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| **C1 - Summary of methodological quality of included studies on basis of six items from QUADAS checklist for each diagnostic study**  |
| **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: unclearMacroscopy: yes | Histology: unclearMacroscopy: 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: unclearMacroscopy: yes | Histology: unclearMacroscopy: 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 or 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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| **C2 - Summary of methodological quality of included studies on basis of the QUIPS tool for each prognostic study** |
| **Study, setting** | **Study Participation** | **Study attrition** | **Prognostic factor measurement** | **Outcome measurement** | **Study confounding** | **Statistical analysis and reporting** |
| **El-Serag (2004) (10)**  | MODERATE | HIGH | HIGH | LOW | NA | LOW |
| **Orenstein (2006) (11)**  | HIGH | HIGH | NA | LOW | NA | LOW |
| **Ruigomez (2015) (12)**  | LOW | MODERATE | LOW | MODERATE | NA | MODERATE |
| **Shepherd (1987) (13)**  | HIGH | HIGH | NA | MODERATE | NA | LOW |

NA = Not applicable

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