T. (2004). What causes seasonality of birth in schizophrenia? *Neuroscience Research, 48*(1), 1–11. <https://doi.org/10.1016/j.neures.2003.09.002>
- Torrey, E. F., Bartko, J. J., & Yolken, R. H. (2012). Toxoplasma gondii and Other Risk Factors for Schizophrenia: An Update. *Schizophrenia Bulletin, 38*(3), 642–647. <https://doi.org/10.1093/schbul/sbs043>
- Trudeau, K. J., Burtner, J., Villapiano, A. J., Jones, M., Butler, S. F., & Joshi, K. (2018). Burden of schizophrenia or psychosis-related symptoms in adults undergoing substance abuse evaluation. *Journal of Nervous and Mental Disease, 206*(7), 528–536.
- Tsapakis, E.-M., Guillin, O., & Murray, R. M. (2003). Does dopamine sensitization underlie the association between schizophrenia and drug abuse? *Current Opinion in Psychiatry, 16*, S45–S52. <https://doi.org/10.1097/00001504-200304002-00008>
- Turkington, D., Dudley, R., Warman, D. M., & Beck, A. T. (2004). Cognitive-behavioral therapy for schizophrenia: A review. *Journal of Psychiatric Practice, 10*(1), 5–16. <https://doi.org/10.1097/00131746-200401000-00002>
- Turkington, D., Kingdon, D., & Chadwick, P. (2003). Cognitive-behavioural therapy for schizophrenia: Filling the therapeutic vacuum. *British Journal of Psychiatry, 183*(2), 98–99. <https://doi.org/10.1192/bjp.183.2.98>
- Valon, P. (2020). Gisela Pankow (1914–1998): Towards a psychoanalytic treatment of the psychoses. *The International Journal of Psychoanalysis, 101*(1), 169–185. <https://doi.org/10.1080/00207578.2020.1716628>
- Vaucher, J., Keating, B. J., Lasserre, A. M., Gan, W., Lyall, D. M., Ward, J., Smith, D. J., Pell, J. P., Sattar, N., Paré, G., & Holmes, M. V. (2018). Cannabis use and risk of schizophrenia: A Mendelian randomization study. *Molecular Psychiatry, 23*(5), 1287–1292. <https://doi.org/10.1038/mp.2016.252>
- Vidal, S., & Huguelet, P. (2019). Thérapie cognitive basée sur le concept de rétablissement pour la schizophrénie: Un cas clinique = Recovery Oriented Cognitive Therapy for schizophrenia: A case report. *Journal de Thérapie Comportementale et Cognitive, 29*(2), 57–66. <https://doi.org/10.1016/j.jtcc.2018.11.001>
- Vogel, M., Meier, J., Grönke, S., Waage, M., Schneider, W., Freyberger, H. J., & Klauer, T. (2011). Differential effects of childhood abuse and neglect: Mediation by posttraumatic distress in neurotic disorder and negative symptoms in schizophrenia? *Psychiatry Research, 189*(1), 121–127. <https://doi.org/10.1016/j.psychres.2011.01.008>
- Volkan, V. D. (2012). *Psychoanalytic Technique Expanded: A Textbook on Psychoanalytic Treatment*. Pitchstone Publishing.
- Volkan, V. D. (1995). *The infantile psychotic self and its fates: Understanding and treating schizophrenics and other difficult patients* (1995-98163-000). Jason Aronson.
- Wang, A. W., Avramopoulos, D., Lori, A., Mulle, J., Conneely, K., Powers, A., Duncan, E., Almli, L., Massa, N., McGrath, J., Schwartz, A. C., Goes, F. S., Weng, L., Wang, R., Yolken, R., Ruczinski, I., Gillespie, C. F., Jovanovic, T., Ressler, K., ... Pearce, B. D. (2019). Genome-wide association study in two populations to determine genetic variants associated with Toxoplasma gondii infection and relationship to schizophrenia risk. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 92*, 133–147. <https://doi.org/10.1016/j.pnpbp.2018.12.019>
- Wang, L.-Y., Chen, S.-F., Chiang, J.-H., Hsu, C.-Y., & Shen, Y.-C. (2018). Autoimmune diseases are associated with an increased risk of schizophrenia: A nationwide population-based cohort study. *Schizophrenia Research, 202*, 297–302. <https://doi.org/10.1016/j.schres.2018.06.033>
- Warman, D. M., & Beck, A. T. (2003). Cognitive behavioral therapy for schizophrenia: An overview of treatment. *Cognitive and Behavioral Practice, 10*(3), 248–254. [https://doi.org/10.1016/S1077-7229\(03\)80037-8](https://doi.org/10.1016/S1077-7229(03)80037-8)
- Weininger, B. I. (1938). Psychotherapy during convalescence from psychosis. *Psychiatry: Journal for the Study of Interpersonal Processes, 2*, 257–264.
- Weiser, M., Reichenberg, A., Rabinowitz, J., Kaplan, Z., Caspi, A., Yasvizky, R., Mark, M., Knobler, H. Y., Nahon, D., & Davidson, M. (2003). Self-Reported Drug Abuse in Male Adolescents with Behavioral Disturbances, and Follow-up for Future Schizophrenia. *Biological Psychiatry, 54*(6), 655–660. [https://doi.org/10.1016/S0006-3223\(03\)00110-0](https://doi.org/10.1016/S0006-3223(03)00110-0)
- Whitaker, R. (2002). *Mad in America: Bad Science, Bad Medicine, And the Enduring Mistreatment Of The Mentally Ill* (1st Edition edition). Basic Books.

- White, T., Cullen, K., Rohrer, L. M., Karatekin, C., Luciana, M., Schmidt, M., Hongwanishkul, D., Kumra, S., Schulz, S. C., & Lim, K. O. (2008). Limbic structures and networks in children and adolescents with schizophrenia. *Schizophrenia Bulletin*, *34*(1), 18–29. <https://doi.org/10.1093/schbul/sbm110>
- Williams, L. (Lea) M., Das, P., Liddell, B. J., Olivieri, G., Peduto, A. S., David, A. S., Gordon, E., & Harris, A. W. F. (2007). Fronto-limbic and autonomic disjunctions to negative emotion distinguish schizophrenia subtypes. *Psychiatry Research: Neuroimaging*, *155*(1), 29–44. <https://doi.org/10.1016/j.psychres.2006.12.018>
- Winterer, G. (2006). Cortical Microcircuits in Schizophrenia—The Dopamine Hypothesis Revisited. *Pharmacopsychiatry*, *39*, S68-s71. <https://doi.org/10.1055/s-2006-931498>
- Włodarczyk, A., Szarmach, J., Cubała, W. J., & Wiglusz, M. S. (2017). Benzodiazepines in combination with antipsychotic drugs for schizophrenia: GABA-ergic targeted therapy. *Psychiatria Danubina*, *29*(Suppl 3), 345–348.
- Wortinger, L. A., Engen, K., Barth, C., Lonning, V., Jørgensen, K. N., Andreassen, O. A., Haukvik, U. K., Vaskinn, A., Ueland, T., & Agartz, I. (2020). Obstetric complications and intelligence in patients on the schizophrenia-bipolar spectrum and healthy participants. *Psychological Medicine*, *50*(11), 1914–1922. <https://doi.org/10.1017/S0033291719002046>
- Wotruba, D., Michels, L., Buechler, R., Metzler, S., Theodoridou, A., Gerstenberg, M., Walitza, S., Kollias, S., Rössler, W., & Heekeren, K. (2014). Aberrant Coupling Within and Across the Default Mode, Task-Positive, and Salience Network in Subjects at Risk for Psychosis. *Schizophrenia Bulletin*, *40*(5), 1095–1104. <https://doi.org/10.1093/schbul/sbt161>
- Xiao, J., Prandovszky, E., Kannan, G., Pletnikov, M. V., Dickerson, F., Severance, E. G., & Yolken, R. H. (2018). *Toxoplasma gondii*: Biological parameters of the connection to schizophrenia. *Schizophrenia Bulletin*, *44*(5), 983–992. <https://doi.org/10.1093/schbul/sby082>
- Xu, J., He, G., Zhu, J., Zhou, X., St Clair, D., Wang, T., Xiang, Y., Zhao, Q., Xing, Q., Liu, Y., Wang, L., Li, Q., He, L., & Zhao, X. (2015). Prenatal nutritional deficiency reprogrammed postnatal gene expression in mammal brains: Implications for schizophrenia. *International Journal of Neuropsychopharmacology*, *18*(4), 1–9. <https://doi.org/10.1093/ijnp/pyu054>
- Xu, L., Qi, X., Zhu, C., & Wan, L. (2018). Activation of IL-8 and its participation in cancer in schizophrenia patients: New evidence for the autoimmune hypothesis of schizophrenia. *Neuropsychiatric Disease and Treatment*, *14*. <https://doi.org/10.2147/NDT.S188210>
- Xu, X. J., & Jiang, G. S. (2015). Niacin-respondent subset of schizophrenia – a therapeutic review. *European Review for Medical and Pharmacological Sciences*, *19*(6), 988–997.
- Zandifar, A., & Badrfam, R. (2020). COVID-19: Considering the prevalence of schizophrenia in the coming decades. *Psychiatry Research*, *288*, 112982. <https://doi.org/10.1016/j.psychres.2020.112982>
- Zhenxing, Y., Longkun, L., & Miaoxin, L. (2018). De novo mutations as causes of schizophrenia. *Psychiatry Research*, *270*, 1168–1169. <https://doi.org/10.1016/j.psychres.2018.05.037>
- Zullino, D. F., Manghi, R., Rathelot, T., Khan, R., & Khazaal, Y. (2010). Cannabis causes schizophrenia? So does nicotine. *Addiction Research & Theory*, *18*(6), 601–605. <https://doi.org/10.3109/16066359.2010.489999>



Knowledge, Attitude and Practice of Medical Students towards COVID-19 Pandemic in a Nigerian Tertiary Institution

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Abstract

The novel Coronavirus disease (COVID-19) SARS-CoV-2, is an evolving respiratory disease which was first detected in December, 2019 in Wuhan, China, and has eventually spread to larger parts of the world. COVID-19 may result in mild to severe respiratory distress, depending on the individuals' age and immune system as well as the presence of any underlying conditions. The objective of the study was to assess the knowledge, attitude and practice of medical students towards COVID-19. The study was a descriptive cross-sectional study that involved all the medical students in Enugu State University College of Medicine, Enugu State, Nigeria. Data was collected with an online questionnaire formulated in Google form. It was shared through their different class online platforms (WhatsApp). All the data were analyzed using SPSS version 25. Categorical variables were presented in the form of frequencies and percentages. Majority of the students were within the 15-24 years age group (79.3%), females (62.1%) and single (98.3%). All the students were of Igbo Ethnic group and Christians. Most of them were in their 5th year of study (39.7%). About 65.4% of the students had good knowledge of COVID-19, while 48.6% of them had good attitude towards COVID-19. Majority of them (77.6%) however, had good practice towards COVID-19. There is poor attitude of the medical students towards the COVID-19 pandemic but they had better knowledge and practice towards the pandemic. Measures should be put in place to address attitudinal change among this group of students towards infectious diseases like the present COVID-19.

Keywords: COVID-19, Enugu State, Medical Students, Nigeria, Tertiary Health Facility

1. INTRODUCTION

In December 2019, an outbreak of viral pneumonia of unknown aetiology was reported in Wuhan City in the East of China (Lu, Stratton & Tang, 2020). It was linked to a seafood and wild animal wholesale market in Wuhan, Hubei Province, China (Li et al, 2020). Gene sequencing showed that the pathogens were enveloped positive-stranded RNA viruses that belong to the family Coronaviridae and the order Nidovirales (Habibzadeh & Stoneman, 2020). The virus was first named 2019-nCoV by the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses and then changed to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Gorbalenya, 2020). On February 11, 2020, the World Health Organization (WHO) gave a new name to the disease caused by this virus – Coronavirus disease 2019 (COVID-19). WHO on 30th January, 2020 declared the outbreak as a Public Health Emergency of International Concern (PHEIC) and described it as pandemic on March 11, same year (World Health Organization, 2020). The most important transmission route that is currently agreed upon, is human-to-human via respiratory droplets or direct contacts (Lai, Shih, Ko, Tang & Hsueh, 2020). Like other viruses of the Coronaviridae family, the major clinical presentations of the disease are fever which occurs in 99% of the affected persons, dry cough, dyspnoea and bilateral patchy infiltration on imaging (Lai, Shih, Ko, Tang & Hsueh, 2020; Huang et al, 2020).

COVID-19 may result in mild to severe respiratory distress, depending on the individuals' age, immune system and the presence of any other underlying chronic conditions. The WHO earlier this year reported that approximately 80% of patients infected with COVID-19 showed mild symptoms or were asymptomatic, and eventually recovered without any medical intervention, whereas 15% of infected persons presented with severe illness, including shortness of breath, septic shock and multiple-organ failure, and remaining 5% of cases categorized as fatal requiring specialized care (World Health Organization, 2020).

Worldwide the strategies established to reduce the transmission of COVID-19 were mostly behavioural, like, social distancing and regular washing of hands. These, largely depend on rapid change in behaviour, which relies on one's knowledge about the problem, ability to perceive the risk, and willingness to change their attitude and behaviours (Wise, Zbozinek, Michelini & Hagan, 2020).

Countries with large cases of COVID-19 patients such as Italy, the United States of America, and the United Kingdom, fast-tracked final year medical students and foundation year doctors into the next level of their career with expedited assessment to help the severely overwhelmed health workforce (Harvey A, 2020; Wang, Tan & Raubenheimer, 2020). Empowering medical students with adequate knowledge will help them to give the public correct information and refute myths and false information about COVID-19 being at the forefront of health education (Shimizu, 2020). A recent study among Iranian medical students spending their clinical courses in university teaching hospitals all over Iran, found a significantly negative correlation between self-reported preventive behaviours and risk perception, which is needed to reduce stress, anxiety, and risk perception, which are the major problems in disease outbreaks (Taghrir, Borazjani & Shiraly, 2020).

Medical students are the first individuals who may have close contact with the affected people due to their presence in the clinics, wards and hospital environment. Lack of proper knowledge among this population can make them overestimate the situation, increase their stress and anxiety level and may interrupt the appropriateness of their medical judgments (Kim & Choi). A basic study of medical students' knowledge, attitude and practice towards COVID-19 is necessary since COVID-19 is currently spreading in Nigerian hospitals and all over the world. To the best of our knowledge, no study is available yet to assess medical students' COVID-19 related knowledge, attitude and practice. This study thus, aims to assess these parameters in medical students in Enugu State, Nigeria.

2. METHODOLOGY

2.1. Study Area

This study was a descriptive cross-sectional study conducted at the Enugu State University College of Medicine, Enugu, Nigeria. Enugu State is located at the South-Eastern part of Nigeria and Enugu is the capital and the economic hub of the State.

2.2. Study design and population

All the medical students in the college of medicine were used for the study. The first year medical students were excluded from the study as they were still in the main campus of the University and have not joined the college of Medicine. There were about 552 medical students in the college as at the time of data collection.

2.3. Data collection

Data was collected between May-June 2020 through an online questionnaire formulated with Google form and shared through the different class WhatsApp chat group.

The questionnaire was formulated by the principal investigator after extensive literature review and based on recommendations of the Nigeria Center for Disease Control (NCDC) and WHO on the means of transmission and possible preventive measures. The questionnaire was divided into four sections. The socio-demographic characteristics of the medical students was on the first part, the second section was on knowledge, and the third was on attitude, while the fourth was on the practice of the medical students towards COVID-19. Eleven questions were used to access the students' knowledge of COVID-19. A correct answer scores one while a wrong answer scores 0. The higher the score the, more knowledgeable the student is. Twenty-one questions were used to assess the attitude of the students. A 5 Likert scale was used. The responses were strongly disagree, disagree, neutral, agree and strongly agree weighing 1, 2, 3, 4 and 5 respectively. The higher the score the better the student's attitude towards COVID-19. Some of the questions were reversed to eliminate the bias of giving a single similar response in all the questions. Ten questions were used to access the practice score using 3 Likert-scale questions. The responses were never, sometimes, and always weighing 1, 2, and, 3 respectively. The higher the score the better the students practice towards COVID-19.

2.4. Data analysis

All the responses in Google form were entered into SPSS version 25. All the data were edited for errors by generating frequencies. The categorical variables were summarized using frequencies and percentages. The significance level was placed at ≤ 0.05 . The knowledge, attitude, and practice scores were categorized into poor and good. Scores of $< 80\%$ were classified as poor while scores of $\geq 80\%$ were classified as good.

RESULTS

Table 1: Socio-demographic characteristics of the students

Variable	Frequency	Percentage
Age		
15-24	230	79.3
25-34	50	17.2
35-44	10	3.4
Gender		
Male	110	37.9
Female	180	62.1
Marital status		
Single	285	98.3
Married	5	1.7
Ethnicity		
Igbo	290	100.0
Others	0	0.0
Religion		
Christianity	290	100.0
Others	0	0.0
Year of study		
2	75	25.9
3	20	6.9
4	45	15.5
5	115	39.7
6	35	12.1

About 552 students were reached out for the study but only 290 responded giving a 53% response rate. Table 1 shows the socio-demographic characteristics of the students. Majority of them were within the 15-24 years age group 230(79.3%), females 180(62.1%) and single 285(98.3%). All were of Igbo ethnic group and Christians. Highest proportion of the students were in their 5th year 115(39.7%) while the least proportion were the 3rd year students 20(6.9%).

Table 2: Knowledge of COVID-19 among the students

Variable	Frequency	Percentage
Have heard about COVID-19		
Yes	290	100.0
No	0	0.0
If yes, sources of information*		
Government	175	60.3
Internet	255	87.9
Mass media	215	74.1
Family and friends	185	63.8
Social media	235	81.0
Colleagues	175	60.3
Hospital management	90	31.0
COVID-19 is a viral infection		
Yes	285	98.3
No	5	1.7
Its incubation period is 2-14days		
Yes	285	98.3
No	5	1.7
COVID-19 can spread by*		
Droplet from infected persons	290	100.0
Surfaces touched by infected persons	270	93.1
Touching bank notes	160	55.2
Asymptomatic persons	230	79.3
Shaking of hands	255	87.9
Hugging	205	70.7
Staying together in a crowded room	255	87.9
Goods imported from China	15	5.2
Common symptoms of COVID-19 include*		
Fever	270	93.1
Dry cough	265	91.4
Body aches	180	62.1
Difficulty in breathing	285	98.3
Vomiting	45	15.5
Sneezing	215	74.1
Vaccine for COVID-19 is available		
Yes	5	1.7
No	285	98.3
Effective treatment for COVID-19 is available		
Yes	25	8.6
No	265	91.4
People with co-morbidities are more at risk		
Yes	270	93.1
No	20	6.9
Children have no risk of death from COVID-19		
Yes	0	0.0
No	290	100.0

COVID-19 may be more dangerous for the elderly		
Yes	285	98.3
No	5	1.7
COVID-19 spreads through close contact		
Yes	260	89.7
No	30	10.3
All COVID-19 patients develop severe acute respiratory illness		
Yes	100	34.5
No	190	65.5
Influenza vaccine also gives protection for COVID-19		
Yes	10	3.4
No	280	96.6
COVID-19 can be prevented by *		
Proper and regular hand washing with soap and water	280	96.6
Use of hand sanitizers	280	96.6
Social distancing	280	96.6
Wearing of face mask	280	96.6
Eating garlic, ginger and local herbs	20	6.9
Avoid touching of the eyes, nose and mouth	270	93.1
Good cough etiquette	260	89.7
Drinking/inhaling hot water	65	22.4
Drinking alcohol	5	1.7
Taking chloroquin tablets	15	5.2
Taking antibiotics	5	1.7
Knowledge categorized		
Good	190	65.4
Poor	100	34.6

*Multiple response allowed

Table 2 shows the knowledge of the medical students to COVID-19. All the students have heard about COVID-19 and their major source of information was the internet 255(87.9%) followed by social media 235(81.0%). The least source of information was through the hospital management (31.0%). Majority knew that COVID-19 is a viral infection 285(98.3%) and that the incubation period is 2-14days 285(98.3%). All the students knew that COVID-19 can spread by droplet from infected persons while a minority of them expressed that it can spread by goods from China 15(5.2%). Majority of the students knew the symptoms of COVID-19 like fever 270(93.1%), cough 265(91.4%) and difficulty in breathing 285(98.3%). Majority asserted that vaccine for COVID-19 was not available 285(98.3%), no effective treatment for COVID-19 265(91.4%), that people with co-morbidity 270(93.1%) and elderly 285(98.3%) are more at risk. Majority of the students knew that COVID-19 could be prevented by proper and regular hand washing 280(96.6%), social distancing 280(96.6%), use of hand sanitizers 280(96.6%), wearing of face mask 280(96.6%) while minor proportions said that it can be prevented by eating garlic, ginger and local herbs 20(6.9%), taking chloroquine tablets 15(5.2%) and antibiotics 5(1.7%).

Table 3: Attitude of the students towards COVID-19

Variable	Frequency	Percentage
You think you will contact COVID-19		
Yes	40	13.8
No	250	86.2
You are worried that a family member may contact COVID-19		
Yes	100	34.5
No	190	65.5
Infection is associated with stigma		
Yes	235	81.0
No	55	19.0
Media coverage is exaggerated		
Yes	125	43.1
No	165	56.9
The virus was initially designed as a biological weapon		
Yes	105	36.2
No	185	63.8
It is a plague caused by sin and unbelief		
Yes	20	6.9
No	270	93.1
It was designed to control population		
Yes	45	15.5
No	245	84.5
Designed by pharmaceutical companies to sell drug		
Yes	5	1.7
No	285	98.3
COVID-19 can be successfully controlled.		
Yes	220	75.9
No	70	24.1
Self- protection is necessary for the protection of others		
Yes	285	98.3
No	5	1.7
Lockdown is an effective control measure		
Yes	205	70.7
No	85	29.3
Nigeria can win the battle against COVID-19		
Yes	170	58.6
No	120	41.4
If I contact a person infected with COVID-19 I will inform NCDC		
Yes	215	74.1
No	75	25.9
If I have symptoms of COVID-19 I will inform NCDC		
Yes	195	67.2
No	95	32.8
If I have contact with an infected person, I agree to be isolated at home		
Yes	240	82.8
No	50	17.2
If I have contact with an infected person, I agree to be isolated at an isolation center		
Yes	200	69.0
No	90	31.0
I am willing to take COVID-19 vaccine if available		
Yes	210	72.4

No	80	27.6
I follow updates about COVID-19 in my country		
Yes	235	81.0
No	55	19.0
Follow updates about COVID-19 worldwide		
Yes	205	70.7
No	85	29.3
Will attend any lecture about the virus around me		
Yes	160	55.2
No	130	44.8
COVID-19 can be controlled by following standard precautions for infection control		
Yes	270	93.1
No	20	6.9
Attitude categorized		
Good	141	48.6
Poor	149	51.4

NCDC; Nigeria Center for Disease Control

Table 3 shows the attitude of the students towards COVID-19. Majority of the students believe that they cannot contact COVID-19 250(86.2%) and that the infection is associated with stigma 235(81.0%). Only a minority of the students are worried that a family member may contact COVID-19 100(34.5%), that the media coverage is exaggerated 125(43.1%), that the virus was initially designed as a biological weapon 105(36.2%), and that it was designed to control population 45(15.5%). Majority of the students however, believe that COVID-19 can be effectively controlled 220(75.9%), that self-protection is necessary for the protection of others 285(98.3%), and that lockdown is an effective control measure 205(70.7%). Also, majority of the students agree that they will accept to be isolated at home if they have contact with an infected person 240(82.8%), are willing to take COVID-19 vaccine if available 210(72.4%), follow updates about COVID-19 in Nigeria 235(81.0%) and worldwide 205(70.7%), believe that COVID-19 can be controlled by following standard precautions for infection control 270(93.1%).

Table 4: Medical students practice towards COVID-19

Variable	Frequency	Percentage
Have been to crowded places in recent time		
Yes	130	44.8
No	160	55.2
Wear mask always while leaving home		
Yes	285	98.3
No	5	1.7
Wear mask in correct way		
Yes	280	96.6
No	10	3.4
Dispose mask when it becomes moist or after 8hours		
Yes	185	63.8
No	105	36.2
Follow WHO hand washing technique		
Yes	265	91.4
No	25	8.6
Practice social distancing		
Yes	275	94.8
No	15	5.2
Follow lockdown regulations		
Yes	265	91.4

No	25	8.6
Cover mouth and nose with tissue while sneezing		
Yes	255	87.9
No	35	12.1
Dispose used tissue in the trash		
Yes	255	87.9
No	35	12.1
Avoid touching of eyes, mouth and nose as much as possible		
Yes	255	87.9
No	35	12.1
Practice categorized		
Good	225	77.6
Poor	65	22.4

Table 4 shows the practice of the students towards COVID-19. Minor proportion of the students 130(44.8%) asserted to have been to crowded places in recent time. Majority wear mask while leaving home 285(98.3%) and in a correct way 280(96.6%), dispose the mask when it becomes moist 185(63.8%), follow WHO hand washing technique 265(91.4%) and practice social distancing 275(94.8%). Also, majority of the students follow lockdown regulations 265(91.4%), cover mouth and nose while sneezing 255(87.9%), and avoid touching of eyes, mouth and nose as much as possible 255(87.9%).

Discussion

The participation of medical students in providing care for patients puts them at higher risk for contracting as well as transmitting infectious diseases. During pandemics such as the present COVID-19 pandemic, healthcare systems are put under great pressure, and a shortage of healthcare workers can drive the health system to co-opt the less experienced medical students into full care of patients. The present study was conducted at the peak of the COVID-19 pandemic in Nigeria.

The knowledge score in our study showed that only 65.4% of the students had good knowledge of COVID-19. This was poor considering that the study was conducted at the peak of the pandemic in Nigeria and the medical students are expected to be much knowledgeable about the disease. The finding was similar to the report of a similar study among medical students in Iran (Taghrir, Borazjani & Shiraly, 2020) but higher than the report of another study among final year medical students in Turkey where only 34.2% of the students had good knowledge of COVID-19 (Çalışkan et al, 2020). The poorer knowledge among the Turkey students may be because the study was conducted at the early stage of the pandemic in the country when much was not yet known about the disease. A Chinese study among healthcare workers however, reported a higher knowledge of 89.0% (Zhang et al, 2020). Medical students who may wish to join HCWs in managing the COVID-19 outbreaks have a high risk of exposure to the infection given their limited clinical experience. It has been shown among medical students that having and enhancing knowledge about a new infectious disease by fostering cooperation between hospitals and universities will help to improve the students' perceptions of the disease and preventive behaviours (Halboub, Al-Maweri, Al-Jamaei, Tarakji & Al-Soneidar, 2015). The risk of medical students acquiring coronavirus infection due to lack of good knowledge about COVID-19 is increased by the fact that there are asymptomatic carrier that transmit the coronavirus (Bai et al, 2020; Rothe et al, 2020).

In this study all the students have heard about COVID 19 and their major source of information was internet 87.9% and social media 81.0%. This was similar to the report of similar studies in Pakistan (Saqlain, Munir & Rehman, 2020), Jordan (Khasawneh et al, 2020) , Uganda (Olum et al, 2020) and Nigeria (Nwoga, Ajuba & Ezeoke, 2020) where 87.68%, 83.4%, 76.0 % and 85.1% of the healthcare workers (HCWs) and medical students got their information through social media.

This was however, higher than the report of other studies where 65.17% and 30% of the students and HCWs used social media as main source of information on COVID 19 (Kushalkumar, Prati, Pushti, Jay, Niraj & Asavari, 2020; Bhagavathula, Aldhaleci, Rahmani, Mahabadi & Bandari, 2020).

There is a wide range of information available on the internet, including unverified, biased and deceptive information's which can easily misguide the public. Thus medical students being at the frontline of medical practice should source information through verified websites. Also the medical community should create more verified websites where important information's like that of the present COVID-19 pandemic can be disseminated easily to the students knowing that internet is their major source of information.

Almost all the students 98.3% knew the incubation period of COVID-19. Knowing the incubation period of the virus would be very useful to identify the suspected cases and to provide medical care at an early stage which will help to reduce the transmission of the infection both among the HCWs and the general public. The finding in this study is similar to the report of similar studies in Iran (Taghrir, Borazjani & Shiraly, 2020), Pakistan (Saqlain, Munir & Rehman, 2020) and Nigeria (Nwoga, Ajuba & Ezeoke, 2020) where 85.4% and 96.38% 90.2% of the respondents knew the incubation period of the virus but higher than the report of a study in China (Zhong, Luo & Li, 2020). Another study among HCWs showed that only 36.4% of them knew the incubation period of COVID-19 (Bhagavathula, Aldhaleei, Rahmani, Mahabadi & Bandari, 2020). Majority of the students had good knowledge about the modes of spread and common symptoms of COVID-19. All of them knew that COVID-19 can spread by droplet from infected persons while majority knew that it can spread by staying together in a crowded place 87.9% and even from asymptomatic persons 79.3%. However, about 5.2% believe that it can be transmitted by goods from China. This can affect the use of products and aids from China for the prevention of COVID-19 and have a negative impact on the general control measures. It can also cause disharmony between the two countries if the information becomes popularized. It is very important that the students should be informed about the modes of spread of COVID-19 infection through validated sources to avoid this form of misconception.

Majority of the students also knew that people with co-morbidities 93.1% and the elderly 98.3% are more at risk. The report of a large survey carried out among general public of the United States of America (USA) and United Kingdom (UK) showed that 96.3% and 97.5% of the people believe that older adults are most likely to die from COVID-19 infection (Geldsetzer, 2020). Similarly, a study conducted among Egyptian public also showed that about 95.0% of study participants believe that COVID-19 is more dangerous for the elderly and those with chronic diseases (Abdelhafiz, Mohammed & Ibrahim, 2020).

A study among medical and allied health science students in India reported that nearly 40% of the participants believed that old/ geriatric or person with co-morbidities are more prone to COVID-19 (Kushalkumar, Prati, Pushti, Jay, Niraj & Asavari, 2020). The higher report in our study may be because all the respondents are medical students while the Indian study involved medical and allied health science students. Medical students by virtue of their training and exposure should have a better knowledge than the allied health science students. Majority of the students knew that COVID-19 can be prevented by proper and regular hand washing, social distancing, wearing face mask and good cough etiquette. The finding is similar to the report of other studies among students (Taghrir, Borazjani & Shiraly, 2020; Kushalkumar, Prati, Pushti, Jay, Niraj & Asavari, 2020; Zhong, Luo & Li, 2020) and HCWs (Saqlain, Munir & Rehman, 2020; Bhagavathula, Aldhaleei, Rahmani, Mahabadi & Bandari, 2020).

A minor proportion of the students (6.9%) however, believe that eating garlic, ginger and local herbs can prevent COVID-19 infection. This can be dangerous as such knowledge can be transferred to the general public who also depend on the medical students for information concerning the pandemic. This can delay seeking medical attention and worsen the disease outcome in such cases. Similar studies among medical students in India (Kushalkumar, Prati, Pushti, Jay, Niraj & Asavari, 2020), HCWs in Nigeria (Nwoga, Ajuba & Ezeoke, 2020) and general population in Egypt (Abdelhafiz, Mohammed & Ibrahim, 2020) also reported this wrong perception.

There was a general poor attitude of the medical students towards COVID-19 as only 48.6% of them had good attitude. This poor attitude was reported in a similar study among HCWs in Uganda (Olum, Chekwech, Wekha, Nassozi & Bongomin, 2020) and Nigeria (Nwoga, Ajuba & Ezeoke, 2020). This was however, lower than the report of other studies in Pakistan (65.4%) (Salman et al, 2020) and Uganda (74.0%) (Olum et al, 2020). It has been reported that forming positive attitudes, and promoting positive behaviours, and attitudes towards diseases affect the effectiveness of the coping strategies and behaviours (McEachan, Taylor, Harrison, Lawton, Gardner & Conner, 2016).

Outbreaks of novel infectious pathogens with poorly understood outcomes are often associated with tremendous fear amongst the general public (Person, Sy, Holton, Govert & Liang, 2004). Fear and stigmatization may impact the intentions of an infected individual to seek medical assistance in the right timing which might contribute to increased morbidity and mortality. This is true for a spectrum of previous coronavirus outbreaks and other infectious diseases including SARS, MERS, HIV infection and tuberculosis (Mak et al, 2009; Nachege et al, 2012; Sim, 2016; Jiang et al, 2018).

Only a minor proportion of the students 13.8% think that they can contact COVID-19. This was much lower than the report of a study among HCWs where 85% of them were afraid that they can contact the virus in their work place (Zhang et al, 2020). The HCWs may be more afraid of contacting the infection due to frequent exposure at work and inadequate provision of PPEs in the workplace. Study have shown that frequency of exposure is associated with risk of infection. About 43.1% of the students believe that the media coverage about COVID-19 is exaggerated. A Nigerian study (Nwoga, Ajuba & Ezeoke, 2020) reported a similar finding of 39.6% while another study reported a much lower finding of 5.38% (Olapegba et al, 2020).

A minority of the students believe that the virus was initially designed as a biological weapon (36.2%). This minority of medical students may constitute a negative source of information to the public as they also depend on these students for information on the pandemic. A nationwide survey in Nigeria however, reported a similar finding where 46.94% of the respondents had similar belief (Olapegba et al, 2020). The sources of information to the general public may have influenced their belief, thus information management is important during pandemics like the present one.

Majority of the students (75.9%) agree that COVID-19 can be successfully controlled. A similar study from Nepal reported a similar finding (Asraf, Garima, Singh, Ram & Tripti, 2020). However, in a Chinese study, 90.8% of the respondents were confident that COVID-19 could be controlled (Zhong, Luo & Li, 2020). The higher positive response among the Chinese participants may be due to better preventive measures put in place both at the health facilities and the country at large. However a study among Turkish final year medical students reported that only about 42.8% of the student believe that COVID-19 can be successfully controlled in Turkey (Çalışkan et al, 2020). Almost all the students (98.3%) agree that self-protection is necessary for the protection of others. A similar study from Nepal reported similar finding (Asraf, Garima, Singh, Ram & Tripti, 2020). This is appropriate and can be achieved by following standard precautions for infection prevention and control as recommended by CDC (Center for Disease Control and Prevention, 2007). About 29.3% of the students does not believe that lockdown is an effective control measure. This shows poor knowledge of the effect of community transmission which escalated cases of COVID-19 in most countries including Nigeria. However, another study reported a more positive response where 96.4% of the students believe that lockdown is an effective control measure (Asraf, Garima, Singh, Ram & Tripti, 2020).

Only about half of the students (58.6%) agree that Nigeria can win the battle against COVID-19. This shows poor attitude towards the preventive measures put in place by the Nigeria Centre for Disease Control and prevention (NCDC) and the government of Nigeria to combat the pandemic. A study from Turkey reported a similar finding (Çalışkan et al, 2020). Studies in Nepal (77.9%) (Asraf, Garima, Singh, Ram & Tripti, 2020) and China (97.1%) (Zhong, Luo & Li, 2020) reported higher positive responses. The better attitude among the respondents of the studies from China and Nepal may probably be because health care facilities in China and Nepal are comparatively better than Nigeria. Also better economic status of these countries may be another factor.

Majority of the students follow updates about COVID-19 in Nigeria (81.0%) and worldwide (70.7%). A study among HCWs in Pakistan showed that about 80% of them agreed that HCWs should acquaint themselves with all information's regarding COVID-19 (Saqlain, Munir & Rehman, 2020).

About 93.1% of the student agree that COVID-19 can be controlled by following standard precautions for infection control. The finding was similar to what was reported in a similar study where more than 96.2% of the participants strongly agreed that COVID-19 could be prevented by following standard precautions (Nwoga, Ajuba & Ezeoke, 2020).

Majority of the students (82.8%) agree to be isolated at home if they have contact with an infected person while a lesser proportion (69.0%) agree to be isolated at an isolation centre. The condition at the isolation centres and the attitude of the HCWs in such centres may contribute to the apparent apathy towards isolation centres in Nigeria. Higher finding was reported in a study conducted among medical students in Uganda (Olum et al, 2020) where 91.0% of the students agree to be isolated at an isolation centre if they come in contact with a patient with COVID-19.

About 77.6% of the students in the present study had good practices towards COVID-19 prevention. Majority of the students took precautions to prevent COVID-19 infection by: wearing face masks when leaving home (98.3%), following WHO hand washing technique (96.6%), practicing social distancing (94.8%) and following lockdown regulations (91.4%). These preventive practices could be primarily attributed to the very strict prevention and control measures implemented by the government of Nigeria such as banning public gatherings and strict lockdown regulations with provision of punishment to defaulters. It could also be the result of the students' knowledge regarding the high infectivity of the COVID-19 virus, which could be easily transmitted between people via invisible respiratory droplets. Unfortunately, the present study showed that about 44.8% of the students still went to crowded places despite the lockdown regulations. The general practice in the present study was higher than what was reported in similar studies in Uganda (Olum et al, 2020) and Ghana (Nkansah et al, 2020) but lower than the report of other studies in Iran (Taghrir, Borazjani & Shiraly, 2020, China (Zhang et al, 2020) and Nigeria (Nwoga, Ajuba & Ezeoke, 2020).

Limitations

This was an online survey and responses mainly depend upon honesty and partly affected by recall ability and thus may be subject to recall bias. Potential sample clustering might also limit the generalizability of the study. Also this is an internet based online survey, students who reside in places without internet access may not be captured which may lead to demographic selection bias.

Conclusion

The study was able to highlight gaps in specific aspects of knowledge, attitude and practice of the students towards COVID-19 that should be focused on in future awareness and educational campaigns. Continued access to online health information resources like free courses, clinical management guidelines, and webinars on COVID-19 offered internationally (e.g. by the International Federation of Medical Students Association (IFMSA) (International Federation of Medical Students' Association, 2020), the CDC (Centers for Disease Control and Prevention, 2020), and the WHO (World Health Organization, 2020) may help improve knowledge, attitude, and practices among these medical students.

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References

- Abdelhafiz AS, Mohammed Z, Ibrahim ME. (2020). Knowledge, perceptions, and attitude of Egyptians towards the novel coronavirus disease (COVID-19). *J Community Health*, 45:881–890.
<https://doi.org/10.1007/s10900-020-00827-7>.
- Asraf H, Garima T, Singh BM, Ram R, Tripti RP. (2020). Knowledge, attitudes, and practices towards COVID-19 among Nepalese Residents: A quick online cross-sectional survey. *Asian Journal of Medical Sciences*, 11(3): 6-11
- Bai Y, Yao L, Wei T, Tian F, Jin D, Chen L, et al. (2020). Presumed asymptomatic carrier transmission of COVID-19. *JAMA*, doi: 10.1001/jama.2020.2565

- Bhagavathula AS, Aldhaleci WA, Rahmani J, Mahabadi MA, Bandari DK. (2020). Knowledge and perceptions of COVID-19 among health care workers: cross sectional study. *JMIR Public Health Surveill*, 6(2):e19160 <https://doi.org/10.2196/19160>
- Çalışkan F, Midik Ö, Baykan Z, Şenol Y, Tanrıverdi EC, Tengiz FI et al. (2020). The knowledge level and perceptions toward COVID-19 among Turkish final year medical students. *Postgraduate Medicine*, doi: 10.1080/00325481.2020.1795486
- Centers for Disease Control and Prevention. 2020. *Coronavirus disease (COVID-19)* URL: <https://www.cdc.gov/coronavirus/2019-ncov/index.html> [Accessed 29/09/2020]
- Centers for Disease Control and Prevention. (2007). Standard precautions. Excerpt from the guideline for isolations; preventing transmission of infectious agents in the healthcare settings 2007. Available at http://www.cdc.gov/ncidod/dhqp/gl_isolation_standard. [Accessed 29/9/2020]
- Geldsetzer P. (2020). Knowledge and perceptions of COVID-19 among the general public in the United States and the United Kingdom: a cross-sectional online survey. *Ann Intern Med*, 1–4. <https://doi.org/10.7326/M20-0912>. 22
- Gorbalenya AE. (2020). Severe acute respiratory syndrome-related coronavirus—The species and its viruses, a statement of the Coronavirus Study Group. *BioRxiv* doi:oi.org/10.1101/2020.02.07.937862
- Habibzadeh P, Stoneman EK. (2020). The Novel Coronavirus: A Bird's Eye View. *Int J Occup Environ Med*, 11(2):65-71. doi: 10.15171/ijoem.2020.1921
- Halboub ES, Al-Maweri SA, Al-Jamaei AA, Tarakji B, Al-Soneidar WA. (2015). Knowledge, attitudes, and practice of infection control among dental students at Sana'a University, Yemen. *J Int Oral Health*, 7(5):15-19
- Harvey A. (2020). Covid-19: medical schools given powers to graduate final year students early to help NHS. *BMJ*. 26;368:m1227. doi: 10.1136/bmj.m1227
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 395(10223):497-506.
- International Federation of Medical Students' Association. (2020). IFMSA COVID19 response URL: <https://ifmsa.org/covid19/> [Accessed 26/09/2020]
- Jiang L, Ng IHL, Hou Y, Li D, Tan LWL, Ho HJA, et al. (2018). Infectious disease transmission: survey of contacts between hospital-based healthcare workers and working adults from the general population. *J Hosp Infect*, 98:404e11.
- Khasawneh AI, Humeidan AA, Alsulaiman JW, Bloukh S, Ramadan M, Al-Shatanawi TN et al. (2020). Medical Students and COVID-19: Knowledge, Attitudes, and Precautionary Measures. A Descriptive Study from Jordan. *Front. Public Health*, 8:253.
- Kim JS, Choi JS. (2016). Middle East respiratory syndrome-related knowledge, preventive behaviours and risk perception among nursing students during outbreak. *J Clin Nurs*, 25(17- 18):2542-9. doi: 10.1111/jocn.13295.
- Kushalkumar HG, Prati BP, Pushti MS, Jay RP, Niraj P, Asavari R. (2020). Knowledge and perceptions about COVID-19 among the medical and allied health science students in India: An online cross-sectional survey. *Clinical Epidemiology and Global Health*, <https://doi.org/10.1016/j.cegh.2020.07.008>
- Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. (2020). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents*, 55(3):105924.
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*, 26;382(13):1199-1207
- Lu H, Stratton CW, Tang Y. (2020). Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. *J Med Virol*, 92(4):401-402
- Mak WWS, Cheung F, Woo J, Lee D, Li P, Chan KS et al. (2009). A comparative study of the stigma associated with infectious diseases (SARS, AIDS, TB). *Hong Kong Med J*, 15:34–7
- McEachan R, Taylor N, Harrison R, Lawton R, Gardner P, Conner M. (2016). Meta-analysis of the reasoned action approach (RAA) to understanding health behaviors. *Ann Behav Med*, 50: 592e612
- Nachege JB, Morroni C, Zuniga JM, Sherer R, Beyrer C, Solomon S et al. (2012). HIV related stigma, isolation, discrimination, and sero status disclosure: a global survey of 2035 HIV-infected adults. *J Int Assoc Physicians AIDS Care*, 11:172–8.
- Nkansah C, Serwaa D, Adarkwah LA, Osei-Boakye F, Mensah K, Tetteh P et al. (2020). Novel coronavirus disease 2019: knowledge, practice and preparedness: a survey of healthcare workers in the Offinso-North District, Ghana. *Pan African Medical Journal*, 35(2):79. [doi: 10.11604/pamj.suppl.2020.35.2.23644]. Available online at: <https://www.panafrican-med-journal.com/content/series/35/2/79/full>
- Nwoga HO, Ajuba MO, Ezeoke UE. (2020). COVID-19: Public Health Implications among Healthcare Workers in a Tertiary Health Facility in Enugu State, Nigeria. *GJMR (F)*, 20 (11):7-15
- Olapegba PO, Ayandele O, Kolawole SO, Oguntayo R, Gandi JC, Dangiwa AL et al. (2020). A preliminary assessment of novel coronavirus (COVID 19) Knowledge and perceptions in Nigeria. *SSRN Electronoc Journal*, doi:10.2139/ssrn.3584408. [Accessed 23/9/2020]

- Olum R, Chekwech G, Wekha G, Nassozi DR, Bongomin F. (2020). Coronavirus Disease-2019: Knowledge, Attitude, and Practices of Health Care Workers at Makerere University Teaching Hospitals, Uganda. *Front. Public Health*, 8:181.
- Olum R, Kajjimu J, Kanyike AM, Chekwech G, Wekha G, Nassozi DR Bongomin F. Perspective of Medical Students on the COVID-19 Pandemic: Survey of Nine Medical Schools in Uganda. *JMIR Public Health Surveill*, 6(2):e19847 URL: <http://publichealth.jmir.org/2020/2/e19847/> doi: 10.2196/19847
- Person B, Sy F, Holton K, Govert B, Liang A. (2004). Fear and stigma: the epidemic within the SARS outbreak. *Emerg Infect Dis*, 10:358– 63.
- Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C et al. (2020). Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med*, 382(10):970-971
- Salman M, Mustafa ZU, Asif N, Zaidi HA, Hussain K, Shehzadi N et al. (2020). Knowledge, attitude and preventive practices related to COVID-19: a cross-sectional study in two Pakistani university populations. *Drugs Ther Perspect*, 09:1-7
- Saqlain M, Munir MM, Rehman SU. (2020). Knowledge, attitude, practice and perceived barriers among healthcare professionals regarding COVID-19: a Cross-sectional survey from Pakistan. *J Hosp Infect*, 105(3):419–423.
- Shimizu K. (2020). 2019-nCoV, fake news, and racism. *Lancet*, 395(10225):685-686. doi: 10.1016/S0140-6736(20)30357-3
- Sim M. (2016). Psychological trauma of middle east respiratory syndrome victims and bereaved families. *Epidemiol Health*, 38:e2016054. doi: 10.4178/epih.e2016054
- Taghrir MH, Borazjani R, Shiraly R. (2020). COVID-19 and Iranian medical students; a survey on their related-knowledge, preventive behaviors and risk perception. *Arch Iran Med*, 01;23(4):249-254. doi: 10.34172/aim.2020.06
- Wang JH, Tan S, Raubenheimer K. (2020). Rethinking the role of senior medical students in the COVID-19 response. *Med J Aust*, 212(10):490-490.
- Wise T, Zbozinek T, Michelini G, Hagan C. (2020). Changes in risk perception and protective behavior during the first week of the COVID-19 pandemic in the United States. Pre Print. PsyArXiv 2020 Mar 19. doi: 10.31234/osf.io/dz428
- World Health Organization. (2020). Emerging respiratory viruses, including COVID-19: methods for detection, prevention, response and control URL: <https://openwho.org/courses/introduction-to-ncov> [Accessed 28/05/2020]
- World Health Organization. (2020). Infection prevention and control (IPC) for novel coronavirus URL: <https://openwho.org/courses/COVID-19-IPC-EN> [Accessed 26/05/2020]
- World Health Organization. Geneva, Switzerland. (2020). WHO Director-General's opening remarks at the media briefing on COVID-19-11 March 2020 URL: <https://www.who.int/dg/speeches/detail/> [Accessed 5th May 2020]
- Zhang M, Zhou M, Tang F, Wang Y, Nie H, Zhang L et al. (2020). Knowledge, attitude, and practice regarding COVID-19 among healthcare workers in Henan, China. *Journal of Hospital Infection*, 105: 183e187
- Zhong BL, Luo W, Li HM. (2020). Knowledge, attitudes, and practices towards COVID19 among Chinese residents during the rapid rise period of the COVID-19 outbreak: a quick online cross-sectional survey. *Int J Biol Sci*, 16(10):1745–1752.



A Qualitative Study of Patients' Perceptions of Dental Care in Primary Health Care

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Abstract

Knowledge of patients' views can contribute to the strengthening of health services. The aim of this study is to describe the patients' perception of a public oral health service, contributing to evaluations in health services. This is a qualitative study in which a focus group was conducted, with the participation of six patients of the oral health system in the city of Belo Horizonte, MG, Brazil, all with a minimum experience of three years of using the service. A theoretical model with dimensions aimed at assessing integrality and primary care services was used. In conducting the research, a semi-structured script was used. The data were analyzed by content analysis. The most representative categories for evaluating oral health actions in primary care are the health unit; the welcoming and its relation with the creation of the bond; service with a strong emphasis on the humanized relationship between professional and patient and on teamwork and; as a highlight, citizen participation, based on the recognition of a "system" that prevents the proper functioning of services and that must be fought with citizenship. Patients' perceptions can be used to assess oral health in primary care from the perspective of those who actually use health services, seeking ultimately to constantly improve them. Knowledge of patients' perceptions may enable organizations to know their performance, through assessment methodologies based on the established perceptions.

Keywords: Primary Health Care, Health Evaluation, Qualitative Research, Patient Participation

1. Introduction

In 2018, the 40th anniversary of the Alma-Ata World Conference was celebrated, when primary health care (PHC) began to occupy a more central place on the countries' agendas. PHC represents a way to rationalize the increasing costs involved in health care and the possibility of including population contingents that were on the margins of this care. Furthermore, the returns on investing in health, based on methods that include both the benefits of improved economic productivity and the intrinsic value of health, can far exceed the costs (Watkins et al, 2018).

The need to improve the oral health conditions of excluded groups motivated the launch of the Oral Health Program of the World Health Organization (WHO, 2002) which includes among its proposals the strengthening of global oral health systems towards PHC (Petersen, 2009).

The Brazilian government decided that oral health should be included in this effort to universalize PHC, through its insertion in the Family Health Strategy (ESF) and based on the guidelines and principles of the Unified Health System (SUS), the Brazilian policy of health. Based on the principle of integrality, public health services must promote health, prevent risk factors and rehabilitate according to the dynamics of the health-disease process (Brasil, 2006).

However, there are challenges in the PHC consolidation process in the Brazilian (Mattos et al, 2014) and worldwide (Mosquera et al, 2014; Gurung et al, 2016) context. To overcome this obstacle, the performance and impact of health services on the population's health must be known and the patients' perception can be a sensitive indicator of the quality of the service provided, related to the greater adequacy in the use of the public health service (Campos, Filho & Castro, 2017). Evaluative research has sought to investigate the expectations and the symbolic universe of these actors, seeking to understand what quality of health services means for them (Amorim et al, 2019). Methodologies that use the patients' view are seen as an effort in which principles related to individual rights and citizenship are reaffirmed, such as expressed in the concepts of humanization, patient rights, empowerment, assuming a political dimension and a social end (Bosi & Uchimura, 2007).

The perception of patients can originate from factors such as their own experience in the use of services, the experience of other members of the family or the community, their health condition, their view on how the care provided by professionals in the area should be, or their perception of what is disclosed in the media (Vaitsman & Andrade, 2005). Even if the perception of a service is a personal judgment, it is important that the health professional or manager knows the patients' expectations for performance improvements (Fadel & Filho, 2009).

The identification of assessment categories for a given group may allow a more consistent assessment, either alone or as a complement to quantitative methodologies (Turato, 2005). The present study aimed to identify categories of evaluation of health services, through the perception of patients about the quality of a public oral health service.

2. Materials and methods

2.1 Qualitative methodology

When working with perception, the qualitative methodology was chosen, focused on the meanings and intentionality of actions in the contexts of social structures (Husserl, 1988). Qualitative research is concerned with deepening the understanding of a given issue, much more than the numerical factor. The focus group was the data collection strategy chosen for allowing, through an explicit interaction between the participants, under the guidance and facilitation of the researcher, to explore people's views and experiences on different aspects of daily life. It is possible to have a shared perception on the researched topic, covering the study object more broadly and to understand what people think and why they think about a certain topic, in this case, health services (Kitzinger, 1995).

2.2 Participants

The subjects of this research were patients of the public oral health system in Belo Horizonte-MG, a large municipality in Brazil, with approximately 2,500,000 inhabitants, divided into nine health districts and with a tradition in the development of its municipal health system within of PHC. The inclusion criteria aimed to guarantee the heterogeneity and multivocality of the participants, according to the different districts of the municipality. Thus, it was requested that dentists based in different basic units, covering the nine health districts, indicate patients who had a minimum experience of three years of effective use of the oral health service (that is, who sought the service seeking treatments and not just emergency care). They should be adults, of both genders and who show a potential interest in participating in the research.

2.3 Data collection

Subsequently, the researcher responsible for data collection contacted the patients indicated by the dentists, when clarifications were made about the research (the objective, the importance of their participation, anonymity), as

well as the invitation to participate in the focus group. After attempts to reconcile the availability of those who were interested in participating, six participants remained, who actually attended the activity. The researcher who conducted the data collection had previous experience in conducting qualitative research and had no connection with the others involved (patients and dentists from the basic units).

Data collection took place in 2015, in a room specially provided by the Research Institution, which provided the necessary adaptation (comfort, silence, tranquility) for the realization of the focus group. The expenses for locomotion of patients to this location were assumed by the researchers. Initially, the participants were again clarified about the research objectives, oriented about their participation in the group, how to avoid overlapping speech or always talking towards the recorder (in the center of the circle). All 6 subjects remained until the conclusion of the group. There were no interruptions during data collection.

For the realization of the focus group, a semi-structured script was used, elaborated from a theoretical model that includes proposals for the evaluation of PHC (Starfield, Shi & Macincko, 2005) and integrality (Silva Jr et al, 2008). After the first conversation with the objective of clarifying and relaxing the group, the motivating question was asked: "How is your arrival, your entry into the dental service at the health unit?" Then the script was explored, in continuity with the established conversation.

2.4 Data analysis

The activity was considered finished when all the topics defined in the script were covered and saturation was observed. The recorder was only turned off after everyone had left the site, allowing observations to be recorded after the formal termination of the group. The content obtained was transcribed by the same researcher who conducted the focus group. Data obtained were processed using the content analysis method. The first stage, called pre-analysis, involved the first contacts with the documents to be analyzed and the formal preparation of the material. Subsequently, a fluctuating, exhaustive and repeated reading of the texts was made, which allowed the transformation of raw data into themes and later the obtaining of categories. Next, inferences were made from the data already treated, qualitatively analyzing the themes and categories that constituted the patients' perception of oral health care in PHC. This process was carried out by two researchers, simultaneously and independently and after discussion between the researchers, the categories were agreed (Bardin, 1977).

This research was approved by the Research Ethics Committee of the Belo Horizonte City Hall, number 0059.0.410.203-10. All subjects signed an informed consent form.

3. Results

The focus group activity was characterized by intense and spontaneous dynamics, lasting 120 minutes, without fatigue or inattention of the participants. All manifested similarly, without the predominance of the speech of some more than others. Of the six participants, five were women and one was a man. The average age of the participants was 40.1 years (25-61). Only one participant had completed high school, and the other five had incomplete high school or complete elementary school. The statements were grouped into four themes, as shown in Chart 1. The patients will be identified at the end of the speeches through a number, as a way of preserving anonymity.

Chart 1: Themes and categories observed in the focus group on dental care in PHC units, Belo Horizonte, Brazil, 2015.

<i>THEMES</i>	<i>CATEGORIES</i>
My health unit	Access Physical structure and inputs Services/procedures offer Attention network
I am welcomed and recognized	Welcoming Bond
The service is good	Humanized relationship

	Team work
My citizen participation	Political system

3.1 My health unit

Participants reported the difficulties in gaining access to dental treatment in PHC. Despite the improvement made possible by the insertion of dentistry at PHC, problems persist. Patients speak in few places and at an inappropriate time, in addition to highlighting the need for easy geographic access as a matter of urban planning.

"The hours should be longer because there are people who work all day, only at night to look for it (P2)"

"... when you are going to create a neighborhood, you have to think about the school, the public health services... the health service unit had to be close to everyone, it is difficult but it had to be. (P4) "

Regarding the physical structure of the basic units and the availability of equipment, inputs and human resources, some aspects were pointed out as important in the day-to-day services.

"I see the following: ... and if it wasn't so bureaucratic, that it wasn't missing so much material (P5)"

"... our biggest difficulty is the number of professionals (P2)"

Regarding the offer of services, patients pointed to PHC as a place where basic clinical procedures are performed, unable to respond to demands. There is dissatisfaction in relation to the functional aspect of access, as there is no provision of enough procedures to the needs of the population.

"At the health center, it is really basic, it is the basic of the basic (P6)"

"Because in the basic [PHC] you did the basics, I dream about orthodontics, I want to make a channel treatment, I want to solve my problem ... (P3)"

3.2 I am welcomed and recognized

Although PHC is considered the priority access door to the health system, paradoxically, the main barrier can be located in PHC itself, due to barriers to reception.

"Well, it is very complicated to go through the" Can I help? "[first contact at reception], the health agent, the doorman ... (P1)"

"The doorman already has to deal with so many things, so many diferente areas of the public health service, if there was an entrance straight to the dentist, it would already make it easier. ... (P3) "

Welcoming may also be in practice a difficulty for those seeking treatment.

"Many times the professional thinks that the reception hours have passed, but does reception have a schedule? And if I left the service, I was feeling sick there, I resisted as long as I could, won't you be welcomed? I can't understand it... (P4) "

The participants perceive what it feels like to be welcomed and point out in the service organization itself an impediment for this to occur. They recognize that "welcoming" is not being a welcoming moment.

"Welcoming is receiving the person, listening to the person, looking at them, even if I had to go back home I would have been treated with respect and I want that from all the professionals, the cleaning lady, the doorman ... I think because due to the demand, they place the reception with a schedule, but reception is not that ... (P4) "

"In the reception they do not let you talk to any professional, or even ask a question to have an answer (P1)"

There may be a greater establishment of a bond when the patient and his demands and needs are welcomed. This relationship was perceived and reported.

"...I also understand because they [health workers] work a lot, and then it affects the welcoming and the bond... the doctor I deal with calls us by name, knows my husband, knows my son but how much time she spent to achieve this? That's where you have a bond, but it could be longer if you had more professional time ... (P4) "

3.3 The service is very good

The quality of care was consistently related to the humanized and compromised relationship that occurs between patients and professionals, capable of overcoming common structural difficulties in the daily lives of countless public health units.

“The conditions of the dentist there... it is basic, but the care he does for any human being who enters there are the best possible (...) he does not do it anymore because he has no conditions, but his care for the patient it is the best possible (P3)”

Teamwork was another category perceived as a quality item in care. The statements indicate the perception that, if there is integration between professionals, there is gain.

“And this fact of helping [team work] is very important because sometimes in the conversations between them [professionals] there is an exchange of information from patients... I have already witnessed this. The dentist also plays this role, they know a little bit of our life, our day-to-day lives they know a little about our history (P6)”

3.4 My citizen participation

The presence of what they called “system” was remarkable, that is, a series of factors, especially related to public policies and management, that hinder or prevent the health care of the population from being offered according to their needs.

“No, it is everybody, he alone [the dentist] will not do anything, the system will not allow him to do anything alone (...) I think it is a huge neglect [structural problems] and I think it's our fault and the politicians' fault, ours because we vote for them.. (P1)”

“It is the system that does not allow certain things (...) this is very sad, this is the system that makes it difficult and then they come and offer us a denture; why didn't you offer a decent treatment back there?? (P3)”

However, some patients are aware of their potential citizens and know the strength that their citizenship has in defining different aspects of service management.

“that's the issue of the city health council. Patients, health professionals mobilize to demand improvements (P2)”

4. Discussion

4.1 My health unit

The patients' perception points to access difficulties in its multiple dimensions. Although there are ethical issues that define health as a good that should be accessible to every human being, this is not what is observed, because for patients access means having public health services available, in places close to the homes, and with permissive hours for use, especially for those who work daily hours. This perception is consistent with other studies (Viegas, Carmo & Luz, 2015; Al-Jaber & Da'Ar, 2016) that pointed to similar difficulties, related to the number of professionals, the geographical issue and the costs of dental treatments, an impediment for many people. This situation, especially in times of financial or political crises, should necessarily lead to reflection among professionals and managers involved, due to the increase in the number of unemployed or people without health insurance coverage, as they may increase the demand for care.

Deficiencies in these aspects compromise the service provided to patients and, consequently, society's view of SUS or any other public health system in the world. The availability of human resources to work in the basic units is, in fact, considered important, as it relates to the possibilities (or not) of providing services that the community needs. The issue of human resources is not limited to just a numerical factor, since the characteristics and attitudes of the professionals involved influence the population's access (Tesser, Neto & Campos, 2010). This situation was highlighted when commenting on the reception at the health unit. Theoretically, the organization of reception of the patients, a moment called welcoming, includes among its purposes, facilitating patients' access (Coelho & Jorge, 2009). However, it was observed that some organizational aspects of health units, aimed at benefiting welcoming, may actually be preventing this from happening. Thus, access and the construction of the SUS itself may be compromised (Souza et al, 2008), as well as other national health policies based on PHC.

It was also possible to verify in the statements that there is dissatisfaction with the list of clinical procedures offered. There is a great demand for oral health among the population, which often requires different procedures. PHC should be able to take care of providing, in addition to curative/restorative procedures, the prevention and promotion of health. In the medium or long term, the population's demand could be reduced (Mc Manus, 2015).

In the Brazilian case, dental services are organized on levels of complexity or healthcare networks (primary, secondary, and tertiary) and it cannot be forgotten that some procedures are performed by the Dental Specialty Centers (CEO). These health units are aimed to perform some clinical procedures that are not performed in basic units, such as surgeries, endodontics and care for special patients, but it also fails to meet these needs (Chaves et al, 2011), compromising the integrality and generating a feeling of dissatisfaction among patients, since they apparently do not know the network operation of the services, but expect attention beyond the "basic". An important benefit of the existence of adequate flows between basic and specialized services is the maintenance of the bond between patients and the professional of origin, considered a reference for the individual or family in primary units. Apparently, there is no uniformity of procedures among the professionals involved in basic and specialized health units, with situations in which the user's "walk" through the health system takes place in an appropriate manner and, at other times, in a unsatisfying way, compromising the integrality and user satisfaction.

Some statements were linked to the lack of human resources in the units' daily lives. These problems could be solved with management mechanisms that are more committed to better structural work conditions and more attractive salary and career plans, for example. However, in addition to technical capacity, team members need to identify themselves with a work proposal that often requires creativity, initiative and a vocation for community and group work, something that should start in training professional (Ronzani & Silva, 2008).

4.2 I am welcomed and recognized

It was observed a relationship between the welcoming and the bond, with the first acting as a facilitator for the second. The coexistence time, despite having its fundamental base in access/reception, is an indispensable factor in longitudinality and can, consequently, interfere in the patients' satisfaction and in the resolution. The bond created is not limited to different clinical moments, it expands to different situations in the participants' daily lives and is not limited to the figure of the dentist, being a category that arises from the humanized relationship that took place with this professional. Bond allows integrality to be more easily achieved and also contributes to longitudinality and long lasting therapeutic bond between patients and professionals, from the recognition of a regular source of primary care (Cunha & Giovanella, 2011).

The bond must be based on the activity of the multidisciplinary team, as the population must believe in the team's ability to solve their health problems and the team must accept these demands. The bond contributes to more accurate diagnoses and treatments, lower costs of care and greater user satisfaction. It can be said that there is a direct relationship, based on access, between welcoming and bonding, the result of which is care, obtained when health professionals feel and experience the reality of patients. Empowered by multiprofessional work, workers must reconcile work and care, which are not opposing categories, but complement each other (Rodrigues, Lima & Roncalli, 2008).

Patients also expressed themselves in relation to the lack of bond in secondary care. They stated that, unlike what happens in PHC, at the secondary level there is no bonding. The service organization itself exacerbates this situation, as the specialized professional is placed as a person who fulfills procedures on patients, does what is requested and forwards them to the unit of origin, not even the documentation remains in place. Everything contributes to the distance perceived by patients. In addition, the majority of professionals working in specialized public care have a dual professional activity, as they work in public and private clinics. Although this double action is not conflicting, it can make it difficult to adjust to the field of public health (Chaves et al, 2011).

4.3 The service is very good

The importance of the humanized relationship between professionals and patients is highlighted. A relationship based on respect and humanistic aspects can overcome several difficulties that PHC units face in their daily lives,

helps to qualify assistance, the quality of care and contributes to a process of reorientation in the production of care (Medeiros, Araújo-Souza & Albuquerque-Barbosal, 2010). Quality is not placed sole under the responsibility of the professional. Patients recognize the limit of this dimension. But a professional with a humanizing capacity can control conflicts that will inevitably not bring benefits in the construction of the desired public health service.

The importance of the humanized relationship in PHC services is pointed out, as humanization is particularly important in this type of service, focused on the most frequent health demands, which are often on the border between “life problems” and “pathology”, as defined by biomedicine (Nora & Junges, 2013). Hence the importance of multi-professional action and intersectoral articulation, since PHC has this vocation as a “gateway” not only for the health service network, but for a multiplicity of other social demands, which end up being translated into health demands or simply present themselves in the absence of other social spaces for expression.

Patients expressed themselves in favor of teamwork. Teamwork is something that, in the view of patients, should happen in the daily life of services and that can qualify the assistance and the relationship between the team and the family. For this, it is essential to develop a communicative practice oriented towards mutual knowledge (Peruzzo et al, 2019; Nora & Junges, 2013). This study confirms the understanding that the specific knowledge of each area can and should be used together to understand certain situations that involve the patients' health.

4.4 My citizen participation

The perception expressed by patients about the political system was highlighted. For them, this system, which is external to the units' daily life, but dictates rules, commands, has immense responsibility in the daily life of public health services, in what they come from positive or negative for the population. It is important to note that this category "system" was addressed several times among the participants, generating debates that revealed a feeling of rejection of political practices that are not committed to the well-being of the population.

One of the reasons for maintaining uncompromised and disconnected management practices from what SUS proposes may be the municipalization of health. This is a principle that guides Brazilian health policy, thought as a possibility to facilitate greater participation of society in health policies, due to a greater proximity between citizens and local managers. However, municipalization does not take into account the demographic reality of most municipalities, which do not have enough population to demand a health system with different levels of complexity, nor the fact that local power in Brazil has traditionally been the basis for representing private interests linked to land ownership and the basis of the oligarchic domination system. There is a natural stimulus for competition between local authorities and power is usually concentrated in a few hands in small municipalities. Power is priority in relation to the broader interests of the population (Rodrigues, 2014).

In contrast to the perceived "system", patients continued to demonstrate, affirming their power as citizens. This citizen vision contributes to social control and integral practices, as they can mobilize managers. It will favor the construction of a society more aware of its rights and responsibilities and contribute to changing the health profile of the population. These perceptions are in line with the concept of empowerment and its interface with health promotion, pointing towards a collective utopia/expectation of social justice and inclusion, especially in national contexts characterized by needs and exclusion. Empowerment contributes to the constant need to debate politicization and health practices (Carvalho & Gastaldo, 2008).

The improvement of any national health policy based on PHC involves the victory over disenchantment or discrediting over that policy. Its concrete performance depends on overcoming the problems historically present in societies, such as uncompromised politics and the lack of efficient management (Campos, 2007). Citizen participation is essential for the promotion of sustainable health and health care. The citizen posture presented is very positive, as it will make it possible to create potential conditions to improve health public services (Willianson, 2014).

5. Conclusions

In this study, it was observed that, for patients, the health unit is an important topic in the evaluation of a public oral health service; welcoming and creating the bond; care with an emphasis on the humanized relationship between professional and patient and teamwork. The critical citizen view on public management was highlighted, which is incompatible with the development of SUS or any other national health policy based on PHC.

The presence of patients, as well as professionals and managers in the effort to build public health systems is essential. The knowledge of the patients' perceptions may enable the elaboration of a characterization of the service provided. The evaluation will allow organizations to know their performance and organize their services not only for the demand, but according to the needs pointed out by the patients, true reasons for the existence of public health services.

Although there is a need to caution in generalizing qualitative studies, the results may have applicability in similar contexts. The fact that not all invited patients wanted or were able to participate generated a small universe of participating patients, which may have omitted unreported perceptions and experiences. It is suggested that further studies be carried out using different qualitative approaches and in different contexts.

References

- Al-Jaber, A., Da'Ar, O. (2016). Primary health care centers, extent of challenges and demand for oral health care in Riyadh, Saudi Arabia, *BMC Health Services Research* 16, 628. <https://doi.org/10.1186/s12913-016-1876-6>
- Amorim, L. P., Senna, M. I. B., Alencar, G. P., Rodrigues, L. G., Paula, J. S., Ferreira, R. C. (2019). User Satisfaction With Public Oral Health Services in the Brazilian Unified Health System, *BMC Oral Health* 19, 126. <https://doi.org/10.1186/s12903-019-0803-8>.
- Bardin, L. (1977). *Análise de conteúdo*. Lisboa: Edições 70.
- Brasil, (2006). Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Atenção Básica, *Saúde Bucal, Cadernos de atenção básica nº. 17*. Brasília. http://bvsmms.saude.gov.br/bvs/publicacoes/saude_bucal.pdf
- Campos, D.F, Filho, R.B.N., Castro, F.N. Castro (2017). Service Quality in Public Health Clinics: Perceptions of Users and Health Professionals. *International Journal of Health Care and Quality Assurance*, 30, 680-692. <https://doi.org/10.1108/IJHCQA-09-2016-0140>.
- Campos, G.W.S. (2007). Health and political reform: is the Brazilian National Health Care System sustainability in question? *Ciencia e Saude Coletiva* 12, 301-306. <https://doi.org/10.1590/S1413-81232007000200002>.
- Carvalho, S.R, Gastaldo, D. (2008). Health promotion and empowerment: a reflection based on critical-social and post-structuralist perspectives, *Ciencia e Saude Coletiva* 13, 2029-2040. <https://doi.org/10.1590/S1413-81232008000900007>
- Chaves, S.C.L., Cruz, D.N., Barros, S.G. et al (2011). Assessing the supply and use of secondary care in specialized dental clinics in Bahia State, Brazil, *Cadernos de Saude Publica* 27, 143-154. <https://doi.org/10.1590/S0102-311X2011000100015>
- Coelho, M.O., Jorge, M.S.B. (2009). Technology of relations as device of humanized attendance in basic attention to health in the perspective of access, sheltering and attachment, *Ciencia e Saude Coletiva* 14, 1523-1531. <https://doi.org/10.1590/S1413-81232009000800026>.
- Cunha, E.M., Giovanella, L., (2011). Longitudinality/continuity of care: identifying dimensions and variables to the evaluation of Primary Health Care in the context of the Brazilian public health system, *Ciencia e Saude Coletiva*. 16, 1029-1042. <https://doi.org/10.1590/S1413-81232011000700036>
- Fadel, M.A.V., Filho, G.I.R (2009). Percepção da qualidade em serviços públicos de saúde: um estudo de caso, *Revista de Administração Publica* 43, 07-22. <https://doi.org/10.1590/S0034-76122009000100002>
- Gurung, G., Derrett, S., Hill, P., et al, (2016). Governance challenges in the Nepalese primary health care system: time to focus on greater community engagement? *International Journal of Health Planning and Management*. 3, 1 167-174. <https://doi.org/10.1002/hpm.2290>
- Husserl. E. (1988). *Investigações lógicas: 6ª investigação: elementos de uma elucidação fenomenológica do conhecimento*, São Paulo, Nova Cultural.
- Kitzinger, J. (1995), Qualitative Research: Introducing focus groups, *British Medical Journal* 311, 299.

- Mattos, G.C.M., Ferreira, E.F., Leite, I.C.G., et al, (2014). The inclusion of the oral health team in the Brazilian Family Health Strategy: barriers, advances and challenges, *Ciencia e Saude Coletiva* 19, 373-382. [https://doi.org/ 10.1590/1413-81232014192.21652012](https://doi.org/10.1590/1413-81232014192.21652012).
- Mc Manus, A. (2015). Health promotion innovation in primary health care, *Australasian Medical Journal*. 6, 15-18. [https://doi.org/ 10.4066/AMJ.2013.1578](https://doi.org/10.4066/AMJ.2013.1578)
- Medeiros, F.A., Araújo-Souza, G.C., Albuquerque-Barbosa, A.A., et al (2010). Basic health unit embracement: focusing on user satisfaction. *Revista de Saude Publica* 12, 402-413.
- Mosquera, P.A., Hernandez, J., Veja, R., et al, (2014). Challenges os implementing a primary health care strategy in a contexto of a market-oriented health care system: the experience of Bogota-Colombia, *International Journal of Health Planning and Management*. 29, 347-367. [https://doi.org/ 10.1002/hpm.2228](https://doi.org/10.1002/hpm.2228)
- Nora, C.R.D., Junges, J.R. (2013). Humanization Policy in Primary Health Care: A Systematic Review, *Revista de Saude Publica*. 47, 1186-200. [https://doi.org/ 10.1590/s0034-8910.2013047004581](https://doi.org/10.1590/s0034-8910.2013047004581)
- Petersen, P.E. (2009). Global policy for improvement of oral health in the 21st century – implications to oral health research of World Health Assembly 2007, World Health Organization, *Community Dentistry and Oral Epidemiology*. 37, 1-8. [https://doi.org/ 10.1111/j.1600-0528.2008.00448.x](https://doi.org/10.1111/j.1600-0528.2008.00448.x)
- Peruzzo, H. E., Silva, E. S., Batista, V. C., Haddad, M. C. F. L., Peres, A. M., Marcon, S. S., (2019). Organizational Climate and Teamwork at the Family Health Strategy, *Revista Brasileira de Enfermagem*. 72, 721-727. [https://doi.org/ 10.1590/0034-7167-2017-0770](https://doi.org/10.1590/0034-7167-2017-0770).
- Rodrigues, P.H.A. (2014). Political challenges facing the consolidation of the Sistema Único de Saúde: a historical approach. *História, Ciencia, Saude-Manguinhos* 21, 37-59. [https://doi.org/ 10.1590/S0104-59702014000100003](https://doi.org/10.1590/S0104-59702014000100003).
- Rodrigues, M.P., Lima, K.C., Roncalli, A.G Roncalli, (2008). Social representation related to care in the family health program in Natal-Brazil. *Ciencia e Saude Coletiva* 13, 71-82. [https://doi.org/ 10.1590/S1413-81232008000100012](https://doi.org/10.1590/S1413-81232008000100012).
- Ronzani, T.M, Silva, C.M. (2008). Brazil's Family Health Program according to healthcare practitioners, managers and users, *Ciencia e Saude Coletiva*. 13, 23-34. [https://doi.org/ 10.1590/S1413-81232008000100007](https://doi.org/10.1590/S1413-81232008000100007).
- Silva Júnior, A.G., Alves, M.G.M., Mascarenhas, M.T.M., et al (2008). Evaluation experiences of the supplementary care sector: contributions of integrality, *Ciencia e Saude Coletiva* 13, 1485-1500. [https://doi.org/ 10.1590/S1413-81232008000500014](https://doi.org/10.1590/S1413-81232008000500014).
- Souza E.C.F., Vilar, R.L.A., Rocha, N.S.P.D., et al (2008). Primary health care access and receptivity to users: an analysis of perceptions by users and health professionals. *Cadernos de Saude Publica* 24, S100-S110. [https://doi.org/ 10.1590/S0102-311X2008001300015](https://doi.org/10.1590/S0102-311X2008001300015)
- Starfield, B., Shi, L., Macincko, J. (2005). Contribution of Primary Care to Health Systems and Health. *The Milbank Quarterly* 83,457–502 <https://doi.org/10.1111/j.1468-0009.2005.00409.x>
- Tesser, C.D., Neto, P.P, Campos, G.W.S. (2010). User embracement and social (de)medicalization: a challenge for the family health teams. *Ciencia e Saude Coletiva* 15, 3615-3624. [https://doi.org/ 10.1590/S1413-81232010000900036](https://doi.org/10.1590/S1413-81232010000900036)
- Turato, E.R (2005). Qualitative and quantitative methods in health: definitions, differences and research subjects, *Revista de Saude Publica* 39, 507-514. [https://doi.org/ 10.1590/S0034-89102005000300025](https://doi.org/10.1590/S0034-89102005000300025)
- Vaitsman, J, Andrade, G.R.B. (2005). Satisfaction and responsiveness: ways to measure quality and humanization of health assistance, *Ciencia e Saude Coletiva* 10, 599-613. [https://doi.org/ 10.1590/S1413-81232005000300017](https://doi.org/10.1590/S1413-81232005000300017)
- Viegas, A.P.B., Carmo, R.F., Luz, Z.M.P. (2015). Factors associated to the access to health services from the point of view of professionals and users of basic reference unit, *Saude e Sociedade* 24, 100-112. [https://doi.org/ 10.1590/S0104-12902015000100008](https://doi.org/10.1590/S0104-12902015000100008).
- Watkins, D.A., et al. (2018). Alma-Ata at 40 years: reflections from the Lancet Commission on Investing in Health. *The Lancet*. 392, 1434–60. [https://doi.org/ 10.1016/S0140-6736\(18\)32389-4](https://doi.org/10.1016/S0140-6736(18)32389-4)
- WHO. The World Health Report 2002. Reducing Risks, Promoting Healthy Life, Geneva, World Health Organization, 2002. https://www.who.int/whr/2002/en/whr02_en.pdf?ua=1
- Williamson, L. (2014). Patient and citizen participation in health: the need for improved ethical support, *American Journal of Bioethics* 14, 4-16. [https://doi.org/ 10.1080/15265161.2014.900139](https://doi.org/10.1080/15265161.2014.900139)



Evaluation of School Health Status, Explanatory Study

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Abstract

Background: Schools are one of the best settings-based approach to promote health. Schools remain for many years been recognized as an important settings for health promotion for the community. The study provides description of schools health status in the city, concerning the activities and services components of school health and the deficiencies, accordingly the requested procedures and processes to improve that health situation, assuming that improvement of schools health status will lead the improvement of health status of the overall community. **Objectives:** The study aims to assess schools health status in Makkah city. **Introduction:** The study conducted to evaluate schools health status and services provided in Makkah city, 20 schools selected randomly for this purpose. **Methodology:** Descriptive study had been implemented, simple random sampling used, (20) schools selected for the evaluation of the six components of school health services and activities, data collected through checklist and interviews. **Results:** The study clarified that most schools in Makkah have a health supervisor, health supervision plan and a committee, but only 32% of schools have healthy foods provided. **Conclusion:** The study concluded that, health supervision was active, but there were weaknesses in the food services, unhealthy foods and drinks were available in schools. **Recommendations:** The study recommends for motivating schools health supervisors for the extra efforts they are providing beside their teaching responsibilities, in addition to that, periodic health education sessions for students is requested to raise their awareness on different health risks especially in school environment.

Keywords: School Health, Evaluation

Introduction

School Health is all the strategies, activities, and services offered by, in, or in association with schools that are designed to promote students' physical, emotional, and social development make up a school's health program.

When a school works with students, their families, and their community to provide these strategies, activities, and services in a coordinated, planned way, then the term coordinated school health program applies (School health IBC, 2009)

School health services: staff can help all students with preventive care such as flu shots and vision and hearing screening, as well as acute and emergency care. Qualified professionals such as school nurses, nurse practitioners, dentists, health educators, physicians, physician assistants and allied health personnel provide these services.

For students with chronic health conditions, school nurses and other health care providers play a large role in the daily management of their conditions. School health services staff also are responsible for coordinating care by communicating with the student's family and health care providers so that they can stay healthy and ready to learn. School health services is part of the Whole School, Whole Community, Whole Child model (WSCC) which promotes a collaborative approach designed to improve learning and health in schools. Another component of the WSCC model, Counseling, Psychological and Social Services, is often an area that overlaps with school health services, because a school nurse or school-based health center for additional care to address these needs may refer students (CDC, 2018).

Objectives

General objective: The assessment of school health status in Makkah.

Specific objective:

- 1) To explore effectiveness of health supervision at schools.
- 2) Assessment of schools physical environment.
- 3) To evaluate quality of schools food services.
- 4) To monitor classrooms health specifications and environment.
- 5) To explore physical activities at schools.

Material and methods

Study area

This study implemented in selected schools located in Makkah city, the total area of Makkah is over 1,200 km², and the total number of schools for boys are (594).

Study population

The total number of schools have been selected for this study were (20) schools.

Study design

Descriptive study design used to evaluate school health status in Makkah through questioners and interviews.

Sample size

Sample size determined by selecting randomly (20) schools for boys in Makkah city.

Inclusion criteria

All schools for boys in Makkah city.

Exclusion criteria

All schools for girls in Makkah city.

Data collection, interpretation

Data has been collected through questionnaires and interviews and interpreted using Excel program.

Ethical issues

No ethical clearance was required.

RESULTS

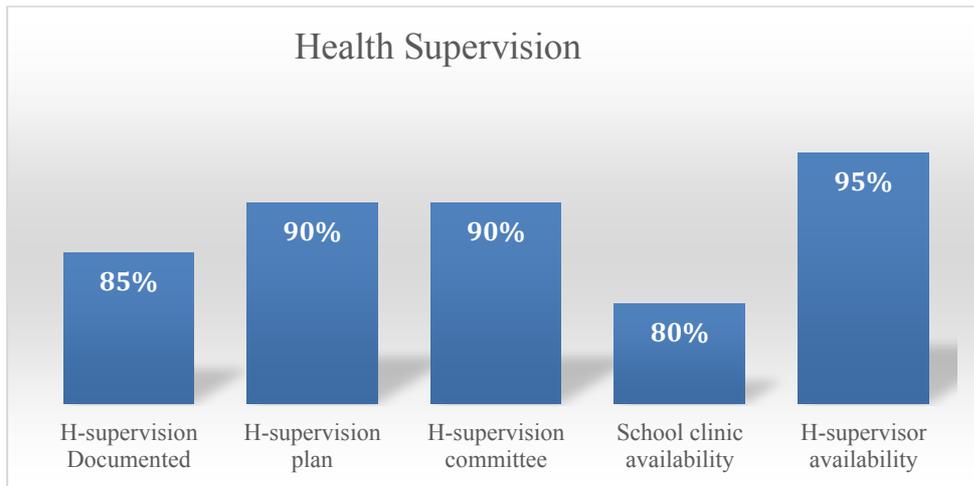


Figure1: Availability of health supervision in schools.

This figure showing that most schools in Makkah have a health supervisor, health supervision plan and committee.

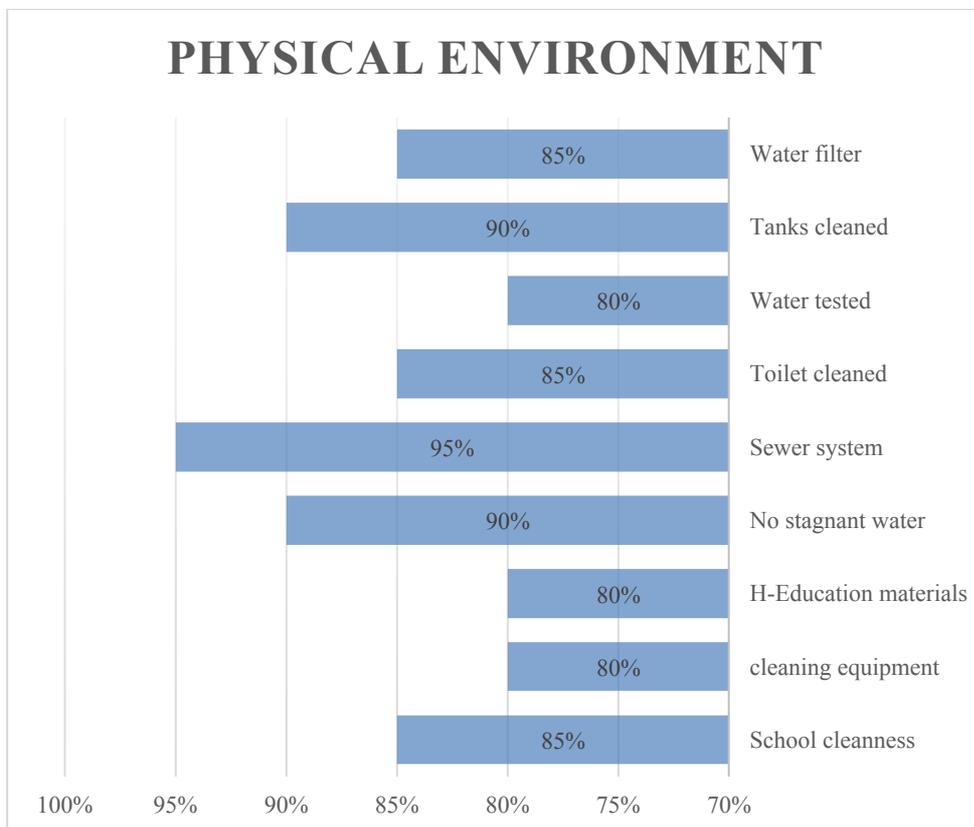


Figure 2: Indicator of physical environment at schools.

The figure showing that 20% of schools water are not tested, tanks periodic cleaning, proper sewer system achieved the best results

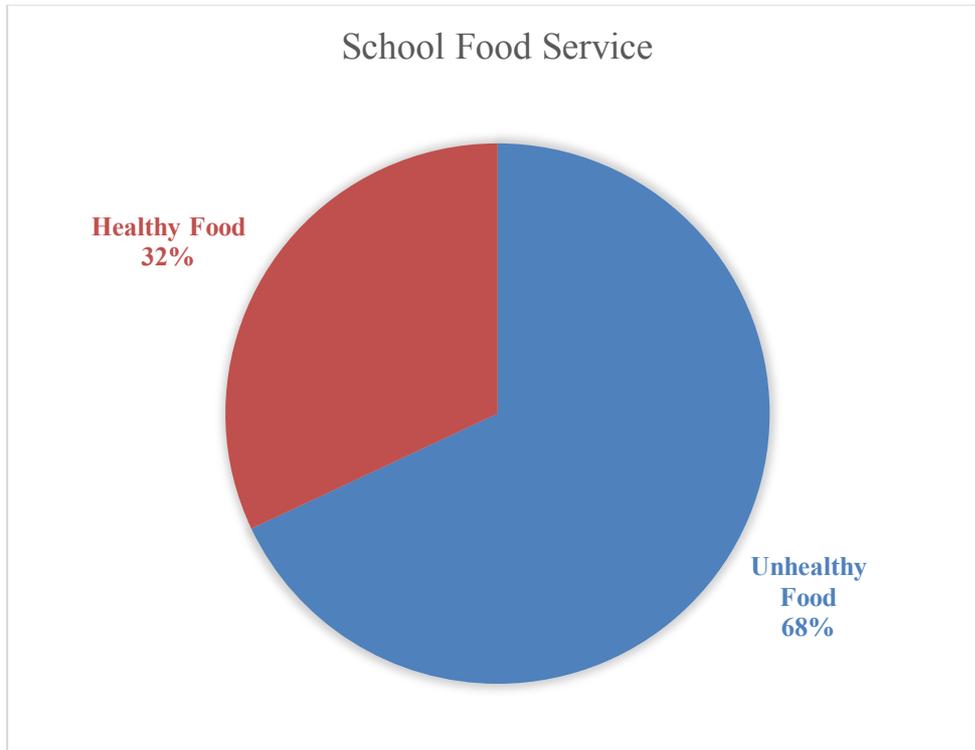


Figure 3: School food services in Makkah.

This figure showing that 68% of Makkah schools with unhealthy foods.

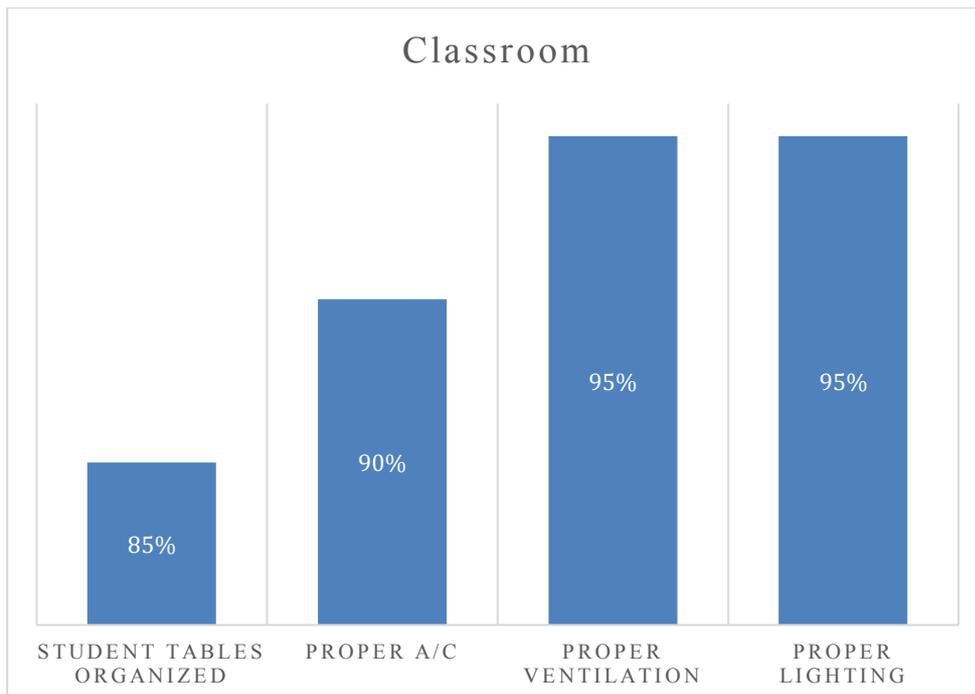


Figure 4: Classroom specifications

The figure shows that specifications and services of the classrooms were generally in good conditions.

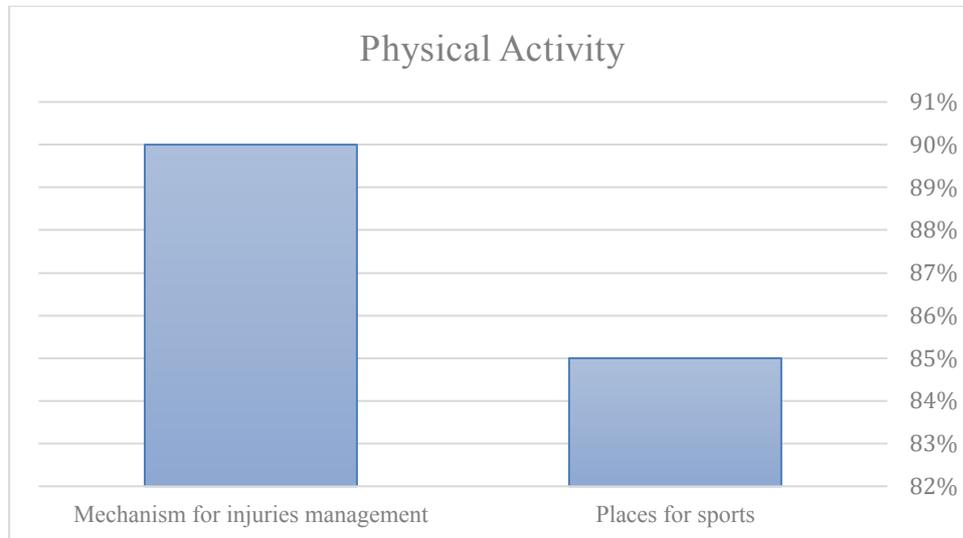


Figure 5: Availability of physical activity in school Health.

The figure showing that most schools have a mechanism for injuries management.

Discussion

The descriptive study designed to evaluate the health services and health status in schools of Makkah city, the evaluation based on the six components of school health services and activities.

Health supervision activities plays an important role in developing school health, its average was 88%. Most schools in Makkah have a health supervisor. Health supervision plans, eventually this leads to improvement in students health.

These findings agreed with the study of Zaine C. Leroy et al, which concluded that supervised school health services play an important role in the promotion of student's health (Leroy, et al., 2017).

Referring to school physical environment component, the study showed that most of the healthy environment activities were being well implemented, results showed that water tanks periodic cleaning and availability of proper sewer system achieved the best results, excluding water inspection in which 20% of schools participated in the study reported that water was not tested.

The study showed that food services in school was generally unhealthy, the percentage of healthy food was 32%, which can affect the health of students, schools are requested for more efforts in order to improve this component, This finding agrees with the study of Bushara MOE, Elqarni MGM, AlHassani ATRLB, Almuterfi H, the study concludes that , extensive efforts are needed from schools to supply healthy food items for students so that the component of food safety and nutrition service within schools will be improved (Bushara, et. al., 2017).

According to classrooms, health specifications and services was generally in good condition 90%, containing ventilation, lightning and proper air conditioning, etc.

The study clarified that most of schools had a mechanism for injuries management when necessary, which is considered as an important component of school health services as well as availability of sufficient places for students physical and sports activities.

Conclusion

The study concluded that there was a weakness in the food services, unhealthy foods and drinks were available in schools, study recommended for more efforts to improve food services.

In the study found that there was a good performance relating health supervision availability and services that contribute positively in the other components of school health services.

According to the study, there was a shortage of periodic check for school water tanks; study recommended for additional efforts on some services mainly water tanks periodic checks. Further, study concluded that school health services in targeted schools were generally good, but there were need for more efforts to develop and improve these services.

Recommendations:

1. Extensive efforts from school health and schools administrations to provide healthy foods.
2. Periodic training refreshment for schools health supervisors.
3. Periodic health education sessions for students to raise their awareness on different health risks.
4. Comprehensive health services directed to school staff organized by health supervisors at schools.
5. Motivating schools health supervisors for the extra efforts they are providing in addition to their teaching responsibilities.
6. Additional efforts on some services mainly water tanks periodic check.
7. More researches requested for the discovering and assessment of school health services and problems.

References

- School health1BC 2009. Definition of School health. Accessed Nov 14, 2018 Available on line at <http://sh1b.blogspot.com/2009/02/definition-of-school-health.html>
- Centers for diseases control and prevention (CDC) 2018. School health services. Accessed Dec 22, 2018, Available on line at <https://www.cdc.gov/healthyschools/schoolhealthservices.htm>
- Government of Western Australia, department of health. Accessed Feb 11, 2019, Available on line at <https://ww2.health.wa.gov.au/About-us/Child-and-Adolescent-Health-Service/Child-and-Adolescent-Community-Health/Community-health-nursing/School-health>
- Anderson, C. L. School Health Practice. Seventh ed. St. Louis: the C. V. Mosby Company; 1972:127-133.
- Department of Health 2018. Accessed Dec 28, 2018, Available on line at https://healthywa.wa.gov.au/Articles/S_T/School-health-services
- NCBI 1997. Accessed Feb 10, 2019 Available on line at <https://www.ncbi.nlm.nih.gov/books/NBK232689/>
- Delaware Department of education 2018. Accessed Dec 16, 2018, Available on line at <https://www.doe.k12.de.us/Domain/150>
- Jessie Haag. School Health Program. 4th ed. United states of America; 1972:1-7
- Jessie Helen Haag. school health program. Revised ed. Oxford. IBH Company: New York;1968:38-45
- Turner Sellery Smith. School health and health education. 4th ed. C V Mosby Company: United states; 1961:42-48
- Zaine C.Leroy.et al. The role of school health services in addressing the needs of students with chronic health conditions. The Journal of school nursing.2017;33:64-72.
- Bushara MOE, Elqarni MGM, AlHassani ATRLB, Almuterfi H. Evaluation of health promoting schools in Makkah city, Saudi Arabia. Int J community Med Public Health 2017;4:2234-9.



Awareness of Long-Term Prednisolone Use Among Patients Attending a Respiratory Clinic in Sri Lanka: A Clinical Audit

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Abstract

Background: Prednisolone is recognized as one of the most commonly used, highly effective anti-inflammatory agent. It plays a pivotal role in the management of various disease conditions in pulmonology, such as interstitial lung diseases, sarcoidosis, bronchial asthma, chronic obstructive airway disease, allergic bronchopulmonary aspergillosis and even in some forms of extrapulmonary tuberculosis. However, this medication with great therapeutic importance is not free of risks. Long-term use and use in higher doses are known to cause various systemic adverse effects. Therefore, complying with recommended precautionary strategies is of paramount importance. **Objectives:** To assess awareness of correct use of prednisolone particularly among long-term, outpatient users. **Methodology:** A structured interviewer-based questionnaire was used to assess awareness of prednisolone usage in patients attending Central chest clinic, Colombo. Forty-one consecutive patients on long term prednisolone were selected from the clinic. The questionnaire was prepared based on recommendations and guidelines related to proper use of corticosteroids. Data were collected by the principal investigator. **Results:** This clinical audit highlighted the inadequacy of awareness about side effects and safety practices among patients on prolonged courses of prednisolone. **Conclusion:** Patients need to be educated more on adverse effects, safety measures and correct use to improve risk/ benefit ratio. Designing a steroid treatment card was identified as a potential method to optimize patient education, monitoring and adverse outcome prevention in long-term steroid therapy. Intended quality improvement will be evaluated by re-auditing the implemented protocol.

Keywords: Audit, Prednisolone, Steroid Treatment Card

INTRODUCTION

Prednisolone is a widely used corticosteroid in various inflammatory disorders involving pulmonary, rheumatological, renal, hematological, ophthalmologic, and gastrointestinal systems (Coutinho and Chapman, 2011). Despite well-known therapeutic benefits of this medication, it is not free of adverse health effects. Side effects of prednisolone include osteoporosis, hyperglycemia, weight gain, hypertension, cataract, immunosuppression, opportunistic infections and poor wound healing, particularly with high dose, long-term use (Liu *et al.*, 2013). Based on National Institute for Health and Care Excellence guidance high dose is defined as a dose of >5 mg oral prednisolone per day and long term as duration of treatment >1 month

Awareness of corticosteroid use and adverse side effects is of paramount important and should be emphasized to patients on long-term prednisolone treatment. Prednisolone should be prescribed at lowest possible dosages and the duration of treatment should be minimized as much as possible. Patients on treatment should be closely monitored for any possible adverse outcomes. Calcium and vitamin D supplementation, antiresorptive therapy (Lekamwasam *et al.*, 2012) and gradual tapering on withdrawal (Bancos *et al.*, 2015) are recommended precautionary strategies.

This knowledge should be clearly and thoroughly disseminated to the patients by the caring physicians. Correct use of prednisolone with recommended safety measures can result in reduction in rate of adverse effects leading to reduced patient morbidity, mortality, hospitalizations and health care cost (Liu *et al.*, 2013; Mundell, Lindemann and Douglas, 2017). This audit was designed to assess awareness about long-term prednisolone usage and to find out the level to which patients are engaged in safety practices among those who attending Central chest clinic.

METHODOLOGY

A structured, interviewer-based questionnaire consisting of 26 questions obtaining data regarding awareness of the patients regarding side effects and safety use of long-term prednisolone was prepared, based on internationally recommended therapeutic guidelines. Forty-one consecutive patients, who are on prednisolone >5mg per day for more than one month, attending central chest clinic were interviewed by the principal investigator. Collected data were tabulated and analyzed.

RESULTS

Selected patients (n=41) were on long term prednisolone for, non-specific interstitial pneumonitis (NSIP), hypersensitivity pneumonitis (HP), organizing pneumonia (OP) or sarcoidosis. Demographic details of the patients are summarized in Table -01. Majority of them were females (82.9 %). Median age of the sample was 51.39 years. Education status of the majority was ordinary level or below (56.1%).

Table 1: Demographic details of selected patients on long-term oral prednisolone therapy. (n=41)

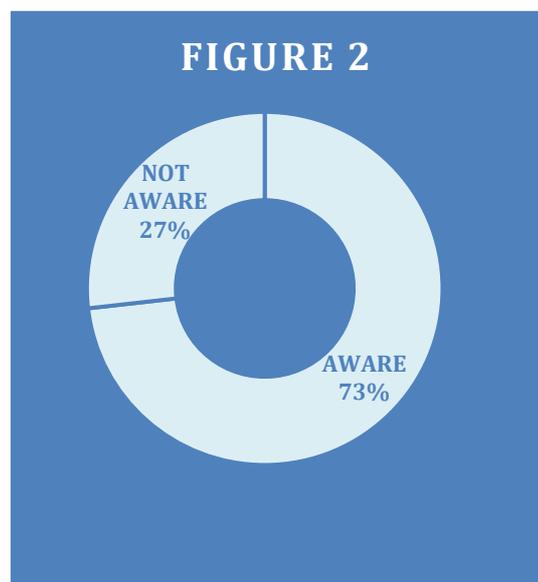
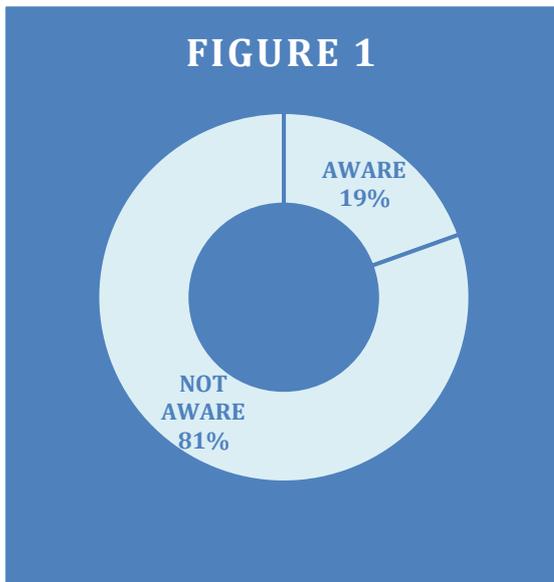
VARIABLE	FREQUENCY (%)
GENDER	
Male	7 (17.1)
Female	34 (82.9)
AGE GROUPS (YEARS)	
25-35	04 (9.75)
36-45	04 (9.75)
46-55	16 (39.02)
56-65	16 (39.02)
66-75	01 (2.43)
EDUCATION	
GCE Ordinary level	23 (56.1)
GCE Advanced level	13 (31.7)

University education	04 (9.8)
Postgraduate education	01 (2.4)

Out of patients included in the audit, only 19.5% (n=8) of patients were aware that they were on a medication of corticosteroid category (Figure 1).

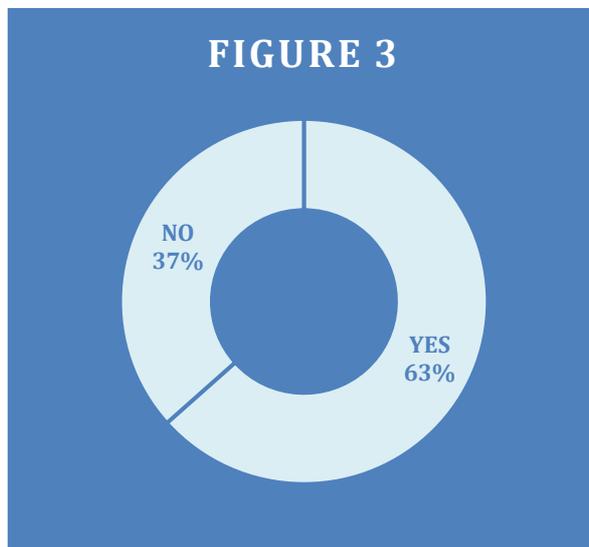
Figure 1: AWARENESS OF PREDNISOLONE AS A CORTICOSTEROID.

Figure 2: AWARENESS ABOUT THE PRESENCE SIDE EFFECTS OF PREDNISOLONE



Thirty patients (73.2%) were aware that long-term prednisolone can have adverse effects. (Figure -02) Twenty-six patients (63.4 %) accepted that they were educated in detail regarding prednisolone therapy and adverse effects by a doctor at the outset (Figure 3).

Figure 3: Percentage of Patients Who Received Detailed Advices Regarding Prednisolone Treatment from A Doctor.



Awareness of patients regarding prednisolone related adverse effects is illustrated in figure 4.

Figure 4: Frequency of Patients Aware About Different Side Effects of Long-Term Prednisolone Related Adverse Effects.

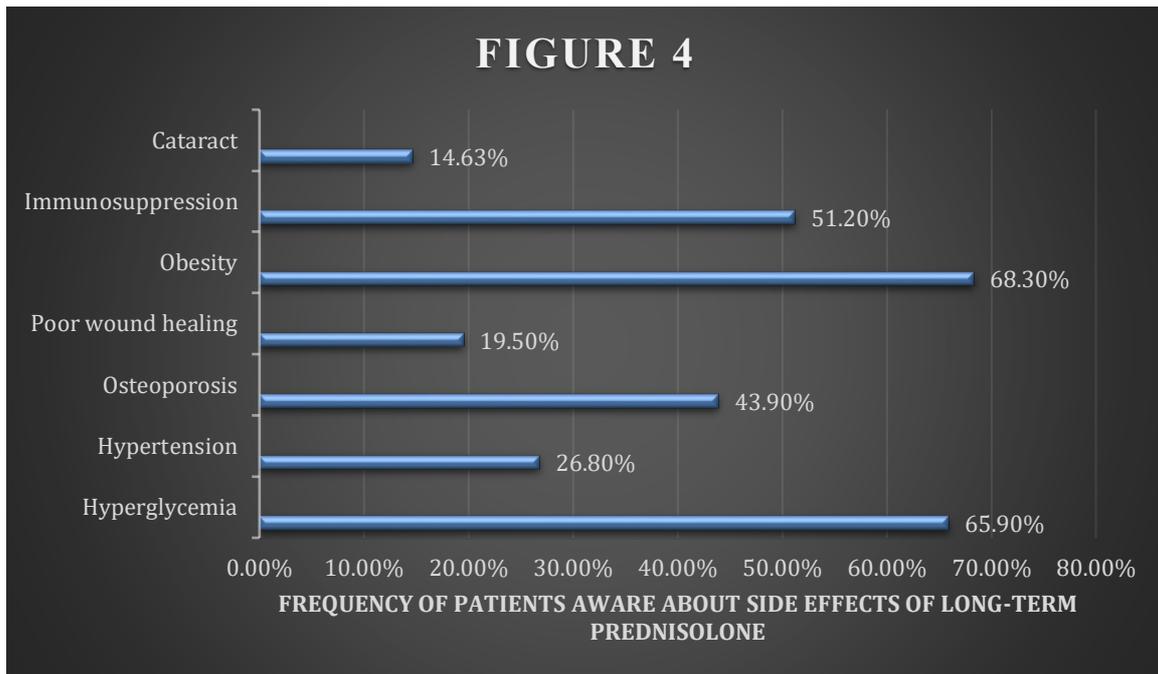


Figure 5 Demonstrates the frequencies of patients aware about the importance of medication safety issues and practices of long-term prednisolone therapy.

Figure 5: Frequency of patients aware about the importance of different safety measures and practices related to long-term prednisolone therapy.

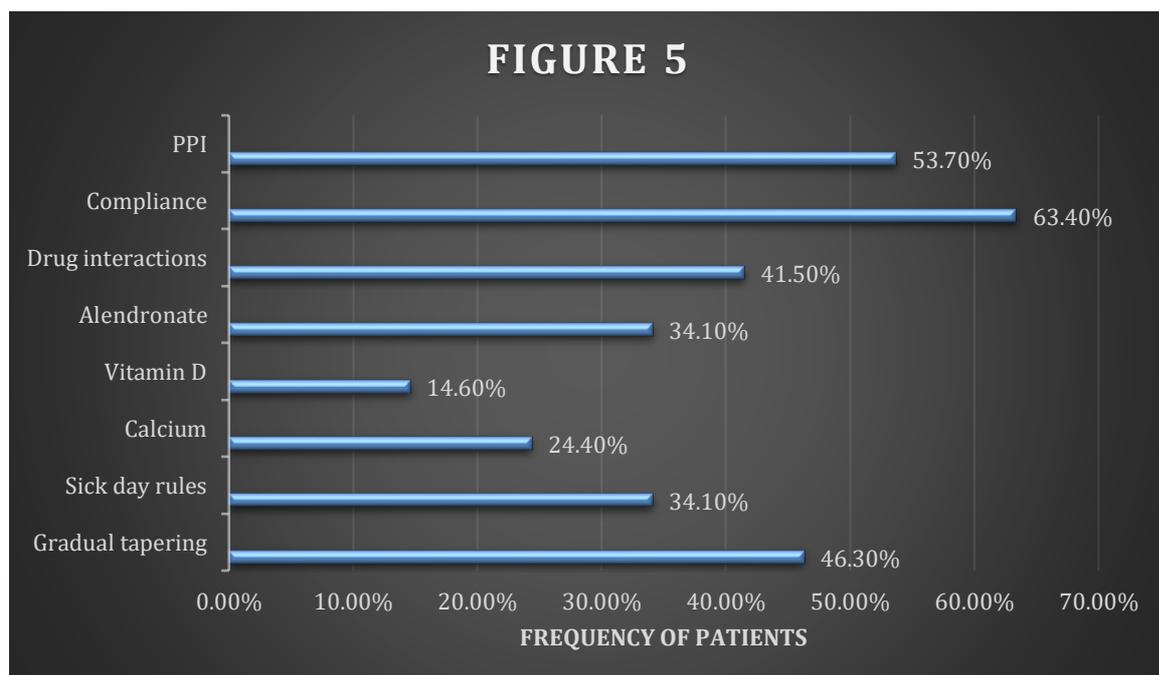
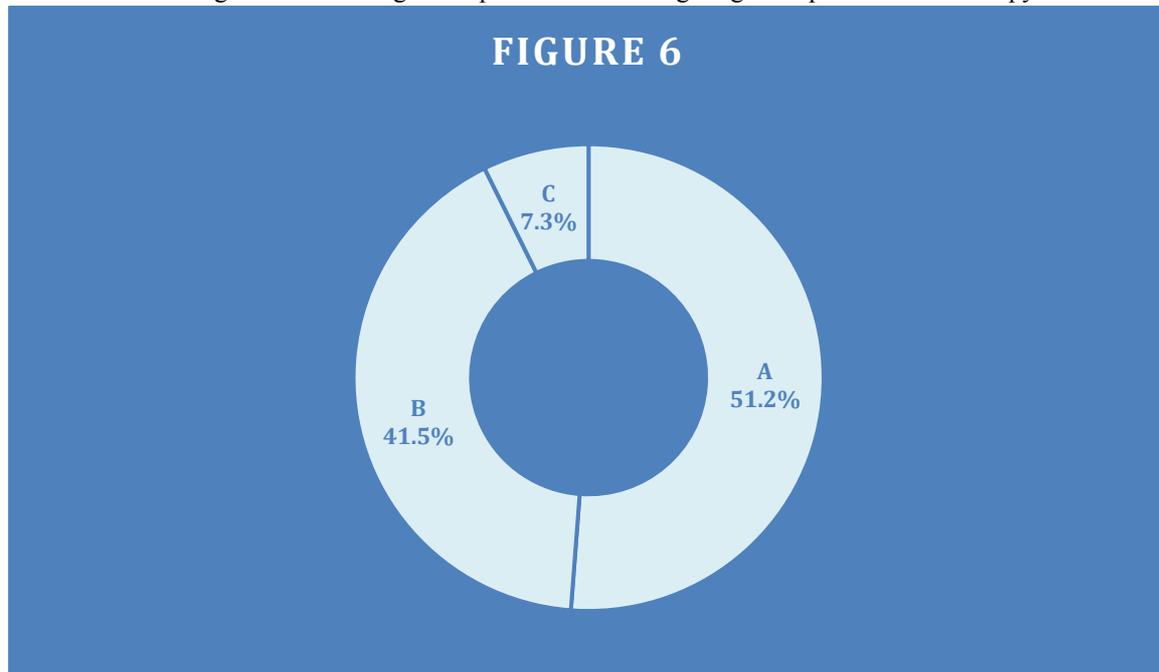


Figure 6 demonstrate details about general practitioner (GP) visits of the patients during last six months.

Figure 6: Visits to general practitioners during long-term prednisolone therapy.



A-GP was not informed regarding concomitant prednisolone treatment by the patient.

B-No GP visits during last six months.

C- GP was informed regarding concomitant prednisolone treatment by the patient.

DISCUSSION

Better patient awareness is of paramount importance when prescribing long term prednisolone considering its significant side effect profile. In our audit, majority of our patients (73.2%) considered oral prednisolone as a drug with devastating systemic side effects, but their awareness about individual side effects was unsatisfactory.

Only, 26.8%, 43.9%, 19.5%, 51.2% and 14.63 % of interviewed patients were aware that long-term prednisolone can cause hypertension, osteoporosis, poor wound healing, low immunity and cataract respectively. These figures correlate with that of previous studies conducted in this field (Mahdy *et al.*, 2017). The frequency of patients aware about most of the side effects was well below 50%. Number of patients aware about cataract as an adverse event was the lowest out of all categories. However, they had a better awareness about hyperglycemia (65.9%) and weight gain (68.3%), compared to other adverse effects.

Around two thirds of the sample were educated in detail regarding prednisolone therapy by a clinic doctor at commencement of the therapy. The proportion of patients who retained that knowledge was low which is probably due to the inadequate time spent for explanation in busy clinics and absence of a written document covering important points to read later. The British National Formulary recommends that all patients on corticosteroids for more than 3 weeks are issued with a steroid treatment card that they carry at all times (BNF, 2017). None the patients in this study have a steroid treatment card.

Overall knowledge about the importance of precautions and medication safety practices was dissatisfying. Percentage of patients who value the importance of safety measures was well below 50% in most of the categories. Only 46.35% and 34.1% of the patients consider gradual tapering and sick day rules are important. Poor knowledge about these measures can result in devastating outcomes like Addisonian crises (Bancos *et al.*, 2015). Only 24.4%, 34.1%, 14.6% and 53.7% of the patients knew the value of concomitant calcium, alendronate, vitamin D and proton pump inhibitors (PPI) respectively.

The proportion of patients knew that prednisolone can interact with other drugs was 41.5%. When a patient is seeking treatment from a GP while on long-term prednisolone therapy, other than the one who prescribed

prednisolone, that doctor need to be informed about the corticosteroid regime. This knowledge will greatly affect clinical decisions, treatment options and even drug doses of the GP. This practice was followed only by 7.3% of the patients interviewed in this study.

This audit highlights the inadequacy of awareness on side effects and precautionary measures of long-term prednisolone treatment. To overcome these issues a steroid treatment card was introduced, which is an essential measure need to be implemented in all health care institutions (Zeppetella, 1998; Rusby, 2010; BNF, 2017). This document contained details about adverse effects, safety practices and dosage and duration of therapy, in both Sinhala and Tamil languages. This will allow the patients to have a clear and better knowledge. Apart from that the card will be useful for healthcare professionals in emergency situations and GP visits. This card was issued to every patient on long-term prednisolone treatment and advised to carry it with them all times. Success of the strategy will be evaluated by a future audit.

We used an interviewer-based questionnaire for data collection. This method allows the interviewer to explain the questions and ensure that the participants are fully understood which may lead to increased reliability of the answers. However, the number of patients interviewed in the audit was relatively small and it was identified as a weak point.

CONCLUSION

Long-term prednisolone therapy is an important therapeutic option in clinical practice. Prevention of side effects is mandatory to increase the benefits of the therapy over hazards. This audit stress the need for better patient education on proper medication usage. Detailed steroid treatment card was introduced to disseminate the particular knowledge to the target patient group.

References

- Bancos, I. *et al.* (2015) 'Diagnosis and management of adrenal insufficiency', *The Lancet Diabetes and Endocrinology*. doi: 10.1016/S2213-8587(14)70142-1.
- BNF (2017) *BNF 73 (British National Formulary) September 2017*, *Bnf.org*.
- Coutinho, A. E. and Chapman, K. E. (2011) 'The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights', *Molecular and Cellular Endocrinology*. doi: 10.1016/j.mce.2010.04.005.
- Lekamwasam, S. *et al.* (2012) 'A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis', *Osteoporosis International*. doi: 10.1007/s00198-012-1958-1.
- Liu, D. *et al.* (2013) 'A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy', *Allergy, Asthma and Clinical Immunology*. doi: 10.1186/1710-1492-9-30.
- Mahdy, A. *et al.* (2017) 'Knowledge, attitude, and practice analysis of corticosteroid use among patients: A study based in the United Arab Emirates', *National Journal of Physiology, Pharmacy and Pharmacology*. doi: 10.5455/njppp.2017.7.1234409022017.
- Mundell, L., Lindemann, R. and Douglas, J. (2017) 'Monitoring long-term oral corticosteroids', *BMJ Open Quality*. doi: 10.1136/bmjopen-2017-000209.
- Rusby, E. (2010) 'Steroid treatment cards: Patient safety remains at risk', *British Journal of General Practice*. doi: 10.3399/bjgp10X515458.
- Zeppetella, G. (1998) 'Steroid treatment cards [8]', *British Journal of General Practice*.