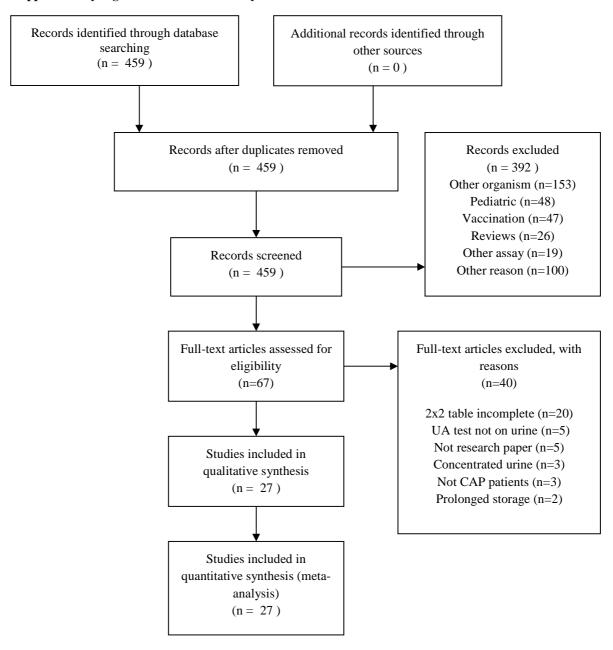
# Supplemental material: Sinclair et al. A urine pneumococcal antigen test (BinaxNOW Streptococcus pneumoniae) for the diagnosis of community acquired Streptococcus pneumoniae pneumonia: A systematic review and meta-analysis

#### Supplementary Figure 1 Flowchart of study selection



Supplementary Figure 2 Forest plot showing sensitivity and specificity of BinaxNOW-SP and prevalence of SP in the studies contributing to the meta-analysis, according to the latent class analysis

Study, year	Prev. [95% Crl]	Sensitivity [95% Crl]	Specificity [95% Crl]
Sorde, 2011 <sup>a;b</sup>	0.46 [0.26,0.55]	0.74 [0.63,0.89]	<b>—</b> 0.98 [0.8,1]
Segonds, 2010 <sup>a</sup>	0.15 [0.08,0.23]	0.73 [0.55,0.9]	<b>-</b> 0.99 [0.93,1]
Garcia Suarez, 2007 <sup>a;c</sup>	0.33 [0.23,0.41]	0.82 [0.71,0.92]	- 0.98 [0.89,1]
Lasocki, 2006	0.41 [0.28,0.53]	0.74 [0.59,0.88]	- 0.99 [0.9,1]
Tzeng, 2006 <sup>d</sup>	0.1 [0.04,0.17]	0.76 [0.58,0.92]	<b>=</b> 0.97 [0.92,1]
Lauderdale, 2005 <sup>a;b;e</sup>	0.26 [0.1,0.39]	0.76 [0.57,0.91]	0.98 [0.85,1]
Ishida, 2004 <sup>a</sup>	0.4 [0.28,0.48]	0.78 [0.68,0.89]	- 0.98 [0.86,1]
Roson, 2004	0.41 [0.22,0.53]	0.72 [0.57,0.88]	0.98 [0.82,1]
Stralin, 2004	0.42 [0.27,0.51]	0.59 [0.47,0.83]	<b>=</b> 0.99 [0.94,1]
Butler, 2003 <sup>a</sup>	0.66 [0.44,0.84]	0.68 [0.53,0.85]	0.98 [0.75,1]
Marcos, 2003 <sup>a</sup>	0.4 [0.28,0.48]	0.67 [0.57,0.84]	- 0.99 [0.91,1]
Burel, 2001	0.47 [0.33,0.61]	0.8 [0.66,0.92]	0.98 [0.85,1]
Shibli, 2011	0.17 [0.03,0.34]	0.71 [0.42,0.91]	- 0.98 [0.86,1]
Charles, 2008 <sup>a;b</sup>	0.13 [0.06,0.19]	0.72 [0.55,0.9]	<b>=</b> 0.98 [0.93,1]
Weatherall, 2008	0.15 [0.04,0.31]	0.78 [0.54,0.93]	- 0.98 [0.88,1]
Diaz, 2007 <sup>a</sup>	0.32 [0.06,0.69]	0.62 [0.3,0.89]	<b>—</b> 0.98 [0.81,1]
Kobashi, 2007 <sup>a</sup>	0.3 [0.16,0.41]	0.83 [0.68,0.94]	0.98 [0.84,1]
Andreo, 2006 <sup>a</sup>	0.25 [0.13,0.4]	0.66 [0.43,0.87]	<b></b> 0.99 [0.92,1]
Ercis, 2006 <sup>f</sup>	0.2 [0.1,0.33]	0.75 [0.53,0.91]	<b>=</b> 0.99 [0.94,1]
Genne, 2006 <sup>f</sup>	0.39 [0.2,0.59]	0.73 [0.51,0.89]	0.98 [0.84,1]
van der Eerden, 2005 <sup>a;b</sup>	0.26 [0.14,0.36]	0.71 [0.54,0.89]	- 0.98 [0.89,1]
Farina, 2002	0.18 [0.11,0.27]	0.77 [0.59,0.92]	<b>0.99</b> [0.96,1]
Murdoch, 2001	0.36 [0.13,0.56]	0.63 [0.43,0.88]	0.98 [0.81,1]
Johansson, 2010 <sup>9</sup>	0.26 [0.14,0.37]	0.72 [0.53,0.89]	- 0.99 [0.9,1]
Perello, 2010 <sup>9</sup>	0.49 [0.22,0.68]	0.76 [0.57,0.91]	0.98 [0.73,1]
Smith, 2009 <sup>a;g;h</sup>	0.52 [0.41,0.62]	0.84 [0.74,0.93]	- 0.98 [0.85,1]
Hohenthal, 2008 <sup>a;g;h</sup>	0.28 [0.12,0.38]	0.79 [0.64,0.92]	0.98 [0.84,1]
	Г		
	0	0.2 0.6 1	0 0.4 0.8

Studies are ordered by date in descending order and grouped according to reference classes, A (11 studies), B (12 studies), and C (4 studies). Footnotes provide additional detail of data interpretation.

<sup>&</sup>lt;sup>a</sup> Definite and probable SP pneumonia were combined into a single category of SP pneumonia.

<sup>&</sup>lt;sup>b</sup> Authors' definition of SP included a positive BinaxNOW-SP result. Patients diagnosed solely on the basis of a positive BinaxNOW-SP were treated as false positive results.

<sup>&</sup>lt;sup>c</sup> Results from the total number of CAP cases derived from the summation of the authors' categories "Pneumococcal infection, Pneumonia", "Pneumococcal infection, Probable pneumococcal pneumonia", "Nonpneumococcal infections, Pneumonia", and "Unknown etiology pneumonia".

<sup>&</sup>lt;sup>d</sup> Data used for those patients with lower respiratory tract infections (LRTIs).

<sup>&</sup>lt;sup>e</sup> Analysis restricted to a subset of patients with complete data.

<sup>&</sup>lt;sup>f</sup> Data used from those patients with CAP. Data from control patients omitted.

<sup>&</sup>lt;sup>g</sup> Complete data to construct a 2x2 table provided only for positive blood culture as a reference standard.

<sup>&</sup>lt;sup>h</sup> Results for the total number of CAP cases derived from the summation of the authors' categories "Pneumococcal bacteremia, With pneumonia" and "Nonbacteremic Pneumonia, Combined subtotal"

## **Supplementary Table 1** Example searches

<u>Search 1</u> used plain text in PubMed and OVID, mapped to keywords, and did not attempt to narrow to diagnostic studies.

pneumonia.mp AND ((bacterial antigens.mp. or Antigens, Bacterial/) AND urin\$.mp) OR binax.mp OR urine antigens.mp)

with limits (language EN, FR; humans; age (adult, all NOT child)

Use of wildcards was also explored in OVID, to expand the search:

pneumococc\$ AND ((urin\$ AND antigen\$) OR (BinaxNOW OR Binax))

## <u>Search 2</u> as designed by a reference librarian, used a diagnostic subheading (EMBASE)

1	
1	exp antigen/
2	exp urine/
3	binax.mp.
4	binaxnow.mp.
5	exp bacterial polysaccharide/
6	or/1-5
7	exp Streptococcus pneumoniae/
8	6 and 7
9	exp pneumonia/di, ep [Diagnosis, Epidemiology]
10	exp pneumococcal infection/di, ep [Diagnosis, Epidemiology]
11	exp diagnosis/
12	exp pneumonia/
13	exp pneumococcal infection/
14	or/12-13
15	11 and 14
16	9 or 10 or 15
17	8 and 16
18	limit 17 to yr="2000 -Current"
19	limit 18 to (english or french)
20	limit 19 to animals
21	19 not 20
22	limit 21 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years>)
23	limit 22 to (adolescent <13 to 17 years> or adult <18 to 64 years> or aged <65+ years>)
24	21 not 22
25	23 or 24

Supplementary Table 2 Risk of bias in studies reporting diagnosis of *S pneumonia* community acquired pneumonia using BinaxNOW

Reference	Representative patient spectrum? <sup>a</sup>	Acceptable ref. standard?b	Acceptable time between tests? <sup>c</sup>	No partial verification? <sup>d</sup>	No differential verification? <sup>e</sup>	No incorporatio n? <sup>f</sup>
Sordé, 2011(23)	Yes	No (A)	Yes: both as part of diagnostic workup.	Unclear - 129/474	Unclear	Yes (data separable)
Segonds, 2010(20)	Yes	No (A)	Unclear: timing not given	Unclear - 247/278	Unclear	Yes (data separable)
Garcia-Suarez, 2007(8)	Yes	No (A)	Yes: samples drawn day 1	Yes	Yes	Yes
Lasocki, 2006(14)	No (All ICU)	No (A)	Unclear: ICU	Yes	Yes	Yes
Tzeng, 2006(25)	Yes	No (A)	Unclear	Yes	Yes	Yes
Lauderdale, 2005(15)	Yes	No (A)	Unclear: urine stored frozen	Unclear – subset with all tests	Yes	Yes
Ishida, 2004(11)	Yes	No (A)	Yes	Yes	Yes	Yes
Róson, 2004(19)	Yes (Minority ambulatory)	No (A)	Unclear	Yes	Yes	Yes
Stralin, 2004(24)	Yes	No (A)	Unclear: urine stored frozen	Yes	Unclear	Yes
Butler, 2003(3)	Yes	No (A)	Unclear	Yes: 147/149	Yes	Yes
Marcos, 2003 (16)	Yes	No (A)	Yes	Yes	Yes	Yes
Burel, 2001 (2)	Yes	No (A)	Unclear	Yes	Yes	Yes
Shibli, 2010 (21)	Yes	No (B)	Yes: sample at admit	Yes	Yes	Yes
Charles, 2008 (4)	Yes	No (B)	Unclear: within 48h	Yes	Yes	Yes (data separable)
Weatherall, 2008 (27)	Yes	No (B)	Yes	Yes	Yes	Yes
Diaz, 2007 (5)	Yes	No (B)	Unclear: time of BinaxNOW-SP not given	Yes	Yes	Yes
Kobashi, 2007 (13)	Yes	No (B)	Unclear: BinaxNOW- SP at "acute stage"	Yes	Yes	Yes
Andreo, 2006 (1)	Yes	No (B)	Unclear: urine stored frozen	Unclear - 92/107	Unclear	Yes (data are separable)
Ercis, 2006 (6)	Yes	No (B)	Yes	Unclear - 52/59	Unclear	Yes

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<sup>&</sup>lt;sup>a</sup> Was the spectrum of patients representative of the patients who will receive the test in practice?

b Was the reference standard likely to classify the target condition correctly? The letter in brackets indicates the reference class.

Was the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?

Did the whole sample or a random selection of the sample, receive verification using the intended reference standard?

Did patients receive the same reference standard irrespective of the index test result?

Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?

Sinclair et al / S Pneumonia diagnosis

Reference	Representative patient spectrum? <sup>a</sup>	Acceptable ref. standard?b	Acceptable time between tests? <sup>c</sup>	No partial verification? <sup>d</sup>	No differential verification? <sup>e</sup>	No incorporatio n? <sup>f</sup>
Genne, 2006 (9)	Yes	No (B)	Unclear: taken at admit, but allowed up to 6 days.	Yes	Yes	Yes
Van der Eerden, 2005 (26)	Yes	No (B)	Yes: sample at admission	Yes	Yes	Yes
Farina, 2002 (7)	Yes	No (B)	Unclear	Yes	Yes	Yes
Murdoch, 2001(17)	Yes	No (B)	Yes	Yes	Yes	Yes
Johansson, 2010(12)	Yes	No (C)	Yes, within 1 day	Yes	Yes	Yes
Perello, 2010(18)	No (All HIV)	No (C)	Yes: sample at admission	Unclear - 96/129	Unclear	Yes
Smith, 2009 (22)	Yes	No (C)	Unclear: blood obtained within 24h abx start	Yes	Yes	Yes
Hohenthal, 2008 (10)	Yes	No (C)	Unclear	Unclear	Yes	Yes

Supplementary Table 2 (cont) Risk of bias in studies reporting diagnosis of S pneumonia community acquired pneumonia using BinaxNOW

Reference	Index results blinded? <sup>g</sup>	Ref. results blinded? <sup>h</sup>	Same clinical info?i	Uninterpretable results explained? <sup>j</sup>	Withdrawals explained? <sup>k</sup>
Sordé, 2011(23)	Unclear	Yes	Yes	None described	No
Segonds, 2010(20)	Unclear	Unclear	Unclear	None described	No
Garcia-Suarez, 2007(8)	Unclear: samples were stored	Yes	Yes	None described	All tested
Lasocki, 2006(14)	Unclear: timing?	Unclear: ICU, so possible later investigations	Unclear: timing?	None described	All tested
Tzeng, 2006(25)	Unclear	Unclear	Yes	None described	All tested
Lauderdale, 2005(15)	Unclear: samples were stored	Unclear	Yes	None described	No - stated did not have samples
Ishida, 2004(11)	Yes: tested at admit	Unclear	Yes	None described	All tested
Róson, 2004(19)	Unclear	Unclear	Yes	None described	All tested
Stralin, 2004(24)	Yes: explicitly stated	Yes	Yes	Yes: described equivocal	All tested
Butler, 2003(3)	Unclear: frozen urine	Unclear	Yes	None described	All but 2 tested
Marcos, 2003 (16)	Unclear	Unclear	Yes	None described	All tested
Burel, 2001 (2)	Unclear	Unclear	Yes	None described	All tested
Shibli, 2010 (21)	Unclear	Unclear	Yes	None described	All tested
Charles, 2008 (4)	Unclear: within 48h	Unclear	Yes	None described	All tested
Weatherall, 2008 (27)	Yes: tested in ED	Unclear	Yes	None described	All tested
Diaz, 2007 (5)	Unclear	Unclear	Yes	None described	All tested
Kobashi, 2007 (13)	Yes: stated	Unclear	Yes	None described	All tested
Andreo, 2006 (1)	Unclear: urine frozen	Unclear	Unclear	None described	No
Ercis, 2006 (6)	Unclear	Unclear	Yes	None described	No
Genne, 2006 (9)	Unclear: timing?	Yes	Yes	None described	All tested
Van der Eerden, 2005 (26)	Unclear	Unclear	Yes	None described	All tested
Farina, 2002(7)	Unclear	Unclear	Yes	None described	All tested
Murdoch, 2001(17)	Unclear: transported for testing	Unclear	Yes	None described	All tested
Johansson, 2010(12)	Unclear	Unclear	Yes	None described	All tested
Perello, 2010(18)	Yes	Unclear	Unclear	None described	No
Smith, 2009 (22)	Yes: "tested prospectively"	Unclear	Unclear	None described	All tested
Hohenthal, 2008 (10)	Unclear	Unclear	Yes	None described	All tested

Were the reference standard results interpreted without knowledge of the results of the index test? Were the index test results interpreted without knowledge of the results of the reference standard?

Were the index test results interpreted without knowledge of the results of the reference standard?

Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?

Were uninterpretable/ intermediate test results reported?

Were withdrawals from the study explained?

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