Syndromic approach in critical microbiology

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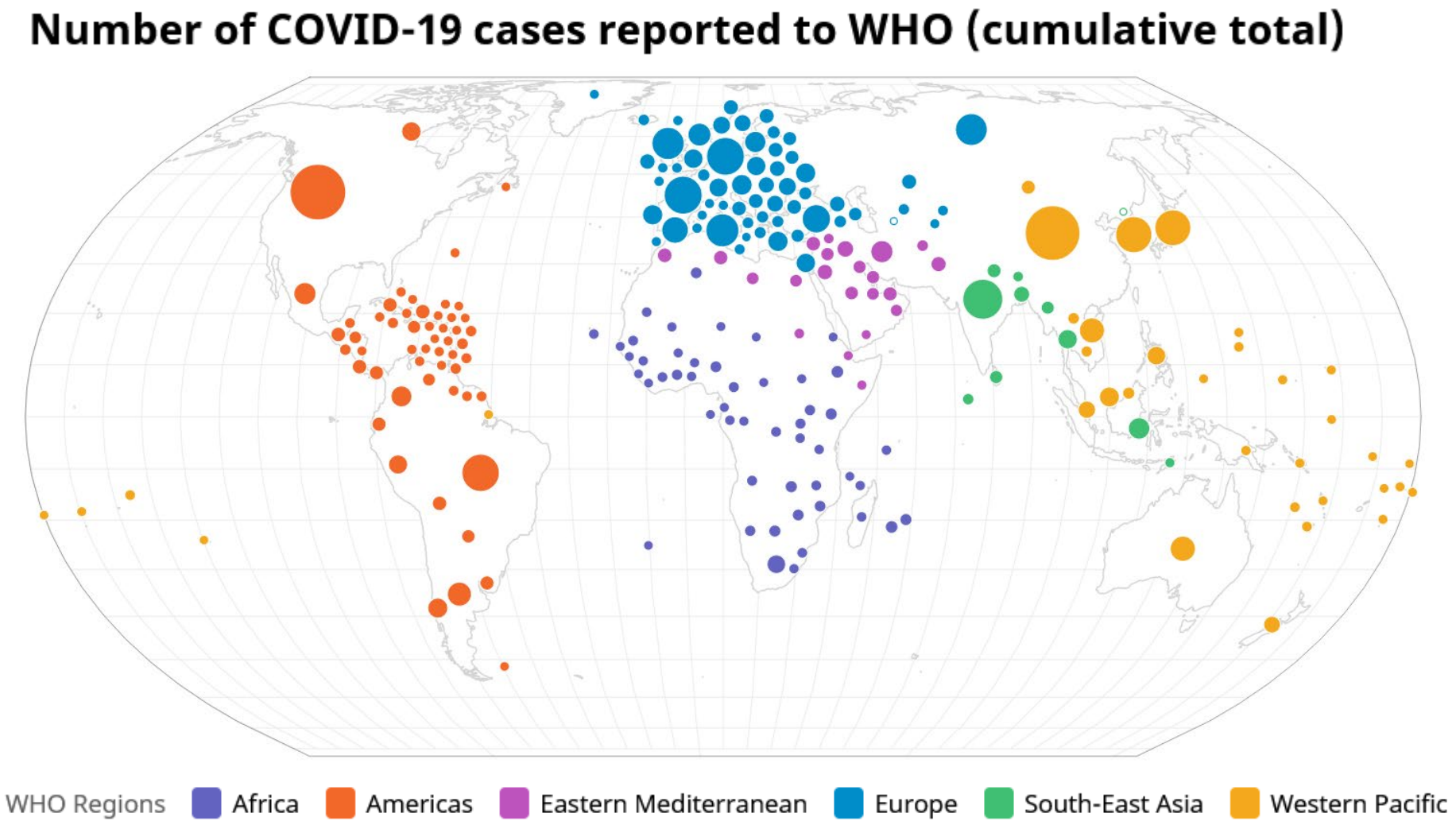
cnrs

Infinity

anrs MALADIES INFECTIEUSES ÉMERGENTES

Saint-Malo – June 13, 2024

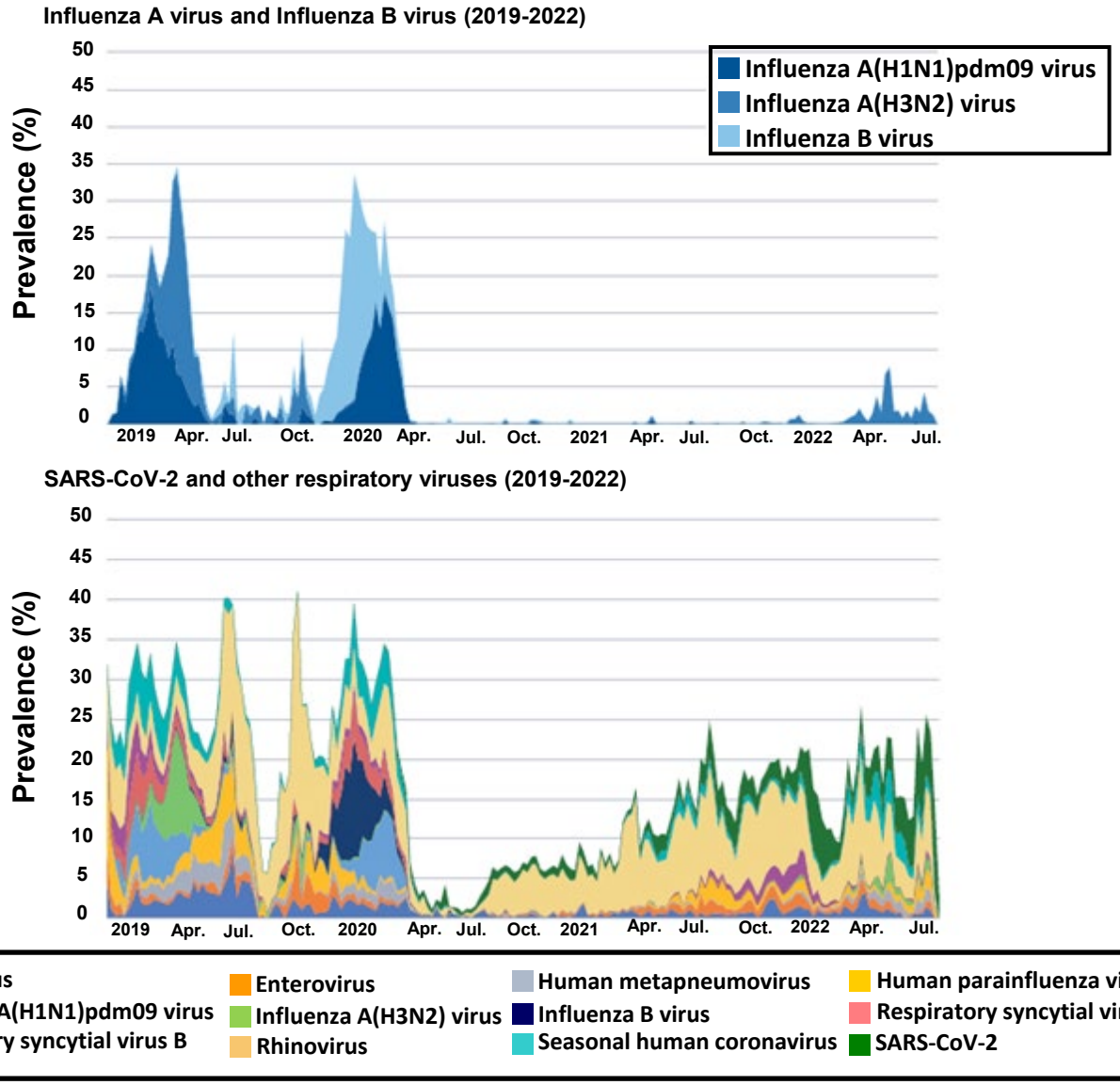
WHO – March 2024



775,251,779
Reported COVID-19 cases
31 March 2024

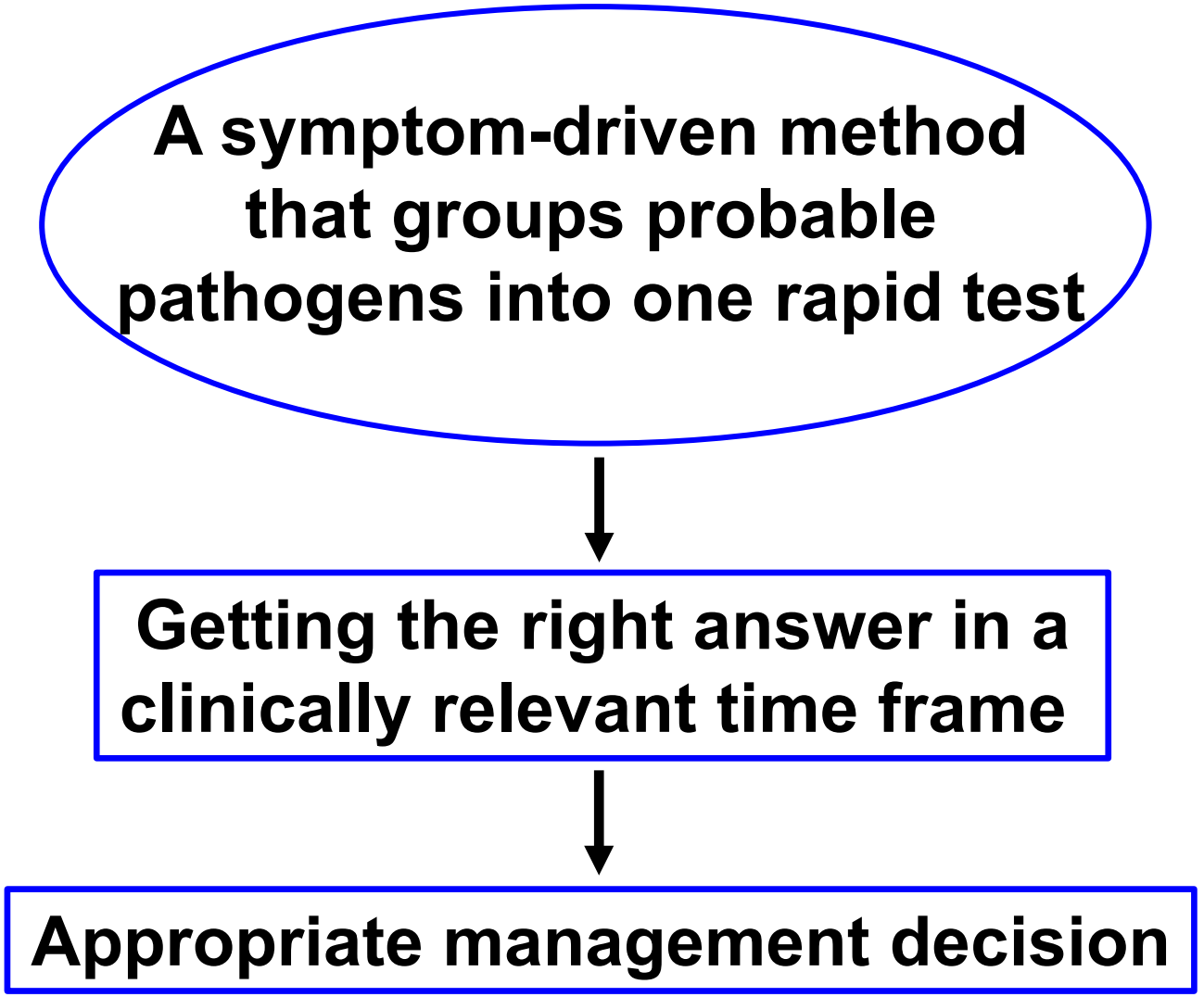
7,043,660
Reported COVID-19 deaths
31 March 2024

The effects of the COVID-19 pandemic on community respiratory virus activity



Chow, *Nature Reviews Microbiology* 2023

What is a syndromic approach ?



Syndromic testing

- ✓ Nucleic Acid Tests & Immunoassays
- ✓ 2 main formats ≠ Multiple single-tests
  - Low-plex : < 5 targets
  - Multi-plex : ≥ 5 targets
- ✓ POC or central lab
- ✓ Systematic or targeted for high-risk patients and/or severe disease

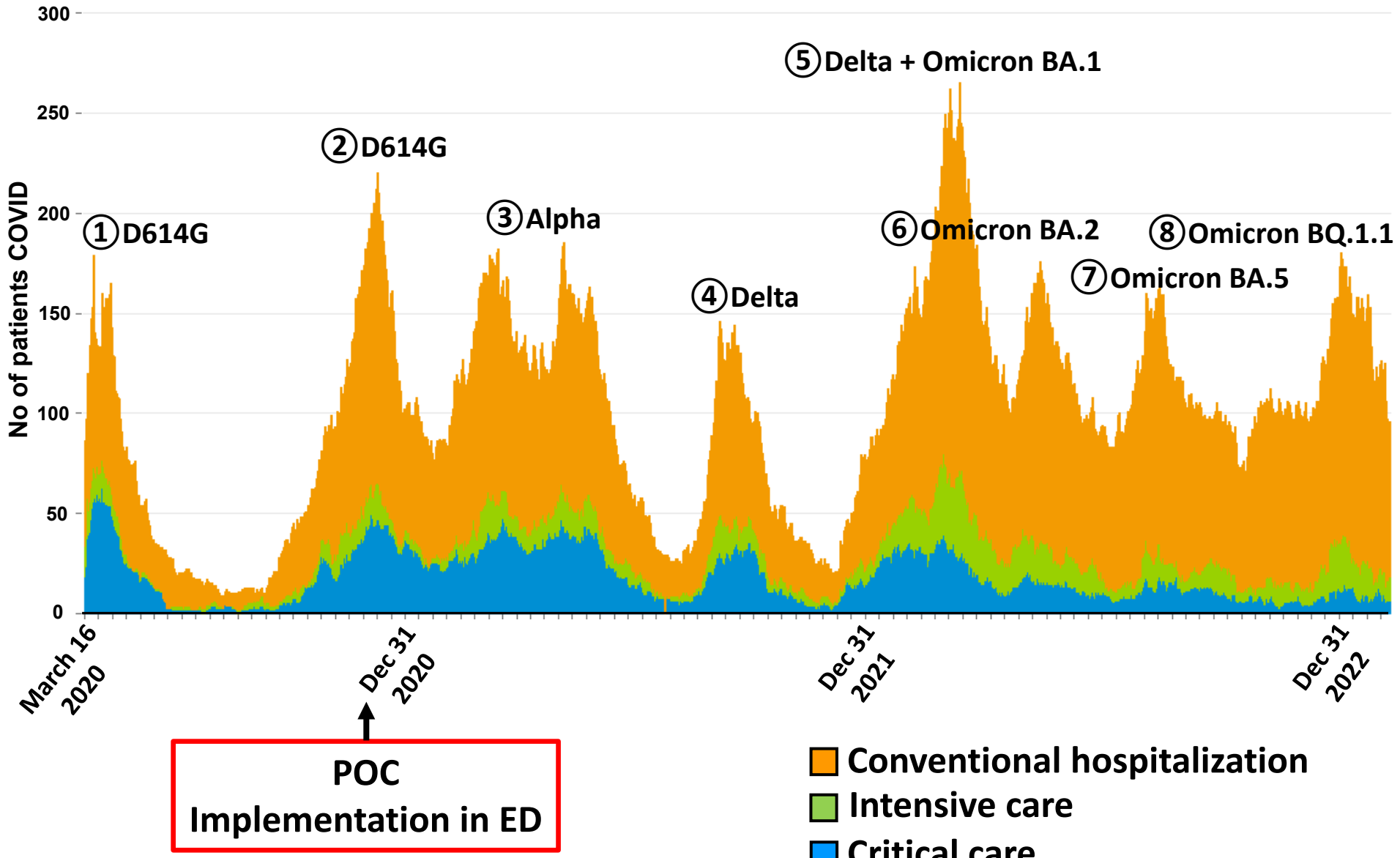
Large clinical spectrum

- ✓ Respiratory pathogens
- ✓ Pathogens associated with CNS infection
- ✓ Gastrointestinal pathogens
- ✓ Other pathogens : fever, sepsis, bone and joint infection,…

Implementation

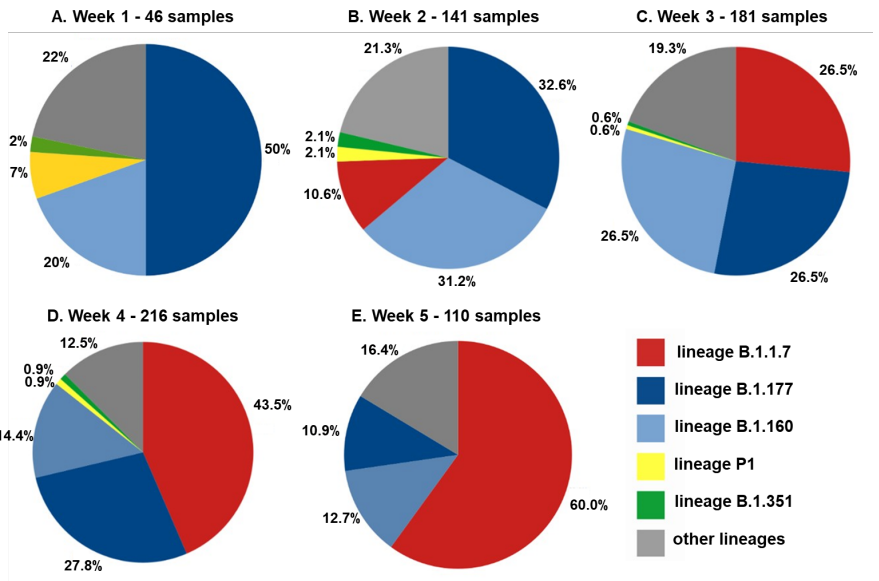
- ✓ **Before SARS-COV-2 emergence**
  - ➔ **contemplation of rapid molecular testing, mostly in central lab**
- ✓ **During the sanitary crisis 2020-2022**
  - ➔ **response in ED with switch to POC, mainly SARS-COV-2**
- ✓ **After the sanitary crisis 2023-**
  - ➔ **consolidation… and extension beyond SARS-COV-2**

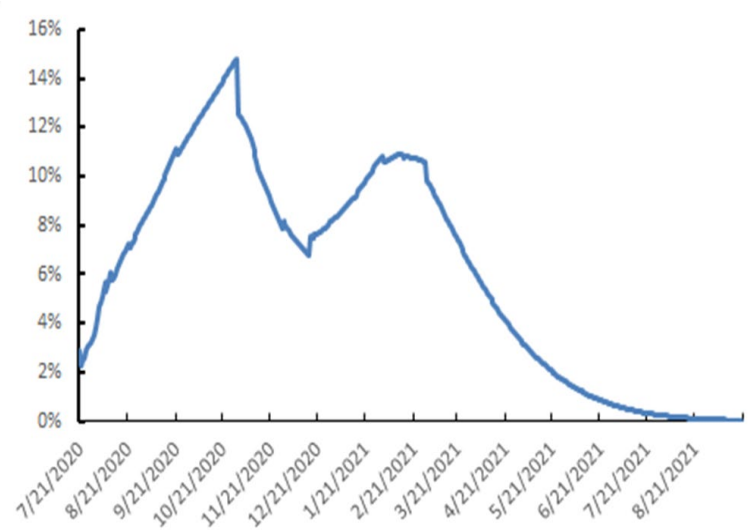
The successive waves



Toulouse University Hospital

- ✓ **Emergence of variant alpha with increased transmissibility**





Dimeglio, *Viruses 2021*

- ✓ **Challenge to reduce the time-to-result in ED despite H24 & 7/7 in the central lab**
  - **specimen shipping : too long**
  - **registration in the LIS: too long**

ID-NOW system - Abbott

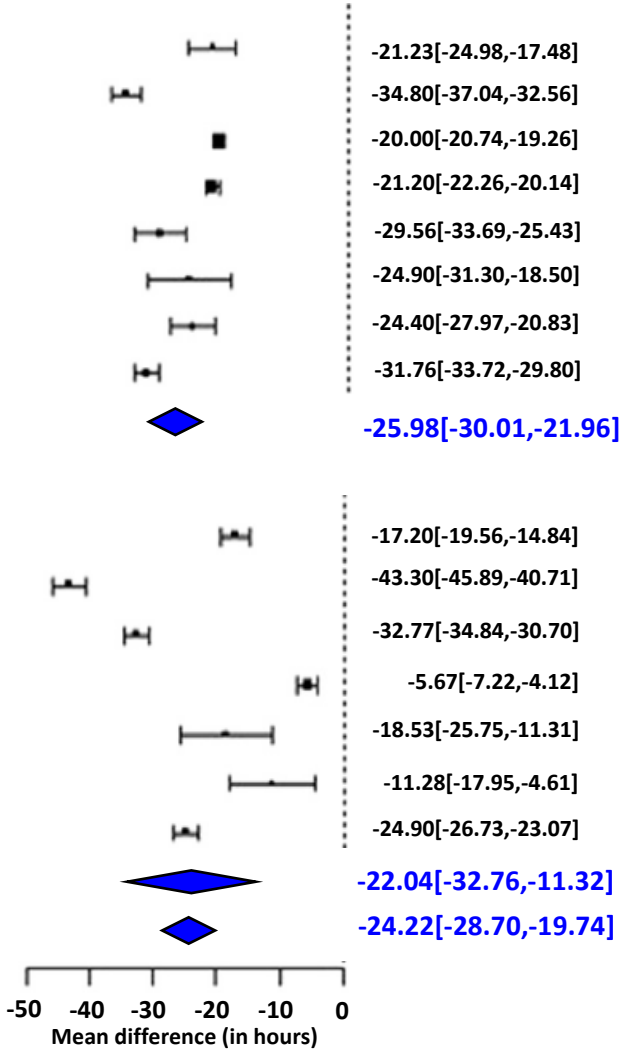
- ✓ 3 instruments / site : 40-50 tests / day on each site
- ✓ Fast installation with connexion to the LIS in less than 1 week
- ✓ Training of 90 (Purpan) and 68 (Rangueil) users
- ✓ Major success :
  - Strong reduction of TAT : 8-12h
  - Strong reduction of phone calls to the lab
  - Invalid results < 3 %

Clinical impact of POC SARS-CoV-2

Type of study	POC system	Comparator Central lab test	Time to result TTR reduction	Length of stay LOS reduction
Monocentric				
Gerlier, 2020	ID-NOW, Abbott	Simplexa, Diasorin	4.34 h vs 10.7min	↓
Baron, 2022	ID-NOW, Abbott	Xpert, Cepheid Film Array BM	4.4 vs 1.9 h	↓
Brendish, 2020	QIA stat-DX, Qiagen	LDT-PCR	21.3 vs 1.7 h	↓
Multicentric (n=6)				
Cancella de Abreu, 2023 1009 pts before 329 pts after	ID-NOW, Abbott QIA stat-DX, Qiagen	Cobas, Roche	10.3 vs 3.1 h	18.1 vs 7.1 h

TTR reduction with rapid multiplex PCR & impact on clinical care

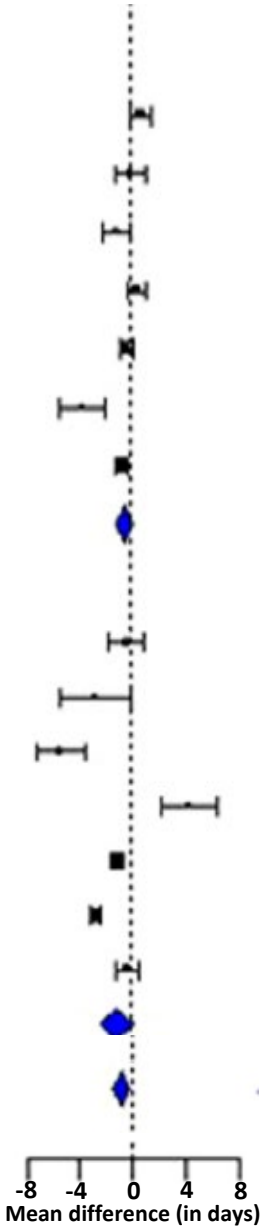
Study ID	Rapid Multiplex PCR			Routine Testing			Risk ratio [95% CI]
RCTs/CCTs	Number of participants	Mean	Standard deviation	Number of participants	Mean	Standard deviation	
Andrews 2017*	334	19.6	17.57	211	40.83	24.04	-21.23[-24.98,-17.48]
Brendish 2017	360	2.3	1.4	354	37.1	21.5	-34.80[-37.04,-32.56]
Brendish 2020*	499	1.73	0.22	555	21.73	8.84	-20.00[-20.74,-19.26]
Clark 2021	307	1.23	0.22	306	22.43	9.46	-21.20[-22.26,-20.14]
Echavarria 2018	176	2	0.65	100	31.56	21.06	-29.56[-33.69,-25.43]
Gelfer 2015	22	1.8	0.3	24	26.7	16	-24.90[-31.30,-18.50]
Gilbert 2016	59	2.1	0.7	68	26.5	15	-24.40[-27.97,-20.83]
Shengchen 2019	398	1.57	0.22	402	33.33	20.09	-31.76[-33.72,-29.80]
Combined mean difference							-25.98[-30.01,-21.96]
Observational studies							
Madigan 2018	124	4.4	0.61	200	21.6	17.02	-17.20[-19.56,-14.84]
Pettit 2015	872	3.1	0.61	230	46.4	20.07	-43.30[-45.89,-40.71]
Poelman 2020	492	3.23	0.61	260	36	17.02	-32.77[-34.84,-30.70]
Rappo2016a	54	1.83	0.46	158	7.5	9.88	-5.67[-7.22,-4.12]
Rappo2016b	85	1.67	0.53	40	20.2	23.3	-18.53[-25.75,-11.31]
Roy 2018b	130	0.72	0.61	25	12	17.02	-11.28[-17.95,-4.61]
Weiss 2019	1043	3	1.17	461	27.9	20.07	-24.90[-26.73,-23.07]
Combined mean difference							-22.04[-32.76,-11.32]
Summary mean difference							-24.22[-28.70,-19.74]



Clark, *Journal of Infection* 2023

LOS rapid multiplex PCR

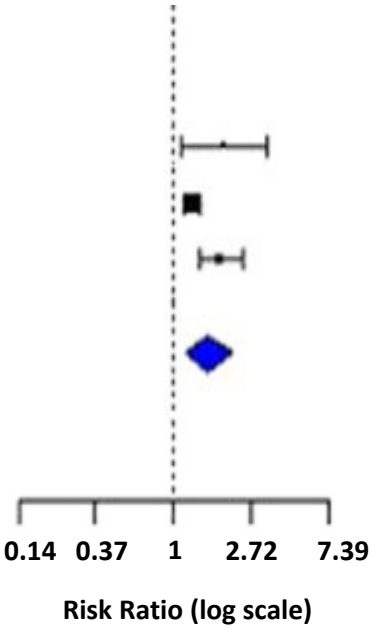
Study ID	Rapid Multiplex PCR			Routine Testing			Risk ratio [95% CI]
RCTs/CCTs	Number of participants	Mean	Standard deviation	Number of participants	Mean	Standard deviation	
Andrews 2017*	334	5.07	5.28	211	4.31	4.57	0.76[-0.08, 1.60]
Branche 2015	151	4	4.78	149	4	5.23	0.00[-1.13, 1.13]
Brendish 2017	360	5.7	6.3	354	6.8	7.7	-1.10[-2.13, -0.07]
Brendish 2020*	499	5.43	5.35	555	5	6.24	0.43[-0.27, 1.13]
Clark 2021	307	3.13	2.76	306	3.47	3.43	-0.34[-0.83, 0.15]
Echavarria 2018	176	4.67	4.48	100	8.33	8.27	-3.66[-5.41, -1.91]
Shengchen 2019	398	8.67	2.98	402	9.33	3.72	-0.66[-1.13, -0.19]
Combined mean difference							-0.44[-1.08, 0.21]
Observational studies							
Esber 2017	128	7	5.21	109	7.35	5.23	-0.35[-1.68, 0.98]
Lee 2020	169	17	14.5	507	19.7	17.2	-2.70[-5.35, -0.05]
Madigan 2018	124	9.94	6.91	200	15.29	10.37	-5.35[-7.23, -3.47]
Qian 2020	112	12.1	4.48	70	7.6	8.27	4.50[2.39, 6.61]
Shadowen 2019	529	8.42	2.98	1994	9.32	3.72	-0.90[-1.20, -0.60]
Timbrook 2015	601	1.33	2.23	219	4	2.99	-2.67[-3.10, -2.24]
Vos 2019	378	6	5.21	192	6.33	5.23	-0.33[-1.24, 0.58]
Combined mean difference							-1.14[-2.38, 0.11]
Summary mean difference							-0.82[-1.52, -0.11]



Clark, *Journal of Infection* 2023

Appropriate infection prevention control

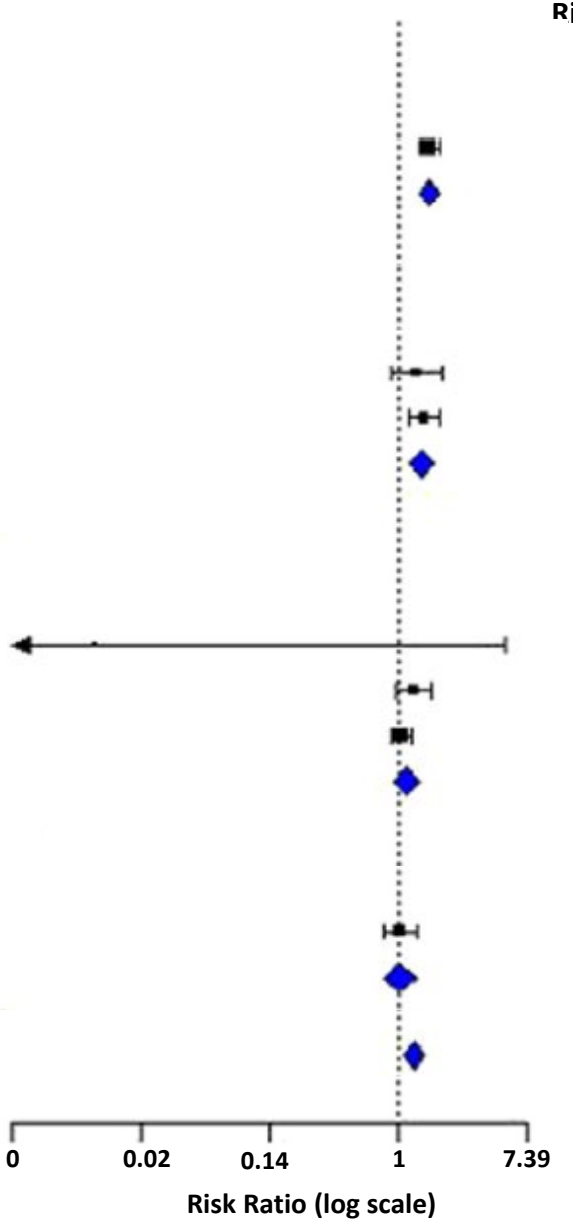
Study ID	Rapid Multiplex PCR		Routine Testing		Risk ratio [95% CI]
RCTs/CCTs	Number with event	Total number	Number with event	Total number	
Brendish 2017	32	191	17	194	1.91[1.10, 3.32]
Brendish 2020*	313	428	242	421	1.27[1.15, 1.41]
Clark 2021	70	100	39	102	1.83[1.39, 2.42]
Summary risk ratio with 95% CI					1.55[1.16, 2.07]



Clark, *Journal of Infection* 2023

Appropriate Influenza antiviral use

Study ID	Rapid Multiplex PCR		Routine Testing		Risk ratio [95% CI]
RCTs/CCTs	Number with event	Total number	Number with event	Total number	
Clark 2021	99	100	63	102	1.60[1.37, 1.87]
Combined risk ratio with 95% CI					1.60[1.37, 1.87]
RCTs/CCTs – Inpatient and emergency department					
Andrews 2017 *	24	30	13	21	1.29[0.88, 1.89]
Brendish 2017	54	57	24	37	1.46[1.14, 1.87]
Combined risk ratio with 95% CI					1.41[1.15, 1.73]
Observational studies – Emergency department					
Mehta 2017	0.1	105.2	2.1	20.2	0.01[0.00, 5.11]
Vos 2019	83	93	17	24	1.26[0.97, 1.64]
Weiss 2019	84	93	23	26	1.02[0.88, 1.19]
Combined risk ratio with 95% CI					1.10[0.90, 1.33]
Observational studies – Inpatient and emergency department					
Rappo 2016a	33	54	96	158	1.01[0.79, 1.29]
Combined risk ratio with 95% CI					1.01[0.79, 1.29]
Summary risk ratio with 95% CI					1.25[1.06, 1.48]



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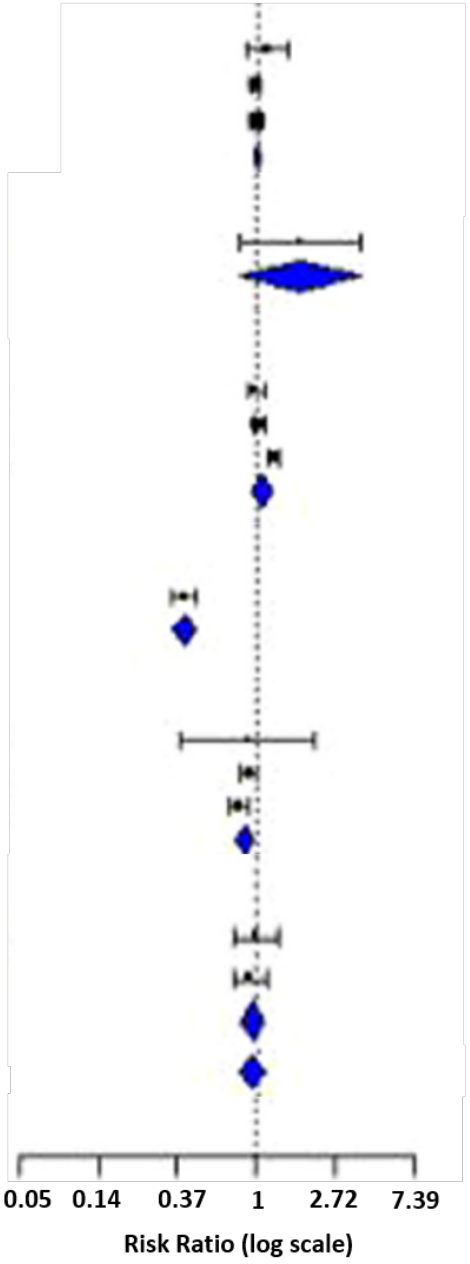
Proportion of patients treated with antibiotics

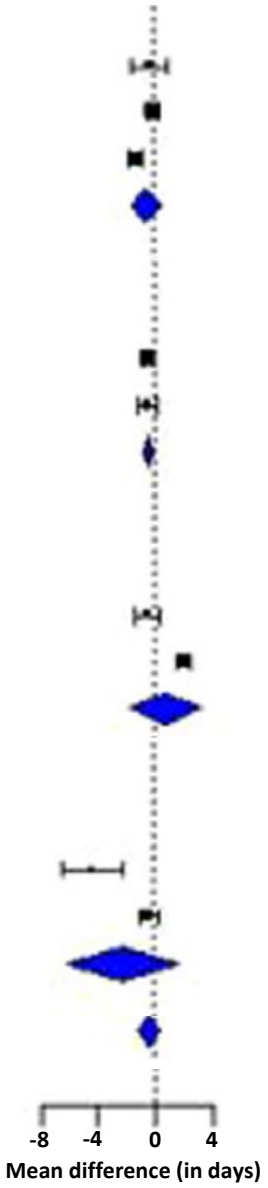
Study ID	Rapid Multiplex PCR		Routine Testing		Risk ratio [95% CI]
RCTs/CCTs	Number with event	Total number	Number with event	Total number	
Branche 2015	69	151	61	149	1.12[0.86, 1.45]
Clark 2021	271	307	278	306	0.97[0.92, 1.03]
Shengchen 2019	367	398	377	402	0.98[0.95, 1.02]
Combined risk ratio with 95% CI					0.98[0.95, 1.01]
RCTs/CCTs – Emergency department					
Gelfer 2015	11	22	7	24	1.71[0.81, 3.63]
Combined risk ratio with 95% CI					1.71[0.81, 3.63]
RCTs/CCTs – Inpatient and emergency department					
Andrews 2017*	243	324	152	198	0.98[0.88, 1.08]
Brendish 2017	301	360	294	354	1.01[0.94, 1.08]
Brendish 2020*	418	499	387	555	1.20[1.12, 1.28]
Combined risk ratio with 95% CI					1.06[0.93, 1.20]
Observational studies – Inpatient					
Timbrock 2015	170	601	156	219	0.40[0.34, 0.46]
Combined risk ratio with 95% CI					0.40[0.34, 0.46]
Observational studies – Emergency department					
Mehta 2017	23	105	5	20	0.88[0.38, 2.03]
Vos 2019	260	378	147	192	0.90[0.81, 1.00]
Weiss 2019	156	234	93	110	0.79[0.70, 0.89]
Combined risk ratio with 95% CI					0.85[0.75, 0.96]
Observational studies – Inpatient and emergency department					
Rappo 2016a	30	54	89	158	0.99[0.75, 1.30]
Rappo 2016b	62	85	32	40	0.91[0.75, 1.12]
Combined risk ratio with 95% CI					0.94[0.80, 1.10]
Summary risk ratio with 95% CI					0.92[0.78, 1.09]



Clark, *Journal of Infection* 2023

Duration of antibiotic use

Study ID	Rapid Multiplex PCR			Routine Testing			Risk ratio [95% CI]
RCTs/CCTs -- Inpatient	Number of participants	Mean	Standard deviation	Number of participants	Mean	Standard deviation	
Branche 2015	151	3.67	4.49	149	4	5.99	-0,33[-1.53, 0.87]
Clark 2021	307	6.3	2.16	306	6.27	2.31	0.03[-0.32, 0.38]
Schengchen 2019	398	7	2.98	402	8.33	3.72	-1.33[-1.80, -0.86]
Combined mean difference							-0.56[-1.60, 0.48]
RCTs/CCTs – Inpatient and emergency department							
Andrews 2017 *	324	5.67	2.23	198	6.1	1.72	-0.43[-0.77, -0.09]
Brendish 2017	360	7.2	5.1	354	7.7	4.9	-0.50[-1.23, 0.23]
Combined mean difference							-0.44[-0.75, -0.13]
Observational studies – Inpatient							
Esber 2017	128	4.5	2.98	109	5.05	3.73	-0.55[-1.42, 0.32]
Timbrock 2015	601	8.5	4.22	219	6.5	3.26	2.00[1.45, 2.55]
Combined mean difference							0.75[-1.75, 3.25]
Observational studies – Emergence department							
Lee 2020	169	12.5	12	507	16.8	13.6	-4.30[-6.46, -2.14]
Vos 2019	378	7.67	2.98	192	8	3.73	-0.33[-0.94, 0.28]
Combined mean difference							-2.17[-6.05, 1.71]
Summary mean difference							-0.41[-1.11, 0.29]



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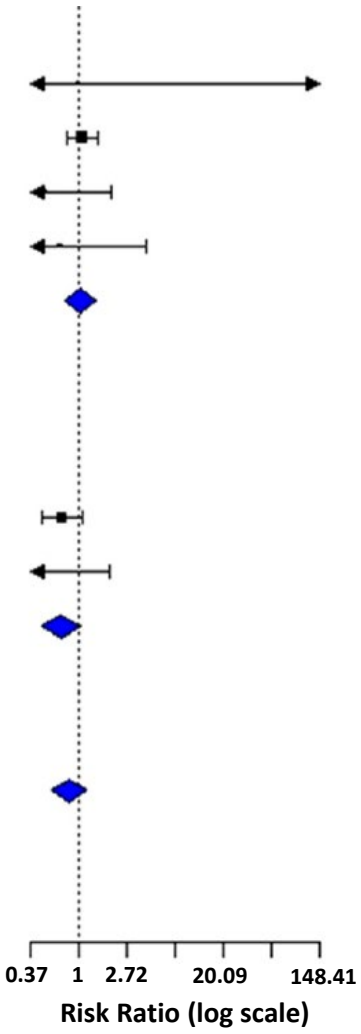
Mortality

Study ID	Rapid Multiplex PCR		Routine Testing		Risk ratio [95% CI]
RCTs/CCTs	Number with event	Total number	Number with event	Total number	
Branche 2015	0.1	151	0.1	149	0.99[0.00, 6304.19]
Brendish 2020*	67	499	69	555	1.08[0.79, 1.48]
Clark 2021	3	307	6	306	0.50[0.13, 1.97]
Shengchen 2019	2	398	3	402	0.67[0.11, 4.01]
Combined risk ratio with 95% CI					1.02[0.74, 1.41]
Observational studies					
Lee 2020	23	169	98	507	0.70[0.46, 1.07]
Weiss 2019	4	234	4	110	0.47[0.12, 1.84]
Combined risk ratio with 95% CI					0.68[0.46, 1.02]
Summary risk ratio with 95% CI					0.82[0.57, 1.18]



Clark, *Journal of Infection* 2023

Clinical outcome of rapid respiratory virus testing in ED

Study	Study design	No. of patients	Age range	Setting: country	Target & type of rapid test	Rapid test	Comparator
Bonner et al, 2023	RCT	391	2 mo to 21 y	ED; US	Influenza ; antigen	FluOIA Biostar	Same test, result unknown
Esposito et al, 2023	RCT	957	0-15 y	ED; Italy	Influenza ; antigen	Sofia Quickvue	No test
Iyer et al, 2005	Quasi-RCT (alternating days)	700	2-24 mo	ED; US	Influenza ; antigen	Sofia Quickvue	No test
Phoeling et al, 2006	Quasi-RCT (randomized days)	305	<5 y	ED; US	Influenza ; antigen	Sofia Quickvue	No test
Doan et al, 2009	RCT	199	3-36 mo	ED; Canada	Multiple; immunofluorescence	SimulFluor	Routine care
Brendish et al, 2017	RCT	279	≥18 y	ED and acute medical unit; UK	Multiple; molecular	BioFire FilmArray	Routine care
Echavarria et al, 2018	RCT	432	2 mo to 6 y	ED; Argentina	Multiple; molecular	BioFire FilmArray	Immunofluorescence
May et al, 2019	RCT	191	≥18 mo	ED; US	Multiple; molecular	BioFire FilmArray	Routine care
Bouzid et al, 2021	Quasi-RCT (alternating weeks)	474	≥18 y	ED; France	Multiple; molecular	QIAstat-Dx	Respiratory panel in centralized laboratory
Rao et al, 2021	RCT	908	1 mo to 18 y	ED; US	Multiple; molecular	BioFire FilmArray	Routine care
Bibby et al, 2022	Quasi-RCT (alternating days)	421	All age groups	ED and inpatients; Canada	Influenza and RSV; molecular	Xpert Xpress	Respiratory panel in centralized laboratory
Matilla et al, 2022	RCT	1243	0-17 y	ED; Finland	Multiple; molecular	QIAstat-Dx	Routine care

Schober, *JAMA Internal Med* 2024

Results for rapid viral test availability

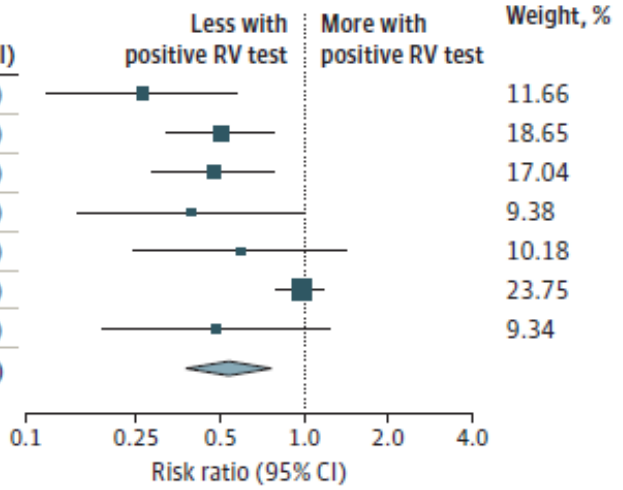
Outcome	No. of studies	No. of patients	Summary
Antibiotic use	11	6068	Little or no difference
Influenza antiviral use	7	2969	Probably increases
Chest radiography	8	4408	Probably decreases
Blood test	5	2552	May decrease
Urine analysis/culture	4	1595	Little or no association
ED length of stay	4	2333	Little or no difference
ED return visit	7	3520	Little or no difference
Hospitalization	9	5489	Little or no difference

Schober, *JAMA Internal Med* 2024

Association of a positive rapid viral test with antibiotic use

RV positive vs negative test result

Study	RV test		Control		Risk ratio (95% CI)	Weight, %
	Antibiotic	Total	Antibiotic	Total		
Bonner et al,[20] 2003	7	96	27	97	0.26 (0.12-0.57)	11.66
Esposito et al,[23] 2003	14	43	282	435	0.50 (0.32-0.78)	18.65
Iyer et al,[17] 2006	15	105	73	240	0.47 (0.28-0.78)	17.04
Poehling et al,[18] 2006	4	28	39	107	0.39 (0.15-1.00)	9.38
Doan et al,[22] 2009	8	56	8	33	0.59 (0.24-1.42)	10.18
Brendish et al,[21] 2017	41	55	60	78	0.97 (0.80-1.18)	23.75
Bibby et al,[15] 2022	5	67	18	117	0.49 (0.19-1.25)	9.34
Random-effects model: $I^2 = 65.69\%$; $\tau^2 = 0.13$					0.53 (0.37-0.77)	



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Antibiotic prescribing according to rapid viral test availability

Category	Subgroup	No. of studies	No. of patients	Relative association estimate (risk ratio)	Absolute association estimate (risk difference)	Subgroup comparison
Age	Children and adolescents	9	5105	0.97 (95% CI, 0.83 to 1.12)	-0.01 (95% CI, 0.05 to 0.02)	*P* = .82
	Adults	4	963	0.98 (95% CI, 0.89 to 1.09)	-0.01 (95% CI, 0.07 to 0.05)	
Test type	Traditional (antigen and immunofluorescence	5	2552	0.91 (95% CI, 0.77 to 1.07)	-0.03 (95% CI, 0.07 to 0.01)	*P* = .26
	Molecular	6	3516	1.01 (95% CI, 0.92 to 1.12)	-0.01 (95% CI, 0.03 to 0.05)	
No. of targets	Monoplex (influenza)	4	2353	0.91 (95% CI, 0.76 to 1.09)	-0.03 (95% CI, 0.08 to 0.02)	*P* = .32
	Multiplex (≥2)	7	3715	1.01 (95% CI, 0.93 to 1.09)	-0.005 (95% CI, 0.03 to 0.04)	
Risk of bias	Low risk of bias	7	4168	0.95 (95% CI, 0.82 to 1.10)	-0.02 (95% CI, 0.06 to 0.03)	*P* = .73
	High risk of bias	4	1900	0.99 (95% CI, 0.87 to 1.12)	-0.0005 (95% CI, 0.04 to 0.05)	
Industry funding	None	7	4074	0.97 (95% CI, 0.90 to 1.03)	-0.02 (95% CI, 0.05 to 0.00)	*P* = .57
	Industry funding	4	1994	1.05 (95% CI, 0.79 to 1.39)	-0.01 (95% CI, 0.05 to 0.07)	

Schober, *JAMA Internal Med* 2024

Potential interest of host response markers

The diagnosis of a virus does not rule out the presence of concomitant bacterial infection

Finger-prick blood & LFD

FebriDx-Lumos Diagnostics
MxA-CRP

NPV > 92 %

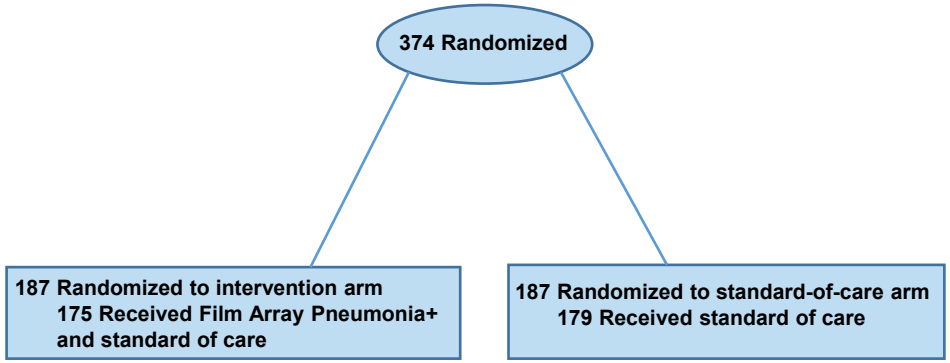
Brendish, *Journal of Infection* 2024

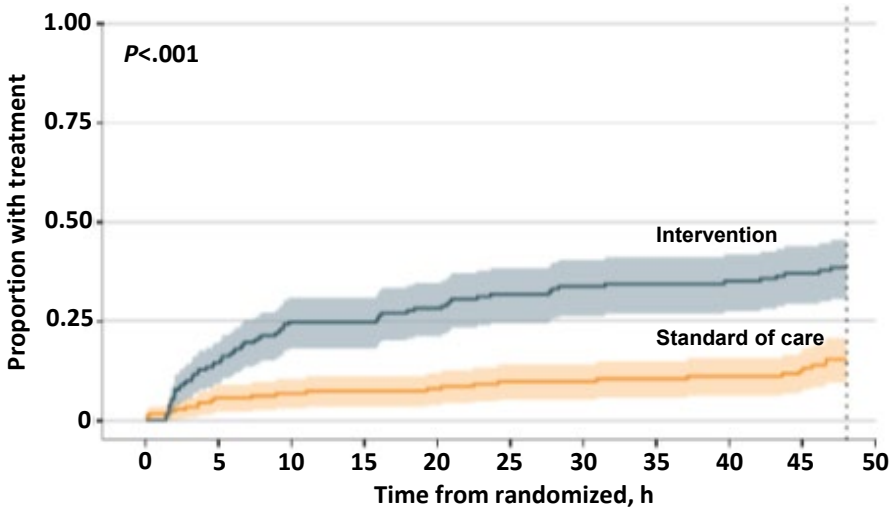
MeMed BV
TRAIL-CRP-IP10

NPV > 98 %

Van Houten, *Lancet ID* 2017
Papan, *Clin Microbiol Infect* 2022

CAPNOR – Monocentric study in Norway of syndromic molecular testing in adult ED



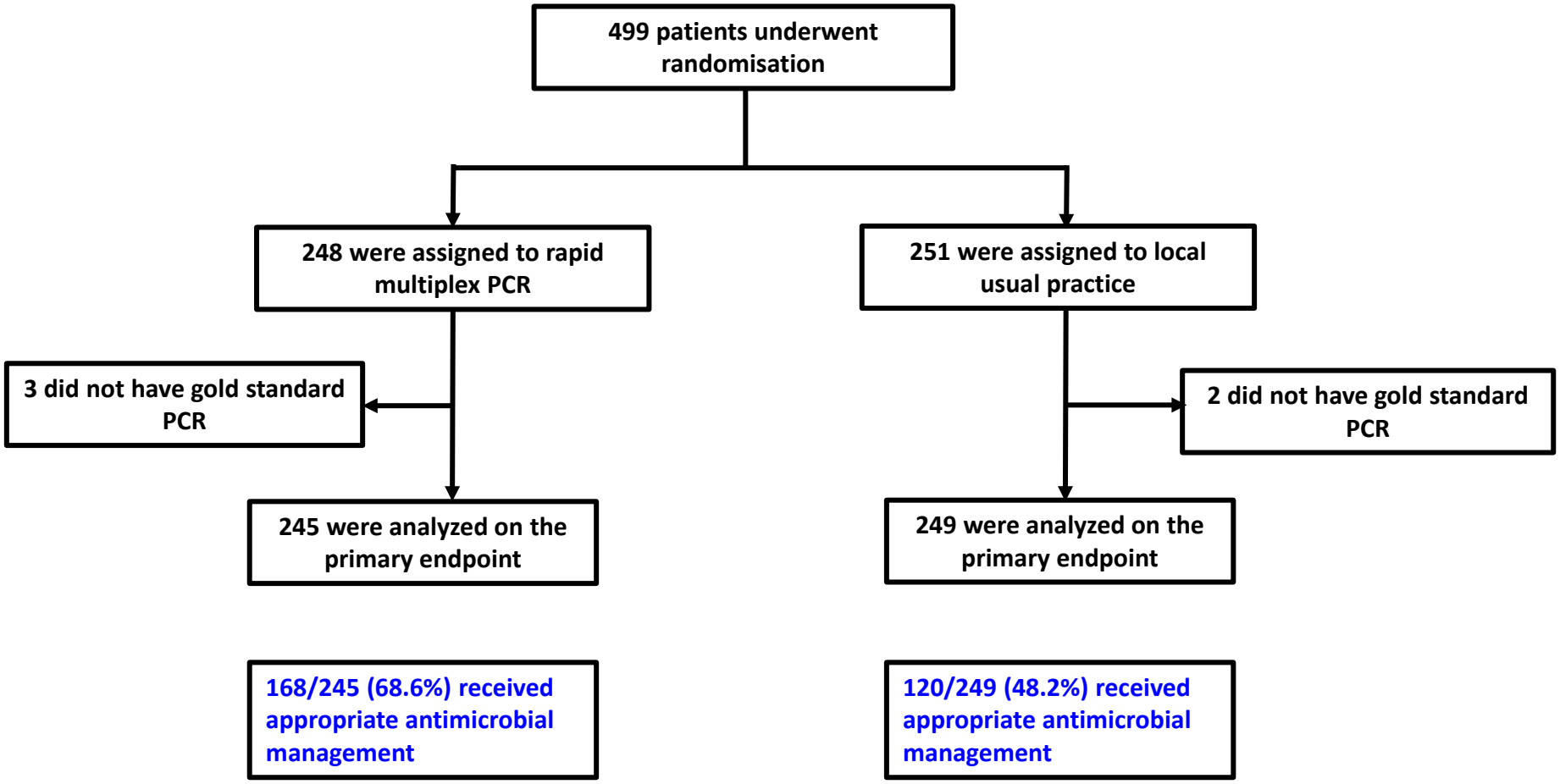


No. at risk

Standard of care	187	163	160	159	155	142	136	134	133	124	0
Intervention	187	149	131	130	120	108	101	100	99	91	0

Markussen, *JAMA Network Open* 2024

OPTIPAC – French multicentre study in paediatric ED (n=11)



Cantais, submitted

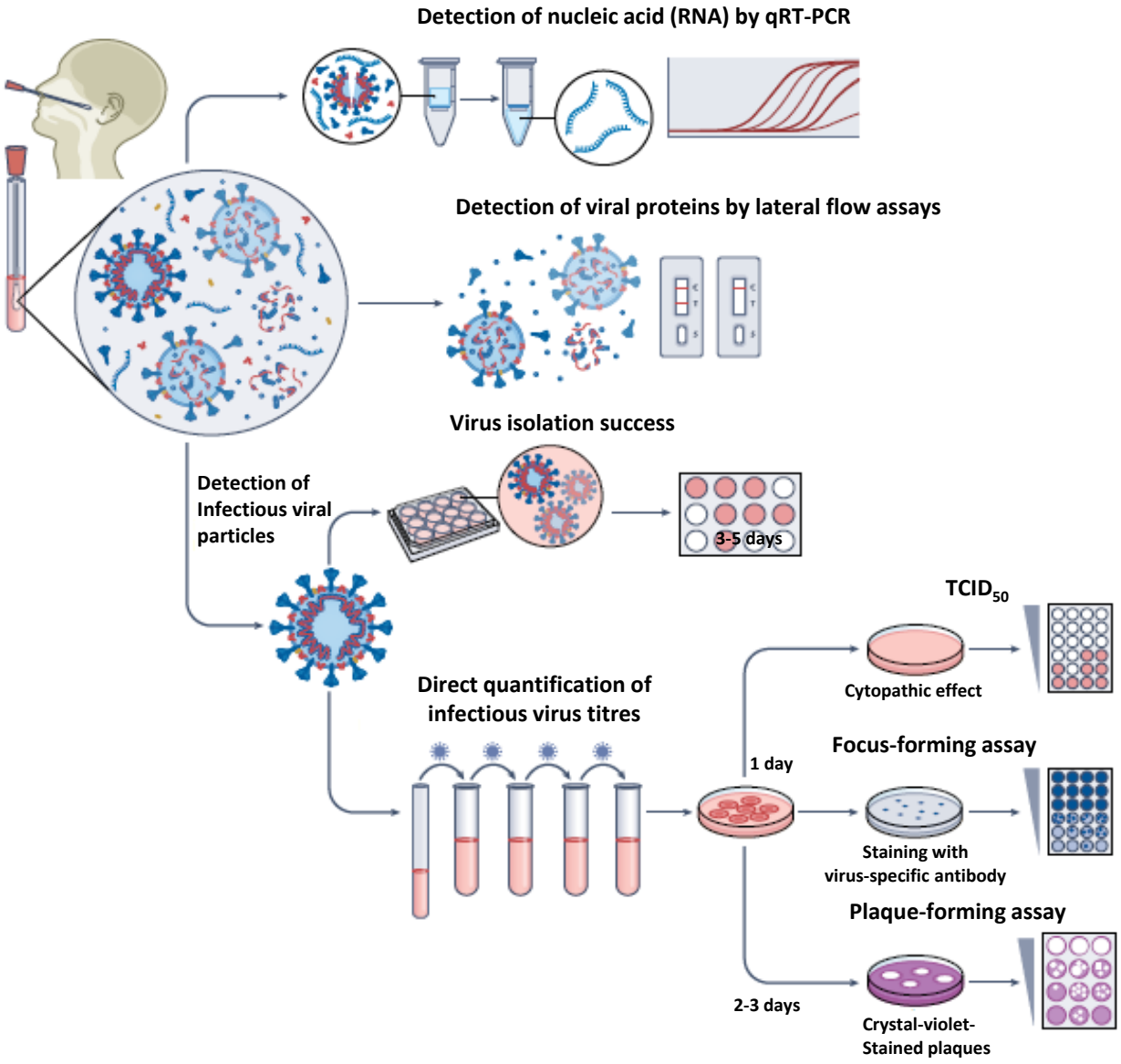
French guidelines

Patient type SYMPTOMATIC HOSPITALIZED and type of service	Quadriplex test detecting: - Influenza A/B virus - RSV - SARS-CoV-2	Extended multiplex PCR or completed panel with adaptation according to local equipment
Adult patient WITHOUT risk of serious form	Recommended	Not recommended
Adult patient WITH risk of serious form	Recommended	Recommended as second-line if quadriplex test negative and impact on treatment
Patient in service of resuscitation#	Recommended	Recommended straight away if possible
Immunocompromised patient	Recommended	Recommended straight away if possible
Medical-social or health establishment or EHPAD	Recommended	Not recommended
Patient in geriatrics department	Recommended	Recommended as second intention if tested negative quadriplex and impact on care or allowing a strengthening of prevention measures and avoiding nosocomial transmissions

French guidelines

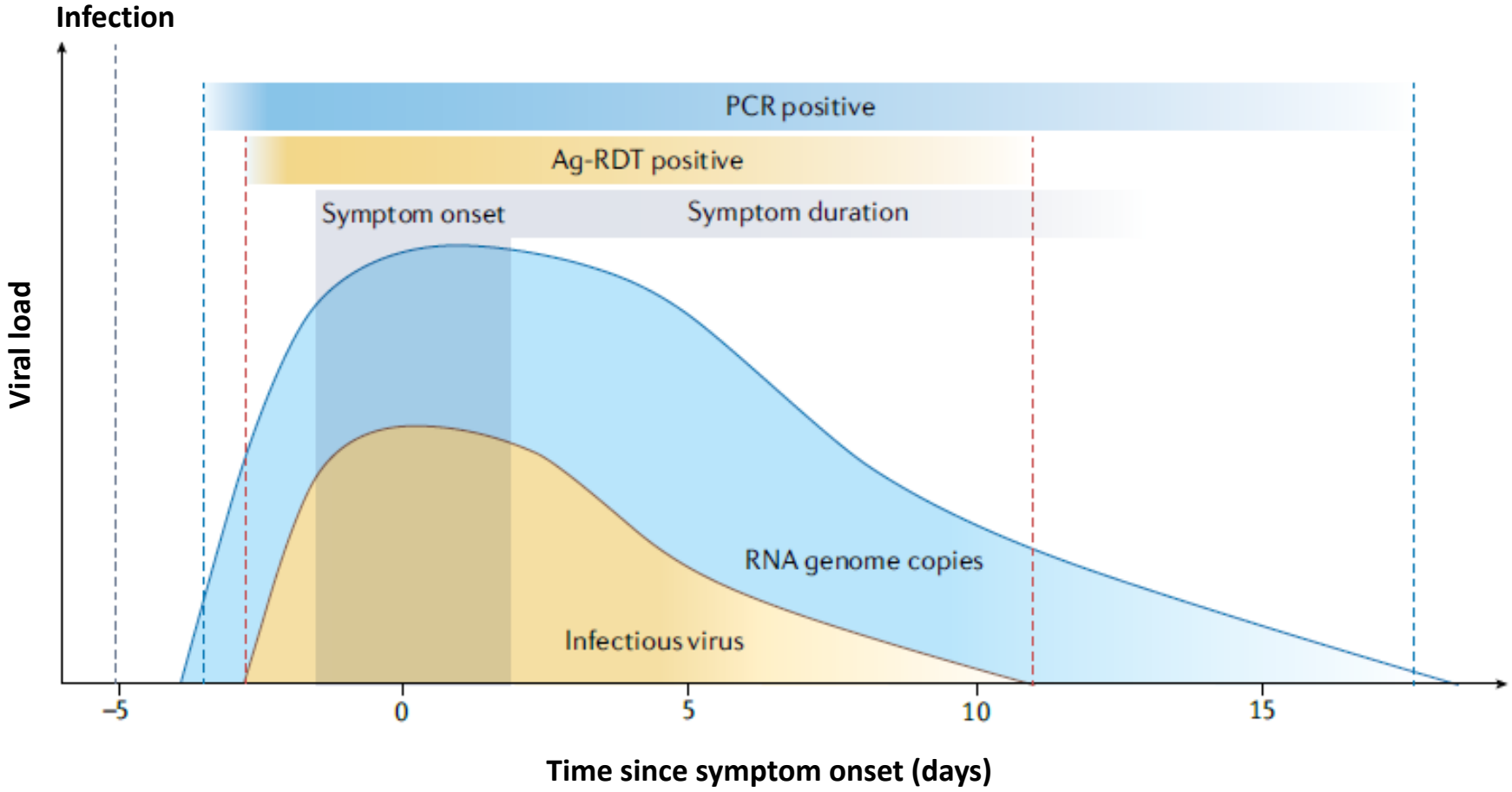
Patient type SYMPTOMATIC HOSPITALIZED and type of service	**Quadriplex test detecting: - Influenza A/B virus - RSV - SARS-CoV-2**	**Extended multiplex PCR or completed panel with adaptation according to local equipment**
Child WITH or WITHOUT risk of serious form	**Recommended**	**Recommended from the outset if foreseeable impact on care, particularly outside periods of circulation of influenza viruses and RSV**
Pregnant woman	**Recommended**	**Not recommended**
Exploring a cluster	**Recommended, use a test detecting the infectious agent responsible for the cluster**	
Healthcare personnel in contact with people likely to make a serious disease	**Recommended**	**Not recommended**

Virological tools



Puhach, *Nat Rev Microbiol* 2023

Interpretation



Puhach, *Nat Rev Microbiol* 2023

Rapid antigenic multiplex test vs multiplex molecular assay in a paediatric population

All in Triplex AAZ POC	Panther Fusion system Hologic on sample dilution buffer Central lab							
	Flu A/B	RSV	SARS- CoV-2	RHV	MPV	ADV	ParaFLu	Negative
Flu A/B	4	0	0	0	0	0	0	0
RSV	0	21	0	8	5	2	0	0
SARS- CoV-2	0	0	6	2	0	1	0	0
Negative	0	6	2	10	5	0	5	
Sensitivity	100 %	75 %	75 %					

Mansuy, *Lancet Microbe* 2024

Respiratory Metagenomics

CLINICAL

Population: intubated ICU patients

Sampling: BAL, tracheal aspirate, or pleural fluid

Median Turnaround time:

6.7 hours

Clinical reporting:

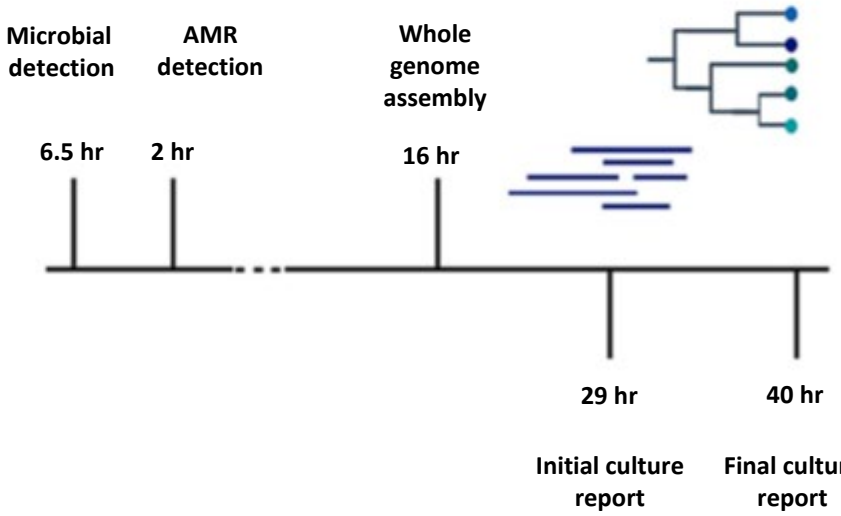
1. Detection of bacterial pathogens and DNA viruses
2. Early tailoring of antibiotics
3. Outbreak investigations

LABORATORY

Patient sample

DNA extraction, library preparation, & nanopore sequencing

Routine microbiology



Lydon, *Am J Respir Crit Care Med* 2024

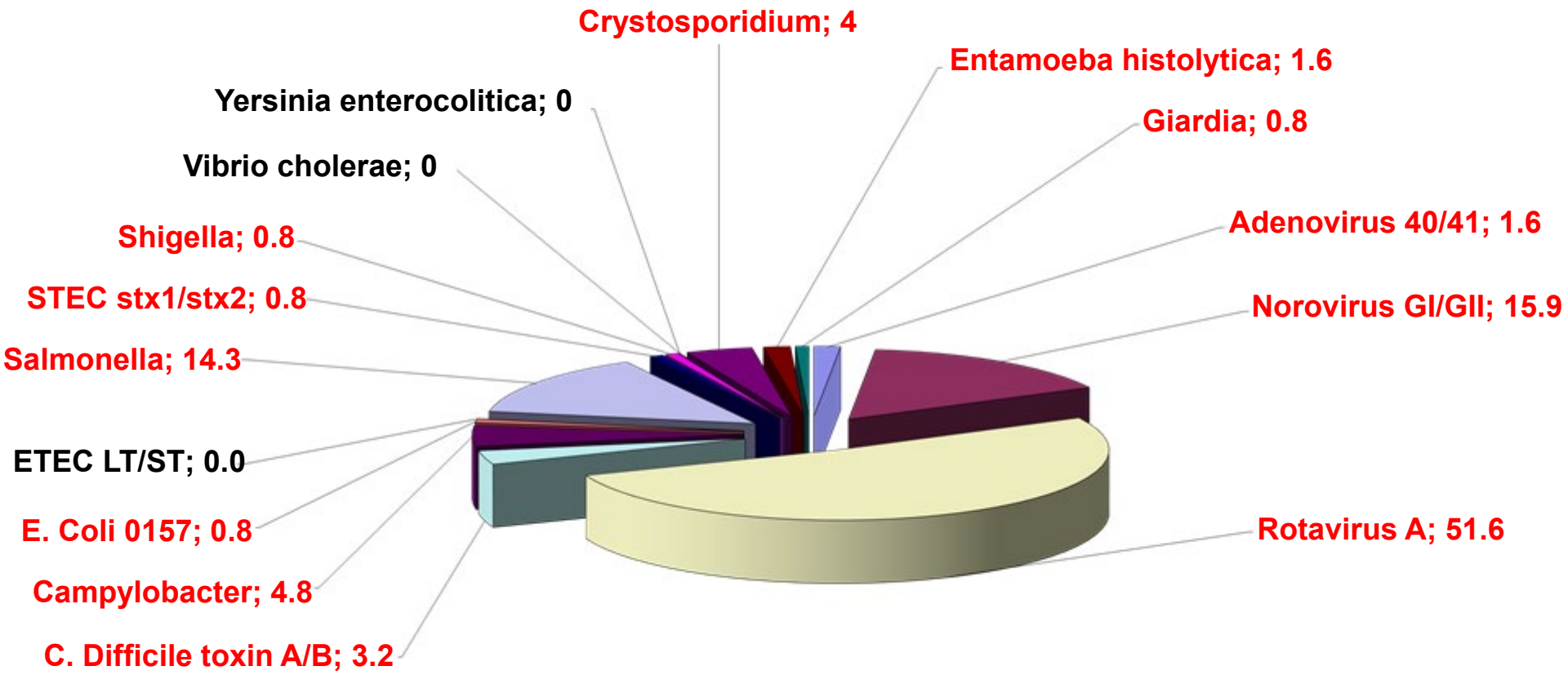
Multiplex PCR gastrointestinal pathogen panels

	Manufacturer	Separate nucleic acid extraction required?	Time to result	Laboratory throughput	Rotavirus	Norovirus	Sapovirus	Adenovirus	Astrovirus
BioCode Gastrointestinal Pathogen Panel	Applied BioCode	Yes	3.5-5h	Up to 96	Yes	Yes	No	Yes	No
BD MAX Enteric Viral Panel	Becton, Dickinson and Company	No	3.5-4h	Up to 24	Yes	Yes	Yes	Yes	Yes
BioFire FilmArray Gastrointestinal Panel	bioMérieux	No	1h	1	Yes	Yes	Yes	Yes	Yes
VERIGENE Enteric Pathogen Test	Luminex Corporation	No	2h	1	Yes	Yes	No	No	No
xTAG Gastrointestinal Pathogen Panel	Luminex Corporation	Yes	5h	Up to 24	Yes	Yes	No	Yes	No
GastroFinder 2Smart	PathoFinder	Yes	2.5h	1	Yes	Yes	Yes	Yes	Yes
QIAstat-Dx Gastrointestinal Panel	QIAGEN	No	1h	1	Yes	Yes	Yes	Yes	Yes
RIDA GENE Viral Stool Panel III	R-Biopharm AG	Yes	1-2h	Up to 96	Yes	Yes	No	Yes	No
Allplex Gastrointestinal Panel	Seegene	Yes	5h	Up to 96	Yes	Yes	Yes	Yes	Yes
EntericBio Viral Panel 3	Serosep	No	1.5-3h	Up to 46	Yes	Yes	Yes	Yes	Yes

Flynn, *Lancet* 2024

Gastrointestinal pathogens

Luminex-based molecular assay – Core lab 4h

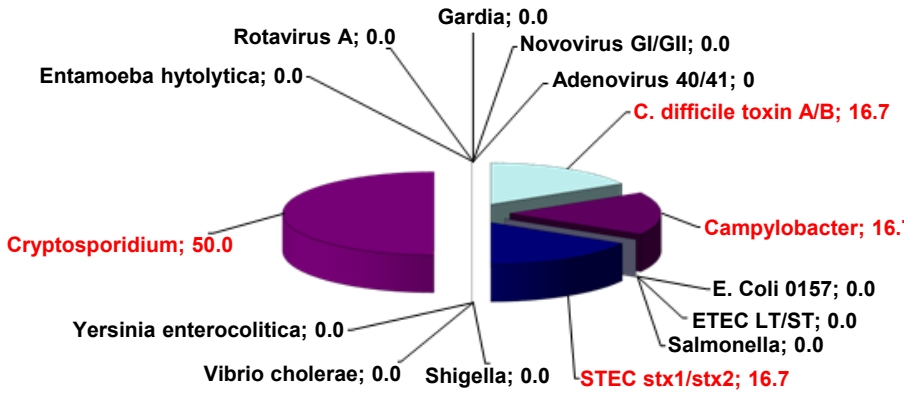


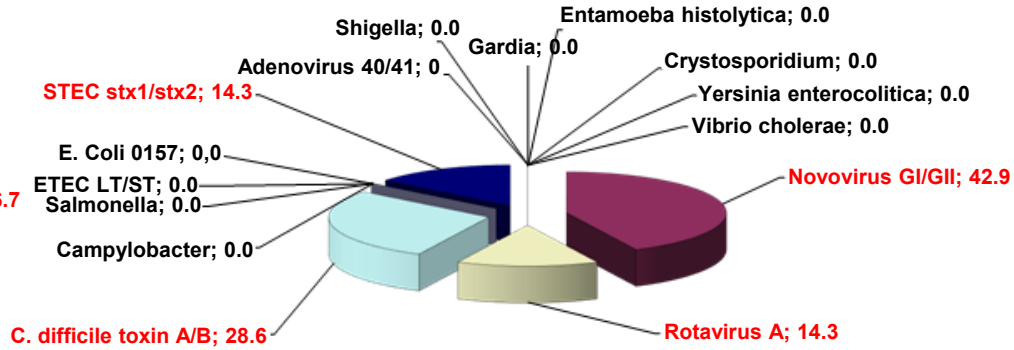
Diarrheic children – Emergency unit
Detected pathogens 93/119 (78 %)
Virus 70 % - Bacteria 25 % - Parasite 5 %

Mengelle, *Clin Microbiol Infect* 2013

Gastrointestinal pathogens

Luminex-based molecular assay – Core lab 4h





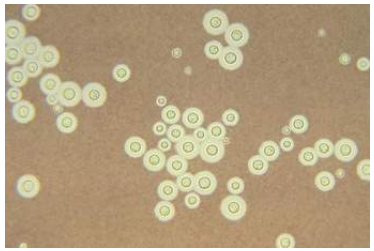
Diarrheic children – Neonatology unit
Detected pathogens 8/60 (13 %)
Co-infections (0 %)

Diarrheic children – Hematology unit
Detected pathogens 9/53 (17 %)
Co-infections (0 %)

Mengelle, *Clin Microbiol Infect* 2013

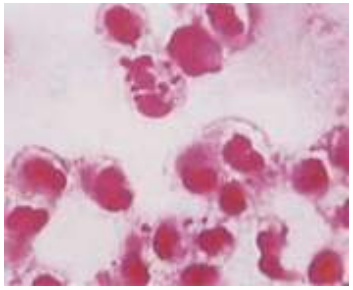
CNS pathogens
Meningitis & encephalitis

Fungi



Cryptococcus

Bacteria



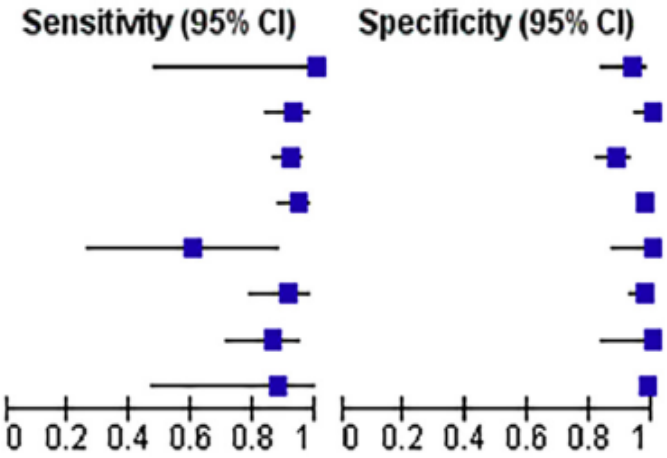
Neisseria meningitidis
S pneumoniae
Listeria m
Haemophilus
S agalactiae
E coli KI

Virus

HSV-1, HSV-2
Enterovirus, VZV, CMV, HHV6,
Parechovirus

Diagnostic test accuracy of the BioFire FilmArray meningitis/encephalitis panel

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arora 2017	5	4	0	57	1.00 [0.48, 1.00]	0.93 [0.84, 0.98]
Graf 2017	62	0	5	66	0.93 [0.83, 0.98]	1.00 [0.95, 1.00]
Hanson 2016	145	19	13	143	0.92 [0.86, 0.96]	0.88 [0.82, 0.93]
Leber 2016	98	33	6	1423	0.94 [0.88, 0.98]	0.98 [0.97, 0.98]
Lee 2019	6	0	4	26	0.60 [0.26, 0.88]	1.00 [0.87, 1.00]
Messacar 2016	41	2	4	93	0.91 [0.79, 0.98]	0.98 [0.93, 1.00]
Piccirilli 2018	36	0	6	21	0.86 [0.71, 0.95]	1.00 [0.84, 1.00]
Radmard 2019	7	12	1	704	0.88 [0.47, 1.00]	0.98 [0.97, 0.99]



PPV : 85.1 %
NPV : 98.7 %

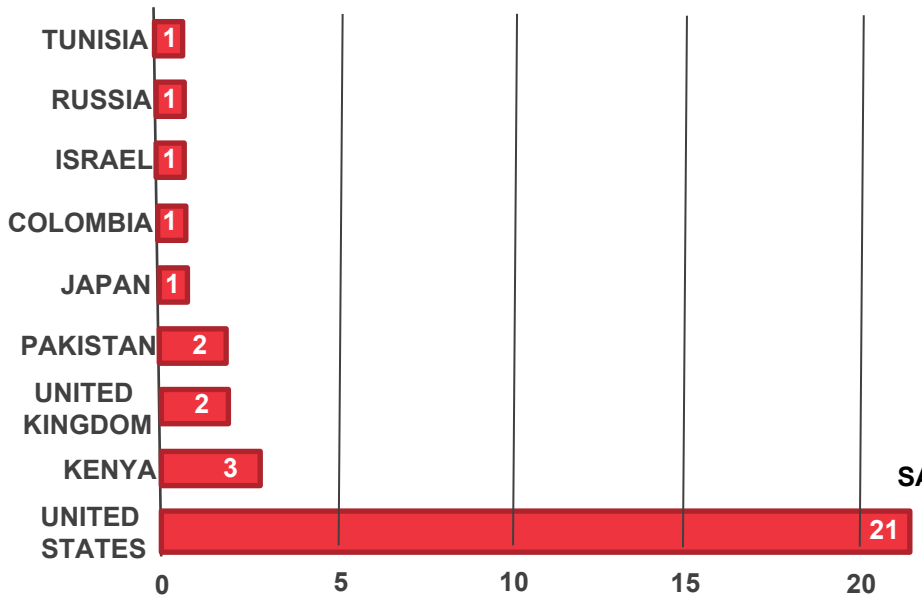
Tansarli, *Clin Microbiol Infect* 2020

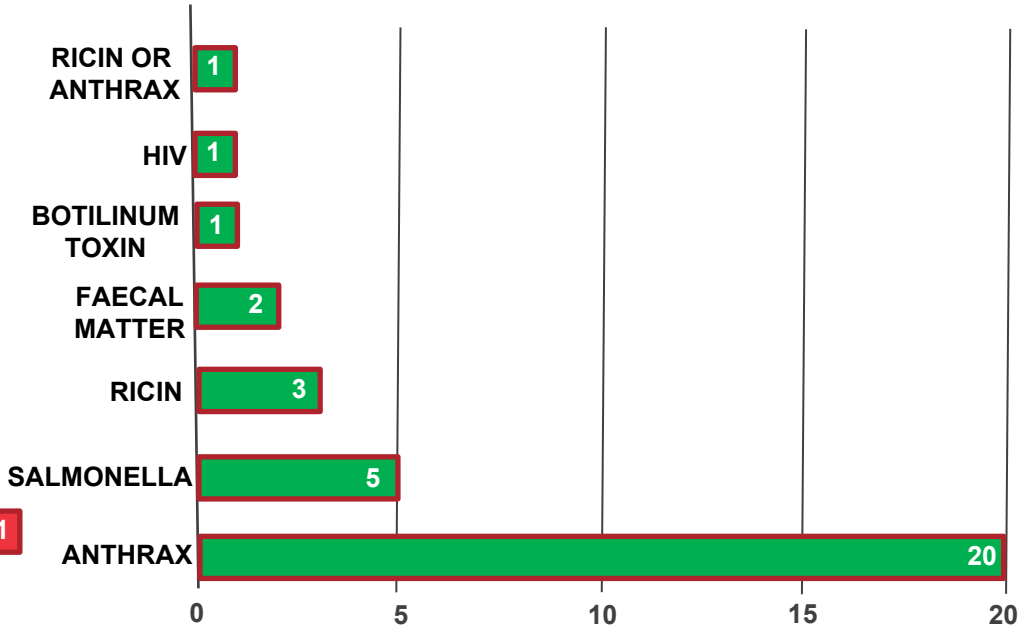
Diagnostic test accuracy of the BioFire FilmArray meningitis/encephalitis panel

	Ref. Test 1			Ref. Test 2		
	No. Studies/No. Patients	Sensitivity (95%CI)	Specificity (95%CI)	No. Studies/No. Patients	Sensitivity (95%CI)	Specificity (95%CI)
All bacteria	16/6183	89.5 (81.1-94.4)	97.4 (94-98.9)	15/5545	93.5 (87.8-96.6)	99.1 (97.8-99.6)
S. *Pneumonia*	16/7090	87.5 (77-94)	98.5 (97-99.3)	10/5287	93 (83.3-97.2)	99.4 (98.2-99.8)
H. *Influenza*	10/4959	64.9 (39.5-84)	99.4 (98.9-99.6)	7/3176	81.1 (55.6-93.6)	99.8 (99.5-99.9)
S. *agalactiae*	10/5266	71.5 (49.6-86;5)	99.5 (98.5-99.9)	5/2543	81.4 (52.3-94.6)	99.4 (97.7-99.9)
E. *coli*	11/4743	70.9 (50.2-85.5)	99.6 (99.1-99.8)	5/2570	76.3 (47.6-91.9)	99.6 (98.7-99.9)
N. *meningitidis*	10/3501	74.5 (52.9-88.4)	99.1 (98.6-99.5)	5/1950	84.4 (53.9-96.2)	99.1 (98.8-99.9)
L. *monocytogens*	7/1332	70.4 (40-89.5)	98.9 (96.9-99.6)	3/550	80.4 (40.4-96.1)	99.5 (97.8-99.9)
Enterovirus	3/6883	93.8 (87-97.2)	99.3 (98.7-99.7)	3/6883	99.8 (86.1-97.4)	99.9 (99.7-100)
HSV-1	3/6883	75.5 (51.2-90.1)	99.9 (94.7-100)	3/6883	78.2 (58.1-90.3)	99.9 (99.8-100)
HSV-2	3/6883	94.4 (83.9-98.2)	99.9 (99.7-100)	3/6883	94.5 (84.2-98.2)	99.9 (99.8-100)
VZV	4/6897	91.4 (78.9-96.9)	99.8 (98.7-100)	4/6897	93.3 (83.6-97.4)	99.9 (99.6-100)

Trujillo-Gomez, e*Clinical Medicine* 2022

Biological agents used in terrorist attacks 1970-2019

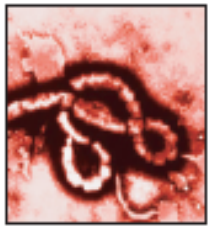




Tin, *Am J Emerg Med* 2022

Global Fever Panel

FilmArray – 19 targets – 1 hour – 2min hands-on time



9
Viruses

Ebola
Marburg
Lassa
Crimean-Congo
Dengue
Zika
Chikungunya
West-Nile
Yellow fever

6
Bacteria

Bacillus anthracis
Francisella tularensis
Leptosira
Salmonella Typhi
Salmonella Paratyphi
Yersinia pestis

4
Protozoa

Leishmania
Plasmodium
P. falciparum
P. vivax/ovale

Performance of clinical metagenomics in France: a prospective observational study

Jacques Fourgeaud*, Béatrice Regnault*, Vichita Ok, Nicolas Da Rocha, Émilie Sitterlé, Meryem Mekouar, Hélène Faury, Catherine Milliancourt-Seels, Florence Jagorel, Delphine Chrétien, Thomas Bigot, Éric Troadec, Isabelle Marques, Alexandra Serris, Danielle Seilhean, Bénédicte Neven, Pierre Frange, Agnès Ferroni, Marc Lecuit, Xavier Nassif, Olivier Lortholary†, Marianne Leruez-Ville†, Philippe Pérot†, Marc Eloit‡, Anne Jamet‡

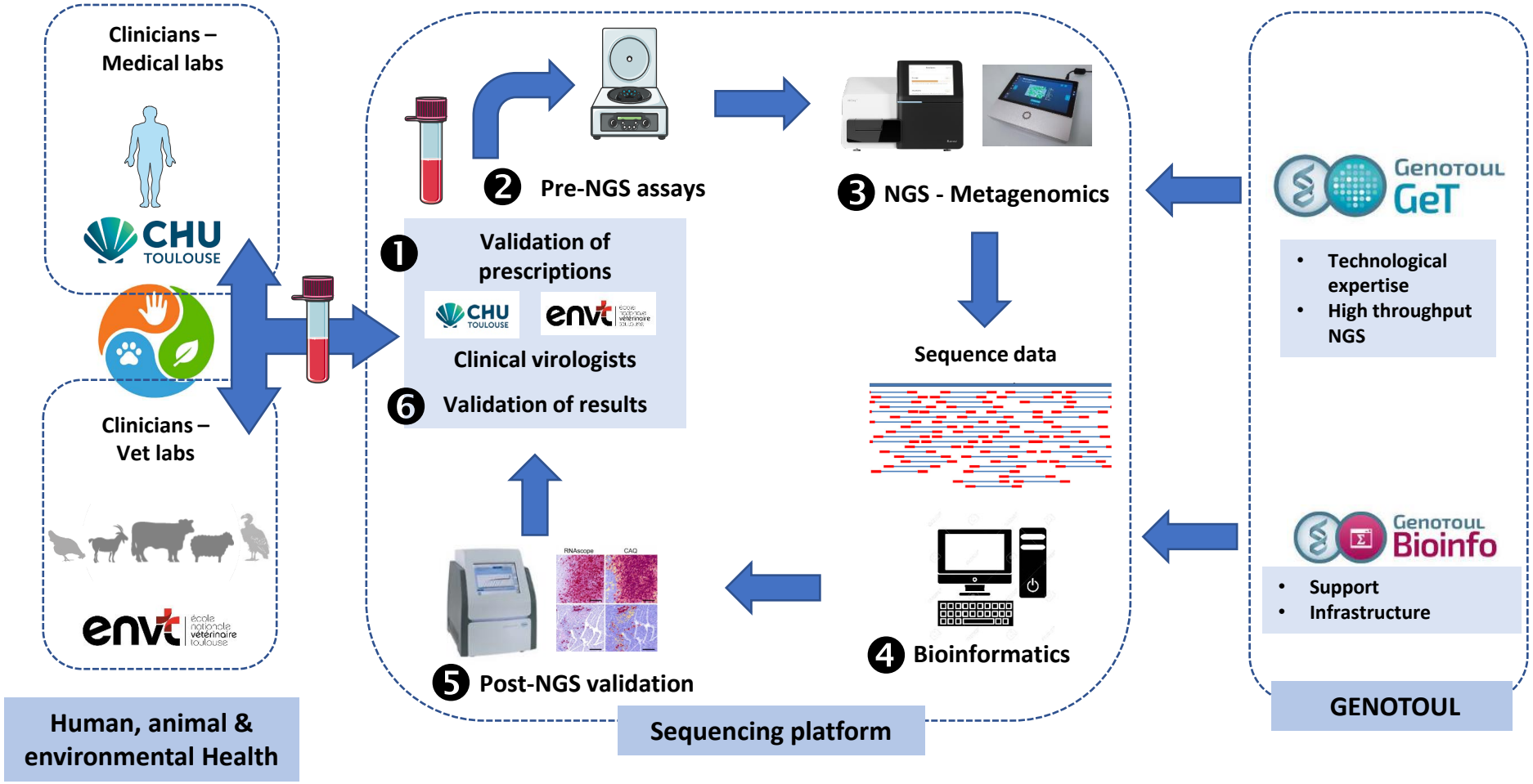
Lancet Microbe 2024; 5: e52–61

Surveillance for Emerging and Reemerging Pathogens Using Pathogen Agnostic Metagenomic Sequencing in the United States: A Critical Role for Federal Government Agencies

Diane L. Downie, Preetika Rao, Corinne David-Ferdon, Sean Courtney, Justin S. Lee, Claire Quiner, Pia D. M. MacDonald, Keegan Barnes, Shelby Fisher, Joanne L. Andreadis, Jasmine Chaitram, Matthew R. Mauldin, Reynolds M. Salerno, Jarad Schiffer, and Adi V. Gundlapalli

Health Security
Volume 22, Number 2, 2024 Mary Ann Liebert, Inc.

Toulouse Metagenomics Platform



Summary

- ✓ Leverage on developments and lessons learned from the COVID-19 pandemic are key for syndromic approaches
- ✓ Rapid diagnostics of respiratory pathogens (cocirculating) is crucial for optimal patient care and control measure to reduce transmission
- ✓ Algorithms for priorization of types of tests / combination of tests
- ✓ Cost-effectiveness studies are needed

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