NHS National Services Scotland

Transmission Based Precautions Definitions literature review

Considered Judgement Forms

Version 1.0

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ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

Executive Summary

There are nine research questions within this considered judgement form. Each research question has two sections, Part A and Part B.

- **Part A** outlines the quality of evidence available to answer the research question and summarises the reliability, consistency, applicability, and generalisability of the evidence as well as risk of publication bias.
- **Part B** will outline draft recommendations and good practice points and will summarise how they were developed (how evidence was combined with expert opinion). This section will detail the intended benefits, potential harms, feasibility of implementation, value judgements, intentional vagueness, and exceptions (scenarios where the recommendation or good practice point would not be applied). Future research needs will also be summarised. **Part B is currently being developed with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.**

The first three research questions assess how contact, droplet and airborne transmission is currently described within the literature, with an additional focus on the evidence cited to support definitions. These research questions will not generate any recommendations or good practice points as they are for information purposes only.

The fourth research question assesses how infectious agents are released into the air from the respiratory tract. Findings from air sampling studies indicate that the current definitions of droplet and airborne transmission are not sufficiently supported by robust evidence. The reasons behind the increased transmission risk associated with specific clinical procedures is explored with a procedure being designated as an aerosol generating procedure (AGP) based on use of high-speed devices on respiratory tract tissue and/or its propensity to induce coughing. Evidence cannot currently support a specific distance from source at which transmission risk is reduced or increased. Evidence also cannot currently support whether a specific size or range of particle sizes drives transmission of infection.

The fifth research question aimed to explore whether there are examples within the literature of person-to-person transmission being described out with the widely acknowledged contact, droplet and airborne framework.

Similarly to research questions one to three, research question six represents an information gathering exercise. This research question assesses how transmission-based precautions (TBPs) are described within the literature, with an additional focus on what specific IPC steps are considered to be TBPs.

Research question seven considers when TBPs should be applied. Limited evidence was identified to support specific contact, droplet and airborne bundled precautions. Most evidence to support general use of TBPs is based on expert opinion. Extant International and national guidance frequently outlines the factors beyond transmission mode which should be considered when implementing TBPs, for example, the consequences of onward transmission, service user symptoms and the nature of the clinical procedure being undertaken.

Research question eight aimed to identify reported occurrences of transmission of infectious agents, within the literature, which do not align with their currently assigned transmission modes of contact, droplet or airborne. Only three limited outbreak reports were identified; one report presented evidence for hypothesised air transmission of *Acinetobacter baumannii* and two suggested long-range air transmission of SARS-CoV-2.

Research question nine assesses the factors which should be considered when discontinuing TBPs. Evidence is limited and highly pathogen specific.

Research Questions

1. What is the current definition of contact transmission?
2. What is the current definition of droplet transmission?
3. What is the current definition of airborne transmission?
4. How are infectious agents released into the air of the health and care environment from the respiratory tract with consideration of particle size, distance and clearance/fallout time?
5. Can person-to-person transmission of infection be described/defined beyond the current categories of contact/droplet and/or airborne?
6. What are Transmission Based Precautions (TBPs)?
7. When should TBPs be applied?
8. Are there reported occurrences of person-to-person infectious agent transmission which do not align with their currently assigned transmission mode(s)?
9. What factors should be considered when determining whether to discontinue TBPs?

Research Question 1: What is the current definition of contact transmission?

A: Quality of Evidence

1.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Thirteen general infection prevention and control (IPC) guidance documents were included for this research question.[1-13] All guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence. Generally, primary evidence cited to support statements within included guidance was of low quality. No primary research studies were included.	13 x SIGN50 level 4 – expert opinion

1.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how the judgement was formed as to the overall direction of the evidence.

Comments
Definitions of indirect and direct contact transmission were consistent across guidance. Direct contact transmission was defined as the physical transfer of infectious agents from an infected or colonised person to another susceptible individual, via touch or contact with blood or body fluids without a contaminated intermediate object or person. Indirect contact transmission was defined as the transfer of an infectious agent to a susceptible host via a contaminated intermediate object. Sources consistently provided examples of scenarios which would be characterised as contact transmission[8-12] and examples of infectious agents considered to be spread via the contact route.[1, 3, 5-8, 10-12] Three sources provided citations to support their definition of contact transmission.[8, 10, 12] These were all low-quality studies; outbreak reports, environmental sampling studies, before-after studies and experimental inoculation studies.

1.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain healthcare settings or groups of infectious agents, for example, care homes or acute respiratory infections. Where appropriate, findings in relation to these documents have been connected, in text, to their respective infectious agent or setting specific guidance.

1.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary research studies were included therefore generalisability is not applicable.

1.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 2: What is the current definition of droplet transmission?

A: Quality of Evidence

2.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Fourteen general infection prevention and control (IPC) guidance documents were identified for this research question.[1, 2, 4-15] All guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence. Generally, evidence cited to support statements within guidance was of low quality.	14 x SIGN50 level 4 – expert opinion

2.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how the judgement was formed as to the overall direction of the evidence.

Comments
Consistency regarding how definition/features are described in guidance:

Comments

- the definition of droplet transmission - infectious respiratory droplets travelling over 'short' distances (<1-2m),[4-6, 8-10, 12, 13] from the respiratory tract of an infectious individual directly through the air, to the susceptible mucosal surfaces (eyes, mouth and/or nose) of the recipient
- droplets being generated when an infected individual coughs, sneezes, or talks

Some consistency regarding how definitions/features are described in guidance:

- the respiratory particles involved in droplet transmission being equal to or greater than 5μm in size, with almost all lacking supportive citations. However, Canadian guidance[8] authors outline droplets as being greater than 10μm
- that droplet production occurs during clinical procedures
- the concept that due to gravitational forces, droplets do not remain suspended in the air for long (time unspecified)[2, 4-10] and cannot traverse large distances (greater than 1-2m).[5, 6, 8-10, 12, 13]
- evidence cited to support the key characteristics of droplet transmission being of low quality[16-24]
- the following infectious agents being considered as transmitted via the droplet route: *Bordetella pertussis*, Adenovirus, Group A *streptococcus*, *Neisseria meningitides*, rubella and influenza. Weak supportive evidence is only cited in one guidance source to support these infectious agent assignations.[12]

Inconsistency across guidance regarding approximate droplet transmission 'at risk' area:

- 3ft around infected individual
- less than one metre
- less than one to two metres

Inconsistency across guidance regarding:

Comments
• whether droplet transmission should be considered a form of contact transmission • whether indirect contact transmission via droplet contaminated surfaces should be considered a form of droplet transmission

2.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain healthcare settings or groups of infectious agents for example care homes or acute respiratory infections. Where appropriate, findings in relation to these documents have been connected, in text, to their respective infectious agent or setting specific guidance.

2.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary studies were included.

2.5. Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 3: What is the current definition of airborne transmission?

A: Quality of Evidence

3.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Fourteen general infection prevention and control (IPC) guidance documents were included for this research question.[1, 2, 4-10, 12-15, 25] All guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence. No primary studies were included.	14 x SIGN50 level 4 – expert opinion

3.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments

Consistency regarding how airborne transmission is described in guidance:

- inhalation of infectious, 'small' aerosol particles (<5μm)[1, 6, 10, 12, 15] (or 'droplet nuclei') which have been generated by the respiratory activities of an infectious host
- particles involved in airborne transmission can be dispersed over undefined large distances and remain infective in the air for prolonged periods (time unspecified), meaning that close contact is not required for transmission to occur
- small particles can be carried on air currents and via ventilation systems

High consistency across guidance regarding the following infectious agents being spread by the 'airborne' route:

- Measles virus
- *Mycobacterium tuberculosis*
- Varicella zoster virus

Supportive citations regarding the airborne transmission status of the infectious agents above are only provided in two sources.[8, 12] Cited studies do not definitively demonstrate long range transmission but provide moderate supportive evidence for its occurrence.

Lack of clarity in guidance regarding defined airtime of small particles. English guidance simply outlines that aerosols "remain in the air for longer" than droplets[9] whilst New Zealand guidance specifies that they, "can stay suspended in the air for hours"[7] with the CDC outlining indefinite airborne suspension.[15]

3.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain healthcare settings or groups of infectious agents for example care homes or acute respiratory infections. Where appropriate, findings in relation to these documents have been connected, in text, to their respective infectious agent or setting specific guidance.

3.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary studies were included.

3.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 4: How are infectious agents released into the air of the health and care environment from the respiratory tract with consideration of particle size, distance and clearance/fallout time?

A: Quality of Evidence

4.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
64 observational air sampling studies.[26-89] Six guidance documents - organisational expert opinion pieces.[4, 8, 9, 12, 90, 91] All 64 air sampling studies represent low quality evidence as they involved observational particle and/or infectious agent detection with no set standards or threshold-based assessment to support overall analysis. Consistent limitations are outlined in section 4.2 below. The six guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence.	64 x SIGN50 level 3 6 x SIGN50 level 4 - expert opinion

4.2 Is the evidence consistent in their conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments
Although there are a limited number of studies which pertain to each specific infectious agent and/or respiratory activity, overall the evidence base was consistent and clear in demonstrating that particles of varying size are released into the air from the respiratory tract through breathing, sneezing, coughing and vocalising. **Respiratory activity** • Three studies reported that when breathing, speaking or coughing, the mean particle diameter of particles produced by healthy participants, near to source (5-20cm), was close to 1µm.[26, 34, 53] • Three studies supported the concept that speaking generates more particles than breathing[26, 60, 81] and that singing, or shouting produces more particles than speaking.[47, 81, 82] • In five studies, increased physical exertion and loudness of speech were associated with increased particle production.[26, 40, 47, 60, 81] **Infectious agent detection** Infectious agent material (see specific infectious agents below) was detected both at source and at a range of distances (<1m-5m) from infected subjects (both hospitalised and un-hospitalised) in varying particle sizes (<1µm-10µm). Studies were heterogeneous in terms of infectious agent studied (including specific variant), population characteristics, procedures reported and environmental parameters during sampling. Of the 39 air sampling studies which involved detection of infectious agents in the air and/or in respiratory exhalations, 15 involved collection of samples at or close to source using apparatus with a mouthpiece, or cone shaped aperture,

Comments

respectively.[33, 36, 37, 44, 56, 59, 64, 68-71, 77, 78, 85, 87] 24 studies involved detection of infectious agents at specified distances from infected persons.

- Viable SARS-CoV-2 virus was detected at source (no particle size assessment, n=2 subjects),[77] approximately 1m away (<1µm, n=3 subjects)[41] and 4.8m away (no particle size assessment, n=1 subject).[35]
- Six studies reported that SARS-CoV-2 RNA was detectable in respiratory exhalations at close range (<1m), in particles <5µm.[41, 64, 66, 68, 83, 85]
- Three studies detected SARS-CoV-2 RNA at approximately 2m from 7 subjects[27, 42, 75] with some positive samples found in small particle size fractions (<4µm).[27, 42]
- SARS-CoV-2 RNA was detected at 4m from a group of 8 infected subjects in one study[75] and on settle plates placed at 0.9-3.1m from 5 dental patients undergoing dental treatment, in another.[63]
- In four studies, viable influenza was detected at close range (<1m) from infected subjects[36, 37, 44, 87] with positive samples found in small particle size fractions (<5µm).[44, 87]
- Four studies reported that influenza RNA was detected at close range (<1m) in particles <5µm.[37, 44, 87, 89]
- In one study influenza RNA was detected at 1-2m from 3 subjects in particles <4µm[49] and in another at 2m from 2 subjects in particles <1µm.[86]
- Three studies reported that viable *Pseudomonas aeruginosa (P. aeruginosa)* was detectable in the coughing exhalations of colonised persons (with cystic fibrosis and/or COPD/bronchiectasis), in particles <5µm diameter, both at source and at 2m.[57, 59, 61] In two studies viable *P. aeruginosa* was detected at 4m from source,[57, 58] with positive samples in particles <3.3µm.[57]

Comments

- Four studies reported detection of viable *Mycobacterium tuberculosis* at source[33, 69, 71, 78] with positive samples in small particle size fractions (<3.3µm).[33, 71]
- Two studies detected *Pneumocystis jirovecii* DNA at 1m from 16 subjects[67, 74] in one of these studies DNA was detected at 3m and 5m also.[67]
- In one study viable *Staphylococcus aureus* was detected in particles <5µm at approximately 3m from source[30] and in an another at 2m and 4m from source.[62]
- Limited evidence demonstrated that the majority of total exhaled influenza viral RNA,[37, 87] viable *P. aeruginosa* [59] and viable *M. tuberculosis* [33, 71] is found in small size fractionated samples (<5µm) close to source (<1m). This finding also applied to *P. aeruginosa* at 2m from source.[61]
- Single studies assessed the presence of the following infectious agents in the air and/or respiratory exhalations; measles virus RNA,[29] viable coagulase negative *staphylococci,*[28] viable respiratory syncytial virus,[50] parainfluenza RNA,[56] rhinovirus RNA,[56] viable *B. cenocepacia*,[59] viable *S. maltophilia*,[61] MERS-CoV RNA,[79] viable MERS-CoV[79] and viable *A. fumigatus*.[70]

Certain limitations were consistently identified within the included air sampling studies. Of the 24 studies where air samples were taken at specified distances, the majority (n=16), were in uncontrolled environments where confidence in maintenance of subject's distance to sampler was poor, precise activities of subjects were unclear and contribution to samples by others could not be ruled out.[27, 29, 35, 41, 42, 49, 50, 63, 66, 67, 72, 74, 79, 83, 86, 89]

The above evidence demonstrates presence of infectious agent material in the air. It does not, in isolation, confirm or refute transmission of these infectious agents from one person to another via the air. In those studies where viable material is ascertained to be present, it is unknown whether it is present in sufficient

Comments

quantities, in line with infectious dose, to result in transmission of infection. Consequently, evidence cannot currently support a specific distance from source at which transmission risk is reduced or increased. Evidence also cannot currently support whether a specific size or range of particle sizes drives transmission of infection.

Contradictory findings were identified in association with SARS-CoV-2 RNA aerosol positivity rates and reported symptoms. Two studies reported that there was a correlation between coughing symptoms and SARS-CoV-2 RNA aerosol positivity[64, 84] whilst one found that clinical symptoms were not significantly different between COVID-19 infected participants with and without detectable SARS-CoV-2 RNA in respiratory exhalations.[68]

Infectious agent clearance time

Very little evidence was identified regarding how long it takes particles carrying infectious agent material to fall out or disperse from an area following release from the respiratory tract. Based on limited evidence (four studies)[50, 57, 58, 62] and the expert opinion of ARHAI Scotland, infectious agent material will likely remain aloft in particles in the air post generation, for an undetermined period of time. This time period may be influenced by air change rates and room pressure.

Clinical procedures

Fifteen air sampling studies assessed particle production during specific medical and/or surgical procedures.

These studies had consistent limitations which included small sample sizes and inappropriate comparative baseline measurements. Procedural particle measurements were compared with those pre-procedure. Pre-procedure measurements were not accompanied by sufficient information on numbers of staff present and nature of activity. Particle counts may not represent those of respiratory tract origin but rather of other sources such as lint or skin squames. In addition, it is unclear whether particle counts correlate with viral/bacterial/fungal levels in the air and thus transmission risk. Numbers of studies providing findings on a specific procedure were small.

Comments

There were a small number of procedures where an increase in particle count was observed compared to forced coughing. This was demonstrated in two studies which assessed upper GI endoscopy,[46, 65] one study which assessed administration of nebulised saline,[55] two studies which assessed ultrasonic scaling[45, 76] and one study which assessed the following dental procedures: drilling (high speed/slow speed/surgical) and 3-in-1 use (with air) however the source of these particles is unclear (for instance instrumental irrigant or respiratory tract fluid).[45]

There were several procedures where particle counts were observed to be lower than that produced by forced coughing. These procedures were as follows; dental hand scaling, routine extractions and 3-in-1 use (water only),[45] manual face mask ventilation,[52, 53] bi-level positive airway pressure (BiPAP) with use of an exhalation filter,[55, 60] continuous positive airway pressure (CPAP) with use of an exhalation filter,[48] breathing with oxygen delivery of up to 15L/min via a face mask,[34, 55] respiratory tract suctioning (beyond the oropharynx),[52] tracheal intubation,[52] tracheal extubation,[52] oral cavity suctioning,[65] chest physiotherapy (induction of sputum),[55] standard spirometry (with filter),[51] peak flow measurements (with filter),[51] supraglottic airway insertion and removal,[54] myringotomy and tympanostomy tube insertion[31] and high flow nasal oxygen (HFNO) at flow rates of 20, 40 and 60L/min.[34, 48, 60] BiPAP, CPAP, manual ventilation, tracheal intubation, tracheal extubation, respiratory tract suctioning beyond the oropharynx, and HFNO all currently feature on the Scottish AGP list.

There are procedures which feature on the current Scottish AGP list for which no studies of adequate quality were included. They were as follows; bronchoscopy, tracheotomy or tracheostomy procedures (including insertion or removal), high frequency oscillatory ventilation (HFOV) and high-speed cutting in surgery or post-mortem procedures (involving the respiratory tract).

Supplementation of the limited evidence base with expert opinion is required to establish which procedures should be included on a high-risk procedure list.

4.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
Of the 64 research studies, 20 were from the U.S.A,[26-44, 87] 12 were from the U.K,[45-55, 89] six were from Australia,[56, 58-62] three each from Germany,[73, 81, 82] France,[67, 72, 74] and Singapore,[66, 68, 83] two each from Canada,[77, 86] Hong Kong,[65, 88] Uganda,[71, 78] South Korea,[79, 80] and Sweden[64, 85] and one from each of the following countries; Italy,[76] Turkey,[63] Norway,[75] South Africa,[69] Japan,[84] and the Netherlands.[70] Clinical procedures performed may utilise differing equipment or techniques depending on country specific practices and there was a lack of detail in the evidence base to confirm whether this was the case or not. The included guidance documents (SIGN level 4 expert opinion) are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Three included guidance documents (SIGN level 4 expert opinion) were general healthcare infection prevention and control documents without a focus on a specific infectious agent or healthcare setting.[8, 12, 90] Three guidance documents (SIGN level 4 expert opinion) focused on respiratory infections[4, 9, 91] with one of these documents outlining that it does not apply to TB, MERS-CoV or human cases of avian influenza[9] and one outlining a focus on epidemic and pandemic prone acute respiratory infections.[4]

4.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
Most included primary studies had highly specific cohorts, environmental conditions, procedures and/or infections (including associated circulating strain); these are challenges to developing evidence-based conclusions. In terms of study populations, in 13 studies where SARS-CoV-2 was identified in air samples, six had sole involvement of hospitalised patients.[27, 35, 41, 66, 83, 84] Of eight studies where influenza was identified in air samples, four had sole involvement of young, otherwise healthy cohorts (~19-21yo).[36, 37, 44, 87] In the review, statements surrounding the respiratory particle production and/or infectious agent evidence base are made, highlighting specific features of studies which limit generalisability where necessary. All study conclusions should be interpreted with an awareness that differing infectious agents, air flow patterns, air change rates, symptoms of participants, humidity conditions, and room temperatures could produce different results.

4.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
ARHAI Scotland theorise that there may be a tendency towards publication of studies where infectious agents were identified in air samples as opposed to studies where they were not. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 5: Can person-to-person transmission of infection be described/defined beyond the current categories of contact/droplet and/or airborne?

A: Quality of Evidence

5.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Six general infection prevention and control (IPC) guidance documents were included for this research question.[4, 8, 12, 90, 92, 93] All guidance documents were published by national organisations and were graded SIGN50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence. No primary research studies were included.	6 x SIGN50 level 4 – expert opinion

5.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how the judgement was formed as to the overall direction of the evidence.

Comments
Little to no consistency was observed regarding descriptions of transmission beyond the framework of contact, droplet and airborne. Two organisations moved away from use of the term 'airborne' with the CDC (2016) suggesting use of the terms 'inhalation' and 'close range inhalation'[92] and the American Society of Heating, Refrigerating and Air-conditioning Engineers (2022) using the phrase 'inhalation of aerosols' with no associated distance descriptors.[90] Some guidance outlines that infectious agents are not exclusively transmitted via one route and that routes of transmission have differing likelihoods attributed to them based on the infectious agent and encounter circumstances. For example, the Canadian Government Pathogen Risk Assessment includes terms which indicate likelihood of transmission via a specific route "none; low, unlikely; moderate, possible; high, preferred route; unknown".[93]

5.3 Are the studies applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain healthcare settings or groups of infectious agents for example care homes or acute respiratory infections. Where appropriate, findings in relation to these documents have been connected, in text, to their respective setting or infectious agent specific guidance.

5.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary studies were included.

5.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 6: What are Transmission Based Precautions (TBPs)?

A: Quality of Evidence

6.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Nineteen general infection prevention and control (IPC) guidance documents were included for this research question.[1-6, 8-12, 14, 25, 94-99] All guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence.	19 x SIGN50 level 4 – expert opinion

6.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments
There was consistency regarding the overall definition of transmission-based precautions (TBPs) which was as follows:

Comments
Transmission Based Precautions (TBPs) are additional measures that should be implemented with standard infection control precautions (SICPs) to prevent the onward transmission of a suspected or confirmed infectious agent. Some sources referred to them as 'additional precautions' – these were considered equivalent to TBPs in the context of this review. Certain types of contact, droplet and airborne precautions were consistently outlined under each bundled heading across the evidence base. Inconsistency within and amongst guidance documents arose through deviation from the initially outlined framework of contact/droplet/airborne precautions for those infected with contact/ droplet/ airborne transmitted infections. These deviations involved TBP recommendations which were based on/specific to: • individual infectious agents • patients' presenting symptoms • certain health and care settings • the performance of certain clinical procedures • certain patient factors • local outbreak information

6.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain infectious agents or healthcare settings for example multi-drug resistant organisms, acute respiratory infections or care homes. Where appropriate, findings in relation to these

Comments
documents have been connected, in text, to their respective infectious agent or setting specific guidance.

6.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary studies were included.

6.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 7: When should TBPs be applied?

A: Quality of Evidence

7.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Twenty guidance documents (SIGN level 4 - expert opinion)[1-5, 8-14, 25, 94-100] one interrupted time series study[101] and one retrospective cohort study[102] (both SIGN level 3) were included for this research question. The guidance documents were published by national organisations and were graded SIGN 50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence.	20 x SIGN50 level 4 – expert opinion 2 x SIGN50 level 3

7.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments

Guidance was consistent in recommending the use of TBPs for patients and/or residents who were confirmed or suspected to be infected or colonised with an infectious agent spread via the contact, droplet or airborne route.

Guidance also consistently outlined that TBPs are required for infectious agents where standard precautions alone are deemed insufficient for the prevention of nosocomial transmission, however, this statement was consistently poorly evidenced.

Guidance consistently outlined the higher risk associated with 'aerosol generating procedures' and the increased volume of smaller infectious particles which they are anticipated to generate and disperse. Different AGP lists are presented across the IPC literature and guidance with weak supportive evidence.[4, 8, 9]

There was a lack of consistency between guidance documents regarding the specific factors which should influence the decision on when to apply TBPs.

Recommendations outlined by more than one source included:

- TBPs for novel or targeted MDROs
- TBPs for 'epidemiologically important' infectious agents
- consideration of severity of illness caused by infection with presenting infectious agent
- consideration of TBP application within the context of local outbreak data
- application of TBPs when a clinical procedure or task is deemed to increase the risk of transmission of a specific infectious agent
- consideration of patient's presenting symptoms
- consideration of patient's ability to maintain personal hygiene
- consideration of the specific health and care setting

Recommendations which were unique to one source included:

- performance of a patient care risk assessment to inform use of TBPs
- consideration of an infectious agent's infective dose

Comments
• consideration of TBP use when “the clinical situation prevent[ed] consistent application of routine practices (for example, care of the young child, incontinent adult or cognitively impaired individual” Efficacy of transmission-based precautions: Only two studies presented results to support the use of precautions, specifically the use of contact precautions to prevent nosocomial MRSA transmission.[101, 102] No evidence was available that assessed the effectiveness of ‘droplet’ or ‘airborne’ precautions.

7.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The included guidance documents are produced by internationally recognised national healthcare associations and are generally relevant to Scottish health and care settings. Some guidance was specific to certain groups of infectious agents or healthcare settings for example multi-drug resistant organisms, acute respiratory infections or care homes. Where appropriate, findings in relation to these documents have been connected, in text, to their specific, named infectious agent or setting specific guidance. The two included studies which assessed contact precaution bundle efficacy both assessed nosocomial acquisition of MRSA in ICU settings (one was a neonatal ICU).[101, 102] The studies were conducted 10-12 years ago, one was conducted in Australia,[101] the other in the U.S.A.[102] Specificity was enhanced in the Australian study through plastic aprons being used for the care of all patients in the before period, not just for those with MRSA.[101]

7.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
The two included studies which assessed contact precaution bundle efficacy both assessed nosocomial acquisition of MRSA in ICU settings (one was a neonatal ICU).[101, 102]

7.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
There is a widely acknowledged publication bias for studies with statistically significant results, however, when screening and appraising evidence in relation to this research question, there were a large number of studies which reported both on changes and an absence of change to infection rates following introduction or discontinuation of contact precautions. It is therefore not expected in this case for publication bias to have significantly hindered the identification of an evidence base to support an effect (or absence of effect) of contact precaution use. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 8: Are there reported occurrences of person-to-person infectious agent transmission which do not align with their currently assigned transmission mode(s)?

A: Quality of Evidence

8.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Three outbreak reports were included for this research question.[103-105] They were graded SIGN50 level 3 evidence. The reports are limited by retrospective data analysis and are at risk of recall bias. Limited information was provided regarding movement of HCWs or sharing of equipment, and active air sampling was not conducted.	3 x SIGN50 level 3

8.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments
One report presented evidence for hypothesised air transmission of *Acinetobacter baumannii* (*A. baumannii*) and two outbreak reports described potential long-range air transmission of SARS-CoV-2. It was not possible to assess consistency due to an insufficient number of studies.

8.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
The *A. baumannii* outbreak investigation was undertaken within a UK burns intensive care unit, making it directly applicable to these settings in Scotland.[103] Of two COVID-19 outbreak investigations, one was undertaken in a haematological ward in South Korea[104] and the other in a general paediatric ward in Israel.[105] Findings from these studies may not be directly applicable to these types of wards in the UK.

8.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
No primary research studies were included.

8.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
No concerns regarding publication bias specifically, however, it is noted that there may be many transmission events which have occurred in health and care settings which have not been published in the literature. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

Research Question 9: What factors should be considered when determining whether to discontinue TBPs?

A: Quality of Evidence

9.1 How reliable is the body of evidence? (see SIGN50, section 5.3.1, 5.3.4)

Comment here on the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.

If there is no available evidence to answer the key question, go to section B.

Comments	Evidence level
Nineteen pieces of evidence were included for this research question; one systematic review (SIGN50 level 1+),[106] three cohort studies,[107-109] (all SIGN50 level 3) five observational studies[89, 110-113] (all SIGN50 level 3) and 10 guidance documents[3, 4, 8-10, 12, 98, 114-116] (all graded SIGN50 level 4 – expert opinion). The guidance documents were published by national organisations and were graded SIGN50 level 4 expert opinion. Expert opinion guidance has potential bias given little detail is provided regarding how recommendations were formulated, and it is not always clear where expert opinion has taken precedence over scientific evidence.	1 x SIGN50 level 1+ 8 x SIGN50 level 3 10 x SIGN50 level 4 – expert opinion

9.2 Is the evidence consistent in its conclusions? (see SIGN50, section 5.3.2)

Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how a judgement was formed as to the overall direction of the evidence.

Comments
There was consistency in reporting that the type of infectious agent and period of infectivity should be used as considerations for discontinuation of TBPs, however, discussion of the complexity of the decision on when to discontinue was also common. Guidance consistently outlined that estimating period of infectivity can be challenging as it can vary depending on patient age, immune status, and presence of co-infection.[4, 8, 9, 12, 106, 112, 114] Guidance also indicated that estimating the end of the infectious period was consistently associated with symptom resolution,[3, 8-10, 12, 114-116] completion of a specific treatment[8, 114-116] and/or testing results.[8, 9, 12, 98, 108, 113, 114] Limited primary studies demonstrated the potential for carriage or recurrence of multi-drug resistant organisms[12, 107, 109, 113, 114] and persons with COVID-19 infection remaining PCR positive for extended periods of time.[106, 108] The CDC and WHO outline recommendations which do not align with considerations presented in other guidance sources. The CDC state that enhanced barrier precautions which are to be used for those “known to be colonized or infected with a MDRO as well as those at increased risk of MDRO acquisition (for example, residents with wounds or indwelling medical devices)” should remain in place for the duration of a patient’s stay or until wounds heal or indwelling devices are removed, although this is specific to care home service users.[3] The WHO do not recommend using testing as a trigger for discontinuation of precautions implemented in association with acute respiratory infection.[4] Both of these recommendations are in direct contradiction with considerations presented by other identified evidence.[8-10, 12, 114-116]

9.3 Is the evidence applicable to Scottish health and care settings? (see SIGN50, section 5.3.3)

For example, do the studies include interventions, comparators or outcomes that are common to Scottish health and care settings?

Comments
Of the included evidence, three pieces were undertaken in or written for UK health and care settings.[9, 89, 115] The findings from these would be directly applicable to NHSScotland. There are a further two pieces of evidence that were written for international or unspecified audiences (1 systematic review,[106] 1 WHO expert opinion[4]). The remaining 13 pieces of evidence were undertaken in or written for North American health and care settings (12 United States,[3, 12, 98, 107-114, 116] 1 Canada[8]), with one additional piece of expert opinion being written for Australian Settings.[10]

9.4 Are the studies generalisable to the target population?

Comment here on sample size and methods of sample selection. Is the sample representative of the specific population/group of interest? Generalisability is only relevant to primary research studies.

Comments
Findings from included primary research may not be generalisable to all infectious agents as evidence was specific to SARS-CoV-2,[106, 108, 112] MRSA,[109, 110, 113] C*arbapenemase-Producing Enterobacteriaceae* (CPE),[107] *Clostridioides difficile* (CDI),[111] and Influenza H1N1.[89] Within studies, testing was undertaking in a variety of ways both directly from patients [106-110, 112, 113] and using staff skin or environmental contamination as a proxy indicator for carriage of infectious agents.[89, 111] These testing and analysis methods will all have differing levels of efficacy and applicability. Of three included studies which involved SARS-CoV-2 infected patients, two included adult patients who were tested upon admission to hospital [108, 112] with one of these specific to solid organ transplant patients.[112] The third SARS-CoV-2 study included both paediatric (<18 years of age) and adult patients, however, it was unclear if patients were assessed within a hospital setting.[106] Of the three studies which included MRSA patients, all were undertaken in hospital settings.[109, 110, 113] Two of these studies presented information on the age of included subjects with the median age of participants reported as 51 and 53 years

Comments
of age respectively.[109, 110] Due to this, findings from these studies may not be generalisable to paediatric populations. The single study which addressed removal of transmission-based precautions for patients colonised with CPE included only adult patients admitted to ICU facilities across four hospitals.[107] A number of comorbidities were reported for the included patient cohort, however none of these were found to be significantly associated with CPE carriage.[107] The single study which included CDI patients did not report on ages of participants and was undertaken in general hospital wards.[111] The findings of this paper are difficult to generalise given the lack of information provided. A single study addressed removal of precautions for patients infected with Influenza (H1N1). This study included adult and paediatric subjects both in the community and admitted to hospital.[89]

9.5 Are there concerns about publication bias? (see SIGN50, section 5.3.5)

Comment here on whether there is a risk in the evidence base that studies have been selectively published based on their results (and thus a risk that results from published studies are systematically different from unpublished evidence).

Comments
Overall, no concerns identified. A formal assessment of publication bias was not conducted.

B: Evidence to Decision

Part B will be completed following consultation with the ARHAI Scotland National Policies Guidance and Evidence (NPGE) Working Group.

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