McMaster University | HEALTH FORUM

RISE Rapid-Improvement Support and Exchange

COVID-19 Rapid Evidence Profile #3 (27 April 2020)

Questions

What is the evidence about international and Canadian experiences with asymptomatic screening to identify COVID-19 cases and to prevent transmission?

What we found

We identified several documents that we deemed to provide highly relevant evidence to the question, including one systematic review, one rapid review, and six guidelines from four groups –Australian National COVID-19 Clinical Evidence Taskforce, Chinese Centre for Disease Control (CDC), U.S. CDC, and World Health Organization – that were developed using some type of evidence synthesis and/or expert opinion. The only highly relevant documents we identified in relation to long-term care settings were two primary studies. The abstracts for the highly relevant documents are included in Appendix 1.

We also identified experiences related to asymptomatic testing from eight international jurisdictions (China, Denmark, France, Germany, Italy, Netherlands, Spain, and United Kingdom).

Evidence about asymptomatic testing

The highly relevant (but low-quality) systematic review found that:

- Enhancing access, determining alternatives to usual specimens, and strengthening the diagnostic pipeline can help overcome testing challenges.

The highly relevant (but low-quality) rapid review found that:

- Asymptomatic transmission of COVID-19 is possible, but efficiency of transmission is unclear.

Box 1: Our approach

We identified evidence addressing the question by searching the guide to COVID-19 evidence sources on 27 April 2020 (www.mcmasterforum.org/find-evidence/guide-to-covid-19-evidence-sources). We identified experiences with implementation by searching jurisdiction-specific sources of evidence on the same website, but with a focus on reviewing those from countries that were affected earliest and most significantly by COVID-19.

We searched for guidelines that were developed using a robust process (e.g., GRADE), full systematic reviews (or review-derived products such as overviews of systematic reviews), rapid reviews, protocols for systematic reviews, and titles/questions for systematic reviews or rapid reviews that have been identified as either being conducted or prioritized to be conducted. Single studies were only included if no relevant systematic reviews were identified.

We appraised the methodological quality of full systematic reviews and rapid reviews using AMSTAR. Note that quality appraisal scores for rapid reviews are often lower because of the methodological shortcuts that need to be taken to accommodate compressed timeframes. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial or governance arrangements within health systems.

This rapid evidence response was prepared in three hours or less to inform next steps in evidence synthesis, guideline development and/or decision-making related to the question that was posed.

Key findings from the highly relevant guidelines that were developed using some type of evidence synthesis and/or expert opinion include:

- Testing of asymptomatic individuals can be considered if they had contact with a COVID-19 case (WHO technical guidance)
- While evaluating and testing, individuals without symptoms should not be a priority (U.S. CDC)
- No baseline investigations are required for mild COVID-19 disease (Australia - National COVID-19 Clinical Evidence Taskforce)
- Asymptomatic persons are not prioritized for testing (U.S. CDC)
- Testing of asymptomatic persons who had close contact with a COVID-19 case may be done in special situations (U.S. CDC guidance for Public Health Personnel Evaluating Persons Under Investigation)
- Monitoring, detection and management of asymptomatic COVID-19 cases (Chinese CDC)

The two highly relevant studies focused on asymptomatic testing in long-term care settings were conducted in the U.S. and found that:

- Testing and treating symptomatic patients is not sufficient as asymptomatic transition is likely in skilled nursing homes
- Symptom-based testing may miss half of residents with COVID-19 infections in skilled nursing facilities

We provide in Table 1 (below) an overview of the type and number of documents that were identified. In addition, we provide in Table 2 a listing of each of the documents (organized by document type and sorted by relevance to the question and COVID-19), with the colour gradient used to reflect high (darkest blue) to low (lightest blue) relevance to the question and to COVID-19. We provide in Appendix 2 a list of documents excluded at the final stage of reviewing.

International and Canadian experiences with implementing asymptomatic testing

We provide evidence related to asymptomatic testing from eight international jurisdictions (China, Denmark, France, Germany, Italy, Netherlands, Spain, United Kingdom) in Table 3. Of these, five jurisdictions have implemented some degree of asymptomatic testing, with priority going to those living or working in long-term care or assisted-living facilities, those who have been recently in contact with someone who has a confirmed case of COVID-19, or those who have travelled back from places with high infection rates of COVID-19. A sixth jurisdiction, Spain, has not implemented asymptomatic testing at a national level, however, it is being rolled out in autonomous communities through anti-body detection tests.

Table 1: Overview of type and number of documents that were identified

Type of document	Asymptomatic testing – general	Asymptomatic testing – long-term care
Guidelines developed using a robust process (e.g., GRADE)	0	0
Full systematic reviews	1	0
Rapid reviews	2	0
Guidelines developed using some type of evidence synthesis and/or expert opinion	7	0
Protocols for reviews that are underway	2	0
Titles/questions for reviews that are being planned	6	0
Single studies in areas where no reviews were identified	2	0

Table 2: Documents that address the question, organized by document type and sorted by relevance to the question and COVID-19

Type of document	Relevance to question	Focus	Recency or status
Guidelines developed using a robust process (e.g., GRADE)		No guidelines developed using robust processes were found	
Full systematic reviews	• Asymptomatic testing – general	Enhancing access, determining alternatives to usual specimens, and strengthening the diagnostic pipeline can help overcome testing challenges (AMSTAR rating 2/9)	13 April 2020
Rapid reviews	• Asymptomatic testing – general	Asymptomatic transmission of COVID-19 is possible, but efficiency of transmission is unclear (AMSTAR rating 0/11 or equivalent due to lack of reporting)	Last updated 13 April 2020
	• Asymptomatic testing – general	Several approaches to testing for COVID-19 and all have advantages and disadvantages	20 April 2020
Guidelines developed using some type of evidence	• Asymptomatic testing – general	Testing of asymptomatic individuals can be considered if they had contact with a COVID-19 case (WHO technical guidance)	19 March 2020

synthesis and/or expert opinion	• Asymptomatic testing – general	While evaluating and testing, individuals without symptoms should not be a priority (U.S. Centers for Disease Control and Prevention)	Last updated 24 March 2020
	• Asymptomatic testing – general	No baseline investigations are required for mild COVID-19 disease (Australia - National COVID-19 Clinical Evidence Taskforce)	19 March 2020
	• Asymptomatic testing – general	Asymptomatic persons are not prioritized for testing (CDC guidance on criteria to guide evaluation and laboratory testing for COVID-19)	24 March 2020
	• Asymptomatic testing – general	Testing of asymptomatic persons who had close contact with a COVID-19 case may be done in special situations (CDC guidance for Public Health Personnel Evaluating Persons Under Investigation)	14 March 2020
	• Asymptomatic testing – general	Monitoring, detection and management of asymptomatic COVID-19 cases (Chinese Center for Disease Control and Prevention)	Last updated 08 April 2020
	• Asymptomatic testing – general	Screening in homeless shelters to identify symptoms that might indicate a respiratory infection (U.S. Centers for Disease Control and Prevention)	Last reviewed 21 April 2020
Protocols for reviews that are underway	• Asymptomatic testing – general	Assessment and management of asymptomatic COVID-19 cases	Anticipated completion 30 April 2020
	• Asymptomatic testing – general	Diagnosis and risk of transmission from asymptomatic COVID-19 cases	Anticipated completion 30 April 2020
Titles/questions for reviews that are being planned	• Asymptomatic testing – general	Evidence about the most effective COVID-19 screening strategy	Underway
	• Asymptomatic testing – general	Screening asymptomatic people for COVID-19	Underway
	• Asymptomatic testing – general	Population screening to achieve long-term isolation	Awaiting prioritization to conduct

	• Asymptomatic testing – general	Diagnostic test accuracy of different tests for the diagnosis of coronavirus infections	Awaiting prioritization to conduct
	• Asymptomatic testing – general	Infection-control practices in non-healthcare settings relevant to primary care	Question under review
	• Asymptomatic testing – long-term care	Effective measures to reduce spread of COVID-19 in care homes	Question under review
Single studies in areas where no reviews were identified	• Asymptomatic testing – long-term care	Testing and treating symptomatic patients is not sufficient as asymptomatic transition is likely in skilled nursing homes (U.S.)	Published 24 April 2020
	• Asymptomatic testing – long-term care	Symptom-based testing may miss half of residents with COVID-19 infections in skilled nursing facilities (U.S.)	3 April 2020
	• Asymptomatic testing – general	Effectiveness of symptom and risk screening for travellers to prevent the spread of COVID-19	Research advance (non-peer reviewed) posted on 24 February 2020
	• Asymptomatic testing – general	Effectiveness of airport screening at detecting travellers infected with COVID-19	Published 6 February 2020

Table 3. Experiences of countries with asymptomatic testing

Countries	Key features of asymptomatic testing
China	• Testing of asymptomatic persons has been prioritized by: o actively testing close contacts of COVID-19 cases; o actively testing during cluster investigations; o actively testing people who have been found to be exposed while tracing an infection source; o actively testing people that have a travel or residential history in areas abroad with sustained COVID-19 transmission; and o actively testing individuals found through epidemiological investigation.
Denmark	• As of 21 April 2020, expanded testing now includes patients with mild respiratory symptoms as well as asymptomatic inhabitants of nursing care homes and front-line nursing-home personnel in case of infection among inhabitants or colleagues. • The next expansion of testing will prioritize close contacts of a person with confirmed COVID-19 four, six or eight days after contact, and inhabitants and personnel in institutions where one or more inhabitants or employees have a confirmed diagnosis of COVID-19.

France	• In early April, the government launched large-scale testing for residents and staff in nursing homes and institutions for disabled individuals using biomedical laboratories, medical-care reserve, and mobile testing buses.
Germany	• As of 25 March 2020, people who have had personal contact with someone confirmed as carrying COVID-19 were asked to immediately contact their health provider, irrespective of symptoms, who was then responsible for deciding whether to refer to testing or not.
Italy	• Testing continues to focus on symptomatic patients with concerns having been expressed about ability of tests to detect active infections in early or asymptomatic stages.
Netherlands	• Testing in the Netherlands is currently focused on symptomatic cases only.
Spain	• Asymptomatic testing has not been implemented at the national level in Spain. • As of 15 April 2020, several autonomous communities have started using rapid antibody detection tests to identify new cases in asymptomatic individuals with priority given to front-line workers, particularly those employed in nursing or assisted-living homes.
United Kingdom	• Asymptomatic testing in the United Kingdom is prioritized for travellers returning from Wuhan (China), Iran, Daegu or Cheongdo (Republic of North Korea) or Northern Italy. As of 16 March 2020, this also includes anyone being discharged from hospital to a care home. • By the end of April, the government has committed to expanding testing to include antibody testing of asymptomatic people, but no details about prioritization of populations has been provided.

Wilson, MG, Waddell K, Gauvin FP, Mansilla C, Moat KA, Wang Q, Lavis JN. COVID-19 rapid evidence profile #3: What is the evidence about international and Canadian experiences with asymptomatic screening to identify COVID-19 cases and to prevent transmission? Hamilton: McMaster Health Forum, 29 April 2020.

The McMaster Health Forum is one of the three co-leads of RISE, which is supported by a grant from the Ontario Ministry of Health to the McMaster Health Forum. To help Ontario Health Team partners and other health- and social-system leaders as they respond to unprecedented challenges related to the COVID-19 pandemic, the Forum is preparing rapid evidence responses like this one. The opinions, results and conclusions are those of the McMaster Health Forum and are independent of the ministry. No endorsement by the ministry is intended or should be inferred.

Appendix 1. Abstracts for highly relevant documents

Note that the table below only includes the abstracts for the documents that we identified on page 1 as being highly relevant to the question.

Type of document	Relevance to question	Abstract and link to full text
Systematic review	Asymptomatic testing – general	Enhancing access, determining alternatives to usual specimens, and strengthening the diagnostic pipeline can help overcome testing challenges **Abstract** Diagnostic testing to identify persons infected with severe acute respiratory syndrome–related coronavirus-2 (SARS–CoV-2) infection is central to control the global pandemic of COVID-19 that began in late 2019. In a few countries, the use of diagnostic testing on a massive scale has been a cornerstone of successful containment strategies. In contrast, the United States, hampered by limited testing capacity, has prioritized testing for specific groups of persons. Real-time reverse transcriptase polymerase chain reaction–based assays performed in a laboratory on respiratory specimens are the reference standard for COVID-19 diagnostics. However, point-of-care technologies and serologic immunoassays are rapidly emerging. Although excellent tools exist for the diagnosis of symptomatic patients in well-equipped laboratories, important gaps remain in screening asymptomatic persons in the incubation phase, as well as in the accurate determination of live viral shedding during convalescence to inform decisions to end isolation. Many affluent countries have encountered challenges in test delivery and specimen collection that have inhibited rapid increases in testing capacity. These challenges may be even greater in low-resource settings. Urgent clinical and public-health needs currently drive an unprecedented global effort to increase testing capacity for SARS–CoV-2 infection. Here, the authors review the current array of tests for SARS–CoV-2, highlight gaps in current diagnostic capacity, and propose potential solutions.
Rapid review	Asymptomatic testing – general	Asymptomatic transmission of COVID-19 is possible, but efficiency of transmission is unclear **Key messages**

		• It is biologically plausible that SARS-CoV-2 can be transmitted when patients are asymptomatic, pre-symptomatic, or mildly symptomatic (potentially from 2.5 days prior to onset of symptoms), based on the finding that RT-PCR levels are high early in infection. Asymptomatic transmission has been documented in individual case reports and reported case series, usually involving close/household contacts. • Importantly, the efficiency of transmission of infection during asymptomatic through pauci-symptomatic infection is unclear, with some conflict between epidemiologic data modelling and other reports. The extent to which RT-PCR positivity in the absence of symptoms reflects cultivatable, and (in the absence of symptoms that strongly promote droplet generation) transmissible virus remains unclear. • Transmission events and their dynamics are complex, but most evidence from other respiratory viruses suggest that transmission events predominantly occur with the peak of symptoms (highest fever, levels of coughing, sneezing and rhinorrhea). • There is minimal data on cultivatable viral loads with SARS-CoV-2 in asymptomatic, pre-symptomatic, and pauci-symptomatic infection, and on the proportion of transmission which may be attributed to these categories, which currently precludes definitive recommendations. • Further evidence is required to elucidate the transmission dynamics of SARS-CoV-2 in multiple populations in the community, long-term care and the acute-care hospital.
Single studies in areas where no reviews were identified	Asymptomatic testing – long-term care	Testing and treating symptomatic patients is not sufficient as asymptomatic transition is likely in skilled nursing homes **Abstract** Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can spread rapidly within skilled nursing facilities. After identification of a case of Covid-19 in a skilled nursing facility, we assessed transmission and evaluated the adequacy of symptom-based screening to identify infections in residents. Methods: We conducted two serial point-prevalence surveys, one week apart, in which assenting residents of the facility underwent nasopharyngeal and oropharyngeal testing for SARS-CoV-2, including real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), viral culture, and sequencing. Symptoms that had been present during the preceding 14 days were recorded. Asymptomatic residents who tested positive were reassessed seven days later.

		Residents with SARS-CoV-2 infection were categorized as symptomatic with typical symptoms (fever, cough, or shortness of breath), symptomatic with only atypical symptoms, pre-symptomatic, or asymptomatic. Results: Twenty-three days after the first positive test result in a resident at this skilled nursing facility, 57 of 89 residents (64%) tested positive for SARS-CoV-2. Among 76 residents who participated in point-prevalence surveys, 48 (63%) tested positive. Of these 48 residents, 27 (56%) were asymptomatic at the time of testing; 24 subsequently developed symptoms (median time to onset, four days). Samples from these 24 pre-symptomatic residents had a median rRT-PCR cycle threshold value of 23.1, and viable virus was recovered from 17 residents. As of April 3, of the 57 residents with SARS-CoV-2 infection, 11 had been hospitalized (three in the intensive care unit) and 15 had died (mortality, 26%). Of the 34 residents whose specimens were sequenced, 27 (79%) had sequences that fit into two clusters with a difference of one nucleotide. Conclusions: Rapid and widespread transmission of SARS-CoV-2 was demonstrated in this skilled nursing facility. More than half of residents with positive test results were asymptomatic at the time of testing and most likely contributed to transmission. Infection-control strategies focused solely on symptomatic residents were not sufficient to prevent transmission after SARS-CoV-2 introduction into this facility.
	Asymptomatic testing – long-term care	Symptom-based testing may miss half of residents with COVID-19 infections in skilled nursing facilities **Abstract** Older adults are susceptible to severe coronavirus disease 2019 (COVID-19) outcomes as a consequence of their age and, in some cases, underlying health conditions. A COVID-19 outbreak in a long-term care skilled nursing facility (SNF) in King County, Washington that was first identified on February 28, 2020, highlighted the potential for rapid spread among residents of these types of facilities. On March 1, a healthcare 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, the novel coronavirus that causes COVID-19, after working while symptomatic on February 26 and 28. By March 6, seven 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 76 (93%) of the 82 facility A residents to

		evaluate the utility of symptom screening for identification of 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 re-categorized as pre-symptomatic at the time of testing. The reverse transcription-polymerase chain reaction (RT-PCR) testing cycle threshold (Ct) values indicated large quantities of viral RNA in asymptomatic, pre-symptomatic, 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. Long-term care facilities should take proactive steps to prevent introduction of SARS-CoV-2. Once a confirmed case is identified in an SNF, all residents should be placed on isolation precautions if possible, with considerations for extended use or reuse of personal protective equipment (PPE) as needed.

Appendix 2: Documents excluded at the final stages of reviewing

Type of document	Focus
Guidelines developed using a robust process (e.g., GRADE)	Not applicable
Full systematic reviews	Not applicable
Rapid reviews	Not applicable
Guidance developed using some type of evidence synthesis and/or expert opinion	COVID-19 guidance on home-care provision
Protocols for reviews that are underway	Use of Biomarkers to identify patients likely to develop severe COVID-19
	Difference in characteristics and infectivity among symptomatic, pre-symptomatic and asymptomatic people with COVID-19
	Proportion and features of asymptomatic COVID-19 infections
Titles/questions for reviews that are being planned	Opportunities for integration of household screening and linkage to care for COVID-19 and TB
	Clinical time course of a detectable SARS-CoV-2 signal by RT-PCR assay in patients with Covid-19
Single studies in areas where no reviews were identified	Asymptomatic SARS-CoV-2 infected patients with persistent negative CT findings