My name is South Africa and I have a drinking a problem:

a multicentre quasi-experimental analysis on alcohol regulation and injury presentations to emergency centres

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Declaration

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Abstract

Background

The South African COVID-19 experience included several national regulatory changes to manage the additional demand placed on the healthcare platform. Since alcohol-related injury contributes a significant healthcare burden in South Africa, regulations to limit alcohol availability were also instituted. In this study we aimed to determine the impact of changing alcohol regulations (full availability, partial availability, and a complete ban on alcohol sales), across three time periods, on injury presentations to emergency centres in the Western Cape, South Africa using a quasi-experimental interrupted time series (ITS) design.

Methods

The study population included all patients who presented to a public sector emergency centre in the Western Cape with injury identified by a trained nurse on triage and identified by an emergency centre clinician by final ICD-10 code in facilities using routine real time electronic capture of emergency centre visits. Since the study design was a quasi-experimental ITS, we used an autoregressive integrated moving average (ARIMA) model with the level and slope of the model in the pre-intervention period being the counterfactual against the observed actual post-intervention level and slope. The primary outcome was the relative percent increase or decrease in the level and slope of injury presentations.

Findings

A total of 31,151 injury patients across the three periods were included in the analyses. A shift from full availability to partial (Monday to Thursday) retail alcohol availability resulted in an overall step reduction in daily injury presentations of 29·0% (absolute reduction [95% CI]: -71·7 [-102·9, -40·4]). A shift from partial to a complete ban resulted in a further step reduction of 26·2% in daily injury presentations (absolute reduction [95% CI]: -4·5 [20·6, -8·4]). This impact was consistent in terms of direction but ranged in magnitude across various sub-populations.

Interpretation

Our findings reflect the considerable impact of alcohol regulation on injury presentations to emergency centres. Partial retail alcohol restrictions, particularly in the South African context, could be considered for longer term, sustainable alcohol regulation policies to reduce the considerable burden of injuries on health services and society.

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Prof. Leslie London and Prof. Charles Parry for tirelessly demonstrating, through their sage example, the impact of public health research and advocacy in action, particularly in the face of strong commercial determinants of health. I continue to learn from their example each day.

Last and perhaps most importantly, to my family. There are few words that can truly encapsulate how grateful I am to them. The past few years have been extremely challenging in many ways, but I found solace in their unwavering love and prayers, and their willingness to help keep the midnight oil burning with a kind word of encouragement and a warm cup of tea.

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List of Abbreviations

Abbreviation	Definition
AB InBEV	Anheuser-Busch InBev
ACF	Autocorrelation Function
AIC	Akaike Information Criterion
AIDS	Acquired Immunodeficiency Disease Syndrome
ARIMA	Autoregressive Integrated Moving Average
BAC	Blood Alcohol Concentration
BIC	Bayesian Information Criterion
CI	Confidence Interval
COVID-19	Coronavirus Disease
DALY	Disability Adjusted Life Years
DMA	Disaster Management Act
EC	Emergency Centre
FASD	Foetal Alcohol Spectrum Disorder
GBV	Gender-Based Violence
GENACIS	Gender, Alcohol, and Culture: An International Study
HECTIS	Hospital and Emergency Centre Tracking Information System
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
ICD-10	International Classification for Diseases 10th edition
IPV	Interpersonal Violence
ITS	Interrupted Time Series
IUGR	Intrauterine Growth Retardation
LMIC	Low- and Middle-Income Countries
NA	Not Applicable
OLS	Ordinary Least Squares
PACF	Partial Autocorrelation Function
PAIA	Promotion of Access to Information Act
POPI	Protection of Personal Information Act
RTI	Road Traffic Incident
SA	South Africa
SAB	South African Breweries
SDG	Sustainable Development Goal
TB	Tuberculosis
UCT	University of Cape Town
WC	Western Cape
WHO	World Health Organization

Chapter 1: Introduction, Literature Review and Protocol

Title (Research Question)

Alcohol regulations and injury presentations to Emergency Centres: a multicentre quasi experimental analysis

Purpose of the Study

The primary purpose of the study is to assess the relationship between changing alcohol availability regulations and trauma injury presentations to Emergency Centres during South Africa's COVID-19 lockdown levels. The working hypothesis considers that alcohol regulation had a positive impact in reducing injury presentations to Emergency Centres.

Background and Literature Review

Introduction

The COVID-19 pandemic in South Africa was accompanied by several regulatory changes to adequately manage both the burden of COVID-19 as well as the additional demand placed on the health service delivery platform. One such change saw the institution of changing regulations to limit alcohol availability and reduce the demand placed on health services secondary to alcohol-related violence and trauma injury. Subsequently, there has been a growing need to formally examine the impact of these changing alcohol regulations on trauma injury presentations to health services across the natural experiment periods that arose. This review will firstly unpack the global context of alcohol and health, the relationship between alcohol, disease and injury and the clear international response and evidence to limit its impact. It will then explore the South African alcohol policy landscape in terms of availability, as well as the health profile of the country as it relates to the use and abuse of alcohol. Lastly, it will explore the recent available evidence within the South African COVID-19 experience as it relates to shifting alcohol regulations and identify gaps currently existing in the literature.

Global context of alcohol and health

In 2015, all member states of the United Nations signed and adopted the Sustainable Development Goals (SDGs) which are a set of global goals to be reached by 2030 (Droogers *et al*, 2020). Under the third SDG target it explicitly states that all countries are to 'strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol'. This was supported and preceded by the WHO's 2010 Global strategy to reduce the harmful use of alcohol (WHO, 2018). At this juncture there was clear consensus that the effects of alcohol use resulted in a significant health and social burden and therefore is a global public health priority. Furthermore, the Global Action Plan, as mandated by the United Nations General Assembly, for the Prevention and Control of Non-Communicable Diseases 2013-2020 clearly reiterates this by putting forward a clear target to relatively reduce the harmful use of alcohol by at least 10% by 2025 as measured by the total alcohol per capita consumption as well as the prevalence of heavy episodic drinking in any given country (WHO, 2013).

This focus on lifting alcohol on the global agenda comes at a time where there is growing evidence highlighting the harms that alcohol has created and continues to create across the world. In 2016

alone the WHO estimates that a total of 3 million deaths, or 5.3% of all deaths, globally, were due to the harmful use of alcohol (WHO, 2018). This impact of alcohol on mortality was even greater than Tuberculosis (at 2.3%), HIV/AIDS (at 1.8%) and Diabetes (at 2.8%).

Relationship between alcohol and disease

Alcohol presents a common upstream determinant of both communicable and non-communicable diseases. The mechanism by which this occurs differs across the disease burdens. HIV/AIDS, for example, is negatively affected both in terms of transmission and infection. Alcohol increases the risk of transmission through inconsistent use of condoms as well as a propensity to engage with multiple sexual partners at the time of intoxication (Reis *et al*, 2016). HIV management is also usually compromised through drug-alcohol interactions, reductions in adherence, and subsequent increased risk of resistance to antiretroviral therapy (Kresina *et al*, 2002). Similarly, there is strong evidence emerging that demonstrate the relationship between Tuberculosis (TB) and alcohol consumption. Imtiaz *et al* (2017) performed a meta-analysis on alcohol consumption as a risk factor for TB and noted that alcohol displays a clear dose-response relationship linked to the risk of developing active TB. A diagnosis of alcohol-use disorder, for example, was linked to a three-fold increased risk of developing active TB. Over and above the mechanism of alcohol-induced immune suppression, alcohol may influence the absorption and metabolism of TB medication (Rehm *et al*, 2009). This, combined with the greater risk of poor adherence, lends itself to the development of drug-resistant TB infection.

On the non-communicable disease front, alcohol is causally related to a multitude of conditions (Parry *et al*, 2011). These include the development of cancers such as breast, colon, rectum, liver, oesophagus, larynx and oropharynx, the development of alcoholic hepatitis, liver cirrhosis, and alcohol-induced liver failure and the development of cardiovascular diseases such as alcoholic cardiomyopathy. Furthermore, many mental health conditions are linked to alcohol use including dependence, depression, delirium, psychosis, and dementia (WHO, 2018). Perhaps the most concerning mental health outcome is the relationship between suicide and intoxication with individuals having a seven-fold increased risk of suicide soon after drinking (Borges *et al*, 2017). This risk increases 37-fold after heavy alcohol use.

Maternal and child health is sadly not spared from the scourge of alcohol use either. There is clear association of alcohol consumption and unprotected sex leading to unintended and delayed recognition of pregnancy (Naimi *et al*, 2003). Fetuses often suffer from prematurity, intrauterine growth retardation (IUGR) and low birth weight (Allebeck and Olsen, 1998). Alcohol exposure during pregnancy is also causally linked to the development of a spectrum of lifelong conditions called Fetal-Alcohol Spectrum Disorder (FASD).

Perhaps the more striking and immediately visible effect of alcohol is its impact on injury and trauma morbidity and mortality. One of the features of this relationship is the importance of the drinking pattern rather than overall consumption (Rehm *et al*, 2003). For chronic diseases, alcohol is harmful due to a cumulative toxic effect, whereas for injury and other acute harms, such as unsafe sex, it is the psychoactive effect of alcohol through heavy episodic or binge drinking that lowers inhibitions, increases aggression and leads to risk-taking behaviour. A recent review of the literature concluded that there is clear evidence “in support of alcohol’s causal and central role in injury” and this

evidence has been strengthened over time (Chikritzhs and Livingston, 2021). Alcohol-related trauma constitutes between 5 and 40% of all injuries to Emergency Departments, as was seen across 27 countries, with young males between the ages of 15-39 contributing approximately 90% of alcohol attributable injury deaths. Injury literature often divides the types of injuries into intentional (e.g. interpersonal violence, self-harm and suicide) and unintentional (e.g. road traffic injuries, falls, drownings, burns, poisonings, workplace injuries and other accidents such as freezing). Unintentional injuries are often subclassified as road traffic injuries or other accidents.

Alcohol has been identified as a clear risk factor of interpersonal violence as it has a direct effect on physical and cognitive functioning leading to reductions in inhibition and judgement (WHO, 2009). Over and above the biological plausibility, there is evidence to suggest that cultural and individual beliefs about alcohol causing aggression can lead to it being used as an excuse to prepare for violent acts. Wilson *et al* (2017) explored this relationship further by performing a grounded theory study and interviewed victims of interpersonal violence. They noted a common 7 stage cycle of drinking and escalated aggression with various levels of intoxication. Three of the stages were noted to be unsafe by the victims including: perpetrators getting drunk and looking for a fight, being intoxicated and "switching" to escalated violence, and being hungover leading to a mean-tempered demeanour. Figure 1 depicts this reported cycle.

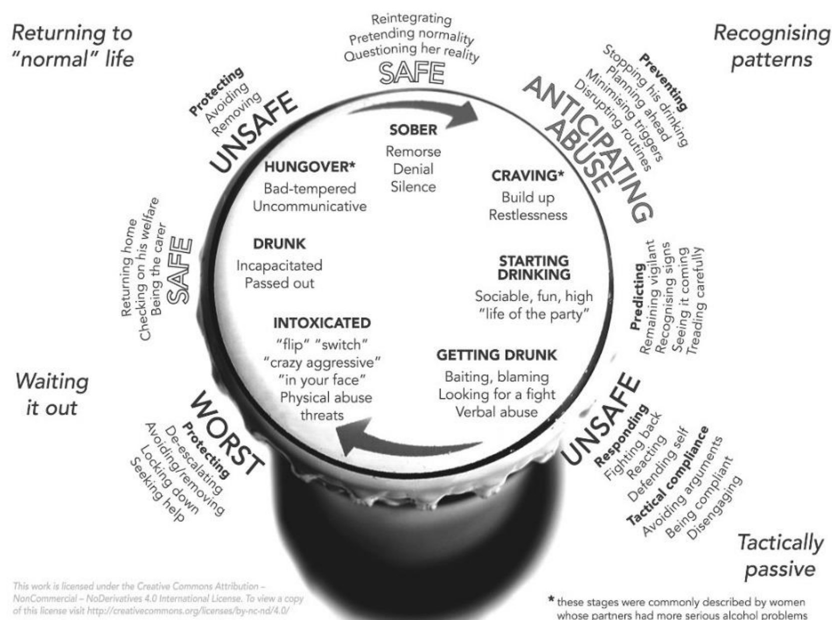

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Figure 1: The cycle of drinking and violence (Wilson et al, 2017)

Cherpitel *et al* (2012) attempted to quantify this attribution of alcohol to violence-related injury by consolidating data from 14 countries around the world, including South Africa. Across all sampled countries, the prevalence of drinking alcohol within 6 hours of the violence-related injury was found to be 62.9%, with the majority believing it to be causal in their injury. This large proportion incorporates both perpetrators, victims or both (perpetrators and victims) that may have been under the influence of alcohol at the time of violence requiring emergency centre admission. This speaks to the multifaceted nature of alcohol's impact directly on those that drink and indirectly on the people around those that drink.

Furthermore, the role of alcohol in relation to gender-based violence (GBV) is well established (Shiva *et al*, 2021). The GENACIS study by Wilsnack (2012) looked at data from 38 countries across 5 continents and concluded that heavier alcohol use showed a strong cross-cultural effect of increased likelihood and severity of interpersonal violence against women. This layer of a gender-based lens is critical as it allows viewing alcohol-related GBV as a tool of control, with economic and financial abuse due to partner drinking and a subsequent burden on families, and an expectation of women to take on caring roles despite being under concomitant threat of violence (Shiva *et al*, 2021).

The evidence above provides a strong basis of biological plausibility, consistency, dose-response relationship, and temporality of effect between alcohol and injury. It is this multifaceted nature of alcohol that supports its strong causal link with alcohol-related violence and injury.

International response and evidence to limit its impact

The WHO Global status report on alcohol and health reflected that strategies to address the impact of alcohol on health need to target multiple levels, components, and determinants such as availability, marketing, and price (WHO, 2018). In 2010 all WHO member states reached consensus on 10 target areas for alcohol policy implementation as well as key components to support these target areas. Over the subsequent years emerging evidence supported the application of these policy options and provided an economic lens to their impact. In May 2017, at the 70th World Health Assembly, the mounting evidence assisted in refining the target areas into stratified "best buys" according to the most cost-effective and feasible interventions. Of note, the three best buys, with an average cost-effectiveness of <$100 per DALY averted in lower-middle income countries, were found to be:

1. Increase prices by, for example, increasing the excise tax on alcoholic beverages
2. Enacting and enforcing restrictions on the physical availability of alcohol (through reduced hours or days of sale)
3. Enacting and enforcing comprehensive exposure to alcohol advertising (across all media types including digital marketing)

Over and above the three "best buys" which focused largely on upstream policy interventions, an additional two, more downstream, interventions were also proposed as effective. They were, though, noted to cost >$100 per DALY averted and included:

4. Enacting drink driving laws (including blood alcohol concentration limits) enforced by sobriety checkpoints
5. Provide and offer brief psychosocial interventions for individuals with a history of harmful and hazardous alcohol use

In 2019, the WHO further solidified these recommendations by launching the SAFER initiative and providing a technical package to support implementation at national and sub-national level (WHO, 2019). SAFER is a mnemonic that encompasses the above recommendations as seen in Figure 2 below:

The SAFER interventions				
STRENGTHEN	**ADVANCE**	**FACILITATE**	**ENFORCE**	**RAISE**
restrictions on alcohol availability	and enforce drink-driving countermeasures	access to screening, brief interventions and treatment	bans or comprehensive restrictions on alcohol advertising, sponsorship and promotion	prices on alcohol through excise taxes and other pricing policies

Figure 2: The SAFER technical package of interventions to reduce alcohol harm at national and sub-national level (WHO, 2019)

Of particular interest is the international evidence supporting the recommendation for restricted availability of alcohol sale. As early as the mid-90's research done in Australia showed that extended trading hours, even by just 1 hour from midnight to 1am resulted in increased assault incidences around the areas where extended hour licenses were given (Chikritzhs and Stockwell, 2002). Similar findings were seen in New Mexico after lifting of a Sunday ban on alcohol sales which amounted to a 42% increase in alcohol-related car crash fatalities (McMillan and Lapham, 2006). In Brazil, in the city of Diadema, a policy was introduced to prohibit on-premise alcohol sales after 11pm which showed an immediate post policy reduction of almost 9 murders per month (Duailibi *et al*, 2007). More recently, Sherk *et al* (2018) performed a systematic review and meta-analysis of availability by retail alcohol sale days and noted that for one additional day of retail sale the per capita consumption of total alcohol increased by 5.3% (95% CI: 3.2, 7.4). The study concluded that the reduction in per capita consumption by limiting days of retail sale would therefore confer public health benefit to all downstream disease burdens. Gruenewald (2011) echoes this sentiment, dismisses the fallacy that there would be displacement of drinking habits to other time periods or days in the week and further supports the WHO's best buys as articulated above.

The South African context of alcohol and injury

On the global stage South Africa emerges as a forerunner and, unfortunately, for the wrong reasons. Even though the majority of South Africans (69%) abstain from alcohol, those that do drink do so heavily (WHO, 2018). The remaining 31%, constituting South Africa's drinking population, consumes 29.9 liters of pure alcohol per year, the sixth highest individual consumption in the world.

This alarming statistic gives credence to the high prevalence of heavy episodic drinking in the South African drinking population (WHO, 2018). Heavy episodic, or binge drinking, is defined as having consumed more than 60g of pure alcohol on one occasion in the preceding 30 days. Considering that a standard drink contains, on average, 8g of pure alcohol (1 unit), this amounts to consuming >7.5 standard drinks on one occasion (Topiwala *et al*, 2017). The prevalence of heavy episodic drinking in the South African drinking population currently stands at 59% across both genders and at >70% in males alone (WHO, 2018). Put another way, almost 1 in 5 people in South Africa (18.3%) are heavy episodic or binge drinkers all of whom are consuming at least 7.5 standard alcoholic drinks at a given time.

Within this context, the legislative and policy landscape of South Africa as it relates to the regulation of alcohol leaves much to be desired. Whilst one third of countries globally have policies in place for regulating days of alcohol sale, and two thirds of countries globally have policies in place for regulating hours of sale, South Africa has limited to no such regulation enforced nationally with much of the responsibility devolved to sub-national/provincial levels with variable implementation and enforcement (WHO, 2018). In addition, South Africa holds no regulation limiting the marketing of alcohol products and, despite having an excise tax in place, recently boasted the cheapest beer in the world at $1.68 (Arney, 2021). When delving into this issue further we see that, whilst the inflation adjusted excise tax increase on cigarettes for the period 1994-2020 increased by >450%, the real excise tax increase on beer was only 70% (Van Walbeek and Chelwa, 2021).

The unhealthy relationship with alcohol and laxity of regulation in South Africa has led to an increasing burden of disease both directly and indirectly related to alcohol as an upstream

determinant. Mabunda *et al* (2008) attempted to quantify this impact on pedestrian vehicle deaths across four cities in South Africa and noted that more than half (58%) of pedestrian deaths tested positive for alcohol at the time of their incident. The Western Cape Injury Mortality Report (2010-2016) also looked at similar metrics and found that amongst pedestrian fatalities, 60% tested positive for alcohol, and amongst all motor vehicle fatalities 48% tested positive for alcohol (Evans *et al*, 2018). Considering the fact that South Africa's road traffic death rate is double the global rate at 39.7 per 100,000 per year, this link starts to make sense (WHO, 2018). Perhaps more concerning was the homicide data emanating from the Western Cape which showed an increasing homicide trend over time (35% increase comparing 2016 to 2010) with these unnatural deaths accounting for 7% of all deaths and 13.5% of years life lost in the province (Davies *et al*, 2019; Evans *et al*, 2018). Furthermore, two thirds of homicides were occurring over weekends with >70% of these homicides over weekends testing positive for alcohol (Evans *et al*, 2018).

Pitpitan *et al* (2013) also explored the intersection between gender-based violence, alcohol use and sexual and HIV risk among women in Cape Town. The authors found that those who consumed more alcohol (quantity and frequency) and who were problematic drinkers were more likely to report being recently abused by their sex partner, experience gender-based violence and engage in risky sexual behaviours. South Africa is also infamous for its burden of Tuberculosis (TB) and Imtiaz *et al* (2017) notes that the country has one of the highest estimated TB incidence rates per 100,000 people attributable to alcohol consumption at ~250 per 100,000 in 2014.

Although steeped in the historical background of an alcohol payment system for farm workers during the Apartheid era, South Africa still struggles with the impact of alcohol on maternal and child health. Fetal Alcohol Spectrum Disorder (FASD) continues to be rife with South Africa having the highest rates in the world. Whilst the global average is 8 per 1000 children born, South Africa is known to have ranges between 29 to 290, with the Western Cape province recently reporting prevalence as high as 196-276 per 1000 children (Adebiyi *et al*, 2019). These overlapping and intersecting burdens of disease had been brewing over time and essentially set the scene before the COVID-19 pandemic in 2020 hit.

Recent emerging evidence within the South African COVID-19 experience as it relates to shifting alcohol regulations

Throughout the COVID-19 pandemic, South Africa implemented several different prohibitions over time on the availability and sale of alcohol products. This was initially premised on the overwhelming resurgence of trauma injury and violence following the lifting of the complete ban in mid-June 2020. What followed was several natural experiments that allowed researchers to investigate the impact on various aspects of the health system and society as a whole.

Barron *et al* (2020) looked at the impact of the 5-week complete alcohol prohibition on mortality due to unnatural causes in South Africa in mid-July 2020. The authors noted a significant reduction of unnatural deaths to the order of 21 per day or a reduction of approximately 740 unnatural deaths averted across the 5-week period. Moultrie *et al* (2021) also looked at excess unnatural deaths across the various regulatory changes and reported compelling evidence in support of restrictions on

sale of alcohol directly, rather than curfew, impacting on the reduction in unnatural deaths seen. This can be seen depicted in Figure 3 and 4 below.

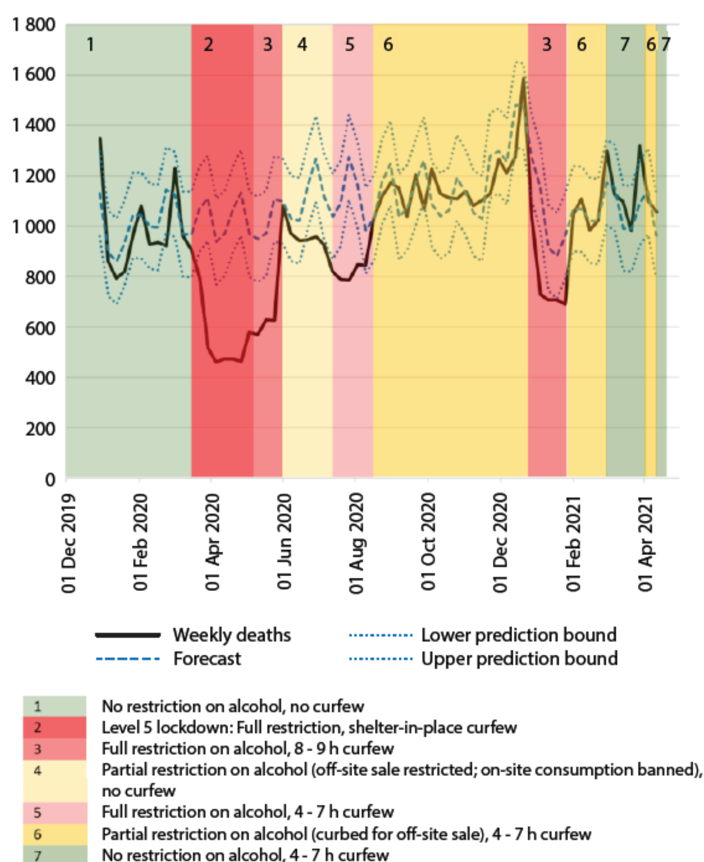

Figure 3: Weekly deaths in South Africa from unnatural causes (29 December 2019 to 17 April 2021) (Moultrie et al, 2021)

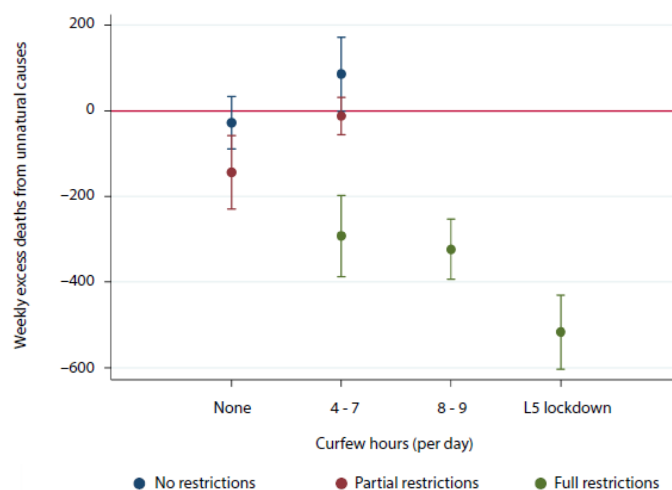

Figure 4: Modelled excess unnatural deaths, by extent of alcohol restriction and curfew duration (Moultrie et al, 2021)

Whilst these analyses provide a rich perspective on the mortality reduction effect of the policy implementation it provides little in the way of understanding the direct effect on the trauma and injury hospitalization burden during the same period. Moreover, they do not consider the effect on different types of injury viz interpersonal violence, road traffic incidents, and self-harm. As a result, several individual hospitals have attempted to analyze and report on this impact. Navsaria *et al* (2021) investigated the impact of the initial and immediate post hard lockdown period in 2020 on the number of patients attending a tertiary urban trauma centre in Cape Town. The authors noted a significant reduction of 53% in total trauma patients during the hard lockdown period. Of note, there were concomitant significant reductions in road traffic accident patients during the hard and immediate post lockdown period. Similar findings were reported by Chu *et al* (2021) based on analysis done at a regional hospital in Cape Town. These authors noted a reduction in stab wounds and trauma admissions during the complete ban periods. Relative to the pre-COVID-19 period the bans saw decreases in the order of 59-69% and relative to the inter-ban period in 2020 saw decreases in the order of 39-46%. Manyoni and Abader (2021) also reported findings from a regional hospital in the Gauteng province, South Africa. Their approach to analysis was slightly different but also noted significant reductions in Emergency Department presentations during the initial hard lockdown (April 2020) in the order of 58% relative to the same period in 2018. Importantly, the proportion of trauma cases dropped from 21% in 2018 to 9% of the total case load in 2020. Lastly,

Shead (2021) looked at blood product usage by trauma areas in a tertiary hospital in Cape Town during the initial hard lockdown period (Figure 5). The author noted a 51% decrease in blood product issuance when comparing the same period in 2020 versus 2018. This translates to a R151,447.10 saving in blood product usage at a single facility.

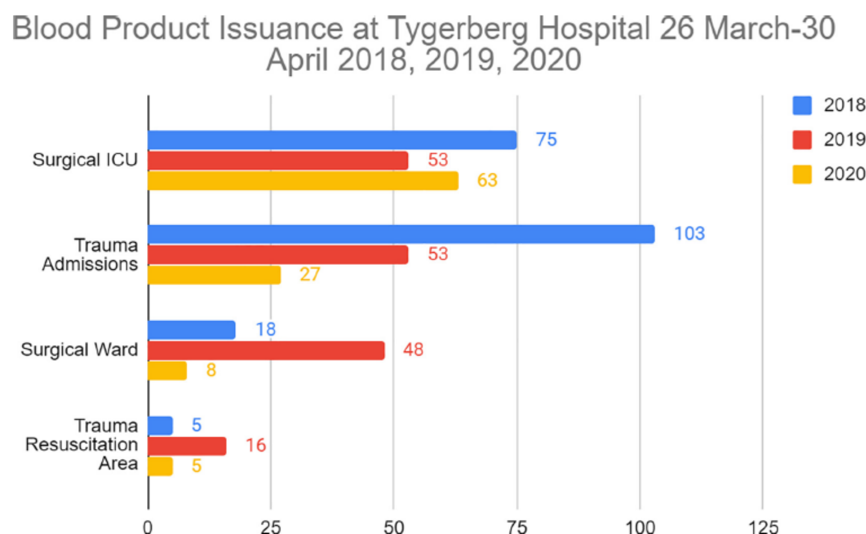

Figure 5: Blood Product Issuance at Tygerberg Hospital 26 March-30 April 2018, 2019, 2020 (Shead, 2021)

Alcohol industry response

The variable changes in alcohol regulation within the Disaster Management Act (DMA) during the COVID-19 pandemic attracted a strong opposing voice from alcohol industry actors (Ngqangashe *et al*, 2021). Several strategies were employed which included framing, lobbying, and on-going litigation or court cases.

Alcohol industry actors, who were largely represented by the top four multi-national corporations viz South African Breweries (SAB), Heineken, Diageo and Distell Group, framed their arguments against the increased regulation with a focus on its impact on the economy, jobs and small business sustainability, instead of their individual company profits (Ngqangashe *et al*, 2021). Furthermore, they repeatedly quoted large financial figures to place emphasis on the economic impact and, for the most part, disregarded the inherent health impact achieved. In April 2021, the industry even went as far as to fund a report that attempted to directly discredit the relationship between alcohol and trauma admissions (Tomlinson, 2021). The authors of the report, who were reportedly independent and had academic statistical backgrounds, framed the report in the grey space between a supposedly peer-reviewed academic paper ladled with scientific jargon and an opinion piece for public consumption. The paper was never published in any reputable scientific peer-reviewed journal and only released as a media statement with some news agencies framing it as undeniable evidence against the alcohol regulations. Tomlinson (2021) comments that this approach is extremely similar to the tobacco industry playbook who delayed tobacco legislation in the 1950's by up to 40 years by sowing seeds of doubt in terms of the evidence around tobacco and lung cancer.

Secondly, the alcohol industry attempted to lobby government by requesting to be a part of the decision-making process, highlighting the economic implications of the regulation, and proposing alternative strategies (Ngqangashe *et al*, 2021). Lobbying saw regular and concerted networking between all alcohol industry role-players and the alternate strategies proposed differed depending on the current state of the regulations – during complete bans, partial restrictions were lobbied, and during partial restrictions self-regulation and individual responsibility were advocated for. This theme of shifting the goalpost to self or deregulation was seen throughout the COVID-19 period.

Lastly, alcohol industry role-players also employed threatened and actual litigation against government in response to the alcohol regulations put in place (Ngqangashe *et al*, 2021). One of the largest of these cases was AB InBev-owned SA Breweries who took the national Minister of Cooperative Governance to the Western Cape High Court to challenge the constitutionality of the alcohol ban. Another court case was the wine producers' body, Vinpro, who challenged the national vs sub-national decision-making function of government as it relates to alcohol regulation. Both these cases were dismissed with the former even requiring SA Breweries to settle the legal costs of the opposing counsel.

Conclusion

There is a strong global movement towards highlighting the harms of alcohol on health and well-being. This is supported by clear, cost-effective upstream policy intervention options as well as downstream individual-based interventions which many WHO-member states have already adopted. South Africa lags significantly behind being plagued by a disadvantaged historical background, a limited impact alcohol regulatory framework to address alcohol-related harms, as well as worsening disease burdens in terms of trauma injury and violence as well as communicable diseases. The COVID-19 pandemic, through the various regulatory changes, allowed for natural experiments to analyze the impact of changing alcohol regulation, despite strong opposition from alcohol industry role-players.

The current mortality studies provided a comprehensive understanding on overall unnatural mortality impact but limited cross-platform understanding on overall or stratified trauma morbidity burden. The current hospital studies, on the other hand, focused on individual isolated hospitals, employed relatively simple analytic techniques, and largely looked at the impact of early lockdown restrictions, which were far more restrictive than only an alcohol ban, and hence may not have adequately accounted for confounding of effects (e.g., curfew times and partial availability). The proposed study, therefore, aims to address these limitations and consider more recent regulatory changes in alcohol availability within the COVID-19 epidemic context in the Western Cape, South Africa.

Aims and Objectives

Primary Aim:

- To analyse the impact of changing alcohol regulations (full availability, partial availability and a complete ban of alcohol sales), across three transitional time periods, on trauma injury presentations to Emergency Centres

Objectives:

1) Describe the alcohol regulatory changes across the three transitional time periods
2) Describe the demographic profile of the patient population experiencing trauma injury grouped by pre- and post-alcohol policy interventions
3) Describe the association between alcohol regulatory changes, across the three transitional time periods, on trauma injury presentations to Emergency Centres
4) Review the impact adjusting for length of curfew, and weekend variability
5) Stratify the interrupted time series analyses by the following subgroups: age category, gender, and type of trauma injury presentation

Methodology

Setting

The proposed study will be performed using secondary data collected during the COVID-19 pandemic from public sector Emergency Centres in the Western Cape province, South Africa. The Western Cape province is reported to have a total of 7.1 million people (StatsSA, 2021). Of this total, 74.9% is reported to be dependent on the public health sector (Day *et al*, 2020). Whilst the Western Cape is lauded as one of the wealthier provinces it sadly suffers from one of the highest population economic inequality indicators with a Gini coefficient >0.5 (Davies *et al*, 2019). Over and above that, the most recent Burden of Disease report for the province (2019) showed that 'intentional injuries' was ranked number 1 across all disease burdens in terms of years of life lost in men. Furthermore, approximately 45% of all homicide victims in the Western Cape tested positive for alcohol with a blood alcohol concentration (BAC) >0.05g/100ml.

During the COVID-19 pandemic the country adopted several stringent legislative responses to curb viral transmission as well as increase the health system's preparedness to respond to the additional burden (Banerjee *et al*, 2020). These restrictions took the form of various lockdown levels that variably restricted movement, restricted gatherings, enforced mask wearing and, importantly, restricted the sale of retail and offsite alcohol products. The key intervention for the proposed study, therefore, relates to the immediate and repeated implementation of national policy to reduce the availability of alcohol sales within the bounds of South Africa's Disaster Management Act (DMA) in the context of the COVID-19 pandemic. The presence of well-defined and adequately communicated public health policy implementation allowed for the development of a real world 'natural experiment' with clear pre- and post-intervention periods. These shifts in the regulatory framework of the country were clearly defined in government gazettes and, on each shift, was publicly announced by the president of South Africa.

Study Population and location of research

The target population proposed for this study would be all adult patients (>18 years) presenting to a public sector Emergency Centre with trauma injury on triage or final ICD-10 code in the Western

Cape, South Africa in facilities involved in routine real time electronic capture of Emergency Centre visits. The time period would be 1st January 2020 to 31st August 2021.

Study Design

The study will employ an interrupted time series design. The decision to utilize this design type is largely based on three main factors (Bernal *et al*, 2017) viz the nature of the intervention being a sudden institution of national policy, the proposed outcome being acute trauma presentations to Emergency Centres and the availability of the data using a routine public sector information system.

Since the study design is a quasi-experimental design, a segmented regression will be developed with the level and slope of the model in the pre-intervention period being used as the counterfactual against the observed actual post-intervention level and slope of the model.

Research procedures and data collection methods

Collection and sources of data

The availability of complete and quality data is an important requirement when it comes to adequate application of interrupted time series design. Fortunately, several emergency centres in the Western Cape province, South Africa have adopted a standard tool for real time capture of all Emergency Centre visits. This routinely collected secondary data, across multiple facilities, allows for a significant amount of data points per unit time within the pre- and post-intervention periods.

The routine information system for Emergency Centre (EC) visits in the Western Cape is known as HECTIS, or Hospital and Emergency Centre Tracking Information System. Patients who present to facilities with the application installed get captured and timestamped on arrival by an admission clerk, subsequently triaged and assessed for history or signs of trauma injury by a triage nurse and then lastly consulted by an attending emergency medicine clinician to be diagnosed by ICD-10 code. All steps in the process are captured in real time by all those involved in the care of the patient. In 2020, a total of 4 facilities across the province (1 tertiary level hospital EC, 2 district level hospital EC's and 1 regional hospital EC) leveraged the application. In 2021, the number of facilities utilizing the application rapidly increased to 17 sites across the province. Depending on the time period under review, the relevant number of sites will be included in the pre- and post-intervention analysis. Addendum D summarizes the facilities included as well as the time when they came online.

Regulatory Changes, including curfew times, would exist at an ecological policy level and will be drawn from formally published national Government Gazettes.

Sampling and Power

Hawley *et al* (2019) noted that, despite interrupted time series analysis being increasingly used in epidemiological research, there is paucity of guidance when it comes to relevant power and sample size calculations. The authors, therefore, proposed a number of scenarios to guide sample size considerations in ordinary least squares (OLS) interrupted time series analysis to ensure adequate power. Importantly, the sample size per time point conferred the greatest impact on adequacy of power, even if the intervention effect was moderate and the number of time points were limited to 12 pre- and post-intervention. This can be seen depicted in Figure 6 and 7 below.

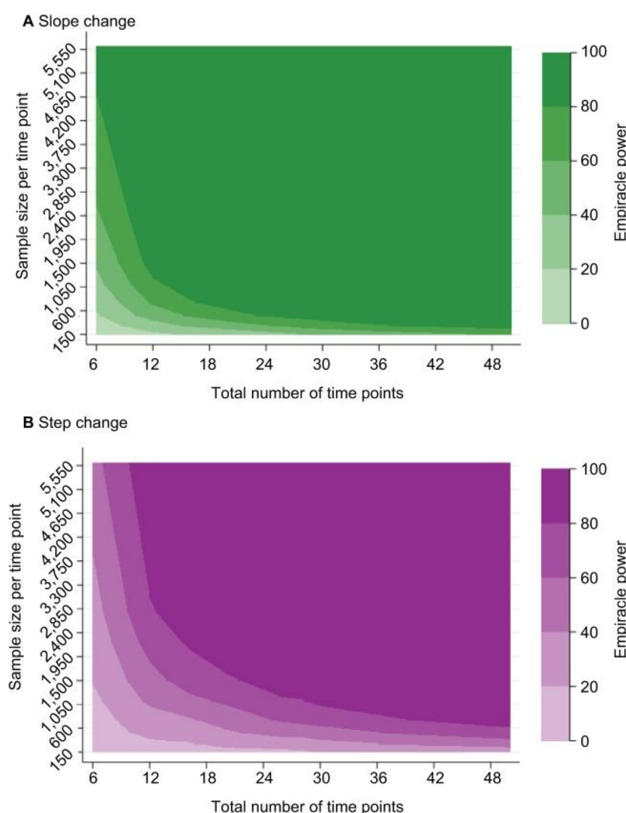

Figure 6: Empirical power to detect a relative reduction in outcome of 34% (Hawley et al, 2019)

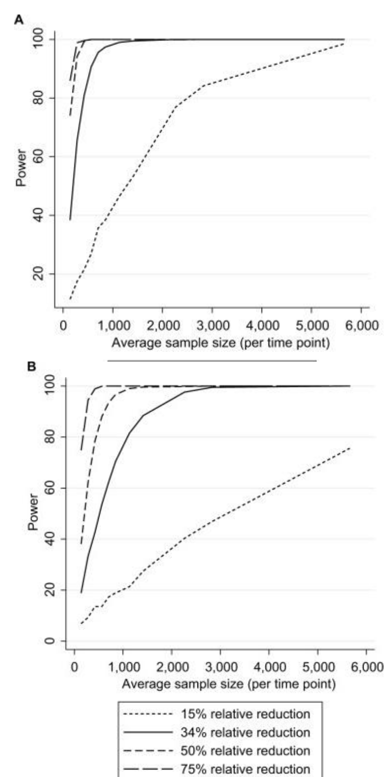

*Figure 7: Empirical power stratified by intervention effect size resulting in a slope change (A) or step change (B) (Hawley et al, 2019)**

*Note: Both graphs in Figure 7 assume a total of 28 time points (i.e. 14 days pre- and post-intervention)

Inclusion and Exclusion criteria

Participants to be included will be all patients that have attended a public sector Emergency Centre during the period under review and presented for a trauma related injury. Exclusion criteria would be facilities that have not fully adopted the routine Emergency Centre information system (including private facilities) as well as patients that had presented to the Emergency Centre for a condition other than trauma (e.g. a medical condition only).

Variables

Outcome:

The natural history of trauma injury morbidity usually involves an acute presentation to an Emergency Centre. The proposed outcome variable of trauma injury presentations, therefore, provides a clear short-term, sensitive indicator of the potential impact of the instituted alcohol policy changes.

Exposure:

The key exposure variable or intervention in this study will be the three transitional policy time periods. The exposure periods under review would be:

1.) Full availability of alcohol sales to partial availability in retail alcohol sales restricted to Monday-Thursday (16/06/2021)

2.) Partial availability in retail alcohol sales, restricted to Monday-Thursday, to a complete ban in alcohol sales (12/07/2020)
3.) Partial availability in retail alcohol sales, restricted to Monday-Thursday, to partial availability in alcohol sales, restricted to Monday-Friday (13/09/2021)

This can be summarized in Figure 8 below:

Figure 8: Alcohol Policy Intervention Period Transitions

Covariates:
The following covariates will be considered in order to adjust for any potential confounding as well as to assess for effect modification:

- Length of curfew (hours) as stipulated in the national government gazettes
- Weekend variability (weekday vs weekend)
- Age category
- Gender (male vs female)
- Type of trauma injury presentation (interpersonal violence, road traffic incident, accidental, etc)

Data Analysis

The primary outcome would be the relative percent increase or decrease of trauma injury presentations to Emergency Centres in the Western Cape in response to changes in the regulatory framework for alcohol sale.

Bernal *et al* (2017) suggests proposing an a priori hypothesis of what the impact would be should the intervention be effective. These may take the form of level changes, slope/gradient/trend changes and gradual/lag effects of the intervention as can be seen by figure 9 below.

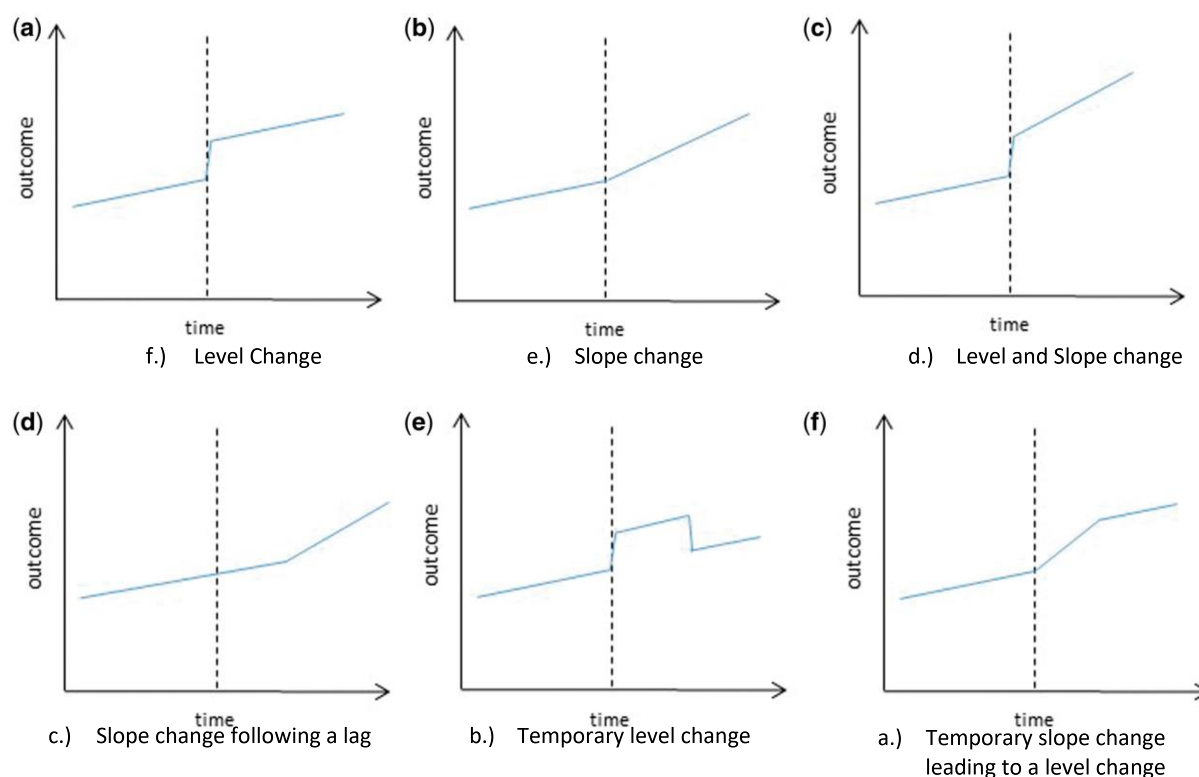

Figure 9: Possible impact models of the ITS study design (Bernal et al, 2017)

Should the alcohol policy interventions be effective the a priori hypothesis for the three periods may perform as follows:

Table 1: Proposed impact models/a priori hypothesis for each time period transition

Policy transition period	Proposed impact model/ a priori hypothesis	Rationale for hypothesis
Full availability of alcohol sales to a partial availability in alcohol sales, retail sales restricted to Monday-Thursdays (16/06/2021)	Level change (with or without a gradient change)	The rationale for this hypothesis is premised on the understanding that the partial ban essentially removed 4 days of alcohol buying opportunities. It is also a significant contextual shift considering the baseline full availability.
Partial availability of alcohol sales to a complete ban in alcohol sales (12/07/2020)	Level change (with or without a gradient change)	This is proposed as a complete ban in alcohol sales may potentially result in minimal to no alcohol-related trauma with both retail and on-site sale being restricted.

Partial availability in retail alcohol sales, restricted to Monday-Thursday, to partial availability in retail alcohol sales, restricted to Monday-Friday (13/09/2021)	Slope change (possibly temporary leading to a level change)	This may be due to a slight and slow increase in alcohol-related trauma with increased access to retail alcohol closer to the weekend period.

Secondary outcomes will review the impact of the policy implementation by adjusting for length of curfew and weekend variability. Furthermore, sub-group analysis will be performed on the regression model to review the impact of age category, gender and type of trauma injury presentation.

Objective 1 will be achieved by a descriptive review of all government gazettes to ascertain the regulatory changes across the three periods identified for the analysis.

To address objective 2, we will describe and compare the study populations in terms of demographic and clinical characteristics between the pre- and post-interventions periods (age, gender, trauma classification recorded). These will be set out in tables and basic statistical analyses applied. This will include chi squared tests for categorical data and t test or Wilcoxon rank sum test for continuous data (should age be used as a continuous variable). Basic scatter plots of the periods under review will also be produced to identify outliers and underlying trends (Bernal *et al*, 2017).

Standard interrupted time series will be employed utilizing a segmented regression model to address objective 3 as follows (Bernal *et al*, 2017):

$$Y_t=\beta_0 +\beta_1 T+\beta_2 X_t + \beta_3 TX_t$$

Where T equates to the time since the start of the period, in our case presented in days, Xt equates to a dummy variable (0,1) representing the pre- and post-intervention period and Yt equates to the outcome, number of trauma injury presentations, at a particular point in time.

The above will provide the basic interrupted time series analysis but won't be able to account for potential confounders. For this reason, the model above will be assessed for objective 4 in terms of seasonal variability (e.g. weekends vs weekdays) and time-varying confounders (e.g. length of curfew).

Thereafter, model-checking will be employed to assess for any residual autocorrelation and sensitivity analysis will be conducted to test for variability in the assumptions initially employed.

The above basic model will also be assessed through individual subgroup analysis for age category, gender and type of trauma injury presentation in order to adequately address objective 5.

Data Safety and Monitoring

All data collected will be de-identified so as to ensure and maintain confidentiality of all personally identifiable patient-level information. This will ensure respect to patient privacy as this data is not needed to achieve the aims and objectives of the study. All de-identified research data will be stored

in a secure, password-protected cloud storage database for the period of the study, will only be accessible to the researchers involved in the study and will be archived and disposed of according to PAIA and POPI regulations within 6 years.

Ethical considerations

Since the study is retrospective in nature and leverages routinely collected data there will be no active or prospective intervention to human subjects. Data will be collected directly from the routine information system's database for the period under review with variables per Addendum A. Routinely collected data will include demographic (age, gender), trauma triage classification, ICD-10 of Final Diagnosis and Date and Time. All secondary analysis will employ de-identified data.

A request for waiver of consent will be submitted along with this protocol. The study will utilize routinely collected secondary data on an anonymized sample population. It will, therefore, not be feasible to contact participants whose data was collected as part of routine care between 1-2 years ago. Some may even be deceased, may no longer live in the province or we do not have adequate contact details for them. Furthermore, the study will involve minimal to no risk to the participants with no direct patient involvement or exposure of the data collectors, will not adversely affect the rights and welfare of the subjects and may justifiably tilt the scales in favour of beneficence hence there is a basis for waiver of the informed consent process.

Risks and Benefits

The proposed methodological approach confers minimal risk to the end-user since it leverages secondary data collected through a routine health information system. No identifiable information except for age and gender will be captured against the participant, therefore the risk of a breach in confidentiality is largely limited.

Conversely, the potential for benefits in terms of scientific value and policy guidance at both provincial and national level would be considerable. The benefit of clear evidence validating or invalidating the approach of restricted availability through partial or complete bans may be able to inform policy decisions for response to sustainable policy considerations in terms of the former approach and national emergencies in terms of the latter approach.

Communication of findings

The findings will be shared with all key stakeholders involved in policy formulation, review and adjudication of the alcohol regulatory framework, will be reported in an accredited peer reviewed journal and presented in forums as seen appropriate. Adequate feedback will also be given to all levels of government, academic forums and public health advocacy structures through presentations and engagement.

Budget

Financial resources will not be required for the review and analysis of the research. Instead, staff time in terms of those employed by academic institutions within the Western Cape and staff employed by the Western Cape Department of Health will be required for the analysis and write-up of the findings emanating from the analysis.

Conclusion

The need for research into the effectiveness of alcohol regulations serves as an important tool to guide policy decisions at a national and sub-national level. The current COVID-19 context has provided a window of opportunity to analyse the potential impact of implementing a WHO Best Buy in terms of the physical availability of alcohol. Ensuring an evidence-based strategy, that leverages local and international research, to address the impact of alcohol-related diseases on our health system will stand us in good stead, both during the COVID-19 pandemic and, perhaps more importantly, beyond.

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Addendum A: Data Elements

1.) **HECTIS**
    a. Type of Data:
        i. Individualized
    b. Data Elements:
        i. Demographic: Age, Gender
        ii. Trauma Triage Classification
        iii. ICD-10 Code of Final Diagnosis
        iv. Date and Time
        v. Weekend vs Weekday
2.) **Government Gazettes**
    a. Type of Data:
        i. Ecological Policy Level
    b. Level:
        i. National
    c. Data Elements:
        i. Lockdown Level
        ii. Period (Start Date – End Date)
        iii. Alcohol Regulation:
            1. Complete Alcohol Sales Ban
            2. Partial Alcohol Sales Allowed
        iv. Retail/Off-site Alcohol Sale
            1. Prohibited (nil availability)
            2. Allowed Mon-Thurs (09:00-17:00) excluding Friday, Sat, Sun and Public Holidays (partial availability)
            3. Allowed Mon-Fri (09:00-17:00) excluding Sat, Sun and Public Holidays (partial availability)
            4. No prohibition on retail Alcohol Sale (full availability)
        v. Licensed/On-site Alcohol Sale
            1. Prohibited
            2. Permitted
        vi. Curfew Regulation:
            1. Number of hours of curfew

Addendum B: Periods of National Regulatory Changes

The following provides an overview of periods of changes in national regulations. Green highlighted rows indicate transition periods to be included in the analysis.

Start Date	End Date	Lockdown Level	Lockdown Level	Start Date	End Date	Alcohol Regulation Change
		→	→			
27/03/2020	30/04/2020	Level 5	Level 4	1/05/2020	31/05/2020	Complete ban
1/05/2020	31/05/2020	Level 4	Level 3 (Part A)	1/06/2020	11/07/2020	Complete to Partial
1/06/2020	**11/07/2020**	**Level 3 (Part A)**	**Level 3 (Part B)**	**12/07/2020**	**30/07/2020**	**Partial (Mon-Thurs) to Complete**
12/07/2020	**30/07/2020**	**Level 3 (Part B)**	**Level 3 (Part B) Amended**	**31/07/2020**	**17/08/2020**	**Curfew change within a complete ban**
31/07/2020	**17/08/2020**	**Level 3 (Part B) Amended**	**Level 2**	**18/08/2020**	**20/09/2020**	**Complete to Partial (no change in curfew, Mon-Thurs)**
18/08/2020	20/09/2020	Level 2	Level 1	21/09/2020	28/12/2020	Curfew extended from 22:00 to 00:00 and Partial changes from Mon-Thurs to Mon-Fri
21/09/2020	28/12/2020	Level 1	Adjusted Level 3	29/12/2020	28/02/2021	Partial to Complete *Public Holidays and NYE
29/12/2020	28/02/2021	Adjusted Level 3	Adjusted Level 1	1/03/2021	01/04/2021	Partial to Full
1/03/2021	01/04/2021	Adjusted Level 1	Adjusted Level 1 (Easter weekend retail ban)	02/04/2021	05/05/2021	
02/04/2021	05/05/2021	Adjusted Level 1 (Easter weekend retail ban)	Adjusted Level 1	06/05/2021	30/05/2021	
06/05/2021	30/05/2021	Adjusted Level 1	Alert Level 2	31/05/2021	15/06/2021	Curfew change only
31/05/2021	**15/06/2021**	**Alert Level 2**	**Adjusted Alert Level 3**	**16/06/2021**	**27/06/2021**	**Full to Partial**
16/06/2021	27/06/2021	Adjusted Alert Level 3	Adjusted Alert Level 4	28/06/2021	25/07/2021	Partial to Complete
28/06/2021	**25/07/2021**	**Adjusted Alert Level 4**	**Adjusted Alert Level 3**	**26/07/2021**	**12/09/2021**	**Complete to Partial Ban (Mon-Thurs)**
26/07/2021	**12/09/2021**	**Adjusted Alert Level 3**	**Adjusted Alert Level 2**	**13/09/2021**	**30/09/2021**	**Partial Ban (Mon-Thurs) to Partial Ban (Mon-Fri)**

Addendum C: Facilities with the HECTIS application installed

The following provides an overview of all facilities in the Western Cape currently involved in routine collection of Emergency Centre data through the use of the HECTIS application, as well as when the relevant facility came online with reliable capturing of the facility's data.

Facility	Start Date
Mitchells Plain Hospital	Monday, November 07, 2016
Heideveld Emergency Centre	Friday, March 31, 2017
George Hospital	Tuesday, October 17, 2017
Groote Schuur Hospital	Saturday, July 07, 2018
Tygerberg Hospital	Tuesday, October 23, 2018
Khayelitsha Hospital	Monday, August 31, 2020
Wesfleur Hospital	Tuesday, November 10, 2020
Mitchells Plain CHC EC	Friday, November 27, 2020
Khayelitsha Site B CHC	Tuesday, December 15, 2020
Hanover Park CHC	Friday, December 25, 2020
Du Noon Clinic	Monday, January 11, 2021
Karl Bremer Hospital	Monday, February 08, 2021
False Bay Hospital	Wednesday, February 10, 2021
Victoria Hospital	Tuesday, February 23, 2021
Elsies River CHC	Thursday, March 04, 2021
Eerste River Hospital	Thursday, March 11, 2021

Chapter 2: Publication-ready Manuscript (for submission to Lancet Public Health)

My name is South Africa and I have a drinking a problem: a multicentre quasi-experimental analysis on alcohol regulation and injury presentations to emergency centres

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Abstract

Background

The South African COVID-19 experience included several national regulatory changes to manage the additional demand placed on the healthcare platform. Since alcohol-related injury contributes a significant acute healthcare burden in South Africa, regulations to limit alcohol availability were also instituted. In this study we aimed to determine the impact of changing alcohol regulations (full availability, partial availability, and a complete ban on alcohol sales), across three time periods, on injury presentations to emergency centres in the Western Cape, South Africa using a quasi-experimental interrupted time series (ITS) design.

Methods

The study population included all patients who presented to a public sector emergency centre in the Western Cape with injury identified by a trained nurse on triage and identified by an emergency centre clinician by final ICD-10 code in facilities using routine real time electronic capture of emergency centre visits. Since the study design was a quasi-experimental ITS, we used an autoregressive integrated moving average (ARIMA) model with the level and slope of the model in the pre-intervention period being the counterfactual against the observed actual post-intervention level and slope. The primary outcome was the relative percent increase or decrease in the level and slope of injury presentations.

Findings

A total of 31,151 injury patients across the three periods were included in the analyses. A shift from full availability to partial (Monday to Thursday) retail alcohol availability resulted in an overall step reduction in daily injury presentations of 29·0% (absolute reduction [95% CI]: -71·7 [-102·9, -40·4]). A shift from partial to a complete ban resulted in a further step reduction of 26·2% in daily injury presentations (absolute reduction [95% CI]: -4·5 [20·6, -8·4]). This impact was consistent in terms of direction but ranged in magnitude across various sub-populations.

Interpretation

Our findings reflect the considerable impact of alcohol regulation on injury presentations to emergency centres. Partial retail alcohol restrictions, particularly in the South African context, could be considered for longer term, sustainable alcohol regulation policies to reduce the considerable burden of injuries on health services and society.

Funding

None

Introduction

More than two thirds of South Africans (69%) abstain from alcohol, but those that do drink do so heavily, consuming 29·9 litres of pure alcohol per year, the sixth highest individual consumption in the world.[1] Among South African drinkers, 59% are heavy episodic drinkers.[1] While one third of countries globally regulate days of alcohol sale, and two thirds of countries globally regulate hours of sale, South Africa has limited regulation enforced nationally with much of the responsibility devolved to sub-national/provincial levels with variable implementation and enforcement.[1] In addition, alcohol marketing is not subject to government oversight in South Africa[1] and, despite having an excise tax in place, in 2021 boasted the cheapest beer in the world at an average price of $1·68 per 330ml bottle ($5·09 per liter).[2]

The harmful drinking pattern and laxity of regulation in South Africa has led to a substantial burden of disease with alcohol as a key direct or indirect upstream determinant.[3] With respect to violence and injury, two thirds of homicides reported in South Africa's Western Cape province from 2010 to 2016 occurred over weekends with >70% of these weekend homicide victims testing positive for alcohol.[4] Furthermore, research has shown a strong nexus between heavy episodic drinking and gender-based violence, HIV and TB risk as well as maternal-foetal health (e.g. Foetal Alcohol Spectrum Disorder) in South Africa.[5–8]

Throughout the COVID-19 pandemic, South Africa implemented several different prohibitions on the availability and sale of alcohol products. These restrictions were premised on the empiric understanding that there is a close relationship between alcohol use and health service demand. This was reinforced with the overwhelming resurgence of injury and violence following the end of the complete alcohol ban mid-June 2020. These restrictions effectively created "natural experiments" that allowed researchers to investigate the impact of differing alcohol availability and sale restrictions on various aspects of the health system and society. Barron *et al.* (2020) and Moultrie *et al.* (2021) both reported reductions in unnatural deaths during alcohol ban periods. Several individual hospitals corroborated this experience of the reduction on injury presentations but were limited in their ability to provide a cross-platform understanding on overall or stratified injury morbidity burden.[11–13]

We aimed to determine the impact of changing alcohol regulations (full availability, partial availability, and a complete ban on alcohol sales), on injury presentations to emergency centres (ECs) in the Western Cape overall and in different subgroups (gender, age, and type of injury), across three time periods when alcohol regulations changed, using a quasi-experimental interrupted time series design.

Methods

Study design

We conducted an interrupted time series analysis of trauma presentations to emergency centres with the study period from 1 June 2020 to 30 September 2021. The key interventions that acted as the interruptions were the abruptly implemented national policies to change the availability of alcohol within the bounds of South Africa's Disaster Management Act (DMA) in the context of the COVID-19 pandemic. The decision to utilize an interrupted time series design was based on three main factors as follows:[14] the sudden nature of the intervention with national policies requiring immediate implementation, acute trauma presentations to emergency centres as the proposed outcome, and the availability of data from a routine public sector information system. Since the study design was quasi-experimental, we used an autoregressive integrated moving average (ARIMA) model with the level and slope of the model in the pre-intervention period as the counterfactual against the observed actual post-intervention level and slope.

Setting and study participants

The Western Cape has a population of 7·2 million, with 75% dependent on the public health sector.[15,16] While it is one of the wealthier provinces it suffers from high economic inequality with a Gini coefficient >0·5.[17] In 2016, intentional injuries were noted to be the leading cause of years of life lost in males in the province.[18] Furthermore, research has shown that, from 2010 to 2016, approximately 45% of all homicide victims in the Western Cape had a blood alcohol concentration (BAC) >0·05g/100ml.[4]

The study population were all patients who presented to a public sector EC in the Western Cape with injury identified by a trained nurse on triage and confirmed by an EC clinician by final ICD-10 code in facilities using routine real time electronic capture of EC visits.

Data sources and disease definitions

In 2020, four facilities across the province (one tertiary level hospital EC, one regional level hospital EC, and two district level hospital ECs) leveraged the electronic EC information system. This increased to 23 facilities across the province by the end of 2021. Depending on the period under review, only sites using the application both before and after the intervention were included in the interruption analysis. Policy regulatory changes, reflecting the interruption, were drawn from formally published national Government Gazettes and, on the day of each shift, were publicly announced by the South African president.

Complete and correct data are required for adequate application of an interrupted time series design. The real time routinely collected emergency centre data, across 23 facilities, allowed for several data points per unit time within the pre- and post-intervention periods. Patients who presented to facilities with the application installed were captured and timestamped on arrival by an admission clerk, subsequently triaged and assessed for history or signs of injury by a triage nurse and then, lastly, consulted by an attending emergency medicine clinician to be diagnosed and assigned an ICD-10 code. Interpersonal violence was further classified from history or signs of a stab, gunshot, or blunt trauma injury at triage presentation. All steps in the process were captured in real time by admin clerks, nurses, and clinicians in the patient's care. The application of two independent healthcare practitioners' assessments, conferred strong internal validity for the diagnosis.

Procedures

Variables were classified according to their role as either outcome, exposure, or covariates within the ARIMA ITS model. The primary outcome variable was the number of acute injury presentations presenting to an emergency centre. This provided a clear short-term, sensitive indicator of the immediate impact of the instituted alcohol policy changes.

The key exposure variables in this study were three transitional policy time periods (Table 1). Period 1, which occurred from 1 June 2020 to 17 August 2020 (11 weeks), explored the impact of shifting from partial retail alcohol availability restrictions (Monday-Thursday: 09:00-17:00) to a complete retail alcohol ban. Importantly, there was no change in regulation for on-site consumption as a complete on-site ban was instituted throughout the entire period. Period 2, which occurred from 31 May 2021 to 27 June 2021 (4 weeks), explored the impact of shifting from full retail availability to partial retail regulations (Monday-Thursday: 10:00-18:00), with, once again, minimal change to onsite consumption regulations. Both period 1 and 2, therefore, measured the effect of imposing stronger restrictions specifically on retail alcohol availability. Period 3 (26 July 2021 to 30 September 2021; 9·5 weeks), on the other hand, looked at the effect of relaxing restrictions by including a shift in regulation from partial retail availability (Monday-Thursday: 10:00-18:00) to an amended partial retail availability (Monday-Friday: 10:00-18:00). The addition of a single day of retail trade also occurred in the context of an additional two hours in on-site consumption per day.

The following covariates were drawn directly from the information system source and included in the analyses: gender defined as male or female; age category defined as children and adolescents (<17 years), young adults (18-39 years), and older adults (>40 years); and type of trauma injury presentation on triage as defined as interpersonal violence (e.g., stab, gun shot, or blunt trauma injury), road traffic incidents (pedestrian or motor vehicle), reported self-harm and non-traffic related accidental injuries (e.g. falls, burns, unspecified mechanisms of injury). Both weekend and end-of-month variability were accounted for by the seasonal component of the ARIMA model.

Table 1: Overview of South African Alcohol Sale Regulations 2020-2021

Year	Dates	Lockdown Level	Regulations for off-site (retail) alcohol consumption	Regulations for on-site alcohol consumption	Period under analysis
2020	01/01/2020 – 18/03/2020	Pre-Lockdown Level	Normal	Normal	
	19/03/2020 – 26/03/2020	Pre-Lockdown Level	Mon-Fri: 09:00-18:00 Sat-Sun: 09:00-13:00	Mon-Fri: 09:00-18:00 Sat-Sun: 09:00-13:00	
	27/03/2020 – 30/04/2020	Level 5 (Hard Lockdown)	Complete ban	Complete ban	
	01/05/2020 – 01/05/2020	Level 4 (Hard Lockdown)	Complete ban	Complete ban	
	01/06/2020 – 12/07/2020	Level 3 (Part A)	Mon-Thurs: 09:00-17:00	Complete ban	**Period 1:** Partial retail availability to complete retail ban (complete ban on on-site throughout)
	13/07/2020 – 30/07/2020	Level 3 (Part B)	Complete ban	Complete ban	
	31/07/2020 – 17/08/2020	Level 3 (Part B) Curfew Amended	Complete ban	Complete ban	
	18/08/2020 – 20/09/2020	Level 2	Mon-Thurs: 09:00-17:00	Normal	
	21/09/2020 – 28/12/2020	Level 1	Mon-Fri: 09:00-17:00	Normal	
2021	29/12/2020 – 01/02/2021	Adjusted Level 3	Complete ban	Complete ban	
	02/02/2021 – 28/02/2021	Adjusted Level 3	Mon-Thurs: 10:00-18:00	Mon-Sun: 10:00-22:00	
	01/03/2021 – 01/04/2021	Adjusted Level 1	Normal	Normal	
	02/04/2021 – 05/05/2021	Adjusted Level 1 (Easter weekend retail ban)	Complete ban	Normal	
	06/05/2021 – 30/05/2021	Adjusted Level 1	Normal	Normal	
	31/05/2021 – 15/06/2021	Alert Level 2	Normal	Normal (restaurants/ bars to close at 22:00)	**Period 2:** Full retail availability to partial retail availability
	16/06/2021 – 27/06/2021	Adjusted Alert Level 3	Mon-Thurs: 10:00-18:00	Normal (restaurants/ bars to close at 21:00)	
	28/06/2021 – 25/07/2021	Adjusted Alert Level 4	Complete ban	Complete ban	
	26/07/2021 – 12/09/2021	Adjusted Alert Level 3	Mon-Thurs: 10:00-18:00	Mon-Sun: Till 20:00	**Period 3:** Partial retail availability (Mon-Thurs) to partial retail availability (Mon-Fri)
	13/09/2021 – 30/09/2021	Adjusted Alert Level 2	Mon-Fri: 10:00-18:00	Mon-Sun: Till 22:00	
	01/10/2021 – 31/12/2021	Adjusted Alert Level 1	Normal	Normal	

Abbreviations: Mon, Monday; Thurs, Thursday; Fri, Friday; Sat, Saturday; Sun, Sunday

Outcomes

The primary outcomes were the relative percent increase or decrease in the immediate level of injury presentations (S, T, and V to Z ICD-10 codes) as well as the gradual slope/gradient change of injury presentations following the regulatory change to alcohol sales. Each transitional time period was divided into a pre- and post-intervention period with the date of policy implementation being the level exposure variable, and the number of days from the policy implementation date being the slope exposure variable. Secondary outcomes reviewed the impact of the transitional periods stratified by sex, age, and specific subgroups namely females who experienced interpersonal violence, young adult males who experienced interpersonal violence, and non-traffic related accidents only.

Statistical analysis

We tabulated key demographic characteristics in each of the alcohol regulatory transition periods according to pre- and post-intervention groups. We then applied an interrupted time series analysis using an autoregressive integrated moving average (ARIMA) model approach for evaluating large-scale health interventions.[19] In contrast to more common segmented regression which does not account for seasonality or autocorrelation (or non-independence), ARIMA models combine three components: an autoregressive (AR) model, a Moving Average (MA) model, and an Integration (or Differencing) term. The AR component addresses the intrinsic issue with time series data where serial data points are correlated. This results in non-independent data so segmented linear regression is a challenge to apply. The MA component also addresses non-independence, but specifically does so for autocorrelation of the error terms. The Integration term addresses non-stationarity (where there is not a constant mean, variance, and covariance) by introducing a differencing (or integration) term. ARIMA models also account for seasonality by considering the amount of autocorrelation at the seasonal difference i.e., seasonal lags of 4, 12 and of 365 for quarterly, monthly, and daily data respectively.

ARIMA models were fitted for each of the overall periods as well as each of the subgroups. Fitting involved plotting the data to understand any obvious trends, seasonality or outliers, transforming the data as required, and selecting the values for the ARIMA model through either assessment of autocorrelation and partial autocorrelation function (ACF/PACF) plots

or running multiple models to obtain the lowest value for the Akaike information criterion (AIC) or Bayesian information criterion (BIC). Goodness of fit and sensitivity analyses were done through an iterative process and an assessment of residuals once the model was run. This included a p-value for the Ljung-Box test for signs of autocorrelation with a $p>0{\cdot}05$ depicting a well-fitted model.

ARIMA models for interrupted time series analyses assess intervention effects through step changes (sudden and sustained change in level in the post-intervention period vs the pre-intervention period) and ramp changes (change in slope in the post-intervention period vs the pre-intervention period).[19] We assessed step changes as a percent increase or decrease relative to the model intercept by incorporating a binary variable (0,1) indicating the pre- or post-intervention periods and ramp changes as daily percent increase or decrease relative to the intercept by incorporating a consistently increasing numeric variable (starting at one) at the start of the post-intervention period.

Pre-intervention period data was used to forecast the counterfactual in the absence of the intervention. This counterfactual used the ARIMA model fitted for the respective pre-intervention period and assisted in visualizing the impact of the counterfactual relative to the actual data reported.

Role of the funding source and ethical approval

There were no funding sources for this study. The corresponding author had full access to the data utilized in the study and took final responsibility in the decision to submit for publication. Ethical approval for the study was obtained from the University of Cape Town Human Research Ethics Committee (ref. no. HREC 224/2022).

Results

We included 31,151 injury patients. Period 1 included 3,883 patients from four facilities (Table 2) with the intervention, on 12 July 2020, of a complete alcohol ban following partial alcohol availability (off-site retail sale allowed from Monday-Thursday). Period 2 included 6,402 patients from 17 facilities sampled, with the intervention, on 16 June 2021, of partial alcohol availability (off-site retail sale allowed only from Monday-Thursday)

following previous full availability (Monday-Sunday). Period 3 included 20,866 patients from 23 facilities with the intervention, on 14 September 2021, of amended partial alcohol availability (off-site retail sale allowed from Monday-Friday) following partial alcohol availability (off-site retail sale allowed from Monday-Thursday).

Table 2: Participant characteristics across alcohol regulatory periods (n=31,151)

	Period 1 (No. of Facilities: 4)			**Period 2** (No. of Facilities: 17)			**Period 3** (No. of Facilities: 23)		
Participant characteristics[1]	**Pre-intervention:** Partial alcohol availability (1 June 2020 – 12 July 2020) **(n=3,059)**	**Post-intervention:** Complete alcohol ban (13 July 2020 – 17 August 2020) **(n=824)**	**Total:** **(n=3,883)**	**Pre-intervention:** Full alcohol availability (31 May 2021 – 16 June 2021) **(n=4,087)**	**Post-intervention:** Partial alcohol availability (17 June 2021 – 27 June 2021) **(n=2,315)**	**Total:** **(n=6,402)**	**Pre-intervention:** Partial alcohol availability Monday-Thursday (26 July 2021 – 13 Sept 2021) **(n=14,891)**	**Post-intervention:** Partial alcohol availability Monday-Friday (14 Sept 2021 – 30 Sept 2021) **(n=5,975)**	**Total:** **(n=20,866)**
Gender									
Male	2,240 (73·2%)	608 (73·8%)	2,848 (73·3%)	2,695 (65·9%)	1,523 (65·8%)	4,218 (65·9%)	9,846 (66·1%)	3,970 (66·4%)	13,816 (66·2%)
Female	819 (26·8%)	216 (26·2%)	1,035 (26·7%)	1,392 (34·1%)	792 (34·2%)	2,184 (34·1%)	5,045 (33·9%)	2,005 (33·6%)	7,050 (33·8%)
Age, years									
<17 years old	497 (16·3%)	174 (21·1%)	671 (17·3%)	874 (21·4%)	480 (20·7%)	1,354 (21·2%)	3,339 (22·4%)	1,363 (22·8%)	4,702 (22·5%)
18 to 39 years old	1,834 (59·9%)	474 (57·5%)	2,308 (59·4%)	2,266 (55·4%)	1,313 (56·7%)	3,579 (55·9%)	8,150 (54·7%)	3,263 (54·6%)	11,413 (54·7%)
>40 years old	728 (23·8%)	176 (21·4%)	904 (23·3%)	947 (23·2%)	522 (22·6%)	1,469 (22·9%)	3,402 (22·9%)	1,349 (22·6%)	4,751 (22·8%)
Weekend vs weekday presentation									
Weekday	1,912 (62·5%)	528 (64·1%)	2,440 (62·8%)	2,681 (65·6%)	1,107 (47·8%)	3,788 (59·2%)	8,893 (59·7%)	3,789 (63·4%)	12,682 (60·8%)
Weekend	1,147 (37·5%)	296 (35·9%)	1,443 (37·2%)	1,406 (34·4%)	1,208 (52·2%)	2,614 (40·8%)	5,998 (40·3%)	2,186 (36·6%)	8,184 (39·2%)
Time of day presenting									
00:00-06:00	581 (19·0%)	137 (16·6%)	718 (18·5%)	564 (13·8%)	368 (15·9%)	932 (14·6%)	2,106 (14·1%)	844 (14·1%)	2,950 (14·1%)
06:00-12:00	603 (19·7%)	150 (18·2%)	753 (19·4%)	1,158 (28·3%)	587 (25·4%)	1,745 (27·3%)	4,273 (28·7%)	1,714 (28·7%)	5,987 (28·7%)
12:00-18:00	834 (27·3%)	262 (31·8%)	1,096 (28·2%)	1,235 (30·2%)	704 (30·4%)	1,939 (30·3%)	4,500 (30·2%)	1,783 (29·8%)	6,283 (30·1%)
18:00-00:00	1,041 (34·0%)	275 (33·4%)	1,316 (33·9%)	1,130 (27·7%)	656 (28·3%)	1,786 (27·9%)	4,012 (26·9%)	1,634 (27·4%)	5,646 (27·1%)
Trauma category									
Interpersonal Violence	1462 (47·8%)	381 (46·2%)	1843 (47·5%)	1,751 (42·8%)	1,091 (47·1%)	2,842 (44·4%)	6,905 (46·4%)	2,757 (46·1%)	9,662 (46·3%)
Road Traffic Incidents (RTIs)	245 (8·0%)	72 (8·7%)	317 (8·2%)	556 (13·6%)	280 (12·1%)	836 (13·1%)	1,738 (11·7%)	643 (10·8%)	2,381 (11·4%)
Accidental (non-RTI)	698 (22·8%)	237 (28·8%)	935 (24·1%)	1,721 (42·1%)	901 (38·9%)	2,622 (41·0%)	6,027 (40·5%)	2,454 (41·1%)	8,481 (40·6%)
Self-Harm	61 (2·0%)	19 (2·3%)	80 (2·1%)	59 (1·4%)	43 (1·9%)	102 (1·6%)	221 (1·5%)	121 (2·0%)	342 (1·6%)
Other	593 (19·4%)	115 (14·0%)	708 (18·2%)						

[1]Reported as n (% within pre- or post-intervention period) unless otherwise specified. Note: Trauma Category Other removed from data collection tool in periods 2 and 3.

The imposition of restrictions on alcohol sales in Periods 1 and 2 were associated with a reduction in the incidence of injury presentations to emergency centres. Shifting from full to partial (Monday-Thursday) alcohol availability had a step effect reduction of 29·0% (absolute reduction [95% CI]: -71·7 [-102·9, -40·4]) in daily injury presentations. Further restricting alcohol availability from a partial (Monday-Thursday) to a complete sales ban in Period 1 resulted in a step effect of reduced trauma injuries of 26·2% (absolute reduction [95% CI]: -4·5 [20·6, -8·4]). These reductions were sustained based on the ramp effect for Periods 1 and 2 (Table 3 and 4). Period 3, the addition of a single day of alcohol availability (Friday), however did not have significant step or ramp effects.

The direction of the above step effects was consistent across all subgroups (Table 3, Figure 2). Of note, in Period 1, a complete ban had a >23% relative reduction (step effect) in all subgroups (range: -23·4% to -42·3%). The largest step effects were in young adults and females who experienced interpersonal violence (IPV) with a complete ban. In Period 2, when a partial ban was instituted, all subgroups had a nearly 15% or more relative reduction in step effect (Range: -14·8% to -37·1%). Conversely, with extension of partial availability to include Friday in Period 3, there were substantial increases in injury presentations in certain subgroups with relative step increases of 25·4% in injuries in females and 35·5% in non-traffic related accidents.

Despite no overall ramp effects for any of the interventions, specific subgroups experienced these effects (Table 4). The complete alcohol ban had no step effect in injury for children and adolescents, but a reduction ramp effect over time. Ramp effects showed an attenuation of step reduction in certain subgroups e.g., during the complete ban (Period 1) for accidents only, and for partial alcohol availability Monday-Thursday (Period 2) for males. Lastly, although there were limited step effects in Period 3 (Friday availability), there were ramp effects of increasing injuries for both females and young adult males who experience interpersonal violence.

Table 3: Autoregressive Integrated Moving Average (ARIMA) model outputs - absolute and relative step effects overall and across subgroups

		Relative STEP effect across alcohol regulatory periods								
		Period 1 Partial alcohol availability [Mon-Thurs] to **a complete alcohol ban**			**Period 2** Full alcohol availability to **partial alcohol availability [Mon-Thurs]**			**Period 3** Partial alcohol availability [Mon-Thurs] to **partial alcohol availability [Mon-Fri]**		
		Intercept (95% CI)	**Absolute Step Effect (95% CI)**	**Relative Step Effect**	**Intercept (95% CI)**	**Absolute Step Effect (95% CI)**	**Relative Step Effect**	**Intercept (95% CI)**	**Step Effect (95% CI)**	**Relative Step Effect**
Overall Step Effect		55·5 (53·7, 57·4)	-14·5 (-20·6, -8·4)	**↓ -26·2%**	247·2 (239·7, 254·7)	-71·7 (-102·9, -40·4)	**↓ -29·0%**	299·5 (271·9, 327·1)	17·3 (-53·7, 88·3)	NA
Stratified subgroup step effects	Males only	43·1 (37·1, 49·0)	-15·4 (-23·0, -7·7)	**↓ -35·7**	165·0 (162·7, 167·3)	-61·3 (-78·5, -44·0)	**↓ -37·1%**	197·1 (162·7, 167·3)	19·7 (-75·9, 42·1)	NA
	Females only	14·5 (13·1, 15·9)	-3·4 (-6·8, -0·0)	**↓ -23·4%**	84·2 (70·7, 97·7)	-3·3 (-9·1, 2·6)	NA	99·7 (93·0, 106·3)	25·3 (0·1, 50·6)	**↑ +25·4%**
	Children and Adolescents	8·7 (8·1, 9·3)	0·9 (-0·7, 2·5)	NA	53·5 (52·9, 54·1)	-14·0 (-19·9, -8·0)	**↓ -26·1%**	65·6 (56·0, 75·1)	15·4 (-4·3, 35·0)	NA
	Young Adults	35·0 (30·6, 39·4)	-14·8 (-21·1, -8·5)	**↓ -42·3%**	136·8 (130·5, 143·2)	-44·3 (-66·2, -22·4)	**↓ -32·4%**	164·3 (152·6, 175·9)	17·3 (-13·6, 48·2)	NA
	Older Adults	13·2 (12·2, 14·2)	-4·6 (-6·6, -2·6)	**↓ -34·5%**	54·2 (42·1, 66·3)	5·3 (-10·8, 21·3)	NA	67·1 (60·8, 73·4)	12·5 (-3·9, 28·9)	NA
	Females who experience IPV	4·2 (12·2, 14·2)	-1·7 (-3·2, -0·3)	**↓ -41·3%**	24·9 (24·4, 25·3)	-3·7 (-7·0, -0·4)	**↓ -14·8%†**	34·3 (31·5, 37·1)	2·3 (-6·2, 10·8)	NA
	Young adult males who experience IPV	16·5 (15·5, 17·4)	-4·2 (-7·7, -0·7)	**↓ -25·4%**	64·0 (62·6, 65·4)	-20·7 (-32·9, -8·4)	**↓ -32·3%†**	77·9 (70·4, 85·4)	11·9 (-3·4, 27·2)	NA
	Accidents only	10·5 (9·6, 11·5)	0·6 (-1·9, 3·0)	NA	102·8 (100·0, 105·6)	-36·1 (-57·0, -15·2)	**↓ -35·1%**	119·5 (112·6, 126·5)	42·4 (14·9, 69·9)	**↑ +35·5%**

Abbreviations: Mon, Monday; Thurs, Thursday; Fri, Friday; Sat, Saturday; Sun, Sunday. †p-value for residuals <0·05. Grey font used for all step effects with p>0·05. Bold font used for all relative step effects with p<0·05. NA: Not applicable as no absolute statistical effect noted.

Table 4: Autoregressive Integrated Moving Average (ARIMA) model outputs – absolute and relative ramp effects overall and across subgroups

		Relative RAMP effect across alcohol regulatory periods								
		Period 1 Partial alcohol availability [Mon-Thurs] to a complete alcohol ban			**Period 2** Full alcohol availability to partial alcohol availability [Mon-Thurs]			**Period 3** Partial alcohol availability [Mon-Thurs] to partial alcohol availability [Mon-Fri]		
		Absolute Intercept (95% CI)	Ramp Effect (95% CI)	Relative Ramp Effect	Absolute Intercept (95% CI)	Ramp Effect (95% CI)	Relative Ramp Effect	Absolute Intercept (95% CI)	Ramp Effect (95% CI)	Relative Ramp Effect
Overall Ramp Effect		55·5 (53·7, 57·4)	0·1 (-0·2, 0·4)	NA	247·2 (239·7, 254·7)	4·5 (-0·5, 9·5)	NA	299·5 (271·9, 327·1)	5·7 (-1·3, 12·7)	NA
Stratified subgroup ramp effects	Males only	43·1 (37·1, 49·0)	0·1 (-0·3, 0·4)	NA	165·0 (162·7, 167·3)	4·6 (1·5, 7·6)	**↑ 2·8%**	197·1 (162·7, 167·3)	4·2 (1·5, 7·3)	**↑ 2·2%**
	Females only	14·3 (13·7, 14·8)	0·1 (-0·0, 0·2)	NA	84·2 (70·7, 97·7)	-0·6 (-2·3, 1·1)	NA	99·7 (93·0, 106·3)	0·2 (-2·7, 3·1)	NA
	Children and Adolescents	8·7 (8·1, 9·3)	-0·1 (-0·1, -0·0)	**↓ -0·8%**	53·5 (52·9, 54·1)	0·7 (-0·4, 1·8)	NA	65·6 (56·0, 75·1)	-0·3 (-2·4, 1·8)	NA
	Young Adults	35·0 (30·6, 39·4)	0·1 (-0·1, 0·4)	NA	136·8 (130·5, 143·2)	3·3 (-0·0, 6·6)	NA	164·3 (152·6, 175·9)	4·4 (1·1, 7·6)	**↑ 2·7%**
	Older Adults	13·2 (12·2, 14·2)	0·1 (-0·0, 0·1)	NA	54·2 (42·1, 66·3)	-1·1 (-3·4, 1·2)	NA	67·1 (60·8, 73·4)	0·4 (-1·6, 2·4)	NA
	Females who experience IPV	4·2 (12·2, 14·2)	0·0 (-0·0, 0·1)	NA	24·9 (24·4, 25·3)	-0·1 (-0·6, 0·5)	NA	34·3 (31·5, 37·1)	1·1 (0·1, 2·1)	**↑ 3·1%†**
	Young adult males who experience IPV	16·5 (15·5, 17·4)	0·1 (-0·1, 0·2)	NA	64·0 (62·6, 65·4)	1·9 (-0·1, 3·8)	NA	77·9 (70·4, 85·4)	2·1 (0·5, 3·8)	**↑ 2·8%**
	Accident only	10·5 (9·6, 11·5)	0·1 (0·0, 0·3)	**↑ 1·3%**	102·8 (100·0, 105·6)	2·4 (-1·0, 5·7)	NA	119·5 (112·6, 126·5)	-1·4 (-4·6, 1·7)	NA

Abbreviations: Mon, Monday; Thurs, Thursday; Fri, Friday; Sat, Saturday; Sun, Sunday. †p-value for residuals <0·05. Grey font used for all step effects with p>0·05. Bold font used for all relative step effects with p<0·05. NA: Not applicable as no absolute statistical effect noted.

Discussion

Our analysis of more than 20,000 injury patients across three different alcohol regulatory periods in South Africa showed a significant, consistent, and sustained impact of alcohol regulation in reducing injury presentations to hospital emergency centres. Implementing only a partial retail ban (Monday to Thursday availability) reduced trauma injuries presenting to ECs by 29% and shifting from a partial retail ban to a complete ban resulted in a further 26% reduction. This impact aligns with and further validates previous evidence that showed the impact of alcohol regulation on unnatural deaths and injury morbidity during the South African COVID-19 experience.[9–12]

In this study, populations most affected by injury presentations included males, young adults (18-39 years), and those with interpersonal violence as the cause of their presentation, correlating well with intentional injuries as the leading cause of male years of life lost in the province.[18] Furthermore, trauma injuries may be under-ascertained in this data as the second highest trauma category was non-traffic related accidental injuries. Since the nature of the injury is self-reported, interpersonal violence experienced by vulnerable populations may be under-reported. Road traffic incidents were a smaller proportion of trauma injuries, but this may be skewed by the dataset reflecting public sector admissions and not adequately reflecting wealthier people with better access to private transportation. The proportion of weekday vs. weekend injury presentations shows a clear weekend spike effect. This may be due to risk factors for injury such as heavy drinking, more leisure time, and increased opportunity at home to engage in domestic violence being more prevalent over weekends compared to the week.

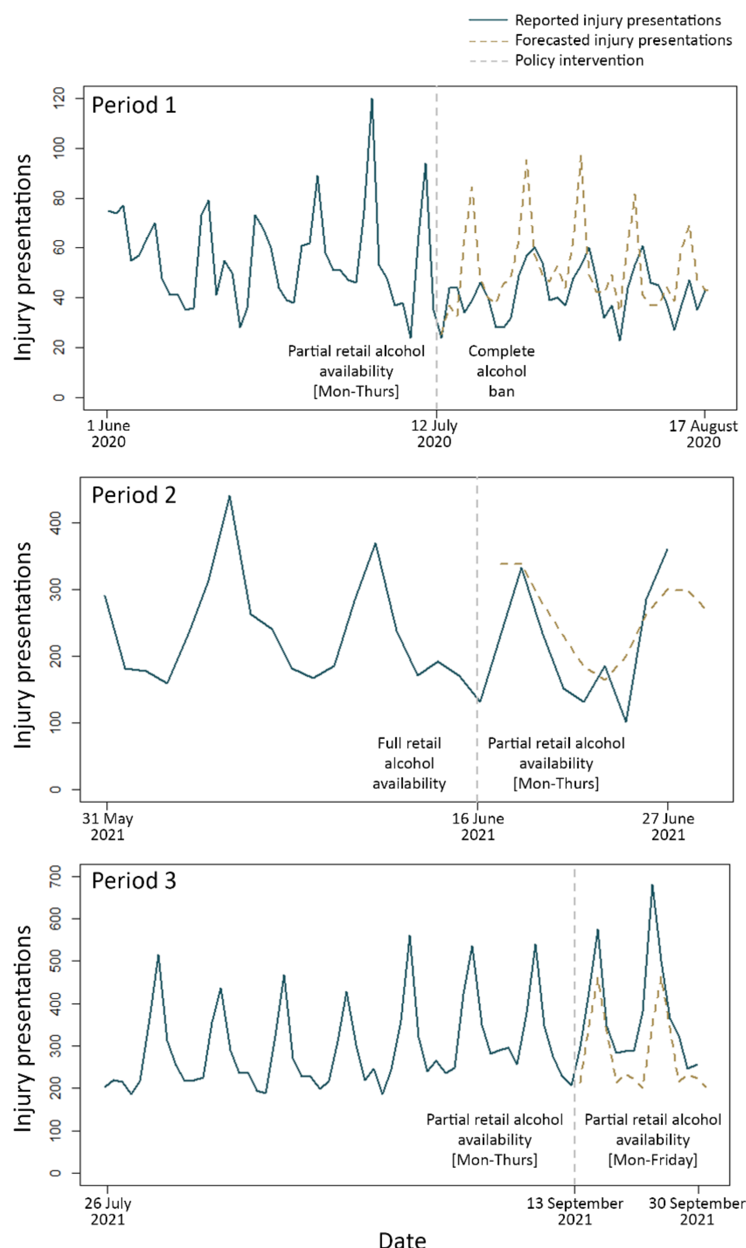

Figure 3: Overall ARIMA interrupted time series analysis by period

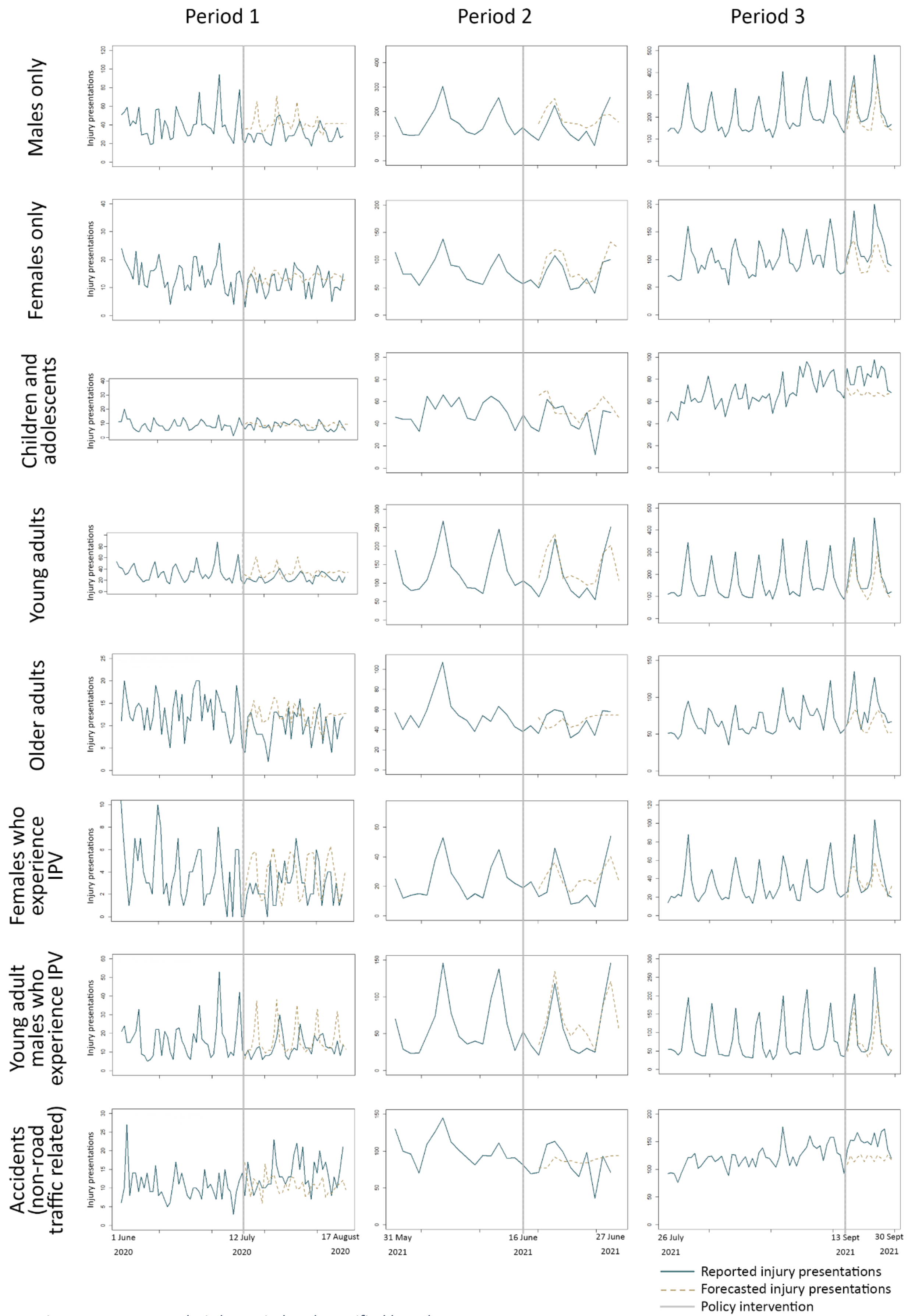

Figure 4: ARIMA analysis by period and stratified by sub-groups

The key finding of this study is the considerable impact of alcohol regulation on injury presentations to ECs, especially with complete cessation in alcohol availability with clear and consistent injury reductions in almost every subgroup. While this demonstrates the harmful relationship with alcohol in South Africa and its implications for healthcare system capacity, complete alcohol bans are not sustainable.

The shift from full to partial Monday-Thursday retail alcohol availability, however, could be considered for longer term, sustainable alcohol regulation policies. This period led to sustained reductions in injury presentations across most subgroups, while among men potential attenuation during the period post introduction was demonstrated. Across the 17 facilities, partially restricting alcohol resulted in, on average, 70 less trauma patients presenting per day or a nearly 30% reduction in daily trauma presentations across the healthcare platform. This is a substantial public health impact and could amount to significant cost savings to the health system, notwithstanding the physical, psychological, and financial saving directly to the patient and their respective communities.

Period 3 allowed assessing the implications of additional Friday availability in the context of partial alcohol availability which impacts weekly wage workers and alcohol abusers that do not or cannot stockpile. Although no immediate overall step effect was noted, there were small increases in trauma injuries over time across several subgroups including males, young adults, and particularly females and young adult males experiencing IPV (Range: +2·2% to +3·1% daily). Given that IPV in young men and violence against women are major contributors to morbidity and premature mortality in South Africa, the increase in IPV over time with Friday availability is concerning and suggests heavy weekend drinking is, indeed, a risk factor. This is further brought to the fore when considering the significant immediate increase in female trauma injuries (+25·4%) and non-road traffic related accidents (+35·5%) with the inclusion of Friday alcohol sales, both of which may indicate a preponderance toward gender-based violence (GBV) and IPV in general with accidents potentially masking the under-reporting from vulnerable victims of IPV/GBV.

To our knowledge, this is the first multi-centre injury morbidity study, leveraging a large and reliable healthcare data set, to analyse the alcohol regulation impact. The focus on

morbidity is important as this has direct implications for healthcare system capacity and resource use. Furthermore, without these alcohol regulation “natural experiments”, there would be little opportunity to practically demonstrate the impact of restricting alcohol availability on injury presentations through experimental study designs. Using a robust quasi-experimental approach, our study improves on previously applied methodologies and implies a causal interpretation of the observed relationship.

Our study had several limitations. Firstly, the fewer facilities available for analysis in period 1 may limit external generalizability as compared to later periods. Secondly, the post-intervention period in Period 2 coincided with an end of month weekend, which together with Period 2 being shorter may have biased the ramp results. The attenuation during the post-implementation period of the large step reduction in trauma presentations in males may be because of inadequate adjustment for an end of month effect in the limited dataset rather than a true attenuation over time. In Period 3, end of month seasonality was adjusted for due to longer pre-intervention data including prior end of month weekends, however some of the increases over time in certain subgroups may still be end of month effects despite adjustment. We could not separately account for changing curfew times which often occurred simultaneously with the alcohol regulation transition dates leading to collinearity. However, prior mortality studies suggested curfews were unlikely to cause a major impact (and there was limited biological plausibility for a curfew impact) apart from potential effect modification through decreased physical alcohol availability due to the curfew itself.[9,10] Lastly, goodness of fit in some of the subgroup analyses were suboptimal, especially for shorter time periods with limited data for the respective subgroup.

Research into the effectiveness of alcohol regulations serves as an important tool to guide policy decisions at a national and sub-national level. This research contributes to the broader evidence base related to the impact of alcohol control measures and particularly helps to contribute to the much-needed research on this topic from low- and middle-income countries (LMICs).[20] Our findings provide clear evidence that alcohol regulation can be a powerful tool to limit the burden of injury on society and relieve the healthcare platform from preventable alcohol-related trauma harms, both in the context of a pandemic, but perhaps more importantly to inform sustainable policy options beyond.

Author contributions

MI conceptualized the study, analysed, and interpreted the data and was the major contributor in writing the manuscript. MP assisted in information system development, data collection and data availability. EM, MM, CP, and LL assisted with study conceptualization and manuscript revisions and review. RM and MAD supported with academic supervision throughout the process, study conceptualization, supervision of analysis and manuscript revisions with critical review. All authors read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

Deidentified, aggregate data are available on reasonable request to the corresponding author.

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Appendices

Appendix 1: Human Research Ethics Council (HREC) Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

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12 April 2022

HREC REF: 224/2022

Prof R Matzopoulos
School of Public Health & Family Medicine
Falmouth Building-FHS
Email: Richard.matzipoulos@uct.ac.za
Student: ismmuz001@myuct.ac.za

Dear Prof Matzopoulos

PROJECT TITLE : ALCOHOL REGULATIONS AND INJURY PRESENTATIONS TO EMERGENCY CENTRES: A MULTICENTRE QUASI EXPERIMENTAL ANALYSIS- (MASTERS CANDIDATE-DR MUZZAMMIL ISMAIL)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, our letter dated 02 February 2022 provides guidance found on our website: http://www.health.uct.ac.za/fhs/research/humanethics/forms

Approval is granted for one year until the 30 April 2023.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

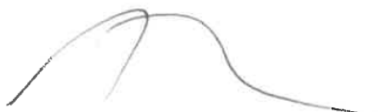
The HREC acknowledge that the student: Dr Muzzammil Ismail will also be involved in this study.

Please quote the HREC REF 224/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely



PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix 2: Lancet Public Health Guidelines (target journal)

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- At the end of the text, under a subheading "Declaration of interests", all authors must disclose any financial and personal relationships with other people or organisations, even if it does not directly relate to the submitted work. Examples of financial conflicts include employment, consultancies, stock ownership, honoraria, paid expert testimony, patents or patent applications, and travel grants, all within 3 years of beginning the work submitted. If there are no conflicts of interest, authors should state that none exist
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- For Comments, *The Lancet Public Health* will not publish if an author, within the past 3 years, and with a relevant company or competitor, has any stocks or shares, equity, a contract of employment, or a named position on a company board; or has been asked by any organisation other than *The Lancet Public Health* to write, be named on, or to submit the paper (see *Lancet* 2004; **363:** 2–3).

Patient Consent form
http://www.thelancet.com/pb/assets/raw/Lancet/authors/lancet-consent-form.pdf

Role of the funding source

- All sources of funding should be declared as an acknowledgment at the end of the text
- At the end of the Methods section, under a subheading "Role of the funding source", authors must describe the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication
- If there is no Methods section, the role of the funding source should be stated as an acknowledgment. If the funding source had no such involvement, the authors should state this

Role of medical writer or editor

- If a medical writer or editor was involved in the creation of your manuscript, we need a signed statement from the corresponding author to include their name and information about funding of this person
- This information should be added to the Acknowledgments or Contributors section
- We require signed statements from any medical writers or editors declaring that they have given permission to be named as an author, as a contributor, or in the Acknowledgments section

Patient and other consents

- Appropriate written consents, permissions, and releases must be obtained where you wish to include any case details, personal information, and/or images of patients or other individuals in *The Lancet* journals in order to comply with all applicable laws and regulations concerning privacy and/or security of personal information. Studies on patients or volunteers need approval from an ethics committee and informed consent from participants. These should be documented in your paper.
- Do not use "blackout" bars or similar devices to anonymise patients in clinical images: if you have taken consent appropriately masking is not needed.
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Please instead complete the patient consent section of the Author statements while retaining copies of the signed forms in the event they should be needed.

- If consent, permission, or release is made subject to any conditions, *The Lancet Public Health* must be made aware in writing of all such conditions before publication.
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Types of article and manuscript requirements

Please ensure that anything you submit to *The Lancet Public Health* follows the guidelines provided for each article type. For instruction on how to format the text of your paper, including tables, figures, panels, and references, please see our **Formatting guidelines**.

Red section (Articles)

Articles

- *The Lancet Public Health* prioritises reports of original research that are likely to change practice or thinking
- We invite submission of all trials, whether phase 1, 2, 3, or 4. For phase 1 trials, we consider those of a novel substance for a novel indication, if there is a strong or unexpected beneficial or adverse response, or a novel mechanism of action
- We require the registration of all interventional trials, whether early or late phase, in a primary register that participates in WHO's International Clinical Trial Registry Platform (see *Lancet* 2007; **369**: 1909–11) or in ClinicalTrials.gov, in accord with ICMJE recommendations. We also encourage full public disclosure of the minimum 21-item trial registration dataset at the time of registration and before recruitment of the first participant (see *Lancet* 2006; **367**: 1631–35). The registry must be independent of for-profit interest
- Reports of trials must conform to CONSORT 2010 guidelines and should be submitted with their protocols
- All reports of randomised trials should include a section entitled Randomisation and masking, within the Methods section. Please refer to *The Lancet's* formatting guidelines for randomised trials
- Cluster-randomised trials must be reported according to CONSORT extended guidelines
- Randomised trials that report harms must be described according to extended CONSORT guidelines
- Studies of diagnostic accuracy must be reported according to STARD guidelines
- Observational studies (cohort, case-control, or cross-sectional designs) must be reported according to the STROBE statement, and should be submitted with their protocols
- We encourage the registration of all observational studies on a WHO-compliant registry (see *Lancet* 2010; **375**: 348)
- Genetic association studies must be reported according to STREGA guidelines
- Systematic reviews and meta-analyses must be reported according to PRISMA guidelines. Please refer to *The Lancet's* formatting guidelines for systematic reviews and meta-analyses.
- Reports of studies of global health estimates should be reported according to the GATHER statement (see *Lancet* 2016; **388**: e19–23)
- Clinical trials that report interventions using artificial intelligence must be described according to the CONSORT-AI Extension guidelines and their protocols must be described according to the SPIRIT-AI Extension guidelines
- To find reporting guidelines see: http://www.equator-network.org
- When using a study group, collaborator group, or Consortia instead of authors' names, please be aware that individuals' names will not explicitly appear when your published Article is uploaded to MEDLINE/PubMed. Your Article will still be discoverable via a search for a specific named author, but only the collective name given to the study will appear on that platform. If you need more information, please contact us.

All Articles should, as relevant:

- Be up to 3500 words (4500 for randomised controlled trials) with 30 references (the word count is for the manuscript text only)
- Include an abstract (semistructured summary), with five paragraphs (Background, Methods, Findings, Interpretation, and Funding), not exceeding 250 words. Our electronic submission system will ask you to copy and paste this section at the "Submit Abstract" stage
- For randomised trials, the abstract should adhere to CONSORT extensions: abstracts (see *Lancet* 2008; **371**: 281–83)
- When reporting Kaplan-Meier survival data, at each timepoint, authors must include numbers at risk, and are encouraged to include the number of censored patients.
- For intervention studies, the abstract should include the primary outcome expressed as the difference between groups with a confidence interval on that difference (absolute differences are more useful than relative ones). Secondary outcomes can be included as long as they are clearly marked as secondary and all such outcomes are reported
- Use the recommended international non-proprietary name (rINN) for drug names. Ensure that the dose, route, and frequency of administration of any drug you mention are correct
- Use gene names approved by the Human Gene Organisation. Novel gene sequences should be deposited in a public database (GenBank, EMBL, or DDBJ), and the accession number provided. Authors of microarray papers should include in their submission the information recommended by the MIAME guidelines. Authors should also submit their experimental details to one of the publicly available databases: ArrayExpress or GEO
- Include any necessary additional data as part of your EM submission
- All accepted Articles should include a link to the full study protocol published on the authors' institutional website (see *Lancet* 2009; **373**: 992 and *Lancet* 2010; **375**: 348)
- We encourage researchers to enrol women and ethnic groups into clinical trials of all phases, and to plan to analyse data by sex and by race
- For all study types, we encourage correct use of the terms sex (when reporting biological factors) and gender (when reporting identity, psychosocial, or cultural factors). Where possible, report the sex and/or gender of study participants, and describe the methods used to determine sex and gender. Separate reporting of data by demographic variables, such as age and sex, facilitates pooling of data for subgroups across studies and should be

WHO's International Clinical Trial Registry Platform
http://www.who.int/ictrp/network/trds/en/index.html

Clinical trials
http://clinicaltrials.gov

ICMJE recommendations
http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

CONSORT 2010 guidelines
http://www.consort-statement.org/consort-2010

Formatting guidelines for randomised trials
https://www.thelancet.com/for-authors/forms?section=rct

CONSORT extended guidelines
http://www.consort-statement.org/extensions/extensions/

STARD guidelines
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Formatting guidelines for meta-analyses
https://www.thelancet.com/for-authors/forms?section=meta-analysis

CONSORT-AI Extension guidelines
https://doi.org/10.1016/S2589-7500(20)30218-1

SPRIT-AI Extension guidelines
https://doi.org/10.1016/S2589-7500(20)30219-3

To find reporting guidelines, see
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Array and GEO
http://www.ebi.ac.uk/microarray-as/ae/
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routine, unless inappropriate. Discuss the influence or association of variables, such as sex and/or gender, on your findings, where appropriate, and the limitations of the data.

Putting research into context

- All research papers (including systematic reviews/meta-analyses) submitted to any journal in *The Lancet* family must include a panel putting their research into context with previous work in the format outlined below (see *Lancet* 2014; **384**: 2176–77, for the original rationale). This panel should not contain references. Editors will use this information at the first assessment stage and peer reviewers will be specifically asked to check the content and accuracy
- The Discussion section should contain a full description and discussion of the context. Authors are also invited to either report their own, up-to-date systematic review or cite a recent systematic review of other trials, putting their trial into context of the review

MENDELEY data
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Research in context

Evidence before this study
This section should include a description of all the evidence that the authors considered before undertaking this study. Authors should briefly state: the sources (databases, journal or book reference lists, etc) searched; the criteria used to include or exclude studies (including the exact start and end dates of the search), which should not be limited to English language publications; the search terms used; the quality (risk of bias) of that evidence; and the pooled estimate derived from meta-analysis of the evidence, if appropriate.

Added value of this study
Authors should describe here how their findings add value to the existing evidence.

Implications of all the available evidence
Authors should state the implications for practice or policy and future research of their study combined with existing evidence.

Research in context panels should not contain references; key studies mentioned here should be referenced in the main text.

Data sharing

From September 21, 2020, all submitted research Articles must contain a data sharing statement, to be included at the end of the manuscript. Data sharing statements must include:

- Whether data collected for the study, including individual participant data and a data dictionary defining each field in the set, will be made available to others ("undecided" is not an acceptable answer);
- What data will be made available (deidentified participant data, participant data with identifiers, data dictionary, or other specified data set);
- Whether additional, related documents will be available (eg, study protocol, statistical analysis plan, informed consent form);
- When these data will be available (beginning and end date, or "with publication", as applicable);
- Where the data will be made available (including complete URLs or email addresses if relevant);
- By what access criteria data will be shared (including with whom, for what types of analyses, by what mechanism – eg, with or without investigator support, after approval of a proposal, with a signed data access agreement - or any additional restrictions).

For *The Lancet* journals' policy on corrections of errors see https://www.thelancet.com/for-authors/forms?section=correction

See table for examples. Clinical trials that begin enrolling participants on or after Jan 1, 2019, must include a data sharing plan in the trial's registration. If the data sharing plan changes after registration, this should be reflected in the statement submitted and published, and updated in the registry record. Mendeley Data is a secure online repository for research data, permitting archiving of any file type and assigning a permanent and unique digital object identifier (DOI) so that the files can be easily referenced. If authors wish to share their supporting data, and have not already made alternative arrangements, a Mendeley DOI can be referred to in the data sharing statement.

Blue section (Comment, Correspondence, etc)

Editorial

- Editorials are the voice of *The Lancet Public Health*, and are written in-house by the journal's editorial-writing team and signed "*The Lancet Public Health*"

Comment

- This section contains Commentaries that accompany papers published in *The Lancet Public Health* or on issues of wide-reaching concern in Public Health. Comments linked to policy decisions are welcomed. Most Comments are commissioned, but unsolicited Comments (no more than 750 words, ten references, and one figure, panel, or small table) are also welcome. Comments may be peer reviewed
- The place to respond to something we have published is in our **Correspondence** section
- See **Conflicts of Interest** guidelines for comments

Correspondence

- Letters should be written in response to previous content published in *The Lancet Public Health*
- Letters for publication must reach us within 4 weeks of publication of the original item and should be no longer than 250 words and 5 references
- Letters of general interest, unlinked to items published in the journal, can be up to 400 words long
- Correspondence letters are not usually peer reviewed, but we might invite replies from the authors of the original publication, or pass on letters to these authors
- Only one table or figure is permitted, and there should be no more than five references and five authors
- All accepted letters are edited. Proofs will be sent out to authors before publication

Corrections

- Any substantial error in any article published in *The Lancet Public Health* should be corrected as soon as possible. Blame is not apportioned; the important thing is to set the record straight.
- The *Lancet* journals have a policy for types of errors that we do and do not correct. We will always correct any error affecting a non-proprietory drug name, dose, or unit, any numerical error in the results, or any factual error in the interpretation

of results. Authorship format changes after publication to facilitate a different visualisation in MEDLINE/PubMed will not be done.

Essay

- Essays should be up to 2000 words in descriptive prose, and can be on any topic related to public health. If you are a medical professional, this is your opportunity to shine light on a neglected area, highlight an inspirational experience, or share your insights.

Green section (Reviews, Viewpoints, Health Policy, Commission)

Reviews

Most reviews are commissioned, but unsolicited short outlines (300–400 words) can be directed to the Editor. If you have already written the paper, please submit it for consideration via our online system.

- Reviews should be either a definitive overview of a major topic connected with public health
- Manuscripts will be assessed in-house and those judged suitable will be peer reviewed before an editorial decision is made
- Reviews should be no more than 4500 words, with a maximum of 75 references
- References selected for publication should be chosen for their importance, ease of access, and for the "further reading" opportunities they provide; citations to papers published in non-peer-reviewed supplements are discouraged. In addition to references, authors should consider supplying a short list of useful websites where readers can find further information on the subject
- A 150 word unstructured summary should be included. Use of up to 5–6 illustrations is encouraged to aid the reader
- Complete transparency about the choice of material included is important to any Review paper. Therefore, all Reviews should include a brief section entitled "Search strategy and selection criteria" stating the sources (including databases, MeSH and free text search terms and filters, and reference lists from journals or books) of the material covered, and the criteria used to include or exclude studies. Citations to papers published in non-peer-reviewed supplements are discouraged. Since these papers should be comprehensive, we encourage citation of publications in non-English languages.

Systematic reviews should be prepared according to the PRISMA guidelines

Viewpoint

Viewpoints are opinion pieces that use the best evidence to develop a robust argument on a topic of immediate relevance to public health. They should have a novel and clear point to make, with the aim of provoking transformational thinking at a high level. Length guidelines are up to 2500 words and 35 references.

Health Policy

Manuscripts considered for this section are narrative reviews (not original research) and should follow the same guidelines as a Review. These papers should cover developments in public health related to policy, health systems, or economics. Other related topics will be considered. Please contact the Editor before submitting to ensure the proposed topic is suitable.

Commissions

Topics for *The Lancet Public Health* Commissions are selected by our editors, who work with academic partners to identify the most pressing issues in public health with the aim of producing recommendations to change policy or practice. All Commissions are academic publications and are subject to the same rigorous peer review process as all other research papers published in our journals. *The Lancet Public Health* does not provide direct financial support to Commissioners for the research or writing of the reports. Funding is sought directly by authors, with oversight from our editors.

Formatting guidelines

Language

- Manuscripts should be submitted in English. Authors writing in Chinese, Portuguese, or Spanish may wish to use the Webshop (http://webshop.elsevier.com/languageservices) to provide an English translation of their manuscript for submission.

For online system see
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- Type a single space at the end of each sentence
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- We use a comma before the final "and" or "or" in a list of items
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- Use single hard-returns to separate paragraphs. Do not use tabs or indents to start a paragraph
- Do not use the automated features of your software, such as hyphenation, endnotes, headers, or footers (especially for references). Please use page numbering
- Guidelines on formatting tables are available in the artwork guidelines

Formatting guidelines for text, tables, and figures
Guidelines on formatting of text, tables, and figures can be found at **https://www.thelancet.com/pb/assets/raw/Lancet//authors/artwork-guidelines.pdf**

References

- If preprints are central to your work or cover crucial developments in the topic(s) covered in your paper, but are not yet formally published, these may be referenced. Preprints should be clearly marked as such, for example by including [preprint] before the reference, and specifically referred to as a preprint in the main text. Where a preprint has subsequently become available as a peer-reviewed article, the formal publication should be used as the reference.
- Cite references in the text sequentially in the Vancouver numbering style, as a superscripted number after any punctuation mark. For example:

  "...as reported by Saito and colleagues.[15]"

- Two references are cited separated by a comma, with no space. Three or more consecutive references are given as a range with an en rule. To create an en rule on a PC: hold down CTRL key and minus sign on the number pad, or on a Mac: ALT hyphen
- References in tables, figures, and panels should be in numerical order according to where the item is cited in the text
- Here is an example for a journal reference (note the use of tab, bold, italic, and the en rule or "long" hyphen):
  "15[tab]Saito N, Ebara S, Ohotsuka K, Kumeta J, Takaoka K. Natural history of scoliosis in spastic cerebral palsy. *Lancet* 1998; **351**: 1687–[en rule]92."
- Give any subpart to the title of the article
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  surname space initials comma
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- For a chapter or section of a book, also give the authors and title of the section, and the page numbers
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- Online journal articles can be cited using the DOI number
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- For trial profiles, study profiles, and CONSORT diagrams, please supply as an editable flow diagram in Word (.doc) or PowerPoint (.ppt) file
- For illustrations (all non-photographic line-work and general drawing) we require editable vector files that contain selectable geometry and fonts (editable text). The editability of files depends on the package they were created in, but as a rule we would prefer to receive any of the following: Adobe Illustrator (.ai) file; Adobe Illustrator or generic .eps files exported from a graphics program; vector-based PDF, PowerPoint, or Word file; or SVG file. If authors are unable to supply files in any these formats, our in-house illustrators can offer guidance on whether it is more economical to export or convert the file into another format, or to redraw from scratch. When files are exported to eps files, we would prefer text to be exported "as text" rather than "as objects", which is especially crucial for files such as forest plots in which there is a lot of text
- If your figures are annotated, please supply two copies of each of these figures as separate files (one annotated copy and one non-annotated and editable copy). Our in-house illustrators will annotate according to journal style using the annotated figures as a guide. For multi-part figures, please supply the individual parts as well as a combined version to be used as a guide for our illustrators to recreate the files
- Images that have been published previously should be accompanied by a statement indicating permission to reproduce the image. If required, further assistance can be obtained from the editorial team. If you have used previously published images, you must obtain permission from the copyright holder of the paper, which might be the authors or the publisher. If all the figures are your own and have not been published before, then this requirement does not apply

Drug names

For more on neuroscience-based nomenclature see http://www.thelancet.com/pdfs/journals/lanpsy/PIIS2215-0366(17)30098-6.pdf

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All material should be submitted as one PDF (with a table of contents and numbered pages) with the paper and will be peer reviewed. Material will be published at the discretion of *The Lancet* journals' editors. For clinical trials, we encourage authors to include a copy of the study protocol. All material should be provided in English.

Text

- Main heading for the web extra material should be in 12 point Times New Roman font **BOLD**
- Text should be in 10 point Times New Roman font, single spaced
- Headings should be in 10 point **BOLD**

Tables

- Main table heading should be in 10 point Times New Roman font **BOLD**
- Legends should be in 10 point, single spaced
- Tables should be in 8 point Times New Roman font, single spaced
- Headings within tables should be in 8 point **BOLD**

Data

- Numbers in text and tables should always be provided if % is shown
- Means should be accompanied by SDs, and medians by IQR
- p values should be given to two significant figures, unless p<0·0001

Drug names

- Recommended international non-proprietary name (rINN) is required
- We encourage use of neuroscience-based nomenclature for psychotropic drugs

References

- Vancouver style—eg,
  Smith A, Jones B, Clements S. Clinical transplantation of tissue-engineered airway. *Lancet* 2008; **372**: 1201–09.
  Hourigan P. Ankle injuries. In: Chan D, ed. Sports medicine. London: *Elsevier*, 2008: 230–47.
- Numbered in order of mention in appendix and numbered separately from references in the full paper

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- All video files can be submitted alongside your article in EM

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- Presentation of data at a scientific meeting, as a poster, abstract, orally, on a CD, or as an abstract on the web, or on a preprint server does not conflict with submission to the *Lancet* journals. As a member journal of the International Committee for Medical Journal Editors, *The Lancet Public Health* does not regard results that are posted in the same clinical trials registry in which primary registration resides as a previous publication, if the results are presented in the form of a brief structured abstract or table
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Decision
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- Two copies of the revised version should be sent back, one of which should be highlighted to show where changes have been made. Detailed responses to reviewers' comments, in a covering letter, are also necessary

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- All figures will be redrawn into *The Lancet Public Health* style by our in-house illustrators
- You will receive a proof from an Assistant Editor. That proof should be corrected and returned within 48 h

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Press release **http://www.thelancet.com/press-room**

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Ombudsperson

For information about what our ombudsperson can and cannot investigate, articles about past ombudspeople, and how to contact the current ombudsperson see https://www.thelancet.com/ombudsperson.

What happens after publication?

Press release

Press releases are issued by *The Lancet* journals' press office for selected content published in our journals. You will be advised in advance if your paper has been selected for press release. *The Lancet* journals' media relations team will contact you with detailed instructions about the embargo for your paper, and will provide a draft press release for your comments ahead of the publication date. If your institute or funder are planning to press release your paper, please let your Assistant Editor know in the first instance, and they will provide you with details on *The Lancet*'s press release policy, embargo dates, and how to receive finalised PDFs of your paper to share with journalists.

Author interview

Your paper may be selected for a podcast. If so, the Web Editor will contact you to arrange a pre recorded interview to discuss your paper. For more information, see **Audio**.

Data storage

Authors may be required to provide the raw data for research papers when they are under review and up to 10 years after publication in *The Lancet Public Health*.

Responsible sharing

The Lancet supports responsible sharing. We recognise that authors want to share their papers and we encourage this. Find out how you can share your paper here.

Appendix 3: MMed Minor Dissertation Guidelines (UCT, FHS)

MMed Minor dissertation guidelines (Excluding Public Health Medicine, Occupational Medicine and Family Medicine)
As approved in PC: September 2017

MMed Part III (minor dissertation)
Guidelines for candidates, supervisors and examiners

The MMed minor dissertation is one of three examination components of the MMed degree. This minor dissertation carries one third of the weight of a full master's dissertation in terms of it's credit weighting, i.e. 60 credits (nominally 600 hours of work). In order to register as a specialist in South Africa, the Health Professions Council of South Africa (HPCSA) requires all specialist trainees who register for training after 1 January 2011 to have completed a relevant research study. The MMed Part III fulfils HPCSA research requirements as well as research requirements by the specialties who include a research project as part of their examination process by the Colleges of Medicine of South Africa (CMSA).

Educational aims

The research project should demonstrate that the student:

- can work independently and ethically under supervision (contributions/assistance must be acknowledged);
- is sufficiently acquainted with the relevant literature to provide appropriate motivation for the research question;
- can plan research or clinical audit (write a protocol), which is approved by an assessor group (delegated by the head of department) and ethics committee where relevant, that contributes new or additional data to the collective knowledge base (the specific data has not been presented as part of other research), but need not produce a unique contribution to the scientific literature;
- uses an appropriate method/design/technique and analysis;
- can adequately present and discuss the significance of the results of the study;
- can present the study in an academically acceptable manner.

Type and scope of the research

The following types of studies are acceptable:

- A clinical audit with or without a repeat data collection cycle;
- A systematic review of the literature on its own **with** extraction and extrapolation of data **OR** a meta-analysis using recognised research methods (eg Cochrane, PRISMA);
- A research study – pro-/retrospective lab or clinical or database review;
- Description and analysis of a case series or cohort, deemed sufficient to supply new knowledge/data, even if only contextual or exploratory;
- Epidemiological research;
- Health service/systems/education research;
- Qualitative research;

Noting:

- *The sample size* can be limited by time (Registrars have limited time allocated/available to collect data and write it up concurrently with their clinical training) - data collection and write up should be possible to complete within two consecutive or cumulative months.

- *Data analysis* may use simple descriptive statistics alone – more advanced analysis can be used, but the student must demonstrate (in the write up) insight into the choice of analysis.

- The above limitations may be associated with the use of descriptive cohort studies based on medical record review; exploratory or pilot studies with small convenience samples; or audits without a repeat data collection cycle to prove quality improvement (QI). Despite limitations, these studies can provide an adequate basis for learning research methodology and can add new data to the collective knowledge base – they may also provide the basis for further publishable work such as a second audit to complete a full QI cycle. As long as these limitations are appropriately acknowledged, these studies should still be acceptable.

- The topic, study design and scope of research may depend on the particular discipline and must be agreed on in consultation with the supervisor(s). The topic must be approved as being suitable for MMed dissertation by the Departmental Research Committee (DRC) and/or a group appointed for this purpose by the head of department.

Submission formats

The dissertation may be presented in one of three formats:

I: Publication-ready format;
II: Published (or accepted for publication) Paper format
III: Monograph format.

As disciplines differ in their requirements, it is important that the format chosen is acceptable to the discipline and appropriate College within the CMSA.

Research protocol

NOTE: All communication from UCT regarding the MMed and the examination process will occur via student UCT e-mailaddress – [student number]@myuct.ac.za. Students must also make sure they have username and password and are able to access the PeopleSoft Student Administration Self Service.

Candidates intending to register for the MMed Part III are required to submit a research protocol for approval to their respective Departmental Research Committees (DRC). The research protocol should briefly summarise the existing knowledge on the topic and justify the research question; it should clearly describe the objectives and methodology and should be structured according to the guidelines in Form FHS015. Write a synopsis according to Form FHS014. Complete a new protocol application form FHS 013. All FHS forms are available at http://www.health.uct.ac.za/fhs/research/humanethics/forms.

The candidate must then obtain approval from the UCT Faculty of Health Sciences Research Ethics Committee (HREC) prior to conducting their research. Studies that involve the audit of clinical records or services also require formal HREC approval. Any primary research that is taking place in a provincial or local authority health facility, such as public sector hospitals or clinics, must also be submitted to the provincial government for approval, after the UCT Research Ethics Committee approval has been obtained. **Approval to access public sector facilities for research is needed for all provincial and local authority facilities.** There are five points where approval for research can be applied for; Groote Schuur Hospital, Red Cross War Memorial Children's Hospital, Tygerberg Hospital), the local authorities and "all other province". Teaching hospitals and the local authorities approve research projects in-house. "All other province" approvals are done via the Directorate: Health Impact Assessment (Sub-directorate: Research) at provincial head office. If research crosses these boundaries, up to five approvals may be needed. Further details can be found at https://www.westerncape.gov.za/general-publication/health-research-approval-process
The Provincial Health Research Committee does not approve research proposals itself, but oversees this approval process by reviewing difficult applications on referral.

The proposal contents should comply with requirements stipulated in Form D1a. This full research protocol together with FHS 013, a copy of the HREC approval letter and completed Forms D1 (Protocol approval), D3 (supervisor appointment form), and D1a must be submitted to the postgraduate administration office, for approval by the Professional Masters Committee (PMC) Chair

and the Board of the Faculty of Health Sciences, prior to commencement of the research. If the title, aims, objectives or any other aspect of the research change following initial submission, an ammendment must be submitted to HREC. **All D-forms are available from the post graduate faculty office or on the UCT Vula Mmed/Mphil site (All registrars and supervisors must be added to this site – your departmental programme manager must send names and email addresses to gregory.doyle@uct.ac.za in order to be added to the site).**

Timelines

Submission of the research protocol for approval should generally be made within the first 12 - 24 months of the registrar programme (this varies between disciplines). Heads of Departments or Divisions should meet with their registrars at least biannually to review progress towards their research project. Unless otherwise stipulated by your Division / Department, the research project should generally be completed by the end of Year 3. For a number of specialties, a dissertation must be submitted before writing the Part II examination. Often the research component of specialist training is only initiated after successful completion of the Part I examination.

Supervisors

The supervisor must: have research experience, ideally a Master's degree, equivalent (eg appropriate publications), or higher; be able relate to the candidate's research project; be available for regular discussion and advice; and be someone with whom the candidate can develop a good working relationship. If the primary supervisor does not have adequate experience, then a secondary supervisor who has appropriate experience will need to be appointed in addition. **Supervisors who have not had extensive experience supervising are required to attend a supervisor training course.** Where specialised equipment and/or laboratory work is required for the study, the supervisor should assist in facilitating access to appropriate facilities.

The primary supervisor may be based outside the candidate's home department, faculty or university. In such a case, a member of UCT staff will also be required as co-supervisor in addition to the primary supervisor, to serve as a guide and link to UCT faculty and discipline-specific procedures. Primary supervisors retain responsibilities to the candidate and the university until the dissertation process is complete. In addition to the forms mentioned above, the supervisor and student must complete D2a which describes the contractual memorandum of agreement (MOU) between supervisor and student regarding the minor dissertation.

The dissertation

Submission of all formats of the dissertation should include the following:

The title page should contain the candidate's name, dissertation title and the name of the university. It must also state the degree, e.g. Master of Medicine (MMed) in, Medicine, Paediatrics, etc.

The Table of contents

The declaration page should include a statement to the effect that the research reported is based on independent work performed by the candidate and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to any other university. It must also state that this work has not been reported or published *prior to registration* for the abovementioned degree.

The abstract should summarise the study rationale, methods, results, discussion and conclusion in fewer than 500 words.

Acknowledgements and contributions. This section should acknowledge and describe the support or input from supervisors and other co-author(s) if applicable. In a dissertation derived from work started by others, e.g. analysis of data collected for another project, the origin of the data and the candidate's contribution must be clearly stated. The candidate must complete the dissertation after his/her registration for the degree and therefore under supervision. In a published manuscript from a

multi-authored project, the candidate must be first author.

List of Tables
List of Figures
Abbreviations

The remainder of the dissertation must be presented in one of three formats:
I: Publication-ready format;
II: Published (or accepted for publication) paper format
II: Monograph format.

I: Publication format

The dissertation must include a manuscript in publication-ready format. The body of the dissertation must be structured as follows:

Chapter 1: Introduction and Literature review

This section must give the background and context of the research question and must include a review of the literature relevant to the subject matter and methods of the study. The review should summarise and interpret the existing knowledge in the field with relevance to the research setting and should identify knowledge gaps and hence the rationale for the dissertation. This chapter should end with a clear statement reflecting the aims and objectives of the research reported in the publication-ready manuscript. References quoted in this chapter should appear at the end of the chapter, not at the end of the thesis. This chapter should be between 2 000 and 5 000 words.

Chapter 2: Publication-ready Manuscript

This chapter must be presented in the form of a manuscript of an article for a named peer reviewed journal, meeting all the requirements of the “Instructions for Authors” of that journal, including the word count and referencing style. Unless specially motivated, the journal chosen should allow for at least 2000 words (not more than 5000 words) excluding abstract, tables, figures and references. The “Instructions to Authors” of the journal must be appended. The co-authors should be listed in the appropriate order, and each of their contributions to the manuscript stated. The journal chosen for publication must be appropriate to the subject matter of the dissertation and listed in the citation index of the Institute for Scientific Information (ISI) or accredited by the Department of Education http://www.lib.uct.ac.za/medical/index.php?html=/libs/accredjnls.htm&libid=24); *other journals with similar review processes, particularly South African journals may be acceptable if permission is obtained from the PMC Chair after appropriate motivation is provided.*

Note 1: In this format, the candidate need not have submitted the article for publication, nor is the acceptance of the article for publication a requirement for passing the degree. However, the norm is to publish the study with the supervisor(s) as co-author(s), and candidates are strongly encouraged to submit their manuscript for publication after examination of the minor dissertation.

NOTE 2: IF THE RESEARCH IS A FULL SYSTEMATIC REVIEW, THERE IS NO NEED FOR A SEPARATE CHAPTER 1 – THE REVIEW SHULD BE SUBMITTED AS ONE CHAPTER.

Appendices

Append all supporting documents including:

- Questionnaire/data capture instrument(s)
- Consent forms and any related participant information sheets
- Technical appendices, including, if considered necessary, any additional tables not included in the main manuscript for the examiner to have available. These should be accompanied by a brief narrative.
- Official Ethics approval letter from the Faculty Research Ethics Committee (except for a full systematic review) and any other approvals required (e.g. Provincial Government).
- Instructions to Authors of the chosen journal

II: Published (or accepted for publication) paper format

A manuscript that has already been published or accepted for publication in a journal that is listed in the citation index of the Institute for Scientific Information (ISI) or accredited by the Department of Education (*other journals with similar review processes, particularly South African journals may be acceptable if permission is obtained from the PMC Chair after appropriate motivation is provided),* may be submitted **if the candidate was the first author, the candidate's contribution was completed under supervision during his/her registration for the degree, and the paper is in line with the educational aims and scope of research described in the first part of this document.**

The dissertation must be submitted in similar format to the publication-ready format – the only differences being: a separate literature review is not required; the accepted publication is submitted as a single chapter following the same format as described above under "Chapter 2"; and the reviewer comments from the journal should be attached as an appendix. *When this format is used, the contributions of all the authors must be very clearly stated under a sub-heading in the "Acknowledgments and contributions" section in the first part of the thesis.*

III: Standard monograph format

Some disciplines and constituent Colleges of the Colleges of Medicine of South Africa require a standard monograph presented in a comprehensive and scholarly style to be submitted as part of the examination. The length is typically 16 000 to 20 000 words in length, but may vary. If the length is not stipulated, the monograph should be 6000 – 16000 words, excluding references and tables.

A recommended structure for the body of the dissertation is as follows;

Chapter 1: Introduction and Literature review
(see guidelines above)

Chapter 2: Methods
Material and methods of the study must be fully described and factually presented.

Chapter 3: Results

Chapter 4: Discussion and conclusions

Appendices

(see guidelines above - omit the instructions to authors)

Language and writing

Clear, grammatically correct English is essential.

Supervisors may assist candidates in developing scientific communication skills but they are not required to do detailed editing or correction of spelling, grammar, or style. Training in scientific writing is available at the Health sciences Writing Centre. Registrars need to make an appointment via the website: http://www.writingcentre.uct.ac.za/about/healthsciences

Candidates should refer to Form D4, Guidelines on the Layout and Style of the Dissertation or Thesis. As long as the dissertation is readable and internally consistent, any of a number of styles are acceptable. For a publication-ready manuscript, references should be formatted according to the instructions to authors for the journal selected, and candidates should use the same style throughout their dissertation. For a monograph format manuscript, the Harvard style for referencing is

recommended, but not compulsory. For reference management, Refworks or Endnote can be downloaded from the ICTS or UCT library website.

Candidates should look at previous examples of Master's dissertations in the library. Master's dissertations are available in the Health Sciences Library. A search will need to be done to obtain a list of titles and authors. This search can be done using search words (e.g. dissertation, health, health sciences, etc.). The librarian can be asked for assistance. Some of these dissertations are available via: http://www.medical.lib.uct.ac.za/hsl/theses-dissertations

Annual approval

After 1 year, apply to HREC for continuing approval Form FHS016 (for intervention study) or FHS017 (for record review) or submit a study closure form, FHS010, if the study is complete. If registration in MMED III is required for more than one year then complete form D2(b) and submit to Post Grad Office when re-registering.

Submission of dissertations

On completion, the dissertation and a Turn-it-in originality report must be submitted to the Faculty Postgraduate Office. The candidate should inform the Faculty Officer one month in advance of the intention to submit, using Form D8 (Intention to submit) online with PeopleSoft system and should subsequently submit their dissertation using the same system – **guidelines for this process and the use of Turn-it-in are on the Mmed/Mphil Vula Website and detailed guidelines are also available in the UCT student help document: " Digital submission of a thesis/dissertation for examination and library access"**. This document is available online at http://www.uct.ac.za/usr/current_students/postgrad/digital_upload_dissertations_theses.pdf

Supervisors will be requested by the Faculty Postgraduate Officer to submit a letter supporting submission, and clearly specifying whether the format of submission, so that the appropriate instructions are sent to the examiners. This letter should be supplied by the primary supervisor. If this supervisor is external, the internal supervisor must be kept informed at every stage of the process.

Please note: In the event that any of your external examiners request a hard copy of your dissertation/ thesis, you will be required to supply this. The Faculty office will inform you should this be necessary.

Specific submission requirements may be set by individual disciplines or constituent Colleges of the CMSA, and registrars are obliged to ensure that their research projects and dissertations meet these specific requirements. UCT Dissertation submission deadlines:

1. March 15th for June graduation
2. August 15th for December graduation

Note on fees: To avoid attracting fees, dissertations need to be submitted before the beginning of the first quarter (first day of academic year), and before the start of the second semester (mid July) to qualify for a 50% fee rebate.

Examiners

The full dissertation will be submitted for examination through the Postgraduate Office to two examiners (nominated by the supervisors and HOD) – at least one examiner must be external to UCT. An internal examiner must not be involved in the research.

It is the supervisors' responsibility to submit names of three potential examiners (or two examiners who have already agreed to examine pending approval of the Post Graduate Office) to the Faculty Officer when the candidate is ready to submit. Appointment of examiners from outside South Africa is encouraged. These nominations need to be approved by the Deputy Dean: Postgraduate Affairs on behalf of the Faculty Board and submitted to the Faculty Board for ratification via a Dean's Circular.

Details required for each examiner are: academic qualifications, postal and/or physical address, telephone and fax numbers and e-mail address, and one paragraph description of their standing in the relevant field (drawn from their CV if need be). The examiners will be sent a copy of these guidelines as well as a guideline for marking. *The candidate may not be informed of the identity of the examiners.* After the outcome of the minor dissertation has been finalised, the examiners' identities are made known if the examiners have indicated that they do not object to this.

Publication agreement

The university has a moral responsibilty to publish all research undertaken when publication is stated as an anticipated output. A candidate who fails to submit a manuscript to a journal for publication within 1 year of submission of their thesis, must accept that their supervisor(s) are entitled to publish their data on their behalf, with the student as co-author - this should be stated in the memorandum of understanding.