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The Impact of Obesity During Covid 19 Outbreak

Siphesihle Sithole*

Environmental Officer at Eskom Rotek Industries, United States

Review Article

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***For Correspondence**

Siphesihle Sithole, Environmental Officer at Eskom Rotek Industries, United States.

E-mail: siphesihlesithole26@icloud.com

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ABSTRACT

The burden of disease caused by infectious diseases has gradually decreased over the years. In 2017 it was estimated that only 30% of the total disease burden globally was due to infectious diseases. Obesity is the modern-day public health challenge as it is one of the underlying factorsto the burden of many chronic diseases.

INTRODUCTION

The burden of disease caused by infectious diseases has gradually decreased over the years. In 2017 it was estimated that only 30% of the total disease burden globally was due to infectious diseases [1]. However, this has not always been the case during the 20th century the largest global burden of disability and premature deaths was attributed to infectious disease. The sporadic pandemics of infectious disease such as cholera, smallpox and influenza have largely posed a threat to the survival of populations [2]. The 1918 influenza pandemic killed an estimate of 50 million people globally [3]. According to Osterhaus, viruses can stay dormant and later reoccur in a population with a waned immunity thus causing a new pandemic wave [4]. This can be seen with the 1977 Russian flu which was caused by the same H1N1 virus that gave rise to the major 1950's Spanish flu pandemic.

Since 1975 the global obesity rates have tripled with approximately 1.9 billion people overweight and 650 million obese [5]. This means over 45% of adults globally have a Body mass index (BMI) of 25 to 30 and >30 respectively [6]. The 2009 influenza a pandemic (H1N1) saw a surge in infectious diseases and the high burden of overweight and obese populous did not provide any relief during the pandemic. Sheridan states through study that obesity is an independent risk factor for mortality and morbidity from H1N1 influenza pandemic. In modern day society the high prevalence of individuals that have waned immunity due to malnutrition such as obesity pose a severe consequence on the body's response to infection of any sort [7,8].

For the purpose of this proposal data will be drawn from previous influenza outbreaks which aims to highlight obesity as a congruent comorbidity risk factor on the current novel corona virus 2019 (Covid-19). The paper aims to expand on the rapid exponential growth of obesity in South Africa and the problems that come with it during pandemic times. This article will elaborate on risk of infection, hospitalization risk and risk of death.

BACKGROUND

Obesity is the modern-day public health challenge as it is one of the underlying factors to the burden of many chronic diseases. In South Africa, 42% of women are reported to be obese this is the highest prevalence rate in sub-Saharan Africa [9]. In 2013

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it was recorded that 12% of men in South Africa are obese [10]. The South African Department of health [DOH] (2016) aims to reduce obesity by 10% in the year 2020 however this target is slowly becoming unobtainable for the time frame given. According to a cross-sectional study conducted amongst adults in the Eastern Cape province of South Africa. The prevalence of overweight and obesity was 24% and 46% respectively in a population of 1077 adults [11]. Females had a higher prevalence of obesity of 53.4% compared to males who were at 27.4% [12]. According to figure 1 below, Obesity is ranked 5th as a risk factor for disability adjusted life years (DALY's). One should take note that figure 1 was captured during 2005 -2007. Therefore, rate of obesity has since been on an exponential rise in South Africa.

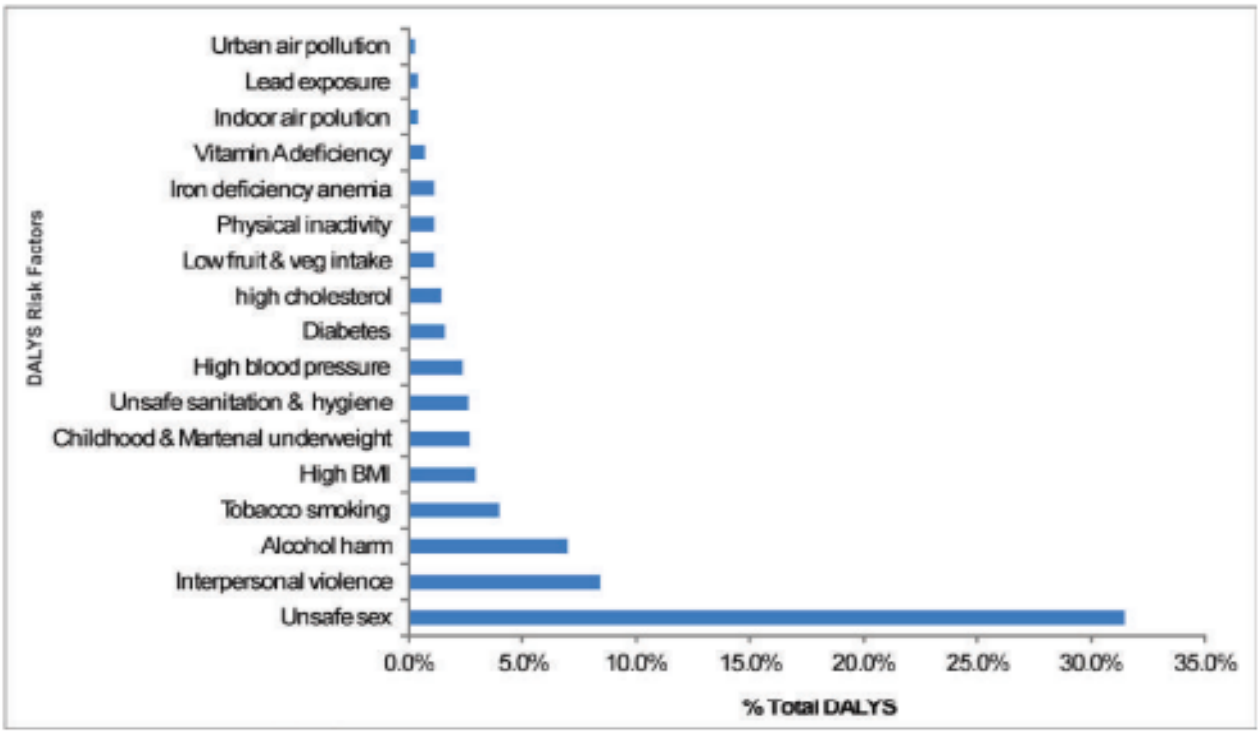

Figure 1. Bar graph showing ranking of risk factors for DALY's in South Africa

South Africa like many other Low-Middle income countries continues to endure the effects of a double burden of disease in the country. With the rapid rise of Non-communicable diseases such as obesity and dealing with infectious disease, it has become very common to find a population within the same community and even in the same household whereby individuals suffer from under nutrition, obesity, and an underlying infectious disease such HIV/AIDS [13]. The exposure to high energy dense foods, over consumption of these foods, lack of physical activity and unemployment has not helped ease the growing problem of obesity. Consistent with other studies, initially 42% of obese women were prevalent in urban areas [14]. Alaba and Chola research shows that men from a higher income percentile are 0.27 Concentration index (CI) more likely to be obese compare to men in the low-income percentile [15]. Owolabi attributes this disparity to the perception that many South Africans still see obesity as a sign of affluency and wealth [16].

OBESITY AND INFLUENZA PANDEMIC

The H1N1 influenza A pandemic affected South Africa late 2009 which posed an extra burden on the health system that was already dealing with a high prevalence of chronic lung disease (specifically Tuberculosis) and HIV as well as emerging NCD's such as diabetes mellitus. A literature review on the research study conducted by Koegelenberg will be done to emphasise on the ramifications of obesity and the H1N1 influenza virus [17].

Koegelenberg conducted a 6 weeks observational study of (n=19) patients confirmed for H1N1. n=15 patients were female between the ages of +/- 20-63 and n=4 males between the ages of +/- 33-64 (appendix 1). n=16 of these patients had an underlying risk factors which were: Pregnancy n=6, type 2 diabetes mellitus n=6 and obesity n=4 (appendix 2). The study observed the patients during the hospital admission and post admission. Figure 2 below shows the baseline characteristics, risk factors, disease severity, management, complications and outcome. As highlighted in figure 2, 3 out of the 4 obese patients died. 3 of which had 2 or more morbidities. Out of the 19 patients only 6 survived.

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No	Age	Sex	Risk factors	Other co-morbidities	APACHE II	P_aO_2/F_IO_2	CXR score	Oseltamivir: SD or DD (days)	Ventilation (mode)	Complications (S=Septic shock)	Length of ICU stay (days)	Outcome
1	25	F	HIV, Pregnant (40/40)		15	112.8	6	SD (5)	NIPPV	—	12	Survived
2	34	F	Pregnant (31/40)		21	176.3	15	SD (5)	SIMV	ARDS, VAP, S, ARF	18	Died
3	43	F	SLE, Renal transplant[a]		23	186.3	24	SD (5)	NIPPV,SIMV	ARDS, S, ARF	5	Died
4	45	F	Type 2 DM		12	268.5	2	SD (5)	SIMV	VAP, S	5	Survived
5	19	F	Pregnant (30/40)		11	127.8	20	SD (5)	SIMV	ARDS, ARF	12	Died
6	36	F	Type 2 DM, Obesity		23	65.4	14	SD (10)	SIMV	ARDS, VAP, S, ARF	17	Died
7	51	M	Type 2 DM, Renal transplant[a]		18	270.8	19	SD (5)	SIMV	—	13	Survived
8	48	F	HIV, Active PTB, RA	Previous PTB, MTX	23	287.5	11	SD (5)	NIPPV, SIMV	ARDS, ARF	13	Died
9	29	F	HIV, Pregnant (27/40)		22	97.7	23	SD (5)	SIMV	ARDS, ARF	7	Died
10	20	F	—		10	298.3	9	SD (5)	NIPPV	—	10	Survived
11	46	F	Type 2 DM, COPD, Obesity	Previous PTB, Smoker	19	75.9	23	DD (4)	SIMV	ARDS, ARF	6	Died
12	39	F	Obesity	Dyslipidaemia	18	268.8	12	SD (5)	NIPPV, SIMV	—	3	Survived
13	69	M	—		20	146.6	16	SD (2); DD (3)	SIMV	VAP, S, ARF	7	Died
14	19	F	Pregnant (38/40)	Smoker	10	103.8	11	DD (5)	SIMV	ARDS, VAP	22	Died
15	68	F	—	Smoker	18	195.4	20	SD (5)	SIMV	ARDS, VAP, ARF	25	Died
16	42	F	Active PTB, Obesity	Idiopathic PAH	30	125.0	16	DD (10)	SIMV	VAP, S, ARF	30	Died
17	43	M	Type 2 DM		17	131.8	20	DD (5)	SIMV	ARDS, VAP, S, ARF	12	Died
18	24	F	Pregnant (27/40)		16	150.9	24	DD (5)	SIMV	ARDS, VAP, ARF	47	Survived
19	50	M	Type 2 DM		19	163.5	16	DD (5)	NIPPV, SIMV	ARDS, VAP, S, ARF	30	Died
Mean	39.5				18.2	171.2	15.8				15.5	
SD	14.8				5.1	74.4	6.2				11.2	

Note: APACHE II, acute physiology and chronic health evaluation (APACHE) II score; P_aO_2/F_IO_2: partial pressure of arterial O_2 to the fraction of inspired O_2; CXR: chest X-ray; SD: single dose (75 mg twice daily); DD: double dose (150 mg twice daily); ICU: intensive care unit; F: female; M: male; HIV: human immunodeficiency virus; SLE: systemic lupus erythematosus; DM: diabetes mellitus; PTB: pulmonary tuberculosis; RA: rheumatoid arthritis; COPD: chronic obstructive pulmonary disease; MTX methotrexate therapy; PAH: pulmonary arterial hypertension; NIPPV: non-invasive positive pressure ventilation; SIMV pressure control synchronised intermittent mandatory ventilation (with pressure support ventilation); ARDS: acute respiratory distress syndrome; VAP: ventilator-associated pneumonia; ARF: acute renal failure; S: septic shock.
[a]Patient on immunosuppression following renal transplant.

C.F.N. Koegelenberg et al.

Figure 2. Table showing baseline characteristics, risk factors, disease severity, management, complications and outcome.

RISK OF INFECTION

Studies that asses risk of infection in the obese populous have been based on analysing infection rate among individuals who had previously been vaccinated against seasonal influenza [18]. No coherent study shows risk of infection with any influenza pandemic virus. However, studies do show a near true replica of the susceptibility that obese individuals possess an increased risk of infection. Neidich conducted a study between vaccinated obese adults (BMI>30) and vaccinated healthy weight adults (BMI 18.5-24.9) to assess the risk of susceptibility to seasonal influenza amongst both populations. In this study 9.8% of obese adults and only 5.1% of healthy weight patients were laboratory confirmed to been infected with the seasonal influenza [19]. The relative risk (RR) of infection amongst the obese participants proved to be 2.1 with a 95% probability that the true RR lie between 1,12-3,60. This shows that compared to the healthy weight, the obese participants had a double risk of influenza infection. Thus, corroborating that obesity undermines the efforts to provide immunity as will further on be explored.

HOSPITALISATION RISK

Risk of hospitalisation increases amongst individuals >20years of age infected with the H1N1 influenza [20]. The author continues to state that this risk of hospitalization increases drastically when the individual also has a severe case of obesity regardless of the individual being predisposed to other chronic medical conditions (Morgan et al, 2010). As noted from Koegelenberg, the mean age of the participants was 32 years. In the study all 4 obese patients were hospitalised. In the Koegelenberg study, Patient 12 was hospitalised but was the only obese patient to survive. This maybe inconclusively due to her not having any other underlying issues as compared to the other 3 obese patients. However, regardless of the outcome the hospitalisation risk in Koegelenberg study reiterates Morgan assessment that obesity increases risk of hospitalisations. Therefore, Han concluded that obesity has been highly associated with an increased number of hospitalisations in adults who were exposed to seasonal influenza [21].

RISK ICU ADMISSION AND RISK OF DEATH

In the study conducted by Koegelenberg 68.4% of the study population died during ICU admission. The study observed that these patients had identifiable risks for severe infection which were mainly pregnancy, type 2 diabetes and obesity. According to Akinnusi obesity is parallel to complications in ICU which includes prolonged stay, longer ventilation period and higher mortalities. A global pooled analysis amongst 19 countries was conducted by Van Kerkhove which identifies obesity as a risk that has increased disease severity. Obesity represented a median of 6% hospitalizations, 11.3% ICU admissions and 12% fatal H1N1 cases (appendix 4). The study found that compared to the general population the risk connected to obesity and morbid obesity was increased with a Relative Risk (death) of 36.3%. The cohort study conducted by Bercault found to have a odds ratio (OR) of 2.1 which suggest a 95% probability that the true OR lie between 1.2-3.6 CI for the association between obesity and mortality.

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Thus, proving that obesity is an autonomous risk factor for ICU admissions and increased deaths therefore should be noted as critical co morbidity.

RESPONSE TO VACCINATION

Obesity on its own is an immunosuppressive condition [18]. However, there have not been many studies conducted that compare influenza infection rate and cellular immune response amongst healthy weight, overweight and obese populations. Sheridan conducted a prospective observational study in the aim to understand the effectiveness of the influenza vaccine in healthy weight, overweight and obese participants. The study had 499 participants with 29.7% healthy weight, 33.4% overweight and 35.5% obese. 12 months post vaccination the study found that a higher BMI was associated with a substantial decline in influenza antibody titers (appendix 3). Although the participants had underlying morbidities such as diabetes, the study states that there was no association of antibody response and these conditions. Ethnicity had a marginal significance of (P=0,03) as well as sex had a marginal significance (P=0,08). Results from Sheridan show that the potential to form an immune response to influenza virus may be impaired by obesity.

GAPS

The lack of coherent research which aims to associate obesity as a direct or indirect co-morbidity during novel virus outbreaks highlights the dire need for extensive studies to continue being conducted in south Africa. The proposal of this paper reinforces the need to target and identify high risk populations. Which in return aims to provide better immunization, early medical advice and use of appropriate antiviral medications. Thus, reducing the infection rate amongst individuals with high risk factors especially overweight and obese populations. Henceforth, during the current impact of Covid-19 it is with great honour to propose research which aims to study these pandemics extensively

(Appendix 1-4)

Gender and age distribution

Age categories (years)	<20	20–39	40–59	≥60
Female	2	7	5	1
Male	0	0	3	1

Appendix 1. Table showing gender and age distribution amongst study participants.

Individual risk factors and disease severity indices

	Frequency amongst all cases (*n* = 19) (%)	Frequency amongst survivors (*n* = 6)	Frequency amongst non-survivors (*n* = 13)	OR (95% CI)	*P*-value
HIV infection	3 (15.8)	1	2	1.10 (0.08–15.14)	0.483
Immunosuppressive therapy	3 (15.8)	1	2	1.10 (0.08–15.14)	0.483
Pregnancy	6 (31.6)	2	4	1.13 (0.14–8.88)	0.395
Type 2 diabetes mellitus	6 (31.6)	2	4	1.13 (0.14–8.88)	0.395
Obesity	4 (21.1)	1	3	1.50 (0.12–18.17)	0.443
Active pulmonary TB	2 (10.5)	0	2	NA	0.456
Previous pulmonary TB	2 (10.5)	0	2	NA	0.456
APACHE II score ≥20	7 (36.8)	0	7	NA	0.034
PaO2/FIO2 <200	12 (63.2)	2	10	6.67 (0.87–50.80)	0.085
CXR score ≥12	14 (73.7)	3	11	5.50 (0.67–44.82)	0.134

Appendix 2. Table showing individual risk factors and disease severity indices.

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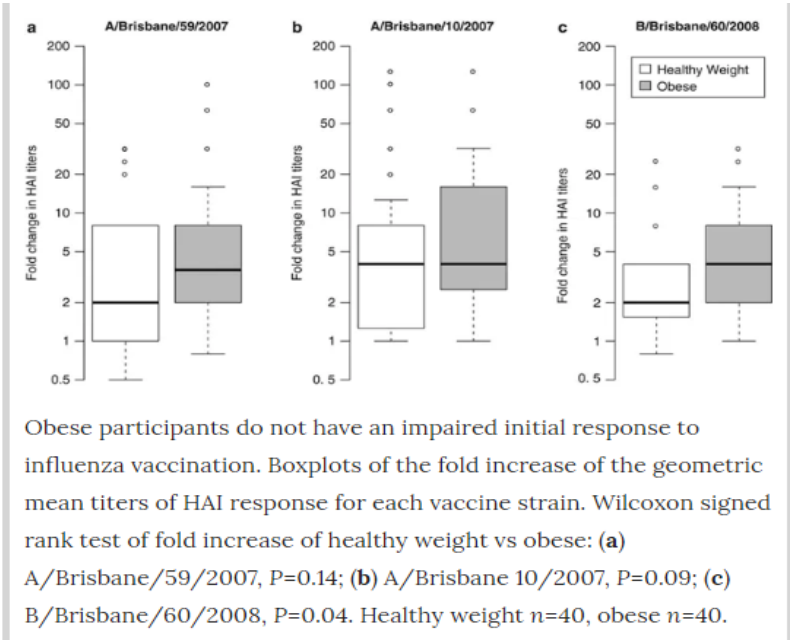

Obese participants do not have an impaired initial response to influenza vaccination. Boxplots of the fold increase of the geometric mean titers of HAI response for each vaccine strain. Wilcoxon signed rank test of fold increase of healthy weight vs obese: (**a**) A/Brisbane/59/2007, P=0.14; (**b**) A/Brisbane 10/2007, P=0.09; (**c**) B/Brisbane/60/2008, P=0.04. Healthy weight n=40, obese n=40.

Appendix 3. box plot showing antibody titers in different BMI's.

Factor[a]	Severity Level[b]						RR of Severe Disease (IQR)[b]			
	n^d	Hospitalized Cases	n^d	ICU-Admitted Cases	n^d	Fatal Cases	n^d	RR_{hosp}	n^d	RR_{death}
	14	19.0 (14.8–27.5)	9	42.0 (35.0–45.0)	13	46.0 (37.0–52.0)		—[e]		—[e]
ler (percent female)	12	49.8 (46.2–51.5)	11	47.0 (41.9–50.5)	14	44.7 (41.5–48.7)	12	1.0 (0.8–1.1)	14	0.8 (0.7–1
nic medical illness										
atory disease	12	10.3 (5.0–21.7)	11	17.2 (10.5–29.9)	16	20.4 (9.3–29.5)	5	3.3 (2.0–5.8)	8	7.8 (4.9–2
a	11	17.6 (10.0–20.4)	9	9.8 (5.6–14.3)	15	5.3 (4.0–10.6)	3	1.8 (1.2–2.6)	6	1.7 (1.5–2
tes	14	9.0 (3.5–12.6)	12	13.6 (9.3–17.3)	17	14.4 (13.0–18.0)	7	0.9 (0.5–1.7)	10	4.0 (3.1–6
c disease	12	7.1 (3.7–10.9)	11	10.9 (8.8–15.0)	15	12.1 (10.0–16.4)	6	2.0 (1.5–2.2)	8	9.2 (5.4–1
disease	13	4.0 (2.0–5.1)	11	6.3 (3.5–8.4)	16	7.1 (5.0–8.1)	2	4.4 (4.2–4.5)	3	22.7 (21.0
disease	9	1.1 (0.3–2.0)	9	2.4 (0.9–5.0)	12	4.9 (2.7–6.0)	3	5.7 (3.2–15.7)	4	17.4 (11.6
logical disease	11	4.0 (2.5–7.5)	11	7.0 (3.5–9.5)	14	13.9 (5.5–18.4)	2	1.1 (0.9–1.3)	3	13.1 (8.4–
ne compromised	13	5.0 (2.0–7.2)	11	6.7 (3.2–18.4)	15	12.5 (7.9–18.4)	2	24.3 (16.1–32.6)	4	27.7 (14.0
with ≥1 chronic al illnesses	14	31.1 (19.0–47.1)	10	52.3 (41.1–58.7)	16	61.8 (48.5–67.9)		NA		NA
nancy[f]										
rimester	7	2.0 (1.0–3.5)	6	2.0 (1.5–2.5)	5	0.9 (0.0–2.5)				
d trimester	7	7.0 (3.9–9.3)	7	5.0 (1.7–6.2)	5	2.5 (0.0–14.1)				
trimester	7	9.5 (7.6–21.3)	8	8.0 (4.0–14.6)	6	16.9 (5.1–32.0)				
own trimester	8	6.0 (1.9–9.3)	6	2.8 (1.7–3.2)	7	0.0 (0.0–2.1)				
(any trimester)	10	17.4 (13.5–30.2)	9	15.0 (9.4–24.2)	11	6.9 (0.0–9.1)	10	6.8 (4.5–12.3)	11	1.9 (0.0–2
ity										
30 or clinically obese	11	6.0 (1.5–7.5)	8	11.3 (7.9–15.8)	13	12.0 (10.0–21.0)	6	0.6 (0.2–1.8)	7	1.5 (0.9–2
30–40	3	7.0 (4.4–16.0)	3	10.0 (6.9–18.5)	4	15.8 (7.7–25.2)		NA		NA
40	5	3.0 (1.4–11.5)	5	5.0 (3.4–16.4)	6	15.2 (4.0–30.8)	2	15.0 (9.5–20.4)	2	36.3 (22.4
ot measured but d clinically obese	8	4.3 (1.8–13.3)	4	4.4 (3.4–5.3)	8	7.8 (3.8–17.3)		NA		NA
erable social/ c group	4	5.2 (2.3–10.6)	4	5.0 (1.5–10.7)	4	10.1 (5.3–18.5)	4	1.0 (0.2–3.7)	4	2.4 (1.2–3
	2	1.7 (0.9–1.8)	2	1.3 (1.0–1.6)	4	2.6 (0.8–5.9)		NA		NA

ext S1 for definitions of risk factors.
ata given as median percent (IQR), except for age, which is median (in years) (IQR).
$_{hp}$ is the unadjusted RR of hospitalization among H1N1pdm patients with the risk factor compared to the risk of hospitalization among H1N1pdm patients v
isk factor, and RR_{death} is the unadjusted RR of death among H1N1pdm patients with the risk factor compared to the risk of death among H1N1pdm pa
out the risk factor; range of RR provided if ≥2 countries provided data.
number of countries providing data for cell directly to the right; the full list of countries that provided data for each risk factor is provided in Text S1.
$_{hp}$ and RR_{death} calculated by age group and shown in Figure 1.
minator is women of childbearing age in each level of severity.

Appendix 4. Table showing risk factor, severity level of cases and serverity of disease interquartile range.

CONCLUSION

The proposal extensively indicates how obesity on its own is an immunosuppressive condition.Risk of hospitalization increases drastically when the individual also has a severe case of obesity regardless of the individual being predisposed to other chronic medical conditions. Compared to the general population the risk connected to obesity and morbid obesity was increased with a Relative Risk (death) of 36,3%.The findings stipulated in this proposal prove evident that a substantial proportion of people with severe and fatal cases of H1N1 had pre-existing chronic illness, which indicates that the presence of chronic illness increases the likelihood of infection, hospitalisation, admissions to ICU and death. Obesity acts as a "silver lining" for other noncommunicable and infectious diseases to continue thriving. With the current obesity projectile in South Africa the ramifications that develop due to its existence prove to be too intense for the country's overwhelmed health system.

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