Correction

'Diagnosing Asthma in General Practice with Portable Exhaled Nitric Oxide Measurement – Results of a Prospective Diagnostic Study: FENO ≤ 16 ppb better than FENO ≤ 12 ppb to rule out mild and moderate to severe asthma

Antonius Schneider*1, Lisa Tilemann1, Tjard Schermer2, Lena Gindner1, Gunter Laux1, Joachim Szecsenyi1 and Franz Joachim Meyer3

Address: 1Department of General Practice and Health Services Research, University Hospital, University of Heidelberg, Heidelberg, Germany, 2Department of Primary Care Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands and 3Department of Cardiology, Pulmonology and Angiology, Medical Centre, University of Heidelberg, Heidelberg, Germany

Email: Antonius Schneider* - antonius.schneider@med.uni-heidelberg.de; Lisa Tilemann - lisa.tilemann@med.uni-heidelberg.de; Tjard Schermer - T.Schermer@hag.umcn.nl; Lena Gindner - lena.gindner@med.uni-heidelberg.de; Gunter Laux - gunter.laux@med.uni-heidelberg.de; Joachim Szecsenyi - joachim.szecsenyi@med.uni-heidelberg.de; Franz Joachim Meyer - joachim.meyer@med.uni-heidelberg.de

* Corresponding author

Published: 7 July 2009
Received: 1 July 2009
Accepted: 7 July 2009

In our study to evaluate the diagnostic accuracy of FENO measurement with NioxMino® for the diagnosis of asthma in general practice, we found the cut-off at FENO ≤ 12 ppb to rule out mild and moderate to severe asthma with a negative predictive value of 81% (95%CI 64–91%) [1]. We oriented ourselves at the already established value of 12 ppb [2]. However, we overlooked in the ROC analysis that the overall diagnostic accuracy improves slightly when the cut-off is chosen at FENO ≤ 16 ppb; and the range of the confidence interval narrows. Thus three patients need to be diagnosed for excluding asthma in order to save one bronchial provocation test when FENO ≤ 16 ppb is used as the cut-off point. With FENO ≤ 12 ppb five patients need to be tested in order to exclude asthma in one of them. Therefore, we suggest choosing FENO ≤ 16 ppb to rule out mild and moderate to severe asthma. This improves diagnostic efficiency compared to the ≤ 12 ppb cut-off point.

We would like to correct the following points in the manuscript:

In the Results section of the Abstract lines 6–7 should read as:

"16 ppb (n = 68; 42.5%), sensitivity was 79% (95%CI 67–88), specificity 55% (95%CI 45–64), PPV 50% (95%CI 40–60), NPV 82% (95%CI 72–90)*."

Also in line 7, "Three" should say "Two".

Table two [see Table 1 below] illustrates that the patient group with correctly excluded asthma by FENO measurement increases at FENO ≤ 16 ppb; and the range of the confidence interval narrows. Thus three patients need to be diagnosed for excluding asthma in order to save one bronchial provocation test when FENO ≤ 16 ppb is used as the cut-off point. With FENO ≤ 12 ppb five patients need to be tested in order to exclude asthma in one of them. Therefore, we suggest choosing FENO ≤ 16 ppb to rule out mild and moderate to severe asthma. This improves diagnostic efficiency compared to the ≤ 12 ppb cut-off point.

We would like to correct the following points in the manuscript:

In the Results section of the Abstract lines 6–7 should read as:

"16 ppb (n = 68; 42.5%), sensitivity was 79% (95%CI 67–88), specificity 55% (95%CI 45–64), PPV 50% (95%CI 40–60), NPV 82% (95%CI 72–90)*."

Also in line 7, "Three" should say "Two".
In the Conclusion section of the Abstract, in line 2, "FENO £ 12 ppb" should say "FENO £ 16 ppb".

In the Sensitivity analyses section, in line 2 of the third paragraph, "FENO £ 12 ppb" should say "FENO £ 16 ppb", "81% (95% CI 64–91)" should say "82% (95% CI 72–90)" and "34" should say "68". In line 4, "12 ppb" should say "16 ppb" and "increased up to 82% (95% CI 64–92)" should say "was 77% (95% CI 61–88)".

In the Discussion section, in line 4, "81%" should say "82%" and in line 5, "FENO £ 12" should say "FENO £ 16"

In the second paragraph, in line 1, "five" should say "three". In line 5, "16 patients had FENO £ 12 ppb" should say "37 patients had FENO £ 16 ppb". Also in line 5, "three" should say "two" and in lines 11 and 12 "FENO £ 12 ppb" should say "FENO £ 16 ppb" and 12 ppb<FENO should say 16 ppb<FENO.

In the third line of the third paragraph "12 to 46 ppb" should say "16 to 46 ppb" and in the seventh line, the sec-

| Table 1: Sensitivity (sens), specificity (spec), positive predictive value (PPV) and negative predictive value (NPV) at different cut-off points (n = 160); unit of FENO is parts per billion |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Asthma diagnoses               | FENO             | sens [%] (95%CI) | spec [%] (95%CI) | PPV [%] (95%CI) | NPV [%] (95%CI) |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Borderline BHR mild BHR moderate to severe BHR positive bronchodilator reversibility (n = 75)* | > 12            | 85 (76–92)      | 24 (16–34)      | 50 (41–58)      | 65 (47–79)      | 126             |                 |
|                                 | > 16            | 69 (58–79)      | 53 (42–63)      | 57 (46–66)      | 66 (54–76)      | 92              |                 |
|                                 | > 20            | 64 (53–74)      | 58 (47–77)      | 57 (47–67)      | 65 (53–74)      | 82              |                 |
|                                 | > 35            | 32 (25–42)      | 84 (74–90)      | 63 (47–77)      | 58 (49–67)      | 38              |                 |
|                                 | > 46            | 32 (23–43)      | 93 (85–97)      | 80 (63–91)      | 61 (52–69)      | 30              |                 |
|                                 | > 76            | 13 (7–23)       | 100 (96–100)    | 100 (72–100)    | 57 (49–65)      | 11              |                 |
| Mild BHR moderate to severe BHR positive bronchodilator reversibility (n = 58)§ | > 12            | 90 (79–95)      | 25 (17–34)      | 40 (32–49)      | 81 (64–91)      | 126             |                 |
|                                 | > 16            | 79 (67–88)      | 55 (45–64)      | 50 (40–60)      | 82 (72–90)      | 92              |                 |
|                                 | > 20            | 67 (54–78)      | 62 (52–71)      | 50 (39–61)      | 77 (67–85)      | 82              |                 |
|                                 | > 35            | 36 (25–49)      | 83 (75–89)      | 55 (40–70)      | 70 (61–77)      | 38              |                 |
|                                 | > 46            | 36 (25–49)      | 91 (84–95)      | 70 (52–83)      | 72 (63–79)      | 30              |                 |
|                                 | > 76            | 17 (10–29)      | 100 (96–100)    | 100 (72–100)    | 68 (60–75)      | 11              |                 |

* prevalence of asthma = 46.9%, prevalence of 'no asthma' = 53.1%
§ prevalence of asthma = 36.3%, prevalence of 'no asthma' = 63.7%

In the Conclusion section of the Abstract, in line 2, "FENO £ 12 ppb" should say "FENO £ 16 ppb".

In the Sensitivity analyses section, in line 2 of the third paragraph, "FENO £ 12 ppb" should say "FENO £ 16 ppb", "81% (95% CI 64–91)" should say "82% (95% CI 72–90)" and "34" should say "68". In line 3, "FENO £ 12 ppb" should say "FENO £ 16 ppb" and "five" should say "three". In line 4 "12 ppb" should say "16 ppb". The sentence starting in line 5 and ending in line 6 should read: "Sensitivity was 78% (95% CI 63–89), specificity was 45% (95% CI 34–57), PPV was 45% (95% CI 34–57), NPV was 78 (95% CI 63–89)". In line 6, "16 (15.8%)" should say "37 (36.6%)", "FENO £ 12 ppb" should say "FENO £ 16 ppb" and "increased up to 82% (95% CI 64–92)" should say "was 77% (95% CI 61–88)".

In the Discussion section, in line 4, "81%" should say "82%" and in line 5, "FENO £ 12" should say "FENO £ 16"

In the second paragraph, in line 1, "five" should say "three". In line 5, "16 patients had FENO £ 12 ppb" should say "37 patients had FENO £ 16 ppb". Also in line 5, "three" should say "two" and in lines 11 and 12 "FENO £ 12 ppb" should say "FENO £ 16 ppb" and 12 ppb<FENO should say 16 ppb<FENO.

In the third line of the third paragraph "12 to 46 ppb" should say "16 to 46 ppb" and in the seventh line, the sec-

| Table 2: Likelihood ratio at different cut-off points (n = 160); unit of FENO is parts per billion; LR+ is positive likelihood ratio, LR- is negative likelihood ratio |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Asthma diagnoses               | FENO             | LR+ (95%CI)     | LR- (95%CI)     |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Borderline BHR, mild BHR, moderate to severe BHR, positive bronchodilator reversibility (n = 75) | > 12            | 1.12 (0.96–1.30) | 0.62 (0.32–1.21) |
|                                 | > 16            | 1.47 (1.12–1.93) | 0.58 (0.39–0.86) |
|                                 | > 20            | 1.55 (1.12–2.14) | 0.65 (0.47–0.91) |
|                                 | > 35            | 1.94 (1.09–3.48) | 0.81 (0.68–0.98) |
|                                 | > 46            | 4.53 (1.96–10.49)| 0.73 (0.62–0.86) |
|                                 | > 76            | not calculable  | not calculable  |                 |                 |
| Mild BHR, moderate to severe BHR, positive bronchodilator reversibility (n = 58) | > 12            | 1.19 (1.03–1.37) | 0.42 (0.18–0.97) |
|                                 | > 16            | 1.76 (1.37–2.26) | 0.38 (0.22–0.64) |
|                                 | > 20            | 1.76 (1.30–2.39) | 0.53 (0.36–0.79) |
|                                 | > 35            | 2.17 (1.25–3.77) | 0.77 (0.62–0.95) |
|                                 | > 46            | 4.10 (2.02–8.36) | 0.70 (0.57–0.86) |
|                                 | > 76            | not calculable  | not calculable  |                 |                 |
ond half of the sentence that reads "and the difference of the 95%CI (-9.8 ppb) and 20 ppb is close to our best cut-off point (12 ppb) to rule out asthma" should not be there.

In the conclusion section, in line 3 "FENO ≤12 ppb" should say "FENO ≤16 ppb" and "three" should say "two".

References