The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate.

YOUR QUESTION

What is the rate of asymptomatic carriage of COVID-19 amongst both older people [65+] and the general population?

IN A NUTSHELL

As the CDC[5] point out, since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood. The WHO[1] suggest that based upon the data available, 80% of COVID-19 infections are mild or asymptomatic. An analysis of available data published by the CEBM[22] on April 6th suggested that 5% and 80% of people testing positive for SARS-CoV-2 may be asymptomatic, that symptom-based screening will miss cases, perhaps many cases, and that asymptomatic cases may become symptomatic. Similarly, an Evidence Summary from HIQA published on 21 April notes the difficulties inherent in identifying truly asymptomatic carriers. There is significant variability in the data arising from the original studies. Much of the data from original studies is derived from closed settings, such as cruise ships, prisons and long term care facilities, which may limit the generalisability. Two American papers have been published regarding older people who are asymptomatic[8,9].

IRISH AND INTERNATIONAL GUIDANCE

What does the World Health Organization say?

Coronavirus disease 2019 (COVID-19) Situation Report 46 (6 March 2020)[1]
For COVID-19, data to date suggest that 80% of infections are mild or asymptomatic, 15% are severe infection requiring oxygen and 5% are critical infections requiring ventilation. These fractions of severe and critical infection would be higher than those observed for influenza infection.

Coronavirus disease 2019 (COVID-19) Situation Report 73 (2 April 2020)[2]

There are few reports of laboratory-confirmed asymptomatic cases and to date there have been no documented instances of asymptomatic transmission. This does not exclude the possibility that asymptomatic transmission may occur. Asymptomatic cases have been reported as part of contact tracing efforts in some countries.

What does the European Centre for Disease Prevention and Control say?

Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK. Ninth update (23 April 2020)[3]

Infection in Asymptomatic Individuals

Asymptomatic infection at time of laboratory confirmation has been reported from many settings. Some of these cases developed some symptoms at a later stage of infection; however, the proportion of cases that will develop symptoms is not yet fully understood. There are also reports of cases remaining asymptomatic throughout the whole duration of laboratory monitoring which revealed viral RNA shedding in various sample types. A recent modelling study suggested that asymptomatic individuals might be major drivers for the growth of the COVID-19 pandemic. For more information on asymptomatic infection, please refer to ECDC's seventh RRA update and to the website."

The update referenced here is:

Coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK. Seventh update (25 March 2020)[4]

Infection in Asymptomatic Individuals

Asymptomatic infection at time of laboratory confirmation has been reported from many settings; a large proportion of these cases developed some symptoms at a later stage of infection. There are, however, also reports of cases remaining asymptomatic throughout the whole duration of laboratory and clinical monitoring. Viral RNA and infectious virus particles were detected in throat swabs from two German citizens evacuated from Hubei province on 1 February 2020 who remained well and afebrile seven days after admission to a hospital in Frankfurt. A mother and her child from a family cluster who both tested positive by quantitative RT-PCR [nasopharyngeal swab samples] remained asymptomatic including normal chest CT images during the observation period. Similar viral loads in asymptomatic versus symptomatic cases were reported in a study including 18 patients. Persistent positivity of viral RNA in throat and anal swabs was reported in an asymptomatic female patient after 17 days of clinical observation and treatment.

…Asymptomatic cases in infants and children have also been reported. Two studies on patients with positive laboratory results reported that 10/15 (66.7%) and 4/31 (13%) of the children were asymptomatic. Exposure to COVID-19 among children is likely to occur within the family or in a household context."

This report also identifies as a research need identification of the proportion of asymptomatic cases and their role in transmission.

What do the Centers for Disease Control and Prevention (United States) say?

Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19) (3 April 2020)[5]
Asymptomatic and Pre-Symptomatic Infection
Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms [asymptomatic] and in patients not yet symptomatic [pre-symptomatic]. Since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood. One study found that as many as 13% of RT-PCR-confirmed cases of SARS-CoV-2 infection in children were asymptomatic. Another study of skilled nursing facility residents infected with SARS-CoV-2 from a healthcare worker demonstrated that half were asymptomatic or pre-symptomatic at the time of contact tracing evaluation and testing. Patients may have abnormalities on chest imaging before the onset of symptoms. Some data suggest that pre-symptomatic infection tended to be detected in younger individuals and was less likely to be associated with viral pneumonia.

POINT-OF-CARE TOOLS

What does BMJ Best Practice say?

COVID-19[6]
Aetiology
Asymptomatic Transmission

- An asymptomatic case is a laboratory-confirmed case who does not develop symptoms. There is some evidence that spread from asymptomatic carriers is possible, although it is thought that transmission is greatest when people are symptomatic, especially around the time of symptom onset.
- Estimating the prevalence of asymptomatic cases in the population is difficult. The best evidence so far comes from the Diamond Princess

cruise ship, which was quarantined with all passengers and crew members repeatedly tested and closely monitored. A modelling study found that approximately 700 people with confirmed infection (18%) were asymptomatic. However, a Japanese study of citizens evacuated from Wuhan City estimates the rate to be closer to 31%. Early data from an isolated village of 3,000 people in Italy estimates the figure to be higher at 50% to 75%. Other studies ranged from 4% to 80%.

- Data from a long-term care facility in the US found that 30% of patients with positive test results were asymptomatic or presymptomatic on the day of testing. In a skilled nursing facility, 64% of residents tested positive 3 days after one resident tested positive; 56% of the residents who tested positive and participated in point-prevalence surveys were asymptomatic at the time of testing, although most went on to develop symptoms.
- Asymptomatic or paucisymptomatic transmission has been reported in family clusters.
- A study in a New York obstetric population found that 88% of women who tested positive for SARS-CoV-2 at admission were asymptomatic at presentation.
- The proportion of asymptomatic cases in children is thought to be significant, and children may play a role in community spread. However, there is a case report of an asymptomatic child who did not transmit the disease to 172 close contacts despite close interactions within schools. This suggests that there may be different transmission dynamics in children.

What does UpToDate say?

Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention[7]

Asymptomatic Infections

Asymptomatic infections have been well documented. Their precise frequency is unknown, but several studies performed in various settings suggest that they are common. As examples:

- In a COVID-19 outbreak on a cruise ship where nearly all passengers and staff were screened for SARS-CoV-2, approximately 17 percent of the population on board tested positive as of February 20; about half of the 619 confirmed COVID-19 cases were asymptomatic at the time

of diagnosis. A modeling study estimated that 18 percent were true asymptomatic cases [ie did not go on to develop symptoms] although this was based on a number of assumptions, including the incubation period.

- In a smaller COVID-19 outbreak within a skilled nursing facility, 27 of the 48 residents who had a positive screening test were asymptomatic at the time of diagnosis, but 24 ultimately developed symptoms over the next seven days.
- Other studies have reported even higher proportions of asymptomatic cases. In a report of a universal screening program of pregnant women presenting for delivery at two New York hospitals at the height of the pandemic there, 29 of 210 asymptomatic women without fever had a positive SARS-CoV-2 reverse transcription polymerase chain reaction test on a nasopharyngeal specimen. 4 additional women had fever or symptoms and also tested positive. Thus, of 33 women with a positive SARS-CoV-2 test, 29 (88%) were asymptomatic on presentation.

Even patients with asymptomatic infection may have objective clinical abnormalities. In a study of 24 patients with asymptomatic infection who all underwent chest computed tomography, 50% had typical ground-glass opacities or patchy shadowing, and another 20% had atypical imaging abnormalities. Five patients developed low-grade fever, with or without other typical symptoms, a few days after diagnosis. In another study of 55 patients with asymptomatic infection identified through contact tracing, 67% had CT evidence of pneumonia on admission; only two patients developed hypoxia, and all recovered.

INTERNATIONAL LITERATURE

What does the international literature say?

SPECIFIC TO OLDER PEOPLE

Kimball et al (3 April 2020) Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility - King County, Washington[8]

On March 1, a health care provider at a second long-term care skilled nursing facility [facility A] in King County, Washington, had a positive test result for SARS-CoV-2 after working while symptomatic on February 26 and 28. By March 6, 7 residents of this second facility were symptomatic and had positive test results for SARS-CoV-2. On March 13, CDC performed symptom assessments and SARS-CoV-2 testing for 93% of facility A residents to evaluate the utility of symptom screening to identify COVID-19 in SNF residents. Residents were categorized as asymptomatic or symptomatic at the time of testing based on the absence or presence of fever, cough, shortness of breath or other symptoms on the day of testing or during the preceding 14 days. Among 23 (30%) residents with positive test results, 10 (43%) had symptoms on the date of testing, and 13 (57%) were asymptomatic. Seven days after testing, 10 of these 13 previously asymptomatic residents had developed symptoms and were recategorized as presymptomatic at the time of testing. The reverse transcription–polymerase chain reaction testing cycle threshold values indicated large quantities of viral RNA in asymptomatic, presymptomatic, and symptomatic residents, suggesting the potential for transmission regardless of symptoms. Symptom-based screening in SNFs could fail to identify approximately half of residents with COVID-19.

Roxby et al (10 April 2020) Detection of SARS-CoV-2 Among Residents and Staff Members of an Independent and Assisted Living Community for Older Adults - Seattle, Washington[9]

Following identification of two COVID-19 cases in a Seattle independent and assisted living facility, stringent preventive measures were implemented. Testing of all residents and staff members found few cases of COVID-19. Three of four residents who had positive test results were asymptomatic.

GENERAL POPULATION PAPERS

Zhu et al (15 April 2020) Clinical characteristics of 3,062 COVID-19 patients: a meta-analysis[10]

In this review of 38 studies involving 3,062 COVID-19 positive patients the percentage of asymptomatic patients was 11.9%.

Nishiura et al (13 March 2020) [Letter] Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19)[11]

The authors suggest that "despite a small sample size, our estimation indicates that perhaps less than a half of COVID-19-infected individuals are asymptomatic**.** This ratio is slightly smaller than that of influenza, which was estimated at 56–80% using similar definitions for symptomatic individuals … There is a need for further studies on the prevalence of asymptomatic COVID-19 infections to guide epidemic control efforts." Asymptomatic infections cannot be recognized if they are not confirmed by RT-PCR or other laboratory testing, and symptomatic cases may not be detected if they do not seek medical attention. Estimates provide important insight by using a targeted population to assess prevalence of asymptomatic viral shedding. It should be noted that limited sensitivity of RT-PCR does not affect the estimate of asymptomatic ratio because the sensitivity is cancelled out from the right-hand side of equation.

Abduljalil and Abduljalil (31 March 2020) Epidemiology, genome, and clinical features of the pandemic SARS-CoV-2: a recent view[12]

Most infected individuals are asymptomatic or only exhibit mild symptoms. After the incubation period, the most common symptoms are fever, cough and fatigue. Asymptomatic carrier state is of paramount importance because of carriers' ability to spread the infection and to shed the virus into the air and surroundings. Although much is still unknown about SARS-CoV-2, the scientific research is moving at an unprecedented pace towards understanding the nature, effective control, prevention and treatment of SARS-CoV-2.

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team [China CDC] (2020) The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19)[13]

A study of 72,314 patient records — 44,672 (61.8%) confirmed cases, 16,186 (22.4%) suspected cases, 10,567 (14.6%) clinically diagnosed cases, and 889 asymptomatic cases (1.2%) — contributed data for the analysis. Asymptomatic cases were diagnosed based on positive viral nucleic acid test results but without any COVID-19 symptoms such as fever, dry cough.

COVID-19 National Emergency Response Center, Epidemiology and Case Management Team, Korea Centers for Disease Control and Prevention. (February 2020) Early Epidemiological and Clinical Characteristics of 28 Cases of Coronavirus Disease in South Korea[14]

Objectives: The first confirmed case of coronavirus disease 2019 (COVID-19) in South Korea was reported in January 2020, with 28 confirmed cases reported as of February 14th, 2020. The epidemiological and clinical characteristics of all 28 cases were analyzed in response to this disease. 3 cases were asymptomatic.

Zhang et al (April 2020) Asymptomatic carriers of COVID-19 as a concern for disease prevention and control: more testing, more follow-up[15]

"According to daily reports from the National Health Commission of the People's Republic of China from March 31, 2020 to April 7, 2020, the number of new asymptomatic cases reported daily greatly exceeded that of new imported cases. As of 24:00 on April 7, there were a total of 1,095 asymptomatic cases with COVID-19 under medical observation on the Chinese mainland, including 358 imported cases".

Tian S et al. (April 2020) Characteristics of COVID-19 infection in Beijing[16]

A retrospective study which included 262 patients with confirmed COVID-19 infection in Beijing. Among 262 patients, 46 [17.6%] were severe cases, 216 [82.4%] were common cases, which including 192 [73.3%] mild cases, 11 [4.2%] non-pneumonia cases and 13 [5.0%] asymptomatic cases respectively. The median age of patients was 47.5 years and 48.5% were male. 192 [73.3%] patients were residents of Beijing; among those residents, 50 [26.0%] had been to Wuhan, 116 [60.4%] had close contact with confirmed cases and 21 [10.9%] had no contact history. The most common symptoms at the onset of illness were fever [82.1%], cough [45.8%], fatigue [26.3%],

dyspnea [6.9%] and headache [6.5%]. The median incubation period was 6.7 days; the interval time from between illness onset and seeing a doctor was 4.5 days. As of February 10, 17.2% patients have discharged and 81.7% patients remain in hospital. The fatality of COVID-19 infection in Beijing was 0.9%.

Mizumoto et al (12 March 2020) Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020[17]

On 5 February 2020 in Yokohama, Japan, a cruise ship hosting 3,711 people underwent a 2-week quarantine after a former passenger was found with COVID-19 post-disembarking. As at 20 February, 634 persons on board tested positive for the causative virus. We conducted statistical modelling to derive the delay-adjusted asymptomatic proportion of infections along with the timeline of the infection. The estimated asymptomatic proportion was 17.9% (95% CI: 15.5–20.2%). Most infections occurred before the quarantine start.

Lai et al (4 March 2020) Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths[18]

This review provides updated information about COVID-19. SARS-CoV-2 can affect patients of all ages. COVID-19 can present as asymptomatic carriage, ARDS and pneumonia. Severe cases are more likely to be older and to have increased underlying comorbidities compared to mild cases. Age and disease severity can be correlated with the outcomes of COVID-19.

Hu Z, Song C, Xu C, et al. (May 2020) Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China[19]

This study aims to present the clinical characteristics of 24 cases with asymptomatic infection screened from close contacts and to show the transmission potential of asymptomatic COVID-19 virus carriers. Epidemiological investigations were conducted among all close contacts of COVID-19 patients (or suspected patients) in Nanjing, Jiangsu Province, China, from Jan 28 to Feb 9, 2020, both in clinic and in community. Asymptomatic carriers were laboratory-confirmed positive for the COVID-19 virus by testing the nucleic acid of the pharyngeal swab samples.

Overall, the asymptomatic carriers identified from close contacts were prone to be mildly ill during hospitalization**.** However, the communicable period could be up to three weeks and the communicated patients could develop severe illness. These results highlighted the importance of close contact tracing and longitudinally surveillance via virus nucleic acid tests. Further isolation recommendation and continuous nucleic acid tests may also be recommended to the patients discharged.

Yu and Yang (4 April 2020) [Letter] COVID-19 transmission through asymptomatic carriers is a challenge to containment[20]

On February 25, a case of COVID-19 transmission occurring in a prison in Rencheng District, Shandong Province [China] sounded an alarm. On February 9, a man was released from prison and returned home but was informed to isolate himself because a prison officer was confirmed to have tested positive for COVID-19 infection on February 14. In order to avoid isolation and observation, the man absconded from his home. Later, it was confirmed that the man was an asymptomatic carrier and that his brother who had come into close contact with him had become infected with COVID-19. This case is an example of asymptomatic transmission. One study has reported that the viral load detected in asymptomatic patients was similar to that in symptomatic patients which also theoretically suggests the potential transmission of asymptomatic patients.

OTHER

HIQA Evidence Summary for asymptomatic transmission of COVID-19[21]

Conclusion

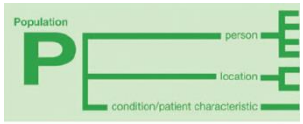
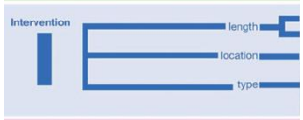
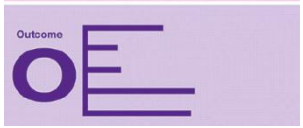
Based on the totality of the evidence presented in this report, it seems likely that pre-symptomatic transmission is occurring. Evidence of asymptomatic transmission from asymptomatic carriers is more limited (perhaps due to difficulties in identifying truly asymptomatic carriers); it appears plausible, but it may not be a driver of transmission.

Centre for Evidence-Based Medicine (6 April 2020) COVID-19: What proportion are asymptomatic?[22]

What did we learn?

- That between 5% and 80% of people testing positive for SARS-CoV-2 may be asymptomatic.
- That symptom-based screening will miss cases, perhaps a lot of cases.
- That some asymptomatic cases will become symptomatic over the next week — sometimes known as pre-symptomatic
- That children and young adults can be asymptomatic.

Produced by the members of the National Health Library and Knowledge Service Evidence Team†. Current as at 30 April 2020]This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.
The following PICO(T) was used as a basis for the evidence summary:

	OLDER PEOPLE [65+] AND GENERAL POPULATION
	
	
	RATE OF ASYMPTOMATIC CARRIAGE OF COVID-19 AMONGST BOTH

The following search strategy was used:

PUBMED
#1 2019-NCOV OR 2019NCOV OR COVID-19 OR SARS-COV-2 OR ((WUHAN AND CORONAVIRUS)
#2 "ASYMPTOMATIC DISEASES"[MESH TERMS] OR "ASYMPTOMATIC"[ALL FIELDS] OR "ASYMPTOMATICALLY"[ALL FIELDS] OR "ASYMPTOMATICS"[ALL FIELDS] OR "PRESYMPTOMATIC"[ALL FIELDS] OR "PRESYMPTOMATICALLY"[ALL FIELDS]
#3 "CAUSALITY"[MESH TERMS] OR "AETIOLOGIE"[ALL FIELDS] OR "AETIOLOGIES"[ALL FIELDS] OR "AETIOLOGY"[ALL FIELDS] OR "ETIOLOGIES"[ALL FIELDS] OR "ETIOLOGY OR "RATE"[ALL FIELDS] OR " OR "EPIDEMIOLOGY"[ALL FIELDS] OR "PREVALENCE"[ALL FIELDS] OR "PREVALENCE"[MESH TERMS] OR "PREVALANCE"[ALL FIELDS] OR "PREVALENCES"[ALL FIELDS] OR "PREVALENCE S"[ALL FIELDS] OR "PREVALENT"[ALL FIELDS] OR "PREVALENTLY"[ALL FIELDS] OR "PREVALENTS"[ALL FIELDS] OR "RATIO"

EMBASE
1 CORONAVIRINAE/EXP OR (COVID-19 OR CORONAVIRUS OR CORONA VIRUS OR (WUHAN ADJ3 VIRUS) OR (2019-NCOV) OR (2019 NCOV) OR SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS OR (2019 AND (NEW OR NOVEL AND CORONAVIRUS) AB, TI)
2 ASYMPTOMATIC INFECTION/EXP OR (ASYMPTOMATIC OR PRESYMTOMATIC AB TI)

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