#### Frampton and Shepherd: Appendix A

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## Appendix A: Symptom assessment instruments reported in randomised controlled trials of inhaled asthma drugs

Data below correspond to those summarised in manuscript Table 2. Study numbers (*in brackets*) refer to the studies as numbered in Table 1. All data tables use the following format, with supporting text provided to clarify similarities or differences between assessment instruments:

| Column 1: A list of studies | Column 2: The | Column 3: Descriptions of the response |
|-----------------------------|---------------|----------------------------------------|
| that used the assessment    | numeric scale | categories on the numeric scale        |
| instrument as characterised |               |                                        |
| in columns 2 and 3          |               |                                        |

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#### Table A1. Asthma severity (day): 11 studies, 2-3 different instruments

2-3 different measurement instruments may have been used (due to differences in wording and in the number of response categories reported it is unclear whether study 14 shared the same instrument as studies 20, 45, 46, 57, 58, 78, 85).

| Connolly et al.    | 0 | No symptoms               |
|--------------------|---|---------------------------|
| (14)               | 3 | Symptoms most of the time |
|                    |   |                           |
| Aubier et al. (31) | 0 | No symptoms               |
| Tal et al. (52)    | 5 | Severe symptoms           |
| Bateman et al.     |   |                           |
| (64)               |   |                           |
|                    |   |                           |
| Basran et al. (20) | 0 | None                      |
| Zetterström et al. | 1 | Mild                      |
| (45)               | 2 | Moderate                  |
| de Benedictis et   | 3 | Severe                    |
| al. (46)           |   |                           |
| Lalloo et al. (57) |   |                           |
| Buhl et al. (58)   |   |                           |
| Kuna et al. (78)   |   |                           |
| Rabe et al. (85)   |   |                           |

#### Table A2. Asthma severity (night): 9 studies, 2-3 different instruments

2-3 different measurement instruments may have been used (due to differences in wording and in the number of response categories reported it is unclear whether study 14 shared the same instrument as studies 20, 45, 46, 57, 58, 78, 85).

| Connolly et al.    | 0 | No symptoms               |
|--------------------|---|---------------------------|
| (14)               | 3 | Symptoms most of the time |
|                    |   |                           |
| Tal et al. (52)    | 0 | No symptoms               |
|                    | 5 | Severe symptoms           |
|                    |   |                           |
| Basran et al. (20) | 0 | None                      |
| Zetterström et al. | 1 | Mild                      |
| (45)               | 2 | Moderate                  |
| de Benedictis et   | 3 | Severe                    |
| al. (46)           |   |                           |
| Lalloo et al. (57) |   |                           |
| Buhl et al. (58)   |   |                           |
| Kuna et al. (78)   |   |                           |
| Rabe et al. (85)   |   |                           |

#### Table A3. Asthma severity (AM): 3 studies, 2-3 different instruments

2-3 different measurement instruments may have been used (due to differences in wording of response category 3, it is unclear whether the instruments used in studies 54 and 56 were equivalent).

| Kuna et al. (54) | 0 | No symptoms             |  |
|------------------|---|-------------------------|--|
|                  | 3 | Incapacitating symptoms |  |
|                  |   |                         |  |
| Bateman et al.   | 0 | No symptoms             |  |

| (56)            | 3                                         | Severe symptoms                                               |  |
|-----------------|-------------------------------------------|---------------------------------------------------------------|--|
|                 |                                           |                                                               |  |
| Molimard et al. | Indi                                      | vidual symptom question from Asthma Control Questionnaire     |  |
| (68)            | (Jur                                      | niper et al. European Respiratory Journal, 1999; 14: 902-907) |  |
|                 |                                           |                                                               |  |
|                 | On                                        | average, during the past week, how bad were your asthma       |  |
|                 | symptoms when you woke up in the morning? |                                                               |  |
|                 | 0 No symptoms                             |                                                               |  |
|                 | 1                                         | 1 Very mild symptoms                                          |  |
|                 | 2 Mild symptoms                           |                                                               |  |
|                 | 3 Moderate symptoms                       |                                                               |  |
|                 | 4 Quite severe symptoms                   |                                                               |  |
|                 | 5                                         | 5 Severe symptoms                                             |  |
|                 | 6                                         | Very severe symptoms                                          |  |

#### Table A4. Asthma severity (PM): 2 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to differences in wording of response category 3, it is unclear whether the instruments used in studies 54 and 56 were equivalent).

| Kuna et al. (54) | 0 | No symptoms             |
|------------------|---|-------------------------|
|                  | 3 | Incapacitating symptoms |
|                  |   |                         |
| Bateman et al.   | 0 | No symptoms             |
| (56)             | 3 | Severe symptoms         |

#### Table A5. Asthma severity ('daily'): 3 studies, 2 different instruments

| Langdon &           | 0 | No description provided |
|---------------------|---|-------------------------|
| Thompson (11)       | 9 | No description provided |
|                     |   |                         |
| Busse et al. (55)   | 0 | No symptoms             |
| Jarjour et al. (86) | 5 | Severe symptoms         |

# **Table A6.** Asthma severity (timing not reported): 2 studies, 1-2 different instruments 1-2 different measurement instruments may have been used (due to incomplete reporting, it is unclear whether the instruments used in studies 1 and 26 were equivalent).

| Rafferty et al. (1) | Sc  | ale not | No symptoms     |
|---------------------|-----|---------|-----------------|
| (visual analogue    | rej | oorted  | Severe symptoms |
| scale)              |     |         |                 |
|                     |     |         |                 |
| Raphael et al.      | 0   | No astl | hma symptoms    |
| (26)                | 3   | Severe  | asthma symptoms |

#### Table A7. Asthma severity + activity (day): 16 studies, 3-14 different scales

3-14 different measurement instruments may have been used (due to differences in wording the response categories and in the number of items reported it is unclear whether studies 8, 9, 17, 21, 22, 23, 48, 63, 82, 87 shared the same instrument and whether studies 38, 73, 80 shared the same instrument).

| Fabbri et al. (6)   | 0                                                                 | Very well, no symptoms                                           |  |
|---------------------|-------------------------------------------------------------------|------------------------------------------------------------------|--|
| Pauwels et al.      | 1                                                                 | A few symptoms (not troublesome)                                 |  |
| (23)                | 2                                                                 | Asthma troublesome                                               |  |
|                     | 3                                                                 | Asthma bad, not able to carry out daily activities as normal     |  |
|                     |                                                                   |                                                                  |  |
| Agertoft &          | 0                                                                 | None (very good day, activities not restricted)                  |  |
| Pedersen (21)       | 1                                                                 | Mild wheezing or breathlessness (e.g., when exercising or in a   |  |
|                     |                                                                   | hurry but activities not restricted)                             |  |
|                     | 2                                                                 | Moderate (some discomfort but able to carry out most of daily    |  |
|                     |                                                                   | activities)                                                      |  |
|                     | 3                                                                 | Severe or incapacitating (inability to attend school or do usual |  |
|                     |                                                                   | activities)                                                      |  |
|                     |                                                                   |                                                                  |  |
| Ige et al. (48)     | 0                                                                 | No asthmatic symptoms                                            |  |
|                     | 1                                                                 | Mild asthmatic symptoms                                          |  |
|                     | 2                                                                 | Moderate asthmatic symptoms which interfered with some           |  |
|                     |                                                                   | activities                                                       |  |
|                     | 3                                                                 | Severe asthmatic symptoms which interfered with most             |  |
|                     |                                                                   | activities                                                       |  |
|                     | 1.                                                                |                                                                  |  |
| Schiccitano et al.  | 0                                                                 | No symptoms                                                      |  |
| (63)                | 1                                                                 | Aware of asthma symptoms but can easily tolerate them            |  |
|                     | 2                                                                 | Asthma causing enough discomfort to cause problems with          |  |
|                     | _                                                                 | normal activities/sleep                                          |  |
|                     | 3                                                                 | Unable to do normal activities/sleep because of asthma           |  |
| T 11 1 . 1          |                                                                   |                                                                  |  |
| Lundback et al.     | 0                                                                 | No asthma, normal unrestricted activity                          |  |
| (8)                 | 3                                                                 | Asthma bad; could not go to work or do housework or carry        |  |
|                     |                                                                   | out usual activities at all because short of breath              |  |
| Custoffson et al    |                                                                   | No symptoms                                                      |  |
| Gustaffson et al.   | 3                                                                 | No symptoms                                                      |  |
| (9)                 | 3                                                                 | Unable to carry out daily activities                             |  |
| Lorentzen et al.    | 0                                                                 | No oothmo                                                        |  |
|                     | 3                                                                 | No asthma                                                        |  |
| (17)                | 3                                                                 | Unable to carry out usual activities                             |  |
| O'Ryma at al        | 0                                                                 | No asthma symptoms                                               |  |
| O'Byrne et al. (71) | 3                                                                 | Unable to undertake normal activities [or to sleep] because of   |  |
| Pohunek et al.      | 3                                                                 | symptoms                                                         |  |
| (87)                |                                                                   | Symptoms                                                         |  |
| (01)                | 1                                                                 |                                                                  |  |
| Bateman et al.      | 0                                                                 | No symptoms                                                      |  |
| (82)                | 3                                                                 | Symptoms so severe that patient could not perform normal         |  |
| (=)                 |                                                                   | daily activities                                                 |  |
| <u> </u>            | 1                                                                 |                                                                  |  |
|                     |                                                                   |                                                                  |  |
| Yiallouros et al.   | 4-point   Severity + activity assessed but no description provide |                                                                  |  |
| (22)                | sca                                                               |                                                                  |  |
|                     | •                                                                 |                                                                  |  |
| Zietlowski et al.   | 0                                                                 | No symptoms                                                      |  |
| (83)                | 4                                                                 | Asthma very bad, unable to carry out daily activities as usual   |  |
|                     | •                                                                 |                                                                  |  |
| Malone et al.       | 0                                                                 | No symptoms                                                      |  |
|                     |                                                                   | ·                                                                |  |

| (73)             | 5 | Severe symptoms that prevented normal daily activities        |
|------------------|---|---------------------------------------------------------------|
|                  |   |                                                               |
| Jenkins et al.   | 0 | No symptoms                                                   |
| (38)             | 5 | Symptoms so severe that the patient could not (go to) work or |
| Dahl et al. (80) |   | perform normal daily activities                               |

#### Table A8. Asthma severity + symptom duration + activity (day): 12 studies, 3-12 different instruments

3-12 different measurement instruments may have been used (due to differences in wording the ared the

|                  | es it | is unclear whether studies 12, 18, 24, 32, 34, 41, 44, 49, 65, 69 s            |
|------------------|-------|--------------------------------------------------------------------------------|
| Bergmann et al.  | 0     | No symptoms                                                                    |
| (61)             | 1     | Symptoms for one short period during the day                                   |
|                  | 2     | Symptoms for two or more short periods, which did not affect normal activity   |
|                  | 3     | Frequent symptoms during the day, which did not affect normal activity         |
|                  | 4     | Symptoms for most of the day which affected normal daily activity              |
| Boe et al. (12)  | 0     | No symptoms during the day                                                     |
| Ringdal et al.   | 1     | Symptoms for one short period during the day                                   |
| (18)             | 2     | Symptoms for two or more short periods during the day                          |
| Bateman et al.   | 3     | Symptoms for most of the day which did not affect my normal                    |
| (24)             |       | daily activities                                                               |
| Chapman et al.   | 4     | Symptoms for most of the day which did affect my normal                        |
| (32)             |       | daily activities                                                               |
| Van den Berg et  | 5     | Symptoms so severe that I could not go to work or perform                      |
| al. (41)         |       | normal daily activities                                                        |
| Johansson et al. |       |                                                                                |
| (44)             |       |                                                                                |
| Ringdal et al.   | 0     | No symptoms during the day                                                     |
| (49)             | 1     | Symptoms for one short period during the day                                   |
| ,                | 2     | Symptoms for two or more short periods during the day                          |
|                  | 3     | Symptoms for most of the day that did not affect normal daily activity         |
|                  | 4     | Symptoms for most of the day that did affect normal daily activity             |
|                  | 5     | Symptoms so severe that they affected work or school and normal daily activity |
| A -11 ( 1        |       | NT                                                                             |
| Aalbers et al.   | 0     | No symptoms                                                                    |
| (65)             | 1     | Symptoms for one short period                                                  |
|                  | 2     | Symptoms for two or more short periods                                         |
|                  | 3     | Symptoms for most of the day that did not affect normal daily activities       |
|                  | 1 1   | Symptoms for most of the day that did affect normal daily                      |

| Aalbers et al. | 0 | No symptoms                                                   |
|----------------|---|---------------------------------------------------------------|
| (65)           | 1 | Symptoms for one short period                                 |
|                | 2 | Symptoms for two or more short periods                        |
|                | 3 | Symptoms for most of the day that did not affect normal daily |
|                |   | activities                                                    |
|                | 4 | Symptoms for most of the day that did affect normal daily     |
|                |   | activities                                                    |
|                | 5 | Symptoms so severe that normal daily activities could not be  |
|                |   | performed                                                     |

| FitzGerald et al.     | 0 No symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| (69)                  | 1 Symptoms for one short period                                                                                                                                                                                                                                                                                                                                                                                                                             |
|                       | 2 Symptoms for two or more short periods                                                                                                                                                                                                                                                                                                                                                                                                                    |
|                       | 3 Symptoms for most of the 24-hour period that did not affect                                                                                                                                                                                                                                                                                                                                                                                               |
|                       | normal activities                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|                       | 4 Symptoms for most of the 24-hour period that did affect                                                                                                                                                                                                                                                                                                                                                                                                   |
|                       | normal activities                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|                       | 5 Symptoms so severe that normal activities could not be                                                                                                                                                                                                                                                                                                                                                                                                    |
|                       | performed                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Ferguson et al.       | 0 None                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| (34)                  | 1 1 short period                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|                       | 2 2 or more short periods                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|                       | 3 Most of the day, activity not affected                                                                                                                                                                                                                                                                                                                                                                                                                    |
|                       | 4 Most of the day, activity reduced                                                                                                                                                                                                                                                                                                                                                                                                                         |
|                       | 5 Severe, unable to go to school                                                                                                                                                                                                                                                                                                                                                                                                                            |
|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Horiguchi et al.      | Mean score calculated from 4 questions using a                                                                                                                                                                                                                                                                                                                                                                                                              |
| Horiguchi et al. (84) | symptom diary scale from Santanello et al. European Respiratory                                                                                                                                                                                                                                                                                                                                                                                             |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651                                                                                                                                                                                                                                                                                                                                                                  |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?                                                                                                                                                                                                                                                                                                        |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651                                                                                                                                                                                                                                                                                                                                                                  |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?                                                                                                                                                                                                                                                                                                        |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time                                                                                                                                                                                                                                                                                    |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time                                                                                                                                                                                                                                                                  |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today?                                                                                                                                                                                                         |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today?  0 Not at all bothered                                                                                                                                                                                  |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today?  0 Not at all bothered 6 Severely bothered                                                                                                                                                              |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today?  0 Not at all bothered 6 Severely bothered (Q3) How much activity could you do today?  0 More than usual activity 6 Less than usual activity                                                            |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today? 0 Not at all bothered 6 Severely bothered (Q3) How much activity could you do today? 0 More than usual activity 6 Less than usual activity (Q4) How often did your asthma affect your activities today? |
| _                     | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today?  0 Not at all bothered 6 Severely bothered (Q3) How much activity could you do today?  0 More than usual activity 6 Less than usual activity                                                            |
|                       | symptom diary scale from Santanello et al. European Respiratory Journal, 1997; 10: 646-651  (Q1) How often did you experience asthma symptoms today?  0 None of the time 6 All of the time (Q2) How much did your asthma symptoms bother you today? 0 Not at all bothered 6 Severely bothered (Q3) How much activity could you do today? 0 More than usual activity 6 Less than usual activity (Q4) How often did your asthma affect your activities today? |

#### Table A9. Cough (day): 4 studies, 1-3 different instruments

1-3 different measurement instruments may have been used (due to differences in coding the 3-4-point numeric scales by studies 2, 13, 35 and lack of description of the response categories in study 22 it is unclear whether these studies shared the same instrument).

| Tjwa (13)         | 0       | No sy  | ymptoms                                    |
|-------------------|---------|--------|--------------------------------------------|
| Jager et al. (35) | 1       | Mild   |                                            |
|                   | 2       | Mode   | erate                                      |
|                   | 3       | Sever  | re symptoms                                |
|                   |         |        |                                            |
| Ebden et al. (2)  | 1       | None   |                                            |
|                   | 2       | Little |                                            |
|                   | 3       | Mode   | erately bad                                |
|                   | 4       | Sever  | re                                         |
|                   |         |        |                                            |
| Yiallouros et al. | 4-point |        | Cough assessed but no description provided |
| (22)              | scale   |        |                                            |

1-2 different measurement instruments may have been used (due to lack of description of the response categories in study 22 it is unclear whether this shared the same instrument as studies 13, 35).

| Tjwa (13)         | 0 | No symptoms     |
|-------------------|---|-----------------|
| Jager et al. (35) | 1 | Mild            |
|                   | 2 | Moderate        |
|                   | 3 | Severe symptoms |

| Yiallouros et al. | 4-point | Cough assessed but no description provided |
|-------------------|---------|--------------------------------------------|
| (22)              | scale   |                                            |

#### Table A11. Cough (AM): 3 studies, 1 instrument

1 measurement instrument appears to have been used as there is only a minor difference between studies, in the wording of response category 2.

| Bousquet et al.  | 0 | None                                                   |
|------------------|---|--------------------------------------------------------|
| (37)             | 1 | Noticeable                                             |
| O' Connor et al. | 2 | Annoying, some interference with daily activities      |
| (42)             | 3 | Very uncomfortable, interference with daily activities |

| Corren et al. (53) | 0 | None                                                     |
|--------------------|---|----------------------------------------------------------|
|                    | 1 | Noticeable                                               |
|                    | 2 | Annoying                                                 |
|                    | 3 | Very uncomfortable and interfered with normal activities |

#### Table A12. Cough (PM): 2 studies, 1 instrument

1 measurement instrument appears to have been used as there are only minor differences between studies, in the wording of response categories 2 and 3.

| Bousquet et al. | 0 | None                                                   |
|-----------------|---|--------------------------------------------------------|
| (37)            | 1 | Noticeable                                             |
|                 | 2 | Annoying, some interference with daily activities      |
|                 | 3 | Very uncomfortable, interference with daily activities |

| Corren et al. (53) | 0 | None                                                     |
|--------------------|---|----------------------------------------------------------|
|                    | 1 | Noticeable                                               |
|                    | 2 | Annoying                                                 |
|                    | 3 | Very uncomfortable and interfered with normal activities |

#### Table A13. Cough ('daily'): 2 studies, 1 instrument

| Kavuru et al.  | 0 | No symptoms                                             |
|----------------|---|---------------------------------------------------------|
| (39)           | 5 | Symptoms that severely interfered with daily activities |
| Shapiro et al. |   |                                                         |
| (40)           |   |                                                         |

#### Table A14. Cough (24-hour period): 2 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to lack of description of the instrument in study 43 it is unclear whether this study shared the same instrument as study 25).

| Dal Negro et al. | 0 | None     |
|------------------|---|----------|
| (25)             | 1 | Mild     |
|                  | 2 | Moderate |
|                  | 3 | Severe   |

| Aubier et al. (43) | Scale not | No description provided |
|--------------------|-----------|-------------------------|
|                    | reported  |                         |

#### Table A15. Dyspnea (day): 4 studies, 3 different instruments

| Tjwa (13)         | 0 | No symptoms     |
|-------------------|---|-----------------|
| Jager et al. (35) | 1 | Mild            |
|                   | 2 | Moderate        |
|                   | 3 | Severe symptoms |

| Bootsma et al. | 0-100 visual analogue scale |
|----------------|-----------------------------|
| (15)           |                             |

| Molimard et al. | Indiv  | Individual symptom question from Asthma Control Questionnaire    |  |  |  |
|-----------------|--------|------------------------------------------------------------------|--|--|--|
| (68)            | (Juni) | (Juniper et al. European Respiratory Journal, 1999; 14: 902-907) |  |  |  |
|                 |        |                                                                  |  |  |  |
|                 | In ger | In general, during the past week, how much shortness of breath   |  |  |  |
|                 | did yo | did you experience because of you asthma?                        |  |  |  |
|                 | 0      | 0 None                                                           |  |  |  |
|                 | 1      | A very little                                                    |  |  |  |
|                 | 2      | A little                                                         |  |  |  |
|                 | 3      | 3 A moderate amount                                              |  |  |  |
|                 | 4      | 4 Quite a lot                                                    |  |  |  |
|                 | 5      | 5 A great deal                                                   |  |  |  |
|                 | 6      | A very great deal                                                |  |  |  |

#### Table A16. Dyspnea (night): 3 studies, 2 different instruments

| Tjwa (13)         | 0 | No symptoms     |
|-------------------|---|-----------------|
| Jager et al. (35) | 1 | Mild            |
|                   | 2 | Moderate        |
|                   | 3 | Severe symptoms |

| Bootsma et al. | 0-100 visual analogue scale |
|----------------|-----------------------------|
| (15)           |                             |

#### Table A17. Dyspnea (AM): 3 studies, 1 instrument

1 measurement instrument appears to have been used as there are only minor differences between studies, in the wording of response categories 2 and 3.

| Bousquet et al.  | 0 | None                                                   |
|------------------|---|--------------------------------------------------------|
| (37)             | 1 | Noticeable                                             |
| O' Connor et al. | 2 | Annoying, some interference with daily activities      |
| (42)             | 3 | Very uncomfortable, interference with daily activities |

| Corren et al. (53) | 0 | None                                                     |
|--------------------|---|----------------------------------------------------------|
|                    | 1 | Noticeable                                               |
|                    | 2 | Annoying                                                 |
|                    | 3 | Very uncomfortable and interfered with normal activities |

#### Table A18. Dyspnea (PM): 2 studies, 1 instrument

1 measurement instrument appears to have been used as there are only minor differences between studies, in the wording of response categories 2 and 3.

| Bousquet et al. | 0 | None                                                   |  |
|-----------------|---|--------------------------------------------------------|--|
| (37)            | 1 | Noticeable                                             |  |
|                 | 2 | Annoying, some interference with daily activities      |  |
|                 | 3 | Very uncomfortable, interference with daily activities |  |

| Corren et al. (53) | 0 | None                                                     |
|--------------------|---|----------------------------------------------------------|
|                    | 1 | Noticeable                                               |
|                    | 2 | Annoying                                                 |
|                    | 3 | Very uncomfortable and interfered with normal activities |

#### Table A19. Dyspnea ('daily'): 2 studies, 1 instrument

| Kavuru et al.  | 0 | No symptoms                                             |
|----------------|---|---------------------------------------------------------|
| (39)           | 5 | Symptoms that severely interfered with daily activities |
| Shapiro et al. |   |                                                         |
| (40)           |   |                                                         |

#### Table A20. Dyspnea (24-hour period): 2 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to lack of description of the instrument in study 43 it is unclear whether this study shared the same instrument as study 25).

| Dal Negro et al. | 0 | None     |
|------------------|---|----------|
| (25)             | 1 | Mild     |
|                  | 2 | Moderate |
|                  | 3 | Severe   |

| Aubier et al. (43) | Scale not | No description provided |
|--------------------|-----------|-------------------------|
|                    | reported  |                         |

#### Table A21. Dyspnea (timing not reported): 1 study, 1 instrument

| Prasad et al. (60) | 0 | No dyspnea       |  |
|--------------------|---|------------------|--|
|                    | 1 | Mild dyspnea     |  |
|                    | 2 | Moderate dyspnea |  |
|                    | 3 | Severe dyspnea   |  |

#### Table A22. Wheeze (day): 5 studies, 2-4 different instruments

2-4 different measurement instruments may have been used (due to differences in coding the 3-4-point numeric scales by studies 2, 13, 35 and lack of description of the response categories in study 22 it is unclear whether these studies shared the same instrument).

| Ebden et al. (2)  | 1 N                                                              | lone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |
|-------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|                   | 2 L                                                              | ittle                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
|                   | 3 N                                                              | Inderately bad                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
|                   | 4 S                                                              | evere                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
|                   |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
| Tjwa (13)         | 0 N                                                              | lo symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |  |
| Jager et al. (35) | 1 N                                                              | fild                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |
| _                 | 2 N                                                              | Noderate Today Tod |  |
|                   | 3 S                                                              | evere symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
|                   |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
| Molimard et al.   | Individual symptom question from Asthma Control Questionnaire    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
| (68)              | (Juniper et al. European Respiratory Journal, 1999; 14: 902-907) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   | In general, during the past week, how much of the time did you   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   | wheeze?                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   | 0                                                                | 0 Not at all                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |
|                   | 1                                                                | 1 Hardly any of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |
|                   | 2                                                                | 2 A little of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|                   | 3                                                                | A moderate amount of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |
|                   | 4                                                                | A lot of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |
|                   | 5                                                                | Most of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  |
|                   | 6                                                                | All of the time                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
| Yiallouros et al. | 4-                                                               | Wheeze assessed but no description provided                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |  |
| (22)              | point                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                   | scale                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |

#### Table A23. Wheeze (night): 3 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to lack of description of the instrument in study 22 it is unclear whether this study shared the same instrument as studies 13, 35).

| Tjwa (13)         | 0 | No symptoms     |  |
|-------------------|---|-----------------|--|
| Jager et al. (35) | 1 | Mild            |  |
|                   | 2 | Moderate        |  |
|                   | 3 | Severe symptoms |  |

| Yiallouros et al. | 4-    | Wheeze assessed but no description provided |
|-------------------|-------|---------------------------------------------|
| (22)              | point |                                             |
|                   | scale |                                             |

#### Table A24. Wheeze (AM): 3 studies, 1 instrument

1 measurement instrument appears to have been used as there are only minor differences between studies, in the wording of response categories 2 and 3.

| Bousquet et al.  | 0 | None                                                   |  |
|------------------|---|--------------------------------------------------------|--|
| (37)             | 1 | Noticeable                                             |  |
| O' Connor et al. | 2 | Annoying, some interference with daily activities      |  |
| (42)             | 3 | Very uncomfortable, interference with daily activities |  |

| Corren et al. (53) | 0 | None       |
|--------------------|---|------------|
|                    | 1 | Noticeable |

| 2 | Annoying                                                 |
|---|----------------------------------------------------------|
| 3 | Very uncomfortable and interfered with normal activities |

#### Table A25. Wheeze (PM): 2 studies, 1 instrument

1 measurement instrument appears to have been used as there are only minor differences between studies, in the wording of response categories 2 and 3.

| Bousquet et al. | 0 | None                                                   |  |
|-----------------|---|--------------------------------------------------------|--|
| (37)            | 1 | Noticeable                                             |  |
|                 | 2 | Annoying, some interference with daily activities      |  |
|                 | 3 | Very uncomfortable, interference with daily activities |  |

| Corren et al. (53) | 0 | None                                                     |  |
|--------------------|---|----------------------------------------------------------|--|
|                    | 1 | Noticeable                                               |  |
|                    | 2 | Annoying                                                 |  |
|                    | 3 | Very uncomfortable and interfered with normal activities |  |

#### Table A26. Wheeze ('daily'): 1 study, 1 instrument

| Kavuru et al.  | 0 | No symptoms                                             |
|----------------|---|---------------------------------------------------------|
| (39)           | 5 | Symptoms that severely interfered with daily activities |
| Shapiro et al. |   |                                                         |
| (40)           |   |                                                         |

#### Table A27. Wheeze (24-hour period): 2 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to lack of description of the instrument in study 43 it is unclear whether this study shared the same instrument as study 25).

| Dal Negro et al. | 0 | None     |  |
|------------------|---|----------|--|
| (25)             | 1 | Mild     |  |
|                  | 2 | Moderate |  |
|                  | 3 | Severe   |  |

| Aubier et al. (43) | Scale not | No description provided |
|--------------------|-----------|-------------------------|
|                    | reported  |                         |

#### Table A28. Cough + dyspnea ('daily'): 1 study, 1 instrument

| Parakh et al. (50)   | Scale not | No description provided  |
|----------------------|-----------|--------------------------|
| 1 arakii ct ai. (37) |           | Two description provided |
|                      | reported  |                          |

#### Table A29. Cough + dyspnea + wheeze ('daily'): 1 study, 1 instrument

| Nathan et al. (80) | 0 | No symptoms                                              |
|--------------------|---|----------------------------------------------------------|
| (stated that used  | 5 | Symptoms so severe they interfered with daily activities |
| the same           |   |                                                          |
| instrument as      |   |                                                          |
| studies 39, 40)    |   |                                                          |

#### Table A30. Dyspnea + wheeze + activity (day): 2 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (due to differences in wording response category 3 it is unclear whether studies 7, 16 shared the same instrument).

| Barnes et al. (7) | 0 | None                                                          |
|-------------------|---|---------------------------------------------------------------|
|                   | 1 | Wheezing or shortness of breath on strenuous                  |
|                   |   | exercise/hurrying, otherwise asthma not unduly troublesome    |
|                   | 2 | Wheezing or shortness of breath most of the day, normal       |
|                   |   | activities difficult                                          |
|                   | 3 | Unable to carry out normal activities because of shortness of |
|                   |   | breath                                                        |
|                   |   |                                                               |
| Ayres et al. (16) | 0 | No asthma, normal unrestricted activity                       |
|                   | 1 | Wheezing or shortness of breath on strenuous                  |
|                   |   | exercise/hurrying, otherwise asthma not unduly troublesome    |
|                   | 2 | Wheezing or shortness of breath most of the day, normal       |
|                   |   | activities difficult                                          |

# **Table A31. Dyspnea** + wheeze + activity (on exercise): 2 studies, 1-2 different instruments 1-2 different measurement instruments may have been used (due to differences in the wording of response categories it is unclear whether studies 9, 21 measured the same symptoms).

out usual activities because of shortness of breath

Asthma bad, could not go to work or do housework or carry

| Gustaffson et al. | 0 | Not breathless                                                  |  |
|-------------------|---|-----------------------------------------------------------------|--|
| (9)               | 3 | Very breathless, tight chested, and wheezy when walking;        |  |
|                   |   | unable to run or play games                                     |  |
|                   |   |                                                                 |  |
| Agertoft &        | 0 | None (can walk, run, or participate in sports and play with no  |  |
| Pedersen (21)     |   | problems)                                                       |  |
|                   | 1 | Mild (no problems when walking but a little wheezing and        |  |
|                   |   | breathlessness when running, participating in sports/playing or |  |
|                   |   | when in a hurry; otherwise activities not restricted)           |  |
|                   | 2 | Moderate (breathlessness and wheezing when walking, which       |  |
|                   |   | worsens when running or participating in sports/playing)        |  |
|                   | 3 | Severe or incapacitating (difficulties when walking and         |  |
|                   |   | inability to run or participate in sports/play)                 |  |

#### Table A32. Unspecified symptoms (day): 6 studies, 3-6 different instruments

2-5 different measurement instruments may have been used (due to lack of description of the instruments in studies 19, 66, 77 it is unclear whether these studies shared the same instrument as study 62 or study 75).

| Hoekx et al. (19) | Scale not | No description provided |
|-------------------|-----------|-------------------------|
| Niphadkar et al.  | reported  | •                       |
| (66)              | •         |                         |
| Lundbäck et al.   |           |                         |
| (77)              |           |                         |

| Jenkins et al. | 0 | No description provided |
|----------------|---|-------------------------|
| (81)           | 3 | No description provided |

| Zhong et al. (62) | 0 | No description provided                                   |  |
|-------------------|---|-----------------------------------------------------------|--|
|                   | 5 | No description provided                                   |  |
|                   |   |                                                           |  |
| Buhl et al. (75)  | 0 | No asthma-related symptoms                                |  |
|                   | 4 | Highest discomfort resulting from asthma-related symptoms |  |

#### Table A33. Unspecified symptoms (night): 6 studies, 3-6 different scales

2-5 different measurement instruments may have been used (due to lack of description of the instruments in studies 19, 29, 75, 77 it is unclear whether these studies shared the same instrument).

| Hoekx et al. (19)<br>Lundbäck et al.<br>(77) | Scale not reported |                            | No description provided                             |
|----------------------------------------------|--------------------|----------------------------|-----------------------------------------------------|
| Jenkins et al.                               | 0 1                | Vo des                     | cription provided                                   |
| (81)                                         | 3 <i>N</i>         | Vo des                     | cription provided                                   |
|                                              |                    |                            |                                                     |
| Heinig et al. (29)                           | 0 <i>N</i>         | Vo des                     | cription provided                                   |
|                                              | 4 <i>N</i>         | Vo des                     | cription provided                                   |
|                                              |                    |                            |                                                     |
| Buhl et al. (75)                             | 0 N                | No asthma-related symptoms |                                                     |
|                                              | 4 F                | Highes                     | t discomfort resulting from asthma-related symptoms |
|                                              |                    |                            |                                                     |
| Zhong et al. (62)                            | 0 <i>N</i>         | Vo des                     | cription provided                                   |
|                                              | 5 <i>N</i>         | Vo des                     | cription provided                                   |

#### Table A34. Unspecified symptoms (AM): 1 study, 1 instrument

| Koopmans et al. | 0 | No description provided |
|-----------------|---|-------------------------|
| (76)            | 4 | No description provided |

#### Table A35. Unspecified symptoms (PM): 1 study, 1 instrument

| Koopmans et al. | 0 | No description provided |
|-----------------|---|-------------------------|
| (76)            | 5 | No description provided |

#### Table A36. Unspecified symptoms ('daily'): 3 studies, 2-3 different instruments

2-3 different measurement instruments may have been used (due to lack of description of the instrument in study 47 it is unclear whether this was the same as used in study 10 or study 33).

| Langdon &       | 0 No description provided                                        |
|-----------------|------------------------------------------------------------------|
| Capsey (10)     | 3 No description provided                                        |
|                 |                                                                  |
| Rao et al. (33) | 0 No description provided (scale = sum of 0-2 day, 0-2 night, 0- |
|                 | 6 2 activity                                                     |
|                 |                                                                  |
| Szefler et al.  | Scale not   No description provided                              |
| (47)            | renorted                                                         |

## **Table A37.** Unspecified symptoms (timing not reported): 2 studies, 1-2 different instruments 1-2 different measurement instruments may have been used (due to lack of description of the instrument in study 72 it is unclear whether this was the same as used in study 29).

| Heinig et al. (29) | 0   | No des  | scription provided      |
|--------------------|-----|---------|-------------------------|
|                    | 5   | No des  | scription provided      |
|                    |     |         |                         |
| Altintas et al.    | Sco | ale not | No description provided |
| (72)               | rep | orted   |                         |

# **Table A38.** Waking due to asthma severity (night): 15 studies, 2-15 different scales 2-15 different measurement instruments may have been used (due to differences in wording the response categories it is unclear whether studies 21, 48, 71, 82 87 shared the same 4-point instrument and whether studies 12, 18, 24, 32, 34, 41, 44, 49, 61, 80 shared the same 5-point instrument).

| msuument).       |   |                                                                  |
|------------------|---|------------------------------------------------------------------|
| Agertoft &       | 0 | None (peaceful night, slept well)                                |
| Pedersen (21)    | 1 | Mild (peaceful night but woke once or woke early because of      |
|                  |   | asthma symptoms)                                                 |
|                  | 2 | Moderate (woke two or three times because of asthma              |
|                  |   | symptoms)                                                        |
|                  | 3 | Severe (awake most of the night because of asthma                |
|                  |   | symptoms)                                                        |
|                  |   |                                                                  |
| Ige et al. (48)  | 0 | No asthmatic symptoms                                            |
|                  | 1 | Mild asthmatic symptoms                                          |
| (Same wording    | 2 | Moderate asthmatic symptoms which interfered with some           |
| used for day     |   | activities                                                       |
| activity & night | 3 | Severe asthmatic symptoms which interfered with most             |
| waking)          |   | activities                                                       |
| <b>-</b>         |   |                                                                  |
| O'Byrne et al.   | 0 | No asthma symptoms                                               |
| (71)             | 3 | Unable to undertake normal activities [or to sleep] because of   |
| Pohunek et al.   |   | symptoms                                                         |
| (87)             |   |                                                                  |
| Bateman et al.   | Λ | No symptoms                                                      |
| (82)             | 3 | No symptoms Symptoms so severe that patient did not sleep at all |
| (02)             | J | Symptoms so severe that patient did not sleep at an              |
| Boe et al. (12)  | 0 | No symptoms during the night                                     |
| Ringdal et al.   | 1 | Symptoms causing you/the patient to wake once or to wake         |
| (18)             |   | early                                                            |
| Bateman et al.   | 2 | Symptoms causing you/the patient to wake twice or more           |
| (24)             |   | (including waking early)                                         |
| Chapman et al.   | 3 | Symptoms causing you/the patient to be awake for most of the     |
| (32)             |   | night                                                            |
| van den Berg et  | 4 | Symptoms so severe that you/the patient did not sleep at all     |
| al. (41)         |   |                                                                  |
| Johannson et al. |   |                                                                  |
| (44)             |   |                                                                  |
| Ringdal et al.   |   |                                                                  |
| (49)             |   |                                                                  |

| Bergmann et al.  |   |                                                         |
|------------------|---|---------------------------------------------------------|
| (61)             |   |                                                         |
|                  |   |                                                         |
| Ferguson et al.  | 0 | None                                                    |
| (34)             | 1 | Wakened once                                            |
|                  | 2 | Wakened 2 or more times                                 |
|                  | 3 | Awake most of the night                                 |
|                  | 4 | Severe, unable to sleep                                 |
|                  |   |                                                         |
| Dahl et al. (80) | 0 | No symptoms                                             |
|                  | 4 | Symptoms so severe that the patient was unable to sleep |

#### Table A39. Waking due to cough or asthma (night): 2 studies, 1 instrument

| Fabbri et al. (6) | 0 | Slept through the night                            |
|-------------------|---|----------------------------------------------------|
| Pauwels et al.    | 1 | Slept well, woken early or once by asthma or cough |
| (23)              | 2 | Woken 2 or 3 times by cough or asthma              |
|                   | 3 | Bad night, kept awake most of the night by asthma  |

## Table A40. Waking due to cough, dyspnea or wheeze (night): 4 studies, 1-2 different instruments

1-2 different measurement instruments may have been used (for studies 5, 7, 16 differences in the wording of response categories appear minor, suggesting 1 instrument was used in these studies; study 8 did not report all response categories and it is unclear whether it shared the same instrument).

| Fitzgerald et al. | 0 | None                                                          |
|-------------------|---|---------------------------------------------------------------|
| (5)               | 1 | Symptoms caused by waking once or early                       |
| Barnes et al. (7) | 2 | Woken 2 or 3 times by cough, wheeze, breathlessness or asthma |
|                   | _ |                                                               |
|                   | 3 | Awake most of the night with cough, wheeze, breathlessness    |
|                   |   | or asthma                                                     |
|                   |   |                                                               |
| Ayres et al. (16) | 0 | Good night, slept well, no asthma                             |
|                   | 1 | Good night, slept well but woke early with wheeze or cough    |
|                   | 2 | Woken 2 or 3 times by cough, wheeze, breathlessness or        |
|                   |   | asthma                                                        |
|                   | 3 | Bad night, awake most of the night with cough, wheeze,        |
|                   |   | breathlessness or asthma                                      |
|                   |   |                                                               |
| Lundback et al.   | 0 | Good night, slept well, no asthma                             |
| (8)               | 3 | Bad night, awake most of the night with cough, wheeze,        |
|                   |   | breathlessness or asthma                                      |

#### Table A41. Waking due to unspecified symptoms (night): 10 studies, 4-10 different scales

4-10 different measurement instruments may have been used (due to differences in wording and lack of reporting response categories it is unclear whether studies 9, 17, 21, 31, 63 shared the same 4-point instrument, whether studies 38, 83 shared the same 5-point instrument and whether study 43 shared a 4- or 5-point instrument).

| Agertoft &             | 0                                        | None (peaceful night, slept well)                                                                                                                                                                                                                                                                                                                                                                                               |  |
|------------------------|------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Pedersen (21)          | 1                                        | Mild (peaceful night but woke once or early because of                                                                                                                                                                                                                                                                                                                                                                          |  |
| 1 caersen (21)         | 1                                        | asthma symptoms)                                                                                                                                                                                                                                                                                                                                                                                                                |  |
|                        | 2                                        | Moderate (woke two or three times because of asthma                                                                                                                                                                                                                                                                                                                                                                             |  |
|                        | -                                        | symptoms)                                                                                                                                                                                                                                                                                                                                                                                                                       |  |
|                        | 3                                        | Severe (awake most of the night because of asthma                                                                                                                                                                                                                                                                                                                                                                               |  |
|                        |                                          | symptoms)                                                                                                                                                                                                                                                                                                                                                                                                                       |  |
|                        |                                          | oj inpromoj                                                                                                                                                                                                                                                                                                                                                                                                                     |  |
| Schiccitano et al.     | 0                                        | No symptoms                                                                                                                                                                                                                                                                                                                                                                                                                     |  |
| (63)                   | 1                                        | Aware of asthma symptoms but can easily tolerate them                                                                                                                                                                                                                                                                                                                                                                           |  |
|                        | 2                                        | Asthma causing enough discomfort to cause problems with                                                                                                                                                                                                                                                                                                                                                                         |  |
|                        |                                          | normal activities/sleep                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|                        | 3                                        | Unable to do normal activities/sleep because of asthma                                                                                                                                                                                                                                                                                                                                                                          |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| Gustaffson et al.      | 0                                        | Slept through the night                                                                                                                                                                                                                                                                                                                                                                                                         |  |
| (9)                    | 3                                        | Awake most of the night                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| Lorentzen et al.       | 0                                        | Slept well, no asthma                                                                                                                                                                                                                                                                                                                                                                                                           |  |
| (17)                   | 3                                        | Awake most of the night                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| Aubier et al. (31)     | 0                                        | No symptoms                                                                                                                                                                                                                                                                                                                                                                                                                     |  |
|                        | 3                                        | Symptoms preventing and sleep [sic]                                                                                                                                                                                                                                                                                                                                                                                             |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| Jenkins et al.         | 0                                        | No symptoms                                                                                                                                                                                                                                                                                                                                                                                                                     |  |
| (38)                   | 4                                        | Unable to sleep at all because of asthma symptoms                                                                                                                                                                                                                                                                                                                                                                               |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| Zietlowski et al.      | 0                                        | No symptoms                                                                                                                                                                                                                                                                                                                                                                                                                     |  |
| (83)                   | 4                                        | Bad night, awake most of the night because of asthma                                                                                                                                                                                                                                                                                                                                                                            |  |
|                        |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
|                        |                                          | lividual symptom question from Asthma Control Questionnaire                                                                                                                                                                                                                                                                                                                                                                     |  |
| Molimard et al.        |                                          | (Juniper et al. European Respiratory Journal, 1999; 14: 902-907)                                                                                                                                                                                                                                                                                                                                                                |  |
| Molimard et al. (68)   |                                          | niper et al. European Respiratory Journal, 1999; 14: 902-907)                                                                                                                                                                                                                                                                                                                                                                   |  |
|                        | (Ju                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
|                        | (Ju                                      | average, during the past week, how often were you woken by                                                                                                                                                                                                                                                                                                                                                                      |  |
|                        | (Ju<br>On<br>you                         | average, during the past week, how often were you woken by a sthma during the night?                                                                                                                                                                                                                                                                                                                                            |  |
|                        | On you                                   | average, during the past week, how often were you woken by ar asthma during the night?  Never                                                                                                                                                                                                                                                                                                                                   |  |
|                        | On you 0                                 | average, during the past week, how often were you woken by ar asthma during the night?  Never  Hardly ever                                                                                                                                                                                                                                                                                                                      |  |
|                        | On you 0 1 2                             | average, during the past week, how often were you woken by ar asthma during the night?  Never  Hardly ever  A few minutes                                                                                                                                                                                                                                                                                                       |  |
|                        | On you 0 1 2 3                           | average, during the past week, how often were you woken by ar asthma during the night?  Never  Hardly ever  A few minutes  Several times                                                                                                                                                                                                                                                                                        |  |
|                        | On you 0 1 2 3 4                         | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times                                                                                                                                                                                                                                                                                |  |
|                        | On you 0 1 2 3 4 5                       | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times                                                                                                                                                                                                                                                             |  |
|                        | On you 0 1 2 3 4                         | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times                                                                                                                                                                                                                                                                                |  |
| (68)                   | On you 0 1 2 3 4 5 6                     | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma                                                                                                                                                                                                                           |  |
| (68)  Horiguchi et al. | On you 0 1 2 3 4 5 6                     | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma                                                                                                                                                                                                                           |  |
| (68)                   | On you 0 1 2 3 4 5 6                     | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma                                                                                                                                                                                                                           |  |
| (68)  Horiguchi et al. | (Ju On you 0 1 2 3 4 5 6                 | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  Imptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.                                                                                                                                 |  |
| (68)  Horiguchi et al. | (Ju On you 0 1 2 3 4 5 6                 | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  Imptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.  In dyou wake up with asthma symptoms. (This can be awakening                                                                   |  |
| (68)  Horiguchi et al. | (Ju On you 0 1 2 3 4 5 6                 | average, during the past week, how often were you woken by a asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  mptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.  d you wake up with asthma symptoms. (This can be awakening the middle of the night or on awakening in the morning)?              |  |
| (68)  Horiguchi et al. | (Ju   On you   O   1   2   3   4   5   6 | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  Imptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.  In you wake up with asthma symptoms. (This can be awakening the middle of the night or on awakening in the morning)?  No       |  |
| (68)  Horiguchi et al. | (Ju   On you   O   1   2   3   4   5   6 | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  Imptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.  In dyou wake up with asthma symptoms. (This can be awakening the middle of the night or on awakening in the morning)?  No Once |  |
| (68)  Horiguchi et al. | (Ju   On you   O   1   2   3   4   5   6 | average, during the past week, how often were you woken by ar asthma during the night?  Never Hardly ever A few minutes Several times Many times A great many times Unable to sleep because of asthma  Imptom diary scale from Santanello et al. European Respiratory arnal, 1997; 10: 646-651.  In you wake up with asthma symptoms. (This can be awakening the middle of the night or on awakening in the morning)?  No       |  |

reported

## $\begin{tabular}{ll} Table~A42.~Waking+dyspnea+wheeze+asthma~severity+activity~(24-hour~period):\\ 2~studies,~2~different~instruments \end{tabular}$

| Vogelmeier et al. | Sco                                                         | re calculated from symptoms section of ACQ-5 Asthma           |  |
|-------------------|-------------------------------------------------------------|---------------------------------------------------------------|--|
| (70)              | Control Questionnaire (Juniper et al. American Journal of   |                                                               |  |
| , ,               | Respiratory & Critical Care Medicine, 2000; 162: 1330-1334) |                                                               |  |
|                   |                                                             |                                                               |  |
|                   | (Q1                                                         | ) On average, during the past week, how often were you        |  |
|                   | wol                                                         | ken by your asthma during the night?                          |  |
|                   | 1                                                           | Hardly ever                                                   |  |
|                   | 2                                                           | A few times                                                   |  |
|                   | 3                                                           | Several times                                                 |  |
|                   | 4                                                           | Many times                                                    |  |
|                   | 5                                                           | A great many times                                            |  |
|                   | 6                                                           | Unable to sleep because of asthma                             |  |
|                   | (Q2                                                         | 2) On average, during the past week, how bad were your        |  |
|                   | asth                                                        | nma symptoms when you woke up in the morning?                 |  |
|                   | 0                                                           | No symptoms                                                   |  |
|                   | 1                                                           | Very mild symptoms                                            |  |
|                   | 2                                                           | Mild symptoms                                                 |  |
|                   | 3                                                           | Moderate symptoms                                             |  |
|                   | 4                                                           | Quite severe symptoms                                         |  |
|                   | 5                                                           | Severe symptoms                                               |  |
|                   | 6                                                           | Very severe symptoms                                          |  |
|                   | (Q3                                                         | 3) In general, during the past week, how limited were you in  |  |
|                   | you                                                         | r activities because of your asthma?                          |  |
|                   | 0                                                           | Not limited at all                                            |  |
|                   | 1                                                           | Very slightly limited                                         |  |
|                   | 2                                                           | Slightly limited                                              |  |
|                   | 3                                                           | Moderately limited                                            |  |
|                   | 4                                                           | Very limited                                                  |  |
|                   | 5                                                           | Extremely limited                                             |  |
|                   | 6                                                           | Totally limited                                               |  |
|                   |                                                             | ) In general, during the past week, how much shortness of     |  |
|                   | brea                                                        | ath did you experience because of your asthma?                |  |
|                   | 0                                                           | None                                                          |  |
|                   | 1                                                           | A very little                                                 |  |
|                   | 2                                                           | A little                                                      |  |
|                   | 3                                                           | A moderate amount                                             |  |
|                   | 4                                                           | Quite a lot                                                   |  |
|                   | 5                                                           | A great deal                                                  |  |
|                   | 6                                                           | A very great deal                                             |  |
|                   |                                                             | 5) In general, during the past week, how much of the time did |  |
|                   | you                                                         | wheeze?                                                       |  |
|                   | 0                                                           | Not at all                                                    |  |
|                   | 1                                                           | Hardly any of the time                                        |  |
|                   | 2                                                           | A little of the time                                          |  |
|                   | 3                                                           | A moderate amount of the time                                 |  |
|                   | 4                                                           | A lot of the time                                             |  |
|                   | 5                                                           | Most of the time                                              |  |
|                   | 6                                                           | All the time                                                  |  |

| Decembell of al  | C                                                                    |  |  |
|------------------|----------------------------------------------------------------------|--|--|
| Rosenhall et al. | Score calculated from symptoms section of mini Asthma Quality        |  |  |
| (50)             | of Life Questionnaire (miniAQLQ) (Juniper et al. European            |  |  |
|                  | Respiratory Journal, 1999; 14 : 32-38)                               |  |  |
|                  | (Q1) In general, how much of the time during the last 2 weeks did    |  |  |
|                  | you feel short of breath as a result of your asthma?                 |  |  |
|                  | (Q2) In general, how much of the time during the last 2 weeks did    |  |  |
|                  | you feel bothered by coughing?                                       |  |  |
|                  | (Q3) In general, how much of the time during the last 2 weeks did    |  |  |
|                  | you experience a feeling of chest tightness or chest heaviness?      |  |  |
|                  | (Q4) In general, how much of the time during the last 2 weeks did    |  |  |
|                  | you have difficulty getting a good night's sleep as a result of your |  |  |
|                  | asthma?                                                              |  |  |
|                  | (Q5) In general, how much of the time during the last 2 weeks did    |  |  |
|                  | you experience a wheeze in your chest?                               |  |  |
|                  | 0 All of the time                                                    |  |  |
|                  | 1 Most of the time                                                   |  |  |
|                  | 2 A good bit of the time                                             |  |  |
|                  | 3 Some of the time                                                   |  |  |
|                  | 4 A little of the time                                               |  |  |
|                  | 5 Hardly any of the time                                             |  |  |
|                  | 6 None of the time                                                   |  |  |
|                  | 7 All of the time                                                    |  |  |