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Presymptomatic, asymptomatic and post-symptomatic transmission of SARS-CoV-2: joint British Infection Association (BIA), Healthcare Infection Society (HIS), Infection Prevention Society (IPS) and Royal College of pathologists (RCPATH) guidance

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1 **Presymptomatic, asymptomatic and post-symptomatic transmission of SARS-**  
2 **CoV-2: joint British Infection Association (BIA), Healthcare Infection Society**  
3 **(HIS), Infection Prevention Society (IPS) and Royal College of Pathologists**  
4 **(RCPATH) guidance**

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17 **Keywords**

18 SARS-CoV-2, COVID-19, infection, transmission, presymptomatic, asymptomatic, post-symptomatic,  
19 guideline

## 1 **1. Executive summary**

2 This is the second of two guidance articles produced by the British Infection Association (BIA), the  
3 Healthcare Infection Society (HIS), the Infection Prevention Society (IPS) and the Royal College of  
4 Pathologists (RCPATH). Both articles refer to the pandemic of coronavirus disease 2019 (COVID-19)  
5 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Using evidence that  
6 emerged during the first wave of the pandemic, the articles summarise aspects of the transmission  
7 dynamics of SARS-CoV-2 and provide guidance on how to reduce the risk of transmission. This article  
8 focuses on the risks of presymptomatic, asymptomatic and post-symptomatic SARS-CoV-2  
9 transmission, allowing healthcare workers and the public to understand how transmission occurs  
10 and to take action to protect themselves and others. The guidance recognises further waves of the  
11 pandemic, the possibility of reinfection, the emergence of new variants of the virus and ongoing  
12 immunisation programmes.

13 Having considered the evidence, the COVID-19 Rapid Guidance Working Party concluded that:

- 14 • presymptomatic transmission (meaning that an index case has no symptoms during the  
15 exposure period of their close contacts, but later develops symptoms) is **confirmed**
- 16 • asymptomatic transmission (meaning that an index case never develops symptoms or signs  
17 of infection) is **probable**.

18 The Working Party was unable to assess the likelihood of post-symptomatic transmission (meaning  
19 that an index case has no symptoms during the exposure period of their close contacts, but  
20 previously had symptoms) because of an absence of evidence.

21 The Working Party formulated recommendations for practice taking account of the evidence  
22 reviewed. The recommendations were developed for acute healthcare settings (with particular  
23 reference to clinical staff and infection prevention and control teams), but they might be useful in  
24 other health and care settings such as dental practices and care homes. The Working Party also  
25 identified areas for future research.

### 26 ***Recommendations***

27 Be aware that:

- 28 • people without noticeable symptoms may transmit the SARS-CoV-2 virus to other people
- 29 • transmission of SARS-CoV-2 from people without symptoms may occur in all settings in  
30 which people are in close proximity
- 31 • however, it is likely that the risk of transmission of SARS-CoV-2 is greater from people who  
32 have symptoms compared with those who do not.

33 Even in the absence of symptoms, adhere to legislation and guidance regarding measures to reduce  
34 the risk of transmission of SARS-CoV-2 (such as social distancing, hand hygiene, use of personal  
35 protective equipment and ventilation of enclosed spaces).

36 Be aware that the future transmissibility of SARS-CoV-2 from people carrying the virus without  
37 symptoms might depend on the:

- 38 • nature of further waves or outbreaks of COVID-19
- 39 • emergence and circulation of SARS-CoV-2 variants of concern
- 40 • potential for people who have had COVID-19 previously to be reinfected
- 41 • effectiveness of available vaccines, including the longevity of immunity they confer.

1 Be aware that it is not yet known to what extent or for how long people recovering from acute  
2 infection can transmit the SARS-CoV-2 virus to other people.

### 3 **2. Lay summary**

4 Covid-19 is a worldwide ~~problem~~~~problem~~, and we are learning not just how to treat and vaccinate  
5 (immunise) people, but also how and when the infection is spread from person to person. Unlike  
6 some infections, you cannot necessarily see who is likely to infect another person; this is because  
7 sometimes the infection is transmitted before (pre) someone develops symptoms. It is also the case  
8 that some people have the infection and can transmit it but never develop symptoms themselves;  
9 this we call asymptomatic transmission.

10 This guidance document is one of a pair which have reviewed the scientific evidence on how Covid-  
11 19 is spread. This part of the guide provides recommendations on how to help stop the spread of  
12 infection before someone becomes obviously ill (presymptomatic) and for those who never become  
13 ill themselves (asymptomatic). We ~~could did~~ not find evidence for post symptomatic transmission  
14 (someone transmitting Covid-19 after they have recovered), ~~however this may emerge as we learn~~  
15 ~~more about this relatively new infection~~.

16 The recommendations based on the evidence we have reviewed give confidence that the things we  
17 are all doing such as social distancing, hand washing, wearing face coverings and keeping rooms well  
18 ventilated by opening windows are the things that we should be doing to prevent people getting  
19 infected with Covid-19. We hope that this guide will help everyone try and prevent spreading Covid-  
20 19.

### 21 **3. Introduction**

22 Coronavirus disease 2019 (COVID-19) was first detected in Wuhan, Hubei province, China; it spread  
23 around the world as a pandemic and by November 2021 had affected more than 260 million  
24 people.<sup>[1]</sup> COVID-19 is caused by a beta-coronavirus, severe acute respiratory syndrome coronavirus  
25 2 (SARS-CoV-2); other beta-coronaviruses associated with respiratory syndromes are severe acute  
26 respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus  
27 (MERS-CoV).

28 As an emerging and pandemic disease, COVID-19 attracted worldwide attention and interest in  
29 understanding the dynamics of SARS-CoV-2 transmission and treatment options for COVID-19  
30 patients. This Working Party Report is the second of two guidance articles developed using evidence  
31 published during the first wave of the pandemic to summarise aspects of the transmission dynamics  
32 of SARS-CoV-2 and advise on measures to reduce the risk of transmission in health and care settings.  
33 The article examines the risks of presymptomatic, asymptomatic and post-symptomatic SARS-CoV-2  
34 transmission. Understanding the risk of transmission according to the index case's symptom status  
35 at the time of exposure of (and potential transmission to) their close contacts is important to allow  
36 healthcare workers and the public to take action to protect themselves and others. The guidance  
37 acknowledges the possibility of reinfection, the emergence of new variants of the virus (particularly  
38 variants of concern), and ongoing immunisation programmes.

39 Key technical terms used in this guidance article are explained in the accompanying glossary (see  
40 Appendix A).

41

## 1 **4. Guideline Development Team**

### 2 **4.1. Acknowledgements**

3 The authors would like to acknowledge the support of their employing institutions, which allowed  
4 time required for producing this guidance. We thank the National Institute for Health Research  
5 Biomedical Research Centre at University College London Hospitals, which partly supported APRW's  
6 involvement in this guidance. We would also like to thank the Healthcare Infection Society (HIS)  
7 Guidelines Committee for reviewing this document.

### 8 **4.2. Source of funding**

9 The authors received no specific funding for this work. Financial support for time required to identify  
10 and synthesise the evidence and to write the manuscript was provided by the authors' respective  
11 employing institutions.

### 12 **4.3. Disclosure of potential conflicts of interest**

13 No authors reported any conflicts of interest (see Appendix B).

### 14 **4.4. Relationship of authors with sponsor**

15 The British Infection Association (BIA), HIS, the Infection Prevention Society (IPS) and the Royal  
16 College of Pathologists (RCPath) commissioned the authors to develop the Working Party Report.  
17 The authors are members of the participating organisations and together comprise the COVID-19  
18 Rapid Guidance Working Party convened to develop the guidance. MAM and AB are employed by  
19 HIS as guideline developers. Further information is provided in Appendix B.

### 20 **4.5. Responsibility for the guidance**

21 The views expressed in this publication are those of the authors and have been endorsed by BIA, HIS,  
22 IPS and RCPath following rapid consultation.

## 23 **5. Working Party Report**

### 24 **5.1. What is the Working Party Report?**

25 This report is the second in a pair of guidance documents covering key aspects in the prevention of  
26 SARS-CoV-2 transmission in health and care settings. The guidance also reviews the evidence for  
27 SARS-CoV-2 transmission dynamics in broader settings. The diagnosis and management of COVID-19  
28 in general is outside the remit of this guidance.

29 The Working Party recommendations have been developed systematically through multidisciplinary  
30 discussions based on currently available evidence from published, preprint and grey literature  
31 sources. They should be used in the development of local protocols for relevant health and care  
32 settings such as hospitals, nursing/care homes, primary care and dental practices.

### 33 **5.2. Why do we need a Working Party Report for this topic?**

34 The first wave of the COVID-19 pandemic occurred amid uncertainty as to how it could be prevented  
35 and controlled. Concern still exists about further waves and new outbreaks occurring. Evidence that  
36 emerged during the first wave provides an opportunity to develop evidence-based guidance for  
37 preventing and controlling future waves/outbreaks, acknowledging the possibility of reinfection, the  
38 context of newly emerging variants of SARS-CoV-2, and ongoing immunisation programmes.

1 **5.3. What is the purpose of the Working Party Report’s recommendations?**

2 The main purpose of the recommendations is to inform clinicians, managers and policy makers  
3 about SARS-CoV-2 transmission dynamics and to provide evidence-based guidance to prevent and  
4 control the spread of SARS-CoV-2 in health and care settings. The report highlights current gaps in  
5 knowledge, which will help to direct future areas of research.

6 **5.4. What is the scope of the guidance?**

7 The scope of the guidance is to provide advice for the optimal provision of effective and safe health  
8 and care services during the period in which COVID-19 remains a health threat. The guidance was  
9 developed for acute healthcare settings, but it might be useful in other health and care settings such  
10 as dental practices and care homes.

11 **5.5. What is the evidence for the guidance?**

12 Topics for this guidance were derived from initial discussions of the Working Party and specific  
13 review questions were developed in accordance with the population–exposure–comparator–  
14 outcome (PECO) framework for investigating the likelihood of developing a certain condition after an  
15 exposure event. To prepare the recommendations, the Working Party collectively reviewed relevant  
16 evidence from published, preprint and grey literature sources. The processes and methods used  
17 were in accordance with the National Institute for Health and Care Excellence (NICE) manual for  
18 developing guidelines (hereafter the NICE guidelines manual).<sup>[2]</sup> The processes and methods were  
19 moreover aligned with those described in the first Working Party Report.<sup>[3]</sup> See below for further  
20 details.

21 **5.6. Who developed the guidance?**

22 The Working Party included infectious diseases, microbiology and virology clinicians, academic  
23 infection prevention and control experts, systematic ~~reviewers~~reviewers, and a lay representative.

24 **5.7. Who is the guidance for?**

25 Any healthcare practitioner, manager or policy maker may use this guidance and adapt it for their  
26 use. It is anticipated that most users will be clinical staff and infection prevention and control teams.  
27 Some aspects of this guidance might also be beneficial to patients, their families/~~carers~~carers, and  
28 the public.

29 **5.8. How is the guidance structured?**

30 To provide advice rapidly, the guidance is being produced as two separate articles, each addressing a  
31 different review question. Each article will comprise an introduction, a summary of the evidence,  
32 and recommendations graded according to the available evidence.

33 **5.9. How frequently is the guidance reviewed and updated?**

34 The guidance will be considered for update within 1 year of publication to determine whether new  
35 evidence exists that would require a change in the recommendations.

36 **5.10. Aim**

37 The aim of the guidance is to evaluate evidence for presymptomatic, asymptomatic and post-  
38 symptomatic transmission of SARS-COV-2 with the intention of preventing transmission in hospitals  
39 and other health and care settings.

## 1 **6. Methodology**

### 2 **6.1. Evidence search and appraisal**

3 As noted above, the processes and methods used to produce this Working Party Report were aligned  
4 with those described in the first Working Party Report.<sup>[3]</sup> Topics for the COVID-19 rapid guidance  
5 were derived from initial discussions of the Working Party. An e-newsletter was sent to HIS members  
6 inviting further suggestions for topics to be considered. To develop their recommendations, the  
7 Working Party collectively reviewed evidence gathered from published, preprint and grey literature  
8 sources. The processes and methods used were based on the NICE guidelines manual.<sup>[2]</sup> Some  
9 modifications were made to allow a rapid review process to be followed. For example, the number  
10 of bibliographic databases searched was limited to two, the Working Party was smaller than usual  
11 (with only one lay member), and quality assessment was conducted by one reviewer (with 10% of  
12 records being checked by a second reviewer).

### 13 **6.2. Data sources and search strategy**

14 Two electronic databases (MEDLINE and Embase) were searched for articles published between  
15 1 January and 29 May 2020. Search terms were constructed using medical subject headings (MeSH)  
16 and free-text terms (see Appendix C). Additional hand searching was conducted in several online  
17 databases (WHO Chinese database, CNKI, China Biomedical Literature Service, Epistemonikos COVID-  
18 19 L·OVE platform, EPPI-Centre living systematic map of the evidence, CORD-19, COVID-END, and  
19 HIS COVID-19 resources) to identify preprints, articles in press and grey literature. Reference lists  
20 from included studies and reviews identified through the literature searches were scanned for  
21 additional studies. Searches were restricted to person-to-person transmission of SARS-CoV-2 and no  
22 language restrictions were applied. Due to the large number of papers being published daily during  
23 the first and second waves of the pandemic, a decision was made not to rerun the searches before  
24 publication as this would significantly delay the guidance being made available to readers. Further  
25 details of the searches are presented in Appendix C.

### 26 **6.3. Study eligibility and selection criteria**

27 The members of the Working Party determined study inclusion criteria. Any article presenting  
28 primary data on presymptomatic, asymptomatic or post-symptomatic transmission of SARS-CoV-2  
29 was eligible for inclusion. Search results were screened for relevance, with one reviewer examining  
30 titles, abstracts and full texts of all records identified through the searches. A second reviewer  
31 checked at least 10% of records earmarked for exclusion at each stage of screening. Disagreements  
32 were first discussed between the two reviewers and, if consensus was not reached, a third reviewer  
33 was consulted. The results are presented in the study selection flowchart in Appendix D. A list of  
34 studies excluded after full-text screening is presented in Appendix E.

### 35 **6.4. Data extraction, analysis and quality assessment**

36 The characteristics of included studies are summarised in Appendix F. For each included study, data  
37 were extracted into an evidence table by one reviewer while a second reviewer checked the data  
38 extraction for 10% of studies. Evidence was stratified (organised) according to the type of study  
39 (cluster/outbreak investigations, comparative epidemiological studies, and mathematical modelling  
40 of epidemic spread). The resulting evidence tables are presented in Appendix G.

41 Further stratification of the evidence, for example, according to whether a cluster/outbreak  
42 investigation explored the possibility of presymptomatic transmission (in which the index case had  
43 no symptoms during the exposure period of their close contacts, but later developed symptoms) or

1 asymptomatic transmission (in which the index case never developed symptoms or signs of  
2 infection) was undertaken to aid presentation and interpretation of the evidence.

3 Many of the cluster/outbreak investigations permitted only a categorical (non-numerical or nominal)  
4 assessment of the credibility of transmission by presymptomatic or asymptomatic people (with the  
5 categories assigned in the evidence review being 'yes', 'no' or 'uncertain'). Other cluster/outbreak  
6 investigations allowed calculation of an attack rate (the number of contacts of the index case who  
7 tested positive for SARS-CoV-2 divided by the total number of contacts) and an associated  
8 confidence interval (CI). Stratification of the evidence from cluster/outbreak studies according to the  
9 time at which contacts were exposed to SARS-CoV-2 relative to the index case acquiring the virus  
10 (categorised as < 7 days, 7 to 10 days, 11 to 14 days or not calculable, with day 0 representing the  
11 day on which the index case acquired the virus) was also undertaken.

12 Where cluster/outbreak studies reported the use of personal protective equipment (PPE) this was  
13 noted to aid interpretation of the evidence.

14 The possibility of identifying comparative epidemiological studies relevant to the review question  
15 had not been anticipated because the pandemic was associated with a novel disease and was still in  
16 its early stages when the evidence review was initiated. However, several such studies were  
17 identified and included as noted above. For these epidemiological studies (and the mathematical  
18 modelling studies included in the review – see below) that reported (or allowed calculation of) a  
19 measure of transmission risk according to the index case's symptom status at the time of exposure  
20 of their close contacts, the convention of expressing risks based on exposure to people with fewer  
21 symptoms compared to risks based on exposure to people with more symptoms was applied where  
22 possible.

23 Mathematical modelling studies were included in the review only where they distinguished between  
24 transmission risks according to the index case's symptom status during exposure of their close  
25 contacts.

26 Included epidemiological studies were appraised for quality using checklists recommended in the  
27 NICE guidelines manual.<sup>[2]</sup> Critical appraisal was conducted by one reviewer, and appraisal outcomes  
28 for at least 10% of studies were checked by a second reviewer. The results of study-level quality  
29 appraisal are included in the evidence tables in Appendix G. Mathematical modelling studies were  
30 not appraised for quality at individual study level.

## 31 **6.5. Rating of evidence and recommendations**

32 Evidence was assessed for quality at outcome level using the approach known as Grading of  
33 Recommendations Assessment, Development and Evaluation (GRADE; see  
34 <https://www.gradeworkinggroup.org/> for details). The resulting GRADE tables are presented in  
35 Appendix H (stratified by type of study and, in the case of cluster/outbreak investigations,  
36 exploration of presymptomatic or asymptomatic transmission and time at which contacts were  
37 exposed to SARS-CoV-2 relative to the index case acquiring the virus, as outlined above). Using  
38 GRADE, the overall quality of the evidence for a particular outcome was classified as very low, low,  
39 ~~moderate~~moderate, or high.

40 No overall assessment of the quality of evidence from mathematical modelling studies was  
41 conducted using GRADE because there is no validated approach for applying GRADE to such studies.  
42 However, some domains in the GRADE framework are applicable in the case of mathematical  
43 modelling studies, for example, inconsistency and indirectness. All the evidence from the

1 mathematical modelling studies was downgraded for indirectness by at least one level because such  
2 studies provided indirect estimates of transmission risks compared to epidemiological studies.  
3 Further downgrading for indirectness was assessed on a case-by-case basis (see Appendix H for  
4 details).

5 Evidence statements were constructed by combining the outcome-level classification of evidence  
6 quality determined using GRADE and the following terms reflecting the Working Party's overall  
7 confidence in using the evidence to formulate recommendations:

- 8 • strong evidence – further research is unlikely to alter confidence in the estimated effect
- 9 • moderate evidence – further research might alter the estimated effect and its strength
- 10 • weak evidence – further research is very likely to alter the estimated effect and its strength
- 11 • inconsistent evidence – current studies report conflicting evidence and further research is  
12 very likely to alter the estimated effect.

13 The Working Party further classified the evidence as indicating whether presymptomatic,  
14 asymptomatic and post-symptomatic transmission was confirmed, probable, possible,  
15 ~~unlikely~~unlikely, or confirmed as not occurring. This mirrored the approach taken in the first article  
16 in the pair of guidance documents, which examined routes of transmission of SARS-CoV-2.<sup>[3]</sup>

17 Finally, in accordance with the GRADE approach, the Working Party's recommendations were  
18 phrased to reflect the strength of the evidence and their confidence in using it as the basis for  
19 developing recommendations.

20 Where there was little or no evidence to guide recommendations, the Working Party used informal  
21 consensus to formulate 'good practice recommendations' based on their collective experience and  
22 expertise.

23 Videoconferences were held regularly throughout the guideline development process to discuss and  
24 interpret the evidence and translate it into recommendations for practice (and, where gaps in the  
25 evidence were identified, recommendations for further research).

## 26 **6.6. Consultation process**

27 Feedback on the draft guidance was received from the HIS Guidelines Committee and through rapid  
28 consultation with relevant stakeholders. The draft report was placed on the HIS website for 10  
29 working days along with the HIS standard response form, including a ~~conflict of interest~~conflict-of-  
30 ~~interest~~disclosure form. The availability of the draft guidance was communicated via email and  
31 social media. Stakeholders were invited to comment on format, content, local applicability, patient  
32 acceptability and recommendations. The Working Party reviewed stakeholder comments, and  
33 collectively agreed revisions in response to the comments (see Appendix I). Comments received  
34 from individuals who disclosed conflicts of interest, or who did not submit a ~~conflict of~~  
35 ~~interest~~conflict-of-interest disclosure form, were excluded.

## 36 **7. Results**

### 37 **7.1 Overview of the evidence**

38 Fifty-five articles were included in the evidence review (see Table F.1).<sup>[4-58]</sup> Of these, 44 reported  
39 cluster/outbreak investigations (presented in chronological order in Table G.1),<sup>[4-7, 9, 10, 14, 15, 17, 18, 20-28,</sup>  
40 <sup>30-34, 36-44, 46-51, 53-55, 57, 58]</sup> six reported comparative epidemiological studies that allowed calculation of  
41 relative risks of transmission based on the index case's symptom status during exposure of their

1 close contacts (for example, transmission associated with presymptomatic exposure versus  
2 transmission associated with symptomatic exposure),<sup>[11, 12, 19, 35, 52, 56]</sup> and five reported mathematical  
3 modelling of epidemic spread.<sup>[8, 13, 16, 29, 45]</sup> More than half of the included studies referred to  
4 investigations of SARS-CoV-2 transmission in mainland China, reflecting the emergence and initial  
5 investigation of COVID-19 there; the remainder reported evidence from Germany, Hong Kong, Italy,  
6 Japan, Malaysia, Singapore, South Korea, Switzerland, Taiwan, USA and Vietnam, reflecting the  
7 pandemic spread as time progressed (see Table F.1 for further details).

## 8 **7.2 Cluster/outbreak investigations**

9 In several instances, the same cluster/outbreak was reported independently in more than one article  
10 (for example, three separate articles reported or commented on a single cluster/outbreak in  
11 Germany)<sup>[7, 26, 41]</sup> or the same data were analysed differently across multiple articles (for example,  
12 three articles reported different analyses of relative risks of transmission based on the index case's  
13 symptom status during an outbreak in China).<sup>[11, 19, 52]</sup> Similarly, there were several instances in which  
14 a single article reported multiple clusters/outbreaks (for example, one article summarised evidence  
15 from several clusters in Singapore that were likely to be associated with presymptomatic  
16 transmission).<sup>[46]</sup> Accounting for such overlaps by presenting a combined summary of each distinct  
17 cluster/outbreak or other epidemiological analysis resulted in a total of 45 distinct  
18 clusters/outbreaks and four sets of comparative epidemiological analyses of transmission risks based  
19 on symptom status (see Table G.1 and Table G.2 for further details).

20 The reported cluster/outbreak investigations focused on potential transmission of SARS-CoV-2 in  
21 both community and nosocomial settings (see Table F.1 and Table G.1). The possibility of  
22 presymptomatic transmission was explored in more studies (36 clusters/outbreaks)<sup>[4, 5, 7, 9, 10, 15, 17, 18,</sup>  
23 <sup>20, 21, 23-28, 30-33, 36, 39-41, 43, 44, 46-51, 53, 54, 57, 58]</sup> than was the possibility of asymptomatic transmission (seven  
24 clusters/outbreaks);<sup>[6, 14, 22, 34, 38, 42, 55]</sup> two further clusters/outbreaks were reported in sufficient detail  
25 to determine that presymptomatic or asymptomatic (rather than symptomatic) exposure had  
26 occurred, but not to distinguish between the two (see Table G.1).<sup>[36, 37]</sup> There were no reports of  
27 investigations exploring the possibility of post-symptomatic transmission.

28 Stratification of the evidence from cluster/outbreak investigations according to the time at which  
29 contacts were exposed to SARS-CoV-2 relative to the index case acquiring the virus (< 7 days, 7 to 10  
30 days, 11 to 14 days or not calculable) is reflected in the evidence tables for the cluster/outbreak  
31 studies (see Table G.1) and the corresponding GRADE tables (see Table H.1, Table H.2 and Table H.3).

## 32 **7.3 Comparative epidemiological studies**

33 Relative risks of transmission associated with presymptomatic exposure versus transmission  
34 associated with symptomatic exposure (two studies),<sup>[12, 35]</sup> and transmission associated with  
35 asymptomatic exposure compared to either presymptomatic or symptomatic exposure (four studies  
36 reported across six articles)<sup>[11, 12, 19, 35, 52, 56]</sup> are presented in the evidence tables for the comparative  
37 epidemiological studies (see Table G.2) and the corresponding GRADE table (Table H.4).

## 38 **7.4 Mathematical modelling studies**

39 Three of the mathematical modelling studies included in the review used adaptations of the  
40 susceptible–exposed–infected–recovered (SEIR) compartmental modelling framework to model  
41 transmission dynamics in hypothetical populations.<sup>[16, 29, 45]</sup> Other approaches reflected in the  
42 included studies involved application of a renewal equation framework (one study)<sup>[13]</sup> and modelling  
43 of viral emissions resulting from respiratory and physical activity in indoor commercial environments

1 (such as a supermarket or restaurant) allowing for different ventilation characteristics (one study).<sup>[8]</sup>  
2 Further details are presented in the evidence tables for the mathematical modelling studies (see  
3 Table G.3) and the corresponding GRADE tables (see Table H.5 and Table H.6).

#### 4 **7.5 Quality of the evidence**

5 For each type of study for which it was possible to produce an overall GRADE rating of the quality of  
6 the evidence the rating applied was very low (see Appendix H). This was partly due to observational  
7 studies being assigned an initial rating of low quality, which would be downgraded to very low if  
8 even one serious limitation were identified with the evidence.

9 Frequently occurring reasons for downgrading the quality of evidence from cluster/outbreak  
10 investigations were risk of bias associated with a lack of clarity regarding complete inclusion (for  
11 example, because it was not clear whether all contacts of an index case had been accounted for) and  
12 imprecision associated with no CIs or other measures of precision being reported (or calculable).  
13 Among those cluster/outbreak investigations that evaluated the risk of asymptomatic transmission,  
14 several had evidence downgraded for indirectness because the definition of an asymptomatic  
15 infection included having mild symptoms (such as a pre-existing cough that might or might not have  
16 been associated with or exacerbated by SARS-CoV-2 infection), or signs of infection on a  
17 computerised tomography (CT) scan of the chest. See Table H.1, Table H.2 and Table H.3 for further  
18 details.

19 Another aspect of the evidence from the cluster/outbreak investigations was the use of PPE as  
20 recorded in the evidence tables for these studies (see Table G.1) and the corresponding GRADE  
21 tables (see Table H.1, Table H.2 and Table H.3). One investigation exploring the possibility of  
22 presymptomatic transmission reported that the index case (a transplant surgeon) and their clinical  
23 colleagues used PPE during the index case's presymptomatic phase (the index case used hand  
24 hygiene and wore a surgical mask and gloves for preoperative visits and standard surgical  
25 procedures, while clinical colleagues wore surgical masks at distances of less than 1 metre and  
26 gloves during all contact).<sup>[40]</sup> One investigation exploring the possibility of asymptomatic  
27 transmission reported that during hospital quarantine of the index case, the index case and other  
28 patients and visitors wore masks except when eating or drinking, while hospital staff wore N95  
29 respirators, isolation gowns and goggles.<sup>[14]</sup> Another investigation exploring the possibility of  
30 asymptomatic transmission reported that the index case wore a mask while travelling to a health  
31 clinic, during the clinic visit, and while in the same room as their housemates after returning  
32 home.<sup>[42]</sup>

33 Among the comparative epidemiological studies that reported (or allowed calculation of) relative  
34 measures of transmissibility according to the index case's symptom status during exposure of their  
35 close contacts, a frequently occurring reason for downgrading the quality of the evidence was risk of  
36 bias associated with potential confounding factors (for example, age or a pre-existing condition that  
37 might affect susceptibility to infection) not being accounted for in the design or analysis of the study.  
38 Another common reason for downgrading the quality of evidence from such studies was that CIs for  
39 estimated effects crossed default thresholds for defining imprecision according to the GRADE  
40 approach. See Table H.4 for further details.

41 The quality of the evidence from the mathematical modelling studies included in the review was  
42 downgraded for indirectness in several cases because relative measures of transmissibility according  
43 to the index case's symptom status during exposure of their close contacts were not wholly aligned  
44 with the symptom statuses of interest to the Working Party (that is, presymptomatic and

1 asymptomatic infections). In one such study, asymptomatic infections and mildly symptomatic  
2 infections were grouped together.<sup>[16]</sup> Another study characterised infections as being  
3 ‘undocumented’ (defined as lacking symptoms severe enough to be confirmed/observed) or  
4 ‘documented’ (defined as having symptoms severe enough to be confirmed/observed).<sup>[29]</sup> A third  
5 study incorporated asymptomatic viral load estimates that might be more representative of  
6 presymptomatic or symptomatic viral loads; this study distinguished between asymptomatic and  
7 symptomatic infections only in terms of respiratory and physical activity levels modelled.<sup>[8]</sup> See Table  
8 H.5 and Table H.6 for further details.

## 9 **8. Evidence statements**

### 10 **8.1 Absolute transmissibility of presymptomatic and asymptomatic infections**

11 There was strong evidence from 36 cluster/outbreak investigations (some of which were reported  
12 across multiple articles, as noted above)<sup>[4, 5, 7, 9, 10, 15, 17, 18, 20, 21, 23-28, 30-33, 36, 39-41, 43, 44, 46-51, 53, 54, 57, 58]</sup>  
13 regarding the possibility of SARS-CoV-2 being transmitted by presymptomatic people. Conclusive  
14 evidence of presymptomatic transmission was provided for seven clusters/outbreaks.<sup>[21, 23, 28, 31, 33, 36,  
15 46, 51, 53, 54]</sup> For another 27 clusters/outbreaks it was uncertain whether presymptomatic transmission  
16 had occurred.<sup>[5, 7, 9, 10, 15, 17, 18, 20, 24-28, 30, 32, 39, 41, 43, 44, 46-50, 57, 58]</sup> In the two remaining clusters/outbreaks  
17 presymptomatic transmission did not occur: one of these related to potential community  
18 transmission associated with tourism in which the index case was assumed to have acquired SARS-  
19 CoV-2 in China before travelling to South Korea on holiday, but the timing of acquisition of the virus  
20 by the index case was uncertain;<sup>[4]</sup> the other related to potential nosocomial transmission associated  
21 with a transplant surgery department in which the index case (a transplant surgeon) used hand  
22 hygiene and wore a surgical mask and gloves for preoperative visits and standard surgical  
23 procedures, while clinical colleagues wore surgical masks at distances of less than 1 metre and  
24 gloves during all contact.<sup>[40]</sup> Among the seven clusters/outbreaks for which presymptomatic  
25 transmission was demonstrated, in one instance the index case had acquired the virus less than 7  
26 days previously<sup>[21]</sup> and in another less than 13 days previously;<sup>[23]</sup> the contacts’ exposure period  
27 relative to the index case acquiring the virus was not calculable for the remaining  
28 clusters/outbreaks.<sup>[31, 33, 36, 46, 51, 53, 54]</sup> Attack rates were calculable for only three of the seven  
29 clusters/outbreaks for which presymptomatic transmission was demonstrated (attack rate 40%  
30 based on 22 close contacts of the index case,<sup>[23]</sup> 85% based on 13 close contacts<sup>[21]</sup> and 100% based  
31 on one close contact).<sup>[31]</sup> The settings in which presymptomatic transmission was demonstrated to  
32 occur related to community transmission (via households, gatherings of family and friends, a work  
33 meeting, being in a restaurant, attending church, or sharing transport).

34 There was moderate evidence from seven cluster/outbreak investigations<sup>[6, 14, 22, 34, 38, 42, 55]</sup> regarding  
35 the possibility of SARS-CoV-2 being transmitted by asymptomatic people. Conclusive evidence of  
36 asymptomatic transmission was provided for one cluster/outbreak.<sup>[22]</sup> For another four  
37 clusters/outbreaks it was uncertain whether asymptomatic transmission had occurred.<sup>[6, 34, 38, 55]</sup> In  
38 the two remaining clusters/outbreaks asymptomatic transmission did not occur: one of these  
39 related to potential community and nosocomial transmission associated with exposure of the index  
40 case’s household, rideshare partners and healthcare workers at a clinic attended by the index case –  
41 the index case wore a mask while travelling to the clinic, during the clinic visit and while in the same  
42 room as members of their household after returning home; the other related to potential  
43 nosocomial transmission associated with hospital quarantine of the index case after presenting at  
44 the emergency department – the index case, other patients and visitors all wore masks except when  
45 eating or drinking, while hospital staff wore N95 respirators, isolation gowns and goggles.<sup>[14]</sup> In both

1 instances, the index case had respiratory symptoms attributable to causes other than COVID-19. In  
2 the cluster/outbreak for which asymptomatic transmission was demonstrated, the index case had  
3 acquired the virus less than 7 days previously.<sup>[22]</sup> The attack rate for this cluster/outbreak was 100%  
4 (based on 3 close contacts of the index case) and the setting was related to community transmission  
5 (via the index case's household). Although the index case was asymptomatic, they had  
6 signs typical of viral infection on a CT scan of the chest.

7 There was weak evidence from two further cluster/outbreak investigations<sup>[36, 37]</sup> regarding the  
8 possibility of SARS-CoV-2 being transmitted by presymptomatic or asymptomatic people. For these  
9 clusters/outbreaks it was not possible to determine whether the index case ever developed  
10 symptoms and it was uncertain whether transmission occurred.

## 11 **8.2 Relative transmissibility of presymptomatic and asymptomatic infections**

12 There was moderate evidence from four epidemiological studies reported across six articles<sup>[11, 12, 19,</sup>  
13 <sup>35, 52, 56]</sup> regarding relative transmissibility of presymptomatic, asymptomatic and symptomatic  
14 people. No differences in transmission according to symptom status of the index case during the  
15 exposure period of their close contacts were detected, although there was a trend towards fewer  
16 symptoms in the index case being associated with a lower risk of transmission: presymptomatic  
17 versus symptomatic exposure, odds ratio (OR) 0.22 (95% CI 0.01 to 3.86)<sup>[35]</sup> and OR 0.79 (95% CI 0.18  
18 to 3.40);<sup>[12]</sup> asymptomatic versus symptomatic exposure, OR 0.57 (95% CI 0.03 to 10.80),<sup>[35]</sup> OR 0.63  
19 (95% CI 0.04 to 10.44),<sup>[12]</sup> OR 0.64 (95% CI 0.28 to 1.47)<sup>[11, 19, 52]</sup> and OR 0.83 (95% CI 0.36 to 1.92);<sup>[11,</sup>  
20 <sup>19, 52]</sup> and asymptomatic versus presymptomatic exposure, OR 0.17 (95% CI 0.02 to 1.34).<sup>[56]</sup>

21 Conclusive evidence of presymptomatic transmission was provided by two of the epidemiological  
22 studies;<sup>[12, 56]</sup> conclusive evidence of asymptomatic transmission was provided by two of the studies  
23 reported across four articles,<sup>[11, 19, 52, 56]</sup> although the definition of an asymptomatic infection was not  
24 always reported. Mass testing might have played a role in preventing asymptomatic transmission in  
25 two of the studies<sup>[12, 35]</sup> because asymptomatic people might have self-isolated from household  
26 members when informed about their possible infection.

27 There was inconsistent evidence from four mathematical modelling studies<sup>[13, 16, 29, 45]</sup> regarding  
28 relative transmissibility according to symptom status of the index case during the exposure period of  
29 their close contacts. Fewer symptoms in the index case during exposure of close contacts was  
30 associated with a lower risk of transmission in one study: undocumented infections (assumed to be  
31 associated with fewer symptoms) versus documented infections (assumed to be associated with  
32 more symptoms), risk ratio (RR) 0.42 (95% credible interval (CrI) 0.34 to 0.61) and RR 0.47 (95% CrI  
33 0.36 to 0.64) with containment measures such as travel restrictions and contact precautions, and RR  
34 0.55 (95% CrI 0.49 to 0.60) without containment measures.<sup>[29]</sup> Another study reported a lower risk of  
35 transmission by people who were infectious but asymptomatic compared to those who were  
36 infectious with symptoms, RR 0.81 (95% CrI not reported).<sup>[45]</sup> Another study reported a higher risk of  
37 transmission by infected people with severe symptoms compared to people who were  
38 asymptomatic or had mild symptoms, RR 1.03 (95% CrI 0.79 to 1.38).<sup>[16]</sup> The same study reported a  
39 lower risk of transmission by people who were asymptomatic or had mild symptoms compared to  
40 those who were presymptomatic, RR 0.033 (95% CrI 0.027 to 0.036).<sup>[16]</sup> The remaining study  
41 reported percentages of the total reproduction number accounted for presymptomatic,  
42 asymptomatic and symptomatic transmission (presymptomatic transmission, 47% (95% CrI 11% to  
43 58%), asymptomatic transmission, 6% (95% CrI 0% to 57%), and symptomatic transmission, 28%  
44 (95% CrI 9% to 49%)).<sup>[13]</sup>

1 There was weak evidence from one mathematical modelling study<sup>[8]</sup> regarding the relative  
2 transmissibility of asymptomatic infections according to ventilation characteristics in indoor  
3 commercial environments. Asymptomatic transmission reproduction numbers with mechanical  
4 ventilation were lower than those with natural ventilation (supermarket, 0.12 with mechanical  
5 ventilation versus 0.17 with natural ventilation; post office, 0.17 with mechanical ventilation versus  
6 0.41 with natural ventilation; pharmacy, 0.22 with mechanical ventilation versus 0.49 with natural  
7 ventilation; bank, 0.34 with mechanical ventilation versus 0.81 with natural ventilation; estimates  
8 refer to modelling of lockdown in which restaurants were required to close and additional voluntary  
9 measures included fewer staff on duty, customers queueing outside, and ventilation increased by  
10 keeping external doors open; estimates for restaurant without lockdown, 5.35 with mechanical  
11 ventilation versus 47.3 with natural ventilation; no CIs or other measures of precision reported).

### 12 **8.3 Transmissibility of post-symptomatic infections**

13 No evidence was identified regarding the possibility of SARS-CoV-2 being transmitted by post-  
14 symptomatic people.

## 15 **9. Rationale for recommendations**

### 16 **9.1 Outcomes that matter most**

17 The Working Party's interest focused on ~~whether or not~~whether transmission occurs as a result of  
18 presymptomatic, asymptomatic or post-symptomatic SARS-CoV-2 infection. For the most part, this  
19 was evaluated through consideration of absolute risks of transmission. At the start of the evidence  
20 review process, it was not anticipated that relative risks of transmission based on the symptom  
21 status of an index case would have been examined (because the pandemic was in its early stages  
22 and research was just starting to be published). However, it became evident when sifting the results  
23 of the systematic literature searches that some studies had investigated relative risks of transmission  
24 and this evidence was eligible for inclusion according to the review protocol.

### 25 **9.2 Quality of the evidence**

26 The evidence from the cluster/outbreak investigations and epidemiological studies providing  
27 estimates of relative risks of transmission based on an index case's symptom status during exposure  
28 of their close contacts was assessed for quality using the GRADE framework. All of the evidence from  
29 these studies was classified as being of very low quality. Recurring reasons for downgrading the  
30 evidence included: risk of bias (for example, due to lack of clarity regarding complete inclusion of an  
31 index case's close contacts in the case of cluster/outbreak investigations, and potential confounding  
32 factors (such as pre-existing conditions and strength of the immune system) not being accounted for  
33 in the case of epidemiological studies providing relative risks of transmission based on the index  
34 case's symptom status during exposure of close contacts); imprecision due to CIs for effect estimates  
35 crossing predefined thresholds or being unavailable; and indirectness (for example, in studies  
36 investigating potential asymptomatic transmission the definition of an asymptomatic infection  
37 sometimes included having mild symptoms or signs of infection). The overall assessment of the  
38 evidence as being of very low quality did not, however, prevent the Working Party reaching  
39 conclusions about characteristics of SARS-CoV-2 transmission and making recommendations for  
40 practice (see below).

41 The evidence from the mathematical modelling studies included in the review could not be fully  
42 assessed using the GRADE framework, but some GRADE domains were applicable, for example,  
43 inconsistency and indirectness. A recurring reason for downgrading the evidence from these studies

1 was indirectness due to relative measures of transmissibility according to an index case’s symptom  
2 status during exposure of close contacts not being fully aligned with symptom statuses of interest to  
3 the Working Party (in particular, presymptomatic and asymptomatic infections).

### 4 **9.3 Benefits and harms**

5 Having considered the evidence, the Working Party concluded that:

- 6 • presymptomatic transmission (meaning that an index case has no symptoms during the  
7 exposure period of their close contacts, but later develops symptoms) is **confirmed**
- 8 • asymptomatic transmission (meaning that an index case never develops symptoms or signs  
9 of infection) is **probable**.

10 There was uncertainty regarding the evidence related to asymptomatic transmission, with the  
11 Working Party noting that a lack of awareness of symptoms or suppressed symptoms (for example,  
12 due to taking medication) could not be distinguished from a complete absence of symptoms in the  
13 reported investigations. The Working Party recognised the potential for subclinical or pauci-  
14 symptomatic infection while emphasising that truly asymptomatic infection or carriage of SARS-CoV-  
15 2 occurs and transmission is to be expected.<sup>[59]</sup>

16 The Working Party recognised that the list of symptoms suggesting COVID-19 had expanded during  
17 the pandemic, reflecting growing knowledge of the condition. The evidence review and synthesis  
18 involved extracting any information about symptoms reported by the study investigators, although it  
19 was acknowledged that people’s perceptions of symptoms differ and this could influence the types  
20 of symptoms reported. The Working Party emphasised the importance of clarity in defining and  
21 reporting symptoms in future research related to COVID-19.

22 The settings in which presymptomatic or asymptomatic transmission was demonstrated mirrored  
23 those reported in the first of the pair of guidance articles in which routes of transmission, regardless  
24 of the symptom status of the index case, were explored.<sup>[3]</sup> In particular, presymptomatic  
25 transmission was demonstrated to occur in community settings that included households,  
26 gatherings of family and friends, a work meeting, being in a restaurant, attending church, or sharing  
27 transport. The Working Party agreed that transmission in the absence of noticeable symptoms could  
28 similarly occur in health and care settings that involve people being in close proximity.

29 The Working Party agreed that from the perspective of preventing transmission by people without  
30 symptoms, it is immaterial ~~whether or not~~ whether they later develop symptoms. The  
31 recommendations were therefore phrased in terms of people without symptoms rather than using  
32 the terms presymptomatic and asymptomatic. The Working Party anticipated that this phrasing  
33 would also make the recommendations more meaningful to the public.

34 The benefits of preventing transmission of SARS-CoV-2 by people without symptoms include the  
35 prevention of ill health due to COVID-19 among their close contacts and the prevention of onward  
36 transmission to ever greater numbers of people. Possible harms associated with actions intended to  
37 prevent transmission of SARS-CoV-2 (such as social distancing, hand hygiene and the use of PPE)  
38 arise through restriction of personal freedoms and a need to modify behaviours with potential  
39 adverse consequences in terms of, for example, mental health and wellbeing. These benefits and  
40 harms apply to healthcare workers, patients and their families/carers, and the public. On balance,  
41 the Working Party recognised that since anyone might carry the virus without knowing it, or be  
42 infected without having noticeable symptoms, the recommendations should reinforce the

1 importance of adhering to existing legislation and guidance intended to reduce the risk of  
2 transmission of SARS-CoV-2 in the general population.

3 The Working Party noted that the evidence regarding relative risks of transmission according to  
4 symptom status suggested that presymptomatic infections are less transmissible than are  
5 symptomatic infections, and that asymptomatic infections are less transmissible than are  
6 presymptomatic infections. The Working Party was aware that the viral load associated with  
7 asymptomatic and pauci-symptomatic infections is typically lower than that associated with  
8 symptomatic infection,<sup>[59]</sup> lending plausibility to a lower rate of transmission. Based on the available  
9 evidence, the Working Party therefore agreed that the recommendations should highlight the  
10 likelihood of greater transmissibility from people with symptoms than from those without  
11 symptoms. Due to some uncertainty remaining, the Working Party also prioritised relative risks of  
12 transmission, including the correlation between transmission and quantification of viral shedding, as  
13 an area for future research.

14 Although the evidence from the mathematical modelling studies was regarded as indirect, the  
15 Working Party noted the reported differences in asymptomatic transmission rates in indoor  
16 environments under different ventilation scenarios. This prompted the Working Party to emphasise  
17 the importance of ventilation in enclosed spaces in the recommendations.

18 The Working Party was acutely aware that the development of the guidance was occurring during an  
19 evolving pandemic. When formulating the recommendations, the Working Party recognised the  
20 possibility of reinfection in people who previously had COVID-19,<sup>[60]</sup> the emergence of variants of  
21 concern, and ongoing immunisation programmes. As such, the Working Party highlighted in the  
22 recommendations that the characteristics and implications of transmission of SARS-CoV-2 by people  
23 without symptoms might change in the future.

24 The likelihood of post-symptomatic transmission (meaning that an index case has no symptoms  
25 during the exposure period of their close contacts, but previously had symptoms) could not be  
26 assessed because of an absence of evidence. The Working Party agreed that post-symptomatic  
27 transmission should be prioritised as an area for further research.

#### 28 **9.4 Cost effectiveness and resource use**

29 The Working Party did not undertake a detailed economic analysis because the recommendations  
30 focused on raising awareness of the possibility of presymptomatic and asymptomatic transmission of  
31 SARS-CoV-2 and reinforcing existing legislation and guidance aimed at preventing transmission.  
32 However, the Working Party considered costs and resource use from the perspective of health and  
33 care systems and identified that costs associated with transmission that is not prevented include the  
34 costs of managing COVID-19 in infected patients and the costs of needing additional resources such  
35 as PPE. Considerations related to the value of time as a resource included the time taken to don and  
36 doff PPE and time away from work for healthcare workers who are unwell or required to self-isolate.  
37 Taken together, these considerations emphasise increased pressure on healthcare systems when  
38 COVID-19 is prevalent. The Working Party recognised potential inconvenience and possible adverse  
39 consequences (in terms of mental health and wellbeing of healthcare workers, patients and their  
40 families/carers) of implementing measures such as social distancing and using PPE. The Working  
41 Party also recognised that the cost effectiveness of preventing transmission would be greater in  
42 aspects of healthcare focusing on people more vulnerable to COVID-19.

43

## 1 9.5 Other considerations

2 As outlined above, the Working Party highlighted several areas for future research. These included  
3 consideration of:

- 4 • when a person who has acquired SARS-CoV-2 becomes infectious and
- 5 • how long infectivity lasts in the absence of symptoms.

6 While the evidence available to the Working Party demonstrated presymptomatic transmission  
7 within 7 days of an index case acquiring the virus, later transmission could not be ruled out.  
8 Moreover, the available evidence did not permit a detailed analysis of infectivity during the first 7  
9 days since acquiring the virus, which was of interest to the Working Party and could form part of  
10 future research. The Working Party also highlighted potential seasonality in transmission rates, and  
11 indoor versus outdoor transmission, as areas to explore in future research.

12 The Working Party discussed the relevance and possible consequences of lung damage revealed by  
13 CT scans in people who did not report symptoms. The Working Party questioned whether such  
14 features might have longer-term consequences for a person who although infected has no  
15 noticeable symptoms and recommended this as an area for future research.

16 The Working Party made several observations regarding the quality of the evidence identified in the  
17 review. While the importance of rapid evaluation during a pandemic caused by a novel disease such  
18 as COVID-19 was appreciated, the value in ensuring robust and efficient research activity was also  
19 recognised. The Working Party agreed that this value could be promoted by avoiding duplication and  
20 repetition in data collection, ~~analysis~~analysis, and reporting, and acknowledged the time needed to  
21 ensure high quality research outputs. The Working Party highlighted the desirability of concerted  
22 global action to coordinate research activity and formalised data gathering and sharing in the event  
23 of future pandemics caused by novel diseases. The Working Party acknowledged that some of the  
24 areas recommended for future research might already have been addressed in primary studies or  
25 systematic reviews published after the searches for the evidence review had been completed.  
26 Although the Working Party had considered updating the review to take account of more recently  
27 published evidence, the rate at which additional evidence was being published prohibited such an  
28 approach. For example, rerunning the MEDLINE and Embase searches in April 2021 indicated that  
29 approximately 20,000 further articles would need to be considered; it was, therefore, not feasible to  
30 undertake a timely and systematic update of the review using the original search terms. The  
31 Working Party emphasised that the research recommendations were intended to build on the  
32 evidence review and allow the guidance to be refined or extended, preferably with reference to  
33 evidence of higher quality and allowing more focused or nuanced consideration of SARS-CoV-2  
34 transmission dynamics. By November 2021, rerunning the MEDLINE and Embase searches resulted in  
35 an additional 30,000 articles, which when filtered to select records containing the phrase 'systematic  
36 review' in the title, abstract or keywords identified nearly 600 articles. Among these systematic  
37 reviews, a handful investigated relative transmissibility of presymptomatic, asymptomatic and  
38 symptomatic infections;<sup>[61-69]</sup> however, none evaluated the impact of new variants of SARS-CoV-2 or  
39 the implementation of immunisation programmes. Indeed, most relied on literature searches  
40 conducted in a similar timescale to those of the Working Party. None of the published systematic  
41 reviews evaluated transmissibility of SARS-CoV-2 in the post-symptomatic period. The Working Party  
42 therefore concluded that no published evidence syntheses were available at the time to prompt  
43 reconsideration of the recommendations that had been formulated previously.

1 The Working Party noted that evidence included in the review suggested that using PPE (such as face  
2 masks or coverings) reduced the risk of transmission of SARS-CoV-2 by people with presymptomatic  
3 or asymptomatic infection. The current evidence review was not designed to explore this  
4 systematically, whereas the first of the pair of guidance articles<sup>[3]</sup> includes recommendations  
5 regarding appropriate PPE in various circumstances. The Working Party also noted that in an  
6 investigation exploring the possibility of asymptomatic transmission, hospital quarantine of the  
7 index case involved the index case and other patients and visitors wearing masks except when eating  
8 or drinking.<sup>[14]</sup> The Working Party recognised the removal of masks to allow eating and drinking as  
9 being increasingly important in nosocomial outbreaks of COVID-19, and this could have implications  
10 for activities in the community such as visiting restaurants.

## 11 ***Recommendations***

12 Be aware that:

- 13 • people without noticeable symptoms may transmit the SARS-CoV-2 virus to other people
- 14 • transmission of SARS-CoV-2 from people without symptoms may occur in all settings in  
15 which people are in close proximity
- 16 • however, it is likely that the risk of transmission of SARS-CoV-2 is greater from people who  
17 have symptoms compared with those who do not.

18 Even in the absence of symptoms, adhere to legislation and guidance regarding measures to reduce  
19 the risk of transmission of SARS-CoV-2 (such as social distancing, hand hygiene, use of personal  
20 protective equipment and ventilation of enclosed spaces).

21 Be aware that the future transmissibility of SARS-CoV-2 from people carrying the virus without  
22 symptoms might depend on the:

- 23 • nature of further waves or outbreaks of COVID-19
- 24 • emergence and circulation of SARS-CoV-2 variants of concern
- 25 • potential for people who have had COVID-19 previously to be reinfected
- 26 • effectiveness of available vaccines, including the longevity of immunity they confer.

27 Be aware that it is not yet known to what extent or for how long people recovering from acute  
28 infection can transmit the SARS-CoV-2 virus to other people.

## 29 **10. Conclusions**

30 Based on the evidence review, which included research published to the end of May 2020, the  
31 Working Party considered presymptomatic transmission of SARS-CoV-2 to be confirmed, and  
32 asymptomatic transmission to be probable. The evidence for these forms of transmission was  
33 sufficient for the Working Party to formulate several strong recommendations with the intention of  
34 raising awareness in health and care settings of the potential for transmission in the absence of  
35 symptoms. The recommendations were intended to reinforce existing legislation and guidance  
36 specifying measures for reducing the risk of transmission from people who have no noticeable  
37 symptoms. The Working Party formulated recommendations for future research to address areas of  
38 uncertainty, such as the relative transmissibility of presymptomatic, asymptomatic and symptomatic  
39 infections, the period of infectivity in people without symptoms, and the possibility of transmission  
40 in the post-symptomatic period. The Working Party emphasised the importance of good quality  
41 design, analysis and reporting of research studies even in pandemic situations. The Working Party

1 also highlighted the desirability of concerted action to coordinate research activity and share  
2 outputs effectively.

### 3 **11. Further research**

4 The rationale for the following research recommendations is presented in Section 9.

#### 5 ***Research recommendations***

6 What is the relative transmissibility of SARS-CoV-2 from people with presymptomatic, asymptomatic  
7 and symptomatic infection, and how does transmission correlate with quantification of viral  
8 shedding?

9 How long after acquiring SARS-CoV-2 do people without symptoms become infectious and how long  
10 does infectivity last?

11 To what extent or for how long can people who have acquired SARS-CoV-2 and are post-  
12 symptomatic transmit the virus to other people?

13 What are the long-term consequences of lung damage associated with SARS-CoV-2 infection in  
14 people who do not report symptoms?

15 What impact do reinfection, variants of concern, and immunisation programmes have on  
16 transmission of SARS-CoV-2?

#### 17 **Declarations**

18 *Ethics approval and consent to participate*

19 Not applicable.

20 *Consent for publication*

21 Not applicable.

22 *Availability of data and materials*

23 All data generated or analysed during this study are included in this published article and its  
24 supplementary information files.

25 *Competing interests*

26 The authors declare that they have no competing interests (see Section 4.3 and Appendix B for  
27 further details).

28 *Funding*

29 See Section 4.2.

30 *Authors' contributions*

31 All authors except LR and SMS were involved in identifying the review question and developing the  
32 review protocol. MAM conducted the literature searches, sifted the search results, prepared  
33 evidence tables, profiles and statements, and documented the Working Party's interpretation of the  
34 evidence and formulation of recommendations. AB supported development of the literature  
35 searches. NVR performed dual sifting of 10% of search results. JB prepared the lay summary. APRW  
36 chaired the Working Party. All authors provided feedback during development of the evidence

1 tables, profiles and statements, were involved in interpreting the evidence and formulating  
2 recommendations (including research recommendations), reviewed and prepared responses to  
3 stakeholder consultation comments and approved the final manuscript.

#### 4 *Acknowledgements*

5 See Section 4.1.

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