



Lenoir-Wijnkoop et al. (2014)***							
McFarland et al. (2002)							
Lucado et. al (2006)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Didari et al. (2014)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Abou Chakra et al. (2014)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
McFarland et al. (1999)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Surawicz et al. (2013)**	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Kwon et al. (2015)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Healthcare Cost and Utilization Project (HCUP) (2015)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Centers for Medicare and Medicaid Services Fee Schedule (2015)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Consumer Price Index (2013)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pharmacy Red Book (2012)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Konijeti et al. (2014)***	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Park et al. (2012)***	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Trallori et al. (1997)***	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cohen et al. (2010)**	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Dellinger et al. (2013)**	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Source Studies:							
Vermeersch et al. (2018)							
Goldenberg et. al. (2013)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hempel et. al. (2012)*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cleemput et. al (2012)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Swartenbroekx et. al (2012)****	N/A	N/A	N/A	N/A	N/A	N/A	N/A

AHS: Alberta Health Services, HCUP: Healthcare Cost and Utilization Project, IPC: Infection Prevention and Control, PSSRU: Personal Social Services Research Unit, US: United States



High risk of bias



Unknown risk of bias



Low risk of bias

\* Systematic reviews/meta-analyses

\*\*Guideline documents

\*\*\*Health economic analyses

\*\*\*\*Public/hospital databases

eAppendix 4B. Risk of bias assessment for source clinical studies utilized in health economic analysis of probiotics (observational studies – utilizing the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies)

	Selection (max 4 stars)	Comparability (max 2 stars)	Outcome (max 3 stars)
<b>Source Studies:</b> Allen et al. (2013)	N/A	N/A	N/A
<b>Source Studies:</b> Branch-Elliman et al. (2015)	N/A	N/A	N/A
<b>Source Studies:</b> Fansi et al. (2012)			
Song et. al (2008)	****	**	***
<b>Source Studies:</b> Leal et al. (2016)	N/A	N/A	N/A
<b>Source Studies:</b> Lenoir-Wijnkoop et al. (2014)			
Pepin et al. (2006)	****	**	***
Miller et al. (2002)	*	0	**
<b>Source Studies:</b> Shen et al. (2017)			
Miller et al. (2002)	*	0	**
Salminen et al. (2002)	****	**	***
Van Walraven et al. (2014)	****	**	***
Lessa et al. (2015)	****	**	***
Kuntz et al. (2012)	****	**	***
<b>Source Studies:</b> Vermeersch et al. (2018)			
Elseviers et al. (2015)	*	*	0
Kyne et al. (2002)	*	0	*
Dubberke et al. (2008)	*	0	*
Song et. al (2008)	****	**	***
Lawrence et. al (2008)	*	0	*
Riley et. al (2008)	*	0	*
Miller et al. (2002)	*	0	**
Ananthakrishnan et al. (2008)	*	0	*
Kofsky et al. (1991)	*	0	*
Wassenberg et al (2010)	*	*	0

**Selection**

- 1) Representativeness of intervention cohort:
  - a. Truly representative of average, treated probiotic patient in hospital\*
  - b. Somewhat representative of average, treated probiotic patient in hospital\*
  - c. Only selected group of patients
  - d. No description of derivation cohort
- 2) Selection of non-intervention cohort:
  - a. Drawn from same community as intervention/exposed cohort\*
  - b. Drawn from different source
  - c. No description of the derivation of the non-exposed cohort
- 3) Ascertainment of intervention:
  - a. Health record\*
  - b. Structured interview\*
  - c. Written self-report
  - d. No description
- 4) Demonstration that outcome of interest was not present the start of the study:
  - a. Yes\*
  - b. No

**Comparability**

- 1) Comparability of cohorts on the basis of the design or analysis:
  - a. Study controls for age, antibiotic/probiotic exposure\*
  - b. Study controls for an additional factors\*

**Outcome**

- 1) Assessment of outcome:
  - a. Independent blind assessment\*
  - b. Record linkage\*
  - c. Self report
  - d. No description
- 2) Was follow-up long enough for outcomes:
  - a. Yes (median duration of follow-up 4 weeks)\*
  - b. No
- 3) Adequacy of follow-up cohort:
  - a. Complete follow-up\*
  - b. Minimal loss to follow-up (<20%)\*
  - c. Follow-up rate <80% and no description of losses to follow-up
  - d. No statement

eAppendix 4C. Risk of bias assessment for source clinical studies utilized in health economic analysis of probiotics (observational studies – utilizing the Newcastle-Ottawa Quality Assessment Scale for Case-Control Studies)

	Selection (max 4 stars)	Comparability (max 2 stars)	Exposure (max 3 stars)
Source Studies: Allen et al. (2013)	N/A	N/A	N/A
Source Studies: Branch-Elliman et al. (2015)	N/A	N/A	N/A
Source Studies: Fansi et al. (2012)			
Suneshine and McDonald (2006) – case report only	0	0	*
Source Studies: Leal et al. (2016)			
Henrich et al. (2009)	****	**	***
Source Studies: Lenoir-Wijnkoop et al. (2014)	N/A	N/A	N/A
Source Studies: Shen et al. (2017)	N/A	N/A	N/A
Source Studies: Vermeersch et al. (2018)	N/A	N/A	N/A

*Selection*

- 1) Is the case definition adequate?:
  - a. Yes, with independent validation\*
  - b. Yes (i.e. record linkage), or based on self-reports
  - c. No description
- 2) Representativeness:
  - a. Consecutive or obvious representative series of cases\*
  - b. Potential for selection biases or not stated
- 3) Selection of controls:
  - a. Hospital controls\*
  - b. No description
- 4) Definition of controls:
  - a. No history of disease (end-point)\*
  - b. No description of source



















*Comparability*

- 1) Comparability of cases and controls on the basis of design or analysis:
  - a. Study controls for age, antibiotic/probiotic exposure\*
  - b. Study controls for an additional factors\*

*Outcome*

- 1) Ascertainment of outcome:
  - a. Secure medical record\*
  - b. Structured interview where to blind to case/control status\*
  - c. Interview not blinded to case/control status
  - d. Written self-report or medical record only
  - e. No description
- 2) Same method of ascertainment of cases and controls:
  - a. Yes\*
  - b. No
- 3) Non-response rate:
  - a. Same rate for both groups\*
  - b. Non-respondents described
  - c. Rate different and no designation

eAppendix 4D. Risk of bias assessment for source clinical studies utilized in health economic analysis of probiotics (Evidence Partners and CLARITY for Risk of Bias of Surveys)

	Source population	Response Rate	Missing Data	Survey Clinical Sensible	Reliability/Validity of Survey Instrument
<u>Source Studies:</u> Allen et al. (2013)	N/A	N/A	N/A	N/A	N/A
<u>Source Studies:</u> Branch-Elliman et al. (2015)					
Branch-Elliman et. al (2013)					
<u>Source Studies:</u> Fansi et al. (2012)	N/A	N/A	N/A	N/A	N/A
<u>Source Studies:</u> Leal et al. (2016)	N/A	N/A	N/A	N/A	N/A
<u>Source Studies:</u> Lenoir-Wijnkoop et al. (2014)					
Baeur et al (2011)		Probably 			
<u>Source Studies:</u> Shen et al. (2017)					
Magill et al. (2014)					Probably 
Sullivan et al. (2006)					
<u>Source Studies:</u> Vermeersch et al. (2018)	N/A	N/A	N/A	N/A	N/A

CLARITY: Clinical Advances through Research and Information Translation



High risk of bias



Low risk of bias

Risk of Bias Instrument for Cross-Sectional Surveys of Attitudes and Practices (Agarwal et. al, evidencepartners.com)

- 1) Is the source population representative of the population of interest?
- 2) Is the response rate adequate?
- 3) Is there little missing data?
- 4) Is the survey clinically sensible?
- 5) Is there any evidence for the reliability and validity of the survey instrument?