Influenza and RSV-infections: current standard in accurate, time- and cost-efficient diagnosis.

Auteur: Klaas Dewaele

Supervisor: Johan Frans, Erwin Ho

	Eerste lijn	Tweede lijn
1	BD Max BioGX GeneXpert Flu/RSV	bioMérieux Biofire FilmArray
2	BD Veritor Alere i	Pathofinder Respifinder
3	BD Veritor Custom multiplex PCR	
4	GeneXpert Flu/RSV Alere RSV antigeentest	Custom multiplex PCR
5	Quidel Sofia Custom multiplex PCR	
6	BD Veritor Custom multiplex PCR	
7	Quidel Sofia Directe immunofluorescentie Virale kweek	
8	BD Veritor	Custom multiplex PCR (extern)
9	BD Veritor GeneXpert Flu/RSV	Pathofinder Respifinder

BILULU

	Eerste lijn	Tweede lijn
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6	BD Veritor Custom multiplex PCR	
7	Quidel Sofia **Directe immunofluorescentie** **Virale kweek**	
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BILULU

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	Eerste lijn	
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3	BD Veritor Custom multiplex PC	
4	GeneXpert Flu/RSV Alere RSV antigeen	
5	Quidel Sofia Custom multiplex F	
6	BD Veritor Custom multiplex PC	
7	Quidel Sofia Directe immunofluoresce Virale kweek	
8	BD Veritor	
9	BD Veritor GeneXpert Flu/RSV	

“Rapid NAATs”

Nieuw!

BILULU

Twee perspectieven

1) Labo-perspectief: welke van beschikbare tests zijn meest **accuraat, tijdsefficiënt?**
2) Klinisch perspectief: wat is de rol van influenza/RSV testing in klinisch praktijk: **welke test hebben we (eventueel) nodig?**

→ Literatuurstudie, benchmark, queries …

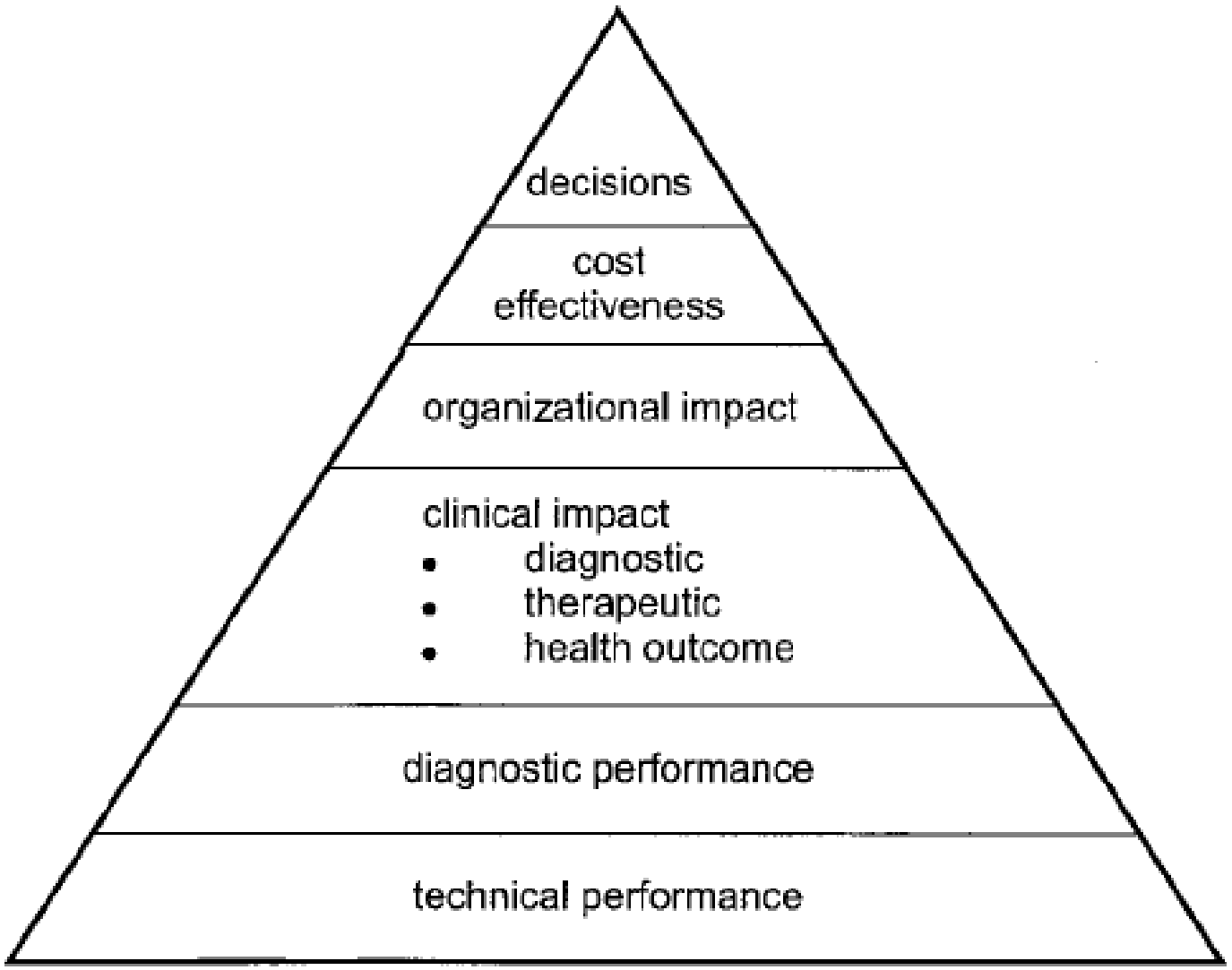
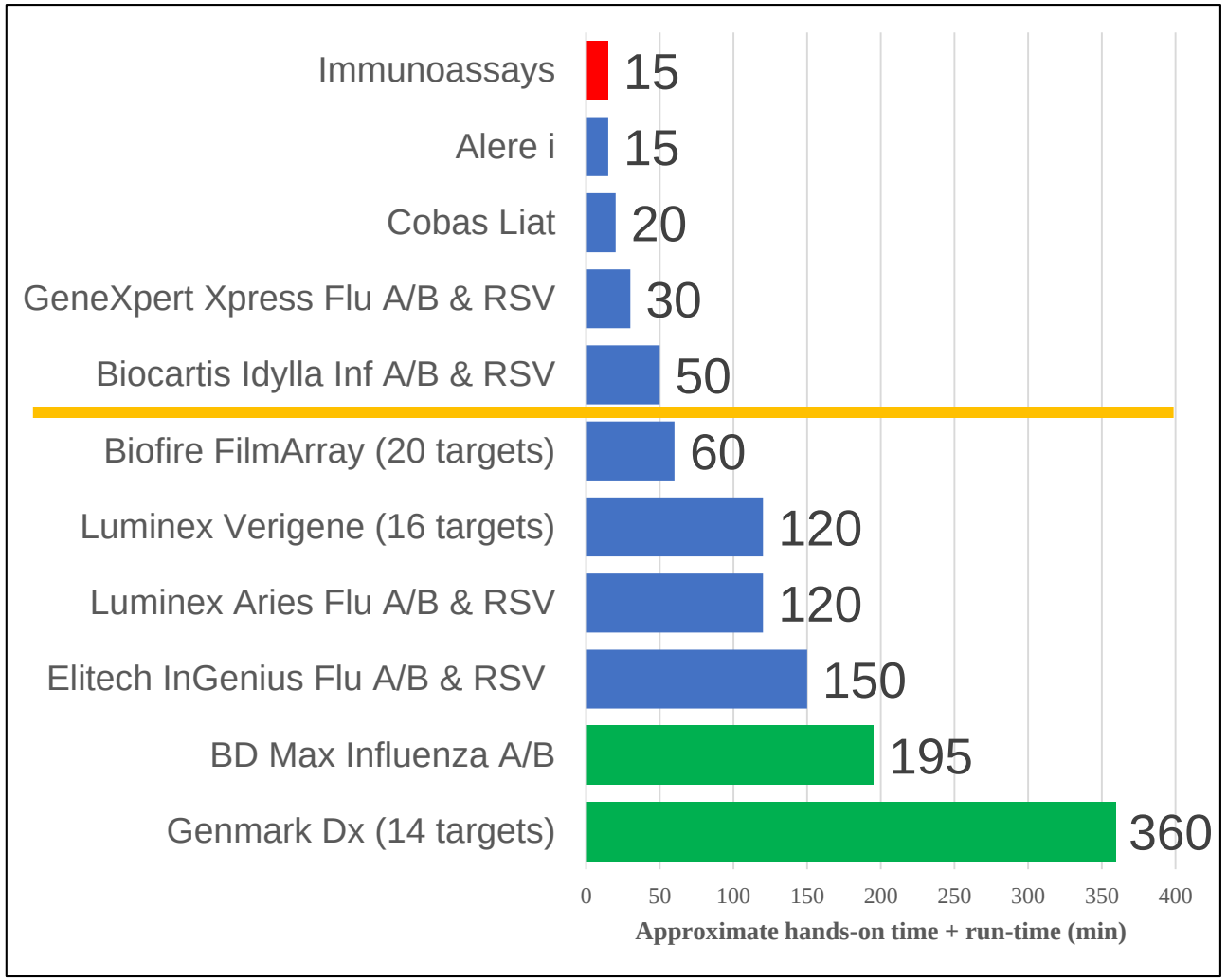


Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Overzicht tests

- **Traditionele methodes:**
  - Virale kweek
  - Serologie
  - Immunofluorescentie
- **Antigeentests**
- **“NAATs” (PCR, …)**
- **“Rapid NAATs” (< 1h)**



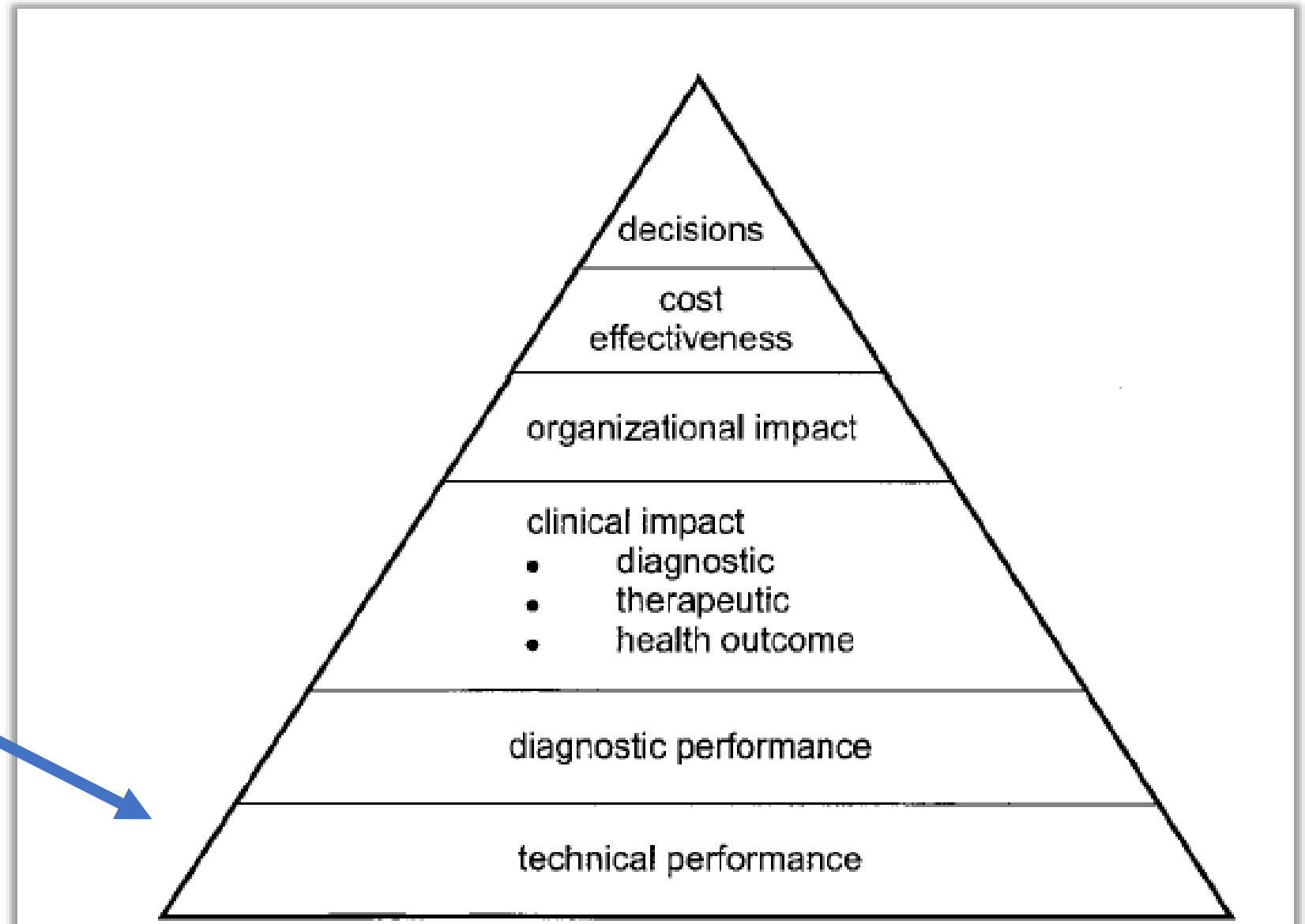


Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Analytische performantie

- **Pre-analytische factoren?**
  - **Geen systematische reviews**
  - Relevant?
    - Interindividuele verschillen viral load
    - Interfererende factoren?
    - Staalstabiliteit
    - Transportmedium?
    - Staaltype

Analytische performantie

- **Pre-analytische factoren?**
  - **Geen systematische reviews**
  - Relevant?
    - **Interindividuele verschillen viral load**
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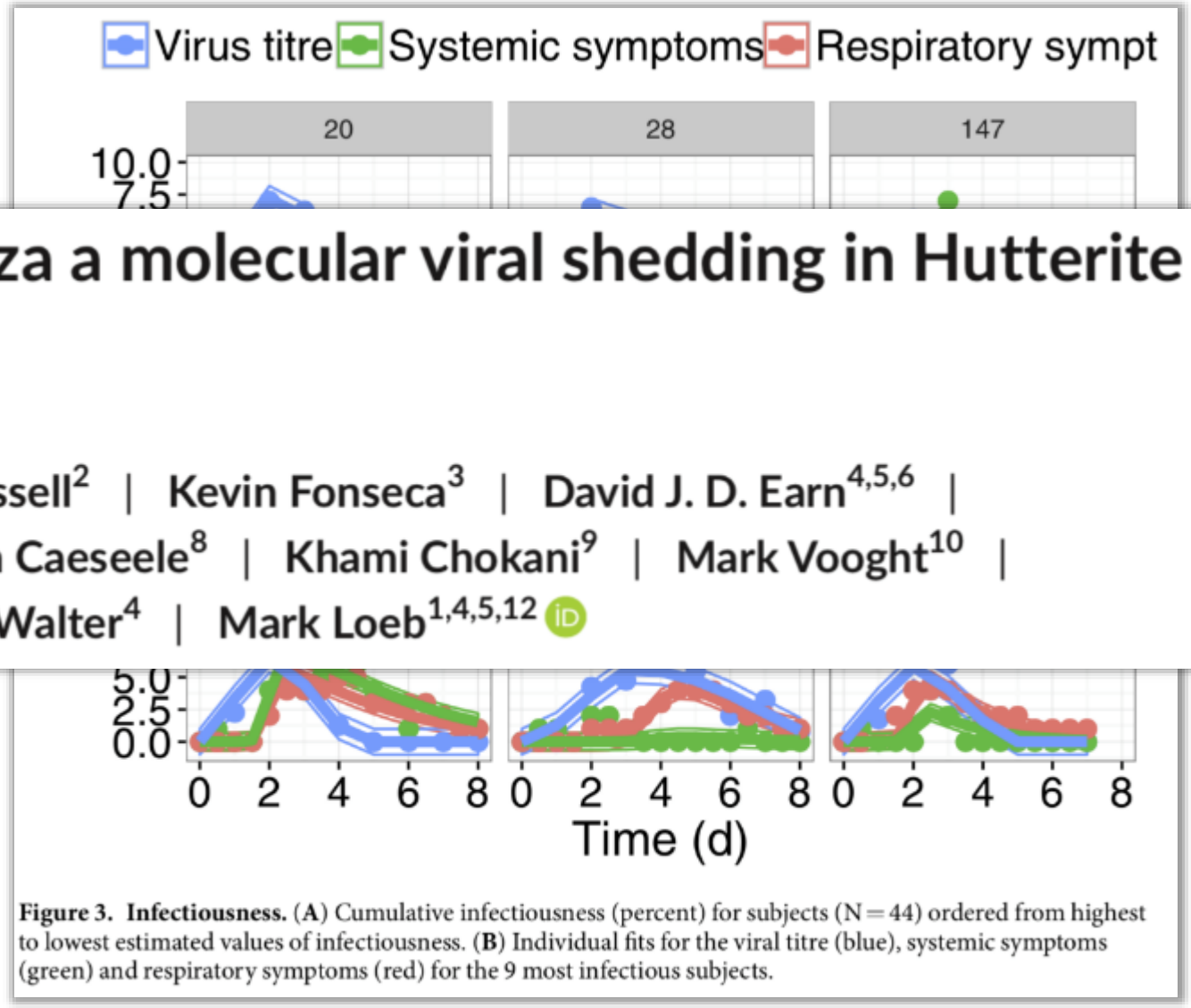
Viral load



Predictors of influenza a molecular viral shedding in Hutterite communities

Biao Wang[1] | Margaret L. Russell[2] | Kevin Fonseca[3] | David J. D. Earn[4,5,6] | Gregory Horsman[7] | Paul Van Caeseele[8] | Khami Chokani[9] | Mark Vooght[10] | Lorne Babiuk[11] | Stephen D. Walter[4] | Mark Loeb[1,4,5,12]

Kinderen hoger,
mannen hoger,
comorbiditeit hoger

Figure 3. Infectiousness. (**A**) Cumulative infectiousness (percent) for subjects (N = 44) ordered from highest to lowest estimated values of infectiousness. (**B**) Individual fits for the viral titre (blue), systemic symptoms (green) and respiratory symptoms (red) for the 9 most infectious subjects.

Canini et al., 2016

Viral load: impact op RSV

Parent-collected respiratory specimens—A novel method for respiratory virus and vaccine efficacy research

Stephen B. Lambert*, Kelly M. All

Summary Population-based respiratory research and vaccine efficacy studies have previously required clinic or home visits when a subject had an acute respiratory illness. This method may mean parents are unwilling to enrol their child or report an illness of interest. We conducted a community-based cohort study into respiratory illnesses in 234 pre-school aged children using parent-collected specimens. Between January 2003 and January 2004 there were 563 specimens collected from 730 identified illnesses and these were tested using a panel of respiratory virus polymerase chain reaction (PCR) assays; 409 (73%) were positive for any virus. Specimens were not more likely to be positive when collected by a healthcare worker parent, when they included a throat swab, or when a very good collection technique was reported. A delay from illness onset to specimen collection of up to 5 days did not appear to impact on sensitivity of virus identification, but a delay of six or more days with minor delays in testing saw positivity fall. Combined with daily symptom diary completion and PCR testing, parent-collected specimens are an efficient and acceptable method for the conduct of future vaccine efficacy studies and other community-based respiratory virus research.

Analytische performantie

- **Pre-analytische factoren?**
  - **Geen systematische reviews**
  - Relevant?
    - Interindividuele verschillen viral load
    - **Interfererende factoren?**
    - Staalstabiliteit
    - Transportmedium?
    - Staaltype

Analytische performantie

- **Pre-analytische factoren?**
  - **Geen systematische reviews**
  - Relevant?
    - Interindividuele verschillen viral load
    - Interfererende factoren?
    - **Staalstabiliteit**
    - Transportmedium?
    - Staaltype

Staalstabiliteit

RSV (Maris et al., 2

Table 2 Stability of the r

Interval (days)	No. of patients	No. of positive swabs
0	44	30
1	42	30
2–5	26	21
Total	112	81

The interval is the time between
freezing of the swab. The swabs
frozen at −70°C for 1–6 months
RSV using reverse transcription-
chain reaction (RT-PCR). The pos
were compared with those in co
nasopharyngeal aspirates (NPAs
time-resolved immunoassay (TR-
RT-PCR.

Table 4 ERV3 and respiratory virus positive samples detected by polymerase chain reaction assays in 3366 parent collected nasal swab specimens

Variable		No. samples (%)	ERV3 Positive			Respiratory virus positive		
			No. samples (%)	Univariate OR (95% CI); P value	*Multivariate OR (95%); P value	No. samples (%)	Univariate OR (95% CI); P value	*Multivariate OR (95%); P value
Age (months)	*< 6*	1293 (38.4%)	995 (77.0)	1	1	208 (16.1)	1	1
	6- <12	1295 (38.5%)	1061 (81.9)	1.20 (0.94-1.53); 0.15	1.28 (0.98-1.68); 0.07	411 (31.7)	2.59 (2.07-3.24); <0.001	2.38 (1.89-3.01); <0.001
	≥12	778 (23.1%)	662 (85.1)	1.49 (1.06-2.10); 0.02	1.93 (1.27-2.93); 0.002	266 (34.2)	2.98 (2.26-3.92); <0.001	2.16 (1.57-2.99); <0.001
Gender	*Male*	1647 (48.9%)	1335 (81.1)	1	1	461 (28.1)	1	1
	Female	1719 (51.06%)	1383 (80.4)	0.81 (0.54-1.22); 0.32	0.87 (0.58-1.29); 0.48	424 (24.7)	0.82 (0.60-1.12); 0.21	0.83 (0.61-1.12); 0.23
Collector	*Mother*	2845 (84.5%)	2307 (81.1)	1	1	766 (26.9)	1	1
	Father	441 (13.1%)	342 (77.6)	0.91 (0.66-1.27); 0.60	0.87 (0.62-1.22); 0.42	109 (24.7)	0.94 (0.70-1.26); 0.67	0.88 (0.65-1.19); 0.41
	Research staff	45 (1.3%)	40 (88.9)	2.71 (1.00-7.36); 0.05	1.76 (0.65-4.81); 0.27	3 (6.7)	0.24 (0.07-0.79); 0.02	0.36 (0.11-1.21); 0.10
	Other	35 (1.0%)	29 (82.9)	1.31 (0.49-3.51); 0.59	1.39 (0.46-4.16); 0.56	7 (20.0)	0.72 (0.30-1.74); 0.47	0.87 (0.35-2.13); 0.76
Season	*Summer*	926 (27.5%)	729 (78.7)	1	1	178 (19.2)	1	1
	Autumn	1059 (31.5%)	802 (75.7)	0.90 (0.71-1.13); 0.37	0.74 (0.58-0.96); 0.02	304 (28.7)	1.99 (1.59-2.49); <0.001	1.74 (1.38-2.20); <0.001
	Winter	541 (16.1%)	482 (89.1)	2.63 (1.87-3.70); <0.001	2.41 (1.67-3.49); <0.001	198 (36.6)	3.06 (2.36-3.97); <0.001	2.63 (2.01-3.45); <0.001
	Spring	840 (25.0%)	705 (83.9)	1.39 (1.07-1.79); 0.01	1.50 (1.13-1.99); 0.005	205 (24.4)	1.27 (1.00-1.61); 0.05	1.43 (1.11-1.84); 0.005
Mould	*None*	2604 (77.4%)	2189 (84.1)	1	1	707 (27.2)	1	1
	Low	411 (12.2%)	308 (74.9)	0.47 (0.36-0.62); <0.001	0.69 (0.52-0.93); 0.01	97 (23.6)	0.73 (0.56-0.95); 0.02	0.81 (0.61-1.07); 0.14
	Medium	252 (7.5%)	163 (64.7)	0.27 (0.20-0.37); <0.001	0.47 (0.33-0.66); <0.001	60 (23.8)	0.70 (0.50-0.96); 0.03	0.70 (0.49-0.99); 0.05
	High	99 (2.9%)	58 (58.6)	0.20 (0.13-0.33); <0.001	0.40 (0.24-0.66); <0.001	21 (21.2)	0.57 (0.34-0.96); 0.04	0.53 (0.31-0.93); 0.03
Time to reach Laboratory (days)	*0-3*	2281 (67.8%)	1983 (86.9)	1	1	587 (25.7)	1	1
	4-7	723 (21.5%)	513 (71.0)	0.32 (0.25-0.40); <0.001	0.39 (0.30-0.50); <0.001	187 (25.9)	0.96 (0.78-1.18); 0.69	1.03 (0.82-1.29);0.80
	>7	362 (10.8%)	222 (61.3)	0.17 (0.13-0.24); <0.001	0.24 (0.17-0.34); <0.001	111 (30.7)	1.16 (0.89-1.52); 0.28	1.42 (1.05-1.94); 0.02

*Adjusted for all variables in the Table.

Alsaleh, 2014

Analytische performantie

- **Pre-analytische factoren?**
  - **Geen systematische reviews**
  - Relevant?
    - Interindividuele verschillen viral load
    - Interfererende factoren?
    - Staalstabiliteit
    - **Transportmedium?**
    - Staaltype

Analytische performantie

- **Pre-analytische factoren?**
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    - **Staaltype?**

Influenza Specimen Collection

Nieuw!

	Nasopharyngeal Swab	Nasopharyngeal/Nasal Aspirate	Nasopharyngeal/Nasal Wash	Deep Nasal Swab	Combined Nasal & Throat Swab
Materials	• Sterile Dacron/nylon swab • Viral transport media tube	• Sterile suction catheter/suction apparatus	• Sterile suction catheter/suction apparatus	• Sterile polyester swab *(aluminum or plastic shaft preferred)*	• 2 dry sterile polyester swabs *(aluminum or plastic shafts preferred)*
Procedure	1 2 3 4				tube *L of sterile* *n)* k 70 degrees. the swab, insert ch into nostril t at turbinates). ral times against t in other nostril into sterile viral and cut off the

JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 2010, p. 3340–3342 Vol. 48, No. 9
0095-1137/10/$12.00 doi:10.1128/JCM.02235-09

Development and Evaluation of a Flocked Nasal Midturbinate Swab for Self-Collection in Respiratory Virus Infection Diagnostic Testing▽

Marek Smieja,[1,2,3,4]* Santina Castriciano,[2,5] Susan Carruthers,[2] Geoffrey So,[3] Sylvia Chong,[2] Kathy Luinstra,[2] James B. Mahony,[1,2,4] Astrid Petrich,[1,2,4] Max Chernesky[2]

Beste balans gebruiksvriendelijkheid en opbrengst?

Note: NP aspirate may not be possible to conduct in infants

and swab the posterior pharynx and tonsillar areas. (Avoid the tongue.)

6 Place tip of swab into the same tube and cut off the applicator tip.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Staalafname

- **Geen systematic reviews**
- **Studies die methodes parallel vergelijken:**
  - **Traditionele methodes (swab, aspirate, brush, wash)**
    - Wash hoogste yield?
    - Cotton swabs minste discomfort

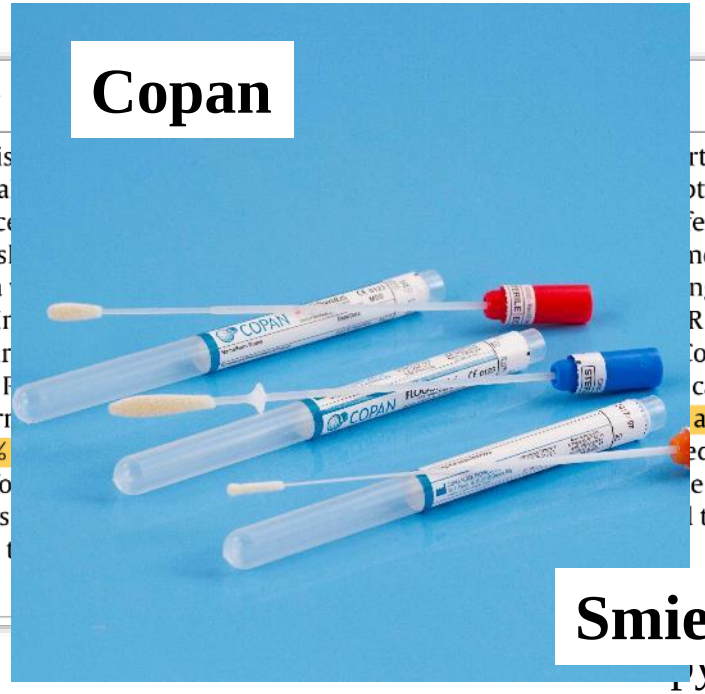
A B S T R A C T

The aim of this study was to compare the efficacy and patient discomfort between four techniques for obtaining nasal secretions. Nasal secretions from 58 patients with symptoms of a common cold, from three clinical centers (Amsterdam, Lodz, Oslo), were obtained by four different methods: swab, aspirate, brush, and wash. In each patient all four sampling procedures were performed and patient discomfort was evaluated by a visual discomfort scale (scale 1–5) after each procedure. Single pathogen RT-PCRs for Rhinovirus (RV), Influenza virus and Adenovirus, and multiplex real-time PCR for RV, Enterovirus, Influenza virus, Adenovirus, Respiratory Syncytial Virus (RSV), Parainfluenza virus, Coronavirus, Metapneumovirus, Bocavirus and Parechovirus were performed in all samples. A specific viral cause of respiratory tract infection was determined in 48 patients (83%). In these, the detection rate for any virus was 88% (wash), 79% (aspirate), 77% (swab) and 74% (brush). The degree of discomfort reported was 2.54 for swabs, 2.63 for washes, 2.68 for aspirates and 3.61 for brushings. Nasal washes yielded the highest rate of viral detection without excessive patient discomfort. In contrast, nasal brushes produced the lowest detection rates and demonstrated the highest level of discomfort.

Spyridaci et al., 2008.

Staalafname

- **Geen systematic reviews**
- **Studies die methodes parallel vergelijken:**
  - **Traditionele methodes (swab, aspirate, brush, wash)**
    - Wash hoogste yield?
    - Cotton swabs minste discomfort
  - **“Flocked swabs”: meer epitheel**
    - **Nasofaryngeale swab?**
    - **Midturbinate swab?**
  - **Twee studies …**



Smieja, 2011

A B S T R A

The aim of this
obtaining nasa
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Bocavirus and F
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R for RV, Enterovirus, Influenza
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any virus was 88% (wash), 79%
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the lowest detection rates and

reserved.

Pyrrhaki et al., 2008.

Self-Collected Mid-Turbinate Swabs for the Detection of Respiratory Viruses in Adults with Acute Respiratory Illnesses

Oscar E. Larios[1,2], Brenda L. Coleman[3,4]*, Steven J. Drews[5,6], Tony Mazzulli[3,4], Bjug Borgundvaag[4,7], Karen Green[3], STOP-Flu Study[¶], Allison J. McGeer[3,4]

1 Departments of Medicine and Laboratory Medicine, Royal University Hospital, Saskatoon, Saskatchewan, Canada, **2** Faculty of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada, **3** Department of Microbiology, Mount Sinai Hospital, Toronto, Ontario, Canada, **4** Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada, **5** Department of Microbiology, Immunology & Infectious Diseases, University of Calgary, Calgary, Alberta, Canada, **6** Department of Microbiology, Provincial Laboratory for Public Health, Calgary, Alberta, Canada, **7** Department of Emergency Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada

Abstract

healthy adults aged 18 to 69 years were recruited into a cohort and followed up for ed to have NP and MT swabs taken as soon as possible after the onset of a fever or with an acute onset. The swabs were tested for viral respiratory infections using on kit. Seventy six pairs of simultaneous NP and MT swabs were collected from 38 symptomatic subjects. Twenty nine (38%) of these pairs were positive by either NP or MT swabs or both. Sixty nine (91%) of the pair results were concordant. Two samples (3%) for hCV OC43/HKU1 and 1 sample (1%) for rhinovirus A/B were positive by NP but negative by MT. One sample each for hCV 229E/NL63, hCV OC43/HKU1, respiratory syncytial virus A, and influenza B were positive by MT but negative by NP.

Conclusions: Flocked MT swabs are sensitive for the diagnosis of multiple respiratory viruses. Given the ease of MT collection and similar results between the two swabs, it is likely that MT swabs should be the preferred method of respiratory cell collection for outpatient studies. In light of this data, larger studies should be performed to ensure that this still holds true and data should also be collected on the patient preference of collection methods.

MT evenwaardig aan NPS voor "respiratoire virussen"?

Zelfafname!

Accuracy and Discomfort of Different Types of Intranasal Specimen Collection Methods for Molecular Influenza Testing in Emergency Department Patients

Bradley W. Frazee, MD*; Amparo Rodríguez-Hoces de la Guardia, PhD; Harrison Alter, MD, MS; Carol G. Chen, PhD; Eugenia L. Fuentes, MSc; Alison K. Holzer, PhD; Macarena Lolas, MD, PhD; Debkishore Mitra, PhD; Jaspreet Vohra, MD; Cornelia L. Dekker, MD

Results: Four hundred eighty-four subjects were enrolled, and all 3 swabs were obtained for each subject; 14% were children. The prevalence of influenza (A or B) was 30.0% (95% confidence interval [CI] 26.0% to 34.8%). The sensitivity for detecting influenza was 98% (95% CI 94.25% to 99.65%) with the midturbinate swab versus 84.4% (95% CI 77.5% to 89.8%) with the nasal swab, difference 13.6% (95% CI 8.2% to 19.3%). Specificity was 98.5% (95% CI 96.6% to 99.5%) with the midturbinate swab versus 99.1% (95% CI 97.4% to 99.8%) with the nasal swab, difference −0.6% (95% CI −1.8% to 0.6%). Swab discomfort levels correlated with the depth of the swab type. Median discomfort scores for the nasal swab, midturbinate swab, and nasopharyngeal swab were 0, 1, and 3, respectively; the median differences were nasopharyngeal swab–midturbinate swab 2 (95% CI 1 to 2), nasopharyngeal swab–nasal swab 3 (95% CI 2 to 3), and midturbinate swab–nasal swab 1 (95% CI 1 to 2).

Conclusion: Compared with the reference standard nasopharyngeal swab specimen, midturbinate swab specimens provided a significantly more comfortable sampling experience, with only a small sacrifice in sensitivity for influenza detection. Nasal swab specimens were significantly less sensitive than midturbinate swab. Our results suggest the midturbinate swab is the sampling method of choice for molecular influenza testing in ED patients. [Ann Emerg Med. 2018;71:509-517.]

Analytische factoren

“Puur” analytische factoren:

- (Im)precisie
- Analytisch meetbereik
- Within/between runvariatie
- …

→ Zie bijsluiters/FDA

Besluit pre-analytische fase

- **Geen systematische reviews**
- **Impact viral load op diagnose?**
  - Viral load slechts beperkt voorspelbaar (interindividuele verschillen)
  - Lagere sensitiviteit ~ duur ziekte (RSV)
- **Staalstabiliteit**: lagere yield over verloop van dagen
- **Staaltype**: (zelf afgenomen) MT swabs nieuwe standaard? (Te bevestigen)

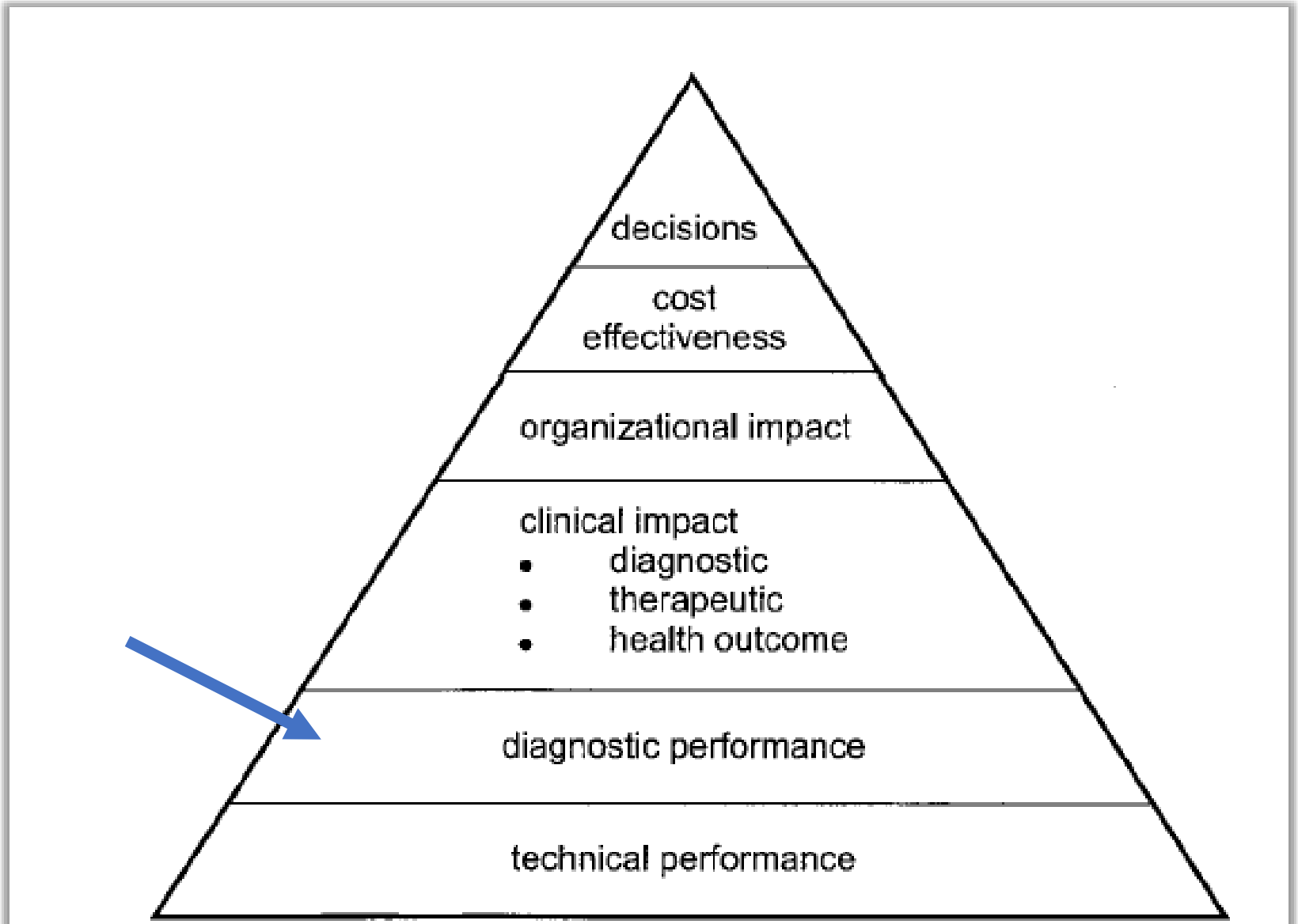


Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Diagnostische performantie

- **Standaard in tijdsefficiënte en accurate diagnostiek?**
- **Sensitiviteit en specificiteit, PPV/NPV**
  - Meta-analyse van rapid tests + eigen update
  - Waarom we zijn afgestapt van sneltests
- **Likelihood ratios**

Merckx et al., 2017

REVIEW

Annals of Internal Medicine

Diagnostic Accuracy of Novel and Traditional Rapid Tests for Influenza Infection Compared With Reverse Transcriptase Polymerase Chain Reaction

A Systematic Review and Meta-analysis

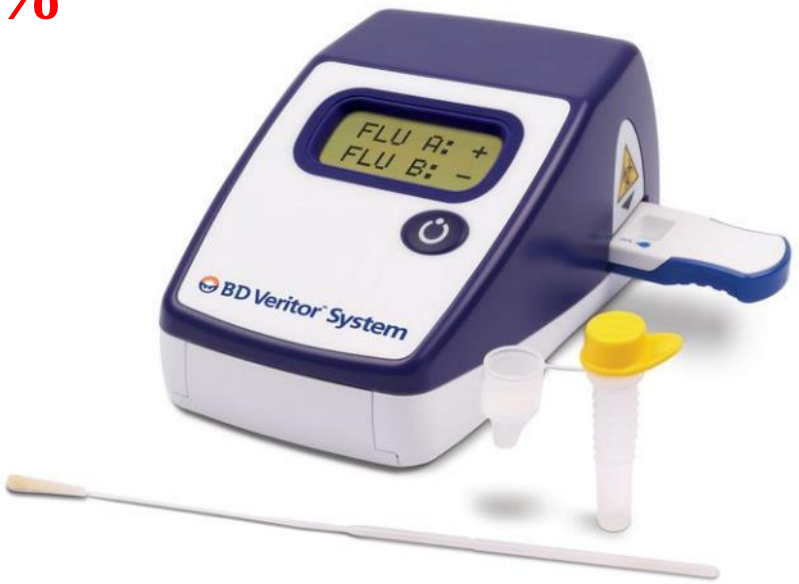
Joanna Merckx, MD, MSc; Rehab Wali, BSc, MBBS; Ian Schiller, MSc; Chelsea Caya, MScPH; Genevieve C. Gore, MLIS; Caroline Chartrand, MD, MSc; Nandini Dendukuri, PhD; and Jesse Papenburg, MD, MSc

Table 2. Overall and Subgroup Analyses of Pooled Rapid Test Accuracy Estimates for Influenza A and B, by Index Test Type*

Index Test Type	Influenza A		Influenza B	
	Pooled Sensitivity (95% CrI), %	Pooled Specificity (95% CrI), %	Pooled Sensitivity (95% CrI), %	Pooled Specificity (95% CrI), %
Subgroup analyses†				
Study population (age)‡				
Traditional RIDTs				
Children (31 influenza A studies; 9 influenza B studies)	61.2 (55.0 to 67.2)	99.2 (98.5 to 99.7)	65.7 (45.3 to 80.5)	99.6 (99.2 to 99.8)
Adults (23 influenza A studies; 5 influenza B studies)	42.6 (34.8 to 50.9)	99.5 (98.6 to 99.8)	33.2 (19.9 to 50.7)	99.9 (99.4 to 100)
Difference in RIDT sensitivity: children vs. adults	**18.5 (8.4 to 28.3)**	–	**31.8 (6.1 to 52.6)**	–
DIAs				
Children (11 influenza A studies; 11 influenza B studies)	87.6 (81.8 to 92.2)	98.1 (96.4 to 99.1)	82.5 (71.2 to 90.2)	98.8 (95.6 to 99.7)
Adults (8 influenza A studies; 7 influenza B studies)	75.4 (66.6 to 82.6)	96.7 (94.7 to 98.0)	57.0 (39.5 to 71.6)	98.8 (97.5 to 99.5)
Difference in DIA sensitivity: children vs. adults	**12.1 (3.1 to 22.1)**	–	**25.3 (6.9 to 44.7)**	–
Rapid NAATs				
Children (4 influenza A studies; 4 influenza B studies)	90.2 (79.2 to 95.8)	99.0 (96.8 to 99.8)	95.9 (82.9 to 99.2)	99.5 (98.2 to 99.9)
Adults (4 influenza A studies; 4 influenza B studies)	87.4 (71.1 to 95.6)	98.0 (93.2 to 99.5)	75.7 (51.8 to 90.7)	99.3 (97.8 to 99.8)
Difference in NAAT sensitivity: children vs. adults	2.7 (−10.7 to 19.7)	–	**19.5 (1.0 to 43.7)**	–

Ervaring met BD Veritor Flu A+B

- **Negatieven hertesten met Luminex xTAG RPP**
- **Sens volwassenen** inf A/B: 105/162 = **64,8%**
- **Sens kinderen** inf A/B: 110/126 = **87,3%**



NAATs: Inf A/B

	Alere i	**Roche Cobas Liat**	**GeneXpert Xpress**
Runtime	15 min	20 min	30 min
Merckx et al.	84,4%/86,6%	97,1%/98,7%	-
Spec Inf A/B	98,9%/99,1%	99,4%/99,5%	-

Update review Merckx

- **Alere i**

Auteur	Jaar	Pathogeen	N	Leeftijd	Sens	Spec
Chen	2018	Influenza A/B & RSV	N = 105/134 (110 vers, 24 ingevoren)	Alle leeftijden	InfA: 97,4% InfB: 81,5%	InfA: 100% InfB: 99,1%
Schnee	2017	RSV	N = 229/533 (vers)	< 18j	93%	96%
Young	2017	Influenza A/B	N = 47/87 (vers)	≥ 18j	InfA: 55,2% InfB: 72,2%	InfA: 98,3% InfB: 97,1%

- **Cijfers H-H. Lier**: influenza: 11/14 = **78,6%** (volwassenen, verse stalen) versus Luminex xTAG (NPS)

Update review Merckx

- **Roche Cobas Liat**

Auteur	Jaar	Pathogeen	N	Leeftijd	Sens	Spec
Gibson	2017	Influenza A/B en RSV	N = 595/1656	Alle leeftijden	InfA: 99.6% InfB: 99.3% RSV: 96.8%	InfA: 97,5% InfB: 99,7% RSV: 98,8%
Young	2017	Influenza A/B	N = 47/87	≥ 18 jaar	InfA:100% InfB: 94,4%	InfA: 98,3% InfB: 100%
Melchers	2017	Influenza A/B	N = 56/121	?	InfA: 96% InfB: 100%	InfA: 100% InfB: 100%

GeneXpert Xpress Inf A/B & RSV

Auteur	Jaar	Pathogeen	N	Leeftijd	Sens	Spec
Chen	2018	Influenza A/B	N = 105/134	Alle leeftijden	InfA: 100% InfB: 96,3%	InfA: 100% InfB: 100%
Ling	2017	Influenza A/B, RSV	N = 50/100	Alle leeftijden	InfA: 100% InfB: 97,8% RSV: 100%	InfA: 100% InfB: 100% RSV: 100%
Cohen	2018	Influenza A/B, RSV	N = 680/2435	Alle leeftijden	InfA: 100% InfB: 100% RSV: 97,1%	InfA: 95,2% InfB: 99,5% RSV: 99,6%

- **Onze ervaring:**
  - **Influenza A/B:** 140/143 = **97,9%** **(ref Luminex xTAG RPP)**
  - **RSV:** geen data

Besluit diagnostische performantie

- Merckx et al.:

personnel. Overall, the rapid tests displayed very high specificities (≥98.3%) and positive LRs (>48). Physicians can therefore diagnose influenza with confidence on the basis of a positive RIDT, DIA, or rapid NAAT result.

Kostenefficiëntie? → klinische impact?

tivity (151). We found that rapid NAATs were the only class of rapid tests with overall negative LRs below 0.1, thereby making a negative result useful to rule out influenza (152). However, the cost of DIAs ($15 to $20 per test) is similar to that of RIDTs, whereas rapid NAATs may cost 2 to 5 times that amount. Whether the incremental gains in sensitivity of rapid NAATs versus DIAs are worth their added costs will likely depend on the patient populations and clinical contexts in which they are used. Moreover, different commercial rapid NAATs

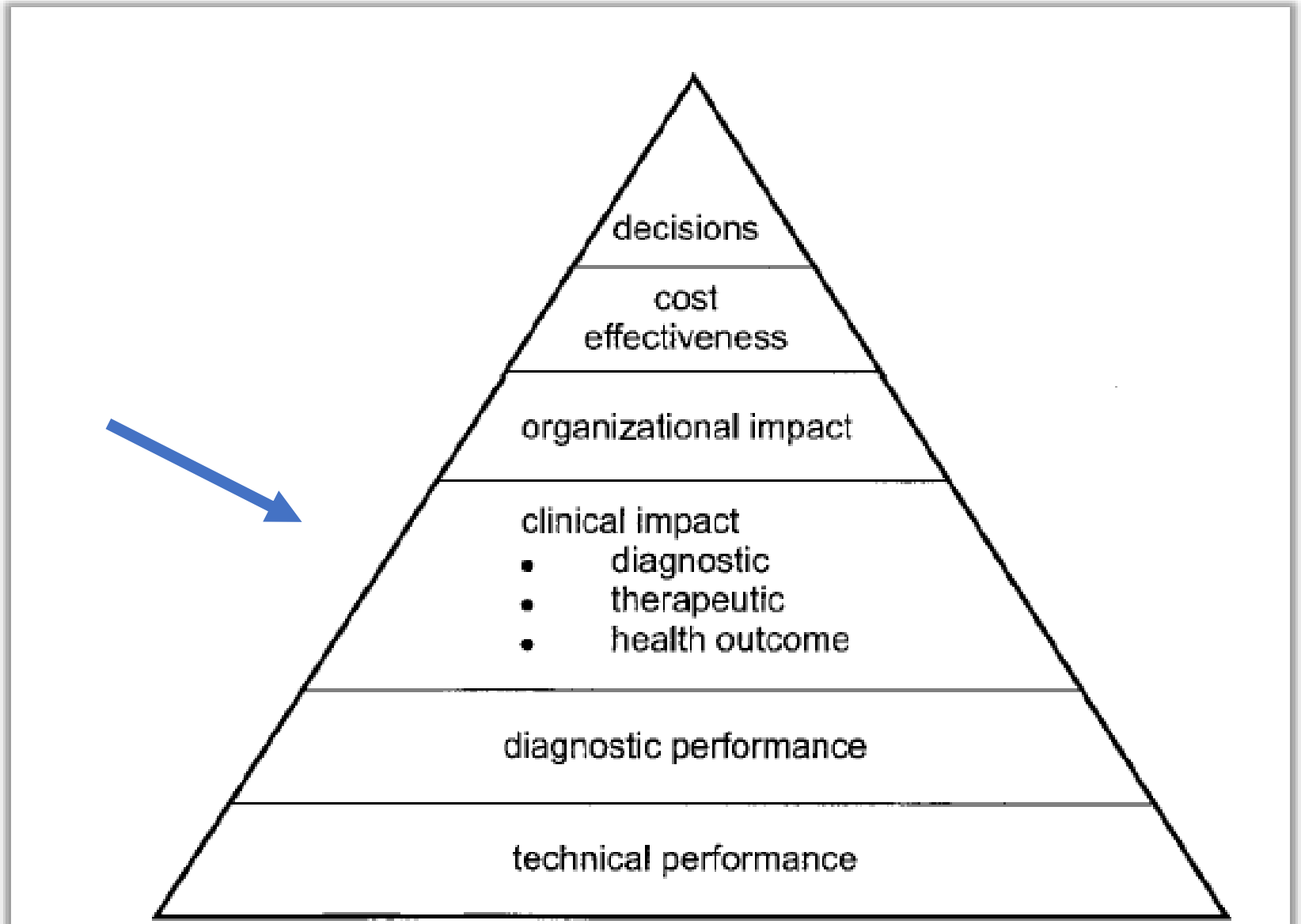


Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Klinische impact

- Zoekstrategie:
  - **Cochrane library Reviews:** “Influenza”, "RSV”, “respiratory viral”
  - **Pubmed:** (impact OR effect OR benefit) AND (Inf OR RSV OR respiratory viral) AND (rapid OR testing OR diagnosis)
  - **SumSearch Guidelines:** “Inf”, "RSV”, “respiratory viral”
  - **Referentie-lijsten**
- **N = 42 trials**

Klinische impact

- **Therapeutische impact**
  - Indicatiestelling antivirale middelen?
  - Indicatiestelling antibiotica?
- **Diagnostische impact**
  - Minder onnodige technische onderzoekingen?
- **Outcome**
  - Hospitalisatieduur?
  - Morbiditeit/mortaliteit?

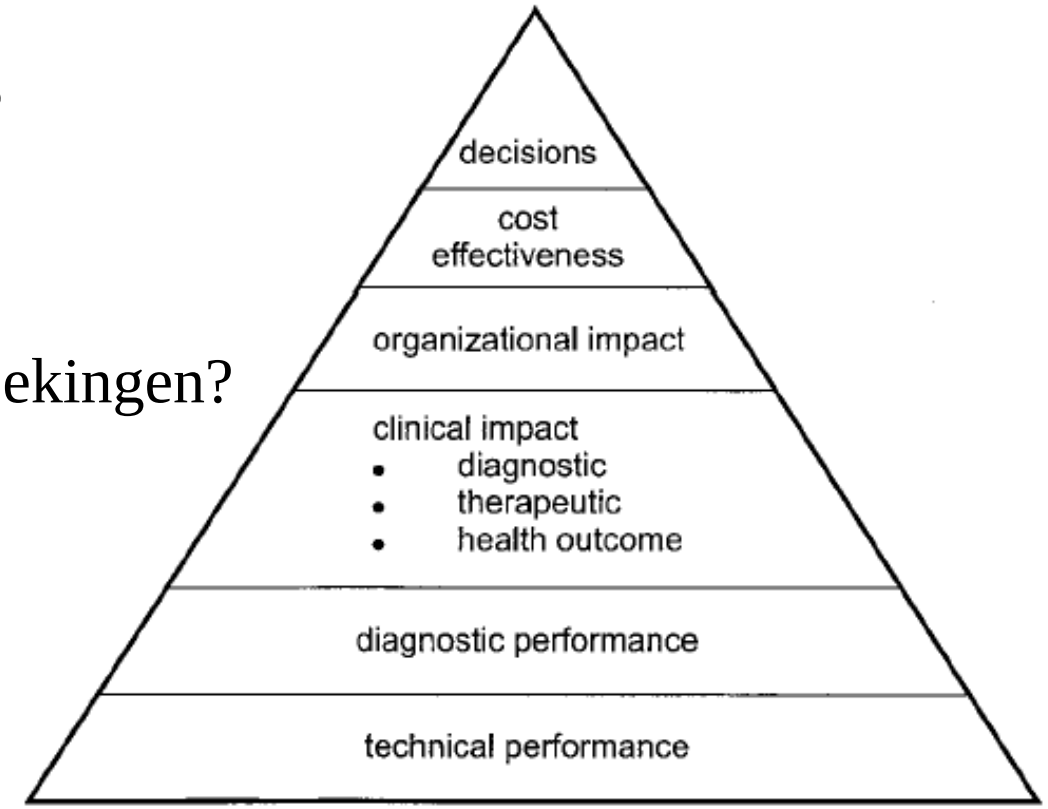


Fig. 2. Evidence of performance designed to facilitate decision-making.

Klinische impact

- **Therapeutische impact**
  - **Indicatiestelling antivirale middelen?**
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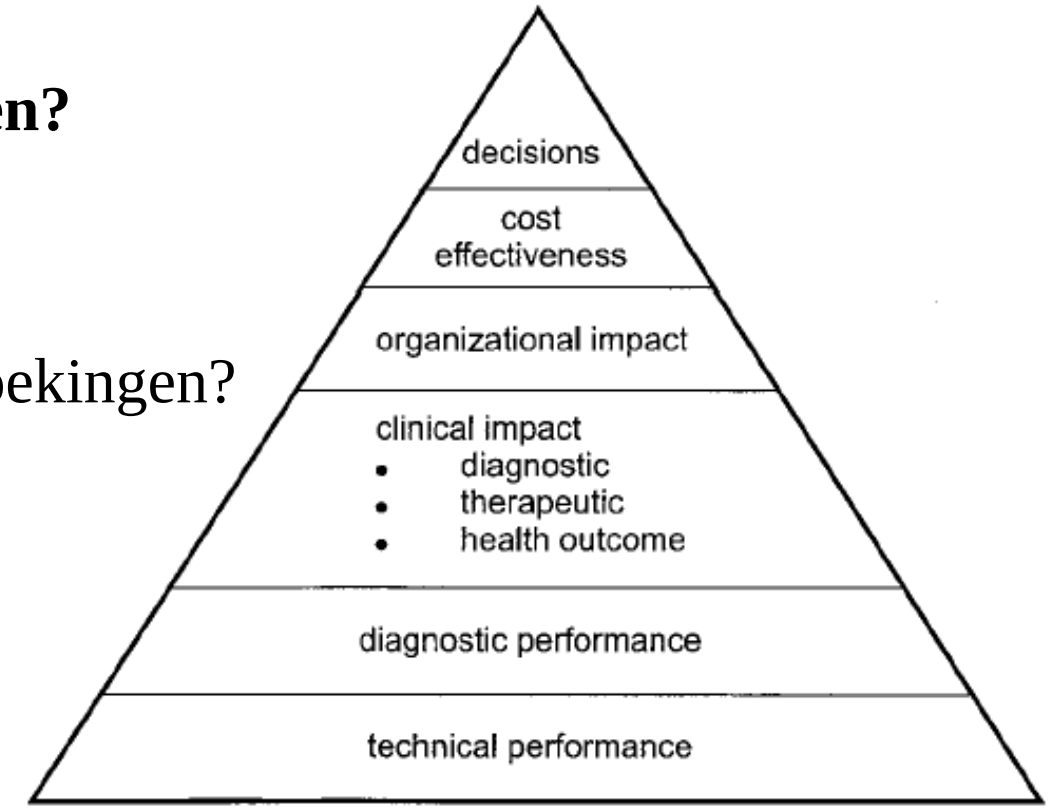


Fig. 2. Evidence of performance designed to facilitate decision-making.

Klinische impact: IDSA 2009

UPDATE IN PROGRESS*

Wie testen?

- Febriele respirat
  - Imuuncomp
    complicatie
  - **Immuunge**
  - **Gehospitali**
  - Kinderen bij
  - Na hospitaal
  - Evt. Voor **lo**
- Ouderen en baby
  sepsis/FUO

Wie behandelen?

s (start < 48u)

italisatie (start <

Who Should Be Tested for Suspected Influenza?

If the result will influence clinical management (decisions on initiation of antiviral treatment, impact on other diagnostic testing, antibiotic treatment decisions, and infection control practices), with consideration for the sensitivity and specificity of the test used and information about local influenza virus circulation, the following persons should be considered for influenza testing (table 2)

Harper et al., 2009

Belang antivirale middelen

- **Cochrane review 2014**
  (Jefferson et al.)

Cochrane Library

Cochrane Database of Systematic Reviews

Neuraminidase inhibitors for preventing and treating influenza in adults and children (Review)

Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, Spencer EA, Onakpoya IJ,

Authors' conclusions

Oseltamivir and zanamivir have small, non-specific effects on reducing the time to alleviation of influenza symptoms in adults, but not in asthmatic children. Using either drug as prophylaxis reduces the risk of developing symptomatic influenza. Treatment trials with oseltamivir or zanamivir do not settle the question of whether the complications of influenza (such as pneumonia) are reduced, because of a lack of diagnostic definitions. The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children. The lower bioavailability may explain the lower toxicity of zanamivir compared

Belang antivirale middelen: oseltamivir

- **Observationele studies?**
  - Geen benefit op **mortaliteit (2009A/H1N1) (Heneghan et al., 2015)**
  - **-19% mortaliteit (Muthuri et al., 2014)**

Study claiming Tamiflu saved lives was based on "flawed" analysis

Zosia Kmietowicz

Neuraminidase inhibitors for influenza: a systematic review and meta-analysis of regulatory and mortality data

Carl J Heneghan, Igho Onakpoya, Mark A Jones, Peter Doshi, Chris B Del Mar, Rokuro Hama, Matthew J Thompson, Elizabeth A Spencer, Kamal R Mahtani, David Nunan, Jeremy Howick and Tom Jefferson

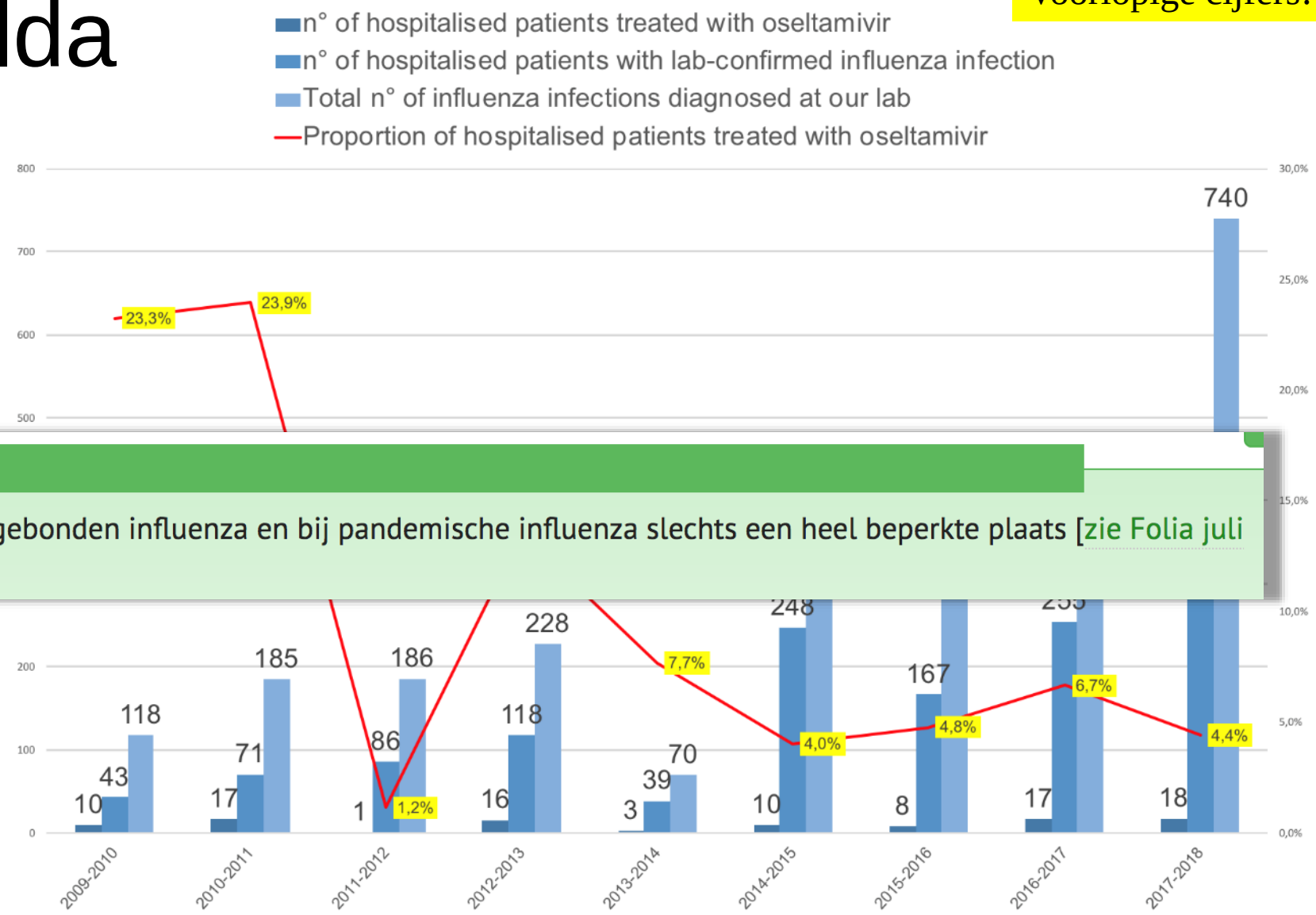
Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data

Stella G Muthuri, Sudhir Venkatesan*, Puja R Myles, Jo Leonardi-Bee, Tarig S A Al Khuwaitir, Adbullah Al Mamun, Ashish P Anovadiya, Eduardo Azziz-Baumgartner, Clarisa Báez, Matteo Bassetti, Bojana Beovic, Barbara Bertisch, Isabelle Bonmarin, Robert Booy, Victor H Borja-Aburto, Heinz Burgmann, Bin Cao, Jordi Carratala, Justin T Denholm, Samuel R Dominguez, Pericles A D Duarte, Gal Dubnov-Raz, Marcela Echavarria, Sergio Fanella, Zhancheng Gao, Patrick Gérardin, Maddalena Giannella, Sophie Gubbels, Jethro Herberg, Anjarath L Higuera Iglesias, Peter H Hoger, Xiaoyun Hu, Quazi T Islam, Mirela F Jiménez, Amr Kandeel, Gerben Keijzers, Hossein Khalili, Marian Knight, Koichiro Kudo, Gabriela Kusznierz, Ilija Kuzman, Arthur M C Kwan, Idriss Lahlou Amine, Eduard Langenegger, Kamran B Lankarani, Yee-Sin Leo, Rita Linko, Pei Liu, Faris Madanat, Elga Mayo-Montero, Allison McGeer, Ziad Memish, Gokhan Metan, Auksė Mickiene, Dragan Mikić, Kristin G I Mohn, Ahmadreza Moradi, Pagbajabyn Nymadawa, Maria E Oliva, Mehpare Ozkan, Dhruv Parekh, Mical Paul, Fernando P Polack, Barbara A Rath, Alejandro H Rodríquez, Elena B Sarrouf, Anna C Seale, Bunyamin Sertogullarindan, Marilda M Siqueira, Joanna Skręt-Magierło, Frank Stephan, Ewa Talarek, J Kelvin K W To, Antoni Torres, Selda H Törün, Dat Tran, Timothy M Uyeki, Annelies Van Zwol, Wendy Vaudry, Tjasa Vidmar, Renata T C Paul Zarogoulidis, PRIDE Consortium Investigators†, Jonathan S Nguyen-Van-Tam*

Roche

Data Imelda

Voorlopige cijfers!



Plaatsbepaling

- Oseltamivir heeft bij seizoensgebonden influenza en bij pandemische influenza slechts een heel beperkte plaats [zie Folia juli 2014 *en* Folia juli 2015].

Klinische impact

- **Therapeutische impact**
  - Indicatiestelling antivirale middelen?
  - **Indicatiestelling antibiotica?**
- **Diagnostische impact**
  - **Minder onnodige technische onderzoekingen?**
- **Outcome**
  - **Hospitalisatieduur?**
  - **Morbiditeit/mortaliteit?**

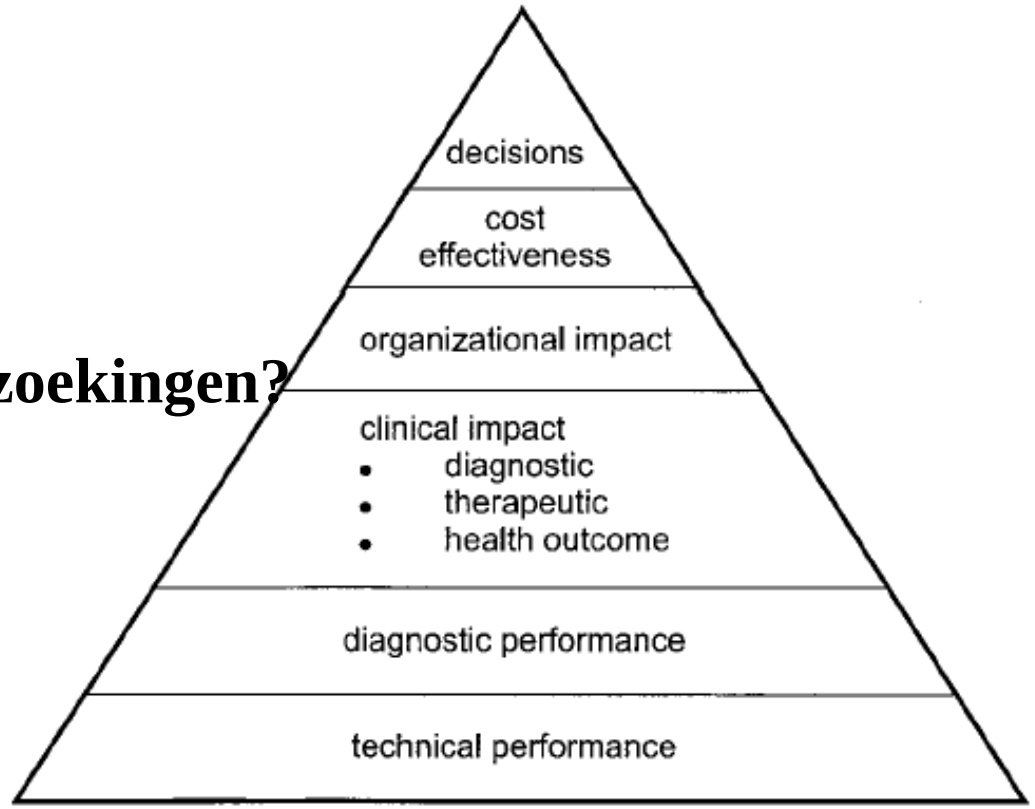


Fig. 2. Evidence of performance designed to facilitate decision-making.

IDSA Antibiotic stewardship guidelines 2016

Clinical Infectious Diseases

IDSA GUIDELINE

Implementing an Antibiotic Stewa
Guidelines by the Infectious Disea
and the Society for Healthcare Ep

**Tamar F. Barlam,[1,a] Sara E. Cosgrove,[2,a] Lilian M. Abbo,[3] Conan MacDougall,[4] Audrey N. Sc
Yngve T. Falck-Ytter,[9] Neil O. Fishman,[10] Cindy W. Hamilton,[11] Timothy C. Jenkins,[12] Pam
Gregory J. Moran,[16] Melinda M. Neuhauser,[17] Jason G. Newland,[18] Christopher A. Ohl,[19]**

[1]Section of Infectious Diseases, Boston University School of Medicine, Boston, Massachusetts; [2]Division of Infect
[3]Division of Infectious Diseases, University of Miami Miller School of Medicine, Miami, Florida; [4]Department of
[5]Department of Medicine, Weill Cornell Medical Center/New York–Presbyterian Hospital, New York, New York;
Medicine, Houston; [7]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atla

XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

Recommendation

17. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics *(weak recommendation, low-quality evidence)*.

Comment: Although rapid viral testing has the potential to reduce inappropriate use of antibiotics, results have been inconsistent. Few studies have been performed to assess whether active ASP intervention would improve those results.

Systematic reviews/meta-analyses

- Doan et al. **Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department (Review).** Cochrane Database Syst Rev. 2014 Sep 15;(9)
- Petrozzino JJ, Smith C, Atkinson MJ. **Rapid diagnostic testing for seasonal Inf: an evidence-based review and comparison with unaided clinical diagnosis.** J Emerg Med. 2010 Oct;39(4):476-490

Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department (Review)

- Negen RCTs; **vier RCTs** van adequate kwaliteit
- n = 759 rapid viral testing, n = 829 controle groep

Authors' conclusions

There is insufficient evidence to support routine rapid viral testing to reduce antibiotic use in pediatric EDs. Rapid viral testing may or may not reduce rates of antibiotic use, and other investigations (urine and blood testing); these studies do not provide enough power to resolve this question. However, rapid viral testing does reduce the rate of chest X-rays in the ED. An adequately powered trial with antibiotic use as an outcome is needed.

- **No effect on length of ED visits or blood or urine** testing in the ED
- No data on adverse effects related to viral testing

RAPID DIAGNOSTIC TESTING FOR SEASONAL INFLUENZA: AN EVIDENCE-BASED REVIEW AND COMPARISON WITH UNAIDED CLINICAL DIAGNOSIS

Jeffrey J. Petrozzino, MD, PHD,* Cynthia Smith, RN,* and Mark J. Atkinson, MED, PHD*†

*The Aequitas Group, Inc., San Diego, California and †Department of Family and Preventive Medicine, University of California, San Diego, San Diego, California

QUIDEL

Table 5. Effect of RFT on Decision-making and Outcomes*

Study (First Author, Year)	RFT	Sample Size	Subject Age	Clinical Setting	DXT	ABX	AV	LOS
Bhavnani, 2007 (21)	QuickVue® Influenza ND	300	All ages	Outpatient		↓		
Bonner, 2003 (23)	FluOIA	391	< 21 months	ED	↓	↓	↑	↓
Falsey, 2007 (24)	Directigen™ Influenza A	166	Adults	Hospital		↓	↑	
Poehling, 2006 (38)	QuickVue® Influenza ND	306 ED 162 Clinic	< 5 years	ED/Clinic	↓			
Sharma, 2002 (78)	Directigen™ Influenza A	72	< 2 years	ED	↓	↓		
Iyer, 2006 (79)	QuickVue® Influenza ND	345	< 2 years	ED	↓	↓		
Esposito, 2003 (80)	QuickVue® Influenza ND	478	0–15 years	ED	↓	↓		
Abanses, 2006 (81)	Directigen™ Influenza A+B	540	3–36 months	ED			↑	↓
Noyola, 2000 (82)	Directigen™ Influenza A	168	1 month–19 years (median 1 year)	ED		↓	↑	
Bonner, 2007 (22)	QuickVue® Influenza A+B	1083	0–18 years	Outpatient		↓	↑	

2010

Tests met langere TAT

- Impact op duur antibiotica? Lengte hospitalisatie?
- Geen systematic reviews/meta-analyses
- Drie RCTs: **inconsistente resultaten**

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Clinical Impact of RT-PCR for Pediatric Acute Respiratory Infections: A Controlled Clinical Trial

TABLE 3 Clinical Outcome Parameters

	Intervention Group ($N = 298$)	Control Group ($N = 285$)	*P*
Hospital admissions, *n* (%)	223 (74.8)	211 (74)	.825[a]
Time in hospital, mean ± SD (range), d	3.68 ± 2.68 (1–18)	3.96 ± 2.67 (1–15)	.170[b]
Antibody therapy initiated, *n* (%)	124 (41.6)	78 (27.4)	.000[a]
Duration of antibody therapy if initiated, mean ± SD (range), d	6.52 ± 2.15 (1–14)	6.97 ± 2.86 (2–21)	.490[b]

We have no satisfying explanation for why antibiotic treatment was started significantly more often in the intervention group. It was not expected that

Wishaupt, 2011

MAJOR ARTICLE

2005

AMERICAN SOCIETY FOR MICROBIOLOGY

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Table 4. Economical outcome associated with hospitalization, diagnostic procedures, and treatment for lower respiratory tract infection.

Variable	Average quantity of resources used per patient[a]		Unit cost in €	Average cost in € per group	
	Intervention group	Control group		Intervention group	Control group
Hospitalization	9.0 days	8.9 days	512	4608	4557
Diagnostic procedure					
Real-time PCR	1	0	331	331	0
CT of thorax and/or pulmonary angiogram	0.07	0.08	164	11.48	13.12
Additional blood-gas analysis	0.11	0.14	4.05	0.44	0.57
Additional blood culture	0.04	0.12	23.15	0.93	2.78
Additional sputum culture	0.06	0.08	8.68	0.52	0.69
Spirometry	0.07	0.04	15	1.05	0.60
Bronchoscopy	0.13	0.04	301	39.13	12.04
Total	…	…	…	384.55	29.80
Duration of antibiotic treatment	12.3 days	10.3 days	15	184.50	154.50
Total hospitalization, diagnostic, and treatment costs per patient	…	…	…	5177.05	4741.30

[a] Data are no. of analyses, unless otherwise indicated.

Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial

Nathan J Brendish, Ahalya K Malachira, Lawrence Armstrong, Rebecca Houghton, Sandra Aitken, Esther Nyimbili, Sean Ewings, Patrick J Lillie, Tristan W Clark

THE LANCET
Respiratory Medicine
Volume 5, Issue 5, May 2017, Pages 401-411

	POCT (n=360)	Control (n=354)	Risk difference (95% CI)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Number needed to test (95% CI)	p value
All antibiotics							
Antibiotics given	301 (84%)	294 (83%)	0·6% (−4·9 to 6·0)	1·04 (0·70 to 1·54)	0·99 (0·57 to 1·70)	..	0·96*

	POCT (n=360)	Control (n=354)	Difference (95% CI)	Odds ratio (95% CI)	p value
Admitted	332 (92%)	327 (92%)	−0·2% (−4·1 to 3·8)	0·98 (0·56 to 1·70)	0·94
Length of hospital stay (days)*	5·7 (6·3)	6·8 (7·7)	−1·1 (−2·2 to −0·3)	..	0·0443
Prolonged inpatient stay†	81/327 (25%)	86/311 (28%)	−2·9% (−9·7 to 3·9)	0·86 (0·61 to 1·23)	0·42

Data are n (%) or mean (SD). POCT=point-of-care testing. *Adjusted for in-hospital mortality. †Defined as ≥7 days (adjusted for in-hospital mortality).

***Table 4*: Length of hospital stay**

Data are n (%) or mean (SD). POCT=point-of-care testing. *Applies to adjusted effect sizes. †Number needed to test to change a standard course to a single dose. ‡Number needed to test to change a standard course to a brief course. §Mean difference. ¶Unadjusted rate ratio. ||Adjusted rate ratio.

***Table 3*: Comparison of antibiotic use**

SHORT REPORT

Arch Dis Child 2003;**88**:525–526

Effect of a rapid influenza diagnosis

S Esposito, P Marchisio, P Morelli, P Crovari, N Principi

Table 1 Comparison of children with a positive (cases) or negative rapid influenza test result (control group 1) and those who did not undergo the test (control group 2)

Characteristic	Cases (n=43)	Control group 1 (n=435)	p value	Control group 2 (n=479)	p value
Gender					
Male	23 (53.5)	242 (55.6)	0.913	254 (53.0)	0.919
Female	20 (46.5)	193 (44.4)		225 (47.0)	
Age (y)					
Median	2.5	2.3	0.643	2.6	0.706
Range	0.3–14.5	0.1–14.7		0.1–14.8	
Underlying illness	2* (4.6)	21† (4.8)	1.000	24‡ (5.0)	1.000
Previous influenza vaccination	0	9 (2.1)	1.000	11 (2.3)	0.611
Diagnosis					
Rhinitis	14 (32.6)	105 (24.1)	0.301	137 (28.6)	0.709
Pharyngitis	16 (37.2)	163 (37.5)	0.133	164 (34.2)	0.821
Acute otitis media	9 (20.9)	72 (16.6)	0.605	86 (18.0)	0.725
Croup	1 (2.3)	8 (1.8)	0.575	15 (3.1)	1.000
Wheezing	1 (2.3)	20 (4.6)	0.709	19 (4.0)	1.000
Acute bronchitis	2 (4.7)	41 (9.4)	0.408	34 (7.1)	0.757
Pneumonia	0	26 (6.0)	0.153	24 (5.0)	0.246
Routine blood examination	1 (2.3)	63 (14.5)	0.045	72 (15.0)	0.038
Chest radiograph	2 (4.6)	50 (11.5)	0.207	56 (11.7)	0.208
Antibiotic use	14 (32.6)	282 (64.8)	<0.0001	296 (61.8)	0.0003
Days of antibiotics					
Median	7	7	0.944	7	0.961
Range	4–10	3–20		5–14	
Admitted	0	20 (4.6)	0.240	28 (5.8)	0.154
Antiviral use	0	0		0	

Besluit klinische impact

- Given the questionable efficacy of influenza medications, and limited use in clinical practice, we believe **viral testing is not justified solely for directing antiviral therapy**. RSV testing might be useful for specific populations, where ribavirin therapy might be beneficial.
- **No definitive benefit on directing antibiotic therapy** has been demonstrated in high-quality trials in children and adults with influenza, although some studies suggest a minor benefit. No RCTs have been performed using the new point-of-care (POC) NAATs.
- **A decrease in the use of chest X-rays** was demonstrated in the pediatric Emergency department. No impact was seen on other technical investigations.
- In high-quality trials, **viral testing does not have an impact on hospital admission rate**. Inconsistent results were obtained for length-of-stay (LOS).

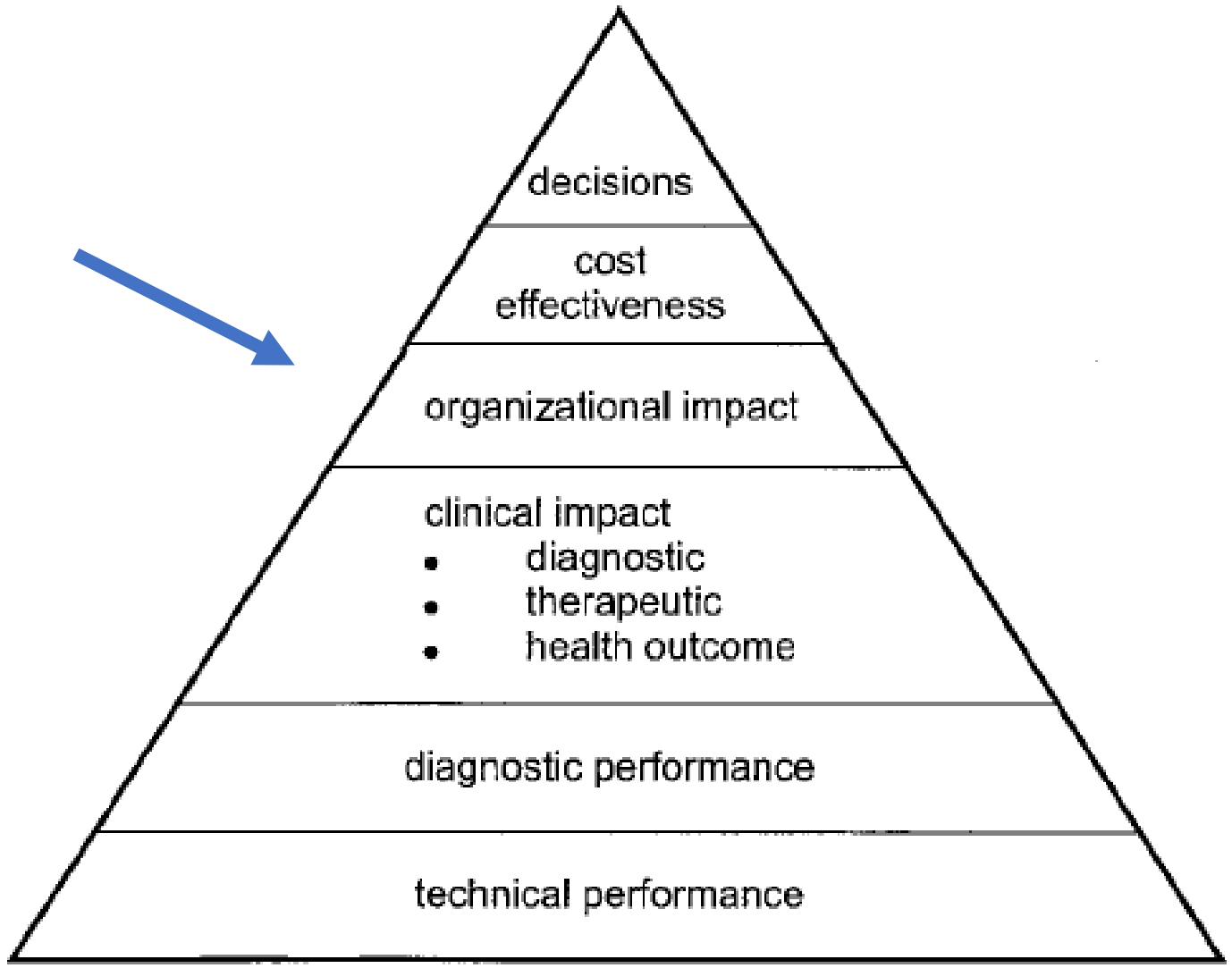

Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Isolatie-maatregelen

- **Isolatie-maatregelen?**

	LCI	CDC
Influenza	Druppel	Druppel
RSV	Druppel	**Contact + standard**

- **Cohortering?**
  - Influenza A vs B?
  - RSV?

Madge P, Paton JY, McColl JH, Mackie PL. Prospective controlled study of four infection-control procedures to prevent nosocomial infection with respiratory syncytial virus. *Lancet* 1992;**340**:1079–1083.

↕

Conclusions—In this multicenter study of children hospitalized with bronchiolitis, RSV was the most common viral etiology, but HRV was detected in one-quarter of children. Since 1 in 3 children had multiple virus infections and HRV was associated with LOS, these data challenge the effectiveness of current RSV-based cohorting practices, the sporadic testing for HRV in bronchiolitis research, and current thinking that the infectious etiology of severe bronchiolitis does not affect short-term outcomes.

Mansbach, 2012 (JAMA)

Impact op isolatie-maatregelen

- **Brendish, 2017 (Lancet)**

	POCT (n=360)	Control (n=354)	Difference (95% CI)	Odds ratio (95% CI)	Number needed to test (95% CI)	p value
Isolation facility use‡						
All patients isolated	63/191 (33%)	49/194 (25%)	7·7% (−1·3 to 16·8)	1·45 (0·94 to 2·27)	..	0·12
Isolated with confirmed respiratory virus infection§	32/191 (17%)	17/194 (9%)	8·0% (1·3 to 14·7)	2·10 (1·12 to 3·92)	13 (6·8 to 73·2)	0·0217
Influenza-positive patients isolated*	20/27 (74%)	13/23 (57%)	17·6% (−8·8 to 43·9)	2·20 (0·67 to 7·24)	..	0·24
Time to isolation (days)¶	0·5 (0·5)	1·0 (0·4)	−0·5 (−0·9 to −0·2)	..	..	0·0071
Time to de-isolation (days)‖	1·0 (0·0)	3·1 (2·2)	−2·1 (−3·6 to −0·7)	..	..	0·0057

- **Nicholson, 2014 (HCA):** te laag aantal patiënten in isolatie

Impact op isolatiemaatregelen

Rapid testing for respiratory syncytial virus in a paediatric emergency department: benefits for infection control and bed management

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SUMMARY

Respiratory syncytial virus (RSV) is responsible for annual winter outbreaks of respiratory tract infection among children in temperate climates, placing severe pressure on hospital beds. Cohorting of affected infants has been demonstrated to be an effective strategy in reducing nosocomial transmission of RSV, and may keep cubicles free for other patients who require them. Testing of symptomatic children for RSV is standard practice, but unfortunately traditional laboratory testing is not rapid enough to aid decision-making processes. Rapid point-of-care testing (POCT) in the emergency department has been suggested as an alternative. We performed a prospective study to quantify the amount of cubicle time saved by using POCT results to allow a targeted cohorting strategy. Over the four-month study period, the POCT allowed 183 children to be admitted directly to a designated cohort area, thus saving 568.5 cubicle-days for other patients. This is equivalent to five cubicles being left free for each day of the study period. This is the first time the benefits of using POCT have been quantified in this way. POCT for RSV is a safe, cost-effective and efficient way to improve bed management.

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Besluit organisatorische impact

- One high-quality trial reported a **benefit in guiding isolation measures in influenza infections**.
- Inconsistent results were obtained for an impact on length of time in the Emergency department. Clinicians at our institution indicated that viral testing plays an important role in triaging patients at the Emergency department.

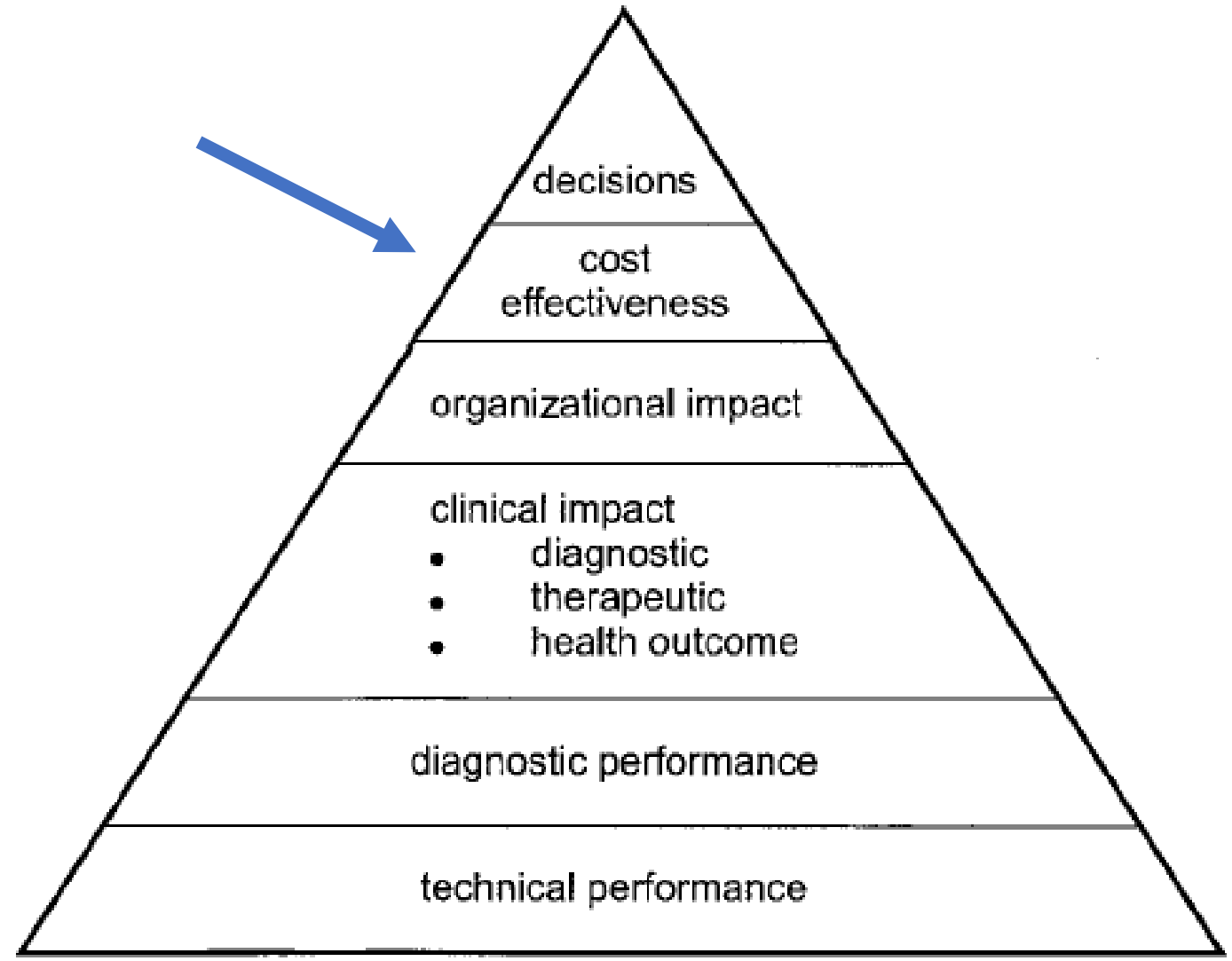
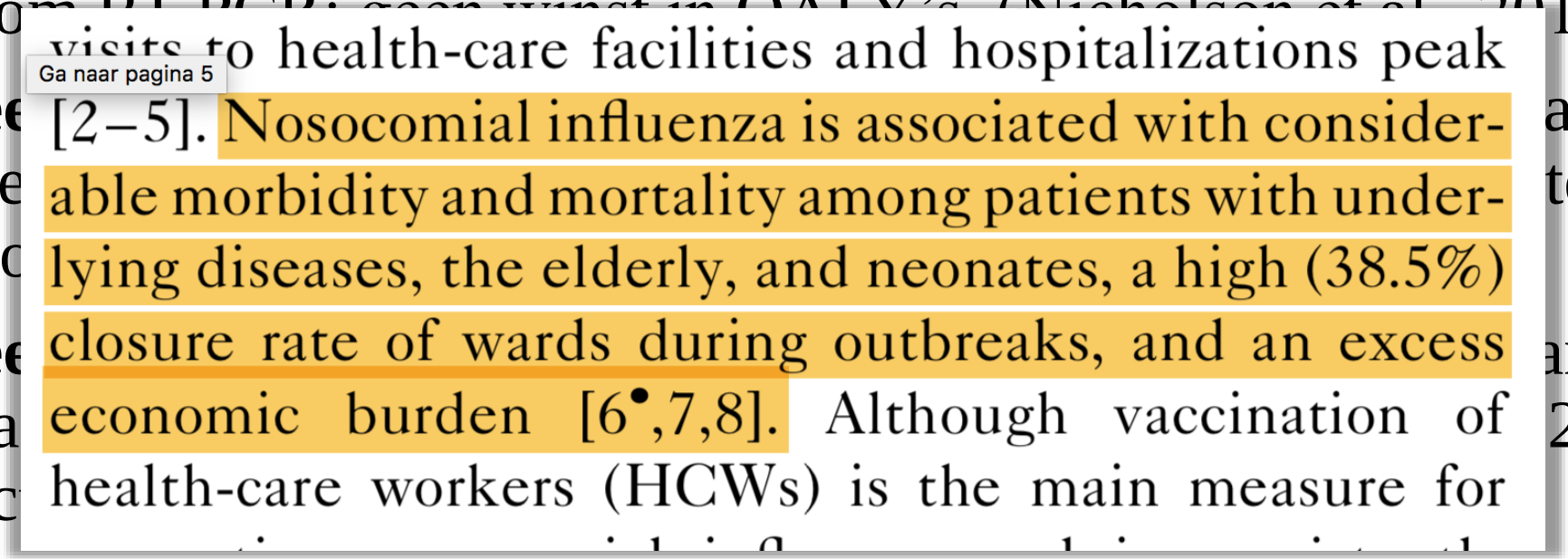


Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Kostenefficiëntie viral testing?

- **Eén RCT**: geen verschil in totale kost van antigeensneltest versus custo
- **Twee** assays): koste teit. (Woc
- **Twee** angrijke impa 2013) → effec
- **<u>Impact op isolatie-maatregelen</u> in geen enkele kostenefficiëntie-studie gekwantificeerd!**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visits to health-care facilities and hospitalizations peak [2–5]. Nosocomial influenza is associated with considerable morbidity and mortality among patients with underlying diseases, the elderly, and neonates, a high (38.5%) closure rate of wards during outbreaks, and an excess economic burden [6•,7,8]. Although vaccination of health-care workers (HCWs) is the main measure for

Besluit kostenefficiëntie

- Hoewel geen overtuigende evidence van kostenefficiëntie van viral testing obv. Klinische impact, **zeer waarschijnlijk wel kostenefficiënt obv organisatorische impact!**
- **(Quid profylactisch oseltamivir?)**

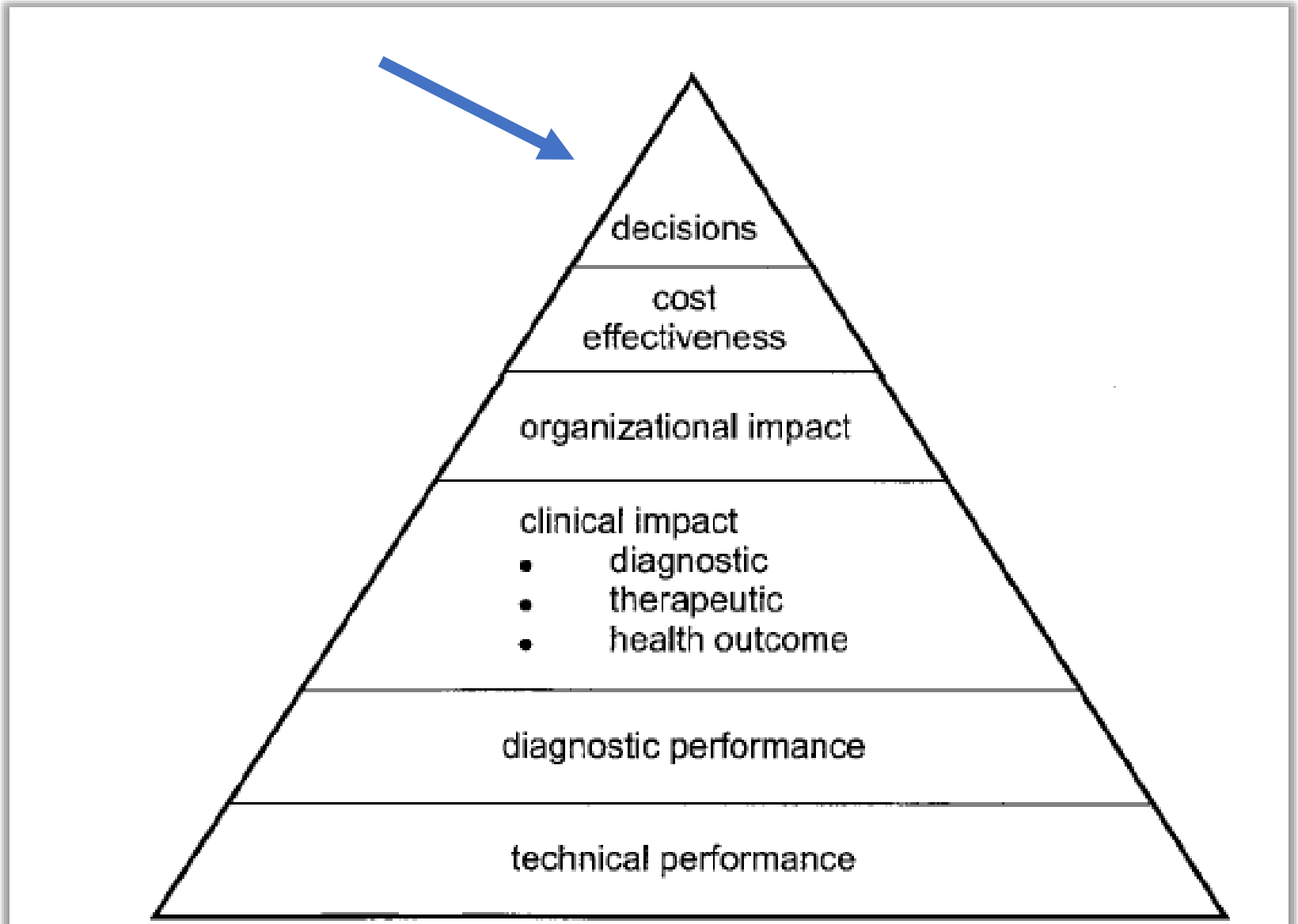

Fig. 2. Evidence of performance designed to facilitate decision-making.

Price, 2000

Besluit: optimale diagnostische workflow

- We propose that rapid (TAT < 1h) or semi-rapid NAATs (TAT < 3h) are preferred diagnostic tests for influenza and RSV, **given the importance of a sensitive test result to guide isolation measures.** Two tier testing using immunoassays in a first step, and confirmatory testing with a (semi-)rapid NAAT in a second step might be equally effective, and more cost-efficient in children.
- **The added value of the newly developed rapid NAATs as opposed to semi-rapid lab assays present in many central laboratories is uncertain**, both regarding clinical impact and in guiding isolation measures: randomized-controlled trials (RCTs) are yet lacking for rapid assays. The only RCT reporting on impact on isolation measures, used a POC multiplex PCR panel, with a mean TAT of 2,4 hours, and demonstrated a significant impact on time to isolation and de-isolation (Brendish et al., 2017).

Besluit/to do's

1. **The use of one-step rapid or semi-rapid NAATs, or two-tier testing (including use of an immunoassay)** are the preferred diagnostic strategies, where their use in **guiding isolation** measures is the best supported test indication.
2. Added value and cost-effectiveness of rapid NAATs in terms of impact on isolation and clinical management is yet to be determined in high-quality trials: **nood aan RCTs!**
3. For implementation of (new, expensive) assays in hospitals, **group purchase/validation/implementation may be beneficial.**