

Appendix 4 – Risk of Bias

4.1. Uitgangsvraag 1 - Diagnostiek

QUADAS items	Salivary pepsin	pH-metry								Endoscopy			GI scintiscan		Upper GI series
	Farhath (2013) (1)	Boix-Ocha (1980) (2)	Arasu (1980) (3)	Da Dalt (1989) (4)	Kahn (1990) ¹ (5)	Cucchiara (1990) (6)	Cucchiara (1993) (7)	Ravelli (2006) (8)	Patra (2011) ² (9)	Cucchiara (1993) (7)	Ravelli (2006) (8)	Arasu (1980) (3)	Arasu (1980) (3)	Patra (2011) (9)	Arasu (1980) (3)
Was the spectrum of patients representative of the patients who will receive the test in practice?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is the reference standard likely to correctly classify the target condition? (yes if reference test was a clinical definition of GERD) ²	No*	No	No	No*	No	No	No*	No	No	No*	No	No	No	No	No
Was the execution of the index test described in sufficient detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the index test results interpreted without knowledge of the results of the reference test?	Unclear	No	Unclear	No	Yes	Yes	Unclear	Yes	Unclear	Histology: unclear Macroscopy: yes	Histology: unclear Macroscopy: yes	Unclear	Unclear	Unclear	Unclear
Were the reference test results interpreted without knowledge of the results of the index test?	Yes	No	Unclear	No	Yes	Yes	Unclear	Yes	Unclear	Histology: unclear Macroscopy: yes	Histology: unclear Macroscopy: yes	Unclear	Unclear	Unclear	Unclear
Were withdrawals from the study explained?	No	No	No	No	No	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No
Quality of evidence (Oxford Centre level of Evidence) ⁴	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

1. This study includes children with ALTE. This study was included because ALTE was regarded as a possible presentation of GERD.

2. This study includes children with recurrent or persistent wheezing (>3 attacks requiring hospital visit or almost daily wheezing for >4 weeks). Within this specific patient group, a division between children with and without a history suggestive of reflux is made. Therefore this study was included, but results should be interpreted in the light of the patient group (wheezers and not the general pediatric population) the study focuses on.

3. Since GERD signs and symptoms are not distinctive, and therefore, difficult to diagnose, it is not clear if the reference standard (signs and symptoms) used in the included studies was correctly classifying the target condition. Studies marked with an (*) however did provide a clear definition/description of GERD.

4. All studies are case-control study, poor or non-independent reference standard and thus level 4 studies: grade of recommendation C.

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References

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