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A rapid review of aerosol generating procedures (AGPs)

An assessment of the UK AGP list conducted on behalf of the UK IPC Cell

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Summary

Background

In response to the SARS-Cov-2 pandemic, infection prevention and control (IPC) guidance was developed for the NHS across the four nations of the UK. This guidance included a list of aerosol generating procedures (AGP) based on the findings of previously conducted reviews. Given that SARS-CoV-2 is a novel pathogen, the evidence base regarding AGPs is still evolving, and the extant AGP list was determined when COVID-19 was classified as an HCID (High consequence infectious disease), a review of the extant AGP list was deemed necessary in support of NHS remobilisation needs across the UK.

Purpose

A rapid review was conducted that sought to assess the available evidence identified for each procedure included on the current UK AGP list and to identify risks specific to SARS-CoV-2 in the current context (epidemiology and vaccination inclusive). The research question of the review was purposefully focused. Specifically, the review sought to answer the following research question: What is the available evidence to support the removal of any procedures currently included on the UK AGP list?

Data Source

Iterative specific and sensitive search strategies, informed in part by the previously conducted AGP reviews, were developed and used to search the Medline (OVID), Cinahl (EBSCOHost), and PubMed bio-medical databases.

Study Selection

The population, intervention, outcome and study designs eligible for inclusion in this review were:

Population: Adults and children with or without clinically suspected or confirmed COVID-19 or other respiratory infection (SARS, MERS, or influenza) or a simulated exposure model (for example, using human volunteers, cadavers, etc.).

Intervention: Procedures currently included on the UK AGP list. (Tracheal intubation and extubation; manual ventilation; tracheostomy; bronchoscopy; dental

procedures using high speed devices; non-invasive ventilation (NIV), bi-level positive airway pressure ventilation (BiPAP), continuous positive airway pressure ventilation (CPAP); high flow nasal oxygen (HFNO); high frequency oscillatory ventilation (HFOV); induction of sputum using nebulised saline; respiratory tract suctioning; upper ENT airway procedures; upper gastro-intestinal endoscopy; surgery/post-mortem if in the respiratory tract or sinuses).

Comparison: As reported in eligible studies.

Outcome: Aerosol generation (size and number of particles), rate/risk of SARS-CoV-2 transmission, or environmental contamination as reported in eligible studies.

Study design: Case-reports, case-series, case-control, cohort studies, outbreak reports, intervention studies (all designs, including empirical studies) were eligible for inclusion in the review.

Titles and abstracts were reviewed by a single reviewer. Two reviewers screened 20% of the titles and abstracts returned via the literature search, to ensure consistency of approach. Conflicts in assessment were resolved via consensus. The remaining titles and abstracts were screened by a single reviewer. Full text screening of results was undertaken using a standardised screening form and was performed by a single reviewer and screening of excluded studies was undertaken by another reviewer.

Data Extraction

Data from eligible full text studies were extracted to a standardised form using Microsoft Excel, which included the main PICOS elements of the review. Specifically, study design, country, location/setting, population, procedure (as per the extant AGP list), exposure/intervention, outcome measure, outcome definition/ascertainment, quantitative outcomes (both absolute and relative), limitations, and any other important comments were extracted.

Evidence synthesis

A total of 37 studies met the eligibility criteria of the review. Fourteen of the studies reported on two or more of the procedures included on the current UK AGP list. Methodological and clinical heterogeneity was observed across the included studies and outcome, ascertainment, definition, and reporting also varied meaning the studies were subject to limitations and uncertainty.

Three studies examined tracheal intubation and extubation. All patients included were anaesthetised and paralysed and underwent urgent, emergency or elective procedures. It was reported that aerosol levels were significantly lower compared

with natural respiratory activities. Therefore, consideration should be given to amending the list to reflect the identified evidence in anaesthetised and paralysed patients by removing intubation and extubation from the UK AGP list.

Three studies assessed manual facemask ventilation and based on the limited volume of evidence identified by the review it appears that consideration should be given to removing manual facemask ventilation from the extant UK AGP list.

Two studies each assessed a single case of tracheostomy insertion and there were limitations and uncertainties in the reported results. Both studies reported low levels of aerosol generated but provide insufficient evidence to support the removal of tracheostomy insertion from the extant UK AGP list.

Two studies examined bronchoscopy which were subject to limitations and uncertainties. Thus, there is currently insufficient evidence to support the removal of bronchoscopy in awake patients from the extant UK AGP list.

Six studies examined dental procedures. It is particularly difficult to distinguish between device-derived and patient-derived aerosols in this setting but there is consensus that dental procedures should remain on the UK AGP list.

Seven studies assessed non-invasive ventilation (NIV) and are consistent in suggesting that NIV is not associated with increased aerosol generation and aerosol concentrations were lower than that associated with natural respiratory activities. Therefore, consideration should be given to removing NIV from the extant UK AGP list.

Nine studies examined high flow nasal oxygen (HFNO). Most of these studies reported that HFNO was either associated with a decrease in aerosol levels or that the aerosol levels were not significantly different to either baseline levels or those generated by coughing. Therefore, consideration should be given to removing HFNO from the extant UK AGP list.

Eight studies assessed ear, nose, and throat (ENT) airways procedures, and available evidence suggests that such procedures should remain on the UK AGP list.

Three studies assessed upper gastro-intestinal endoscopy. The available evidence included in this review indicates that upper gastro-intestinal endoscopy in awake patients should remain on the UK AGP list.

Five studies examined surgical procedures in the respiratory tract or sinuses and the evidence included in this review suggests that these procedures should remain on the extant UK AGP list.

No studies were included in the review that examined high frequency oscillatory ventilation (HFOV), induction of sputum using nebulised saline, respiratory tract suctioning, or post-mortem procedures.

Three studies that examined the relationship between clinicians, AGPs, and COVID-19 infection met the inclusion criteria of this review. The included evidence that examined the risk to clinicians of COVID-19 infection associated with AGPs is insufficient to enable any definitive conclusions to be drawn.

Limitations of included studies

Included studies were subject to potential bias and confounding. The studies were both methodologically and clinically heterogeneous and there was variation in outcome measures and outcome assessment. Not all of the studies may be generalisable to the UK population and clinical practice. The majority of studies did not include patients with respiratory infection, and most were unable to quantify risk or identify specific risk factors for transmission of respiratory infection associated with the interventions examined.

Limitations of the review

Rapid review methodology was employed, and formal quality assessment of the included studies could not be performed. This was due to heterogeneity in outcome measures and therefore outcome reporting precluded pooling of studies for estimation of effect.

Conclusions

The review identified evidence which suggests that consideration should be given to removing some of the procedures currently included on the UK AGP list. However, the evidence assessed was subject to a number of limitations and uncertainties that should be considered before amending the UK AGP list.

Introduction

In response to the SARS-CoV-2 pandemic, infection prevention and control (IPC) guidance was developed for health and care services across the four nations of the UK. This guidance included a list of aerosol generating procedures (AGP).

The AGP list was informed in part by transmission based guidance developed as part of the National Infection Prevention and Control Manual (NIPCM), Scotland, derived from World Health Organization (WHO) recommendations.¹ The NIPCM AGP review was published in 2017 and included an AGP list that was broader than that of the World Health Organization (WHO). In addition, a review² was undertaken by the Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) Scotland group based on AGP enquires received in relation to COVID-19. This review included additional procedures based on the HCID (High consequence infectious disease) classification at the beginning of the pandemic and perceived level of risk based on expert opinion. The recommendations of this review were agreed in collaboration with experts from New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) and Public Health England (PHE). A further systematic review³ was undertaken on behalf of the Independent High Risk AGP Panel, to review specific cough-related procedures that had not been considered in previous reviews and were the subject of enquiries. The panel noted in their advice that there is an absence of evidence for these procedures, and the challenges of the evidence base more generally for AGPs, indicating the urgent need for more research. Given that SARS-CoV-2 is a novel pathogen with disease dynamics that differ markedly from the viruses responsible for SARS and MERS, the evidence base regarding AGPs is still evolving, and the extant AGP list was determined when COVID-19 was classified as an HCID, a review of the extant AGP list was deemed necessary in support of NHS remobilisation needs across the UK.

Objective

The review sought to assess the available evidence identified for each procedure included on the current UK AGP list and to identify risks specific to SARS-CoV-2 in the current context (epidemiology and vaccination inclusive). Therefore, the research question was purposefully focused. Specifically, the review sought to answer the following research question: What is the available evidence to support the removal of procedures currently included on the UK AGP list?

Methods

A formal protocol was not generated or registered on the International Prospective Register of Systematic Reviews (PROSPERO), or equivalents, for the rapid review. The current review does not meet the PROSPERO eligibility criteria as a systematic review methodology was not employed due to time constraints (the service required clarification quickly) and the necessary processes, governance, and responsibilities were not established to conduct a full review. However, an SBAR was developed which summarised the situation and the proposed methodology for conducting this review. Therefore, the rapid review was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)⁴, Cochrane guidance^{5, 6}, and Synthesis without meta-analysis (SWiM) in systematic reviews guidance⁷ where possible and appropriate.

Stakeholders (clinical consultation group)

In lieu of a multi-disciplinary review group (recommended when undertaking systematic reviews⁵) a Clinical consultation group was formed to advise during the review process based on the Cochrane recommendations regarding stakeholder involvement and roles in rapid reviews.⁶ Specifically, the group provided clinical advice and input to the review by assessing:

- the search strategies and identifying any omitted terms or acronyms.
- the appropriateness of the eligibility criteria developed.
- the studies identified for full text review to identify any incorrectly included studies and any additional studies not identified or erroneously excluded.

The Clinical consultation group were involved in the eligibility assessment, but were not involved directly in data extraction, appraisal, or in the initial drafting of the review. However, post assessment the group were consulted to seek their clinical opinion and comments regarding the results and conclusions of the completed draft review before production of the final draft.

Eligibility criteria

Inclusion and exclusion criteria for the review were developed in accordance with PICOS (Population; Intervention; Comparison; Outcome; Study design) and are shown in table 1 below.

Table 1: Eligibility criteria applied during the review process

Eligibility criteria	
Population	Adults and children with or without suspected clinically suspected or confirmed COVID-19 or other respiratory infection (SARS, MERS, or influenza) or a simulated exposure model (for example, using human volunteers, cadavers, etc.).
Exposure / Intervention	Procedures currently included on the UK AGP list: tracheal intubation and extubation; manual ventilation; tracheostomy; bronchoscopy; dental procedures using high speed devices; non-invasive ventilation (NIV), bi-level positive airway pressure ventilation (BiPAP), continuous positive airway pressure ventilation (CPAP); high flow nasal oxygen (HFNO); high frequency oscillatory ventilation (HFOV); induction of sputum using nebulised saline; respiratory tract suctioning; upper ENT (ear, nose, and throat) airway procedures; upper gastro-intestinal endoscopy; surgery/post-mortem if in the respiratory tract or sinuses.
Comparison	As reported in eligible studies.
Outcome	Aerosol generation (number concentration, mass concentration and size distribution of particles), rate of transmission, risk of transmission, or environmental contamination as reported in eligible studies.
Study design	Case-reports, case-series, case-control, cohort studies, outbreak reports, intervention studies (all designs, including empirical studies).
Exclusion criteria	
	Procedures not currently included on the UK AGP list.
	Studies examining the efficacy or effectiveness of mitigation measures used during AGP.
	Studies conducted in environments/settings or using interventions/therapeutics that are not generalisable to the UK health and/or social care setting.
	Clinical and/or consensus guidelines, editorials, opinion/news studies, predictive modelling studies, in-vitro, vaccine studies, systematic reviews, and meta-analyses.
	Grey literature
	Pre-print (not peer reviewed) studies
Date range	2019 to present (cut off as per the latest DB update or day search was run).
Language	English only

Information sources

The extant UK AGP list was determined in part via the recommendations/findings of three prior reviews.¹⁻³ Following an assessment of the sources that were used by these reviews, Medline (OVID), Cinahl (EBSCOHost), and PubMed were identified

as the most appropriate sources to inform the current review. Registries and grey literature sources were not searched as part of the current review; nor were pre-print databases or platforms. No handsearching or snowball searching was performed. However, as part of the review process the Clinical consultation group were asked to suggest any additional studies, they were aware of, that were not identified via the literature searches.

Literature searches

Search strategies were developed iteratively for each database using a combination of subject headings (controlled vocabulary) and free text terms appropriate for each platform. The strategies were informed by the approaches taken in the ARHAI² and Independent High Risk AGP Panel³ reviews. Therefore, specific strategies (based on the ARHAI approach) and sensitive strategies (based on the Panel approach) were developed. The search strategies used are shown in appendix 3 (specific strategies) and appendix 4 (sensitive strategies) for each database searched to inform the review.

Study selection

The screening of titles and abstracts of results yielded via the literature searches was conducted by a single reviewer. Abstract assessment was conducted using a standardised title and abstract form that was developed and used to screen the titles and abstracts of the literature search results. Two reviewers screened 20% of the titles and abstracts returned via the literature search, to ensure consistency of approach. Conflicts in assessment were resolved via consensus. The remaining titles and abstracts were screened by a single reviewer. Full text screening of results was undertaken using a standardised screening form and was performed by a single reviewer and screening of excluded studies was undertaken by another reviewer.

Data collection and data items

Data from eligible full text studies were extracted to a standardised form using Microsoft Excel, which included the main PICOS elements of the review. Specifically, study design, country, location/setting, population, procedure (as per the extant AGP list), exposure/intervention, outcome measure, outcome definition/ascertainment, quantitative outcomes (both absolute and relative), limitations, and any other important comments were extracted.

Outcomes

Outcomes of interest for the review were aerosol generation (including the number concentration, mass concentration and size distribution of particles, where reported), rate of transmission, risk of transmission, or environmental contamination in relation to any of the procedures included on the UK AGP list as reported in the included studies. Due to the anticipated limited volume of evidence, the standard metrics used in the review were as reported in the eligible studies. It was anticipated that these would include measures of absolute effect, such as means as well as particle diameter and that relative effects may also have been reported, such as mean relative difference (proportion), odds ratios (OR), hazard ratios (HR), relative risk (RR), absolute risk reduction (ARR), and relative risk reduction (RRR).

Quality assessment (risk of bias)

Due to the different study designs and methodologies employed across the included studies, quality assessment was anticipated to be complex. Difficulties in assessing the quality of health protection and infection control studies have been well documented.⁸ No published quality assessment tools were deemed appropriate for a formal assessment of the risk of bias in the eligible studies due to the nature of their design. Therefore, assessment using a standardised assessment tool was not undertaken. However, limitations and potential uncertainties of included studies were included in the extraction process and recorded in the evidence table that informed this review.

Synthesis of results

In accordance with SWIM guidance⁷, the method of evidence synthesis was assessed prior to conducting this rapid review. Following this assessment, evidence synthesis was conducted based on grouping of the outcomes (and standard metrics if possible) as reported for each intervention (i.e., each AGP included on the current UK list). Given that the extant UK AGP list is comprised of interventions performed across a range of different specialties it was anticipated that synthesis should be performed for specialties / intervention as this would be clinically appropriate and of most use to the service. It was also anticipated that a lack of data would preclude meta-analysis or quantitative synthesis of estimated effect. Furthermore, it was expected that the results reported in the eligible studies would be heterogeneous in terms of outcome measure. Thus, it was determined a priori that “vote counting” was likely to be the most appropriate method of synthesising the effect reported in the studies for each AGP (that is, if there is evidence of a consistent direction of effect but not magnitude of effect).

Results

Search results

A total of 13,165 results were returned via the sensitive and specific literature searches. Following the removal of duplicates and the exclusion of records based on the screening of titles and abstracts, a total of 80 records underwent full text assessment. After assessment, a total of 53 records were excluded from the review for the following reasons: population (n=1); intervention/exposure (n=9); outcome (n=24); study design (n=14); and not available in full text (n=5). Therefore, 27 records were deemed eligible for inclusion in the review. Full details of the search and screening process are outlined in the PRISMA flow diagram, shown in appendix 1. (A list of the 53 excluded studies, by PICOS, is provided in appendix 2).

Upon review of the 80 articles eligible for full text review, the Clinical consultation group suggested an additional 18 studies as being potentially eligible for inclusion in the review. Following full text assessment, 8 studies were excluded from the review (intervention n=5 and study n=3). Therefore, an additional 10 studies were deemed eligible for inclusion in the review. Full details are shown in the PRISMA flow diagram, appendix 1, and a list of excluded studies is shown in appendix 2. Thus, a total of 37 articles overall were adjudged to be eligible for inclusion in this review.

Characteristics of included studies

Fifteen of the included studies⁹⁻²³ were conducted in the US; 11 studies²⁴⁻³³ were conducted in the UK; five studies³⁴⁻³⁸ were conducted in Australia; one was conducted in Canada³⁹, China⁴⁰, Japan⁴¹, and New Zealand⁴², respectively; two of the included studies^{43, 44} were international studies. Seventeen of these studies^{11, 12, 14, 15, 23, 27, 29-35, 37, 39-41} were conducted using patient populations.

The majority of the included studies used an empirical design, specifically: four studies^{9, 19, 21, 22} were cadaveric studies; 16 studies^{14, 15, 27, 29, 32, 39, 41, 11, 12, 23, 31, 33-35, 37, 40} used environmental monitoring / sampling; seven studies^{10, 13, 16, 17, 36, 38, 42} were conducted with healthy volunteers; one study³⁰ used both healthy volunteers and COVID-19 positive patients (as a reference group); six studies^{20, 24-26, 28, 45} were conducted using a manikin; two were case control studies^{18, 44}; and one was a prospective cohort study.⁴³

Of the studies eligible for inclusion in the review:

- three studies examined tracheal intubation and extubation (n=2 environmental monitoring / sampling^{27, 35}; n=1 manikin study²⁰)
- three studies assessed manual ventilation (n=3 environmental monitoring / sampling^{27, 32, 34})
- two studies assessed tracheostomy (n=2 environmental monitoring / sampling^{31, 37})
- two studies examined bronchoscopy (environmental monitoring /sampling^{23, 39})
- six studies examined dental procedures (n=1 environmental monitoring / sampling¹²; n=5 manikin studies^{24-26, 28, 45})
- seven studies assessed non-invasive ventilation (NIV) (n=1 environmental monitoring / sampling³³; n=5 healthy volunteers^{10, 13, 16, 36, 38}; n=1 healthy volunteers and COVID-19 patients as a reference group³⁰)
- nine studies examined high flow nasal oxygen (HFNO) (n=2 environmental monitoring / sampling^{11, 33}; n=6 healthy volunteers^{10, 13, 16, 36, 38, 42}; n=1 healthy volunteers and COVID-19 patients as a reference group³⁰)
- eight studies assessed ENT procedures (n=3 environmental monitoring / sampling^{14, 15, 23}; n=1 healthy volunteers¹⁷; n=4 cadaveric studies^{9, 19, 21, 22})
- three studies assessed upper gastro-intestinal endoscopy (n=3 environmental monitoring / sampling^{29, 40, 41})
- five studies examined surgical procedures (n=3 environmental monitoring / sampling^{14, 15, 34}; n=2 cadaveric studies^{19, 22})

Fifteen of the eligible studies^{10, 13, 16, 19, 21-23, 27, 33, 34, 36, 38} reported on two or more procedures included on the current UK AGP list.

No studies were included in the review that examined high frequency oscillatory ventilation (HFOV), induction of sputum, respiratory tract suctioning, or post-mortem procedures. Further details regarding the location of studies, populations, and interventions by specific AGP is provided in the next section.

In this review the term “awake” includes patients who are sedated and excludes anaesthetised patients with secured airways.

Results of Individual studies

Tracheal intubation and extubation

Three studies^{20, 27, 35} were included in the review that examined tracheal intubation and extubation and the association with aerosol generation. One study²⁷ was conducted in an ultraclean (highly ventilated and high efficiency particulate air [HEPA] filtered) operating theatre environment, one in a “standard” operating theatre³⁵, and Weber²⁰ in an unspecified room or “chamber”. In two of these studies

the population was comprised of COVID-19 negative patients who were anaesthetised for urgent and emergency orthopaedic trauma and neurosurgical procedures²⁷ and elective endonasal pituitary surgery.³⁵ Weber²⁰ used a training manikin with simulated body fluid (including fluorescein) added to the lungs and stomach. During the intervention a researcher “squeezed” the manikin to imitate coughing and vomiting.

In Brown²⁷ environmental sampling was performed across all phases of the procedure (pre-oxygenation, induction of anaesthesia and neuromuscular blockade with manual facemask ventilation, laryngoscopy and tracheal intubation) by means of an optical particle sizer, sampling 0.5m from patients’ heads (directly above for most but also some observation behind patients’ heads). This study reported on aerosol detected during intubation (n=19 patients) and extubation procedures (n=14 patients); for three patients, multiple attempts at intubation were included in the analysis and were considered in each case as belonging to a single continuous intubation sequence. Environmental sampling was undertaken in the Dhillon³⁵ study, which included three elective patients, by means of air sampling with spectrometry with observations made 0.5m superior and 0.5m caudal to the patient’s nasal aperture. This study also used particle image velocimetry. Weber²⁰ employed air sampling at a stationary location (~1m above the floor and from the procedure) and in the “personal breathing zone” of clinicians and surface sampling at seven locations across the room.

The reported outcome in Brown²⁷ was airborne particle size, distribution, and particle number concentration associated with the procedure. Aerosol associated with background and volitional coughs (n=38 coughs; n=1 healthy volunteer) were used for comparison in this study. In Dhillon³⁵ the outcome was reported as count, size, duration, and direction of any aerosol produced during the procedure. Weber²⁰ reported fluorescein concentration in air particles and surface contamination associated with the procedure.

Tracheal intubation:

- Brown²⁷ reported that volitional coughs were associated with a rapid and transient spike. Mean peak aerosol concentration 2 seconds after the cough was observed as 1,310 particles/L (± 905). Most of these particles were <1 micrometre in diameter.

The mean number of particles detected in a 5 minute period during anaesthetic induction and intubation was 7 particles (± 6), compared with background (empty theatre) ~2 particles per 5 minute period. The mean concentration of particles recorded during the intubation period was 1.4 particles/L (± 1.4), which was reported as 500-fold lower than the mean

concentration recorded during volitional coughs of 732 particles/L (± 418) ($p < 0.0001$). The maximum concentration recorded during intubation, averaged across events, was 77 particles/L (± 49), which was reported as 22-fold lower than the peak concentration during volitional coughs 1,688 particles/L (± 872) ($p < 0.0001$).

- Dhillon³⁵ reported mean particle concentrations during tracheal intubation were 12 times greater than baseline ($p < 0.001$). The study reported an increase in aerosol during facemask ventilation, rather than intubation. Clarification was subsequently provided in another study³⁴ by the same authors and in the same patients (refer to section below).
- Weber²⁰ reported median particles observed at the stationary position during intubation of 3.13 nanograms/m³ (IQR: not detectable to 6.53 nanograms/m³) (50% of sample below detection limit). Median particles from observations made within the personal breathing zone were reported as not detectable (IQR: not detectable to 15.1 nanograms/m³). (70% of samples below detection limit). Aerosol levels observed during tracheal intubation were lower compared with other activities assessed in the study.

Extubation:

- Brown²⁷ reported the mean concentration observed was 21 particles/L (± 18), which was reported as 35-fold lower than observed during a volitional cough ($p < 0.0001$) but 15-fold greater than during intubation ($p = 0.0004$). The maximum concentration during extubation averaged across events was reported as 432 particles/L (± 209) and this was associated with evoked coughing, which was still significantly lower than volitional coughs 1,688 particles/L (± 872) ($p < 0.0001$).

Manual facemask ventilation

Three studies^{27, 32, 34} examining manual facemask ventilation and aerosol generation met the eligibility criteria of this review. The study by Brown²⁷ assessed manual facemask ventilation as part of the intubation sequence (details are outlined in the section above). Two studies were conducted in ultraclean operating theatres located at a single institution in the UK.^{27, 32} The other study was conducted in a “standard” operating theatre with conventional ventilation in Australia.³⁴ All studies included COVID-19 negative patients undergoing either elective surgery^{32, 34} or urgent and emergency orthopaedic trauma and neurosurgical procedures.²⁷ The intervention in Shrimpton³² and Dhillon³⁴ was facemask ventilation; Shrimpton³² included 11 anaesthetised and paralysed patients, Dhillon³⁴ three anaesthetised and paralysed patients. Outcome assessment was via particle image velocimetry

(n=3 locations) and air sampling with spectrometry in one study.³⁴ Shrimpton³² used an optical particle sizer with observations made 20cm directly above the mouth of the patient. The reported outcome in Shrimpton³² was particle size and number concentration associated with the procedure; tidal breathing and volitional cough were also assessed. In Dhillon³⁴ the outcome was reported as count, size, duration, and direction of any aerosol produced. The study by Shrimpton³² was a collaboration of the Brown²⁷ and Dhillon³⁵ intubation groups conducted to investigate the results reported by Dhillon regarding aerosol generation and facemask ventilation. Using a jointly agreed protocol the study examined the relationship between facemask ventilation and aerosol generation, and it was agreed between the groups that the level of aerosol observed was less than observed for tidal breathing.

- It was reported that facemask ventilation produced mostly small particles <5 micrometres in concentrations 30 to 300 times greater than background ($p < 0.001$) in Dhillon.³⁴ (Clarification of the results reported in Dhillon³⁵).
- Shrimpton³² reported a median particle concentration of 191 particles/L (IQR [interquartile range]: 77 to 486 [range: 4 to 1,313]) for tidal breathing, which was consistently detected compared to background levels and the difference was statistically significant ($p = 0.002$). In comparison, volitional coughs were observed to have a peak median aerosol concentration of 1,260 particles/L (IQR: 800 to 3,242 [range: 100 to 3,682]). Most particles (86.5%) measured <1 micrometre.

Median particle concentration during 60 seconds of facemask ventilation without a leak was 3 particles/L (IQR: 0 to 9 [range: 0 to 43]), which was not significantly different compared with background level ($p = 0.43$) and significantly lower than during tidal breathing ($p = 0.001$). Particle concentration during facemask ventilation with a leak was 11 particles/L (IQR: 7 to 26 [range: 1 to 62]), approximately five-fold higher than background ($p = 0.019$) but lower (17-fold) than that during tidal breathing ($p = 0.002$). Median peak particle concentration during the periods of facemask ventilation without a leak was 60 particles/L (IQR: 0 to 60 [range: 0 to 120]) compared with 120 particles/L (IQR: 60 to 180 [range: 60 to 480]) when there was a leak, which is 20-fold ($p = 0.002$) and 10-fold ($p = 0.001$) lower, respectively, than particle count detected during a volitional cough.

- Brown²⁷ reported the mean number of particles detected in a 5 minute period during anaesthetic induction with a period of manual facemask ventilation and intubation was 7 particles (± 6), compared with background (empty theatre) ~2 particles per 5 minute period. The mean concentration of particles recorded during the intubation period was 1.4 particles/L (± 1.4),

which was reported as 500-fold lower than the mean concentration recorded during volitional coughs of 732 particles/L (± 418) ($p < 0.0001$). The maximum concentration recorded during intubation, averaged across events, was 77 particles/L (± 49), which was reported as 22-fold lower than the peak concentration during volitional coughs 1,688 particles/L (± 872) ($p < 0.0001$).

Tracheostomy

The eligible studies^{31, 37} that examined tracheostomy procedures both used environmental monitoring / sampling to determine aerosol generation during a single procedure performed on a single patient. There was clinical heterogeneity across both studies. The procedure was reported as being “semi-elective” and the patient was COVID-19 positive in McGain³⁷; in Ramesh³¹ the COVID-19 status of the patient was unclear. Furthermore, surgical tracheostomy was performed in McGain³⁷ and percutaneous tracheostomy in Ramesh.³¹ However, the procedures in both studies were performed on anaesthetised and paralysed patients. Ramesh³¹ was performed in an ultraclean operating theatre, McGain³⁷ was performed in a standard operating theatre. In both studies a technique was used that aimed to minimise aerosol generation; this included paralysis of muscle activity, passing the tracheal tube beyond the surgical site before opening the trachea and pausing lung ventilation during the open tracheal phases of surgery. The studies were also methodologically heterogeneous. An aerodynamic particle sizer and a combined optical and electrical particle sizer were used in McGain³⁷; an optical particle sizer was used in Ramesh³¹ to assess aerosol generation. In both studies the observations were made at approximately 30cm from the patient airway and surgical site. Both studies reported that aerosol measurement was performed during all phases of the procedure, although there was variation in the timings of measurements. Ramesh³¹ separated the procedure into distinct phases and reported corresponding aerosol levels (per cm^3). McGain³⁷ reported aerosol level as a fold increase compared to baseline for specific phases of the procedure. Therefore, there was also variation in the reporting of the results. However, both studies^{31, 37} reported that aerosol levels observed during the procedures were generally “low”.

Bronchoscopy (awake)

Two studies^{23, 39} that assessed aerosol generation associated with bronchoscopy were eligible for inclusion in this review. There was methodological and clinical heterogeneity between the studies. Environmental sampling was used in Doggett³⁹ and Zheng²³ and both studies assessed aerosol generation by means of an optical particle counter. However, there was some variation in the positioning of the devices in both studies. In Doggett³⁹ observations were made 75cm from the patients’ head (towards their feet); in the Zheng²³ observations were made 60cm

from the patient's oral cavity (positioned to the left of the clinician). Doggett³⁹ included 39 patients (per protocol population) undergoing bronchoscopy in two negative pressure endoscopy suites at two tertiary care centres. Zheng²³ reported aerosol levels observed while conducting several endoscopic procedures in an "standard" operating theatre at a single centre, including one bronchoscopy. The reporting of aerosol levels in the studies also differed. While both studies reported aerosol level as change from baseline, Doggett³⁹ reported the change in relation to specific aerosol diameter whereas Zheng²³ reported a cumulative difference in aerosol level. In Doggett³⁹ observations indicated a fall in aerosol with the median difference compared with baseline was reported as: 0.3 micrometres: -5.5 (-389.2 to 85.3) $p=0.44$; 0.5 micrometres: -29.4 (-46.8 to -16.0) $p<0.001$; 1.0 micrometres: -4.1 (-7.2 to -2.2) $p<0.001$. In Zheng²³, no significant difference compared with baseline was reported in particles 0.3 to 1.0 micrometres but a significant reduction in particles sizes 1.0 to 25 micrometres was reported.

Dental procedures using high speed devices

In total six studies^{12, 24-26, 28, 45} that assessed dental procedures, using high speed devices, met the eligibility criteria for inclusion in this review. Aerosol generation was assessed in five of these studies^{24-26, 28, 45} by conducting dental procedures on a dental manikin and environmental monitoring / sampling was used in Meethil.¹² There was variation in the setting in which the manikin studies were conducted. Two studies^{24, 25} (both by Allison) were conducted in a simulation unit located within the same UK dental school laboratory with one study²⁵ being conducted in an open plan clinic and a dental surgery and the other study²⁴ in a "room" with a "standard hospital ventilation system". Another of the included manikin studies²⁶ (also by Allison) was conducted in an open plan clinic located at the same UK institution. The remaining two manikin studies^{28, 45} were both conducted in a dental surgery located at two different UK institutions. The Meethil study¹² was conducted at a single US institution and included 28 patients, 19 of whom were reported as being COVID-19 positive.

The intervention in four of the manikin studies^{24-26, 45} was crown preparation, although Vernon⁴⁵ also assessed root canal preparation. In Ehtezazi²⁸ six different procedures were performed, including cavity preparation (n=3 locations), use of a three in one syringe, and an ultrasonic scaler (n=2 locations). The duration of the procedures varied across the included studies, for example, whether procedures were performed in sequence, the length of time prior to the interventions when aerosol assessment was performed, and the length of time performing the procedure. There was heterogeneity in the equipment used to carry out the procedures, with the studies reporting the use of air turbines^{24, 25, 28, 45}, electric contra angle handpieces²⁸, ultrasonic scalers^{24, 25, 28}, electric speed controlled handpiece⁴⁵, and three in one syringes.²⁸ Furthermore, one of the studies²⁶

assessed aerosol generation associated with a novel electric micro-motor handpiece. One study¹² assessed aerosol generation associated with dental implants and “restorative procedures” using “high-speed handpieces” and ultrasonic scalars.

The assessment of aerosol generation was also heterogeneous across the included studies. An optical particle sizer (0.5m from the manikin oral cavity and 2m from the dental chair), surface (spectrofluorometric analysis) and air sampling were employed in one study.²⁵ An optical particle sizer (0.5m, 1.5m, and 1.7m from the dental chair) surface (spectrofluorometric analysis) and air sampling were used in another study.²⁶ In Ehtezazi²⁸ a cascade impactor (at n=6 locations across the dental surgery) was used. Photographic image analysis and spectrofluorometric analysis were employed in another study.²⁴ In Vernon⁴⁵ artificial saliva infected with $\Phi 6$ bacteriophage, at approximately 10^8 plaque forming units per mL, was used and two particle counters and sampling (passive and active) on settle and air sampling plates were employed. Surface contamination was utilised in the Meethil¹² environmental monitoring / sampling study. Furthermore, in three studies²⁴⁻²⁶ (all by Allison) assessment was undertaken using fluorescein.

There was variation in the outcomes assessed in the eligible studies. While all of the studies sought to assess particle concentration or dispersal, one study²⁶ sought to assess the efficacy of a novel handpiece; Meethil¹² sought to determine the origin of microbiota in aerosols generated during dental procedures; one study²⁴ aimed to determine aerosol concentration and level associated with the procedures; Vernon⁴⁵ aimed to assess particle distribution associated with the use of different mitigation methods, however reported results included the use of no mitigations as a reference measure. The effect of ventilation on aerosol levels and distribution was examined in another study²⁵; and Ehtezazi²⁸ sought to characterise aerosol generation and mitigation measures. Therefore, the reported outcomes also varied.

- Two studies^{24, 25} reported that aerosol was detected during all procedures performed and that contamination reduced with increasing distance from the dental chair.
- Another study²⁶ reported that the novel handpiece was associated with increased aerosol level, especially at 0.5m where aerosol level was elevated throughout the procedures.
- Ehtezazi²⁸ reported >99.9% particles sampled proximal to patient were <0.3 micrometres and that the highest level of aerosol generated was by air turbine and electric contra angle handpiece. Peak aerosol concentrations were reported as occurring between particle diameters 0.013 to 0.022 micrometres at 9 to 12 minutes.

- Meethil¹² reported that microbiota from irrigants contributed to a median 78% (range: 2.5% to 100%) of the microbiota in condensate detected, irrespective of the procedure performed. Saliva was reported to have contributed to a median 0% (range: 0% to 82%). A median of 20% of the microbiota could not be attributed to either source (range: 0% to 90%). COVID-19 was reported as being undetectable in the condensate on the clinicians, patient, or environment in any of the interventions.
- Vernon⁴⁵ reported that bioaerosol was detected at all sampling points for all procedures conducted using an air turbine and no mitigation.

Non-invasive ventilation (NIV) / Continuous Positive Airway Pressure (CPAP)

In this review non-invasive ventilation (NIV) means ventilation or pressure support via a tightfitting facemask (or other device-patient interfaces such as a nasal mask or helmet). It can be subdivided into constant pressure (Continuous Positive Airways Pressure (CPAP) and alternating pressure (non-invasive positive pressure ventilation (NIPPV) / bi-level non-invasive positive pressure (BiPAP) these latter two terms being interchangeable). This review uses the term NIPPV for two level pressure NIV and CPAP for constant pressure NIV. Seven of the identified studies^{10, 13, 16, 30, 33, 36, 38} eligible for inclusion in this review examined NIV. The population in six of these studies^{10, 13, 16, 36, 38} was reported as being healthy volunteers, the population in Winslow³³ was exclusively COVID-19 positive patients (n=30).

There was variation in the reported settings of the studies. The Wilson³⁸ study of healthy volunteers was performed in an ultraclean sampling chamber. The remaining healthy volunteer studies were conducted in clinical settings, however the settings varied. Two studies were reported as being undertaken in clean³⁶ or ultraclean³⁰ clinical environments. Gaeckle¹⁰ reported being performed in a negative pressure environment and Pearce¹⁶ in a positive pressure environment. The remaining study¹³ conducted in healthy volunteers reported being carried out in an intensive care unit room that was set to “standard pressure”. The environmental sampling study³³ conducted in COVID-19 positive patients was reported as being multi-centre and being conducted in both “cohorted” wards as well as single rooms. The studies by Gaeckle¹⁰, Hamilton³⁰, McGain³⁶, and Wilson³⁸ were all conducted in settings with ultraclean backgrounds.

There was also clinical and methodological heterogeneity across the included studies. Specifically, several different oxygen modalities/delivery methods were assessed across the studies including: alternating pressure modes (NIPPV)^{10, 13, 38} and CPAP.^{16, 30, 33, 36} Five of the studies also included natural respiratory activities: normal, tidal, or quiet breathing via the nose or mouth^{10, 30, 38}; talking, in which

literature was provided to read at a normal volume¹⁰, or speaking³⁰; reciting the alphabet at a loud volume³⁸; repeating a short sentence as loud as could be sustained³⁸; deep breathing¹⁰; coughing^{13, 30, 38}; and exercise with a pedal exerciser.³⁸ Forced expiratory volume (FEV) was also included in the study by Wilson.³⁸ In three of these studies^{13, 30, 38} the interventions were performed with and without a surgical facemask. There was also heterogeneity in the duration and order in which the interventions were conducted across the eligible studies.

Outcome ascertainment varied across the studies: an aerodynamic particle spectrometer was used in two studies^{10, 36}; an aerodynamic particle spectrometer and optical particle sizer were used in Hamilton³⁰; a scanning mobility particle sizer spectrometer was also used in McGain³⁶; a particle counter was used in Miller¹³; a laser aerosol spectrometer was used Pearce¹⁶; an optical particle counter was used Wilson³⁸; and air and surface sampling was used in the Winslow³³ but no aerosol was measured. There was therefore also variation in observations (method, distance, and number of locations) in the different studies and in the corresponding outcomes assessed.

- NIPPV: It was reported in Gaeckle¹⁰ that NIPPV was not associated with increased aerosol generation compared with baseline and that coughing was the only activity associated with increased particle number. No significant difference in particle size or diameter was observed for coughing with or without NIPPV. Similarly, Miller¹³ reported that no statistically significant difference observed between any of aerosol levels associated with NIPPV and low flow nasal cannula ($p=0.79$). Analysis of variance suggested significant differences between the distances (sampling locations) and participants but not in comparison to low flow nasal cannula. Wilson³⁸ reported that in comparison with exercise alone, exercise plus NIPPV significantly reduced observed particle counts ($p=0.002$). This study also reported modest increases in total particle counts for NIPPV associated with increasing pressures (generally <5-fold). However, when NIPPV was applied during exercise NIPPV decreased aerosol generation. BiPAP was observed to have generated “moderate” aerosols (29.7 particles/mL) in McGain.³⁶
- Mask CPAP: Pearce¹⁶ reported that CPAP was associated with a maximum 15% reduction in smaller particles ($p<0.0001$; larger particles showed no significant change from baseline). It was reported in Hamilton³⁰ that CPAP was associated with reduced aerosol generation compared with all other interventions assessed. Even with a large, induced air leak (>50L/min), the aerosol emission measured over that leak during coughing was reported as lower than in participants not receiving CPAP 0.029 vs 1.40 particles/cm³; $p<0.001$). The size distribution of aerosol particles in patients with COVID-19 was very similar to healthy volunteers. Wilson³⁸ included CPAP in their

NIPPV series with the same results as those indicated above. Winslow³³ reported that in COVID-19 positive patients, four patients had a positive or suspected-positive sample in both an air and surface samples. CPAP use or coughing was not associated with significantly more environmental contamination compared to baseline.

High flow nasal oxygen (HFNO)

Nine studies^{10, 11, 13, 16, 30, 33, 36, 38, 42} that examined high flow nasal oxygen (HFNO) and aerosol generation were eligible for inclusion in this review. Seven of the studies described^{10, 13, 16, 30, 33, 36, 38} also assessed NIV. Two additional studies assessed HFNO. Gall¹¹ examined HFNO, performed in a single centre, in infants (aged 4 weeks to 24 months) who required HFNO but were otherwise healthy or who had a respiratory illness but were COVID-19 negative. The study by Jermy⁴² included healthy volunteers (n=10) who received HFNO at a single centre.

As shown in the NIV section above, the eligible studies^{10, 13, 16, 30, 33, 36, 38} were both clinically and methodologically heterogeneous. There was also variation in the Gall¹¹ and Jermy⁴² studies. Aerosol generation associated with HFNO was determined in Gall¹¹ by optical particle sizer and scanning mobility particle sizer. In Jermy⁴², observations were made using high speed camera imaging assessment and use of a chemical marker. This study examined quiet breathing; voluntary snort (mouth closed, expel air through nose with maximum effort); voluntary cough (mouth open); voluntary sneeze (allow mouth to open) with and without HFNO. The reported outcome in Gall¹¹ was near-field aerosol levels and the association with HFNO flow rate. In Jermy⁴² the outcome was reported as particle generation observed during the interventions. Therefore, there was variation in observations (method, distance, and number of locations) in the included studies and in the corresponding outcomes assessed.

- Gaeckle¹⁰ reported that the observed number and size of particles measured from the respiratory tract during HFNO did not significantly change compared with baseline levels and that coughing was the only activity associated with increased particle number. No significant difference in particle size or diameter was observed for coughing with or without HFNO.
- The study by Gall¹¹ reported no association between HFNO use, at any flow rate, and near-field particle counts.
- Hamilton³⁰ reported that HFNO was associated with increased aerosol concentrations compared to baseline measures (p<0.001 for 30L/min vs baseline, p<0.001 for 60L/min vs baseline for all comparisons). Higher flow rates (60L/min) were associated with higher reported aerosol concentrations

than lower flow rates (30L/min) for speaking (0.29 vs 1.71 particles/cm³, p<0.001), breathing (2.40 vs 0.33 particles/cm³, p<0.001), but not coughing (3.70 vs 2.61 particles/cm³, p=0.155), nor coughing with a surgical facemask (0.73 vs 0.34 particles/cm³, p=0.08). However, the aerosol was generated regardless of whether the machine was attached to a patient in a sub-study of HFNO machines (n=4). Therefore, the study states, this aerosol is generated by the machines and is not of clinical relevance and does not pose a risk of infection. HFNO generated particles were reported as small (<1 micrometre). The size distribution of aerosol particles in patients with COVID-19 was reported to be very similar to healthy volunteers.

- Jermy⁴² reported that during quiet breathing with no therapy and with 30L/min HFNO, no particles were detected. Particles were detected during quiet breathing with 60L/min HFNO. The results of the chemical marker analysis showed no significant differences due to HFNO, nor between types of vigorous breathing, nor due to distance (quiet only), nor due to HFNO order, and there were no two-way interactions between these factors.
- The McGain³⁶ study reported a low increase in aerosols was observed for HFNO at 60L/min (0.24 particles/mL).
- Miller¹³ reported that a significant difference was observed between measurement at the 0.6m and 1.8m (p<0.0001) for HFNO. Mean particle concentration 0.6m: 15 micrometres/m³ 1.8m: 10 micrometres/m³. Analysis of variance (ANOVA) suggested the difference was not significant for particles 5 to 10 micrometres. No statistically significant differences related to flow rate (p=0.08) or interaction between flow rate and distance (p=0.2) were observed. No statistically significant difference was observed between any aerosol levels during HFNO compared to during low flow nasal oxygen (p=0.79).
- In the Pearce¹⁶ study, HFNO was reported as being associated with a flow-dependent increase in particles at 60L/minute. HFNO increased generation of small particles 150 to 300 nanometres (55% increase) and large particles 0.5 to 2 micrometres (70% increase) compared to 15L/minute.
- Wilson³⁸ reported that particle counts decreased when HFNO was used during respiratory activities more exertional than quiet breathing, and significantly during coughing where aerosols emissions were halved (p=0.028). During exercise, HFNO reduced particle counts but the difference was not statistically significant.

- Winslow³³ reported that in COVID-19 positive patients (n=4), HFNO use or coughing was not associated with significantly more environmental contamination compared to baseline.

ENT airway procedures

In total, eight studies^{9, 14, 15, 17, 19, 21-23} were included in this review that examined upper ENT airway procedures and aerosol generation. The populations included in the studies varied. Four of these studies^{9, 19, 21, 22} were conducted using a cadaver; three included patients undergoing nasal endoscopy (n=11)¹⁵, nasal and skull based surgery (n=5)¹⁴, and direct laryngoscopy (n=10)²³; and one study¹⁷ included healthy volunteers (n=2).

There was also variation in the settings where studies were performed. Two studies¹⁴ were performed in a “standard” operating theatre/room; the Sharma¹⁹ and Workman²² studies were conducted in surgical laboratories; one study¹⁵ was conducted in a single outpatient setting; the Rameau¹⁷ study was conducted in two laryngology clinic rooms; another study²¹ was carried out in a clinical examination room and surgical laboratory; and the remaining study⁹ was conducted at a single centre but the setting of this study was unclear.

There was also clinical and methodological heterogeneity across the included studies. The reported interventions included in the studies varied. Rigid nasal endoscopy, flexible fiberoptic laryngoscopy, and rigid nasal suctioning was assessed in Boorgu.⁹ One study¹⁵ assessed diagnostic nasal endoscopies (n=11) and nasal endoscopies with debridement (n=19). Another study¹⁴ included skull base tumours (n=3), orbital abscess (n=1), and functional endoscopic sinus surgery (n=1).

Boorgu⁹ assessed fluorescent tracer concentration via a cascade impactor to examine near-field contamination. Both studies but Murr^{14, 15} sought to quantify aerosol generation associated with the interventions, however in one study¹⁴ this related to the increase in aerosol generation. Rameau¹⁷ sought to quantify aerosol and droplet generation associated with the procedure and Sharma¹⁹ examined the number of aerosol concentrations observed during the intervention. All four studies^{14, 15, 17, 19} reported using an optical particle sizer located at different positions and distances. In one of the studies by Workman²¹, the reported outcome was aerosol generation (size and distribution) during procedures and in the other Workman²² study, the reported outcome was aerosol generation in the 1 to 10 micrometres range. An optical particle sizer was used to make observations in both studies. Zheng²³ measured airborne particles 0.3 to 25 micrometres associated with the intervention by means of an optical particle counter. Therefore, there was

variation in observations (method, distance, and number of locations) in the included studies and in the corresponding outcomes assessed.

- The Boorgu⁹ study reported minimal to no field (surface) contamination was observed. Particles ≤ 14.1 micrometres were not detected during rigid nasal endoscopy, flexible fiberoptic laryngoscopy, and rigid nasal suction. However, the study states an overarching generalisation to endoscopy and suctioning could not be made.
- Murr¹⁴ reported 99% of all measured airborne particles were size ≤ 1.0 micrometre with 70.3% of total particulate measured to be 0.3 micrometres and 24.2% as 0.5 micrometres.
- Murr¹⁵ reported 99.2% of measured airborne particles were ≤ 1 micrometres, with 72.9% measured at 0.3 micrometres, 22.4% at 0.5 micrometres, and 4.0% at 1.0 micrometres. Mean particle concentration during diagnostic endoscopy was 6,021 p/ft³ with a nonsignificant mean difference of -173 p/ft³ (95% CI: $-1,139$ to 793; $p=0.698$) compared with pre-procedure concentrations.
- The study by Rameau¹⁷ reported that none of the laryngoscopy interventions produced aerosols above breathing and phonation (the only interventions with a statistically significant increase in aerosol compared with baseline).
- Sharma¹⁹ reported statistically significant increases in concentrations of aerosol 0.30 to 10 micrometres during rhinologic procedures ($p<0.05$).
- Workman²² reported statistically significant particulate generation of 1 to 10 micrometres during the intervention when there was no mitigation ($p<0.001$).
- Workman²¹ reported that the interventions were associated with significant airborne particle generation in the range of 1 to 10 micrometres.
- Zheng²³ reported that during direct laryngoscopies in anaesthetised intubated patients ($n=7$) a mean 6.7% increase in cumulative particles, primarily 0.3 to 1.0 micrometre particles ($p<0.0001$) was observed compared with baseline. Particles of diameter 1.0 to 25 micrometre significantly decreased ($p<0.001$) in comparison with baseline. During direct laryngoscopies with jet ventilation ($n=3$) there was no statistically significant change in cumulative particles compared with baseline, but a significant mean 42.4% increase in particles 1.0 to 25 micrometres compared with baseline ($p=0.002$).

Upper gastro-intestinal endoscopy (awake)

Three studies^{29, 40, 41} that examined aerosol generation associated with upper gastro-intestinal endoscopy met the eligibility criteria of this review. The methodology used in the studies varied and there were also clinical differences. All three studies^{29, 40, 41} employed environmental monitoring / sampling however, there was heterogeneity in the aerosol assessment across the studies. Chan⁴⁰ used a particle counter placed “directly in front of patients’ mouths”; Gregson²⁹ used an optical particle sizer with observation made 20cm from patients’ mouths; and Sagami⁴¹ used an optical particle sizer positioned inside a novel barrier used during the study. The locations of the procedures also differed. While all of the studies reported being conducted at a single institution, in Chan⁴⁰ procedures were conducted in an endoscopy suite, in an ultraclean operating theatres in Gregson²⁹, and in a “positive pressure room” in Sagami.⁴¹ The outcomes of the studies also varied with two of the studies^{29, 40} assessing aerosol generation during the procedure and Sagami⁴¹ assessing the effectiveness of a novel barrier used during the procedure. Furthermore, in two studies^{29, 40} aerosol generation was assessed by examining changes in aerosol concentration compared with baseline. In the Sagami⁴¹, the comparison used in the assessment was also against baseline aerosol levels however a cohort of healthy controls was also included and used for comparison against patients undergoing the procedure. Gregson²⁹ assessed aerosol concentrations associated with three reference activities (tidal breathing, via the mouth; nasal breathing; and volitional cough) and reported aerosol levels observed from burps and coughs observed during the procedure.

All three studies reported using a sample of patients drawn from institutional lists. With studies including 93 patients⁴⁰, 15 patients²⁹, and 103 patients and 90 controls (healthy volunteers).⁴¹ Chan⁴⁰ and Gregson²⁹ included a mixture of sedated and unsedated patients. Sagami⁴¹ included exclusively sedated patients. In two of the studies^{40, 41} the COVID-19 status of patients was not reported, while patients included in Gregson²⁹ were reported as being COVID-19 negative. There was also heterogeneity in the reporting of results across the studies, while all studies reported aerosol concentrations the unit of measure differed. In Chan⁴⁰ aerosol concentrations were reported as particle counts/cubic foot (dcF), in Gregson²⁹ as mean aerosol concentration per litre, and in Sagami⁴¹ as particle counts per cubic metre.

- Chan⁴⁰ reported that aerosol concentrations were higher, compared with baseline, during the procedure and that the observed increase was statistically significant ($p < 0.001$ to $p = 0.02$). In addition, the study also reported that sedation was not observed to influence the amount of aerosol.

- Gregson²⁹ reported mean particle concentration for voluntary coughs of 2,330 particles/L ($\pm 2,120$) and an average total number of particles detected per cough of 192 particles/L (± 183). The mean aerosol particle concentration observed during endoscopy was 595 particles/L ($\pm 1,110$), which was reported as not being significantly greater than tidal breathing via the mouth ($p=0.17$). The study also reported that during the procedure, coughs were frequently evoked and that burps were induced in approximately a third of procedures. Procedure-associated coughs had a mean peak concentration of 11,710 particles/L ($\pm 13,700$) and the total number of particles detected per cough was 780 particles/L ($\pm 1,010$). Procedure-associated coughs were associated with more aerosol than volitional coughs from the same patients ($p=0.008$). The mean peak concentration of particles observed for procedure-associated burps was 3,060 particles/L ($\pm 3,830$) and the total number of particles detected per burp was 205 particles/L (± 280), which were not significantly different compared with volitional coughs.
- In Sagami⁴¹, increased aerosol levels were observed during the procedure compared with prior to the procedure in 81% of patients and 22% of controls ($p<0.001$). Mean increased aerosol levels ($10^6/m^3$) were reported as 5.0 (± 4.5) for patients versus 1.9 (± 3.6) for controls ($p=0.006$). Increased aerosol levels after the procedure compared with before the procedure were observed in 74% of patients and 22% of controls ($p<0.001$). Mean increased aerosol levels ($10^6/m^3$) were reported as 4.4 (± 4.4) for patients versus 3.0 (± 4.1) for controls ($p=0.227$).

Surgical procedures in the respiratory tract or sinuses

Surgical procedures in the respiratory tract or sinuses and aerosol generation were assessed by five studies^{14, 15, 19, 22, 34} included in this review. Four of these studies^{14, 15, 19, 22} also assessed ENT airways procedures and details regarding their methodologies and populations are outlined in the ENT section above. A fifth study by Dhillon³⁴ that assessed surgical procedures was eligible for inclusion in this review. This study was conducted using patients ($n=3$) in an operating theatre located at a single centre. The reported outcome measure was particle size, concentration, airborne duration and spread. Observations were made using a particle sizer spectrometer 50mm superior and distal to the patient's nasal aperture. Particle image velocimetry was also employed in this study.

In addition to the differences identified across these studies (refer to ENT section) there was also variation in the surgical procedures carried out in the studies. Patients in Dhillon³⁴ underwent endonasal pituitary surgery. In Murr¹⁵ nasal endoscopies with debridement were performed on 19 patients. Surgery for skull base tumours ($n=3$), orbital abscess ($n=1$), and functional endoscopic sinus

surgery (n=1) were carried out in Murr.¹⁴ In the study by Sharma¹⁹ several endoscopic and surgical procedures of the sinuses were conducted. The Workman²² study assessed anterior and posterior endonasal drilling and cautery.

- Dhillon³⁴ reported that mean particle concentrations during endonasal access were up to 4.5 times greater than baseline (p=0.01). Turbinectomy and sphenoidotomy using a microdebrider was the only procedural step of endonasal access associated with a mean particle concentration above baseline (18 times greater, p=0.005). Mostly large particles >75 micrometres were observed. High speed drilling of the sphenoid keel, sphenoid septum or sella turcica floor; raising of a nasoseptal flap; and scissors did not produce mean aerosol greater than background values. Mean particle concentrations during pituitary tumour resection were less than baseline values but this difference was not significant (p=0.18). Use of a curved spatula, curettes, or suction within the sella were not associated with increases in aerosol above baseline.
- The study by Murr¹⁴ a mean change in particle concentrations compared to pre-instrumentation levels for cold instrumentation with suction were an increase of 716 particles/ft³ at the surgeon position (p=0.34), a decrease of 112 particles/ft³ at the circulator workstation position (p=0.99), and a decrease of 398 particles/ft³ at the anaesthesia provider position (p=0.76). Mean change in particle concentration following microdebrider use demonstrated an increase of 1,825 particles/ft³ at the surgeon position (p=0.001), an increase of 40 particles/ft³ at the circulator workstation position (p=0.99), and a decrease of 935 particles/ft³ at the anaesthesia provider position (p=0.16). Mean changes in particle concentration after drill use demonstrated an increase of 2,418 particles/ft³ at the surgeon position (p=0.001), a decrease of 34 particles/ft³ at the circulator workstation position (p>0.99), and a decrease of 1,690 particles/ft³ at the anaesthesia provider position (p=0.13). Aerosol concentrations during microdebrider use (1,825 particles/ft³ (95% CI: 508 to 3,141) and drill use (2,445 particles/ft³ (95% CI: 595 to 4,294) did not demonstrate a statistically significant difference (p=0.59).
- Murr¹⁵ reported that mean particle concentration during cold instrumentation was observed at 8,002 particles/ft³, with a significant mean increase of 2,462 particles/ft³ (95% CI: 837 to 4,088; p=0.005) from pre-procedure. Mean particle concentration during suction use was observed at 8,514 particles/ft³ with a significant mean increase of 2,973 particles/ft³ (95% CI: 1,419 to 4,529; p=0.001) compared with pre-procedure. Endoscope use prior to tissue manipulation during endoscopies with debridement was associated with a mean particle concentration of 7,169 particles/ft³ and a nonsignificant mean

increase of 1,629 particles/ft³ (95% CI: -96 to 3,354; p=0.063) from pre-procedure.

- The Sharma¹⁹ study reported statistically significant differences in total aerosol concentrations generated among several surgical procedures: cold functional endoscopic sinus surgery (FESS), microdebrider FESS, powered drilling, needle tip electrocautery, and use of an ultrasonic aspirator (p<0.001) without mitigation. Powered drilling produced a mean total aerosol concentration of 11.4 particles/cm³ which was significantly higher than cold FESS (1.29 particles/cm³; p<0.001), microdebrider FESS (-0.025 particles/cm³; p<0.001), and needle tip electrocautery (1.58 particles/cm³; p<0.001). There was no statistically significant difference between powered drilling and the ultrasonic aspirator (4.41 particles/cm³; p>0.99).
- Workman²² reported that without mitigation, significant particulate generation in the 1 to 10 micrometre range was observed during powered high-speed drilling of both the sphenoid rostrum (p<0.001) and anterior nasal septum / anterior medial maxillary wall (p<0.001). Significant airborne particulate generation in the 1 to 10 micrometre range was also observed in the 60 second period following cautery without mitigation (p<0.001), compared to matched-condition baseline background levels.

Risk of transmission to healthcare workers performing AGPs

Three studies were identified that examined the risk associated with AGPs, two case control^{18, 44} and one prospective cohort study.⁴³ The cohort study⁴³ and one of the case control studies⁴⁴ were international multicentre studies and the remaining case control study¹⁸ was an outbreak report conducted at a single centre.

The prospective cohort study⁴³ included 1,718 clinicians who had performed tracheal intubation (n=5,148) of patients with suspected or confirmed COVID-19. The reported composite outcome in this study was the incidence of laboratory-confirmed COVID-19 diagnosis or new symptoms requiring self-isolation or hospitalisation after a tracheal intubation episode. There was no comparator group included in this study. Lentz⁴⁴ recruited 1,130 clinicians, with 244 reported as cases (COVID-19 positive laboratory confirmed) and 886 as controls (COVID-19 negative). This study assessed the association between exposures within and outside the medical workplace with clinician SARS-CoV-2 infection. The study by Rosser¹⁸ examined exposure to a known index case (including conducting AGP) by clinicians and COVID-19 infection in seven cases and 93 controls linked to the index case.

- In the El-Boghdadly study⁴³ the incidence of the composite endpoint was reported as 10.7% over a median (IQR [range]) follow-up of 32 (18–48 [0–116]) days). The study reported that the risk of the composite endpoint varied by country; was higher in females; and not associated with other factors assessed in the analysis (age, HCW role, setting, personal protective equipment (PPE), procedures). Approximately, 1 in 10 clinicians involved in tracheal intubation of patients with suspected or confirmed COVID-19 subsequently met the composite outcome definition.
- The study by Lentz⁴⁴ reported that respirator use during AGPs (adjusting for age, gender, smoking status, presence of a baseline comorbidity, healthcare role, and world region) was associated with lower odds of clinician infection (adjusted [odds ratio] OR=0.4 (95% CI: 0.2 to 0.8; p=0.005), as was exposure by clinicians to intensive care and dedicated COVID units, negative pressure rooms, and the appropriate use of PPE (adjusted OR range, 0.4 to 0.7).
- Rosser¹⁸ reported that compared with controls, infected individuals reported significantly more patient contact time. Infected individuals were also significantly more likely to have performed airway procedures on the index patient, particularly placing the patient on HFNO, CPAP, or BiPAP (OR=11.6; 95% CI: 1.7 to 132.1).

Evidence synthesis

No eligible studies were identified that examined high frequency oscillatory ventilation (HFOV), induction of sputum using nebulised saline, respiratory tract suctioning, or post-mortem procedures. Therefore, there is insufficient evidence to support the removal of these procedures from the extant UK AGP list. Evidence was identified that examined the other procedures currently include on the extant UK AGP list and a brief synthesis of the evidence by procedure is provided below.

Tracheal intubation and extubation

Three studies^{20, 27, 35} that examined tracheal intubation and extubation met the eligibility criteria of this review. However, there were differences in the reporting of results and disagreement regarding the reporting and interpretation of results across the studies. Dhillon³⁵ argued initially that their results demonstrate that intubation is an AGP and that specific activities or phases of the procedure are associated with greater levels (peaks) of aerosol generation. Dhillon³⁵ did not include any measure of aerosol generation during normal respiration against which to benchmark procedural aerosol generation, therefore the results are difficult to interpret. Furthermore, in a subsequent report of the same patients by Dhillon³⁴

aerosol generation was attributed to manual facemask ventilation rather than intubation. In the studies by Brown²⁷ and Weber²⁰ the interpretation of the results differed. In Brown²⁷ the results also included comparisons against aerosols observed for volitional coughs as a reference measure. Intubation and extubation were reported to generate considerably less aerosol than a volitional cough. Furthermore, this study reported that the aerosol concentration was greater for extubation (due to some patients coughing) compared with intubation, which produced negligible aerosol. Weber²⁰ reported that while aerosol was observed during intubation and extubation the levels observed were lower compared with other activities assessed in the study. Both Brown and Weber argue that the “definition” of AGPs may need to be revised.

There is some uncertainty in the results reported in the eligible studies. The studies all had small sample size (number of interventions). In addition, both the Dhillon³⁵ and Brown²⁷ studies used populations drawn from a single institution, albeit one was located in the UK²⁷, which may restrict generalisability. The study by Weber²⁰ was conducted using a manikin, therefore the study could not simulate natural respiratory activities / behaviours that may be observed in a live patient. Furthermore, aerosol concentration was not reported in this study, and it is unclear if multiplicity was accounted for in the analysis. There was also clinical heterogeneity across the studies. In Brown²⁷ and Dhillon³⁵ the procedures were conducted in accordance with local institutional protocols. There was methodological heterogeneity in the ascertainment and reporting of data across the studies. Furthermore, in the study by Dhillon³⁵ aerosol measurement included very small particles (<0.01 micrometres) which may have introduced artefact into the results. This study was conducted in an environment with high background aerosol levels which is a source of additional uncertainty. The studies by Dhillon³⁵ and Brown²⁷ were conducted in COVID-19 negative patients. Thus, aerosol generation in COVID-19 positive patients is unknown. However, based on the evidence included in this review tracheal intubation and extubation in anaesthetised patients should be removed from the extant UK AGP.

Manual facemask ventilation

Limited evidence that assessed manual facemask ventilation was identified by this review. The study by Brown²⁷ assessed manual facemask ventilation as part of the intubation sequence (details are outlined in the section above). Shrimpton³² included a small sample size. Both of these studies were conducted in an ultraclean environment meaning that the results are likely to have a higher degree of precision. In addition, the study by Shrimpton³² also assessed both tidal breathing and volitional cough for comparison and reported results when there was a leak. Moreover, this study was a collaboration of the Brown²⁷ and Dhillon³⁵ intubation groups and was conducted to investigate the results reported by Dhillon regarding

aerosol generation and facemask ventilation using a jointly agreed protocol. The study reported no significant difference in aerosol generation during facemask ventilation without a leak and the median aerosol level was reported as being significantly lower than tidal breathing. Facemask ventilation with a leak was also significantly lower than tidal breathing. No statistically significant difference in aerosol concentrations was reported between facemask ventilation with and without a leak, and both were reported to be significantly lower than the aerosol concentration observed for volitional coughing. There is uncertainty regarding the reported results in Dhillon³⁴ because it included three patients and therefore was underpowered. Furthermore, the study was not conducted in an ultraclean environment and measured aerosols <0.01 micrometre in diameter which introduces uncertainty into the results. All studies were conducted in COVID-19 negative patients who were anaesthetised and paralysed. Therefore, aerosol generation in COVID-19 positive patients is unknown. However, based on the evidence identified by this review consideration should be given to removing manual facemask ventilation from the extant UK AGP list.

Tracheostomy insertion

The limited volume of evidence (n=2 studies^{31, 37}) examining tracheostomy insertion was consistent in reporting that the procedure was associated with “low” levels of aerosol generation. However, the studies were both methodologically and clinically heterogeneous. Outcome reporting varied across the studies, which makes inference difficult. The sample size was limited to a single patient in both studies meaning that both studies were underpowered; although McGain³⁷ was performed on a COVID-19 positive patient. The studies were also each performed at a single centre, albeit one was located in the UK³¹, which may limit generalisability. Both studies included anaesthetised patients undergoing elective procedures meaning that natural respiratory activities were inhibited during outcome assessment. Due to these limitations and uncertainties, there is currently insufficient evidence to support the removal of tracheostomy insertion from the extant UK AGP list.

Bronchoscopy (awake)

Both eligible studies^{23, 39} that examined aerosol levels associated with bronchoscopy reported a decrease in large particle levels and a statistically non-significant difference in smaller particle levels compared with baseline. However, there was both methodological and clinical heterogeneity across the studies. The sample sizes in both studies were small meaning that they were underpowered. Both studies also used samples, drawn from procedural lists, therefore the populations may not be representative of the UK patient population. Furthermore, while Doggett³⁹ was a multicentre study it was reported that there was variation across both sites, with a high number of protocol violations reported at one site.

There is also some uncertainty regarding aerosol level assessment in Zheng²³, as the optical particle sizer may not have used a cone / funnel. Therefore, results may not be specific to the patient but to changes in aerosols within the room. Patients included in both studies were COVID-19 negative and patients were sedated as per the institutional protocol, which may not be generalisable to current UK practice. Thus, natural respiratory activities were inhibited during outcome assessment. Due to these limitations and uncertainties, there is currently insufficient evidence to support the removal of bronchoscopy from the extant UK AGP list. Discussions with the Clinical consultation group suggested that awake tracheal intubation, should be included under this AGP heading (rather than tracheal intubation) until further evidence is available.

Dental procedures using high speed devices

There is consensus in the eligible studies^{12, 24-26, 28, 45} that aerosol was observed during the dental procedures performed. However, there was both clinical and methodological heterogeneity across the included studies. In most studies there was either no attempt or it was not possible to distinguish non-biological aerosols generated from the device used for the procedure and bioaerosols generated by the patient. Therefore, it is not possible to draw conclusions regarding the magnitude of aerosols associated with dental procedures, nor the origin of the aerosols be it the procedural equipment or the patient. Furthermore, five of the studies^{24-26, 28, 45} were performed using dental manikins. Thus, natural respiratory activities and patient behaviours could not be simulated in these studies; in all of these studies a proxy for blood and bone fragments was not included and only Vernon⁴⁵ included a proxy for saliva. Thus, observed aerosol in these studies related predominately to the intervention (irrigant or coolant) and not the patient, which introduces uncertainty into the reported results. There is also a risk that these studies were performed in an unclean environment, which may have impacted on the precision of results reported. Moreover, these studies included a relatively small number of interventions and it is unclear if these studies accounted for multiplicity. In addition, in most of the manikin studies the interventions were conducted in simulated clinical environments which may not be representative of dental settings across the UK. Meethil¹² included patients undergoing dental procedures in a real-world setting, although the procedures were not clearly defined. However, the study used a convenience sample meaning that the population may not be representative of the UK population. In addition, while Meethil¹² included COVID-19 positive patients and reported that virus was not detected in observed microbiota, the sample size was small, and it is likely that the study was underpowered. It is also unclear if there was a clear distinction between droplet and aerosols in the outcome assessment in this study. The generation of aerosol during dental procedures is further complicated by the impact of mitigation measures that can be employed and an assessment of the effectiveness of such measures is out with the scope of this review. Therefore,

there is a lack of available evidence from which to draw conclusions and dental procedures using high speed devices should remain on the extant UK AGP list.

Non-invasive ventilation (NIV) / Continuous Positive Airways Pressure (CPAP)

There was consensus in the eligible studies that examined NIV that the procedures (NIPPV; CPAP; BiPAP) were not associated with aerosol levels that were above baseline / background levels or compared with natural respiratory activities. However, the eligible studies had small sample sizes meaning that they may have lacked power. In addition, most of the studies^{10, 13, 16, 36, 38} were conducted in healthy volunteers meaning that there may be uncertainty in the generalisability of results to patients. Furthermore, individual variation was observed among participants included in five of the included studies^{10, 13, 16, 30, 38} and it is unclear if multiplicity was adjusted for in all studies, thus introducing uncertainty into the results. However, the results reported in Winslow³³, which was conducted in COVID-19 positive patients, suggest that NIV was not associated with significantly more environmental contamination compared with baseline in this population. McGain³⁶ sought to examine the efficacy of a novel mitigation intervention, which may affect the generalisability of results to UK clinical practice. Heterogeneity in the ascertainment (sampling method, number, and frequency of observations) reporting of aerosol levels (different units of measurement) and interventions (including flow rate) across the included studies means that it is not possible to determine the magnitude of effect associated with the procedures. However, the evidence included in this review is consistent in suggesting that NIV was not associated with aerosol levels that were greater than natural respiratory activities. Therefore, consideration should be given to removing NIV from the extant UK AGP list.

High flow nasal oxygen (HFNO)

The reported results of the nine studies^{10, 11, 13, 16, 30, 33, 36, 38, 42} that examined HFNO included in this review are not consistent. There was both clinical and methodological heterogeneity across the studies, which had small sample sizes meaning they may be underpowered. Most of the studies were conducted in adults, predominately healthy volunteers^{10, 13, 16, 36, 38, 42}, meaning that there may be uncertainty in the generalisability of results to patients. Individual variation was observed among participants included in six of these studies^{10, 13, 16, 30, 38, 42} and it is unclear if multiplicity was adjusted for in all studies, which introduces uncertainty into the results. McGain³⁶ sought to examine the efficacy of a novel mitigation intervention, which may affect the generalisability of results to UK clinical practice. The study by Gall¹¹ was the only study that included an infant population and reported no association between HFNO use, at any flow rate, and near-field particle counts was observed. The study by Jermy⁴² was partially funded by Fisher &

Paykel Healthcare Ltd., a device manufacturer, which may have introduced potential bias into the reported results of this study.

Heterogeneity in the ascertainment (sampling method, number, and frequency of observations) reporting of aerosol levels (different units of measurement) and interventions (including flow rate) across the included studies means that it is not possible to determine the magnitude of effect associated with the procedures.

- Wilson³⁸ reported that particle counts decreased when HFNO was used during respiratory activities, and significantly during coughing where aerosols (emissions) were halved ($p=0.028$).
- Gaeckle¹⁰ reported that HFNO did not result in a statistically significant difference in the number and size of particles observed compared to baseline. Similarly, Winslow³³ reported that HFNO in COVID-19 positive patients was not associated with significantly more environmental contamination compared to baseline. Miller¹³ reported no statistically significant difference between any aerosol levels produced during HFNO compared with low flow nasal canula.
- Hamilton³⁰ reported that HFNO was associated with statistically significant increased aerosol concentrations compared to baseline measures at a flow rate of 30L/min and 60L/min but that rates were lower than those observed for coughing alone. However, the study also reported that most of the aerosol observed was from the HFNO machine and not the patient.
- The study by Hamilton³⁰ also reported that higher flow rates (60L/min) were associated with higher reported aerosol concentrations than lower flow rates (30L/min) in comparison to the natural respiratory activities observed, except coughing, which was observed to generate the largest concentration of aerosol. However, aerosols were observed to be from the machine and not the patient. The McGain³⁶ study reported a low increase in aerosols was observed for HFNO at 60L/min (0.24 particles/mL). Similarly, Wilson³⁸ reported slight increases in total particle counts for HFNO at higher flow rates. Jermy⁴² reported that during quiet breathing with no therapy and with 30L/min HFNO, no particles were detected, however, particles were detected during quiet breathing with 60L/min HFNO. In the Pearce¹⁶ study, HFNO was reported as being associated with a flow-dependent increase in particle at 60 L/minute.

Most of the studies reported that HFNO was either associated with a decrease in aerosol levels or that any difference in levels was not significantly different compared with either baseline levels or those observed for coughing. While more

aerosols were reported by some studies at 60L/min flow rate compared with 30L/min, the addition of HFNO reduced aerosol compared to its absence in exertional respiratory activities. Therefore, consideration should be given to amending the extant UK AGP list.

ENT airways procedures

Seven of the studies^{14, 15, 17, 19, 21-23} included in this review were consistent in reporting upper ENT airways procedures were associated with a statistically significant increase in aerosol levels, without mitigation. The study by Boorgu⁹ reported that the procedures observed did not appear to pose an additional risk, but the result could not be extrapolated to endoscopy. The interpretation of the results of this study and the other studies is subject to uncertainty. Four of the studies^{9, 19, 21, 22} (including Boorgu⁹) were conducted using a cadaver. Therefore, natural respiratory activities and patient behaviours / responses could not be simulated in these studies. The population in the study by Rameau¹⁷ was comprised of healthy volunteers, meaning that the results may not be generalisable to patients. The three studies^{14, 15, 23} that included patients used a convenience sample, which may reduce their generalisability to the UK population. In addition, all of the included studies had a small sample size meaning that they were likely underpowered. It is unclear if studies involving multiple measurement, of the same population, accounted for multiplicity. All of the studies were conducted at a single centre and different ENT interventions were assessed. Therefore, the results may not be generalisable to UK clinical practice. The studies also reported different outcomes and made observations using different devices positioned at different locations. There is also a risk that some of the studies were performed in an unclean environment, which may have impacted on the precision of reported results. The generation of aerosol during some upper ENT airways procedures is further complicated by the impact of mitigation measures that can be employed. An assessment of the effectiveness of such measures is out with the scope of this review. Therefore, there is insufficient available evidence to support the removal of these procedures which should remain on the UK AGP list.

Upper gastro-intestinal endoscopy (awake)

There is consensus in the included studies^{29, 40, 41} that upper gastro-intestinal endoscopy was associated with an increase in aerosol concentrations. Gregson²⁹ reported that the procedure evoked coughing and burping and that both were associated with an increase in aerosol concentration above baseline respiratory activities and volitional coughs measured in the same patients. The studies by Chan⁴⁰ and Gregson²⁹ included a mixture of un-sedated and sedated patients; while Sagami⁴¹ included exclusively sedated patients. Each of the three studies was performed at a single centre which may further limit generalisability, albeit one

was located in the UK²⁹. In addition, the COVID-19 status of patients was unreported in two studies^{40, 41} and patients were reported as being COVID-19 negative in Gregson.²⁹ However, there was clinical and methodological heterogeneity across the eligible studies. Outcome reporting varied across the studies, which makes inference regarding the magnitude of aerosol generation difficult to determine. The measurement of aerosol levels was also heterogeneous. Furthermore, the studies were comprised of patients drawn from institutional lists and the population sizes were relatively small meaning that the results may not be representative of the UK patient population. Therefore, while it is not possible to determine the magnitude of effect associated with the procedure. Available evidence identified by this review suggests that upper gastro-intestinal endoscopy should remain on the extant UK AGP list.

[Surgical procedures in the respiratory tract or sinuses](#)

The results of the five included studies^{14, 15, 19, 22, 34} that assessed surgical interventions were consistent in reporting that increased aerosol levels were observed during the interventions performed. There was clinical and methodological heterogeneity across the included studies. Two of the studies^{19, 22} were conducted using cadavers. Therefore, natural respiratory activities and patient behaviours / responses could not be simulated in these studies. The remaining three included studies^{14, 15, 34} were conducted using a convenience sample of patients and therefore may not be representative of the UK population. Furthermore, all of the studies had small sample sizes (observations) and thus may be underpowered. It is unclear if multiplicity was adjusted for in studies involving multiple measurement of the same population. All of the studies were conducted at a single centre and different surgical interventions were examined. Consequently, the results may not be generalisable to UK clinical practice and potentially cannot be extrapolated to surgical procedures not assessed. The studies also reported different outcomes and made observations using different devices positioned in different locations. Some of the studies were conducted in potentially unclean environments which may influence the precision of the reported outcomes. The generation of aerosol during some surgical interventions is further complicated by the impact of mitigation measures that can be employed, which is out with the scope of this review. Therefore, it is not possible to determine the magnitude of effect associated with the procedures. However, evidence included in this review suggests that surgical procedures in the respiratory tract or sinuses should remain on the extant UK AGP list.

[Risk of transmission to healthcare workers performing AGPs](#)

Interpretation of the results of the studies^{18, 43, 44} included in this review that examined risk is difficult. The studies examined different factors and their

association with COVID-19 infection and the reported outcome also varied. Furthermore, there were differences in the analyses undertaken in the studies (that is, adjustment for potential confounders and effect modifiers). In addition, the study by El-Boghdadly⁴³ included a composite endpoint and the lack of a comparison group further restricts interpretation of the results. There are also uncertainties in the reported results of the studies. All of the studies^{18, 43, 44} used self-reported data and therefore there is a risk of potential recall bias. The studies^{18, 43, 44} also all reported that they recruited volunteers which may have introduced further bias. The studies by El-Boghdadly⁴³ and Lentz⁴⁴ were multicentre, international studies meaning that there may have been clinical heterogeneity. The specific AGP assessed in the studies was only reported in El-Boghdadly⁴³ and were not clearly specified in Lentz⁴⁴ or Rosser.¹⁸ The populations included in the studies may also not have been representative of UK clinicians. Therefore, the included evidence that examined risk to clinicians associated with AGPs is insufficient to enable any conclusions to be drawn.

Discussion

This rapid review included 37 studies that assessed the association between aerosol generation and procedures currently included on the UK AGP list. Seventeen of these studies^{11, 12, 14, 15, 23, 27, 29-35, 37, 39-41} were conducted using patient populations. The number of eligible studies identified for procedures on the AGP list were as follows:

- three studies^{20, 27, 35} examined tracheal intubation and extubation
- three studies^{27, 32, 34} assessed manual ventilation
- two studies^{31, 37} assessed tracheostomy
- two studies^{23, 39} examined bronchoscopy
- six studies^{12, 24-26, 28, 45} examined dental procedures
- seven studies^{10, 13, 16, 30, 33, 36, 38} assessed non-invasive ventilation (NIV)
- nine studies^{10, 11, 13, 16, 30, 33, 36, 38, 42} examined high flow nasal oxygen (HFNO)
- eight studies^{9, 14, 15, 17, 19, 21-23} assessed upper ENT airways procedures
- three studies^{29, 40, 41} assessed upper gastro-intestinal endoscopy
- five studies^{14, 15, 19, 22, 34} examined surgical procedures in the respiratory tract or sinuses

Fifteen of these studies^{10, 13, 16, 19, 21-23, 27, 33, 34, 36, 38} reported on aerosol generation across two procedures (NIV and HFNO; ENT and surgical procedures) included on the current UK AGP list.

No studies were included in this review that examined high frequency oscillatory ventilation (HFOV), induction of sputum, respiratory tract suctioning, or post-mortem procedures involving the respiratory tract or sinuses.

An assessment of included studies suggests that tracheostomy insertion, awake bronchoscopy, dental procedures using high speed devices, ENT airways procedures, awake upper gastro-intestinal endoscopy, and surgical procedures in the respiratory tract or sinuses should remain on the extant UK AGP list.

Patients included in the eligible tracheal intubation and extubation studies were anaesthetised and paralysed. It was reported that observed aerosol levels during the procedures were lower compared with natural respiratory activities. Therefore, consideration should be given to removing intubation and extubation of anaesthetised patients from the UK AGP list. Awake intubation is akin to bronchoscopy and should be included as an AGP.

Based on the limited volume of evidence identified by the review that examined manual facemask ventilation consideration should be given to removing manual ventilation from the extant UK AGP list.

The studies that assessed non-invasive ventilation (NIV) are consistent in suggesting that NIV is not associated with aerosol levels that are greater than background or natural respiratory activities. Rather NIV may reduce aerosol production when applied to exertional respiratory activity, which also applies to mask CPAP which can be regarded as subset of NIV. Therefore, consideration should be given to removing NIV from the UK AGP list.

Most of the studies that examined HFNO reported that the procedure was either associated with a decrease in aerosol levels or that any difference in concentrations was not significantly different compared with either baseline levels or those observed from coughing. Some studies reported an increase in aerosol at 60L/min flow rate compared with 30L/min, however, the addition of HFNO reduced aerosol compared to its absence in exertional respiratory activities. Therefore, consideration should be given to amending the extant UK AGP list.

Three studies met the inclusion criteria of this review that examined the relationship between clinicians, AGPs, and COVID-19 infection. The included evidence that examined risk to clinicians associated with AGPs is insufficient to enable any conclusions to be drawn.

The included studies also illustrate that some of the procedures included on the UK AGP list may not currently be adequately defined. Eligible studies of NIV examined a number of different oxygen modalities, including CPAP which can be delivered in

via different methods (such as, facemask, helmet, or tracheal tube). A further consideration is that the risk of a given procedure is intrinsically linked to the risk of respiratory aerosol generation by the patient and so the same procedure may be considered a high risk AGP in an awake patient (bronchoscopy, endoscopy, awake tracheal intubation) but would not be aerosol generating in an anaesthetised patient whose respiratory reflexes are obtunded and who may be paralysed (tracheal intubation, bronchoscopy, endoscopy).

Clarification of additional procedures

While conducting the review, clarification was requested from the Chief Medical Officer and PHAGE (Public Health Advice, Guidance and Expertise team) to clarify if additional procedures could be reviewed. Specifically, the request related to supraglottic airways (SGA), pleural procedures, and spirometry. These procedures are out with the scope of the review (they are not included on the extant UK AGP list), however four studies that examined these interventions were identified in the excluded studies of this review.

Shrimpton⁴⁶ examined SGA insertion and removal (n=12) and aerosol generation conducted in an ultraclean operating theatre environment. The observation methods were as per those used in the Brown²⁷ study. Shrimpton⁴⁶ reported that there was no statistically significant difference between SGA insertion and removal compared with tidal breathing. The study also reported SGA insertion and removal produced significantly less aerosol compared with breathing or volitional cough (p<0.001).

Two of the studies^{47, 48} assessed spirometry and aerosol generation and both reported that in comparison with a cough, spirometry was associated with less aerosol. Furthermore, in one study⁴⁸ the use of a viral filter during the procedure reduced aerosol level further.

The final study⁴⁹ assessed pleural procedures and aerosol generation and reported that percutaneous pleural procedures were not aerosol generating.

Therefore, limited available evidence suggests these procedures should continue to be excluded from the UK AGP list and consideration should be given to adding additional clarification to reflect this.

Contextual Risk assessment

In the process of conducting the review it became apparent that the major change in the evidence base around AGPs during the pandemic has come from important advances in the ability to detect aerosol produced during medical procedures

(either within hospitals or in simulated models with varying degrees of fidelity). This clinical aerosol science has enabled a quantitative assessment of aerosol generation that can be useful to inform the relative risk association with these activities. In particular, volitional coughing from study participants has been operationalised as a reference for risk, such that aerosol generated from volitional coughs can be used as an appropriate relative risk comparator for aerosol generating procedures. The volitional cough has the advantage that it can be detected above baseline aerosol levels (if in a clean environment) and is a discrete, transient event. There is considerable variation between both individuals and between studies reflecting individual respiratory (patho)physiology, measurement techniques and experimental conditions. Nonetheless using within-subject comparisons has demonstrated that several AGPs on the extant list produce much less aerosol than a cough and so by this measure can be considered as not being high risk for aerosol generation.

Importantly, there is an increasing evidence base of aerosol measurements during normal respiratory activities such as tidal breathing, breathing during exercise, talking, shouting and singing.^{10, 27, 30, 32, 36, 38, 39, 46-48, 50} Each of these activities generates measurable aerosol in a graded and proportionate way and importantly this physiological respiratory aerosol has been demonstrated to contain SARS-CoV-2 in patients with COVID-19.^{51, 52} For many of the reviewed procedures, the aerosol generated by natural respiratory activities exceeded that produced by the actual procedure, often by more than an order of magnitude. It is further apparent that the source of the detected aerosol in several of the AGPs that do generate increased aerosol (such as, upper gastro-intestinal endoscopy) is predominantly from the patient's own respiratory activities (i.e., coughing) rather than from the actual procedure.²⁹

This review examined medical procedures included on the UK AGP list and the relationship with aerosol generation or increased risk of respiratory transmission from an infected patient / individual to those present / undertaking the procedures. This review did not examine the additional standard and transmission based precautions required when treating patients with respiratory infectious agents, which is contained in UK IPC COVID-19 [guidance](#) and the National Infection Prevention and Control Manual (NIPCM) for NHS England. In particular the individual patient placement / assessment for infection risk this should be undertaken based on an individuals' infectious status, the level of interaction and the anticipated level of exposure to the infectious agent. This assessment will determine the required transmission based precautions required including PPE / RPE (respiratory protective equipment). It is worth again emphasising that airborne precautions (PPE / RPE) are not required for AGPs on patients / individuals that are not suspected / confirmed to be suffering from a respiratory infectious agent.

Note: This assessment differs from the requirement for organisation / employers to undertake risk assessments based on the [‘hierarchy of controls’](#) or workplace risk assessments for employees as per Health and Safety legislation / regulations.

Limitations and uncertainties of included evidence

The evidence eligible for inclusion in this review was subject to a number of limitations and uncertainties. Many of these limitations and uncertainties are similar to those identified in previous reviews of AGPs, for example, the systematic review by Tran⁵³ that was used to inform the original WHO AGP recommendations. The Tran⁵³ systematic review acknowledged that studies included in that review were deemed to be of “very low quality”. Predominately this was attributed to the use of observational methodologies in the included studies; therefore, the studies were acknowledged to be subject to potential residual confounding and bias.

The majority of the studies included in the current review employed an empirical approach. Therefore, there is a risk that these studies were subject to systematic error, for example, sampling bias associated with the use of convenience samples and observer bias as they did not employ blinding or randomisation.

The reported sample sizes (or number of procedures performed) were generally small meaning that some studies included in this review may have lacked statistical power. All of the included studies may not also be representative of UK clinical practice or of the eligible UK patient population. Exclusion criteria of the review were intended to increase generalisability, but it cannot be guaranteed. However, some of the included studies (n=11) were conducted in the UK which increases certainty. The review by Tran⁵³ also reported that most of the studies included in that review were performed at a single centre this was identified as potentially restricting generalisability. Furthermore, the review⁵³ also reported that many of the studies included a small number of events and that the “sample size of the studies could potentially bias estimates of effects and limit statistical power.”

The reported outcome and definition varied across the included studies. All of the studies examined the relationship between aerosols or particles and an intervention currently included on the UK AGP list. However, aerosols / particles were reported variously as observed quantity, aerosol size or as a range of sizes, as concentrations (for example, per litre, millilitre, and cubic foot), and spread or dispersal. Therefore, heterogeneity of reporting prevented an assessment of the magnitude of effect and thus assessment was restricted to direction of effect.

There was heterogeneity in the methods and devices used to measure aerosols in the included studies. An assessment of these methods and devices was out with

the scope of this review. Therefore, such variation is a source of potential uncertainty in the results reported across the included studies.

Descriptive statistics were used in the studies as the primary analysis, with most reporting an absolute effect. However, there was variation in the reference measures used across the studies. This included background aerosol level of the setting before the intervention and natural respiratory activities such as breathing and talking. Heterogeneity of reference measure adds further uncertainty to the results and their interpretation. Baselines that include natural respiratory activity, particularly coughing or breathing, are likely the most appropriate as these are the benchmarks against which AGPs have been defined. Conversely, using an increase against a background level is an entirely arbitrary measure dependant on the cleanliness of the experimental setting and provides little insight into the extent of aerosol generation or its absence. The exclusion of studies where background level was the reference measure may have increased the precision of the review. However, the on-going pandemic, limited date range of the literature searches, and use of a rapid review methodology restricted the number of eligible studies included in this review. The exclusion of studies using background reference measures would have further restricted the number of eligible studies. The evidence base examining AGPs is still evolving and the review is intended to inform service need. Furthermore, synthesis and assessment in this review were via evidence of a consistent direction of effect (but not magnitude of effect). Therefore, the inclusion of these studies was deemed appropriate.

Many of the included studies reported taking multiple measurement of the same population and it is unclear if adjustment was made for multiplicity. It is also unclear if all of the studies controlled for potential confounding (for example, temperature, humidity, air changes per hour) of results.

The number of interventions that were included for ENT airways procedures and surgery in the respiratory tract or sinuses was small and may not encompass all procedures in these specialties that might be associated with aerosol generation. There is also some uncertainty regarding the effectiveness of mitigations that can be employed during these procedures, and in dental procedures, as this was out with the scope of this review. In addition, a number of studies were conducted using simulated interventions which may not be reflective of real procedures. The review by Tran⁵³ also acknowledged that “with the exception of tracheal intubation, there were a limited number of studies identified for each procedure, which limits the confidence for an individual observation.”

In a number of the included studies the population was comprised of exclusively anaesthetised and paralysed or conscious patients undergoing procedures. Therefore, the reported effect may be limited to this group of patients and may not

be generalisable to other groups. Given the results of the studies in anaesthetised patients, it is logical for the AGP list to specify whether procedures included apply to patients who are awake or anaesthetised or both.

The generalisability of the included studies is restricted because the majority of patients in the included studies did not have a respiratory infection, with only a limited volume of evidence included for COVID-19 positive patients. However, those studies that did include patients with SARS-CoV-2 (which itself has a very wide spectrum of clinical phenotypes) did not identify major differences in aerosol generation between infected and non-infected participants.

In addition, a number of studies were conducted in manikins or cadavers. Such studies cannot replicate the natural respiratory activities and behaviours associated with live patients undergoing the intervention. However, the inclusion of such studies should be balanced against the service need which the review is intended to address.

Strengths and Limitations of the review

This review was subject to several limitations.

- A full systematic review methodology was not employed, and a rapid review was carried out in accordance with best practice where possible. However, rapid review methodology may not be as robust as that of a systematic review. The review employed both sensitive and specific search strategies, however, no assessment of the precision and recall of the strategies was conducted.
- Literature search results were not updated following completion of the search process and studies not published in English were excluded. Grey literature and preprint repositories were not searched as part of this review. Therefore, some studies that reported on procedures included on the extant UK AGP list may not have been identified. Furthermore, no assessment of publication bias was performed. However, the search strategies and eligibility criteria employed by the review were informed by reviews that were undertaken previously to specifically inform the AGP list. In addition, the search strategies and eligibility criteria were both subject to review by the IPC Cell and the Clinical consultation group and deemed to be both appropriate and suitably robust.
- The risk of bias was not formally assessed, using a standardised and validated instrument, was not undertaken as part of the review. It was determined that there was not a formalised, validated, and published quality

assessment tool suitable for assessment of most of the included studies. While a quality assessment tool could have been developed specifically for this review, it was felt that such an instrument would be of limited use because it would not be formally tested or validated. Furthermore, the urgency of the review precluded the development of such a tool. However, as part of the review process details regarding limitations and uncertainties of the included studies were included in the extraction process, evidence table, and the evidence synthesis of this review.

- A formal check of heterogeneity was not conducted; however, clinical and methodological heterogeneity were qualitatively assessed. Evidence synthesis was conducted using a “vote counting” approach, meaning that only the reported direction of effect was assessed. Furthermore, limitations of the included data reported in the studies meant that meta-analysis or quantitative synthesis of estimated effect could not be conducted. Therefore, this review lacks precision in the reporting of (estimated) effect.

Future research

Methodological heterogeneity was observed across the studies included in this review. Outcome definition, reporting, and reference measure were not consistent and different observation and sampling methods were employed across the studies. Furthermore, the studies were conducted in a number of different environments and it is unclear if confounding (for example, temperature, humidity, and ventilation) was accounted for in all studies. Most of the included studies were unable to quantify risk or identify risk factors for transmission of respiratory infection associated with the interventions examined. No appropriately designed epidemiological studies intended to measure observed risk of transmission associated with the procedures were identified by the review. Such issues introduce potential uncertainty and restrict assessment of the wider AGP evidence base; a limitation which is equally applicable to the evidence on which the current AGP list was based. As highlighted in the National Institute for Health Research (NIHR) AGP research prioritisation report⁵⁴ there is a need for future research to address these issues.

Conclusion

This review identified evidence which supports the removal of the following procedures currently included on the UK AGP list:

- tracheal intubation and extubation (in anaesthetised patients)
- manual facemask ventilation
- non-invasive ventilation (NIV) including CPAP
- high flow nasal oxygen (HFNO)

The evidence assessed was subject to a number of limitations and uncertainties that should be considered before amending the extant UK AGP list. It is also suggested that consideration is given to clarifying the wording of procedures currently included on the UK AGP list. Specifically:

- Removing HFOV as it is a ventilation mode rather than a specific procedure.
- Including awake tracheal intubation under the category of bronchoscopy.
- Specifying that bronchoscopy and endoscopy apply to awake patients and intubation to an anaesthetised patient.
- NIV should include CPAP.
- Sputum induction need not mention saline.

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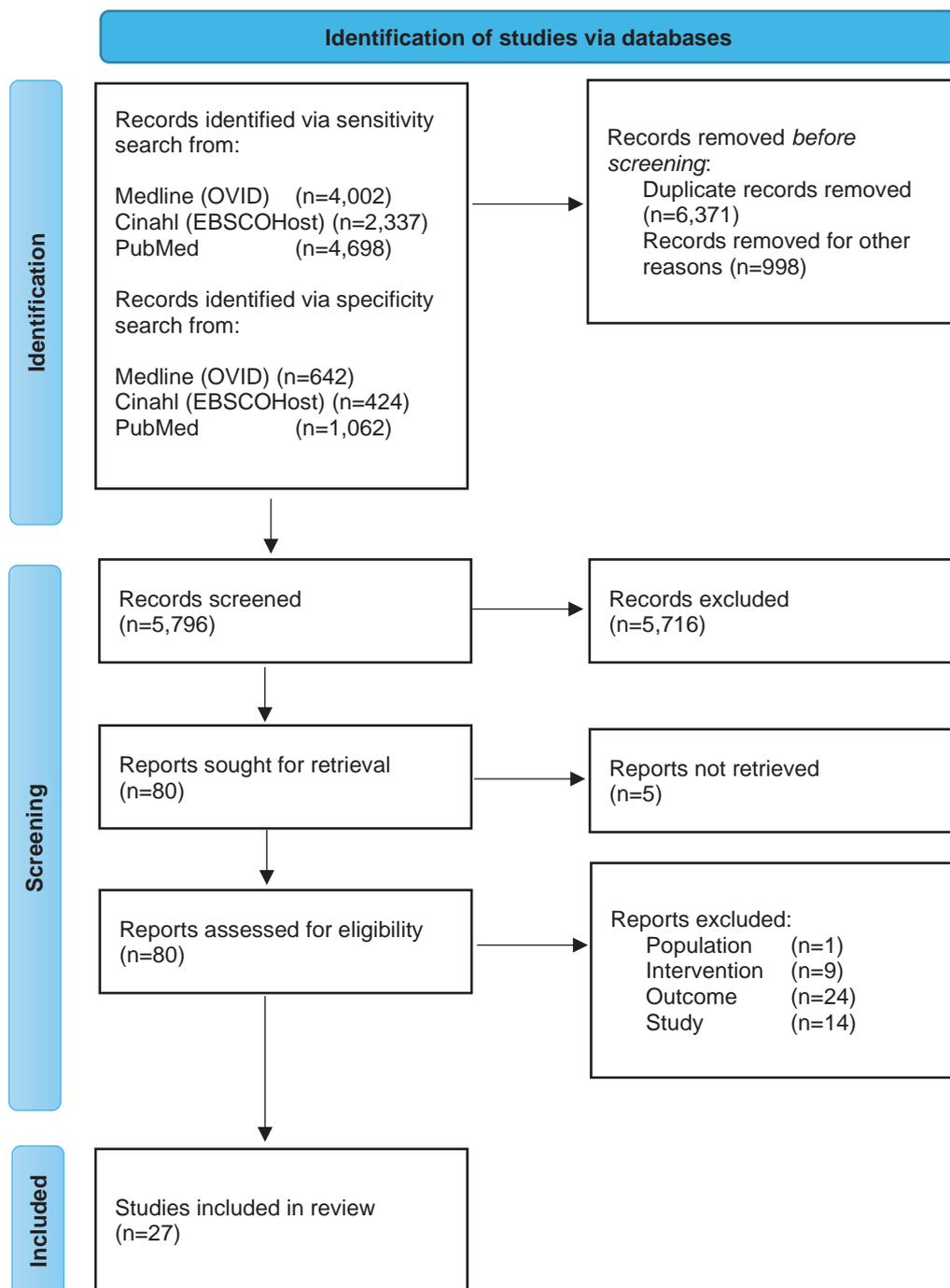
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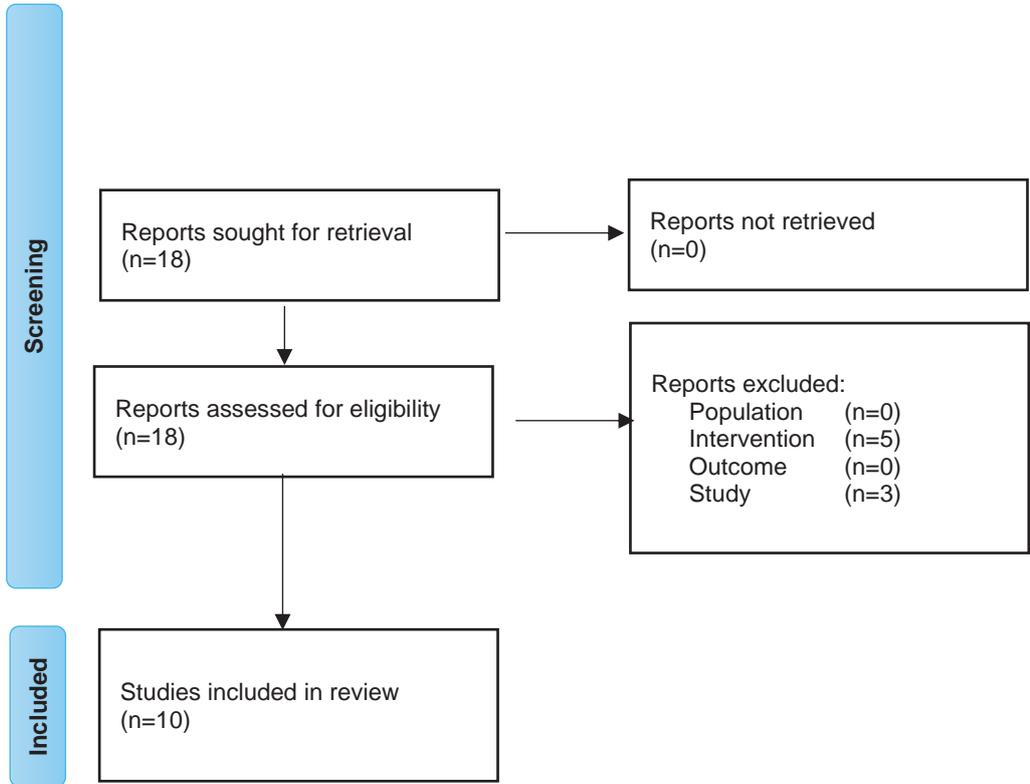
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Appendix 1: PRISMA flow diagrams



Identification of studies via consultation group



Appendix 2: list of excluded studies

Studies excluded from the review following full text assessment, listed by PICOS.

Population

Brown A, Schwarcz L, Counts CR, Barnard LM, Yang BY, Emert JM, et al. Risk for Acquiring Coronavirus Disease Illness among Emergency Medical Service Personnel Exposed to Aerosol-Generating Procedures. *Emerging infectious diseases*. 2021;27(9):2340-8.

Intervention

Arnold DT, Gregson FKA, Sheikh S, Hamilton FW, Welch H, Dipper A, et al. Standard pleural interventions are not high-risk aerosol generating procedures. *Eur Respir J*. 2021;58(4).

Berges AJ, Lina IA, Ospino R, Tsai H-W, Brenner MJ, Pandian V, et al. Quantifying Viral Particle Aerosolization Risk During Tracheostomy Surgery and Tracheostomy Care. *JAMA Otolaryngology-Head & Neck Surgery*. 2021;147(9):797-803.

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Joyce M, McGrath JA, Mac Giolla Eain M, O'Sullivan A, Byrne M, MacLoughlin R. Nebuliser Type Influences Both Patient-Derived Bioaerosol Emissions and Ventilation Parameters during Mechanical Ventilation. *Pharmaceutics*. 2021;13(2).

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Llandro H, Allison JR, Currie CC, Edwards DC, Bowes C, Durham J, et al. Evaluating splatter and settled aerosol during orthodontic debonding: implications for the COVID-19 pandemic. *Br Dent J*. 2021.

Newsom RB, Amara A, Hicks A, Quint M, Pattison C, Bzdek BR, et al. Comparison of droplet spread in standard and laminar flow operating theatres: SPRAY study group. *Journal of Hospital Infection*. 2021;110:194-200.

Sakai W, Hasegawa G, Chaki T, Tachibana S, Yamakage M. Aerosol boxes decrease aerosol exposure only in depressurized rooms during aerosol-generating procedures in a simulation study. *J Anesth*. 2021:1-10.

Sheikh S, Hamilton F, Nava G, Gregson F, Arnold D, Riley C, et al. Are aerosols generated during lung function testing in patients and healthy volunteers? results from the AERATOR study. *Thorax*. 2021:in press.

Shrimpton AJ, Gregson FKA, Brown JM, Cook TM, Bzdek BR, Hamilton F, et al. A quantitative evaluation of aerosol generation during supraglottic airway insertion and removal. *Anaesthesia*. 2021. **(reference was identified via the literature searches and via the clinical consultation group; therefore, it was included twice in total excluded studies)**

Suprono MS, Won J, Savignano R, Zhong Z, Ahmed A, Roque-Torres G, et al. A clinical investigation of dental evacuation systems in reducing aerosols. *Journal of the American Dental Association (1939)*. 2021;152(6):455-62.

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Villa A, Grenon M. The Cupola: an additional layer of protection for providers working in the oropharyngeal region. *BMC research notes*. 2021;14(1):115.

Outcome

Ahmad I, Jeyarajah J, Nair G, Ragbourne SC, Vowles B, Wong DJN, et al. A prospective, observational, cohort study of airway management of patients with COVID-19 by specialist tracheal intubation teams. *Can J Anaesth*. 2021;68(2):196-203.

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Chanpong B, Tang M, Rosenczweig A, Lok P, Tang R. Aerosol-Generating Procedures and Simulated Cough in Dental Anesthesia. *Anesthesia progress*. 2020;67(3):127-34.

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Leong SC, Mogre D, Andrews P, Davies E. Reducing the risks of endoscopic sinonasal surgery in the Covid-19 era. *Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery*. 2021;46(4):809-15.

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Thal AG, Schiff BA, Ahmed Y, Cao A, Mo A, Mehta V, et al. Tracheotomy in a High-Volume Center During the COVID-19 Pandemic: Evaluating the Surgeon's Risk. *Otolaryngol Head Neck Surg*. 2021;164(3):522-7.

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Study design

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Phillips F, Crowley J, Warburton S, Gordon GSD, Parra-Blanco A. Quantifying aerosol and droplet generation during upper and lower gastrointestinal endoscopy: whole procedure and event-based analysis. *medRxiv*. 2021:2021.04.15.21255544.

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Sun M, Li N, Suo X, Xia Z, Zuo M, Zhi H, et al. Acquired infection after intubating patients with COVID-19: Datasets. *Data in brief*. 2020;32:106130.

Workman AD, Welling DB, Carter BS, Curry WT, Holbrook EH, Gray ST, et al. Endonasal instrumentation and aerosolization risk in the era of COVID-19: simulation, literature review, and proposed mitigation strategies. *International forum of allergy & rhinology*. 2020;10(7):798-805.

Yang M, Chaghtai A, Melendez M, Hasson H, Whitaker E, Badi M, et al. Mitigating saliva aerosol contamination in a dental school clinic. *BMC Oral Health*. 2021;21(1):52.

Yang SS, Zhang M, Chong JJR. Comparison of three tracheal intubation methods for reducing droplet spread for use in COVID-19 patients. *British journal of anaesthesia*. 2020;125(1):e190-e1.

Zeidan A, Bamadhaj M, Al-Faraidy M, Ali M. Videolaryngoscopy Intubation in Patients with COVID-19: How to Minimize Risk of Aerosolization? *Anesthesiology*. 2020;133(2):481-3.

Zhang J, Sun M, Li N, Suo X, Xia Z, Zuo M, et al. Acquired infection after intubating patients with COVID-19: A retrospective pilot study. *J Clin Anesth*. 2020;67:110006.

Appendix 3: search strategies (sensitivity)

Database: Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to October 01, 2021>

- 1 positive-pressure respiration/
- 2 high-frequency ventilation/
- 3 high-frequency jet ventilation/
- 4 exp respiration artificial/
- 5 ventilators, mechanical/
- 6 intermittent positive-pressure ventilation/
- 7 Intubation, Intratracheal/
- 8 exp intubation/
- 9 suction/
- 10 exp drainage/
- 11 tracheostomy/
- 12 bronchoscopy/
- 13 thoracostomy/
- 14 "nebulizers and vaporizers"/
- 15 sputum/
- 16 oxygen inhalation therapy/
- 17 Autopsy/
- 18 exp respiratory function tests/
- 19 exp spirometry/

- 20 exp cardiopulmonary resuscitation/
- 21 breathing exercises/
- 22 exp dentistry/
- 23 otorhinolaryngologic surgical procedures/
- 24 oral surgical procedures/
- 25 exp otolaryngology/
- 26 nasal surgical procedures/
- 27 otologic surgical procedures/
- 28 natural orifice endoscopic surgery/
- 29 exp endoscopy/
- 30 physical therapy modalities/
- 31 thorax/
- 32 NIV.tw.
- 33 CPAP.tw.
- 34 BiPAP.tw.
- 35 HFOV.tw.
- 36 "high frequency oscillatory ventilation".tw.
- 37 ventilat\$.tw.
- 38 respirat\$.tw.
- 39 intubat\$.tw.
- 40 extubat\$.tw.
- 41 ((respirat\$ or airway or "air way") adj3 suction\$.tw.
- 42 nebuli\$.tw.

- 43 "heat moisture exchange".tw.
- 44 (chest adj3 phys\$).tw.
- 45 (sputum adj3 induct\$).tw.
- 46 ((lung or pulmonary) adj2 test\$).tw.
- 47 saliva/
- 48 "supra glottic airways".tw.
- 49 SGA.tw.
- 50 "face mask ventilation".tw.
- 51 exp aerosols/
- 52 aerosol genera\$ procedure.tw.
- 53 (aerosol adj3 proced\$).tw.
- 54 AGP.tw.
- 55 AGMP.tw.
- 56 aerosol\$.tw.
- 57 airborne.tw.
- 58 splatter.tw.
- 59 droplet.tw.
- 60 cough/
- 61 cough\$.tw.
- 62 SARS virus/
- 63 SARS-CoV-2/
- 64 middle east respiratory syndrome coronavirus/
- 65 severe acute respiratory syndrome/

- 66 coronavirus infections/
- 67 COVID-19/
- 68 severe acute respiratory syndrome/
- 69 influenza, human/
- 70 exp orthomyxoviridae/
- 71 MERS.tw.
- 72 SARS.tw.
- 73 COVID.tw.
- 74 influenza.tw.
- 75 exp animals/ not exp humans/
- 76 ((or/1-29) or (and/30-31) or (or/32-50)) and (or/51-61) and (or/62-74)
- 77 76 not 75
- 78 limit 77 to yr="2019 -Current"
- 79 limit 78 to english language

Cinahl sensitivity AGP search strategy (4th October 2021)

- S1 MH positive pressure ventilation OR MH ventilation high frequency OR MH jet ventilation, high frequency OR MH "respiration artificial+" OR MH ventilators, mechanical OR MH intermittent positive pressure ventilation OR MH intubation, intracheal OR MH intubation+ OR MH suction+ OR MH drainage+
- S2 MH tracheostomy OR MH bronchoscopy OR MH thoracostomy OR MH (nebulizers and vaporizers) OR MH sputum OR MH oxygen therapy OR MH autopsy OR MH "respiratory function tests+" OR MH spirometry OR MH "resuscitation, cardiopulmonary+"
- S3 MH breathing exercises OR MH dentistry+ OR MH surgery, otorhinolaryngologic OR MH surgery, oral OR TX otolaryngology OR MH ear surgery OR MH endoscopy+
- S4 MH physical therapy AND MH thorax

- S5 TX NIV OR MH continuous positive airway pressure OR TX CPAP OR TX BiPAP OR TX HFOV OR TX "high frequency oscillatory ventilation" OR TX ventilat* OR TX respirat* OR TX intubat* OR MH extubation OR TX (((respirat* or airway or "air way") N3 suction*)) OR TX nebul*
- S6 TX "heat moisture exchange" OR TX chest N3 phys* OR TX sputum N3 induct* OR TX (((lung or pulmonary) N2 test*)) OR MH saliva OR TX "supra glottic airways" OR TX SGA OR TX "face mask ventilation"
- S7 MH aerosols OR TX "aerosol generat* procedure" OR TX aerosol N3 proced* OR TX AGP OR TX AGMP OR TX airborne OR TX splatter OR TX droplet OR MH cough OR TX cough*
- S8 MH SARS virus OR MH SARS-COV-2 OR MH middle east respiratory syndrome coronavirus OR MH severe acute respiratory syndrome OR MH middle east respiratory syndrome OR MH COVID-19 OR MH influenza, human OR MH orthomyxoviridae+ OR TX MERS OR TX SARS OR TX COVID OR TX influenza
- S9 (S1 or S2 or S3 or S4 or S5 or S6) and S7 and S8
- S10 MH animals NOT MH human
- S11 S9 NOT S10

Limited to English language and date range of 2019 to present (4th October 2021)

PubMed sensitivity AGP search strategy (4th October 2021)

- #1 (((((((((((((positive-pressure respiration[MeSH Terms]) OR (high-frequency ventilation[MeSH Terms])) OR (high-frequency jet ventilation[MeSH Terms])) OR (respiration artificial[MeSH Terms])) OR (ventilators, mechanical[MeSH Terms])) OR (intermittent positive-pressure ventilation[MeSH Terms])) OR (Intubation, Intratracheal[MeSH Terms])) OR (intubation[MeSH Terms])) OR (suction[MeSH Terms])) OR (drainage[MeSH Terms])) OR (tracheostomy[MeSH Terms])) OR (bronchoscopy[MeSH Terms])) OR (thoracostomy[MeSH Terms])) OR (nebulizers and vaporizers[MeSH Terms])) OR (sputum[MeSH Terms])
- #2 (((((((((((((oxygen inhalation therapy[MeSH Terms]) OR (Autopsy[MeSH Terms])) OR (respiratory function tests[MeSH Terms])) OR (spirometry[MeSH Terms])) OR (cardiopulmonary resuscitation[MeSH Terms])) OR (breathing exercises[MeSH Terms])) OR (dentistry[MeSH Terms])) OR (otorhinolaryngologic surgical procedures[MeSH Terms])) OR (oral surgical procedures[MeSH Terms])) OR (otolaryngology[MeSH Terms])) OR (nasal surgical procedures[MeSH Terms])) OR (otologic surgical procedures[MeSH Terms])) OR (natural orifice endoscopic surgery[MeSH Terms])) OR (endoscopy[MeSH Terms])
- #3 (physical therapy modalities[MeSH Terms]) AND (thorax[MeSH Terms])

- #4 (((((((((((((((((((((((NIV[Text Word]) OR (CPAP[Text Word])) OR (BiPAP[Text Word])) OR (HFOV[Text Word])) OR ("high frequency oscillatory ventilation"[Text Word])) OR (ventilat*[Text Word])) OR (respirat*[Text Word])) OR (intubat*[Text Word])) OR (extubat*[Text Word])) OR (respirat* N3 suction*[Text Word]))) OR (air way N3 suction*[Text Word])) OR (airway N3 suction*[Text Word]) OR (nebuli*[Text Word])) OR ("heat moisture exchange"[Text Word])) OR (chest aN3 phys*[Text Word])) OR (sputum N3 induct*[Text Word])) OR (lung N2 test*[Text Word])) OR (pulmonary N3 test*[Text Word])) OR (saliva[MeSH Terms])) OR (supra glottic airways[Text Word])) OR (SGA[Text Word])) OR ("face mask ventilation"[Text Word])
- #5 (((((((((aerosols[MeSH Terms]) OR (aerosol genera* procedure[Text Word])) OR (aerosol N3 proced*[Text Word])) OR (AGP[Text Word])) OR (AGMP[Text Word])) OR (aerosol*[Text Word])) OR (airborne[Text Word])) OR (splatter[Text Word])) OR (droplet[Text Word])) OR (cough[MeSH Terms]) OR (cough*[Text Word])
- #6 ((((((((((SARS virus[MeSH Terms]) OR (SARS-CoV-2[MeSH Terms])) OR (middle east respiratory syndrome coronavirus[MeSH Terms])) OR (COVID-19[MeSH Terms])) OR (influenza, human[MeSH Terms])) OR (orthomyxoviridae[MeSH Terms])) OR (MERS[Text Word])) OR (SARS[Text Word])) OR (COVID[Text Word])) OR (influenza[Text Word])
- #7 (#1 or #2 or #3 or #4) and #5 and #6
- #8 (animals[MeSH Terms]) NOT (human[MeSH Terms])
- #9 #7 NOT #8

Limited to English language and date range of 2019 to present (4th October 2021)

Appendix 4: search strategies (specificity)

Database: Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to October 01, 2021>

1 exp aerosols/

2 aerosol genera\$ procedure.tw.

3 (aerosol adj3 proced\$).tw.

4 AGP.tw.

5 AGMP.tw.

6 aerosol\$.tw.

7 airborne.tw.

8 splatter.tw.

9 droplet.tw.

10 cough/

11 cough\$.tw.

12 exp infection control/

13 exp cross infection/

14 preventive medicine/

15 Disease Transmission, Infectious/

16 Infectious Disease Transmission, Patient-to-Professional/

17 Infectious Disease Transmission, Professional-to-Patient/

18 Disease Outbreaks/

19 Occupational Exposure/

20 risk factors/

21 risk assessment/

22 risk management/

23 exp health services/

24 exp health personnel/

25 (or/1-11) and (or/12-22) and (or/23-24)

26 exp animals/ not exp humans/

27 25 not 26

28 limit 27 to yr="2019 -Current"

29 limit 28 to english language

Cinahl (EBSCOHOST) specificity AGP search strategy (4th October 2021)

S1 MH aerosol OR TX "aerosol genera* procedure" OR TX aerosol N3 proced*
OR TX AGP OR TX AGMP OR TX aerosol* OR TX airborne OR TX splatter
OR TX droplet OR MH cough OR TX cough*

S2 MH infection control OR MH cross infection OR MH preventive health care
OR MH disease transmission OR MH disease transmission, patient-to-
professional OR MH disease transmission, professional-to-patient OR MH
disease outbreaks OR MH occupational exposure OR MH risk factors OR
MH risk assessment OR MH risk management

S3 MH "health services+" OR MH "health personnel+"

S4 S1 and S2 and S3

S5 MH animals NOT MH human

S6 S4 NOT S5

Limited to English language and date range of 2019 to present (4th October 2021)

PubMed specificity AGP search strategy (4th October 2021)

- #1 (((((((((aerosols[MeSH Terms] OR (aerosol genera* procedure[Text Word])) OR (aerosol N3 proced*[Text Word])) OR (AGP[Text Word])) OR (AGMP[Text Word])) OR (aerosol*[Text Word])) OR (airborne[Text Word])) OR (splatter[Text Word])) OR (droplet[Text Word])) OR (cough[MeSH Terms])) OR (cough*[Text Word])
- #2 (((((((((infection control[MeSH Terms] OR (cross infection[MeSH Terms])) OR (preventive medicine[MeSH Terms])) OR (disease transmission, infectious[MeSH Terms])) OR (infectious disease transmission, patient-to-professional[MeSH Terms])) OR (infectious disease transmission, professional-to-patient[MeSH Terms])) OR (disease outbreaks[MeSH Terms])) OR (occupational exposure[MeSH Terms])) OR (risk factors[MeSH Terms])) OR (risk assessment[MeSH Terms])) OR (risk management[MeSH Terms])
- #3 (health services[MeSH Terms] OR (health personnel[MeSH Terms])
- #4 #1 AND #2 AND #3
- #5 (animals[MeSH Terms] NOT (humans[MeSH Terms])
- #6 #4 NOT #5

Limited to English language and date range of 2019 to present (4th October 2021)