

## Global Hepatitis Programme

### Guideline development for Hepatitis C virus Screening, Care and Treatment in low- and middle-income countries PICO 1 Testing (Antibody Testing) – Decision Making Table

Health system and public health evidence to recommendations framework

#### Who should be tested for HCV antibodies?

**Population:** People with a history of behaviours or exposures that place them at increased risk of hepatitis C infection.

**Intervention:** Targeted HCV antibody testing. “Targeted” means testing of individuals based either on their being part of a defined risk group (populations with high HCV prevalence such as injecting drug users, people with HIV) or through questions to elicit a history of HCV-risk behaviours

**Comparison:** HCV antibody testing in symptomatic individuals. “Symptomatic” means antibody testing based on the presence of liver-related signs or symptoms.

**Outcomes:** Number of referrals to care/treatment for HCV, number of cases of HCV transmission, HCV disease progression (liver cirrhosis, HCC, DCC), SVR, quality of life, all-cause mortality

#### Background:

The World Health Organization estimates that between 130 and 150 million people are chronically infected with hepatitis C (HCV) virus worldwide<sup>1</sup>, most of whom are unaware of their infection<sup>2</sup>. People at increased risk of HCV include people who inject drugs (PWID), and people undergoing medical procedures in an unsafe setting (including the transfusion of infected blood or blood products, renal dialysis, the reuse of syringes and other medical equipment such as catheters and needles)<sup>3,4</sup>. Intranasal drug use and cosmetic procedures (such as tattooing and body piercing) are also risk factors for HCV acquisition<sup>5</sup>. Sexual transmission of HCV occurs infrequently in HIV-negative couples<sup>6,7</sup> but is commoner in HIV-positive patients, particularly in men-who-have-sex-with-men (MSM)<sup>8</sup>. Perinatal transmission of HCV occurs in up to 4-8% of cases and is commoner in infants infected with HIV (17-25%)<sup>9,10</sup>. The relative importance of these risk factors vary depending on the geographical setting and population studied.

People living with chronic HCV are at increased risk of liver cirrhosis, hepatocellular carcinoma, and liver-related mortality<sup>6</sup>. Targeted testing or screening interventions to detect HCV (in order to facilitate earlier access to HCV treatment and care) may prevent or reduce the risk of liver-related complications<sup>1</sup>.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a priority?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <b>Varies</b> <input type="checkbox"/>	HCV prevalence in low and middle income countries is highest in certain high risk groups including those who have been exposed to HCV through medical interventions and in PWID. Perinatal transmission of HCV is high, especially in individuals who are HIV infected. Intranasal drug use and sexual transmission among MSM are also associated with increased risk of infection.	
	Are a large number of people affected?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <b>Varies</b> <input type="checkbox"/>	HCV affects 170 million people around the world; 3% of the world's population. Medical interventions are still associated with transmission of HCV in many countries. A well documented outbreak of HCV infection associated with unsafe injection practice in Egypt resulted in an estimated seroprevalence of up to 25% in at-risk populations <sup>11</sup> . According to the latest WHO report on blood safety (2011), 39 countries do not routinely screen blood transfusions for blood-borne viruses <a href="http://www.who.int/bloodsafety/global_database/en/">http://www.who.int/bloodsafety/global_database/en/</a> .  Injecting drug use has been reported in 148 countries around the world and is associated with high prevalence rates of HCV <a href="http://www.who.int/substance_abuse/facts/en/">http://www.who.int/substance_abuse/facts/en/</a> .	

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
BENEFITS & HARMS OF THE OPTIONS	Are the desirable anticipated effects large?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input checked="" type="checkbox"/> Yes <input type="checkbox"/> <b>Varies</b> <input type="checkbox"/>	16 studies were reviewed in detail as part of a systematic review; 12 studies reported on direct HCV testing interventions and four studies reported on general HCV testing interventions ( <a href="#">PICO 1 Antibody testing systematic review</a> ). The main findings are summarized in Tables a-c (below). Direct HCV testing strategies (health or social care centre offering risk assessment and HCV testing) are more effective than general strategies (such as invitations to information sessions for care providers, leaflets or posters on HCV testing for use in service settings, TV/radio awareness-raising campaigns) in increasing the number of tests, in detecting HCV antibody positive cases and the number of attendances and referrals to specialist care. Although testing interventions are associated with an increase in HCV treatment commencement, this is not reflected in the literature in an increased chance of SVR or reduced mortality. This is likely to be due to the short period of follow-up used by most studies. Members of the Guidelines Committee felt that although a	
	Are the undesirable anticipated effects small?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <b>Varies</b> <input type="checkbox"/>		

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
<b>What is the overall certainty of this evidence?</b>	<p>No included studies</p> <p>Very low    Low    Moderate    High</p> <p><input type="checkbox"/>    <input type="checkbox"/>    <input type="checkbox"/>    <input checked="" type="checkbox"/>    <input type="checkbox"/></p>	direct connection was not made in the systematic review between testing and reduced mortality that these could be indirectly connected.	

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION																								
VALUES	<p>How certain is the relative importance of the desirable and undesirable outcomes?</p>	<p> <input type="checkbox"/> Important uncertainty or variability                    <input type="checkbox"/> Possibly important uncertainty or variability                    <input type="checkbox"/> Probably no important uncertainty or variability                    <input checked="" type="checkbox"/> No important uncertainty or variability                    <input type="checkbox"/> No known undesirable outcomes             </p>	<p>The balance of desirable and undesirable outcomes was considered to be in favour of HCV antibody testing in high prevalence populations. Potential undesirable outcomes were not highlighted in the systematic review process but were discussed by the Guidelines Committee. Members of the patient representative organizations brought up the possibility of lack of access to treatment as a problem in those known to be HCV infected. Other possible problems considered included stigma and loss of employment as a result of a positive result.</p> <p><i>The relative importance or values of the main outcomes of interest:</i></p> <table border="1" data-bbox="779 555 1664 970"> <thead> <tr> <th>Outcome</th> <th>Relative importance</th> <th>Certainty of the evidence</th> </tr> </thead> <tbody> <tr> <td>Referral to HCV specialist</td> <td></td> <td>High</td> </tr> <tr> <td>Attendance at HCV specialist</td> <td></td> <td>High</td> </tr> <tr> <td>Commenced treatment</td> <td></td> <td>High</td> </tr> <tr> <td>SVR</td> <td></td> <td>Low</td> </tr> <tr> <td>Morbidity</td> <td></td> <td>No evidence</td> </tr> <tr> <td>All-cause mortality</td> <td></td> <td>Very low</td> </tr> <tr> <td>Quality of life</td> <td></td> <td>No evidence</td> </tr> </tbody> </table> <p>Overall, the relative importance of desirable outcomes was felt to outweigh the importance of undesirable outcomes.</p>	Outcome	Relative importance	Certainty of the evidence	Referral to HCV specialist		High	Attendance at HCV specialist		High	Commenced treatment		High	SVR		Low	Morbidity		No evidence	All-cause mortality		Very low	Quality of life		No evidence	
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<p>Are the desirable effects large relative to undesirable effects?</p>	<p>No    Probably No    Uncertain    Probably Yes    Yes    <i>Varies</i></p> <p><input type="checkbox"/>    <input type="checkbox"/>    <input type="checkbox"/>    <input type="checkbox"/>    <input checked="" type="checkbox"/>    <input type="checkbox"/></p>	<p>The anticipated pooled absolute effects of HCV testing interventions among populations eligible for testing and the effect on management among the estimated HCV antibody positive population are described in Tables a and b respectively. The anticipated absolute effects of HCV testing interventions among hypothetical populations with HCV prevalence of 10% and 50% are shown in Table c.</p> <p>The desirable effects were considered by the Guidelines Committee to be large relative to any undesirable effects.</p>	

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION																				
RESOURCE USE	Are the resources required small?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>The comparison of targeted antibody testing against symptomatic screening would require resources as outlined below. The resources required were not considered to be small. Targeted testing has different costs associated with different settings – if HCV is prevalent in the population, wide screening may be indicated and may have significant cost implications.</p> <p><b>Main resource requirements</b></p> <table border="1"> <thead> <tr> <th>Resource</th> <th>Settings</th> </tr> </thead> <tbody> <tr> <td>Training</td> <td>Medical training for blood-letting and antibody testing</td> </tr> <tr> <td>Supervision and monitoring</td> <td>Initial counseling and follow-up including provision of treatment</td> </tr> <tr> <td>Supplies</td> <td>Medical facility for blood-letting and for treatment Screening with an antibody and follow-up PCR and genotype has been estimated at €400-500<sup>12</sup>.</td> </tr> </tbody> </table>	Resource	Settings	Training	Medical training for blood-letting and antibody testing	Supervision and monitoring	Initial counseling and follow-up including provision of treatment	Supplies	Medical facility for blood-letting and for treatment Screening with an antibody and follow-up PCR and genotype has been estimated at €400-500 <sup>12</sup> .	
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	Is the incremental cost small relative to the net benefits?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>Direct targeted HCV testing strategies are more cost-effective than general screening strategies in increasing the number of tests and in detecting HCV antibody positive cases. However this needs to be balanced against costs associated with both screening and treatment.</p>									
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EQUITY	What would be the impact on health inequities?	<table border="0"> <tr> <td>Increased</td> <td>Probably increased</td> <td>Uncertain</td> <td>Probably reduced</td> <td>Reduced</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Increased	Probably increased	Uncertain	Probably reduced	Reduced	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>An intervention targeted at patients most at risk e.g. those of lower socio-economic status, PWID and prisoners and those exposed to high-risk medical interventions is likely to reduce health inequities. Currently, 96% of people in low-income countries have no access to HCV testing. (World Hepatitis Alliance<sup>13</sup> <a href="http://www.worldhepatitisalliance.org/Policy/2010PolicyReport.aspx">www.worldhepatitisalliance.org/Policy/2010PolicyReport.aspx</a>). Testing should be voluntary and not mandatory.</p>									
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	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION												
ACCEPTABILITY	Is the option acceptable to key stakeholders?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	The Guidelines Committee emphasized that access to screening needs to be followed by access to treatment in order to improve health, therefore resource would need to be put into both.	
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
FEASIBILITY	Is the option feasible to implement?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	As above, the Guidelines Committee discussed that the infrastructure for both screening and treatment is necessary for screening to have an impact on key outcomes including quality of life and mortality. Funding for HCV treatment is currently available in 77% of middle-income countries and 33% of low-income countries (World Hepatitis Alliance).	
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>											

<b>Problem:</b> [Problem]	<b>Option:</b> [Option]	<b>Comparison:</b> [Comparison]	<b>Setting:</b> [Setting]		
<b>Balance of consequences</b>	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings <input type="checkbox"/>	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings <input type="checkbox"/>	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> <input type="checkbox"/>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings <input type="checkbox"/>	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings <input checked="" type="checkbox"/>
<b>Type of recommendation</b>	We recommend against the option <input type="checkbox"/>		We suggest considering the option <input type="checkbox"/> Only in the context of rigorous research <input type="checkbox"/> Only with targeted monitoring and evaluation <input type="checkbox"/> Only in specific contexts		We recommend the option <input checked="" type="checkbox"/>
<b>Recommendation</b>	It is recommended that HCV antibody testing is offered to individuals who are part of a population with high HCV prevalence or who have a history of HCV-risk exposure / behavior. Strong recommendation, moderate quality of evidence				
<b>Justification</b>	The systematic review highlighted the benefits of targeted testing in at-risk populations (Tables a-c). The quality of evidence was considered to be high for onward referral to a specialist and for commencement on treatment.				
<b>Implementation considerations</b>	Implementation considerations include cost feasibility in individual settings. Access to treatment following a positive test is highly desirable. However, lifestyle advice following a positive result could lead to reduced progression to disease (for example reducing alcohol intake) and measures taken to prevent transmission. Different populations are at risk in different settings. People at increased risk of HCV include people who inject drugs (PWID), and people undergoing medical procedures in an unsafe setting (including the transfusion of infected blood or blood products) <sup>14,15</sup> . Intranasal drug use and cosmetic procedures (such as tattooing and body piercing) are also risk factors for HCV acquisition <sup>16</sup> . Sexual transmission of HCV occurs infrequently in HIV-negative couples <sup>17, 18</sup> but is commoner in HIV-positive patients, particularly in men-who-have-sex-with-men (MSM) <sup>19</sup> . Perinatal transmission of HCV occurs in up to 4-8% of cases and is commoner in infants infected with HIV (17-25%) <sup>20,21</sup> . Testing should be voluntary and not mandatory.				
<b>Monitoring and evaluation</b>	Monitoring of laboratory and clinical facilities to ensure high standards of practice are required.				
<b>Research priorities</b>	There is a lack of evidence for the effectiveness of HCV testing interventions with regards to treatment outcomes and HCV-related morbidity and mortality. Further research in this area focusing on the longer-term outcomes of testing interventions for HCV would be useful.				

**Evidence profile [title]****Authors:** David Hunt, Esther Aspinall, and Hamish Innes**Date:** 2013-05-16**Question:** Who should be tested for HCV antibodies?**Settings:** Individuals with chronic HCV infection**Bibliography:** [Citation text]**Table a: GRADE summary of findings: testing for HCV, and HCV positive cases detected among the population eligible for testing**

Outcome	Subgroup	Eligible population (studies)	GRADE quality*	Effect size (95% CI)	Baseline risk per 10,000 eligible population	Anticipated absolute effects per 10,000 eligible population (95% CI)
Tested for HCV	All strategies	7,435,283 (16 studies)	MODERATE <sup>a</sup>	2.90 (2.01, 4.17)	59 tests conducted	112 more HCV antibody tests (from 59 more to 186 more)
	General strategy	6,834,938 (4 studies)	LOW <sup>b</sup>	1.47 (0.71, 3.03)	60 tests conducted	28 more HCV antibody tests (from 17 fewer to 122 more)
	Direct strategy	600,345 (12 studies)	MODERATE <sup>c</sup>	3.47 (2.52, 4.79)	44 tests conducted	108 more HCV antibody tests (from 66 more to 166 more)
HCV positive cases detected	All strategies	7,424,451 (14 studies)	MODERATE <sup>d</sup>	1.67 (1.28, 2.20)	2 cases detected	1 more case detected (from 0 more to 2 more)
	General strategy	6,834,938 (4 studies)	MODERATE <sup>e</sup>	1.26 (0.97, 1.64)	1 case detected	0 more cases (from 0 fewer to 1 more)
	Direct strategy	589,513 (10 studies)	MODERATE <sup>f</sup>	2.31 (1.47, 3.62)	8 cases detected	10 more cases detected (from 4 more to 20 more)

\*Marked down for: a) inconsistency; b) inconsistency and imprecision; c) inconsistency; d) inconsistency; e) inconsistency; f) inconsistency.

**Table b: GRADE summary of findings: management of HCV positive individuals among the estimated HCV antibody positive population**

Outcome (mean follow-up)	Population (studies)	GRADE quality*	Effect size (95% CI)	Baseline risk per 10,000 HCV antibody positive population	Anticipated absolute effects per 10,000 HCV antibody positive population (95% CI)
Referral to HCV specialist (Six months)	138 (1 study)	MODERATE <sup>a</sup>	3.01 (1.79, 5.07)	2,000 referrals to specialist	4020 more referrals to a specialist (from 1580 more to 8140 more)
Attendance at HCV specialist (Six months)	138 (1 study)	MODERATE <sup>b</sup>	3.66 (1.92, 6.99)	1,380 attending a specialist	3683 more cases attending a specialist (from 1274 more to 8294 more)
Commenced treatment (Two years)	17,263 (4 studies)	MODERATE <sup>c</sup>	3.02 (0.90, 10.15)	54 commencing treatment	109 more commencing treatment (from 5 fewer to 495 more)
SVR (Three years six months)	980 (2 studies)	VERY LOW <sup>d</sup>	1.34 (0.25, 7.11)	41 achieving SVR	14 more achieving SVR (from 31 fewer to 250 more)
Morbidity	No data available				
All-cause mortality (Six months)	138 (1 study)	LOW <sup>e</sup>	0.89 (0.06, 13.95)	Insufficient data	Insufficient data
Quality of Life	No data available				

\*Marked down for: a) sparse data; b) sparse data; c) sparse data; d) observational studies and sparse data; e) directness and sparse data.

**Table c: Anticipated absolute effects of HCV testing interventions by population HCV prevalence**

Outcome	GRADE quality	Subgroup	HCV prevalence	Anticipated absolute effects of HCV testing interventions per 10,000 population (95% CI)
HCV antibody positive cases detected	MODERATE	All strategies	10%	5 more cases detected (from 2 more to 8 more)
			50%	23 more cases detected (from 9 more to 40 more)
		Direct strategy	10%	8 more cases detected (from 3 more to 15 more)
			50%	39 more cases detected (from 14 more to 77 more)
		General strategy	10%	2 more cases detected (from 0 fewer to 5 more)
			50%	10 more cases detected (from 1 fewer to 26 more)
Referral to specialist	MODERATE	All strategies	10%	330 more cases (from 649 more to 1370 more)
			50%	2812 more cases (from 1017 more to 5935 more)
Attendance at specialist	MODERATE	All strategies	10%	289 more cases (from 100 more to 651 more)
			50%	1735 more cases (from 600 more to 3907 more)
Commenced	MODERATE	All	10%	13 more commencing treatment (from 1 fewer to 60 more)

**Problem:** [Problem]

**Option:** [Option]

**Comparison:** [Comparison]

**Setting:** [Setting]

treatment		strategies	50%	39 more commencing treatment (from 2 fewer to 179 more)
SVR	VERY LOW	All strategies	10%	0 more SVRs (from 0 fewer to 4 more)
			50%	5 more SVRs (from 11 fewer to 86 more)
All-cause mortality	LOW	All strategies	10%	Insufficient data
			50%	Insufficient data

## References

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- 1 World Health Organization 2012
- 2 Lavanchy 2009
- 3 Alter 1990
- 4 Villano 1997
- 5 Karmochine 2006
- 6 Hallam et al, 1993
- 7 Scott et al, 2010
- 8 Danta et al, 2007
- 9 Thomas et al, 1997 JID
- 10 Mast et al, JID, 2005
- 11 Frank et al, 2000
- 12 MSF report 2013
- 13 World Hepatitis Alliance. Viral hepatitis: global policy. World Hepatitis Alliance: London, UK; 2011
- 14 Alter 1990
- 15 Villano 1997
- 16 Karmochine 2006
- 17 Hallam et al, 1993
- 18 Scott et al, 2010
- 19 Danta et al, 2007
- 20 Thomas et al, 1997 JID
- 21 Mast et al, JID, 2005

## Explanations

### Definitions for ratings of the certainty of the evidence (GRADE)\*\*

Ratings	Definitions	Implications
⊕⊕⊕⊕ High	This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different* is low.	This evidence provides a very good basis for making a decision about whether to implement the intervention. Impact evaluation and monitoring of the impact are unlikely to be needed if it is implemented.
⊕⊕⊕○ Moderate	This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different <sup>4</sup> is moderate.	This evidence provides a good basis for making a decision about whether to implement the intervention. Monitoring of the impact is likely to be needed and impact evaluation may be warranted if it is implemented.
⊕⊕○○ Low	This research provides some indication of the likely effect. However, the likelihood that it will be substantially different <sup>4</sup> is high.	This evidence provides some basis for making a decision about whether to implement the intervention. Impact evaluation is likely to be warranted if it is implemented.
⊕○○○ Very low	This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different <sup>4</sup> is very high.	This evidence does not provide a good basis for making a decision about whether to implement the intervention. Impact evaluation is very likely to be warranted if it is implemented.

\*Substantially different: large enough difference that it might have an effect on a decision

\*\*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group began in the year 2000 as an informal collaboration of people with an interest in addressing the shortcomings of present grading systems in health care. The working group has developed a common, sensible and transparent approach to grading quality of evidence and strength of recommendations. Many international organizations have provided input into the development of the approach and have started using it.

(Return)

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