

# THE LANCET

## Infectious Diseases

### Supplementary appendix

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## **Initiation and completion of treatment for latent tuberculosis infection in migrants globally: A systematic review and meta-regression analysis**

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## Appendix 1. Search strategy (with subject headings (/))

### Embase Database

1. migrant/ or migrant worker/ or Migrant\*.mp.
2. Migrat\*.mp.
- 3.refugee/ or refugee\*.mp.
- 4.asylum seeker/ or asylum seeker\*.mp.
- 5.foreigner\*.mp. or foreign worker/
- 6.foreign born.mp.
- 7.immigrant/ or immigra\*.mp.
8. Emigrants/ or emigrant/ or emigration/ or emigra\*.mp.
9. oversea\*.mp.
10. foreign student\*.mp. or foreign student/
11. international student\*.mp.
12. traffick\*.mp.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. adher\*.mp.
15. complian\*.mp.
16. deafult.mp.
17. concordan\*.mp.
18. treatment outcome/ or treatment outcome\*.mp.
19. non adher\*.mp.
20. non complian\*.mp. or patient compliance/
21. treatment uptake.mp.
22. treatment start.mp.
23. treatment initiation.mp.
24. drop out.mp.
25. follow up/ or loss to follow-up.mp.
26. treatment deferral.mp.
27. treatment completion.mp.
28. treatment success.mp. or treatment outcome/
29. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30. latent tuberculosis/ or Latent tuberculosis infection.mp.
31. latent TB infection.mp.
32. LTBI.mp.
33. latent tuberculosis.mp.
34. latent TB.mp.
35. latent mycobacterium tuberculosis.mp.
36. inactive tuberculosis infection.mp.
37. inactive tuberculosis.mp.
- 38.inactive TB.mp.
39. inactive mycobacterium tuberculosis.mp
40. (prophyla\* adj3 tuberculosis).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
41. 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42. 13 and 29 and 41

## MEDLINE Database

1. Migrant\*.mp. or "Emigration and Immigration"/
2. migrat\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3. "Emigrants and Immigrants"/ or Refugees/ or refugee\*.mp.
4. asylum seeker\*.mp.
5. foreigner\*.mp.
6. foreign born.mp.
7. non-native\*.mp.
8. immigra\*.mp.
9. emigra\*.mp.
10. oversea\*.mp.
11. foreign student\*.mp.
12. International Student\*.mp.
13. traffick\*.mp.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. adher\*.mp.
16. complian\*.mp.
17. default.mp.
18. concordan\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
19. Treatment Outcome/ or treatment outcome\*.mp.
20. non-adher\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
21. non-complian\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
22. Treatment uptake.mp.
23. treatment start.mp.
24. treatment initiation.mp.
25. drop out.mp.
26. loss to follow-up.mp.
27. treatment deferral.mp.
28. treatment completion.mp.
29. treatment success.mp.
30. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. Latent tuberculosis infection.mp. or Latent Tuberculosis/
32. Latent TB infection.mp.
33. LTBI.mp.
34. latent TB.mp.
35. latent Mycobacterium tuberculosis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
36. inactive tuberculosis infection.mp.
37. inactive TB infection.mp.
38. Inactive Tuberculosis.mp.
39. Inactive TB.mp.
40. Inactive Mycobacterium Tuberculosis.mp.
41. (prophyla\* adj3 tuberculosis).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
42. 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41
43. 14 and 30 and 42

## Global Health Database

1. migrant labour/ or migrant farm workers/ or Migrant\*.mp.
2. Migrat\*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
3. Refugee\*.mp. or refugees/
4. asylum seeker\*.mp.
5. foreigner\*.mp.
6. foreign-born.mp.
7. non-native\*.mp.
8. immigra\*.mp.
9. emigra\*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
10. Oversea\*.mp.
11. foreign student\*.mp. or foreign students.sh.
12. International Student\*.mp.
13. traffick\*.mp.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. Adher\*.mp.
16. complian\*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
17. default.mp.
18. concordan\*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
19. treatment outcome\*.mp.
20. non-adher\*.mp. or patient compliance.sh.
21. non-complian\*.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
22. treatment uptake.mp.
23. treatment start.mp.
24. treatment initiation.mp.
25. drop out.mp.
26. loss to follow-up.mp.
27. treatment deferral.mp.
28. treatment completion.mp.
29. treatment success.mp. or treatment failure.sh.
30. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. Latent Tuberculosis Infection.mp.
32. latent tb infection.mp.
33. LTBI.mp.
34. latent tuberculosis.mp.
35. latent TB.mp.
36. latent mycobacterium tuberculosis.mp.
37. inactive tuberculosis infection.mp.
38. inactive tb infection.mp.
39. inactive tuberculosis.mp.
40. inactive tb.mp.
41. inactive mycobacterium tuberculosis.mp.
42. (prophyla\* adj3 tuberculosis).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
43. 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42
44. 14 and 30 and 43

**Appendix 2.** Characteristics of included studies

INH = Isoniazid, RMP = Rifampicin, N.R = Not Reported

Citation	Location	StudyType	Study Quality	Dates	Average Age of migrant Population Reported	LTBI diagnostic used	Treatment Adherence definition	LTBI positive migrants (N)	Migrants initiating treatment (n)	Migrants completing treatment (n)	WHO region assigned	Time period Assigned	Migrant Type Assigned	Treatment Regimen assigned
Ailinger, et al. <sup>62</sup> 2007	United States	Cross-sectional	6/8	2004-2005	Mean age of 26.1 (SD = 6.6)	N.R	Completion of 270 doses in 12 months	153	129	52	Americas	2000s	Foreign-born	9 Month INH
Benjumea-Bedoya, et al. <sup>31</sup> 2019	Canada	Retrospective cohort	9/11	Jan 2015 – Dec 2015	Mean age of 32.5 (SD =8.9)	IGRA	≥80% of INH doses within 12 months	59	34	27	Americas	2010s	Refugees	9 Month INH
Bennet, et al. <sup>51</sup> 2014	United States	Retrospective cohort	10/11	Jan 2010-Oct 2012	Median age of 31	TST, IGRA	N.R	823	373	219	Americas	2010s	Refugees	6-9 Month INH
Bishara, et al. <sup>35</sup> 2015	Israel	Retrospective cohort	11/11	2005-2011	Mean age of 28.2 (SD = 16.9)	TST	26 supervised doses with 9 months	849	663	628	Europe	.	Foreign-born	6-9 Month INH
Bodenmann, et al. <sup>46</sup> 2009	Switzerland	Cross-sectional	6/8	Jan 2007 – Jul 2007	Mean age of 34.8	IGRA	N.R	14	10	5	Europe	2000s	Undocumented Immigrants	Unclear
Brassard, et al. <sup>32</sup> 2006	Canada	Retrospective cohort	11/11	1998 - 2003	unclear	TST	>80% prescribed doses taken with 43 weeks of initiating therapy	507	176	111	Americas	2000s	Foreign-born	9 Month INH
Carter, et al. <sup>52</sup> 2017	United States	Retrospective cohort	8/11	Aug 2012-Apr 2016	Median age of 31.8 (Range = 18 – 70)	IGRA	120 doses within 6 months	121	90	85	Americas	2010s	Refugees	4 Month RMP
Chang, et al. <sup>53</sup> 2013	United States	Retrospective cohort	10/11	Jan 2000-Dec 2002	Median age of home follow-up of 22 (interquartile range = 10-31); Median age of clinic follow-up of 24 (interquartile range = 13-35)	TST	≥6 months of INH within 9 months	3417	3417	2669	Americas	2000s	Foreign-born	6-9 Month INH
Dobler, Marks. <sup>28</sup> 2012	Australia	Retrospective Cohort	10/11	Jan 2000-Dec 2010	Mean age of 27 (SD = 16)	TST	6 monthly bottles of INH collected by patient	128	128	96	Western Pacific	.	Foreign-born	6 Month INH
Duchen, et al. <sup>54</sup> 2017	United States	Retrospective cohort	11/11	Jan 2009-Apr 2012	Mean age of 35.2 (SD = 11.3)	TST	>90% of doses received & missed less than three daily doses per month	107	85	41	Americas	.	Refugees	Mixed (inc. RMP & INH regimens)
Elliot, et al. <sup>29</sup> 2018	Australia	Retrospective cohort	8/11	2007 - 2010	Unclear	TST, IGRA	6 Months of preventive therapy	79	33	33	Western Pacific	.	Refugees	6 Month INH
Essadek, et al. <sup>42</sup> 2018	Spain	Retrospective cohort	7/11	2012-2014	unclear	N.R	N.R	54	n/a	43	Europe	2010s	Foreign-born	Unclear
Gacek, et al. <sup>55</sup> 2013	United States	Retrospective cohort	6/11	Jan 2007-Dec 2008	N.R	TST	N.R	105	49	15	Americas	2000s	Foreign-born	Unclear
Goswami, et al. <sup>36</sup> 2012	United States	Prospective cohort	11/11	Jan 2008-May 2009	Unclear	TST	N.R	321	73	44	Americas	2000s	Foreign-born	Mixed (inc. RMP & INH regimens)
Haley, et al. <sup>57</sup> 2008	United States	Retrospective cohort	10/11	Feb 2000-Feb 2004	unclear	TST	4 pill bottles provided & provider determination treatment was complete	598	598	476	Americas	2000s	Foreign-born	4 Month RMP
Hargreaves, et al. <sup>47</sup> 2014	United Kingdom	Cross-sectional	7/8	2013	unclear	IGRA	N.R	6	1	1	Europe	2010s	Foreign-born	Unclear
Harstad, et al. <sup>39</sup> 2010	Norway	Retrospective cohort	11/11	Jan 2005-Jun 2006	N.R	TST	N.R	2293	30	n/a	Europe	2000s	Asylum Seekers	Unclear
Hirsch-Moverman, et al. <sup>58</sup> 2010	United States	RCT	7/9	2002-2005	N.R	N.R (CDC guidelines)	According to CDC guidelines	81	81	47	Americas	2000s	Foreign-born	9 Month INH
Jimenez-Fuentes, et al. <sup>43</sup> 2013	Spain	RCT	8/9	Apr 2001-Apr 2005	26.1	TST	>80% of the prescribed dose taken at each follow-up visit & attendance at clinics	590	590	367	Europe	2000s	Foreign-born	Mixed (inc. RMP & INH regimens)
Kawatsu, et al. <sup>36</sup> 2017	Japan	Cross-sectional	6/8	2007 - 2014	unclear	N.R	≥180 days treatment duration & recorded as treatment completed	2510	2510	1738	Western Pacific	.	Foreign-born	6-9 Month INH
Kim, et al. <sup>41</sup> 2019	South Korea	Prospective cohort	10/11	2008	Mean age of 35.4 (SD = 10)	TST, IGRA	Finishing ≥80% of prescribed pills	172	172	117	Western Pacific	2000s	Refugees	Mixed (inc. RMP & INH regimens)
Lardizabal, et al. <sup>59</sup> 2006	United States	Retrospective cohort	9/11	2000-2003	unclear	N.R	Pill count & extensive discussion between nurses and case managers	432	432	298	Americas	2000s	Foreign-born	Mixed (inc. RMP & INH regimens)
Li, et al. <sup>60</sup> 2010	United States	Retrospective cohort	11/11	Jan 2002-Aug 2004	unclear	TST	Attendance at follow-up appointments	12683	12683	5733	Americas	2000s	Foreign-born	Mixed (inc. RMP & INH regimens)
Lim, et al. <sup>33</sup> 2016	Canada	Retrospective cohort	10/11	2014 - 2016	unclear	TST, IGRA	Filling at least 75% of treatment doses	80	72	62	Americas	2010s	Refugees	3 Month INH + RMP
Loutet, et al. <sup>48</sup> 2018	United Kingdom	Retrospective cohort	11/11	Aug 2014-Aug 2015	unclear	IGRA	N.R	719	449	n/a	Europe	2010s	Foreign-born	3 Month INH + RMP
Nuzzo, et al. <sup>61</sup> 2015	United States	Retrospective cohort	11/11	Feb 2009-Mar 2011	unclear	TST, IGRA	≥6 months INH and attendance at final appointment, or ≥3 months RIF and attendance at final appointment	595	485	409	Americas	.	Foreign-born	Mixed (inc. RMP & INH regimens)
O'Shea, et al. <sup>49</sup> 2014	United Kingdom	Prospective cohort	8/11	Feb 2012 – Sep 2012	Range = 18-21	TST, IGRA	N.R	29	29	29	Europe	2010s	Foreign-born	3 Month INH + RMP

<i>Olsson, et al.</i> <sup>45</sup> 2018	Sweden	Retrospective cohort	11/11	Jan 2008-Mar 2016	N.R	TST	Collected the prescribed treatment	297	297	245	Europe	.	Asylum Seekers	Mixed (inc. RMP & INH regimens)
<i>Sawka, Brigham.</i> <sup>27</sup> 2019	Australia	Retrospective cohort	6/11	Jan 2013-Dec 2017				846	n/a	135	Western Pacific	2010s	Foreign-born	Unclear
<i>Schein, et al.</i> <sup>40</sup> 2018	Norway	Prospective cohort	10/11	2016	Unclear	IGRA	As reported by responsible clinician & verified by duration of treatment	595	595	562	Europe	2010s	Foreign-born	Mixed (inc. RMP & INH regimens)
<i>Shieh, et al.</i> <sup>63</sup> 2006	United States	Prospective cohort	10/11	Jul 2002-Sep 2003	unclear	TST	N.R	196	196	57	Americas	2000s	Foreign-born	6-9 Month INH
<i>Spruijt, Erkens, et al.</i> <sup>37</sup> 2019	Netherlands	Prospective Cohort	10/11	Mar 2016 – Sep 2016	Unclear	TST, IGRA	N.R	94	49	34	Europe	.	Foreign-born	3 Month INH + RMP
<i>Spruijt, Haile, et al.</i> <sup>38</sup> 2019	Netherlands	Prospective cohort	10/11	Nov 2016-Dec 2017	Unclear	IGRA	National Guidelines	178	149	129	Europe	2010s	Asylum Seekers	3 Month INH + RMP
<i>Subedi, et al.</i> <sup>64</sup> 2015	United States	Retrospective cohort	8/11	2010-2012	N.R	TST, IGRA	N.R	57	57	43	Americas	2010s	Refugees	Unclear
<i>Thee, et al.</i> <sup>34</sup> 2019	Germany	Prospective cohort	5/11	2016	Median age of 16.8 (interquartile range = 16-17.2)	IGRA	N.R	38	38	29	Europe	2010s	Refugees	3 Month INH + RMP
<i>Trauer, Krause.</i> <sup>30</sup> 2011	Australia	Prospective cohort	11/11	Feb 2006-Jan 2009	Median age of 15 (Interquartile range = 7-29)	TST	≥80% of 9-month doses taken within 12 months	146	93	41	Western Pacific	2000s	Refugees	9 Month INH
<i>Usdin, et al.</i> <sup>50</sup> 2017	United Kingdom	Prospective cohort	9/11	Feb 2014 – Mar 2014	N.R	IGRA	N.R	71	53	45	Europe	2010s	Foreign-born	3 Month INH + RMP
<i>Villa, et al.</i> <sup>44</sup> 2019	Spain	Prospective Cohort	10/11	Jan 2016-Dec 2017	unclear	TST, IGRA	Patient self-reporting	875	808	768	Europe	2010s	Asylum Seekers	Mixed (inc. RMP & INH regimens)
<i>Walters, Sullivan.</i> <sup>65</sup> 2016	United States	Retrospective cohort	9/11	Nov 2009-Apr 2011	23.8 (SD = 11.9)	TST, IGRA	N.R	680	381	261	Americas	.	Refugees	Mixed (inc. RMP & INH regimens)

**Appendix 3.** Univariable meta-regression analysing heterogeneity between sub-groups

Analyses	Results	
	Variable	P-value
..	..	..
<u>Treatment initiation amongst LTBI positive Migrants</u>	..	..
..	Region	0.82
..	Time period	0.05
..	Screening & Treatment Setting	0.81
..	Migrant Type	0.76
..	Treatment Regimen	0.44
<u>Treatment completion amongst migrants that initiate treatment</u>	..	..
..	Region	0.01
..	Time period	0.00
..	Screening & Treatment Setting	0.26
..	Migrant Type	0.35
..	Treatment Regimen	0.12
<u>Treatment completion amongst LTBI positive migrants</u>	..	..
..	Region	0.02
..	Time period	0.01
..	Screening & Treatment Setting	0.47
..	Migrant Type	0.37
..	Treatment Regimen	0.28



**Appendix 4.** Results of critical appraisal carried out on included studies. Quality scores were calculated as the cumulative numbers of “Yes” responses to the appraisal questions.

Cross-Sectional (prevalence) Studies	Citation	Study Type	Score	1. Were criteria for inclusion in the sample clearly defined?	2. were the study subjects and the setting described in detail?	3. Was the exposure measured in a valid and reliable way?	4. Were objective, standard criteria used for measurement of the condition?	5. Were confounding factors identified?	6. Were strategies to deal with confounding factors stated?	7. Were the outcomes measured in a valid and reliable way?	8. Was appropriate statistical analysis used?			
	<i>Ailinger, et al. 2007</i>	Cross-sectional	6/8	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes			
	<i>Bodenmann, et al. 2009</i>	Cross-sectional	6/8	yes	yes	Yes	Yes	Yes	No	Yes	no			
	<i>Hargreaves, et al. 2014</i>	Cross-sectional	7/8	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes			
	<i>Kawatsu, et al. 2017</i>	Cross-sectional	6/8	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes			
Cohort Studies (Prospective and Retrospective)	Citation	Study Type	Score	1. Did the study address a clearly focused issue?	2. Was the cohort recruited in an acceptable way?	3. Was the exposure accurately measured to minimise bias?	4. Was the outcome measure accurately measured to minimise bias?	5a. Have the authors identified all important confounding factors?	5b. Have they taken account of the confounding factors in the design and/or analysis?	6a. Was the follow up of subjects complete enough?	6b. Was the follow up of subjects long enough?	7. Do you believe the results?	8. Can the results be applied to the local population?	9. Do the results of this study fit with other available evidence?
	<i>Benjumea-Bedoya, et al. 2019</i>	Retrospective Cohort	9/11	Yes	Yes	Yes	Yes	can't tell	can't tell	Yes	Yes	yes	yes	Yes
	<i>Bennet, et al. 2014</i>	Retrospective Cohort	10/11	Yes	Yes	Yes	yes	Yes	Yes	yes	No	yes	yes	yes
	<i>Bishara, et al. 2015</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes
	<i>Brassard, et al. 2006</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Carter, et al. 2017</i>	Retrospective Cohort	8/11	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
	<i>Chang, et al. 2013</i>	Retrospective Cohort	10/11	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Dobler, Marks. 2012</i>	Retrospective Cohort	10/11	Yes	Yes	Can't tell	Yes	yes	yes	yes	yes	yes	yes	yes
	<i>Duchen, et al. 2017</i>	Retrospective Cohort	10/11	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes
	<i>Elliot, et al. 2018</i>	Retrospective Cohort	8/11	Yes	Yes	Yes	Can't tell	no	no	yes	Yes	yes	yes	yes
	<i>Essadek, et al. 2018</i>	Retrospective Cohort	7/11	Yes	Yes	Can't tell	Can't tell	Yes	No	yes	can't tell	yes	yes	yes
	<i>Gacek, et al. 2013</i>	Retrospective Cohort	6/11	Yes	Yes	can't tell	Can't tell	Yes	no	No	can't tell	yes	yes	yes
	<i>Goswamin, et al. 2012</i>	Prospective Cohort	11/11	Yes	Yes	yes	Yes	Yes	Yes	yes	Yes	yes	yes	yes
	<i>Haley, et al. 2008</i>	Retrospective Cohort	10/11	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Harstad, et al. 2010</i>	Prospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Kim, et al. 2019</i>	Retrospective Cohort	10/11	Yes	can't tell	Yes	Yes	yes	yes	Yes	Yes	Yes	yes	Yes
	<i>Lardizabal, et al. 2006</i>	Retrospective Cohort	9/11	Yes	Yes	Can't tell	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
	<i>Li, et al. 2010</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Lim, et al. 2016</i>	Retrospective Cohort	10/11	Yes	Yes	Yes	yes	Yes	no	Yes	Yes	Yes	Yes	Yes
	<i>Loutet, et al. 2018</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Nuzzo, et al. 2015</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>O'Shea, et al. 2014</i>	Prospective Cohort	8/11	Yes	Yes	Yes	Can't tell	No	No	Yes	Yes	Yes	Yes	Yes
	<i>Olsson, et al. 2018</i>	Retrospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	<i>Sawka, Brigham. 2019</i>	Retrospective Cohort	6/11	Yes	Yes	Yes	Can't tell	can't tell	can't tell	yes	can't tell	yes	can't tell	yes
	<i>Schein, et al. 2018</i>	Prospective Cohort	10/11	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Shieh, et al. 2006</i>	Prospective Cohort	10/11	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Sprujit, Erkens, et al. 2019</i>	Retrospective Cohort	10/11	Yes	Yes	Yes	Can't tell	Yes	Yes	yes	yes	Yes	Yes	Yes
	<i>Sprujit, Haile, et al. 2019</i>	Prospective Cohort	10/11	Yes	Yes	Yes	Can't tell	Yes	Yes	yes	yes	Yes	yes	Yes
	<i>Thee, et al. 2019</i>	Prospective cohort	5/11	Yes	No	Yes	Can't tell	No	No	yes	can't tell	yes	no	yes
	<i>Subedi, et al. 2015</i>	Retrospective Cohort	8/11	Yes	Yes	Yes	Can't tell	Yes	No	yes	can't tell	Yes	Yes	Yes
	<i>Trauer, Krause. 2011</i>	Prospective Cohort	11/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	<i>Usdin, et al. 2017</i>	Prospective Cohort	9/11	Yes	Yes	Yes	can't tell	Yes	No	Yes	Yes	Yes	Yes	Yes
	<i>Villa, et al. 2019</i>	Retrospective Cohort	10/11	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
	<i>Walters, Sullivan. 2016</i>	Retrospective Cohort	9/11	Yes	Yes	Yes	Can't tell	Yes	Yes	cant tell	Yes	Yes	Yes	Yes
<b>Randomised Controlled-Trial</b>	<b>Citation</b>	<b>Study Type</b>	<b>Score</b>	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. were patients, health workers and study personnel 'blind' to treatment?	5. were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. Can the results be applied to the local population, or in your context?	8. Were all clinically important outcomes considered?	9. Are the benefits worth the harms and costs?		
	<i>Hirsch-Moverman, et al. 2010</i>	RCT	7/9	Yes	Yes	Yes	Yes	No	Yes	Can't tell	Yes	Yes		
	<i>Jimenez-Fuentes, et al. 2013</i>	RCT	8/9	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes		

**Appendix 5.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2-3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2-3
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	4
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	4

<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1; 5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 2.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix 4.
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	5-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	5-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5-9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9-10
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	10