THE PREVALENCE OF SUBSTANCE USE IN ANAESTHESIA PRACTITIONERS IN SOUTH AFRICA

Master of Medicine in Anaesthesia

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DECLARATION

I, *Justine Van der Westhuizen*, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

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Date: ……15/02/2020…….

Abstract:

Introduction:

Substance abuse has twice the mortality in United States anaesthesia- than non-anaesthesia residents. Since no data exist, the primary objective of this cross-sectional study was to establish the prevalence of substance use in South African anaesthesia practitioners. Secondary objectives were to compare the prevalence in male and female practitioners, and in private- and state practice anaesthetists. Years of experience and level of training were explored as possible risk factors for hazardous or harmful use.

Method:

Participants completed a self-administered, validated WHO questionnaire, run for ten days surrounding the 2018 South African Society of Anaesthesiologists (SASA) congress. All doctors practicing anaesthesia in South Africa were eligible. Recruitment was via an email link sent to all SASA members, as well as a web-based link at the congress.

Results:

A total of 1961 SASA members and 113 non-members (anaesthesiologists, registrars and non-specialists) were invited to participate (total 2074). There were 434 responses (response rate 20.9%, margin of error 4.18%); 364 were suitable for analysis. The most commonly lifetime-used substances were alcohol (92.8%), tobacco (42.3%), cannabis (34.7%), and sedatives (34.4%). Questionnaire scores defined low-, medium- and high-risk categories according to substance use during the previous 3 months. Sedative (12.6%) and alcohol (12.1%) users were deemed to be at moderate risk. The prevalence of opioid use was 1.9% (n=7). Prevalence of substance use was similar in male and female practitioners, as well as in those working in private practice or in state hospitals.

Conclusion:

The prevalence of current use of alcohol and sedatives is of major concern. A significant proportion of respondents were assessed to be at moderate risk of hazardous or harmful substance use. Gender and practice setting have little impact on substance use. Wellness efforts should be aimed at all anaesthesia practitioners in South Africa.

Acknowledgments and Contributions:

1. **J. Van der Westhuizen, Department of Anaesthesia and Perioperative Medicine, University of Cape Town, South Africa:** First author and Mmed candidate. The protocol, data collection and write-up of final manuscript were primarily done by candidate, under supervision.

2. **F. Roodt, Department of Anaesthesia, George Regional Hospital**: Supervised the writing of the protocol and data collection.

3. **R. Dyer, Department of Anaesthesia and Perioperative Medicine, University of Cape Town, South Africa**: Assisted with writing and editing of write-up of final manuscript, as well as journal submission.

4. **M. Nejthardt, Department of Anaesthesia and Perioperative Medicine, University of Cape Town, South Africa:** Supervised the writing of the protocol and data collection, and final manuscript.

5. **T. Esterhuizen, Division of Epidemiology and Biostatistics, Stellenbosch University, South Africa:** Assisted with statistical analysis of data

6. **M. Flint, Department of Anaesthesia and Perioperative Medicine, University of Cape Town, South Africa**: Supervised writing of protocol and write-up.

7. **D. Van Straaten, Research and Development Bioinformatician, Safe Surgery South Africa:** Assisted with data collection process.

8. **P. Magni, MBChB, FC Psych, Private Practice, Cape Town, South Africa:** Supervised the writing of the protocol.

Article published in South African Journal of Anaesthesia under the following citation:

Van der Westhuizen J, Roodt F, Nejthardt M, Esterhuizen T, Flint M, Van Straaten D, Magni P. The prevalence of substance use in anaesthesia practitioners in South Africa. Southern African Journal of Anaesthesia and Analgesia. 2019;25(6):14-20.

Tables:

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Supplementary Files:

Abbreviations:

All abbreviations used are listed within article on first use.

Chapter 1: The prevalence of substance use in anaesthesia practitioners in South Africa

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Introduction

Substance abuse is linked to a more than three times higher incidence of suicide in young male anaesthesia practitioners, when compared with other physicians.[1] The prevalence of

this behaviour should therefore be considered when analysing the complex topic of wellness in anaesthesiologists.

In the United States, anaesthesiology residents are twice as likely to die from chemical dependency abuse than non-anaesthesia residents, [2] and are over-represented by a factor of seven at rehabilitation facilities. [2] The health care system in South Africa is unique and exists as a dichotomy of private and state care, each with its own unique challenges and stressors. No data exists for substance use in South African anaesthesia practitioners, either in private or state practice.

The primary objective of this cross-sectional study was to describe the prevalence of substance use in anaesthesia practitioners in South Africa, in order to establish baseline data. The prevalence of lifetime- and of current use, defined as use within the previous three months, was determined. For this the purpose, a validated WHO questionnaire was used, which defines low-, moderate-, and high-risk categories for addiction to a substance.

The secondary objectives were to compare the prevalence of substance use in male and female practitioners, and in private- and state practice. The number of years spent in anaesthesia practice was also explored as a possible risk factor for addiction. Finally, a comparison was made of the prevalence in non-specialists, training specialists (registrars), and specialist anaesthesiologists. We postulated that the incidence of substance use would be similar in all groups.

Methods

This study was conducted as a self-administered questionnaire, with closed-ended questions, and was only made available online, i.e. in a digital format. Approval was obtained from the Human Research Ethics Committee of the University of Cape Town (HREC 190/2018) prior to distribution. The questionnaire used was available from the World Health Organization, namely the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). It was developed by the WHO in a primary health care setting, in collaboration with an international team of substance abuse researchers, and validated in seven

countries. [3] In the present study, the questionnaire was modified to include demographic data (Supplementary file 1).

The questionnaire screens for use of tobacco products, alcohol, cannabis, cocaine, amphetamine-type stimulants, sedatives, hallucinogenics, inhalants, opioids and 'other' drugs. Examples of each category of substance are listed in the questionnaire. These were altered slightly for the South African context. ASSIST identifies lifetime use (i.e. use of the substance at any time in a practitioner's life), as well as use in the previous three months. A risk score (low-, moderate-, or high risk) is then determined for each category of substance, based only upon use in the previous three months.

The questionnaire is comprised of eight questions: question one examines lifetime use; question two examines frequency of use in the past three months; question three asks about urge or desire to use a substance; question four explores the frequency of social, legal, health or financial problems related to drug use; question five examines interference with responsibilities; question six asks whether anyone has ever expressed concern about usage; question seven asks about any attempt to stop or reduce substance use; and question eight asks about injection of substances. In addition to the physical use of a substance, the urge to use a substance (question three) has been postulated to be consistent with more frequent use, a previous problem with the substance, or a stronger potential for addiction.

Scoring is done per category by adding the scores of questions two through seven. Question eight is not included in the scoring but is used as an indicator of risk. For all substances apart from alcohol, a score 0-3 indicates low risk, 4-26 indicates moderate risk ("likely to indicate hazardous or harmful substance use"), and greater than 27 high risk ("likely to indicate substance dependence"). Low risk alcohol use scores 0-10, moderate risk 11-26, and high risk greater than 27. ASSIST recommends no treatment for low risk scores, a brief intervention for moderate risk users, and specialist referral for high risk users. [4] Since our questionnaire was administered anonymously, no intervention could be provided. However, at the conclusion of the questionnaire, the respondent could see their risk score and

category with a brief explanation, as calculated online. Contact details for drug and alcohol help lines, as well as the SASA Wellness team, were provided.
The questionnaire was run for ten days surrounding the 2018 South African Society of Anaesthesiologists (SASA) congress. Participants were recruited via a public link made available on email sent to all SASA members before the congress, as well as electronic distribution via a web-based link at the congress, on social media. Although not specifically validated for self-completion, it was felt that this method would better assure anonymity. The email was sent out once, with one follow-up/reminder five days later. The link to the questionnaire was then closed after ten days, allowing no further recruitment.

Data was captured using "REDCap", which is a secure web application for building and managing online surveys and databases, specifically designed for research studies. The REDCap system is run by SAFE SURGERY and ANSA.

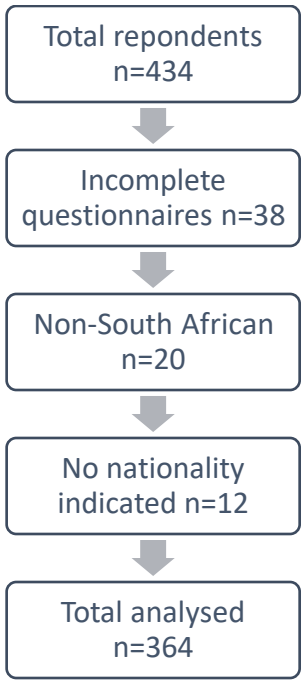
All anaesthesia practitioners who were doctors practicing in South Africa, were eligible. Specialist-, trainee-, and non-specialist Anaesthesiologists were included. The SASA email database was used. The demographic data distinguished between state- versus private practice. Work environment, drug handling, and stressors were postulated to differ in the two settings, which could influence substance use patterns. The prevalence of substance use was postulated to vary according to the length of exposure to both work environment stress, as well as access to drugs. Therefore, the number of years in practice was also captured. The prevalence of substance use in male and female practitioners was also recorded.

Demographic variables were all categorical and were summarised using frequency tables and bar charts. ASSIST scores were categorised as defined in the questionnaire manual, and summarised overall and per stratification variable using frequency tables and percentages. Where comparisons of proportions between groups were possible, Pearson's chi square tests or Fisher's exact tests were conducted, as appropriate. If more than 25% of expected cell counts were less than five, Fisher's exact p values were reported. Incomplete responses were treated as voluntary withdrawal and were discarded from the data set. A p value <0.05 was considered statistically significant. IBM SPSS version 25 was used to analyse the data.

Results

Participants eligible for the study were doctors currently practicing anaesthesia in South Africa. This included specialists, trainee specialists and non-specialists. A total of 1961 SASA members received the email link. In addition, 113 non-members were exposed to the link, via social media and during attendance of sessions, at the congress. Therefore, the total number of potential respondents was 2074. The number of respondents was 434, which gave a response rate of 20.9%, and a margin of error of 4.18%. Incomplete questionnaires (n=38) and non-South African practitioners were excluded (n=20), as well as respondents who did not indicate their nationality (n=12). The total number of analysed responses was 364, as shown in Figure 1. There were 168 female respondents (46.7%) and 192 males (53.3%).

Figure 1



Respondents were stratified according to qualification: specialists (71.7%), trainee specialists (18.4%), and general practitioners or medical officers (9.9%) practicing anaesthesia. Forty four percent of the respondents had had more than 15 years of experience in anaesthesia, 16.2% 10-15 years, 25.5% 5-10 years, and 14.3% less than five

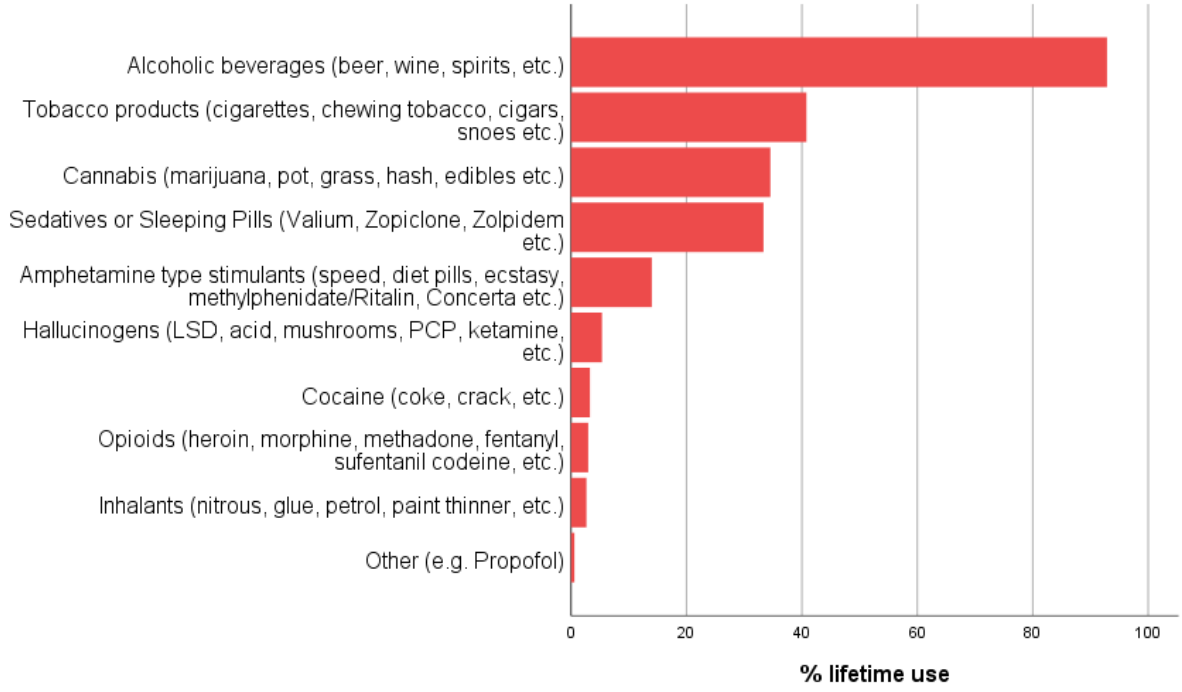
years. Fifty five percent of respondents were from private practice and 45% from state hospitals.

The lifetime use of all agents investigated, in the order listed in the questionnaire, is shown in Table I. Figure 2 is a histogram summarising this information.

Table I – Lifetime use of agents

	N/364	% of users of each agent (CI)
Tobacco products (cigarettes, chewing tobacco, cigars, snus etc.)	153	42.3% (37.3-47.4)
Alcoholic beverages (beer, wine, spirits, etc.)	336	92.8% (89.7-95.1)
Cannabis (marijuana, pot, grass, hash, edibles etc.)	123	34.7% (30.0-39.8)
Cocaine (coke, crack, etc.)	12	3.4% (2.0-5.8)
Amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	53	15.1% (11.7-19.2)
Inhalants (nitrous, glue, petrol, paint thinner, etc.)	9	2.6% (1.4-4.8)
Sedatives or Sleeping Pills (Valium, Zopiclone, Zolpidem etc.)	123	34.4% (29.6-39.4)
Hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)	19	5.4% (3.5-8.3)
Opioids (heroin, morphine, methadone, fentanyl, sufentanil codeine, etc.)	12	3.4% (2.0-5.9)
Other (e.g. Propofol)	2	0.6% (0.2-2.0)

Figure 2 – Lifetime use of substances



A detailed description of substances used in the previous three months, shown as a percentage of users of the individual agent, as well as of the total sample, appears in Table II. Only alcohol fell into the high-risk category, with 1% of users displaying high risk behaviour (n=3). Moderate risk usage was highest for sedatives (12.6%) and alcohol (12.1%). The most commonly used substance was alcohol (n=310), followed by sedatives (n=74).

Table II – Substances used in the previous three months

	Overall prevalence (%; CI) N=364	Low risk			Moderate risk			High risk		
		N	% of users of each agent	% of total sample	N	% of users of each agent	% of total sample	N	% of users of each agent	% of total sample
Tobacco	29 (8.0; 5.6 to 11.2)	4	13.8 (5.5 to 30.6)	1.1 (0.4 to 2.8)	25	86.2	6.9 (4.7 to 9.9)	0	0.0	0.0 (0 to 1.0)
Alcohol	310 (85.1; 81.1 to 88.4)	263	84.8 (80.4 to 88.4)	72.3 (67.4 to 76.6)	44	14.2	12.1 (9.1 to 15.8)	3	1.0	0.8 (0.3 to 2.4)
Cannabis	8 (2.2; 1.1 to 4.3)	8	100.0 (67.6 to100)	2.2 (1.1 to 4.3)	0	0.0	0.0 (0 to 1.0)	0	0.0	0.0
Cocaine	1 (0.3; 0 to 1.5)	1	100.0 (20.7 to 100)	0.3 (0 to 1.5)	0	0.0	0.0 (0 to 1.0)	0	0.0	0.0

Amph *	12 (3.3; 1.9 to 5.7)	8	66.7 (39.1 to 86.2)	2.2 (1.1 to 4.3)	4	33.3	1.1 (0.4 to 2.8)	0	0.0	0.0
Sedatives	74 (20.3; 16.5 to 24.8)	28	37.8 (27.6 to 49.2)	7.7 (5.4 to 10.9)	46	62.2	12.6 (9.6 to 16.4)	0	0.0	0.0
Opioids	7 (1.9; 0.9 to 3.9)	4	57.1 (25.0 to 84.2)	1.1 (0.4 to 2.8)	3	42.9	0.8 (0.3 to 2.4)	0	0.0	0.0

*amph = amphetamine

The overall prevalence of urge to use a substance in practitioners using a particular agent, is shown in Table III. There was a statistically significantly higher prevalence of urge to use alcohol in those who had been in practice 5-10 years, when compared with all other groupings of years of experience (p=0.002). Females were more likely to experience an urge to use alcohol than males (p=0.010). The urge to use sedatives was also significantly higher in non-specialists than in specialists (p=0.016). Detailed data is available in Supplementary file 2.

Table III – Overall prevalence of urge

	Urge to use substance (N) % of each agent, (CI)
Tobacco	25
	86.2% (69.4 to 94.5)
Alcohol	160
	50.5% (45.0 to 55.9)
Cannabis	0
	0.0% (0 to 32.4)
Cocaine	0
	0.0% (0 to 79.3)
Amphetamine	3
	25.0% (8.9 to 53.2)
Sedative	41
	55.4% (44.1 to 66.2)
Opioids	2
	28.6% (8.2 to 64.1)

% = percentage of current users of the individual substance experiencing an urge to use the substance

With respect to secondary outcomes, there was no statistically significant difference between the prevalence of male and female users of any substance. There were also no

differences between the proportions of practitioners in private- versus state hospitals, using any of the substances, or in substance use according to number of years of experience.

Discussion

This study examined the prevalence of lifetime- and previous three-month usage of various potentially addictive substances, by a total of 364 male and female anaesthesia practitioners of varying years of experience. A WHO-validated questionnaire, ASSIST, was used, and practitioners categorised as low-, moderate-, or high risk.

With respect to lifetime use, the five most commonly used agents were alcohol, tobacco products, cannabis, sedatives and amphetamine type stimulants. Risk categories were assigned on the basis of questionnaire scores for substance use during the previous three months. Most commonly used were alcohol, sedatives, tobacco, and amphetamines. The majority of alcohol users were low risk. Practitioners at moderate risk used sedatives, alcohol, tobacco, and amphetamines. The knowledge of the latter scores would make it possible for these practitioners to self-refer for a brief intervention. Alcohol was the only substances with any high-risk use (n=3). These practitioners could self-refer for specialist treatment.

The prevalence of opioid use was low (n=7), although this is likely an underestimate. Opioid dependence is particularly devastating in anaesthesia, and re-integration into the workplace is problematic. [1] The United States is currently battling a worsening opioid crisis, [5] particularly fentanyl use. It is possible that this international trend may impact South Africa in the next few years. Our baseline data may provide valuable information to display a change in usage patterns within the profession in the future, if indeed opioid use becomes more common.

The finding of an increased urge to use a substance, in practitioners of 5-10 years' experience, in women, and on non-specialists, may be helpful in identifying psychological dependence, and is particularly associated with the progression to high risk use. [4]

With respect to secondary outcomes, it was noteworthy that there was a similar prevalence of substance use in male and female practitioners, and in those working in the private practice or state hospital environment. There was inadequate statistical power to establish the relationship between years of experience, or the association between the level of qualification of the practitioner, and substance use.

There are no data available to provide a comparison of the incidence of substance use in South African anaesthesia practitioners and those in other countries. A retrospective survey conducted in 2002 found the prevalence of drug abuse or dependence in 133 anaesthesiology training programmes in the USA, to be 1.0-1.6%, with a higher prevalence in trainee specialist anaesthesiologists. A national survey of anaesthesiologists in France in 2004 [6] found a prevalence of 59.0% for alcohol use, 41.0% for tranquillisers and hypnotics, 6.3% for cannabis, 5.5% for opiates and 1.9% for stimulants. Our data showed a higher overall prevalence of use of alcohol and stimulants, and less cannabis and opioid use.

Amongst the general population, substance use disorders have a higher prevalence in South Africa than in European countries, with a lifetime usage of 13.3%. [7] Although anaesthesia practitioners are not representative of the South African population with respect to age, gender, and average income, we also quote for interest the known prevalence for alcohol and tobacco use in the general population. The prevalence of lifetime use of alcohol, the most commonly misused substance in South Africa, is 25%. Fourteen percent of the population has lifetime diagnosis of alcohol abuse and/or dependence. [7] This is similar to the prevalence found in our questionnaire of 12.9% of moderate- and high-risk users amongst anaesthesia practitioners, and comparable to developed countries. Tobacco use was found to be lower than in the general population; 8% versus 17.6% respectively. [8]

There are several limitations to this study. The response rate for the survey was low (20.9%). Although the margin of error of 4.18% is acceptable, the sample was not randomly- but rather self-selected, and the sensitive nature of the electronic survey is likely to have introduced bias, and an under-estimate of the prevalence of substance use. It is theoretically plausible that respondents to a sensitive topic which includes substance abuse, particularly if the information could potentially result in loss of employment or license to

practice, would not be truthful in their responses to a detailed questionnaire. However, there is evidence that there is little response bias if the questionnaire is anonymous, [9] and the risk of non-response to an emailed link should be offset against the benefit of anonymity.

Our study could have been biased towards obtaining information from physicians with access to the internet, smart phone applications, Twitter accounts, and an active e-mail address. However, this was not expected to be a significant limitation, considering the general easy accessibility and widespread use of email and social media. Response rates to emailed or web-based surveys are comparable to a mail hard copy survey[10]

The survey did not include doses of drugs which had been appropriately prescribed by a physician for a valid diagnosis, that might be used in excessive doses. However, based upon published literature, drugs prescribed and accessed via a treating physician, as opposed to self-prescription, are unlikely to be a major source of abuse. These therapeutic doses were therefore excluded by the questionnaire, to simplify the data collected.

A sign of potential drug abuse in the workplace is a willingness to remain at work, to take extra shifts or to stay late (in order to increase access to drugs). [11] It was therefore a concern that running the survey during a congress might miss the users who had elected to stay at work and forgo the congress in order to improve access to drugs. This was addressed by also emailing the survey to SASA members.

The ASSIST questionnaire classifies drugs in broad categories. It is therefore possible that the respondents may not have remembered or listed a substance that was not included in the list of examples. As many as possible common examples were listed, without making the survey too detailed. While this research aimed to report the prevalence of substance use, it did not explore causation. This is a possible area for future research.

Conclusion

This self-administered WHO questionnaire shows that the prevalence of lifetime use of both alcohol and sedatives by South African anaesthesia practitioners is of major concern. The overall use of alcohol exceeds that of the South African general population, and of anaesthesia practitioners internationally. A significant proportion of practitioners were assessed according to their previous 3 months' use to be at moderate risk, implying the likelihood of hazardous or harmful substance use. Although opioid use was low compared with other substances, the 1.1% prevalence may be an underestimate. Factors such as gender and practice setting appear to have little impact on substance use patterns. It is therefore our recommendation that wellness efforts be aimed at all practitioners of anaesthesia. The impact on the lives of substances users, their families, patients and colleagues is often devastating. This study may be regarded as the first step towards addressing the problem, namely the acknowledgement that it exists.

Other information

I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper.

This research was endorsed by the SASA wellness team. Many thanks for their encouragement.

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Supplementary File 1 – Questionnaire

Incidence of Substance Abuse Amongst Anaesthetists

Dear colleague

Thank you for participating in this important MMed study looking at the Incidence of Substance Abuse amongst Anaesthetists in South Africa. There is limited international data on this subject, and little to no data on South African anaesthetists.

Many of us know, or have known, a colleague who is suffering from substance addiction. Sadly, substance addiction can have a huge negative impact on patient care, work attendance and performance, careers, family life, and in some cases, even results in death due to suicide or overdose.

It is therefore vital that, as a fraternity, we identify the extent of this problem within our context and aim to help and support those who are suffering from its grip. Without fully appreciating the extent, however, we cannot adequately provide care and assistance to those who are suffering.

By continuing with this survey, you are consenting to have your responses form part of a data set which will be used to describe the incidence of substance use amongst anaesthetists in South Africa. Your responses will be completely anonymous. The questionnaire is built using REDCap, a trusted research resource. All responses are automatically disconnected from the respondent, and there is no way to trace the data back to you. The data set itself is also password protected to ensure data protection.

The survey is comprised of 13 questions or less. It should take you no longer than 5-10 minutes to complete, depending on your responses. This research is supported by the Wellness Committee of SASA.

To reiterate, there is absolutely no way to link your responses back to you, even if you have received this questionnaire via email. Absolute anonymity is ensured.

We urge you to be honest in your responses. Without accurate data, future interventions will be hindered.

Thank you for your participation.

Dr Justine Van der Westhuizen (MMEd Candidate)

Co-Investigators : Dr Francois Roodt, Dr Marcin Nejthardt, Dr Paul Magni

Department of Anaesthesia, University of Cape Town

Do you currently practice in South Africa? ◯ Yes ◯ No

What is your current registration/qualification in anaesthesia?

◯ Specialist Anaesthetist
◯ Anaesthetic Registrar
◯ GP Anaesthetist/Medical Officer

How long have you been practicing anaesthesia?

◯ < 5 years
◯ 5 - 10 years
◯ 10 - 15 years
◯ > 15 years

What best describes your current anaesthetic practice?

◯ Private practice only
◯ State practice only
◯ Majority state practice with some private work (10 hours or less per week)
◯ Majority private practice with some state work (10 hours or less per week)

Gender ◯ Male ◯ Female

In your life, which of the following substances have you ever used? (NON-MEDICAL USE ONLY, including self-prescribed)

	No	Yes
Tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	○	
Alcoholic beverages (beer, wine, spirits, etc.)	○	
Cannabis (marijuana, pot, grass, hash, edibles etc.)	○	
Cocaine (coke, crack, etc.)	○	○
Amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	○	
Inhalants (nitrous, glue, petrol, paint thinner, etc.)	○	
Sedatives or Sleeping Pills (Valium, Zopiclone, Zolpidem etc.)	○	
Hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)	○	○
Opioids (heroin, morphine, methadone, fentanyl, sufentanil codeine, etc.)	○	
Other (e.g. Propofol)	○	○

If other, please specify _____

In the past three months, how often have you used the substances you mentioned?

	Never	Once or twice	Weekly	Daily or almost daily
Tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	○	○	○	
Alcoholic beverages (beer, wine, spirits, etc.)	○	○	○	
Cannabis (marijuana, pot, grass, hash, edibles etc.)	○	○	○	
Cocaine (coke, crack, etc.)	○	○	○	○
Amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	○	○	○	
Inhalants (nitrous, glue, petrol, paint thinner, etc.)	○	○	○	
Sedatives or Sleeping Pills (Valium, Zopiclone, Zolpidem etc.)	○	○	○	
Hallucinogens (LSD, acid, mushrooms, PCP, Ketamine, etc.)	○	○	○	○
Opioids (heroin, morphine, methadone, fentanil, sufentanil, codeine, etc.)	○	○	○	○
Other (e.g. Propofol)	○	○	○	○

If other, please specify _____

Tobacco	
During the past three months, how often have you had a strong desire or urge to use tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of the following led to health, social, legal or financial problems? tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Alcohol	
During the past three months, how often have you had a strong desire or urge to use alcoholic beverages (beer, wine, spirits, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of alcoholic beverages (beer, wine, spirits, etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of alcoholic beverages (beer, wine, spirits, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Cannabis	
During the past three months, how often have you had a strong desire or urge to use cannabis (marijuana, pot, grass, hash, edibles etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of cannabis (marijuana, pot, grass, hash, edibles etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of cannabis (marijuana, pot, grass, hash, edibles etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Cocaine	
During the past three months, how often have you had a strong desire or urge to use cocaine (coke, crack, etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of cocaine (coke, crack, etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of cocaine (coke, crack, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Amphetamines	
During the past three months, how often have you had a strong desire or urge to use amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/ Ritalin, Concerta etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/ Ritalin, Concerta etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Inhalants	
During the past three months, how often have you had a strong desire or urge to use inhalants (nitrous, glue, petrol, paint thinner, etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of inhalants (nitrous, glue, petrol, paint thinner, etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of inhalants (nitrous, glue, petrol, paint thinner, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Sedatives or sleeping pills	
During the past three months, how often have you had a strong desire or urge to use sedatives or sleeping pills (Valium, Zopiclone, Zolpidem, etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of sedatives or sleeping pills (Valium, Zopiclone, Zolpidem etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of sedatives or sleeping pills (Valium, Zopiclone, Zolpidem, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Hallucinogens	
During the past three months, how often have you had a strong desire or urge to use hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of hallucinogens (LSD, acid,mushrooms, PCP, ketamine, etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Opioids	
During the past three months, how often have you had a strong desire or urge to use opioids (heroin, morphine, methadone, fentanyl, sufentanil codeine, etc.)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often has your use of opioids (heroin, morphine, methadone, fentanyl, sufentanil, codeine, etc.) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
During the past three months, how often have you failed to do what was normally expected of you because of your use of opioids (heroin, morphine, methadone, fentanyl, sufentanil, codeine, etc.)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily

Other	
During the past three months, how often have you had a strong desire or urge to use other drugs (e.g. Propofol)	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
If other, please specify	_____
During the past three months, how often has your use of other drugs (e.g. Propofol) led to health, social, legal or financial problems?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
If other, please specify	_____
During the past three months, how often have you failed to do what was normally expected of you because of your use of other drugs (e.g. Propofol)?	◯ Never ◯ Once or twice ◯ Monthly ◯ Weekly ◯ Daily or almost daily
If other, please specify	_____

Has a friend or relative or anyone else ever expressed concerns about your use of the following?	
Tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Alcoholic beverages (beer, wine, spirits, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Cannabis (marijuana, pot, grass, hash, edibles etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Cocaine (coke, crack, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Inhalants (nitrous, glue, petrol, paint thinner, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Sedatives or Sleeping Pills (Valium, Zopiclone, Zolpidem etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Opioids (heroin, morphine, methadone, fentanyl, sufentanil, codeine, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Other (e.g. Propofol)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
If other, please specify	_____

Have you ever tried and failed to control, cut down or stop using the following?	
Tobacco products (cigarettes, chewing tobacco, cigars, snoes etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Alcoholic beverages (beer, wine, spirits, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Cannabis (marijuana, pot, grass, hash, edibles etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Cocaine (coke, crack, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Amphetamine type stimulants (speed, diet pills, ecstasy, methylphenidate/Ritalin, Concerta etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Inhalants (nitrous, glue, petrol, paint thinner, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Sedatives or Sleeping Pills (Valium, Zopiclone, Zolpidem etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Hallucinogens (LSD, acid, mushrooms, PCP, ketamine, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Opioids (heroin, morphine, methadone, fentanyl, sufentanil, codeine, etc.)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
Other (e.g. Propofol)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
If other, please specify	_____

Injecting drugs	
Have you ever used any drug by injection? (NON-MEDICAL USE ONLY)	◯ No, Never ◯ Yes, in the past 3 months ◯ Yes, but not in the past 3 months
What was your pattern of injecting during this period?	◯ Once weekly or less ◯ Fewer than 3 days in a row ◯ More than once per week ◯ 3 or more days in a row

Thank you for taking the time to complete this questionnaire. Based on your responses, your risk levels are as follows: (please note, these are for your feedback only, and are anonymous. They are not made known to any other party)

Tobacco

Your risk is: Low

Your risk is: Medium

Your risk is: High

Alcohol

Your risk is: Low

Your risk is: Medium

Your risk is: High

Cannabis

Your risk is: Low

Your risk is: Medium

Your risk is: High

Cocaine

Your risk is: Low

Your risk is: Medium

Your risk is: High

Amphetamines

Your risk is: Low

Your risk is: Medium

Your risk is: High

Inhalants

Your risk is: Low

Your risk is: Medium

Your risk is: High

Sedatives

Your risk is: Low

Your risk is: Medium

Your risk is: High

Hallucinogens

Your risk is: Low

Your risk is: Medium

Your risk is: High

Opioids

Your risk is: Low

Your risk is: Medium

Your risk is: High

Other drugs

Your risk is: Low

Your risk is: Medium

Your risk is: High

What do your scores mean?Low: You are at low risk of health and other problems from your current pattern of use.Moderate: You are at risk of health and other problems from your current pattern of substance use.High: You are at high risk of experiencing severe problems (health, social, financial, legal, relationship) as a result of your current pattern of use and are likely to be dependent

If you would like to speak to someone about your substance use, or your risks, or would like to reach out for help, please contact the SASA Wellness Team

Name	Telephone No	Email
Ms Natalie Zimmelma	082 331 7846	ceo@sasaweb.com
Dr Caroline Lee	082 777 2136	dreamdocsa@gmail.com
Dr Allan Hold	082 655 7792	holdfam@iafrica.com
Dr Bhavika Daya	083 787 1177	bhavikadaya@gmail.com
Dr Megan Jaworska	082 371 2383	madzia2908@gmail.com

b) Alcohol use

Tel: 0861435722

http://www.aasouthafrica.org.za

c) SANCA national

Tel: 011 892 3829

http://www.sancanational.info/contact

WhatsApp: 0765351701

d) Substance use helpline

Tel: 0800121314

SMS: 32312

e) Matrix Instituite on addiction (out patient treatment option) http://www.scienza.co.za/contact-matrixx-place.html

Tel: 0832835278

Supplementary File 2

		Qualification			P value (Chi square or Fisher's exact)
		Specialist	Registrar	GP or MO	
		Positive urge	Positive urge	Positive urge	
Tobacco	N	13	6	6	0.194
	% of each agent	76.5%	100.0%	100.0%	
Alcohol	N	117	28	15	0.932
	% of each agent	50.0%	52.8%	50.0%	

Cannabis	N	0	0	0	-
	% of each agent	0.0%	0.0%	0.0%	
Cocaine	N	0	0	0	-
	% of each agent	0.0%	0.0%		
Amph*	N	1	2	0	0.532
	% of each agent	14.3%	40.0%	0.0%	
Sedatives	N	26	10	5	0.016
	% of each agent	46.4%	76.9%	100.0%	
Opioids	N	1	1	0	1.000
	% of each agent	25.0%	33.3%	0.0%	

		Number of years in practice				P value (Chi square or Fisher's exact)
		< 5 years	5-10 years	10-15 years	>15 years	
		Positive urge	Positive urge	Positive urge	Positive urge	
Tobacco	N	4	6	7	8	0.658
	% of each agent	80.0%	85.7%	100.0%	80.0%	
Alcohol	N	22	52	30	56	0.002
	% of each agent	51.2%	65.0%	57.7%	39.4%	
Cannabis	N	0	0	0	0	-
	% of each agent	0.0%	0.0%	0.0%	0.0%	
Cocaine	N	0	0	0	0	-
	% of each agent	0.0%	0.0%	0.0%	0.0%	
Amph*	N	1	1	0	1	-
	% of each agent	25.0%	25.0%	0.0%	50.0%	
Sedative	N	7	10	8	16	0.230
	% of each agent	87.5%	55.6%	57.1%	47.1%	
Opioids	N	0	1	1	0	-

		Gender		P value (Fisher's exact)
		male	female	
		Positive urge	Positive urge	
Tobacco	N	17	8	1.000
	% of each agent	85.0%	88.9%	
Alcohol	N	76	83	0.010
	% of each agent	43.9%	58.5%	
Cannabis	N	0	0	-
	% of each agent	0.0%	0.0%	
Cocaine	N	0	0	-
	% of each agent	0.0%	0.0%	
Amph*	N	1	2	0.236

	% of each agent	12.5%	50.0%	
Sedative	N	19	22	1.000
	% of each agent	54.3%	56.4%	
Opioids	N	1	1	1.000

		Private or mostly private	State or mostly state	P value (Fisher's exact)
		Positive urge	Positive urge	
Tobacco	N	14	11	0.268
	% of each agent	77.8%	100.0%	
Alcohol	N	83	77	0.113
	% of each agent	46.4%	55.8%	
Cannabis	N	0	0	-
	% of each agent	0.0%	0.0%	
Cocaine	N	0	0	-
	% of each agent	0.0%	0.0%	
Amph*	N	1	2	1.000
	% of each agent	25.0%	25.0%	
Sedative	N	21	20	0.643
	% of each agent	52.5%	58.8%	
Opioids	N	1	1	1.000
	% of each agent	25.0%	33.3%	

Appendix 1: Ethics approval letter

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences Human

Research Ethics Committee

Room E53-46 Old Main Building Groote
Schuur Hospital Observatory
7925
Telephone [021] 406 6338
Email: lamees.emjedi@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

03 April 2018

HREC REF: 190/2018

Dr F Roodt
Anaesthesia Department
D23
NGSH

Dear Dr Roodt

PROJECT TITLE: THE INCIDENCE OF SUBSTANCE ABUSE AMONGST ANAESTHETISTS IN SOUTH AFRICA - (Master's candidate-Dr J van der Westhuizen)

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

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

Approval is granted for one year until the 30 April 2019.

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 acknowledges that the following Master's candidate, Dr J van der Westhuizen, will also be involved in this study.

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.

Please quote the HREC REF in all your correspondence. Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938

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 Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), 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: Instructions to the journal

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

- This manuscript has currently only been submitted to SAJAA and has not been published previously.
- This work is original and all third party contributions (images, ideas and results) have been duly attributed to the originator(s).
- Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval and proof of payment for royalties have been submitted as supplementary files.
- The submitting/corresponding author is duly authorised to herewith assign copyright to the South African Society of Anaesthesiologists (SASA).
- All co-authors have made significant contributions to the manuscript to qualify as co-authors.
- Ethics committee approval has been obtained for original studies and is clearly stated in the methodology as well as provided as a supplementary file.
- A conflict of interest statement has been included where appropriate.
- The submission adheres to the instructions to authors in terms of all technical aspects of the manuscript.
- Plagiarism: The submitting author acknowledges that the Editorial Board reserves the right to use plagiarism detection software on any submitted material.

Author Guidelines

Submitted manuscripts that are not in the correct format and without the required supporting documentation specified in these guidelines will be returned to the author(s) for correction and will delay publication.

AUTHORSHIP

Named authors must consent to publication **by signing a covering letter** which should be submitted as a supplementary file. Authorship should be based on substantial contribution to:

(i) conception, design, analysis and interpretation of data;

(ii) drafting or critical revision for important intellectual content; and

(iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to **www.icmje.org**); and

(iv) exact contribution of each author must be stated.

DECLARATION OF CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute a conflict of interest. If there is no conflict of interest to declare please include the following statement: The authors declare no conflict of interest.

FUNDING SOURCE

All sources of funding should be declared. Also define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the writing of the manuscript; the decision to submit the manuscript for publication. If the study sponsors had no such involvement, this should be stated as follows: No funding source to be declared.

RESEARCH ETHICS COMMITTEE APPROVAL

The submitting author must provide written confirmation of Research Ethics Committee approval for all studies including case reports. The ethics committee as well as the approval number should be included.

STATISTICAL ANALYSIS

Authors are advised to involve medical statisticians at the protocol stage of their research project: to plan sample size, and the selection of appropriate statistical tests for analysis and presentation.

PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or

guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to **www.icmje.org**.

ETHNIC CLASSIFICATION

The rationale for analysis based on racio-ethnic-cultural categorisation should be indicated.

CATEGORIES OF SUBMISSIONS

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles

Original articles on research relevant to anaesthesia and analgesia should not exceed 3 200 words, no more than 30 references, with up to 6 tables or figures. A structured abstract under the following headings, Background, Methods, Results, and Conclusions is a requirement and should not exceed 300 words.

Clinical Review articles

Review articles relevant to anaesthesia and analgesia should not exceed 2 400 words, with a maximum of 20 references and no more than 6 tables or figures. A summary of 300 words or less is required.

Case reports

Case reports should not exceed 1 800 words with no more than 10 references. Figures are limited to 2 figures and may include images or photographs. The case report should have three headings: Summary (not exceeding 100 words), Case report (with no introduction) and Discussion. Case reports will be published online only. The summary and the URL will appear in the printed version.

Scientific Letters

Scientific Letters should not exceed 2 400 words with a maximum of 10 references. Only one table or illustration is permissible. A structured abstract under the following headings, Background, Methods, Results, and Conclusions, is a requirement and should not exceed 250 words.

Letters to the editor

Letters to the editor should be 800 words or less with only one image or table.

MANUSCRIPT PREPARATION

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - **www.icmje.org**. Manuscripts must be provided in **UK English**.

Qualification, affiliation and contact details

This information must be provided for ALL authors and must be submitted as a supplementary file.

Email addresses of all author must be provided.

ORCID number of **ALL** authors must be provided – if authors do not have ORCID, please register at https://orcid.org/

Abbreviations

All abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements

Scientific measurements must be expressed in SI units except blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age) should also be preceded by a space e.g. > 20 years. No spaces should precede ± and °, i.e. '35±6' and '19°C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160…

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
Round **brackets** (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

General formatting

The manuscript must be in Microsoft Word or RTF document format. Text must be 1,5-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, except for Tables). *The manuscript must be free of track changes.*

Disclaimers should follow the Conclusion and it should be in the following order: Acknowledgements, Declaration conflict of interest, Funding source, Ethics declaration and ORCID.

ILLUSTRATIONS AND TABLES

If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file **and** provided as **'supplementary files'**. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes, tabs or enters) and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Figure 1)'. Figure legends: Figure 1: 'Title...'. All illustrations/figures/graphs must be of **high resolution/quality**: 300 dpi or more is preferable, but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached as '**supplementary files**' upon submission (not embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft PowerPoint or Excel must be accompanied by the original workbook.

REFERENCES

Authors must verify references from the original sources. *Only complete, correctly formatted reference lists will be accepted.* Reference lists may be generated with the use of reference manager software, but the final document must be delinked from the reference database or otherwise generated manually. Citations should be inserted in the text as superscript, e.g. These regulations are endorsed by the World Health Organization,[1,2] and others.[3,4-6] The superscript reference number should come after the punctuation mark and should not be in brackets.

All references should be listed at the end of the article in numerical order of appearance in the **Vancouver style** (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given; if there are more than six authors, the first four names should be given followed by et al. First and last page, volume and issue numbers should be given. **Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID).** Authors are encouraged to use the DOI lookup service offered by **CrossRef**. Crossref DOIs should always be displayed as a full URL link in the form https://doi.org/10.xxxx/xxxxx

Journal references:

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Appendix 3: Reviewer comments

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