AEROSOLIZATION DURING INTUBATION AND EXTUBATION AND ITS ASSOCIATED RISK OF TRANSMISSION OF SARS-CoV-2 TO HEALTHCARE WORKERS: A SCOPING REVIEW

By

Dr Verushka Naidoo

(Student No: 201293857)

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I, Dr Komalan Govender, as the candidate's supervisor have approved this thesis for submission.

Signed: [redacted] Date: 20 October 2023

Declaration

I, Dr Vemshka Naidoo, declare that:

(i) The research reported in this dissertation, except where othe1wise indicated, is my original work.

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Dedication

I would like to dedicate this dissertation to my late father, Vishnu Rungiah Naidoo, he was and will always be my greatest motivation. Words cannot express my gratitude towards him and for all the sacrifices he had made to give me the life that I have.

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Abstract:

Background:

Healthcare workers, in particular anesthesiologists, are at risk for many infectious diseases that could potentially be transmitted during intubations and extubations. Although intubation and extubation are known to stimulate coughing and to promote the generation of aerosols, their risk of transmission of COVID-19 infection is still not clearly understood. Among the aerosol generating procedures, intubation and extubation is thought to be especially harmful due to the proximity of the anaesthetist to the patient's airway. The aim this study is to explore and describe the risk of aerosolisation of SARS-CoV-2 to the anaesthetist during airway management.

Methods:

We conducted a scoping review of PubMed, MEDLINE, LANCET, and grey literature related to intubations and extubations, and the risk of transmission of infections to the anaesthetist. The scoping review was conducted using the Arksey and O' Malley framework for scoping reviews. We conducted a narrative synthesis of the evidence gathered. There were no restrictions on study design, year of publication, and study location. The literature search was updated on the 15th of July 2023.

Results:

Our scoping review showed that healthcare workers involved in airway procedures specifically intubation and extubation are at an increased risk of contracting SARS-COV-1 and SARS-COV-2. Aerosol generation during these procedures has been shown to generate less aerosol than that of a cough. Extubations are particularly riskier regarding aerosol exposure than intubations. The relationship between aerosol exposure and virus transmission is uncertain.

Conclusions:

Anaesthetists are at increased risk of infection during intubations and extubations. There remains a lack of evidence of the exact mechanisms of transmission from patients to healthcare workers during aerosol-generating procedures. There is also a lack of consistency in the definition of aerosol-generating procedures.

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Overview of the Thesis

Aerosol generating procedures (AGPs) have been a major reason for concern since the recent COVID-19 pandemic. Many healthcare workers involved in AGPs are at risk of contracting SARS-COV-2 due to their interaction with COVID-19 positive patients especially those that may be asymptomatic. This can have an impact on service delivery and compromise patient care. Multiple health care organisations have raised concern regarding the risk of infection to HCWs involved in AGPs but there is still a lack of evidence regarding the exact mechanisms involved in the spread of the virus during intubation and extubation. There is an urgent need for further research and larger studies involving AGPs so that HCWs can protect themselves from the ongoing risk of infection whilst not compromising patient care and disrupting surgical lists.

This study was conducted to ascertain whether the AGPs (during intubation and extubation) are in fact aerosol generating and to identify the steps during these AGPs that place healthcare workers at increased risk. We also looked at whether there is in fact an increased risk of infection amongst individuals involved in these AGPS. This study was done by conducting a scoping review which we believed would be appropriate to aggregate the current state of the literature to advise on the possible impact of aerosolization to the anaesthetist during airway management. This study aimed to map the existing literature in the field of interest and to identify research gaps in the existing literature.

This scoping review was conducted using the Arksey and O' Malley framework. The following five steps were included in this scoping review: (i) identifying the research question, (ii) identifying relevant studies, (iii) study selection, (iv) charting the data, and (v) collating, summarising, and reporting the results.

It is hoped that the information obtained from this scoping review will help healthcare workers involved in intubation and extubation make informed decisions regarding the risk of infection and have knowledge about the quantity of aerosols generated during these procedures. We also hope that the study will highlight gaps in the current literature and areas that require further inquiry.

Part One: Review of the Literature

Aerosolisation during Intubation and Extubation and its associated Risk of Transmission of SARS-CoV-2 to Healthcare Workers: A Scoping Review

Introduction

The purpose of this scoping review was to define what an aerosol generating procedure is in relation to anaesthetic practice, to review the evidence on aerosolization during intubation and extubation, to explore the literature on aerosol generation in SARS-CoV-2 and the risk to the anaesthetist, and finally to identify gaps in the literature where future research may be directed.

It is now acceptable to recognise airborne transmission as an important route of transmission of Severe Acute Respiratory Syndrome Corona Virus-2 (SARS CoV-2). Medical professionals are frequently involved in airway management that have the potential to generate aerosols which may transmit the infection between humans. Multiple interventions are in place to reduce the risk of infection associated with AGPs in patients presenting for surgery. These include, but are not limited to, decreased staff numbers in operating rooms, use of higher-level personal protective equipment (PPE), change in the anaesthetic plan for example, change from regional anesthesia to general anesthesia. All the above can have a negative impact on the surgical procedure itself and good communication amongst team members becomes vital. It is important for health care workers to make evidence-based decisions on whether enhanced protection during AGPs is in fact still required in the time of reduced transmission risk and personal risk of severe disease.

Aerosol Generating Procedures (AGPs)

A universal definition does not exist in the current literature. There is still no definition that quantitates the amount of aerosol generated during “aerosol generating procedures.” According to the World Health Organization aerosol generating procedures are defined as any medical procedure that can induce the production of aerosols of various sizes, including droplet nuclei (1).

Aerosols are produced during expiration for example, during coughing, talking, breathing, sneezing etc (2). If there is a thin layer of liquid over which high-velocity gas flows then aerosols can be generated and these high gas velocities can be produced by the patient, a procedure or by surgical equipment (3). Wilson et al describes three mechanisms involved in the development of respiratory airborne particles, all of which require surface tension disruption of the respiratory tract lining fluid (4). The three mechanisms include: (i) open-close cycling of glottic structures, (ii) shearing forces due to high velocity gas flow and, (iii) open-close cycling of terminal bronchiole airways (4). Aerosols are microscopic solid, semi-solid, or liquid particles that are often defined as being so small that they remain suspended in air (3). Aerosols can range from 0.1-100 micrometres (μm) in diameter and are categorised as being either coarse (>5 μm) or fine (<5 μm) (5). The aerosols that tend to deposit in the upper airways are usually coarse aerosols whereas those that tend to deposit in the lower airway are fine aerosols (5). Airborne transmission occurs when infected aerosols (often defined as being <5μm) are inhaled over both short and long ranges and there is evidence supporting the airborne transmission of multiple viruses (4,5). Coleman et al tried to determine the viral load of SARS-CoV-2 in coarse and fine respiratory aerosols produced during singing, talking and breathing. They measured viral RNA using a device called a G-11 exhaled breath collector from expiratory samples. Samples were collected from 22 participants. Thirteen of the participants emitted detectable levels of SARS-CoV-2 RNA in the respiratory aerosols (5). It was shown that the viral loads ranged from 63-5821 N-gene copies per respiratory activity per participant (5). There was also a high person-to-person variation in terms of virus emission and they found that patients earlier in the disease process were more likely to emit detectable RNA (5). Fine aerosols make up 85% of the viral load detected in the study and that these fine aerosols contained more SARS-CoV-2 than coarse aerosols (5). The study highlights that fine aerosols may play an important role in the transmission of SARS-CoV-2. There is increasing evidence that support the airborne transmission of SARS-CoV-2 especially in indoor environments were ventilation is poor (4). The phases involved in airborne transmission include the generation and exhalation of aerosol, transportation of the aerosol through air, inhalation by the host and deposition into the respiratory tract and infection (4). The way in which a virus-laden aerosol behaves is determined by its physicochemical properties which include the physical size, viral load and infectivity, other chemical components such as electrolytes, proteins and surfactants, the pH value, the electrical charge, and the air/liquid interfacial properties (4).

The recent pandemic has resulted in the acquisition of a list of medical procedures, these medical procedures are referred to as "aerosol generating procedures" (AGPs). This list is important as it tends to affect the appropriate level of personal protective equipment used by health care workers and puts into play several protocols to assist in protecting medical personnel. There is no consensus or adequate data available to produce a definitive list of which procedures are aerosol generating. It is due to this reason that the list of aerosol-generating procedures varies between countries and different health organisations. A systematic review by Jackson et al found that there was enough evidence available to classify 19 procedure groups as aerosol generating and these included autopsy, surgery/post-mortem procedures with high-speed devices, intubation and extubation procedures, bronchoscopy, sputum induction, manual ventilation, airway suctioning, cardiopulmonary resuscitation, tracheostomy and tracheostomy procedures, non-invasive ventilation, high-flow oxygen therapy, breaking closed ventilation systems, nebulised or aerosol therapy, nasopharyngoscopy or laryngoscopy, high-frequency oscillatory ventilation, coughing, mechanical ventilation, chest physiotherapy and nasopharyngeal aspirate (6). Jackson et al recommend that the procedures above be considered as aerosol generating in order to decide on what personal protective equipment to select (6). It is imperative that health care professionals are aware of procedures that are aerosol generating in order to guide on the level of personal protective equipment required for each procedure. Public health agencies have recommended that health care workers wear N95 respirators, gloves, a fluid-repellent long sleeved gown and eye protection when involved in AGPs with patients suspected or confirmed to have SARS-CoV-2 infection (8). These procedures, if possible, should also be conducted in rooms with adequate ventilation (airborne infection isolation rooms with 12 or more air changes per hour and negative air flow) to decrease the risk of infection (7). However, there is still no general agreement as to which procedures can be deemed aerosol generating. The Centres for Disease Control and Prevention listed the following procedures as aerosol generating procedures: open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BIPAP, CPAP), bronchoscopy and manual ventilation (8). Nebulizer administration and high flow O2 delivery were also listed but it was uncertain as to whether aerosols generated from these procedures may be infectious (8).

Of importance to the anaesthetist, is whether intubations and extubations are in fact aerosol generating procedures and, if these aerosols indeed pose an infective risk to healthcare workers and patients involved in these procedures. The process of tracheal intubation and extubation involves multiple tasks. It places the health care worker at greatest risk because of potential aerosol and fomite transmission of the virus. The intubation process involves many independent procedures: pre-oxygenation with a face mask, bag mask ventilation, direct or video laryngoscopy, airway suctioning, passing the endotracheal tube through the glottis opening, the checking of the correct placement of the endotracheal tube, and the commencement of positive pressure ventilation.

Health care professionals involved in intubation and extubation are close to the patients airway for long periods of time before, during, and after the intubation and extubation process therefore potentially placing them at higher risk than others in the operating theatre.

Intubation and Extubation: Is there an infective risk to healthcare workers?

The assessment of the infectivity risk to healthcare workers from SARS-CoV-2 is on-going. In order for healthcare workers to protect themselves during aerosol generating procedures, like intubation and extubation, it is important to ascertain whether they do indeed increase the risk of transmission of SARS-CoV-2.

An earlier study by Fowler et al investigated whether specific ventilatory strategies were associated with an increased risk of severe acute respiratory syndrome (SARS CoV-1) in healthcare workers. They conducted a retrospective cohort analysis involving seven patients with SARS in an intensive care unit. These patients were being treated with different modes of ventilatory support. They focused their attention on healthcare workers who performed or were involved in endotracheal intubation for patients with SARS. The patients involved in the study were treated in negative pressure isolation rooms. Staff attending to these patients wore gowns, gloves, N95 masks and hairnets. The use of eye and face shields were variable. Fowler et al demonstrated that healthcare workers who were directly involved in endotracheal intubation had an increased risk of developing SARS (RR, 13.29; 95% CI, 2.99 to 59.04; $p = 0.003$) (9). They also found that physicians who performed endotracheal intubation had a 3.8-fold greater likelihood of developing SARS in comparison to physicians caring for patients with SARS than those that did not perform endotracheal intubation (RR, 3.82; 95% CI, 0.23 to 62.24; p = 0.5) (9). This association however was not found to be statistically significant (9). In addition, the study highlighted that nurses who assisted in endotracheal intubation were more likely to develop SARS than nurses who cared for patients with SARS in the ICU (RR, 21.38; 95% CI, 4.89 to 93.37; p = 0.001) (9). Of the five nurses that assisted with intubation in patients with SARS, three of the nurses developed the infection (9). The relative risk was higher amongst nurses than physicians, Fowler et al stated that this may be due to the longer duration of time spent with patients during the intubation procedure as opposed to the shorter duration spent by physicians who were just involved in the procedure itself (9). The important limitations of this study were the small sample size and limited available data; therefore, caution should be taken when interpreting this analysis. It is therefore difficult to extrapolate these findings to the current context of the COVID-19 pandemic.

An article by Harding et al also aimed to establish the risk of SARS-CoV-2 infection associated with AGPs. In their review article they also highlighted that endotracheal intubation of SARS-infected patients has been consistently associated with viral transmission to healthcare workers from the evidence they obtained (10). They also highlighted the substantial gaps in the literature for the SARS-CoV-2 pandemic around transmission routes, risks to healthcare workers and safety of AGPs (10).

Another systematic review published in 2012 by Tran et al looked at the evidence for the risk of transmission of acute respiratory infections to healthcare workers caring for patients undergoing aerosol generating procedures compared to those patients not undergoing AGPs. Their study looked at 5 case-control and 5 retrospective cohort studies which assessed transmission of SARS to HCWs. Tracheal intubation was one of the AGPs found to have an increased risk of transmission [n=4 cohort; Pooled OR=6.6 (95%CI: 2.3, 18.9), and n=4 case-control; Pooled OR=6.6 (95%CI: 4.1, 10.6)] (11). Other procedures associated with an increased risk also included non-invasive ventilation, tracheotomy and manual ventilation (11). The findings of the above study indicated that the most consistent association across the multiple studies was with tracheal intubation (11). This review however did not assess the production of aerosols from specific procedures, and the presence of viable microbes in the aerosols generated during the procedures. Also, the overall quality of the 10 studies included in the systematic review according to the GRADE classification was reported to be of very low quality. The study also looked at the risk of transmission of SARS-CoV-1 and this can therefore not be extrapolated when dealing with the SARS-COV-2 pandemic.

El-Bodhdadly and colleagues designed a self-reporting provider registry to collect data on nosocomial exposure, procedural performance, use of PPE and subsequent COVID-19 related outcomes after tracheal intubation (12). The study included 1718 healthcare workers in 17 countries that were involved in intubations on COVID-19 patients across 503 healthcare institutions. Their aim being to investigate the incidence and risk factors for the development of COVID-19 in healthcare workers after participating in tracheal intubation. The study highlighted that 1 in 10 health care workers involved in tracheal intubation of patients with confirmed or suspected COVID-19 infection in due course reported a COVID-19 outcome, which was a laboratory confirmed COVID-19 diagnosis or the onset of new symptoms that required self-isolation or hospitalisation after a tracheal intubation episode (12). The incidence increased over a certain time period (3.6% within 7 days, to 6.1% within 14 days and 8.5% within 21 days of the participants first recorded intubation) (12). Of interest was that females were identified as being at increased risk of reporting a COVID-19 outcome (12). It was unclear as to what the reasons were for this finding. Although tracheal intubation is often highlighted as a “high-risk procedure” it is still unclear as to which components during the procedure cause an increased risk of infection. The study however did not have a group to compare those healthcare workers that were not involved with tracheal intubations, one therefore cannot draw conclusions as to whether the rates of infection would have been lower, higher, or equal.

A systematic review and meta-analysis of observational studies by Wai-Shun Chan et al was the first to summarize the risk of coronavirus transmission to HCWs via AGPs since the start of the COVID-19 pandemic. The study investigated the risks of SARS-CoV-1, SARS-CoV-2 and MERS-CoV transmission during AGPs. The meta-analysis identified a significant increase in odds of HCWs contracting SARS-CoV-1 or SARS-CoV-2 during endotracheal intubation (OR, 6.69; 95% CI, 3.81–11.72; $p < 0.001$) when compared with those not involved in endotracheal intubation (13).

From the list of commonly performed aerosol generating procedures, it appears that endotracheal intubation is particularly hazardous to anaesthetists and other healthcare workers performing tracheal intubations. It can be deduced that tracheal intubation is the procedure most associated with transmission and should therefore be considered a high-risk aerosol generating procedure increasing the risk of transmission and exposure to SARS-CoV-

2. Although intubation has been shown to be associated with an increased risk of infection to healthcare workers, it still remains unclear to the exact cause of transmission.

Hamilton et al in their article published in 2021 stated that we should also be focusing on other factors that could play a role in the transmission of COVID-19 and that these factors should be included in assessing risk (14). The proposed factors highlighted in the study included, a) patient risk: the possibility of the patient being infected and the time since acquiring the infection; a coughing patient or a patient with increased respiratory effort are more likely to generate infectious aerosols, b) duration of exposure: the length of time exposed to an infected individual increases the likelihood of both aerosol and droplet transmission, c) health-care practitioner risk form COVID-19: age, sex, body mass index, comorbidities, vaccination status, d) proximity risk: close patient contact increases risk and, e) environmental risk: ventilation, humidity, temperature. (14)

What is the evidence supporting aerosolization during intubation and extubation?

There are few studies available using scientific methods to evaluate the generation of aerosol during intubation and extubation.

Due to lack of studies evaluating the quantity and size of aerosol generated during intubation and extubation Brown et al conducted a prospective environmental monitoring study. The study was conducted in four operating theatres with an ultraclean, laminar flow ventilation system with high efficiency particulate air (HEPA) filtration. An optical particle sizer was used for sampling and this detects particles by laser optical scattering. A sampling funnel was placed 0.5m above the aerosol source where the airway procedures were performed. Results were taken for 19 intubations and 14 extubations. The intubations and extubations performed were elective procedures. The study showed that tracheal intubation with facemask ventilation produced very low quantities of aerosolised particles (average concentration, 1.4 (1.4) particles.l^{-1}, n=14) vs. a volitional cough (average concentration, 732 (418) particles.l^{-1}, n = 38, $p < 0.0001$) (15). In comparison tracheal extubation produced a detectable aerosol (21 (18) l^{-1}, n =10) that was 15-fold greater than intubation ($p = 0.0004$) but 35-fold less than a volitional cough ($p < 0.0001$) (15). In 50% of extubations a cough event was clinically noted and this was detected as an aerosol spike (15). Since intubation and extubation have a low risk of generating aerosol compared to that of a volitional cough one needs to reassess whether intubation and extubation can be classified as an actual aerosol generating procedures. In addition, extubation with the presence of a cough produced more aerosol than extubation without a cough, for this reason one needs to try to reduce the incidence of coughing during extubation (15). Since the study only gives a quantitative measure of aerosol generation during intubation and extubation, we still cannot draw conclusions from the study about the risk of transmission of SARS-CoV-2. The study did not include measurements from patients known to have COVID-19 or other respiratory illnesses nor was the concentration of live virions measured withing the particles. In addition, intubations and extubations in an emergency setting were not included. Therefore, caution should be taken when reviewing these results as they may not be generalisable to intubations and extubations in other settings e.g., ill patients coughing prior to intubation or poorly ventilated rooms.

An observational study by Dhillon et al aimed to determine whether procedures like facemask ventilation, tracheal intubation and extubation generated aerosols, however they looked at this in actual clinical practice. They recruited patients undergoing elective endonasal pituitary surgery. They also aimed to characterise the aerosols produced by looking at the size, quantity, duration, and direction of aerosol production. Investigators used two methods to detect aerosol: larger particles were detected using particle image velocity and smaller particles were detected using air sampling with spectrometry. The study demonstrated that tracheal intubation and extubation do indeed generate aerosols. The mean particle concentrations measured during intubation were 12 times more than baseline ($p<0.001$) (16). During induction of anaesthesia, facemask ventilation during apnoeic oxygenation (oxygen flows of 6-10 $L.min^{-1}$) in a paralysed patient, tracheal intubation and inflation of the cuff generated aerosols in concentrations of 30-300 times greater than background noise and most of the particles were less than 5 micrometres in size ($p < 0.001$) (16). During extubation, the mean particle concentrations measured were 12 times greater than the baseline ($p < 0.001$) (16). In addition, positive pressure bag and mask ventilation with high flow oxygen, and the patient coughing into a Hudson mask produced large signal spikes in aerosol concentrations. Of interest, passive oxygenation, introduction of the laryngoscope blade and, throat pack insertion did not produce aerosols above background noise. The study therefore highlights that there are certain steps during airway management that produce aerosols, some more than others like bag mask ventilation (16). It also demonstrated that small particles are produced that can remain suspended in air and spread throughout the operating theatre (16).

In comparison to the other experimental studies reviewed, an observational study by Oksanen et al looked at aerosol generation during each step of airway management in surgical patients in an actual operating room environment. The study was a single-centre observational study that took place in Helsinki University Hospital and included 39 patients who underwent general anaesthesia and tracheal intubation. The steps they investigated included preoxygenation, mask ventilation, intubation and extubation. The measurements were taken in operating rooms with laminar flow and high air change rates per hour. An Optical Particle Sizer was used to measure the size and number of particles generated. The study focused on mean particle concentrations during each step of anaesthesia and compared it to coughing (control data) and this was then used to assess the variation in generation of particles. The reason they compared it to coughing was to determine if aerosol generating procedures produced more aerosol than exposure to patients during routine care. Reference coughing data was collected using the same collection methods used to detect aerosol production during the study. The study highlights that general anaesthesia procedures does not generate more aerosols as compared to coughing(17). Particle measurements were made in the operating theatres with laminar flow and no changes were made to the theatre environment, in addition background aerosol concentrations were also taken into consideration. It was demonstrated that all procedures were equivalent statistically to concentrations seen during coughing in total particle concentration and these did not exceed the mean aerosol generation of coughing (17). Mask ventilation produced the highest measured individual total particle concentration, but this was still lower than mean aerosol generation during coughing (17). The study highlighted that this could be attributed to face-mask seal leakage and this was also demonstrated in the study by Dhillon et al (16). It is therefore necessary to ensure a tight seal using the correct fitting mask when mask ventilation is required. Mean particle generation during intubation also did not exceed coughing statistically (17). What was interesting was that a reported difficult intubation produced less aerosol than a normal intubation (17). Extubation also generated aerosol concentrations comparable to coughing (17). Extubations with coughing tended to produce up to four times more particles than with the patient not coughing during extubation (17). The study also demonstrates what was shown in the other experimental studies above, that aerosol generation during intubation and extubation do indeed produce aerosol but this is still not as much as that compared to coughing.

A simulation study by Feldman et al used fluorescent markers to visualise the deposition of simulated exhaled respiratory secretions on the surface of HCWs involved in endotracheal intubations. The study was performed in an emergency department and made use of adult and paediatric high-fidelity manikins. To simulate the droplets being exhaled by the manikins, an atomizing device was used. Health care personnel involved in the study wore N95 respirators, protective eyewear, gloves, and gowns. The study demonstrated that despite PPE, 8 of the 8 HCWs that participated in the study had fluorescent markers visible on their hair, 7 of the 8 had markers visible on their exposed skin, 6 on the neck, 1 on the ear and 4 had markers on their shoes. The findings suggest that the current recommendations for PPE may not be sufficient to prevent exposures during tracheal intubations in the emergency department setting (18). Aerosols can be deposited on uncovered skin, hair and shoes and this infective material may possibly have the potential to cause infection to HCWs involved in intubations via hand transfer to the nose, mouth and eyes if the HCW does not adhere to strict hand hygiene (18)(19).

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Part 2: A Submission Ready Manuscript

Aerosolization during Intubation and Extubation and its associated Risk of Transmission of SARS-CoV-2 to Healthcare Workers: A Scoping Review

Verushka Naidoo[1], Komalan Govender [1,2]

[1] University of KwaZulu-Natal, Discipline of Anaesthesiology and Critical Care

[2] King Edward VIII Hospital, Intensive Care Unit

Corresponding Author: V Naidoo (vnaidoo1982@yahoo.com)

Abstract

Background:

Healthcare workers in particular anesthesiologists are at risk for many infectious diseases that could potentially be transmitted during intubation and extubation. Although intubation and extubation are known to stimulate coughing and to promote the generation of aerosols, their risk of transmission of COVID-19 infection is still not clearly understood. Among the aerosol generating procedures, intubation and extubation is thought to be especially harmful due to the close proximity of the healthcare worker to the patient’s airway. The aim our study is to explore and describe the risk of aerosolization of SARS-CoV-2 to the anesthetist during management of the airway.

Methods:

We conducted a scoping review of PubMed, MEDLINE, LANCET, Cochrane, and grey literature related to aerosol generating procedures (intubation and extubation) and the risk of transmission of SARS-COV-2 to healthcare workers. The scoping review was conducted using the Arksey and O’ Malley framework. Limitations included few COVID-19 specific studies relating to intubation and extubation and exclusion of non-English language articles. We conducted a narrative synthesis of the evidence gathered. There were no restrictions on study design, year of publication, and study location. The literature search was updated on the 15th July 2023.

Results:

Our scoping review shows that healthcare workers involved in airway procedures specifically intubation and extubation are at an increased risk of contracting SARS-COV-1 and SARS-COV-2. Aerosol generation during these procedures has been shown to generate less aerosol than that of a cough.

Conclusion:

There remains a lack of evidence of the exact mechanism of transmission from patients to health-care workers during aerosol-generating procedures. There is also a lack of consistency in the definition of aerosol-generating procedures, and these may leave anaesthesiologists and other healthcare workers performing intubations and extubations unsure of the risks.

Introduction:

Coronavirus disease 2019 (COVID-19) which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first confirmed in South Africa on the 5th of March 2020. On the 15th of March 2020 President Cyril Ramaphosa declared a national state of disaster. Since then, the pandemic has continued to impact lives during the various levels of lockdown. For many healthcare workers (HCWs) aerosol generating procedures (AGPs) have become a major source of concern due to the risk of transmission of infection by airborne particles. During the current pandemic many HCWs have been infected with SARS-CoV-2 that has resulted in either severe illness or death. COVID-19 may be transmitted through small droplets and/or aerosols and is highly contagious.[1]

There appears to be little consensus on which procedures are deemed aerosol-generating. There is also a lack of evidence regarding quantifying aerosol generation during these procedures and no new high quality epidemiological studies that reveal an increased risk of infection with regards to SARS-CoV-2. [2,3] Healthcare Workers are frequently involved in aerosol generating procedures like intubations and extubations and, may therefore be at an increased risk of contracting COVID-19, however the extent of this risk remains unclear.

The World Health Organization defines an AGP as any medical procedure that can induce the production of aerosols of various sizes, including droplet nuclei. [2] Due to the lack of strong evidence and agreement amongst experts there is still no final or all-inclusive list of AGPs.[4] The Center for Disease Control and Prevention list the following procedures as aerosol generating: open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BiPAP, CPAP), bronchoscopy and manual ventilation.[4] High flow oxygen delivery and nebulized-drug administration are marked as potential aerosol generating procedures due to limited data related to their infectivity.[4] Of importance to our scoping review are the aerosol-generating procedures intubation and extubation. With safety measures in place and the development and availability of COVID-19 vaccines, South Africa has been able to terminate its "state of disaster" and move to a transitional phase. This lifting of restrictions was due to the lower incidence of severe cases and deaths associated with COVID-19 infection rates of late. It is uncertain how health care workers should transition in the workplace when managing patients requiring aerosol generating procedures like intubation and extubation. The aim of this scoping review was to identify the most relevant scientific literature available surrounding the question of aerosol generating procedures like intubation and extubation and its associated risk of transmission to healthcare workers, in particular anaesthetists.

Methods:

Research Protocol:

A scoping review protocol was developed for this study. The protocol was submitted to the University of KwaZulu Natal and an exemption from ethics review was granted by the Biomedical Research Ethics Committee (BREC) on the 20th of December 2021 (Protocol reference: BREC/00003733/2021). BREC is registered with the South African National Health Research Ethics Council. We decided to conduct a scoping review since it aims to highlight different types of evidence on the area of interest and identifies gaps for further research.

The Arksey and O'Malley six stage methodological framework was used to provide guidance when conducting the study [5,6]. The first five steps were be followed in this scoping review: (i) identifying the research question, (ii) identifying relevant studies, (iii) selection of eligible studies, (iv) charting the data, and (v) collating and summarizing the results. The sixth step of this framework which is optional was not conducted in our study. Our findings are presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews reporting standards (PRISMA-ScR). [7]

Eligibility Criteria:

We sought to define and gather evidence related to the aerosolization produced during intubation and extubation and to determine the risk of infection to health care workers involved in these procedures during the COVID-19 pandemic. To be included in the review, the articles needed to focus on aerosolization during intubation and extubation only and the risk of infectivity of SARS-CoV-2 to HCWs during these aerosol generating procedures. No restrictions were placed on the study design. We limited our search to studies published in English. No time restrictions were used in this search.

Information Sources and search strategy:

A formal literature search was performed for evidence on the topic of aerosolization during Intubation and Extubation and its associated risk of transmission of SARS-CoV-2 to anesthetists or healthcare workers. The following electronic databases were included: PUBMED, MEDLINE, Cochrane, LANCET. The search terms 'aerosol-generating procedures', 'intubation', 'extubation', 'anaesthetist', 'anaesthesiology' and 'SARS-CoV-2' were used for the preliminary search.

A subsequent 'hand search' of the above terms and other key terms identified in the literature was also conducted and additional articles were sought from the references of the studies included in the study. A search was also performed in Google Scholar for other "grey literature". We also included websites such as the World Health Organization (WHO) and the Centers for Disease Control and Prevention as part of our search criteria.

Study selection:

The titles and abstracts were screened by two investigators independently (VN and KG) to select publications providing evidence or reporting on aerosolisation during intubation and extubation and its associated risk of transmission of SARS-CoV-2 to anaesthetists.

Any conflicts regarding which articles included was resolved by consensus and discussion with another senior researcher in the Department of Anaesthetics at the University of KwaZulu-Natal. Background reference searching was conducted for the selected studies to ensure that essential references were not omitted.

A final search of the literature was conducted prior to preparing the final manuscript for publication to include the most recent studies.

Inclusion Criteria:

- Articles describing aerosolization at the time of intubation or extubation
- Articles specifically describing aerosolization in any respiratory tract infection

- Articles specifically describing aerosolization in SARS-CoV-2 infections
- Articles published in English
- No date restrictions (Articles published up to July 2023 were included)
- Peer reviewed empirical studies of any design

Exclusion Criteria:

- Animal studies
- Articles not published in English

Data Extraction

A data charting form was developed by the primary investigator (VN) and reviewed by co-investigator (KG) to capture relevant information from each of the included studies. Data extracted from the articles included: authors and the year of publication, aim of the study, the study design, the study setting, sampling method (if applicable) and the most relevant findings (i.e., amount of aerosol generated, risk of infection)

Synthesis of results

The data was collated and assessed on a Microsoft® Excel spreadsheet. Data was summarised in table form. A narrative report and recommendations were generated of all the findings.

Results:

Study Selection and sources of evidence

A full electronic search strntegy was employed using the above databases mentioned. The search was conducted in October 2021 and was updated in July 2023.

Table 1: Electronic databases included in the search

Electronic Database	Keywords searched (advanced search)	Number of studies retrieved	Number of studies selected	Duplicates
PUBMED	"Aerosol Generating Procedmes" AND "COVID-19" AND "Intubation" AND "Extubation"	45	5	4
MEDLINE	As Above	60	6	4
LANCET	As Above	337	3	1
Cochrane	As Above	9	0	0
Grev Literature	As Above	12	0	1
Hand Searches	As Above	8	0	1

Additional key words:

Anaesthesia risk; Vims trnnsmission; Infection risk.

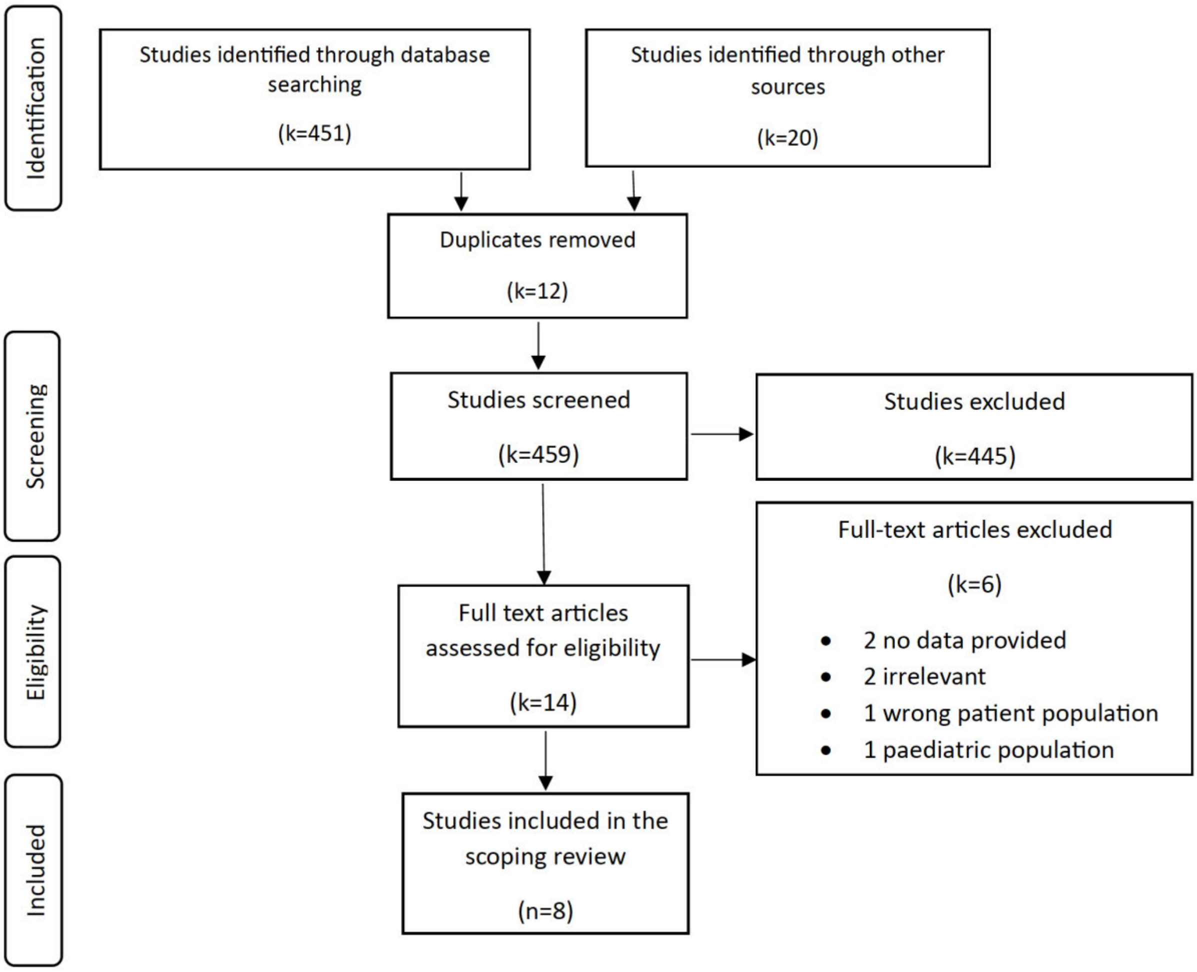

Figure 1: PRISMA flow diagram

Characteristics of sources of evidence

We retrieved a total of 471 articles using an advanced search strategy and hand searching through reference lists of the articles obtained during the review. Eight articles met our inclusion criteria. Of the 8 articles, 4 looked at aerosolization itself during intubation and extubation and the other 4 looked at the risk of transmission of an acute respiratory infection following intubation and extubation. Two studies were a systematic review and meta-analysis and 2 were observational studies, one was a prospective multi-center cohort study, and the other was a retrospective cohort analysis.

Results of individual sources of evidence (Table 2):

A systematic review published in 2012 by Tran et al looked at the evidence for the risk of transmission of acute respiratory infections to healthcare workers caring for patients undergoing aerosol generating procedures compared to those patients not undergoing AGPs. (3). Their study looked at 5 case-control and 5 retrospective cohort studies which assessed transmission of SARS to HCWs. Tracheal intubation was one of the AGPs found to have an increased risk of transmission [n=4 cohort; OR 6.6 (CI 2.3, 18.9), and n=4 case-control; OR 6.6 (CI 4.1, 10.6)]. Other procedures associated with an increased risk also included non-invasive ventilation, tracheotomy and manual ventilation. The findings of the above study indicated that the most consistent association across the multiple studies was with tracheal intubation. This review however did not assess the production of aerosols from specific procedures, and the presence of viable microbes in the aerosols generated during the procedures. Also, the overall quality of the 10 studies included in the systematic review according to the GRADE classification was of very low quality. The study also looked at the risk of transmission of SARS-CoV-1 and this can therefore not be extrapolated when dealing with SARS-CoV-2.

A report by Fowler et al described the occurrence of high rates of transmission to healthcare workers caring for patients with SARS who required ventilatory assistance.[8] Fowler et al observed a greater risk of developing severe acute respiratory syndrome for physicians and nurses performing endotracheal intubation (relative risk [RR], 13.29; 95% confidence interval [CI], 2.99 to 59.04; p = 0.003).[8] It is also interesting that the relative risk may be higher for nurses than physicians. This might be because of a longer duration of exposure that nurses likely had in the peri-intubation period, whereas physician exposure is often limited to the procedure itself.[8]

El-Boghdadly et al evaluated the risks of infection to healthcare workers following tracheal intubation of patients with COVID-19.(9) The study highlighted that 1 in 10 health care workers involved in tracheal intubation of patients with confirmed or suspected COVID-19 infection in due course reported a COVID-19 outcome which was a laboratory confirmed COVID-19 diagnosis or the onset of new symptoms that required self-isolation or hospitalization after a tracheal intubation episode. Although tracheal intubation is often highlighted as a “high-risk procedure” it is still unclear as to which components during the procedure cause an increased risk of infection. The study however did not have a control group to compare those healthcare workers that were not involved with tracheal intubations, one therefore cannot draw conclusions as to whether the rates of infection would have been increased, decreased or similar.

A systematic review by Wai-Shun Chan et al was the first to summarize the risk of coronavirus transmission to HCWs via AGPs since the start of the COVID-19 pandemic. The meta-analysis suggested a significant increase in odds of HCWs contracting SARS-CoV-1 or SARS-CoV-2 during endotracheal intubation (OR, 6.69; 95% CI, 3.81–11.72; $p < 0.001$) when compared with those not involved in endotracheal intubation.[10]

There has been a lack of studies evaluating the quantity of aerosol generated during intubations and extubations specifically. To assess the above, Brown et al conducted a prospective environmental monitoring study. The study showed that tracheal intubation with facemask ventilation produced very low quantities of aerosolised particles. In comparison tracheal extubation produced a detectable aerosol that was 15-fold greater than intubation but 35-fold less than a volitional cough. [11] Since intubation and extubation have a low risk of generating aerosol compared to that of a volitional cough one needs to reassess whether intubation and extubation can be classified as an actual aerosol generating procedure. In addition, extubation with the presence of a cough produced more aerosol than extubation without a cough, for this reason one needs to try to reduce the incidence of coughing during extubation.[11] Since the study only gives a quantitative measure of aerosol generation during intubation and extubation, we still cannot draw conclusions from the study about the risk of transmission of SARS-CoV-2.

An observational study by Dhillon et al aimed to determine whether procedures like facemask ventilation, tracheal intubation and extubation generated aerosols, however they looked at this in actual clinical practice. The study demonstrated that tracheal intubation and extubation do indeed generate aerosols. [12] The mean particle concentrations measured during intubation and extubation were 12 times more than baseline. [12] In addition, positive pressure bag and mask ventilation with high flow oxygen, and the patient coughing into a Hudson mask produced large signal spikes. [12] What was interesting was that passive oxygenation, introduction of the laryngoscope and throat pack insertion did not produce aerosols above background noise. [12] The study therefore highlights that there are certain steps during airway management that produce aerosols, some more than others, like bag mask ventilation. It also demonstrated that small particles are produced that can remain suspended in air and spread throughout the operating theatre.[12]

In comparison to the other experimental studies reviewed, the observational study by Oksanen et al looked at aerosol generation during each step of airway management in surgical patients in a real-life OR environment. These steps included preoxygenation, mask ventilation, intubation and extubation. The study focused on mean particle concentrations during each step of anaesthesia and compared it to coughing (control data) and this was then used to assess the variation in generation of particles. In comparison to coughing the study pointed out that general anaesthesia procedures did not generate more aerosols than previously thought.[13] Reference coughing data was collected using the same collection methods used to detect aerosol production during the study. [13] Particle measurements were made in the operating theatres with laminar flow and no changes were made to the OR environment; in addition, background aerosol concentrations were also taken into consideration.[13] It was demonstrated that all procedures were equivalent statistically to concentrations seen in coughing in total particle concentration and these did not exceed the mean aerosol generation of coughing.[13] Mask ventilation produced the highest measured individual total particle concentration, but this was still lower than mean aerosol generation during coughing.[13] Mean particle generation during intubation also did not exceed coughing statistically.[13] Interestingly, difficult intubations produced less aerosol than a normal intubations.[13] Extubation also generated aerosol concentrations comparable to coughing.[13] Extubations with coughing tended to produce up to four times more particles than with the patient not coughing during extubation.[13]

A simulation study by Feldman et al used fluorescent markers to visualise the deposition of simulated exhaled respiratory secretions on the surface of HCWs involved in endotracheal intubations. The study demonstrated that despite PPE, 8 of the 8 HCWs that participated in the study had fluorescent markers visible on their hair, 7 of the 8 had markers visible on their exposed skin, 6 on the neck, 1 on the ear and 4 had markers on their shoes. [14] The findings suggest that the current recommendations for PPE may not be sufficient to prevent exposures during tracheal intubations in the emergency department setting.[14] Aerosols can be deposited on uncovered skin, hair and shoes.[14] This infective material may possibly have the potential to cause infection to HCWs involved in intubations via hand transfer to the nose, mouth and eyes if the HCW does not adhere to strict hand hygiene.

Table 2. Summruy of ruticles on aerosol generation and transmission of infection to the anaesthetist

Title of Study	Authors and Publication	Aims and Objectives	Study Setting	Sampling Method	Study Design	Findings	Most relevant findings applicable to our study	Comments
A quantitative evaluation of aerosol generation during tracheal intubation and extubation	Brown et al, October 2020	To provide quantitative evidence on the size, distribution and particle number concentration of airborne particles produced during intubation and extubation (aerosol generating procedures)	Four ultraclean laminar flow ventilation operating theatres in a UK hospital	Particle analysis instruments	Prospective environmental monitoring study	Facemask ventilation followed by tracheal intubation produced very low quantities of aerosolised particles smaller than cough particles. Tracheal extubation including coughing produced a detectable aerosol. Particles produced during extubation was 15 times more than with intubation but 35-fold less than a volitional cough. Aerosol generation with a cough during extubation is quantitatively different from extubation without a cough.	Tracheal intubation and extubation produce far less airborne particles than that of a volitional cough. There was also l 5x more detectable aerosol during extubation than intubation and this production of aerosol was increased when the patient coughed. The study was unable to make any conclusions about the risk of transmission of SARS-CoV 2 as aerosol generation is still only a presumed risk factor and particle number concentration is not a proven measure of that infection risk.	The limitations of this study were the small number of observations included (19 intubations and 14 extubations). No measurements were made from subjects known to have COVID-19 and the concentration of live virions within the particles were not measured.
Aerosolisation during tracheal intubation and extubation in an operating theatre setting	Dhillon et al, Se p tember 2020	To determine whether facemask ventilation, intubation and extubation generate aerosols in clinical practice and to characterise any aerosol production.	Operating theatre	Larger particles detected using laser-based particle image velocimetry and smaller particles detected using spectrometry with continuous air sampling.	Observational study	Mean particle concentrations measured during tracheal intubation were 12 times greater than baseline. Facemask ventilation in a patient who received neuromuscular blockers, tracheal tube insertion and inflation of cuff produced mostly small particles of <5 micrometers, however concentrations were 30-300 times greater than background noise.	The study demonstrates that positive pressure mask ventilation, tracheal intubation and procedures and events following extubation produce small particles in counts several hundred times over baseline. These remain suspended in air and can spread throughout the operating theatre. The patient coughing into the Hudson mask also produced large signal spikes during measurements.	The study had several limitations one being the small sample size. The study did not measure virions present in the aerosol particles. Also, the proceduralists hands during measurement of particles could have interfered with the data recording.
Aerosol Generating Procedures and Risk of transmission of acute respiratory infections to Healthcare Workers : A Systematic Review	Tran et al, April 2012	To evaluate the risk of transmission of Acute Respiratory Infections to health care workers caring for patients undergoing aerosol generating procedures in comparison to HCWs caring for	NIA	NIA	Systematic Review and meta-analysis	The study has demonstrated that there are some AGPs that have been associated with an increased risk of SARS transmission to HCWs. Tracheal intubation was found to be the most consistent association across the numerous studies included in this systematic review.	Tracheal intubation had a higher risk of SARS-COV transmission compared to unexposed health care workers- this was demonstrated in 7 of the 8 studies included in the article. Four cohort studies revealed that healthcare workers involved in tracheal intubation had a higher risk of disease transmission compared to those not exposed. Four case-control studies showed that tracheal intubation was a significant risk factor for transmission of SARS to HCWs. The authors using multivariate	The generation of aerosols from specific procedures was not looked at in this article nor was the presence of microbes within the aerosols produced during these aerosol generating procedures. The findings could not exclude that the transmission of SARS was due to direct and indirect contact transmission. The overall evidence in this systematic review was very low quality of evidence according to GRADE. Due to the low-quality evidence and the small number of

		patients not undergoing AGPs					analysis in three of the case-control studies, also reported that tracheal intubation was an independent risk factor for transmission of SARS.	studies included in this review, it should be interpreted with caution.
Risks to healthcare workers following tracheal intubation of patients with COVID-19: a prospective international multicenter cohort study	El-Boghdadly et al, June 2020	To evaluate the incidence of laboratory-confirmed COVID-19 diagnosis or new symptoms that required self-isolation or hospitalisation after being involved in tracheal intubation.	Hospitals in 17 countries	The Intubate-COVID registry	Prospective multicenter cohort study	Following a tracheal intubation with a confirmed or suspected COVID-19 patient 1 in 10 healthcare workers subsequently reported a COVID 19 outcome.	184 participants (10.7%) reported a COVID-19 outcome. 144 (8.4%) reported symptomatic self-isolation. 53 (3.1%) reported a laboratory confirmed COVID-19 infection and 2 (0.1%) reported hospital admission with COVID-19 symptoms. Univariable associations indicated a higher incidence of COVID-19 infection between countries in women and assistant vs intubators. The study also identified women as being at increased risk of reporting a COVID-19 outcome.	It is unclear as to which elements of the procedure contributed to the increased risk. There was also insufficient utilization of PPE in more than 12% of cases which could have contributed to the increased risk of infection. Direct causality linked to tracheal intubations per se cannot be demonstrated as HCWs may be exposed to SARS-COV-2 from other sources. Asymptomatic seroconversion was not recorded therefore the results may be underestimated.
Exposure to a Surrogate Measure of Contamination from simulated patients by Emergency Department Personnel wearing Personal Protective Equipment	Feldman et al, April 2020	To assess the protection of HCWs wearing the recommended PPE (WHO and CDC recommendations) while caring for a simulated patient with respiratory distress.	An emergency department	Fluorescent markers were used to visualise deposition of simulated exhaled respiratory secretions on the surface of HCWs involved in endotracheal intubations.	A Simulation Study	The study demonstrated that despite PPE, 8 of the 8 HCWs had fluorescent markers visible on their hair, 7 of the 8 had markers visible on their exposed skin, 6 on the neck, 1 on the ear and 4 had markers on their shoes.	The findings suggest that the current recommendations for PPE may not be sufficient to prevent exposures during tracheal intubations in the emergency department setting.	Aerosols can be deposited on uncovered skin, hair and shoes. This infective material may possibly have the potential to cause infection to HCWs involved in intubations via hand transfer to the nose, mouth and eyes if the HCW does not adhere to strict hand hygiene.
Aerosol generation during general anesthesia is comparable to coughing: An observational clinical study	Oksanen et al, December 2021	To assess staff exposure to potentially infectious particle generation during general anesthesia	University Hospital	Particle Optical Sizer	An observational clinical study	Induction during anesthesia generates small aerosol particles (<1micrometre). General anesthesia procedures ie. preoxygenation, mask ventilation, intubation and extubation are not highly aerosol-generating in comparison to coughing.	The highest total aerosol concentration was seen with mask ventilation. Preoxygenations, mask ventilations, uncomplicated intubations and extubations produced mean aerosol concentrations statistically comparable to coughing. Difficult intubations produced fewer aerosols than uncomplicated intubation or coughing.	The study looked at aerosolisation of particles during all steps of airway management in an OR. The link between aerosol generation and viral transmission was not investigated.

Transmission of Severe Acute Respiratory Syndrome Coronavirus 1 and Severe Acute Respiratory Syndrome Coronavirus 2 During Aerosol-Generating Procedures in Critical Care: A Systematic Review and Meta-Analysis of Observational Studies	Chan et al, July 2021	To assess the risk of coronavirus transmission to healthcare workers performing aerosol-generating procedures and the potential benefits of personal protective equipment during these procedures	N/A	N/A	Systematic Review and meta-analysis	Significant increase in odds of HCWs contracting SARS-CoV-1 or SARS-CoV-2 during Endotracheal intubation (OR, 6.69; 95% CI, 3.81–11.72; $p < 0.001$) when compared with their those not involved in Endotracheal intubation	This systematic review was the first to summarize the risk of coronavirus transmission to HCWs via AGPs since the COVID-19 pandemic	This review is mainly based on retrospective observational studies. Furthermore, the studies from the SARS epidemic may not be entirely generalizable to the current COVID-19 pandemic clinically.
Transmission of Severe Acute Respiratory Syndrome during Intubation and Mechanical Ventilation	Fowler et al, February 2004	To determine whether specific ventilatory strategies were associated with an increased risk of SARS development in healthcare workers	Hospital setting, critical care units	N/A	Retrospective cohort analyses	Greater risk of developing severe acute respiratory syndrome for physicians and nurses performing endotracheal intubation (relative risk [RR], 13.29; 95% confidence interval [CI], 2.99 to 59.04; $p = 0.003$)	Healthcare workers performing intubations are at increased risk of infective aerosol transmission. Nurses may be more at risk than physicians	There may be multiple reasons for the finding of increased risk in nurses; time in contact with the patient may be the most important. As the article looked at SARS we cannot draw definitive conclusions about COVID-19 based on this study.

Discussion:

Tracheal intubation and extubation are procedures involving multiple steps. These procedures require the healthcare worker to be in close contact to the patient and the airway. It therefore places healthcare workers at risk due to both droplet and fomite transmission of the virus. From our scoping review we find that evidence supports the infective risk of SARS-CoV-1 and SARS-CoV-2 to healthcare workers involved in airway procedures such as intubation and extubation [3,8,9,10]. Although intubation is associated with an increased risk of infections, other factors may also play an infective risk. These may include the proximity to the patient, for example, heavy breathing and coughing before intubation and bag mask ventilation, as these also generate aerosols [12,13], instead of intubation itself. In addition, exposure time to the patient may also play a role in the risk of infection.

As demonstrated in the study by Feldman et al, aerosols can be deposited on areas such as the skin of the neck and face [14]. Self-inoculation of the contaminated material to the eyes, mouth and nose may also play role in the mechanism of spread of the virus. Self-inoculation may arise due to poor hand hygiene or by lack of adherence to common disease-controlling etiquettes.

Three studies in our scoping review confirmed that tracheal intubation and extubation do produce aerosols which can remain suspended in air and spread through the operating theatre [11,12,13]. However, the quantities and sizes of these aerosols differ between the various studies. Brown et al found that tracheal intubation including mask ventilation produced very low quantities of aerosolized particles [11]. In addition, Brown demonstrated that tracheal extubation when the patient coughed produced detectable levels of aerosol which was more than that produced during intubation but less than a volitional cough [11]. Due to their definition used that "aerosol generating procedures are considered to have a greater likelihood of producing aerosols compared with coughing", they emphasize that elective tracheal intubation should not be designated as an aerosol generating procedure [11]. Dhillon et al also highlighted aerosol generation during airway management and demonstrated that there are specific steps during airway management that are particularly aerosol-generating (positive pressure bag and mask ventilation and the patient coughing into a mask[12]. Dhillon et al appeared to demonstrate higher concentrations of aerosol produced during airway management in comparison to the study by Brown et al [15]. As mentioned in an editorial by Nestor et al these varying concentrations of aerosol production during intubation and extubation from baseline levels could be as a result of the different background ventilation systems, sampling locations and particle counters used [15].

Oksanen et al also demonstrated that general anaesthesia procedures do not produce more aerosol when compared with coughing [13]. Their study however showed that aerosol generation was comparable to that of coughing [13]. From the above studies investigating aerosol generation, intubation and extubation is as high-risk a procedure as coughing [11,12,13].

There are numerous strategies in place at different institutions to reduce the risk of infection when carrying out AGPs during surgical interventions. Some of these strategies include the use of a higher level of PPE, decreasing the number of staff members in the theatre and a reduction in the amount of unnecessary equipment in the OT. These interventions can impact negatively on patient care. It is important for us as health care workers to make evidence-based decisions on whether these procedures are still required in the future given the above findings, whilst still maintaining safe practice. However there has still been no change in the policies regarding what is defined as an AGP and the use of PPE.

The use of a barrier device to limit the exposure to aerosol was evaluated by one South African study. Swart and colleagues used a Perspex box (designed by their own team) to limit the exposure to aerosol during intubation. The use of the box increased the total time to successful intubation. This may negatively impact patients who are already severely hypoxaemic from a COVID pneumonia needing intubation and ventilation. The time to intubation was not affected by the type of laryngoscope used or the seniority or expertise of the person performing the intubation. [17]

If procedures such as tracheal intubation do not produce as much aerosol as a volitional cough but are still found to be high risk with regards to infection, we should then evaluate other mechanisms to account for this increased risk as discussed in the article by Klompas et al for example, forced air over moist respiratory mucosa generating virus-laden respiratory particles, symptoms and disease severity of the patient, distance from respiratory emissions and the time period that one is exposed to virus-laden aerosols [16].

Limitations

This scoping review is limited to only the aerosol generating procedures of intubation and extubation and therefore cannot apply to other aerosol generating procedures associated with risk to healthcare workers. There are inconsistent methodologies between studies which make drawing conclusions from the studies difficult. Newer evidence or recommendations may have been published following finalizing this manuscript, however the incidence and severity of the COVID-19 pandemic is reducing.

Conclusions

The aerosol generating procedures of intubation and extubation are high risk for the transmission of SARS-COV-1 and SARS-COV-2 from infected patients to healthcare workers. The quantity of aerosol generated seems to be less than that generated by a cough. Procedures known to generate aerosol still require further research in terms of the risk of transmission of viral particles. The actual mechanisms of increased infective risk are still unclear. In addition, the definition of high-risk aerosol generating procedures needs to be reevaluated as exposures during normal patient care may also place an individual at risk for example, a coughing patient in the general ward. It is our opinion that healthcare workers, for both patient care and for their own safety, continue with current PPE practices until further research is available.

Considerations and Recommendations:

1. Intubation, mask ventilation and events around extubations increase aerosol production above baseline levels; these tend to be <5μm in size and may be suspended in air for longer.
2. Aerosol has been found to deposit on various sites on HCWs that may not be protected with PPE and therefore HCWs should be encouraged to sanitise areas not covered with PPE.

3. Intubations and extubations have been shown to produce less aerosol than volitional coughing. HCWs should try to avoid unnecessarily stimulating a patient's airway during extubation, which may trigger coughing.
4. The link between aerosol generation and viral transmission has not conclusively been proven and remains a gap in the literature; however, HCWs are encouraged to use the appropriate PPE (including an FFP2 or N95 respiratory).
5. The procedure of tracheal intubation has been shown to have an increased risk of viral transmission and this should be performed by the most experienced HCW wearing the appropriate PPE.

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Appendices

Appendix 1: The Final Study Protocol

University of KwaZulu-Natal
College of Health Sciences
School of Clinical Medicine

Aerosolisation during Intubation and Extubation and its associated Risk of Transmission of SARS-CoV-2 to Healthcare Workers: A Scoping Review

Degree: MMED Anaesthetics

Principal Investigator: Dr Verushka Naidoo
Student number: 201293859

Contact details:
Address: 3 La Pianta, Ballito Gardens, Ballito
Tel: 032 9470228
Cell: 0842758543
E-mail: vnaidoo1982@yahoo.com

Supervisor : Dr Komalan Govender
E-mail address: Komgovender@gmail.com

Date: 13 November 2021

Table of Contents

1. Background and Literature Review

Coronavirus disease 2019 (COVID-19) which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) was first confirmed in South Africa on the 5th of March 2020. On the 15th of March 2020 President Cyril Ramaphosa declared a national state of disaster. Since then, the pandemic has continued to impact our daily lives during the various levels of lockdown. For many healthcare workers (HCWs) aerosol generating procedures (AGPs) have become a major source of concern due to the risk of transmission of infection by airborne particles. During the current pandemic many HCWs have been infected with SARS-CoV-2 that has resulted in either severe illness or death.

There appears to be little consensus on which procedures are deemed aerosol-generating. There is also a lack of evidence regarding quantifying aerosol generation during these procedures and any new high quality epidemiological studies that reveal an increased risk of infection with regards to SARS-CoV-2 [1,2]. As HCWs, we are frequently involved in aerosol generating procedures like intubation and extubation and may therefore be at an increased risk of contracting COVID-19, however the extent of this risk remains unclear.

The World Health Organization defines an AGP as any medical procedure that can induce the production of aerosols of various sizes, including droplet nuclei. [1] Due to the lack of strong evidence and agreement amongst experts there is still no final or all-inclusive list of AGPs.[3] The Center for Disease control and Prevention list the following procedures as aerosol generating: open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BiPAP, CPAP), bronchoscopy and manual ventilation.[3]

High flow oxygen delivery and nebulized-drug administration are marked as potential aerosol generating procedures due to limited data related to their infectivity.[3] Of importance to our scoping review are the aerosol-generating procedures of intubation and extubation. A study conducted by Tran *et* al. had demonstrated that certain aerosol-generating procedures are associated with an increased risk of SARS-CoV-1 transmission.[2] Across most of the studies evaluated in this systematic literature review and meta-analysis it was found that tracheal intubation was the most consistent associated factor with regards to transmission.[2] The authors also noted tracheal intubation as an independent risk factor for the acquisition of SARS-CoV-1.[2] The results of this study dealt with SARS-CoV-1 and therefore cannot be generalised to other acute respiratory infections, but given the fact that the novel coronavirus also infects the upper and lower respiratory tracts and the high viral loads found in these secretions, it could be postulated that this may also apply to SARS-CoV-2. This notion is reaffirmed in a study by El-Boghdadly *et* al. where it was demonstrated that approximately 1 in 10 healthcare workers that were involved in tracheal intubation of patients with suspected or confirmed COVID-19 subsequently reported a COVID-19 outcome.[4]

An observational study by Dhillon *et* al. showed that mean particle concentrations measured during tracheal intubation were 12 times greater than baseline ($p<0.001$).[5] In addition facemask ventilation in a patient who received neuromuscular blockers using oxygen at 6-10 L/min, tracheal tube insertion and inflation of cuff produced mostly small particles <5 micrometres in concentrations 30-300 times greater than background noise ($p<0.0001$). [5] This study confirms that intubation and extubation are aerosol-generating procedures but conclusions cannot be made about the risk of transmission of COVID-19.

In contrast, a study by Brown *et* al. a minimal increase in aerosol production was demonstrated during controlled intubation and extubation, for this reason the authors questioned whether these procedures can actually be classified as AGPs as they produced less aerosol than a volitional cough.[6] There was also 15x more detectable aerosol during extubation than intubation and this production of aerosol was increased when the patient coughed.[6] The study was unable to make any conclusions about the risk of transmission of SARS-CoV-2 as aerosol generation is still only a presumed risk factor and particle number concentration is not a proven measure of that infection risk.[6] In an article by Klompas *et* al. the authors identified 4 factors that may explain the risk of transmission during medical procedures. These being: (1) forced air over the respiratory mucosa, (2) symptomatic patients and disease severity, (3) distance from the source and (4) the duration that one is exposed to aerosols.[7] They concluded that a combination of these factors may increase one's risk of infection even further.

The above factors could also explain why HCWs involved in intubation and extubation are at a higher risk of infection than other aerosol-generating procedures due to the close proximity to the airway. Although intubation and extubation are known to stimulate coughing and to increase aerosol generation their risk of transmission is still not clearly identified. It is important that HCWs are informed about this risk and consider the implications this may have in their daily practice. COVID-19 is said to continue to disrupt our lives into the near future and with vaccinations now in progress we may also come into contact with patients that may be asymptomatic who require tracheal intubation for certain surgical procedures. It is for this reason that we are in urgent need for high quality research in this area so that we can minimise the risk of transmission of SARS-COV-2.

2. Aim and Objectives

The aim of this project is to explore and describe the risk of aerosolization of SARS-CoV-2 to the anaesthetist during management of the airway.

The objectives are to:

a) Define what an aerosol generating procedure is in relation to anaesthetic practice
b) Review the evidence on aerosolization during intubation and extubation in anaesthetic practice
c) Explore the literature on aerosol generation in SARS-CoV-2 and the risk to the anaesthetist
d) Summarize the recommendations of guidelines published by different organizations on the management of AGP's and the anaesthetist during intubation or extubation of a SARS-CoV-2 positive patient.
e) To identify gaps in the literature where future research may be directed

3. Methodology

Scoping Review

The current literature is inconsistent regarding the definition, method of measurement of aerosolization, assessment of risk of disease transmission, and lacks specificity to SARS-CoV-2 infections. For these reasons, a scoping review would be appropriate to aggregate the current state of the literature to advise on the possible impact of aerosolization to the anaesthetist during airway management. This method is most appropriate for areas of the literature that are not supported by large, randomized control trials or robust observational data. We therefore hope to map the existing literature in the field of interest and to identify research gaps in the existing literature.

This scoping review will be conducted using the Arksey and O' Malley framework.[8,9] The following five steps will be included in this scoping review: (i) identifying the research question, (ii) identifying relevant studies, (iii) study selection, (iv) charting the data, and (v) collating, summarizing, and reporting the results. The sixth step of this framework which is optional will not be conducted in our study.

i. Identifying the research question

The research question is:

- What is the risk of transmission of SARS-CoV-2 to an anaesthetist exposed to during routine management of the airway (i.e. during intubation or extubation)?

ii. Identifying relevant studies

A formal literature search was performed for evidence on the topic of Aerosolisation during Intubation and Extubation and its associated Risk of Transmission of SARS-CoV-2 to anaesthetists. The following electronic databases will be included: PUBMED, EMBASE, Cochrane Library. The search terms 'aerosol-generating procedures', 'intubation', 'extubation', 'anaesthetist', 'anaesthesiology' and 'SAR-CoV-2' will be used for the search.

A ‘hand search’ of key terms will also be conducted from the references of the studies included in the study. We also included websites such as the World Health Organization (WHO) and the Centers for Disease Control and Prevention as part of our search criteria.

iii. Study Selection

The titles and abstracts will be screened by two authors independently (VN and KG) to select publications providing evidence or reporting on aerosolisation during intubation and extubation and its associated risk of transmission of SARS-CoV-2 to anaesthetists.

Any conflicts regarding which articles would be included will be resolved by consensus and discussion with another senior researcher in the Dept. of Anaesthetic at UKZN. Background reference searching will be conducted for the selected studies to ensure that any essential references will not be left out of the study.

A final search of the literature will be conducted prior to preparing the final manuscript for publication to include the most recent studies.

Inclusion Criteria:

- Articles describing aerosolization at the time of intubation or extubation
- Articles specifically describing aerosolization in any respiratory tract infection
- Articles specifically describing aerosolization in SARS-CoV-2 infections
- Articles published in English
- No Date restrictions
- Peer reviewed empirical studies of any design

Exclusion Criteria:

- Animal studies

iv. Charting the Data

A data charting form will be developed by the primary investigator (VN) and reviewed by co-investigator (KG) to capture relevant information from each of the included studies. The data extracted will include the following headings:

1. Title of Study
2. Publication
3. Aim of Study
4. Study Setting
5. Sampling Method
6. Study Design
7. Conclusion
8. Most relevant findings to our study
9. Comments

v. Collating, summarizing, and reporting of results

The data will be collated and assessed on a Microsoft Excel Spreadsheet. Data will be summarized in table form. A narrative report and recommendations will be generated of all the findings.

4. Ethical Considerations

This scoping review will not include animals or humans as participants. All the information sourced will be from published literature. An application for ethics exemption will be submitted to the UKZN Biomedical Research Ethics Committee.

5. Budget (including Funding obtained)

This study is self-funded.

6. Timelines and Project Management

The literature review will be conducted over 12 weeks. Summarizing the data will take approximately 4 weeks. Interpreting the data and resolving conflicts will take approximately 4 weeks. Preparing the manuscript will take approximately 4 weeks. The project should take 6 months from the time of scientific and ethical approval.

7. Contributors and Authorship

Names: Verushka Naidoo (VN) and Komalan Govender (KG)
University of KwaZulu-Natal, Discipline of Anaesthesiology and Critical Care
Contribution: VN and KG conceived of the study, VN participated in the design of the study, VN will undertake the literature review process and data extraction. Both authors will draft the manuscript. Both authors will read and approve the final manuscript.

Authors or acknowledgements:
First author: VN
Second author: KG

Proposed Target Journal:
South African Journal of Anaesthesia and Analgesia

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Appendix 2: The Guidelines for Authorship for the Journal selected for submission of the manuscript

South African Journal of Anaesthesia and Analgesia

Accredited by the Department of Higher Education and Training (DHET) for research subsidy.

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:

- conception, design, analysis and interpretation of data;
- drafting or critical revision for important intellectual content; and
- 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
- 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.

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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.

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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.

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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: '...'
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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.

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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.

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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,[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

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A covering letter to the editor is mandatory and must include statements that the manuscript has not been published previously and is not under review elsewhere. It should state details of any prior publication of the research in abstract form or in Congress proceedings. The letter must declare if any of the authors have a conflict of interest and that the requirements for submission, including ethics approval and patient permission for case reports have been fulfilled. All authors must sign the covering letter.

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Case Studies
(1 800 words) (3 pages)

Clinical reviews
(2 400 words) (3-4 pages)

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Appendix 3: Ethical Approval

Appendix 4: Expanded Summary of data extraction

Title of Study	Authors and Publication	Aims and Objectives	Study Setting	Sampling Method	Study Design	Conclusion	Most relevant findings applicable to our study	Comments
A quantitative evaluation of aerosol generation during tracheal intubation and extubation	Brown et al, October 2020	To provide quantitative evidence on the size, distribution and particle number concentration of airborne particles produced during intubation and extubation (aerosol generating procedures)	Four ultraclean laminar flow ventilation operating theatres in a UK hospital	Particle analysis instruments	Prospective environmental monitoring study	Facemask ventilation followed by tracheal intubation produced very low quantities of aerosolised particles (1.4 (1.4) particles.l^{-1}, n=14, p<0,0001 vs cough). Tracheal extubation especially when the patient coughed produced a detectable aerosol (21 (18) particles.l^{-1}, n= 10). Particles produced during extubation was 15 times more than that with intubation (p=0,0004) but 35-fold less than a volitional cough (p=0,0001) which produced 732 (418) particles.l^{-1}, n=38). Aerosol generation with a cough during extubation is quantitatively different from extubation without a cough therefore making it important to reduce the risk of coughing during extubation.	Tracheal intubation and extubation produce far less airborne particles than that of a volitional cough. There was also 15x more detectable aerosol during extubation than intubation and this production of aerosol was increased when the patient coughed. The study was unable to make any conclusions about the risk of transmission of SARS-CoV 2 as aerosol generation is still only a presumed risk factor and particle number concentration is not a proven measure of that infection risk.	The limitations of this study were the small number of observations included (19 intubations and 14 extubations). Also no measurements were made from subjects known to have COVID-19 and the concentration of live virions within the particles were not measured.
Aerosolisation during tracheal intubation and extubation in an operating theatre setting	Dhillon et al, September 2020	To determine whether facemask ventilation, intubation and extubation generate aerosols in clinical practice and to characterise any aerosol production.	Operating theatre	Larger particles detected using laser-based particle image velocimetry and smaller particles detected using spectrometry with continuous air sampling.	Observational study	Mean particle concentrations measured during tracheal intubation were 12 times greater than baseline (p<0.001). Facemask ventilation in a patient who received neuromuscular blockers using oxygen at 6-10 $l.min^{-1}$, tracheal tube insertion and inflation of cuff produced mostly small particles <5 micrometers in concentrations 30-300 times greater than background noise (p<0.0001).	The study demonstrates that positive pressure mask ventilation, tracheal intubation and procedures and events following extubation produce small particles in counts several hundred times over baseline. These remain suspended in air and can spread throughout the operating theatre. The patient coughing into the Hudson mask also produced large signal spikes during measurements.	The study has several limitations one being the small sample size. The study also does not measure virions present in the aerosol particles. Also the proceduralists hands during measurement of particles could have interfered with the data analysed.

Aerosol Generating Procedures and Risk of transmission of acute respiratory infections to Healthcare Workers : A Systematic Review	Tran et al, April 2012	To evaluate using clinical evidence the risk of transmission of Acute Respiratory Infections to health care workers caring for patients undergoing aerosol generating procedures in comparison to HCWs caring for patients not undergoing AGPs	N/A	N/A	Systematic Review and meta-analysis	The study has demonstrated that there are some aerosol generating procedures that have been associated with an increased risk of SARS transmission to HCWs. Tracheal intubation was found to be the most consistent association across the numerous studies included in this systematic review.	Tracheal intubation had a higher risk of SARS-COV transmission compared to unexposed health care workers- this was demonstrated in 7 of the 8 studies included in the article. 4 cohort studies revealed that healthcare workers involved in tracheal intubation had a higher risk of disease transmission compared to those not exposed. 4 case-control studies showed that tracheal intubation was a significant risk factor for transmission of SARS to HCWs. The authors using multivariate analysis in three of the case-control studies, also reported that tracheal intubation was an independent risk factor for transmission of SARS.	The generation of aerosols from specifics procedures was not looked at in this article nor was the presence of microbes within the aerosols produced during these aerosol generating procedures. The findings could not exclude that the transmission of SARS was due to direct and indirect contact transmission. The overall evidence in this systematic review was very low quality of evidence according to GRADE. Due to the low-quality evidence and the small number of studies included in this review, it should be interpreted with caution.
Risks to healthcare workers following tracheal intubation of patients with COVID-19: a prospective international multicenter cohort study	El-Boghdadly et al, June 2020	To evaluate the incidence of laboratory-confirmed COVID-19 diagnosis or new symptoms that required self-isolation or hospitalisation after being involved in tracheal intubation.	Hospitals in 17 countries	The Intubate-COVID registry	Prospective multicenter cohort study	Following a tracheal intubation with a confirmed or suspected COVID-19 patient 1 in 10 healthcare workers subsequently reported a COVID 19 outcome.	184 participants(10.7%) reported a COVID-19 outcome. 144(8.4%) reported symptomatic self-isolation. 53(3.1%) reported a laboratory confirmed COVID-19 infection and 2(0.1%) reported hospital admission with COVID-19 symptoms. Univariable associations using Cox regression models in the study indicated a higher incidence of the primary endpoint of COVID-19 infection between countries in women and in assistants vs intubators. The study also identified women as being at increased risk of reporting a COVID-19 outcome.	In the study it is unclear as to which elements of the procedure contributed to the increased risk. There was also insufficient utilisation of PPE in more than 12% of cases which could have contributed to the increased risk of infection. Direct causality linked to tracheal intubations per se cannot be demonstrated as HCWs may be exposed to SARS-COV-2 from other sources. The authors also did not consider asymptomatic seroconversion therefore the results may be underestimated.
Exposure to a Surrogate Measure of Contamination from simulated patients by Emergency Department Personnel wearing Personal Protective Equipment	Feldman et al, April 2020	To assess the protection of HCWs wearing the recommended PPE (WHO and CDC recommendations) while caring for a simulated patient with respiratory distress.	An emergency department	Fluorescent markers were used to visualise deposition of simulated exhaled respiratory secretions on the surface of HCWs involved in endotracheal intubations.	A Simulation Study	The study demonstrated that despite PPE, 8 of the 8 HCWs had fluorescent markers visible on their hair, 7 of the 8 had markers visible on their exposed skin, 6 on the neck, 1 on the ear and 4 had markers on their shoes.	The findings suggest that the current recommendations for PPE may not be sufficient to prevent exposures during tracheal intubations in the emergency department setting.	Aerosols can be deposited on uncovered skin, hair and shoes. This infective material may possibly have the potential to cause infection to HCWs involved in intubations via hand transfer to the nose, mouth and eyes if the HCW does not adhere to strict hand hygiene.

Aerosol generation during general anesthesia is comparable to coughing: An observational clinical study	Oksanen et al, December 2021	To assess staff exposure to potentially infectious particle generation during general anesthesia	University Hospital	Particle Optical Sizer	An observational clinical study	Induction during anesthesia generates small aerosol particles (<1micrometre). General anesthesia procedures ie. preoxygenation, mask ventilation, intubation and extubation are not highly aerosol-generating in comparison to coughing.	The highest total aerosol concentration was seen with mask ventilation. Preoxygenations, mask ventilations, uncomplicated intubations and extubations produced mean aerosol concentrations statistically comparable to coughing. Difficult intubations produced fewer aerosols than uncomplicated intubation or coughing.	The study looked at aerosolisation of particles during all steps of airway management in an OR,
Transmission of Severe Acute Respiratory Syndrome Coronavirus 1 and Severe Acute Respiratory Syndrome Coronavirus 2 During Aerosol-Generating Procedures in Critical Care: A Systematic Review and Meta-Analysis of Observational Studies	Chan et al, July 2021	To assess the risk of coronavirus transmission to healthcare workers performing aerosol-generating procedures and the potential benefits of personal protective equipment during these procedures	N/A	N/A	Systematic Review and meta-analysis	Significant increase in odds of HCWs contracting SARS-CoV-1 or SARS-CoV-2 during Endotracheal intubation (OR, 6.69; 95% CI, 3.81–11.72; $p < 0.001$) when compared with their those not involved in Endotracheal intubation	This systematic review was the first to summarize the risk of coronavirus transmission to HCWs via AGPs since the COVID-19 pandemic	This review is mainly based on retrospective observational studies. Furthermore, the studies from the SARS epidemic may not be entirely generalizable to the current COVID-19 pandemic clinically.
Transmission of Severe Acute Respiratory Syndrome during Intubation and Mechanical Ventilation	Fowler et al, February 2004	To determine whether specific ventilatory strategies were associated with an increased risk of SARS development in healthcare workers	Hospital setting, critical care units	N/A	Retrospective cohort analyses	Greater risk of developing severe acute respiratory syndrome for physicians and nurses performing endotracheal intubation (relative risk [RR], 13.29; 95% confidence interval [CI], 2.99 to 59.04; $p = 0.003$)	Healthcare workers performing intubations are at increased risk of infective aerosol transmission. Nurses may be more at risk than physicians	There may be multiple reasons for the finding of increased risk in nurses; time in contact with the patient may be the most important. As the article looked at SARS we cannot draw definitive conclusions about COVID-19 based on this study.