Epidemiology of the respiratory viruses in all age groups
Symposium BVIKM-SBIMC
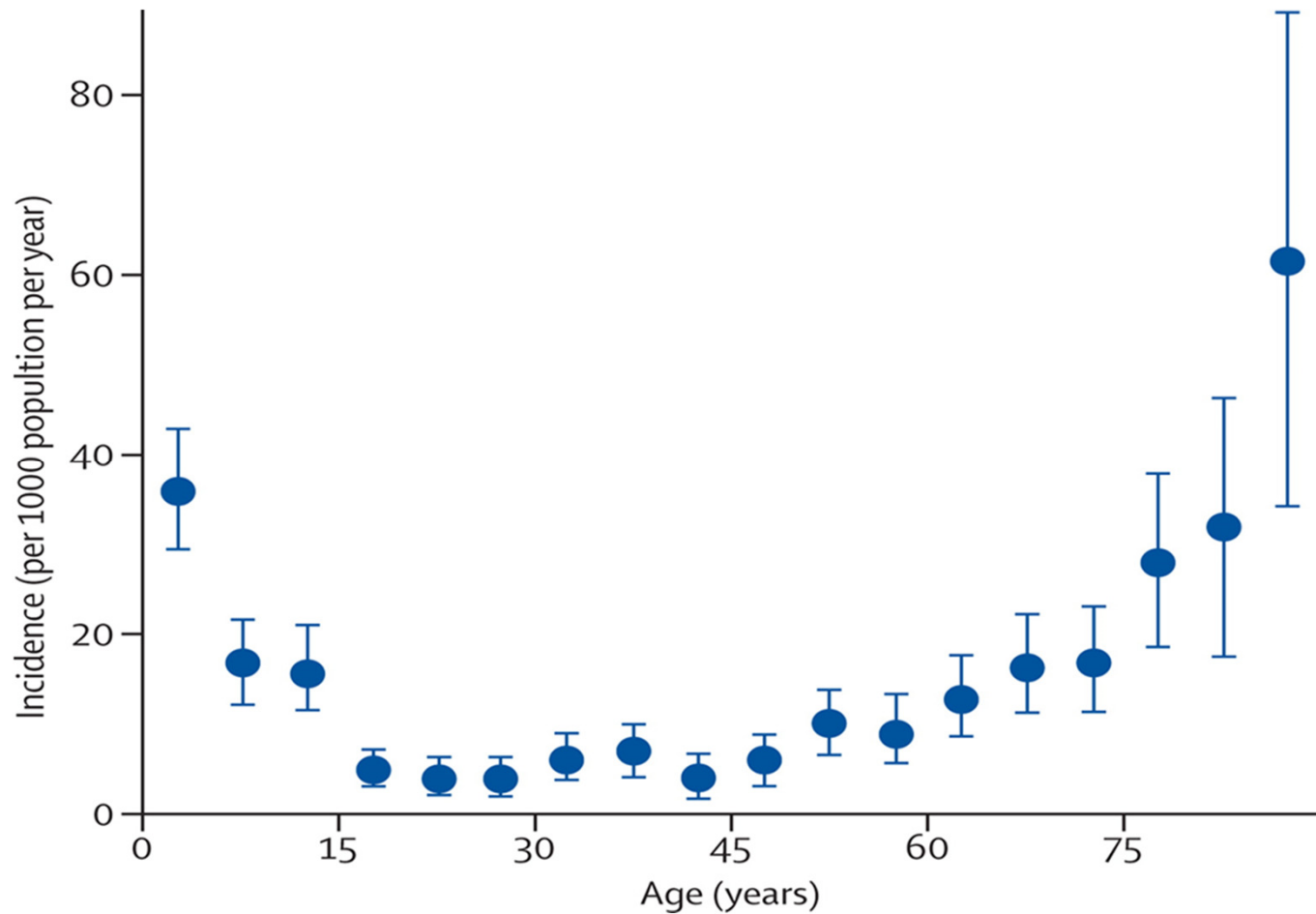

Marijke Reynders

La Hulpe, October 29th 2015

Age-distribution of CAP

Jokinen C, Heiskanen L, Juvonen H, et al. Incidence of community-acquired pneumonia in the population of four municipalities in eastern Finland. *Am J Epidemiol* 1993; **137**: 977–88.

Causative Viral Agents of RTI

« Old » chaps

- Influenza A
- Influenza B
- RSV (A/B)
- Parainfluenza 1-3
- Adenovirus 4, 7, 21
- Rhinovirus (species A & B)
- Enterovirus: echo, coxsackie, entero
- CMV
- EBV
- Varicella-zoster virus
- Human Herpes Virus 6
- Coronavirus (OC43, 229E)
- Measles
- Hantavirus

« New » chaps

- hMPV
- Parainfluenza 4
- hCoV-NL63,-HKU1, -SARS, -MERS
- hBoV 1-4
- (PARV4 & 5)
- Polyoma KI, WU
- Rhinovirus species C
- Mimivirus
- Parechovirus 1-16
- "New " enteroviruses EV-D68 (polio-like), EV-C105

....

Emerg Infect Dis. 2015 Oct;21(10):1858-60. doi: 10.3201/eid2110.150759.

Acute Flaccid Paralysis Associated with Novel Enterovirus C105.

Horner LM, Poulter MD, Brenton JN, Turner RB.

-- Common causes of pneumonia, -- Uncommon causes of pneumonia

EV-D68

KEEP CALM
Enterovirus D68
Is Just A
Cold

- USA: August 2014 severe RTI in children in Missouri & Illionois
  (sequencing by CDC: Missouri EV-D68 & Illionois EV-D68)
- Outbreak 2014 in other states & Canada:
  at least 1121 positives; 68% prior history of wheezing; mostly
  severe bronchiolitis; ICU requirement; 12 children died
- How much EV-D68 is there really in Europe?

ECDC: I see no problem............

- ESCV Annual Meeting, Sept 2014 in Prague:
  start European EV-D68 surveillance network

17TH ANNUAL MEETING
OF ESCV | PRAGUE 2014
28. 9.–1. 10. 2014

az sint-jan
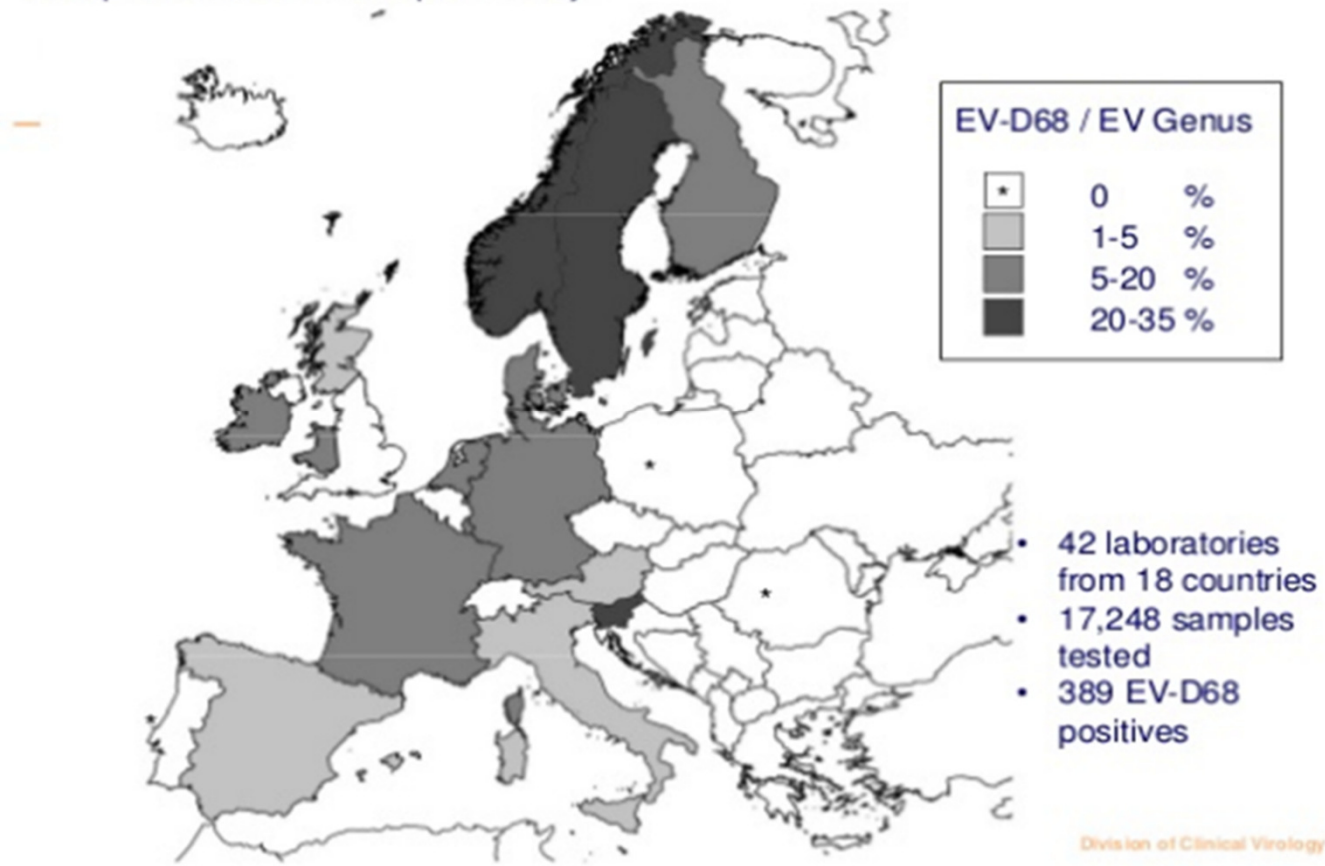brugge - oostende av

EV-D68

Is EV-D68 detected?

- QCMD: most laboratories do not detect or look for EV-D68
- Commercial assays:
    - Fast-track diagnostics YES
    - Argene YES
    - GenMark NOT
    - Cepheid YES, but not validated
    - FilmArray YES, but rhino/entero together
    - Luminex YES, but rhino/entero together
    - Pathofinder MLPA YES, but rhino/entero together
    - Seegene, NOT
    - bioMerieux NASBA NucliSENS EasyQ Enterovirus, NOT
- Laboratory Developed Tests: not always
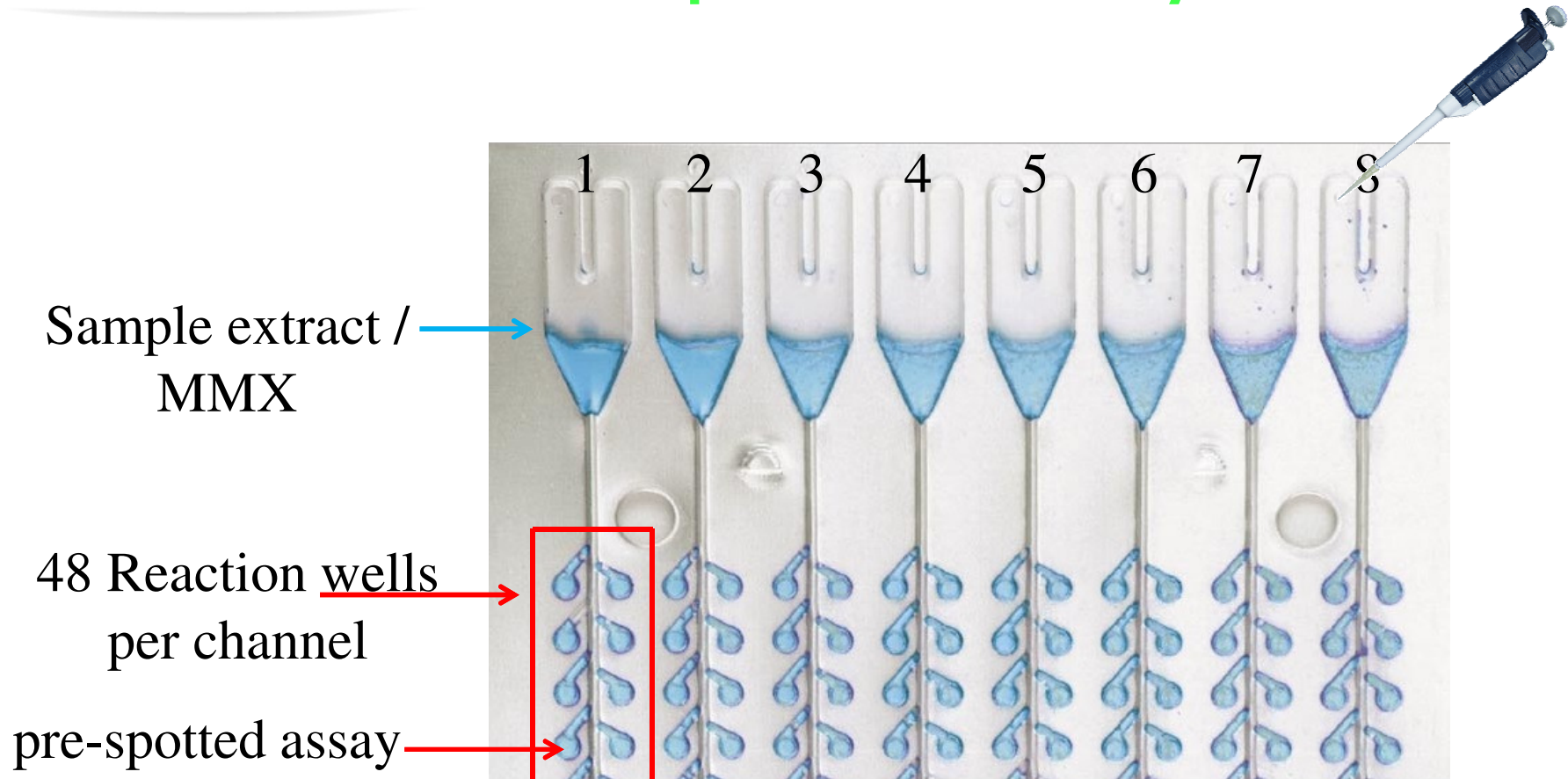- Routinely, enterovirus is not always included for respiratory diagnostics

Niesters B, UMC Groningen, situation 12/2014

EV-D68

European detection rates per country

EV-D68 / EV Genus

*	0	%
	1-5	%
	5-20	%
	20-35	%

- 42 laboratories from 18 countries
- 17,248 samples tested
- 389 EV-D68 positives

Division of Clinical Virology

TaqMan® Array Card

Sample extract / MMX

48 Reaction wells per channel

pre-spotted assay

1 well = 1 μl reaction volume = 1 Real Time PCR reaction

Composition Respi TAC v 9,0 Bruges

az sint-jan
brugge - oostende av

Viruses		Viruses		Bacteria	
1	Rhinoviruses #1	20	Human adenovirus (all types)	35	*Bordetella holmesii*
2	Rhinoviruses #2	21	Human adenovirus (all types)	36	*Bordetella parapertussis*
3	Enteroviruses #1	22	Human metapneumoviruses	37	*Bordetella pertussis*
4	Enteroviruses #2	23	Human parechovirus	38	*Bordetella pertussis 2*
5	Influenza A DC	24	Bocavirus	39	*Mycoplasma pneumoniae*
6	Influenza A H1	25	Cytomegalovirus	40	*Chlamydophila pneumoniae*
7	Influenza A H3	26	Human coronavirus 229E	41	*Legionella pneumophila*
8	Influenza A H7N9	27	Human coronavirus GP2 OC43/HKU1	42	*Coxiella burnetii*
9	Influenza A 2	28	Human coronavirus NL63	43	*Chlamydophila psittaci*
10	Influenza A Y	29	Human coronavirus OC43		
11	Influenza B	30	Measles virus		**Fungi**
12	Influenza B 2	31	Mumps virus	44	*Aspergillus fumigatus*
13	Human respiratory syncytial virus A	32	MERS CoV (1) ⟶ EV-D68	45	*Pneumocystis jiroveci*
14	Human respiratory syncytial virus B	33	MERS CoV (2)		
15	Human respiratory syncytial virus	34	HSV-1/2		**Controls**
16	Parainfluenza 1			46	18S
17	Parainfluenza 2		**34 pathogens**	47	PDV control
18	Parainfluenza 3			48	Human Rnase P gene
19	Parainfluenza 4				

INFANT FEBRILE ILNESS: SEARCH FOR THE RESPONSIBLE MICROORGANISMS BY DIFFERENT MOLECULAR TECHNIQUES

ESPID 2014

n=51 infants between 0-3 months

Table I. Diagnostic gain from different techniques

Viral Pathogens	Ag detection n	Viral Culture n	Home made real-time PCR n	Pneumovir® n	Smartfinder® n	Home made TLDA n
RSV A&B	8	9	10	11	11	11
Influenza A/B	0	2 A, 1 B	2 A, 1 B	2 A, 3 B	2 A, 2 B	2 A, 2 B
Rhino/Entero	na	6°	7	14	23	24
Paraecho	na	0*	na	na	na	3
Adeno	0	1°	2	2	1	1
hMPV A&B	2	1*	6	7	7	7
Coronavirus (OC43, NL63, HKU-1, 229E)	na	0*	7	1	5	8
Parainfluenza 1-4[x]	1	3	3	4	4	4
Bocavirus	na	na	1	2	2	1
Total viruses	11	23	39	46	57	63 (+4 CMV=67)

na: not applicable; *cell growth very difficult to practically impossible, °huge variety of genotypes of which some can't be cultured; [x]PIV 4 not detectable by Ag test nor culture

Epidemiology of viral/atypical RTI

- Period: January 2013-September 2015

- Patient population: 0-102 years of age with T°>37,8°C and/or respiratory symptoms (>75y: + acute deterioration/anorexia w/o etiology)

- 55% of samples < ♂

- Total number of samples: n=12397 <different episodes; from 11686 different patients

- Sample types:
  4% nasopharyngeal aspirates, 29% BAL fluids, 67% NPS/TS

- Positivity rate overall: 57,7% (35,0% monoinfection ⇔ 22,7% co)

- Children (0-15y): mean age: 28m – median age: 14m

- Positivity rate pediatrics: 87,3% of samples (47,3% co ⇔ 39,9% monoinfection)

Epidemiology of viral/atypical RTI

- Sample distribution
  - 2708 < ICU
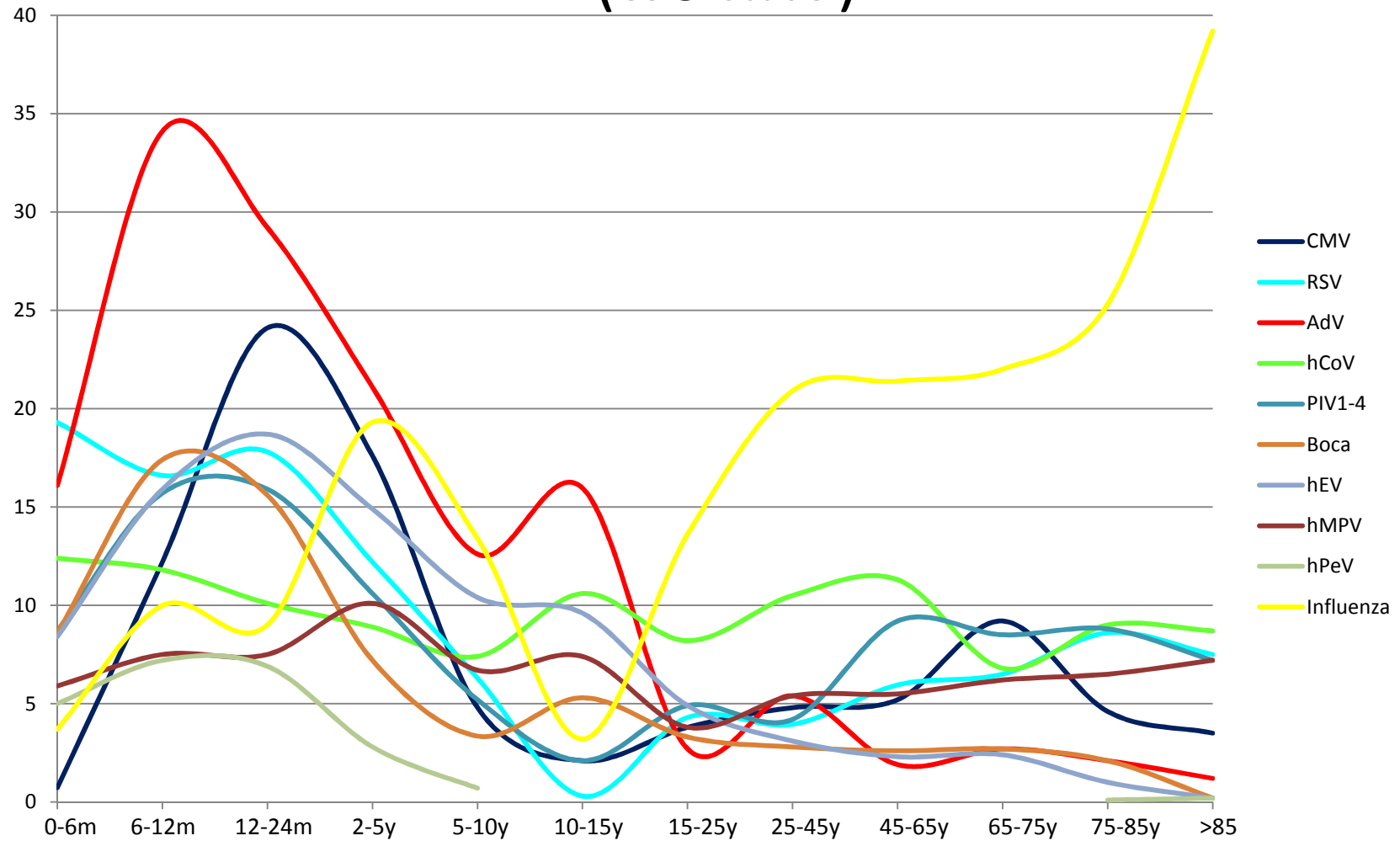 - 207 < NICU
  - 4131 < pediatrics
  - 896 hematology
  - 746 oncology
  - 1527 pneumology
  - 107 MICU/gynaeco

    83,3% of samples

  - Consultation/emergency w/o hospitalization: 2075
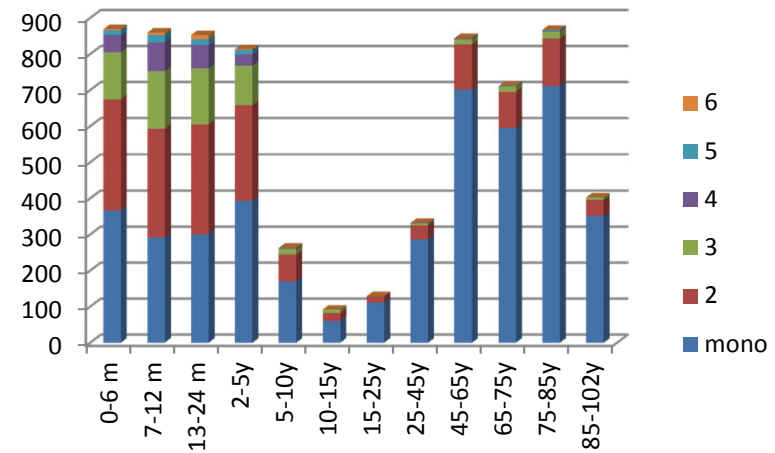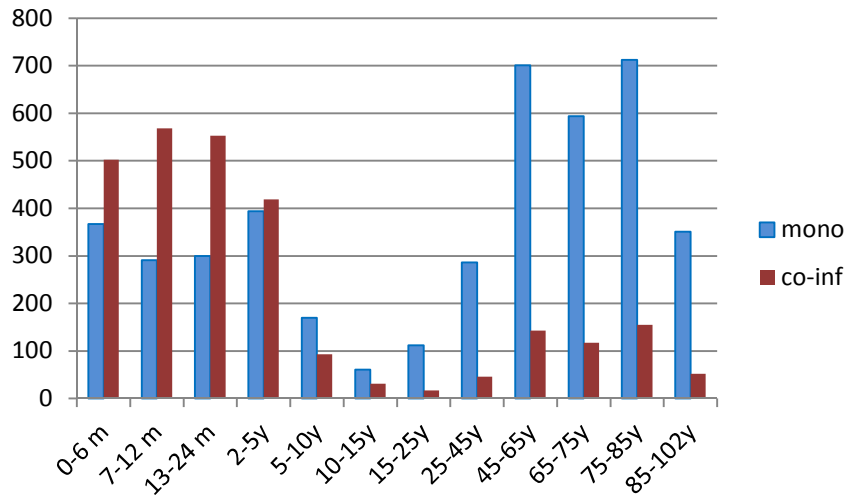
Prevalence all detected pathogens

Respiratory Viruses in function of age

Respiratory Viruses in function of age
(wo hRV)

Legend: CMV, RSV, AdV, hCoV, PIV1-4, Boca, hEV, hMPV, hPeV, Influenza
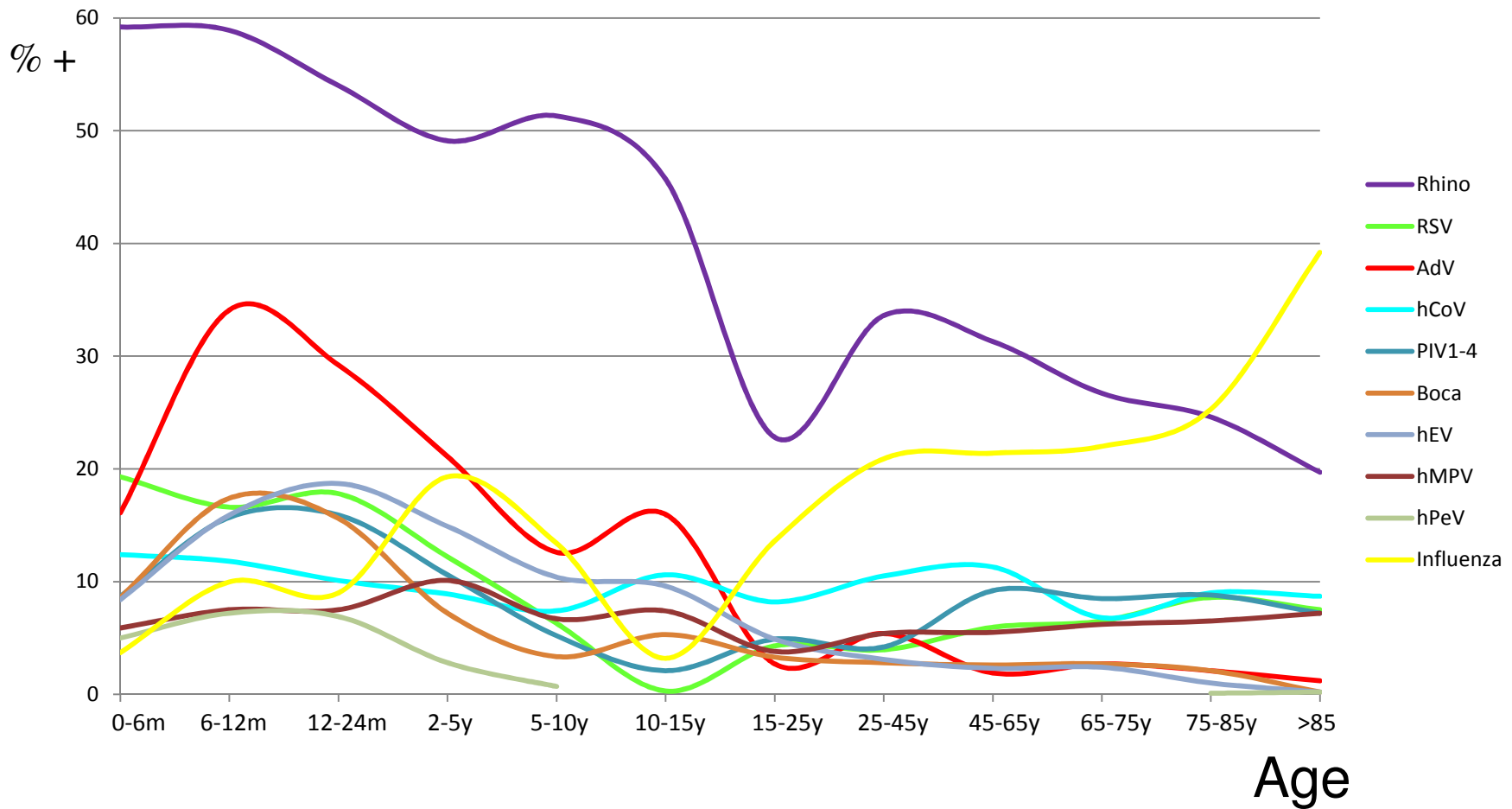
Mono- versus coinfection

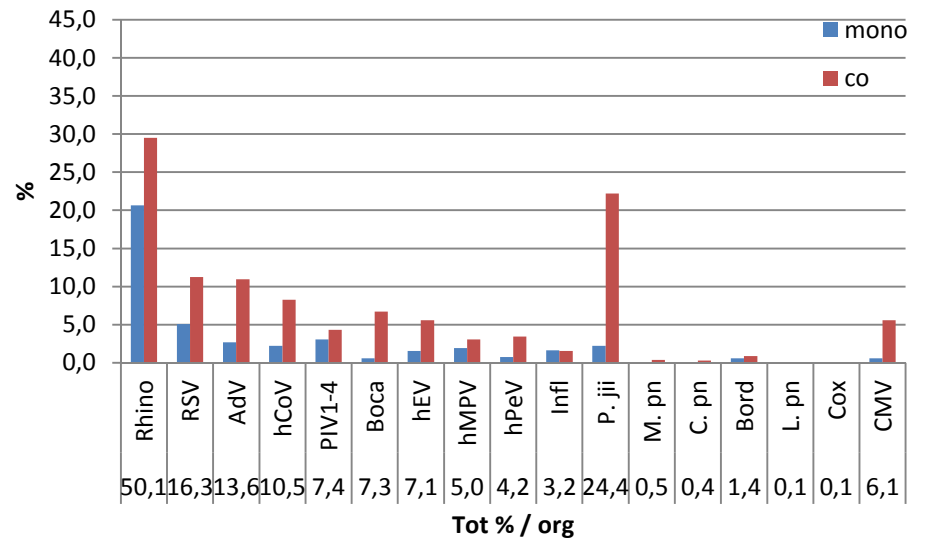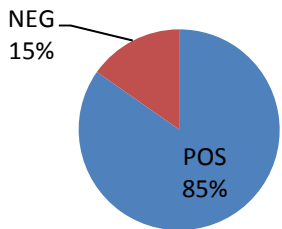|	mono	2	3	4	5	6
0-6 m	367	307	131	47	14	3
7-12 m	291	302	159	80	21	6
13-24 m	300	305	155	65	16	12
2-5y	394	264	110	31	13	1
5-10y	170	74	16	2	1	0
10-15y	61	22	8	1	0	0
15-25y	112	16	0	1	0	0
25-45y	286	40	5	1	0	0
45-65y	701	126	14	3	0	0
65-75y	594	101	14	1	1	0
75-85y	712	131	19	3	2	0
85-102y	351	44	7	0	1	0
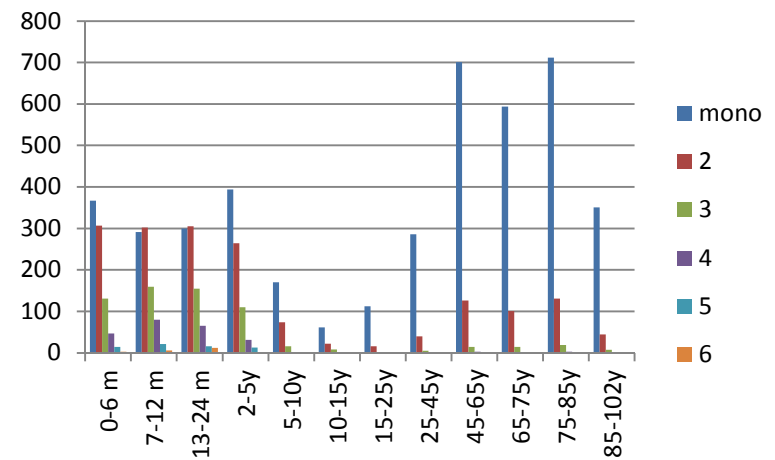
Age 0-6 months
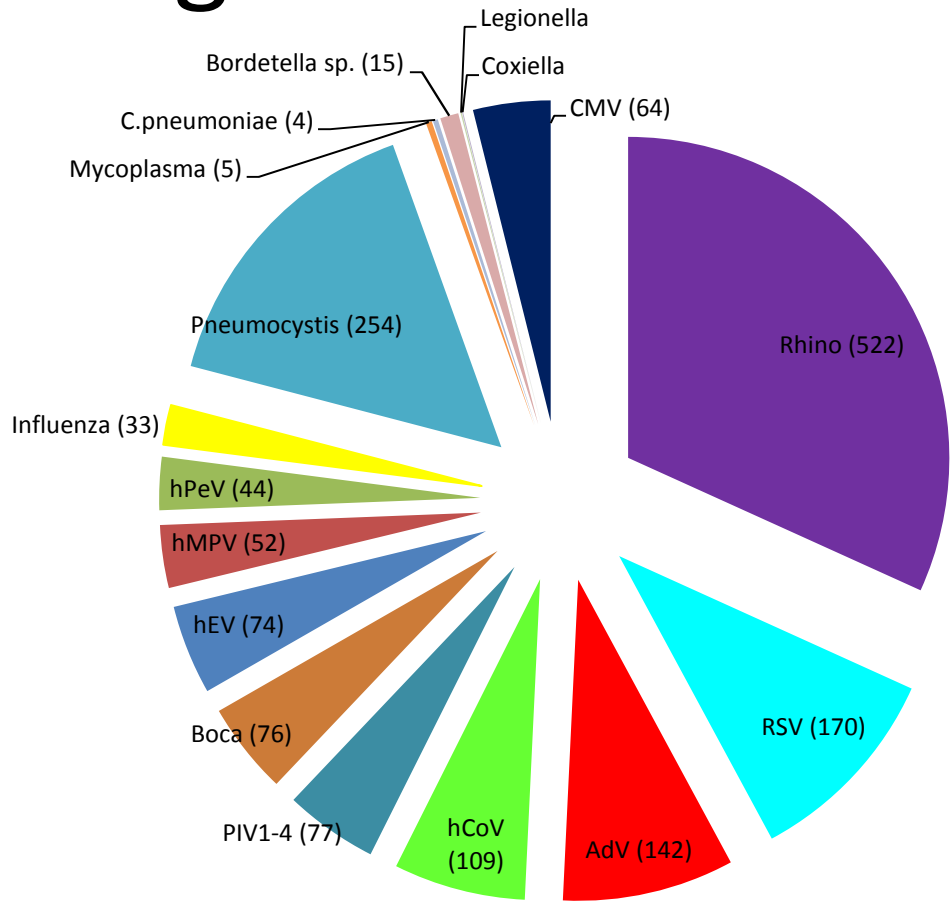
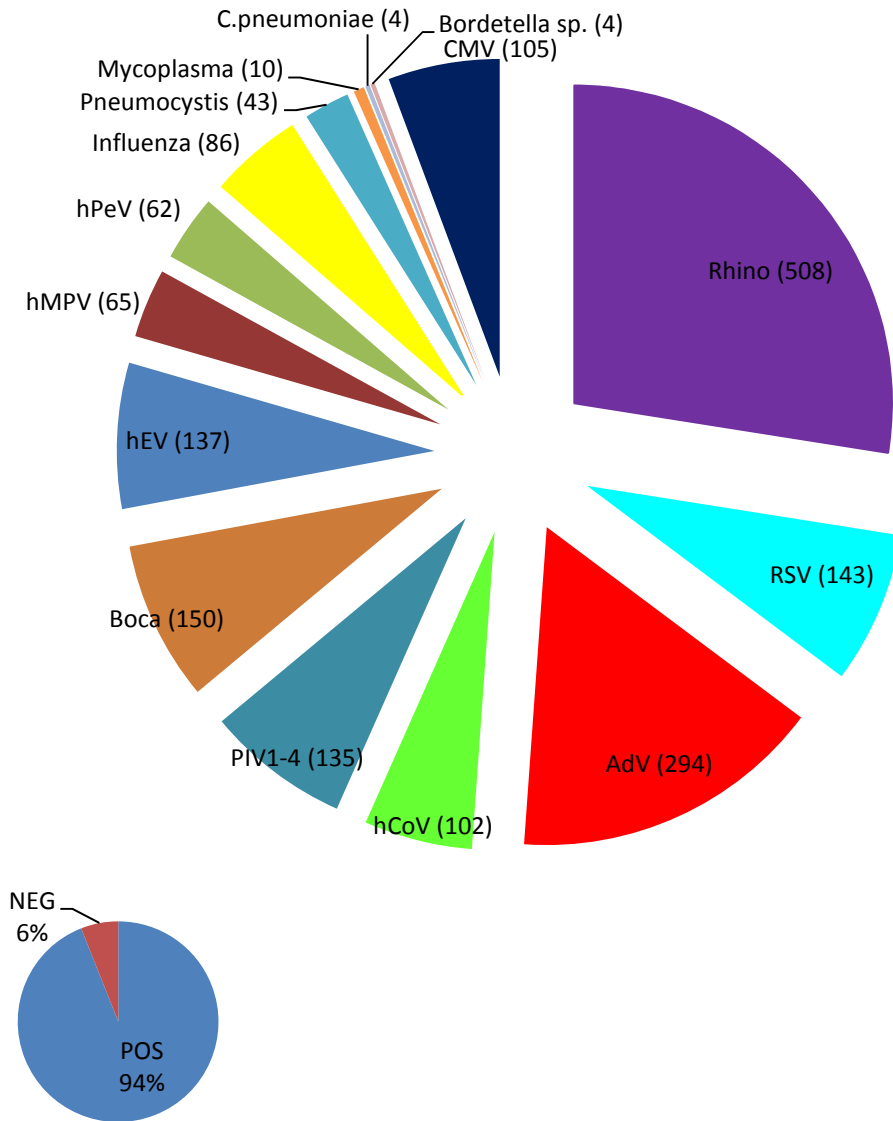n=1041 → 882+

TOP 5:
1)hRV: 59,2%
2)RSV: 19,3%
3)AdV: 16,1%
4)hCoV: 12,4%
5)PIV1-4: 8,7%

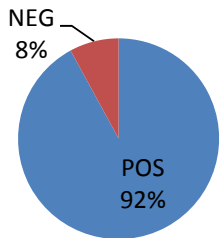Pie chart labels: Legionella, Coxiella, CMV (64), Bordetella sp. (15), C.pneumoniae (4), Mycoplasma (5), Pneumocystis (254), Influenza (33), hPeV (44), hMPV (52), hEV (74), Boca (76), PIV1-4 (77), hCoV (109), AdV (142), RSV (170), Rhino (522)

NEG 15%, POS 85%

	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	50,1	16,3	13,6	10,5	7,4	7,3	7,1	5,0	4,2	3,2	24,4	0,5	0,4	1,4	0,1	0,1	6,1

Age >6-12 months

C.pneumoniae (4)
Bordetella sp. (4)
CMV (105)
Mycoplasma (10)
Pneumocystis (43)
Influenza (86)
hPeV (62)
hMPV (65)
hEV (137)
Boca (150)
PIV1-4 (135)
hCoV (102)
AdV (294)
RSV (143)
Rhino (508)

NEG 6%
POS 94%

n=917 → 862+

TOP 5:
1) hRV: 58,9%
2) AdV: 34,1%
3) Boca: 17,4%
4) RSV: 16,6%
5) hEV: 15,9%

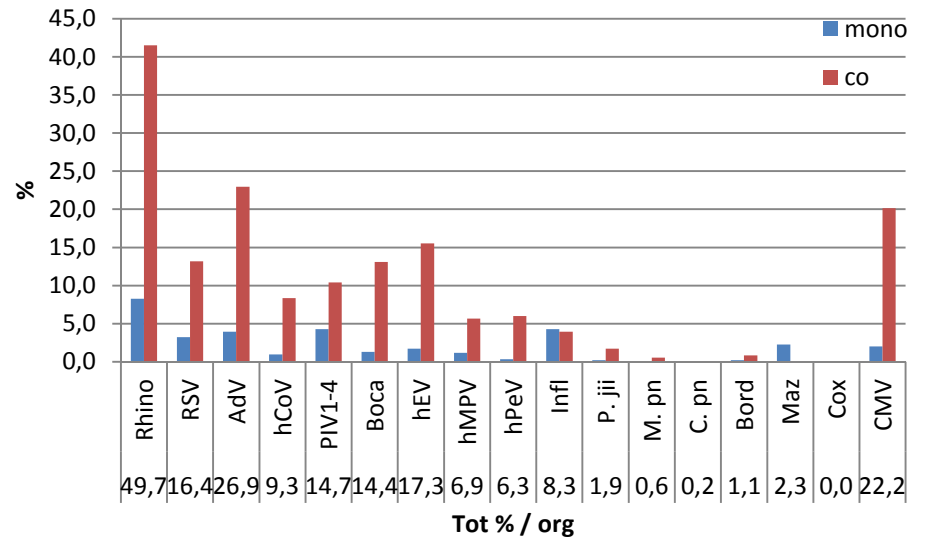|	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	55,4	15,6	32,1	11,1	14,7	16,4	14,9	7,1	6,8	9,4	4,7	1,1	0,4	0,4	0,0	0,0	11,5

mono
co
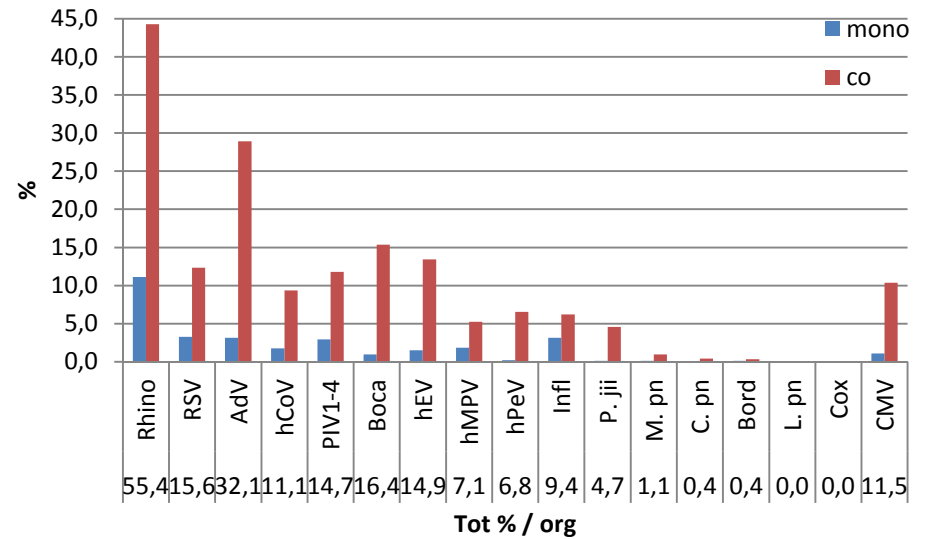
Age >12-24 months
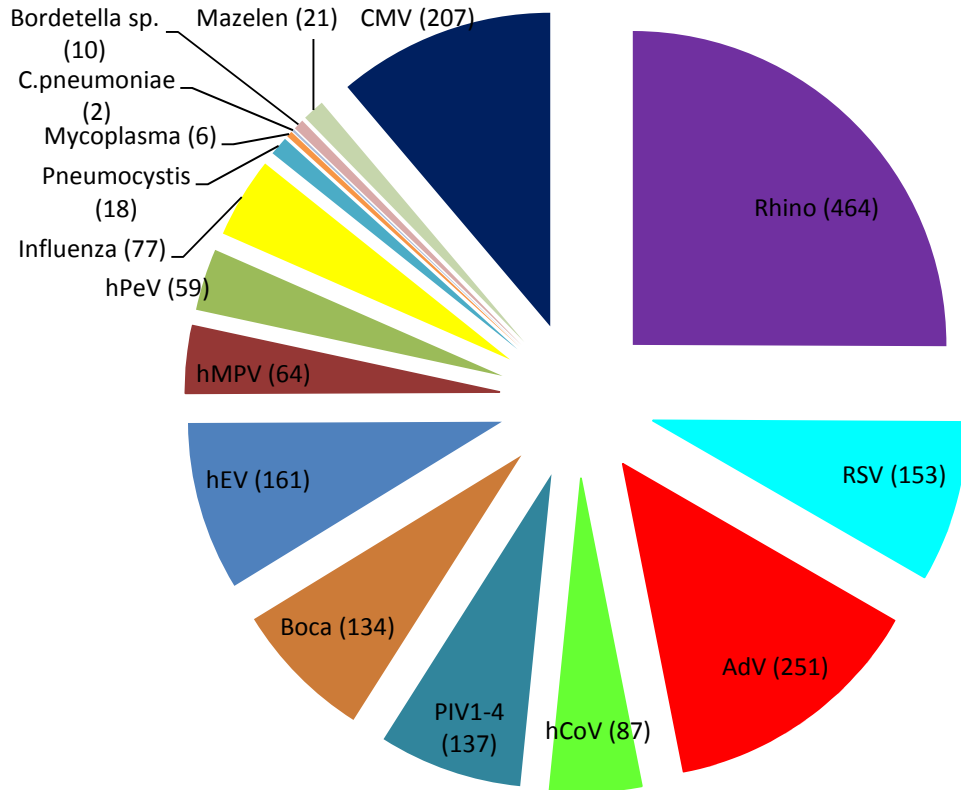
n=933 → 859+

TOP 5:
1) hRV: 54,0%
2) AdV: 29,2%
3) hEV: 18,7%
4) RSV: 17,8%
5) PIV1-4: 15,9%

Age >2-5 years

C.pneumoniae (4)
Bordetella sp. (15)
CMV (144)
Mycoplasma (30)
Pneumocystis (7)
Rhino (403)
Influenza (158)
hPeV (23)
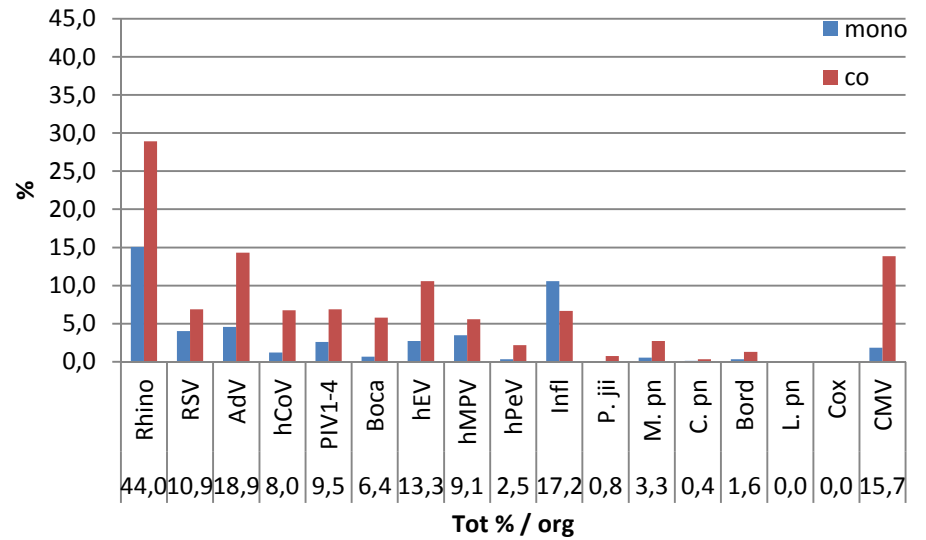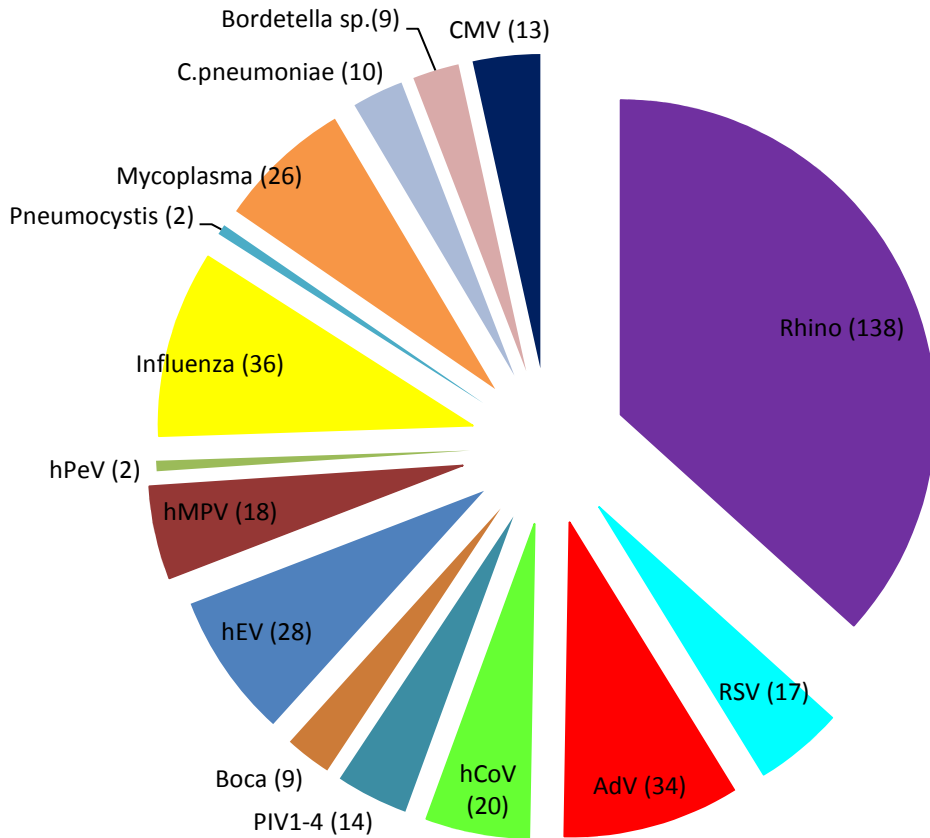hMPV (83)
hEV (122)
Boca (59)
PIV1-4 (87)
hCoV (73)
AdV (173)
RSV (100)

NEG 10%
POS 90%
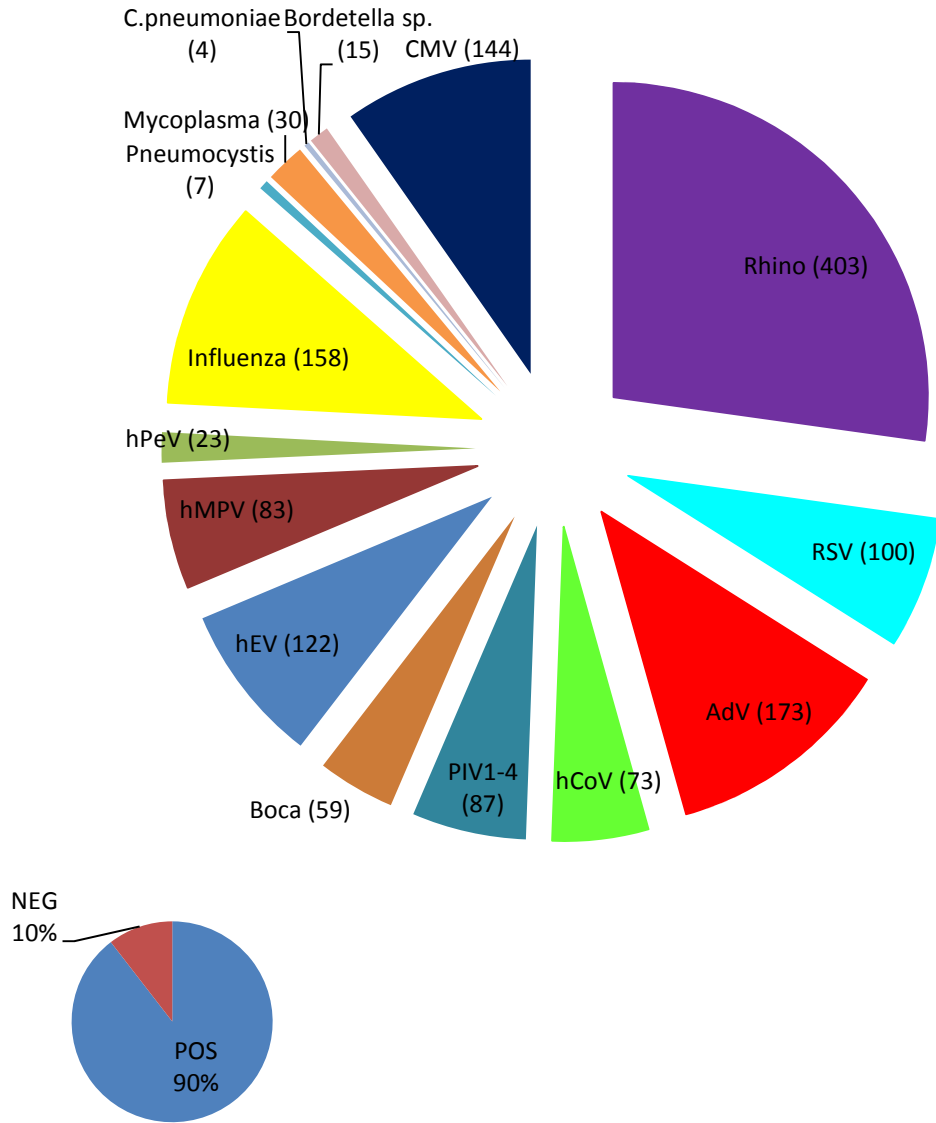
n=916 → 820+

TOP 5:
1)hRV: 49,1%
2)AdV: 21,1%
3)Infl: 19,3%
4)hEV: 14,9%
5)RSV: 12,2%

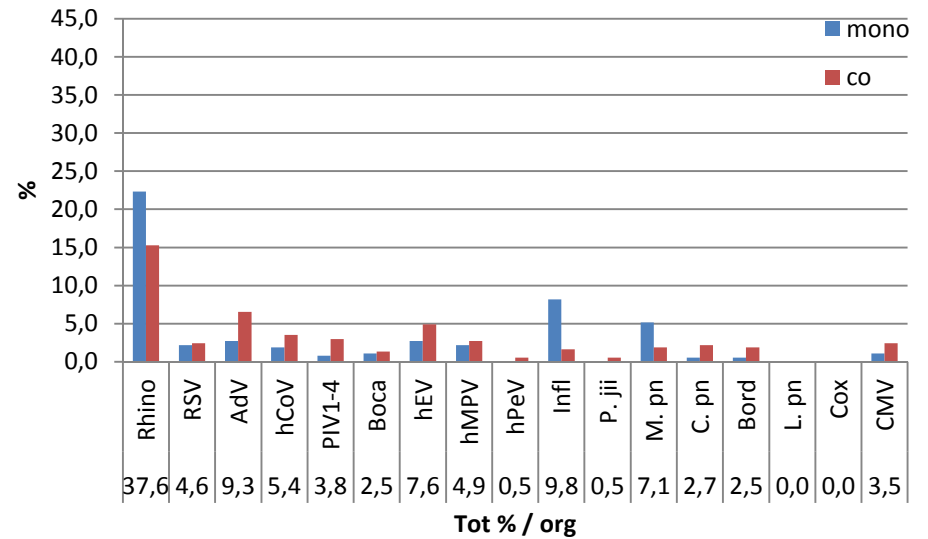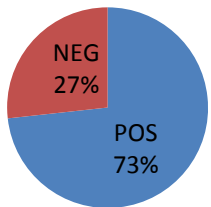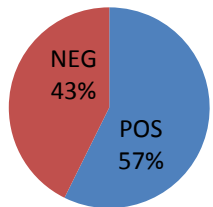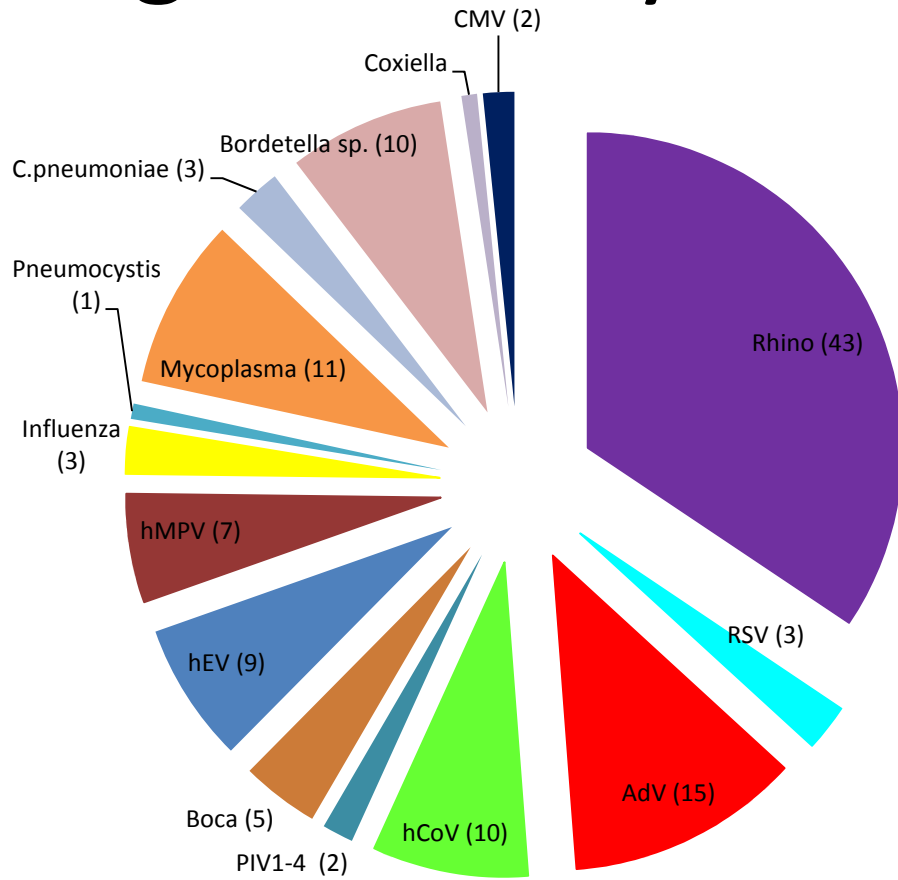|	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	44,0	10,9	18,9	8,0	9,5	6,4	13,3	9,1	2,5	17,2	0,8	3,3	0,4	1,6	0,0	0,0	15,7

Age >5-10 years

n=367 →269+

TOP 5:
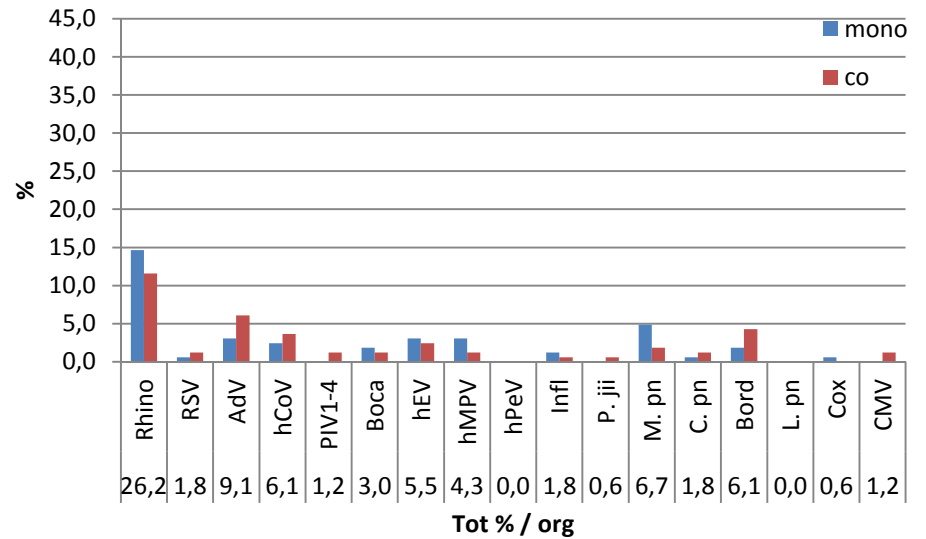1)hRV: 51,3%
2)Infl: 13,4%
3)AdV: 12,6%
4)hEV: 10,4%
5)M.pneu: 9,7%

Age >10-15 years

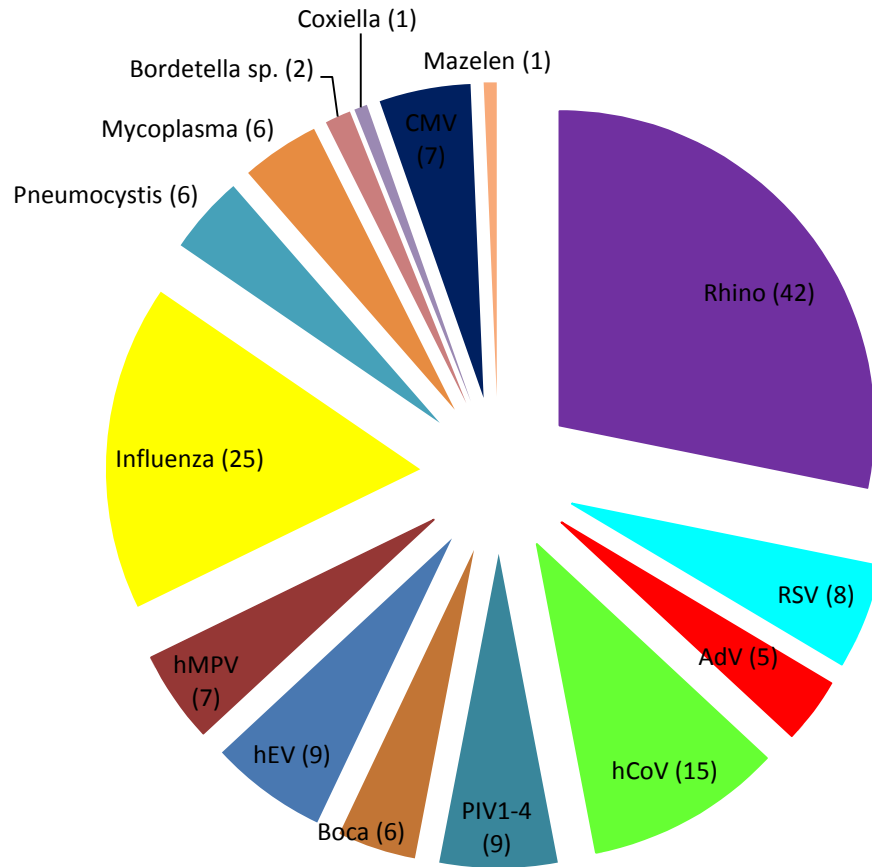
n=166 →94+

TOP 5:
1)hRV: 45,7%
2)AdV: 16%
3)M.pneu: 11,7%
4)Bord/hCoV: 10,6%
5)hEV: 9,6%

Pie chart labels: CMV (2), Coxiella, Bordetella sp. (10), C.pneumoniae (3), Pneumocystis (1), Mycoplasma (11), Influenza (3), hMPV (7), hEV (9), Boca (5), PIV1-4 (2), hCoV (10), AdV (15), RSV (3), Rhino (43)

NEG 43%, POS 57%

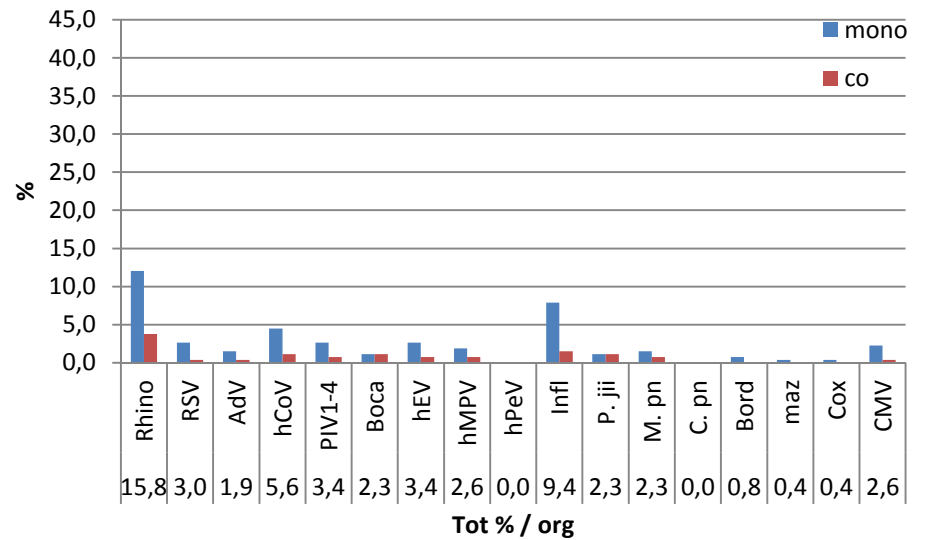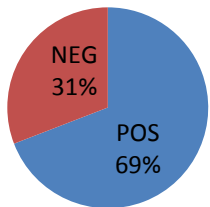|	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	26,2	1,8	9,1	6,1	1,2	3,0	5,5	4,3	0,0	1,8	0,6	6,7	1,8	6,1	0,0	0,6	1,2

mono / co

Age >15-25 years

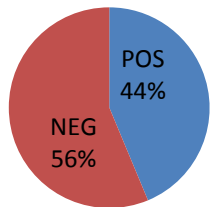
n=266 → 184+

TOP 5:
1)hRV: 22,8%
2)Infl: 13,6%
3)hCoV: 8,2%
4)hEV/PIV: 4,9%
5)RSV: 4,3%

Pie chart labels: Rhino (42), RSV (8), AdV (5), hCoV (15), PIV1-4 (9), Boca (6), hEV (9), hMPV (7), Influenza (25), Pneumocystis (6), Mycoplasma (6), Bordetella sp. (2), Coxiella (1), CMV (7), Mazelen (1)

NEG 31%, POS 69%

Bar chart (mono / co):

	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	maz	Cox	CMV
Tot % / org	15,8	3,0	1,9	5,6	3,4	2,3	3,4	2,6	0,0	9,4	2,3	2,3	0,0	0,8	0,4	0,4	2,6

Age >25-45 years
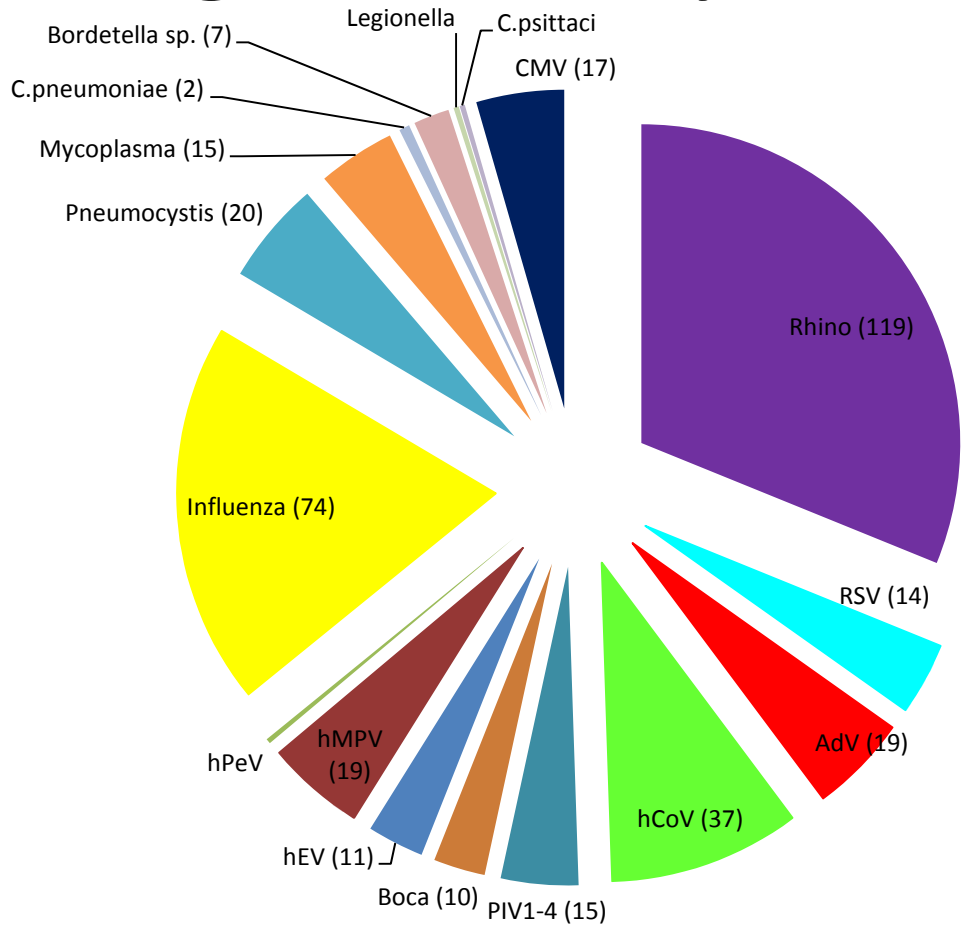
n=810 → 354+

TOP 5:
1)hRV: 33,6%
2)Infl: 20,9%
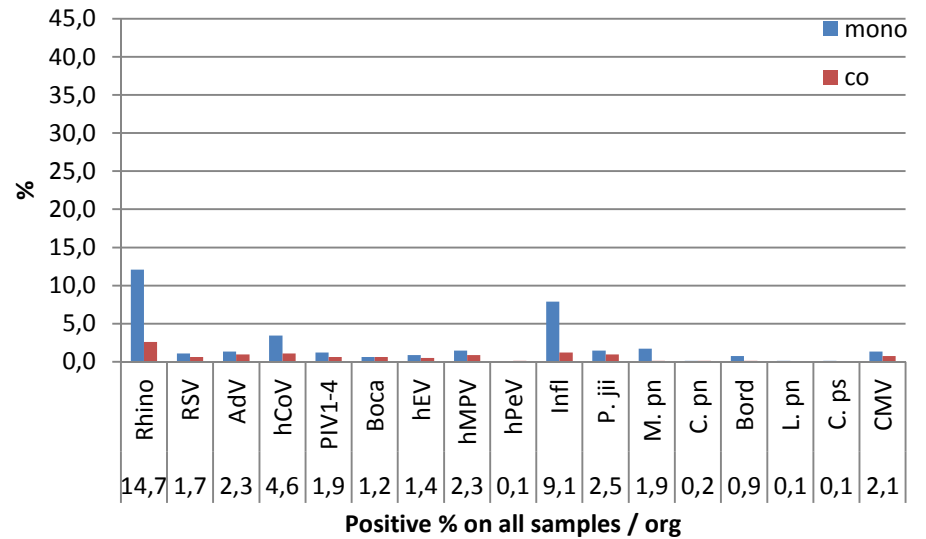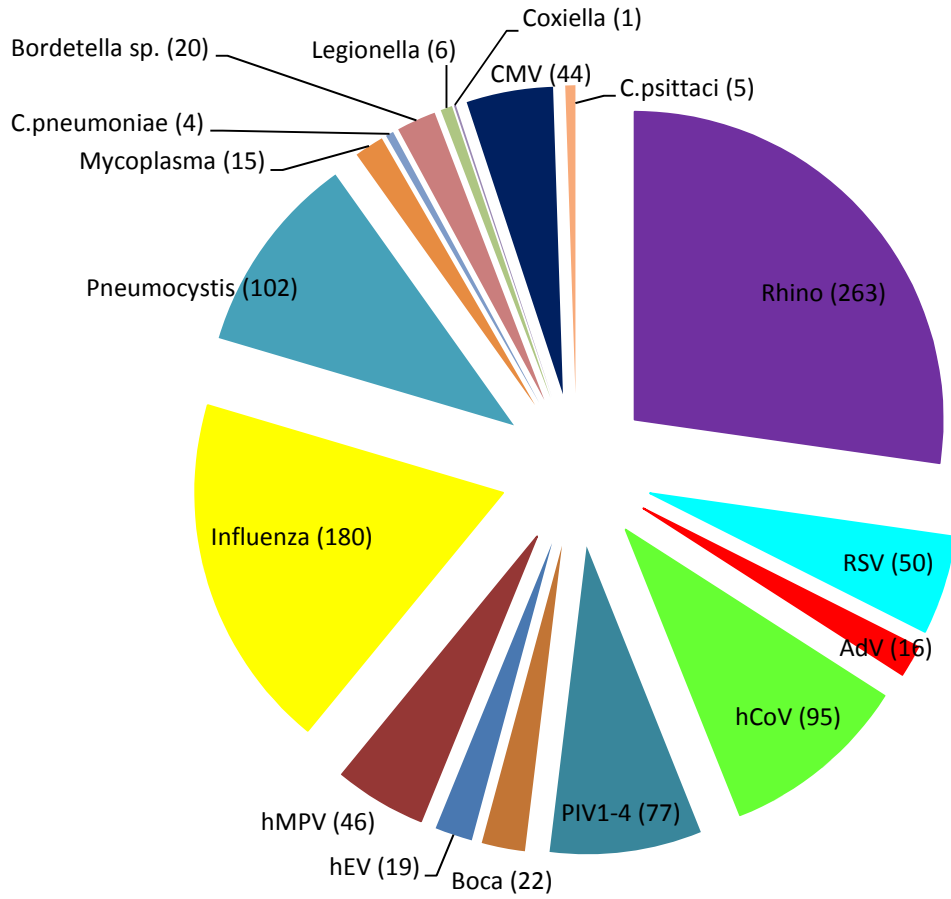3)hCoV: 10,5%
4)AdV/hMPV: 5,4%
5)PIV1-4/M.pn: 4,2%

Pie chart labels:
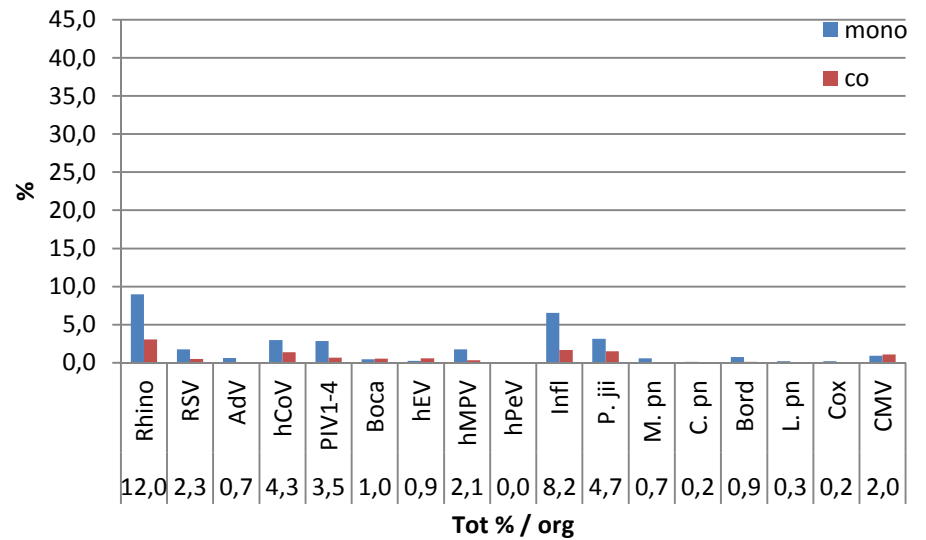- Bordetella sp. (7)
- C.pneumoniae (2)
- Mycoplasma (15)
- Pneumocystis (20)
- Legionella
- C.psittaci
- CMV (17)
- Rhino (119)
- RSV (14)
- AdV (19)
- hCoV (37)
- PIV1-4 (15)
- Boca (10)
- hEV (11)
- hMPV (19)
- hPeV
- Influenza (74)

POS 44%
NEG 56%

Bar chart (Positive % on all samples / org):

Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	C. ps	CMV
14,7	1,7	2,3	4,6	1,9	1,2	1,4	2,3	0,1	9,1	2,5	1,9	0,2	0,9	0,1	0,1	2,1

mono
co

Age >45-65 years

Pie chart organisms:
- Rhino (263)
- RSV (50)
- AdV (16)
- hCoV (95)
- PIV1-4 (77)
- Boca (22)
- hEV (19)
- hMPV (46)
- Influenza (180)
- Pneumocystis (102)
- Mycoplasma (15)
- C.pneumoniae (4)
- Bordetella sp. (20)
- Legionella (6)
- Coxiella (1)
- CMV (44)
- C.psittaci (5)

POS 38% / NEG 62%

n=2186 → 840+

TOP 5:
1) hRV: 31,3%
2) Infl: 21,4%
3) hCoV: 11,3%
4) PIV1-4: 9,2%
5) RSV: 6,0%

Legend: mono, co

	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	12,0	2,3	0,7	4,3	3,5	1,0	0,9	2,1	0,0	8,2	4,7	0,7	0,2	0,9	0,3	0,2	2,0

Age >65-75 years

Bordetella sp. (14)
Legionella (6)
CMV (65)
C.pneumoniae (1)
Mycoplasma (14)
Rhino (189)
Pneumocystis (122)
RSV (46)
AdV (19)
hCoV (48)
Influenza (156)
PIV1-4 (60)
hMPV (44)
hEV (17)
Boca (19)

POS 38%
NEG 62%
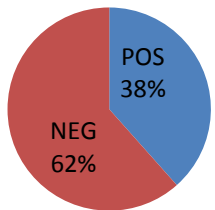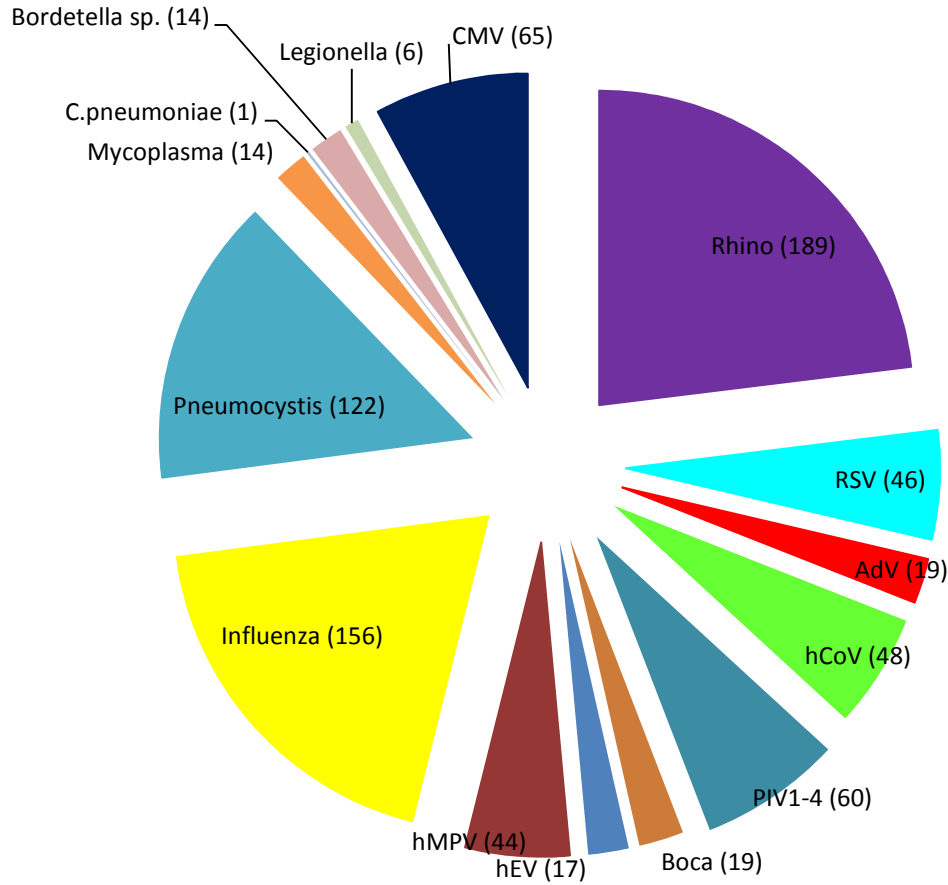
n=1850 →708+

TOP 5:
1)hRV:26,7%
2)Infl: 22,0%
3)PIV1-4: 8,5%
4)hCoV: 6,8%
5)RSV: 6,5%

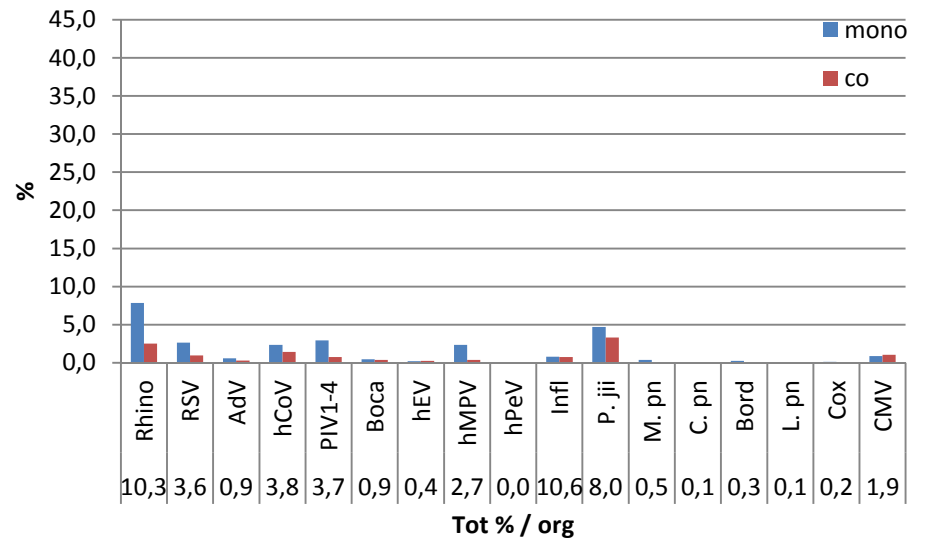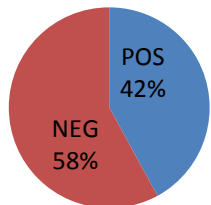|	mono	co
Rhino	10,2	
RSV	2,5	
AdV	1,0	
hCoV	2,6	
PIV1-4	3,2	
Boca	1,0	
hEV	0,9	
hMPV	2,4	
hPeV	0,0	
Infl	8,4	
P. jii	6,6	
M. pn	0,8	
C. pn	0,1	
Bord	0,8	
L. pn	0,3	
Cox	0,0	
CMV	3,5	

Tot % / org
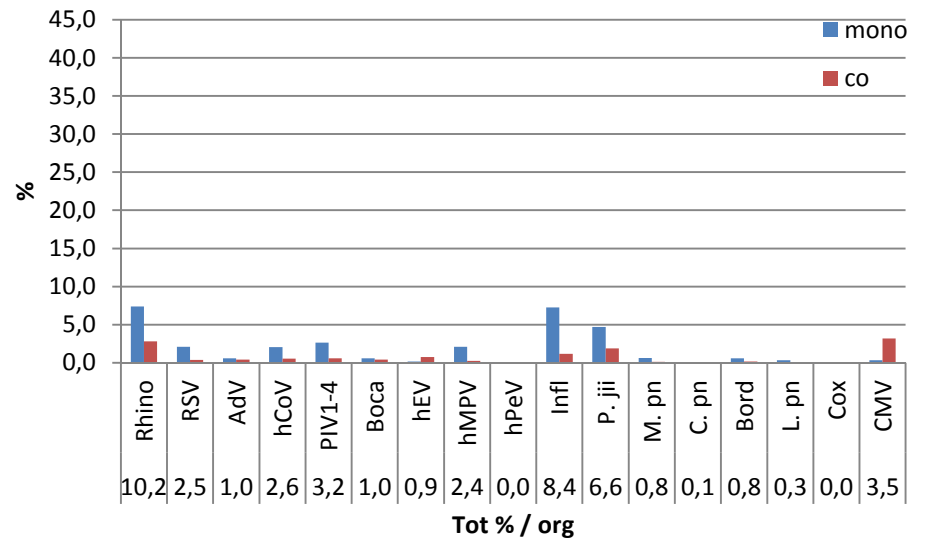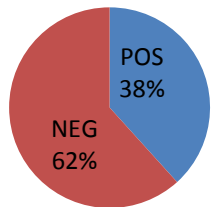
Age >75-85 years
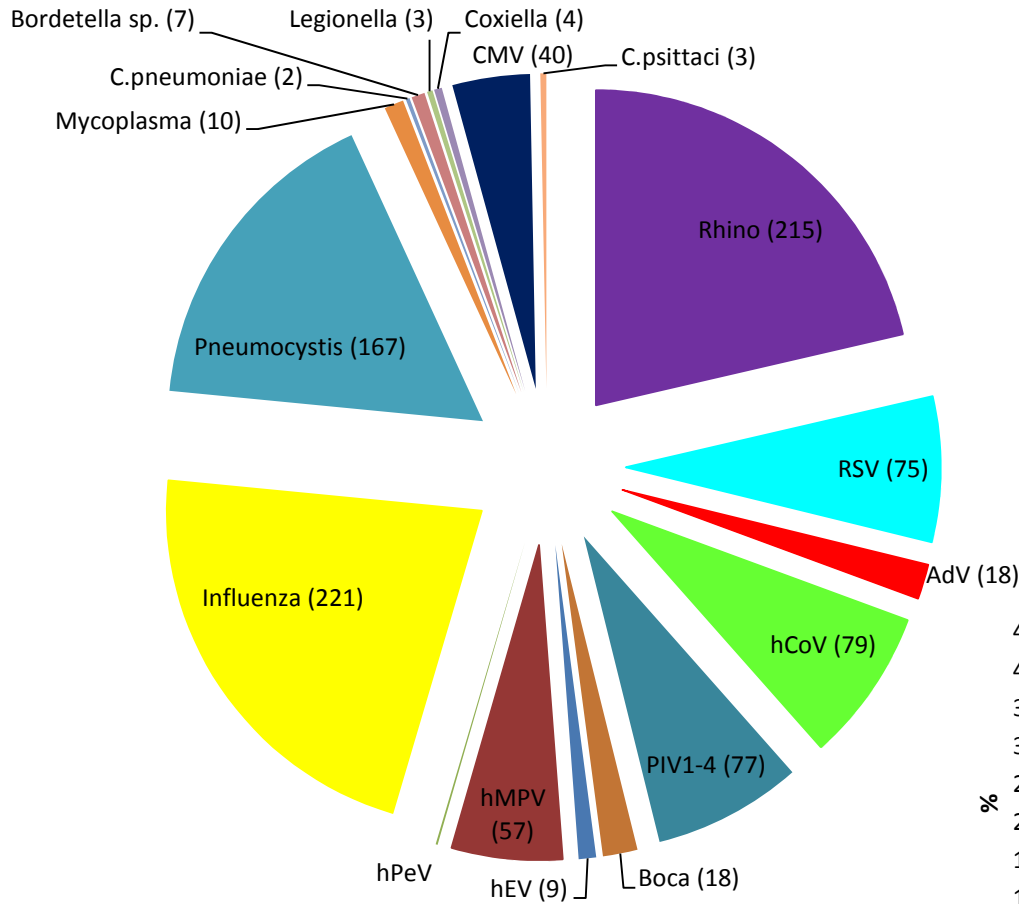
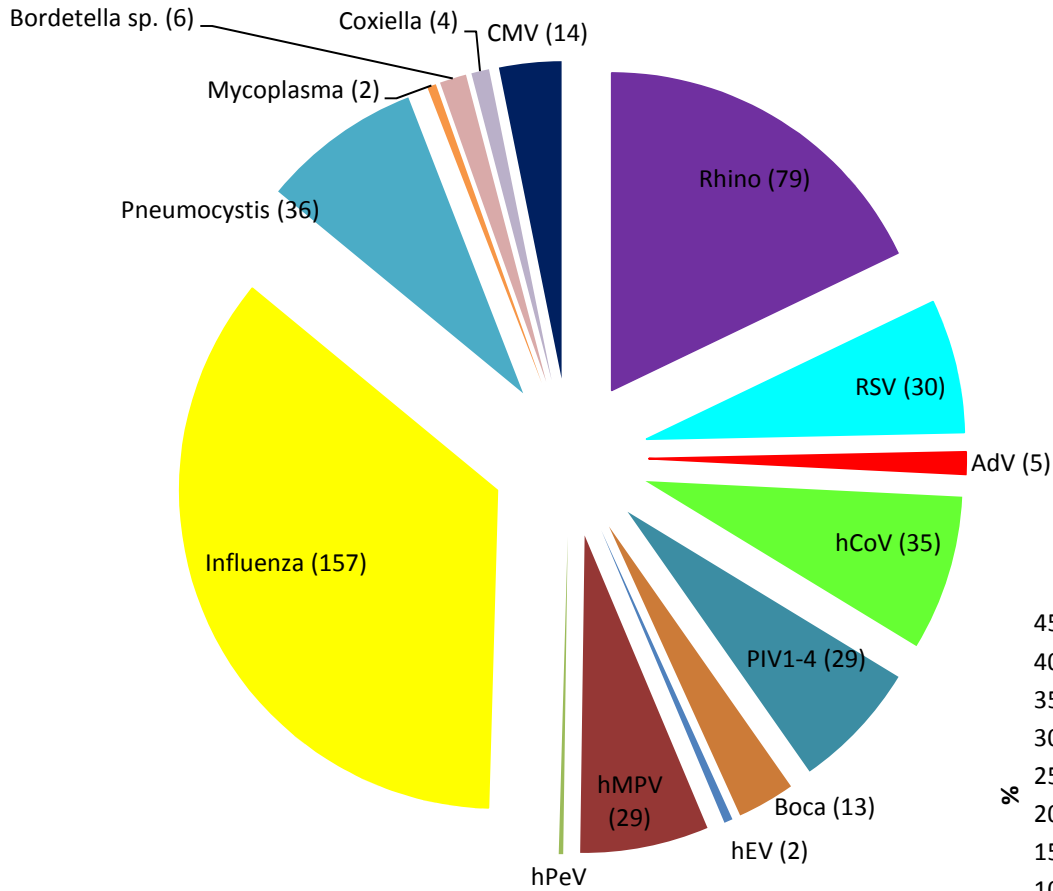
n=2078 → 873+

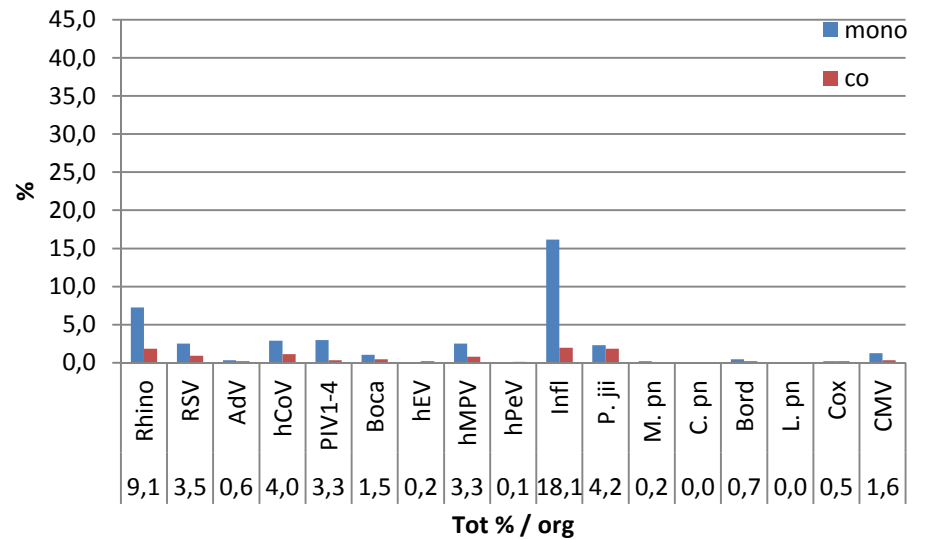TOP 5:
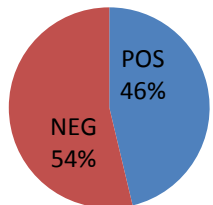1) Infl: 25,3%
2) hRV: 24,6%
3) hCoV: 9,0%
4) PIV1-4: 8,8%
5) RSV: 8,6%

Age >85-102 years

n=867 → 401+

TOP 5:
1)Infl: 39,2%
2)hRV: 19,7%
3)hCoV: 8,7%
4)RSV: 7,5%
5)PIV1-4/hMPV:7,2%

Pie chart labels:
- Bordetella sp. (6)
- Coxiella (4)
- CMV (14)
- Mycoplasma (2)
- Rhino (79)
- Pneumocystis (36)
- RSV (30)
- AdV (5)
- hCoV (35)
- Influenza (157)
- PIV1-4 (29)
- Boca (13)
- hEV (2)
- hMPV (29)
- hPeV

POS 46%
NEG 54%

Bar chart:

	Rhino	RSV	AdV	hCoV	PIV1-4	Boca	hEV	hMPV	hPeV	Infl	P. jii	M. pn	C. pn	Bord	L. pn	Cox	CMV
Tot % / org	9,1	3,5	0,6	4,0	3,3	1,5	0,2	3,3	0,1	18,1	4,2	0,2	0,0	0,7	0,0	0,5	1,6

Legend: ■ mono ■ co
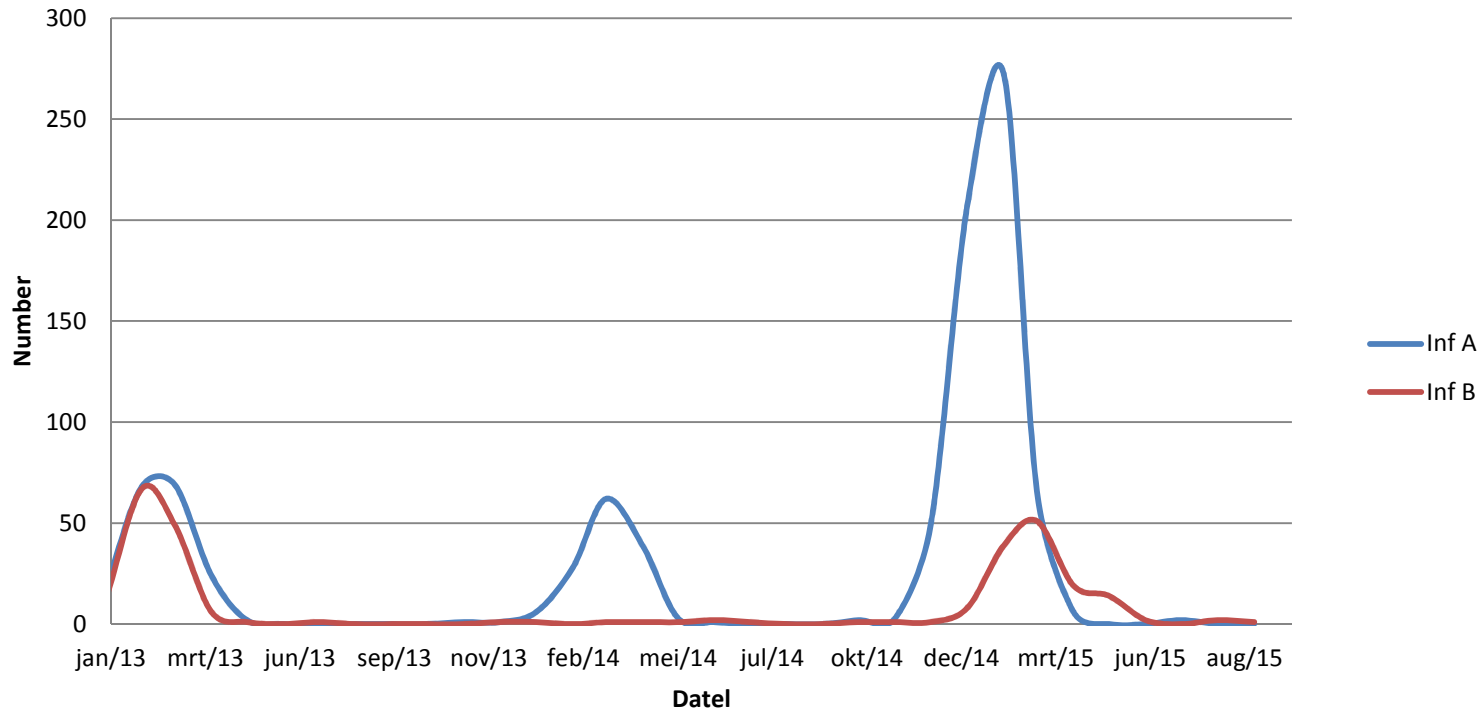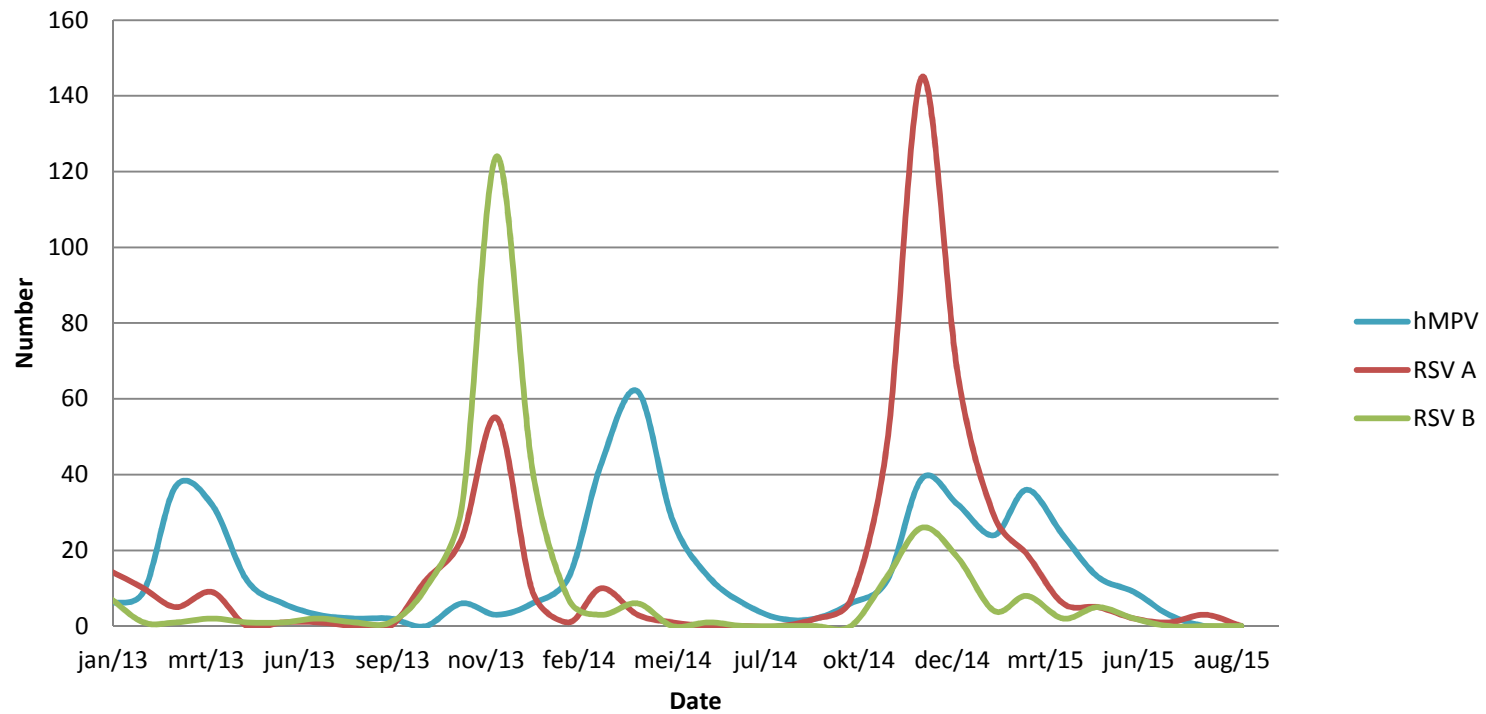
Dynamics of Parainfluenza viruses
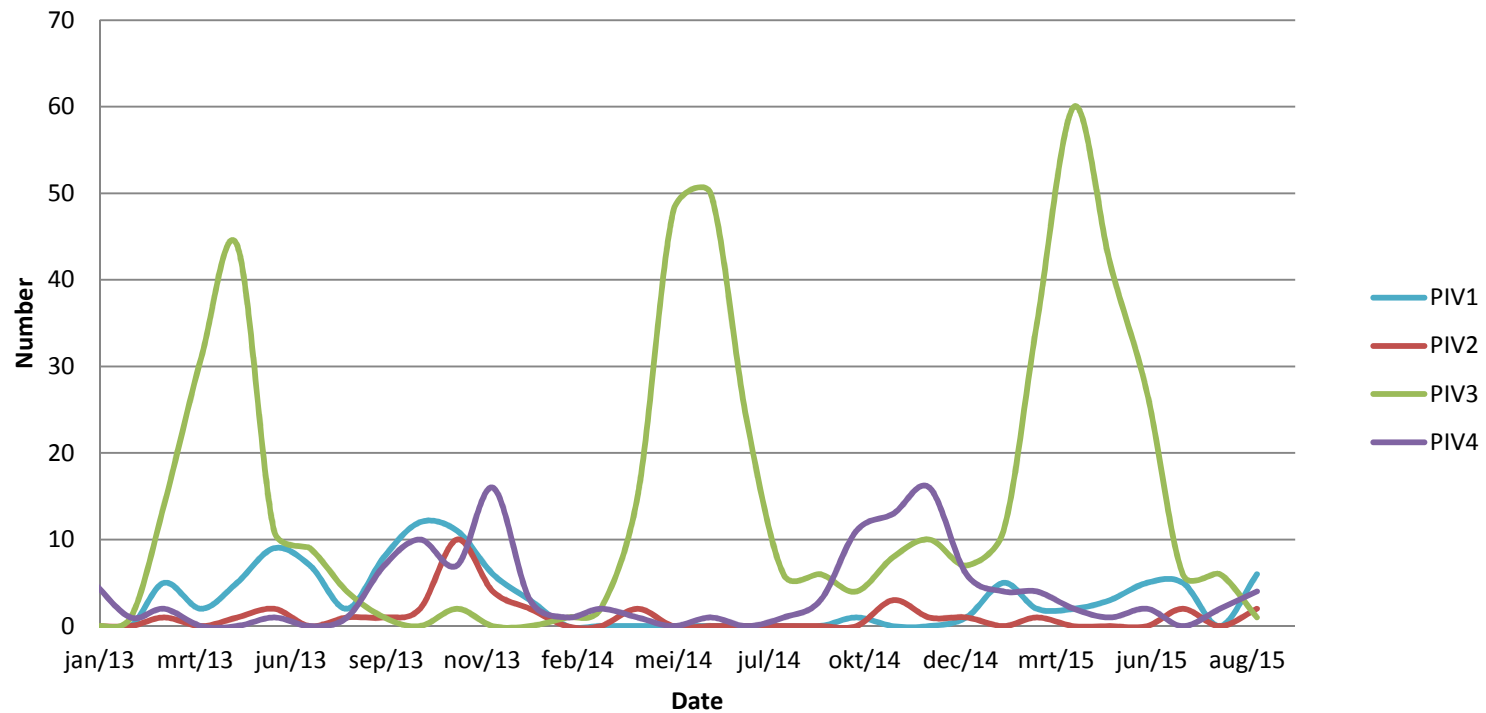
PIV-3: "summer" virus, most prevalent within parainfluenza family

Dynamics of coronaviruses
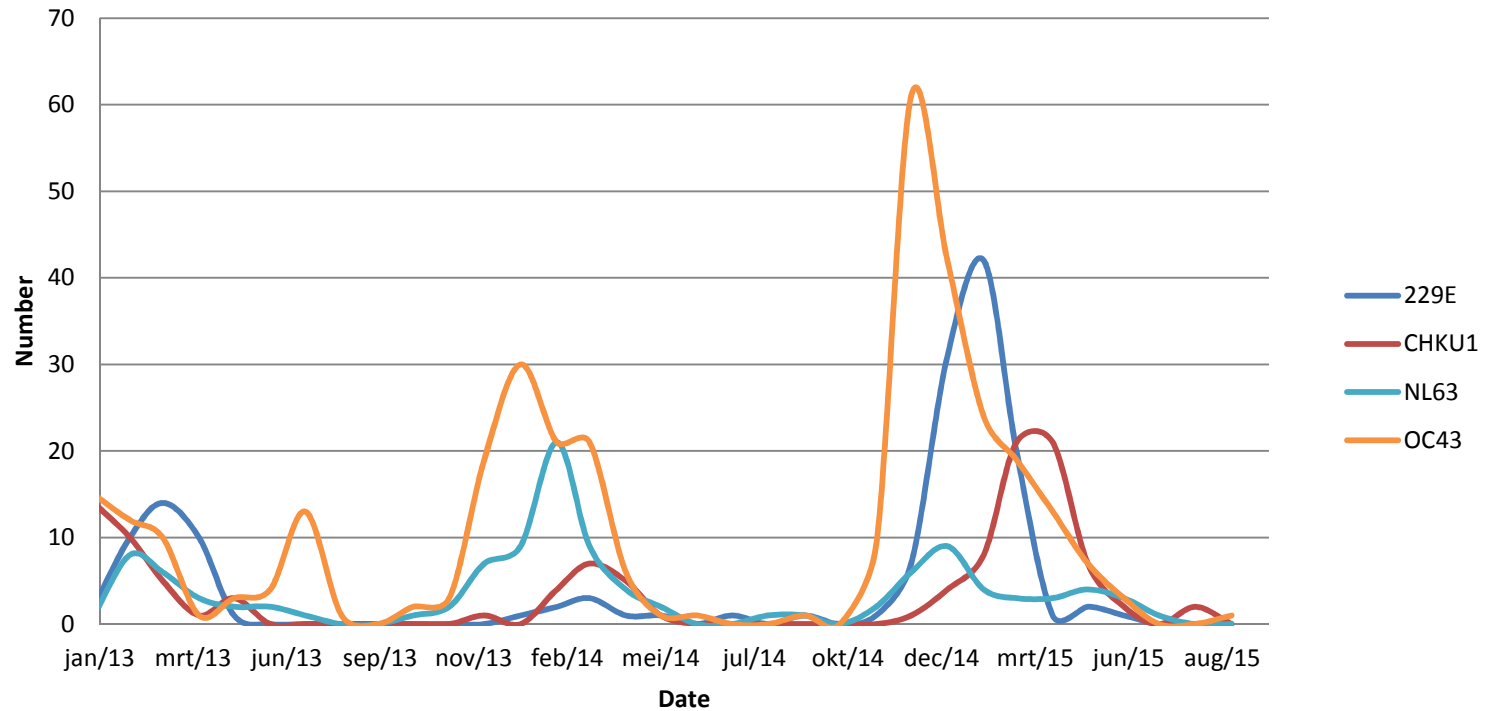
hCoV-OC43: most prevalent coronavirus overall

Human coronaviruses in function of age
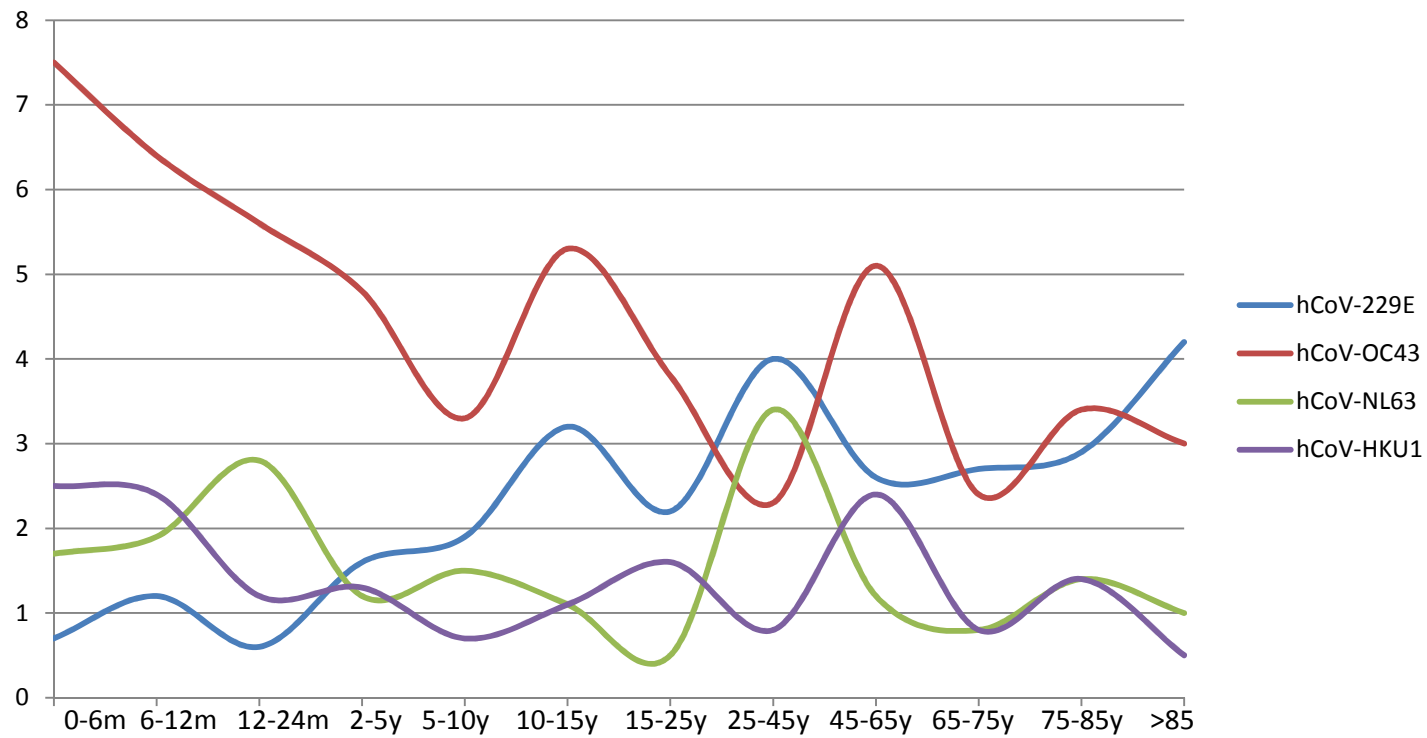
Atypical bacteria over the seasons
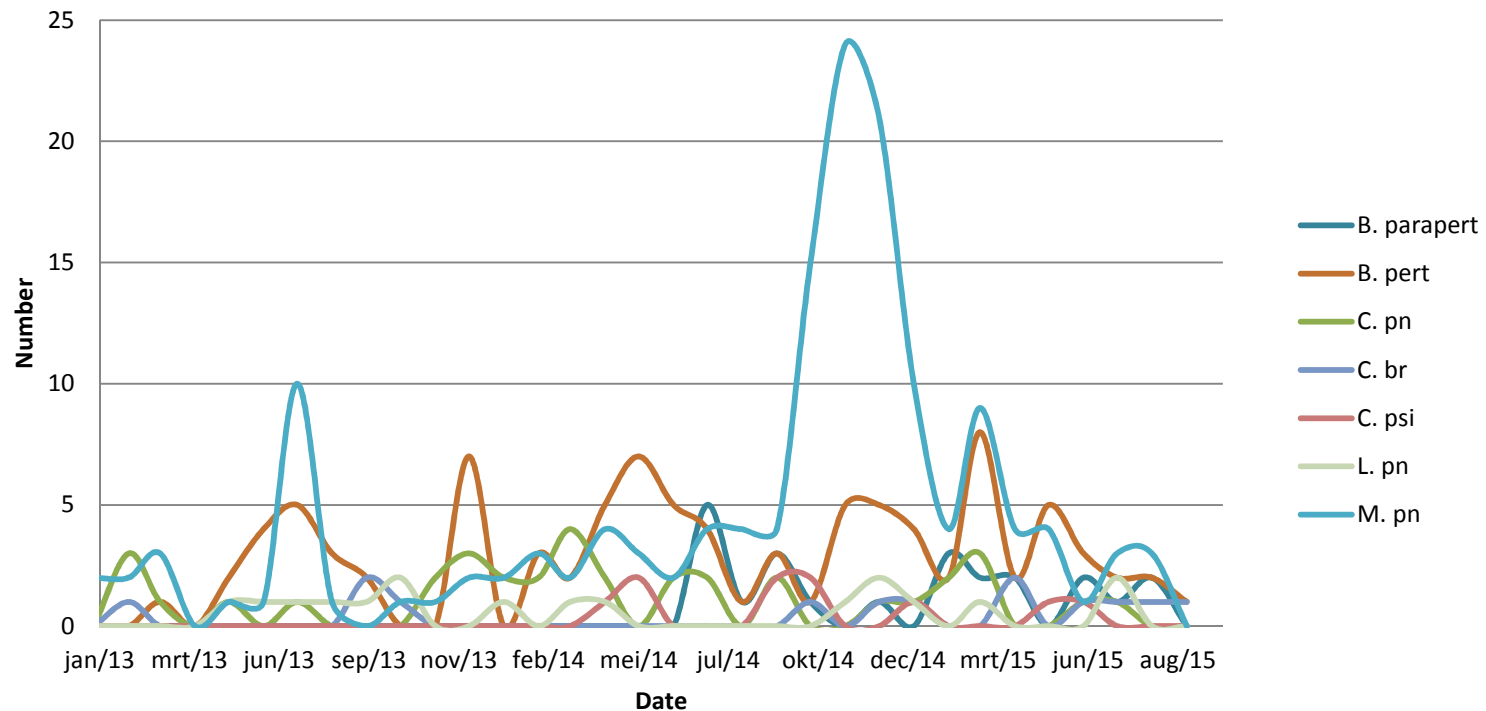
Frequency Atypical bacteria over all:

M.pneumoniae (150)> Bordetella pertussis (94) > C.pneumoniae (36) > Bordetella parapertussis (24) > Legionella pneumophila (17) > Coxiella burnetii (13) > C.psittaci (10)

Atypical bacterial pathogens over the ages

% +/all +

Age

Legend:
- Mycoplasma
- C.pneumoniae
- Bordetella sp.
- Legionella
- Coxiella
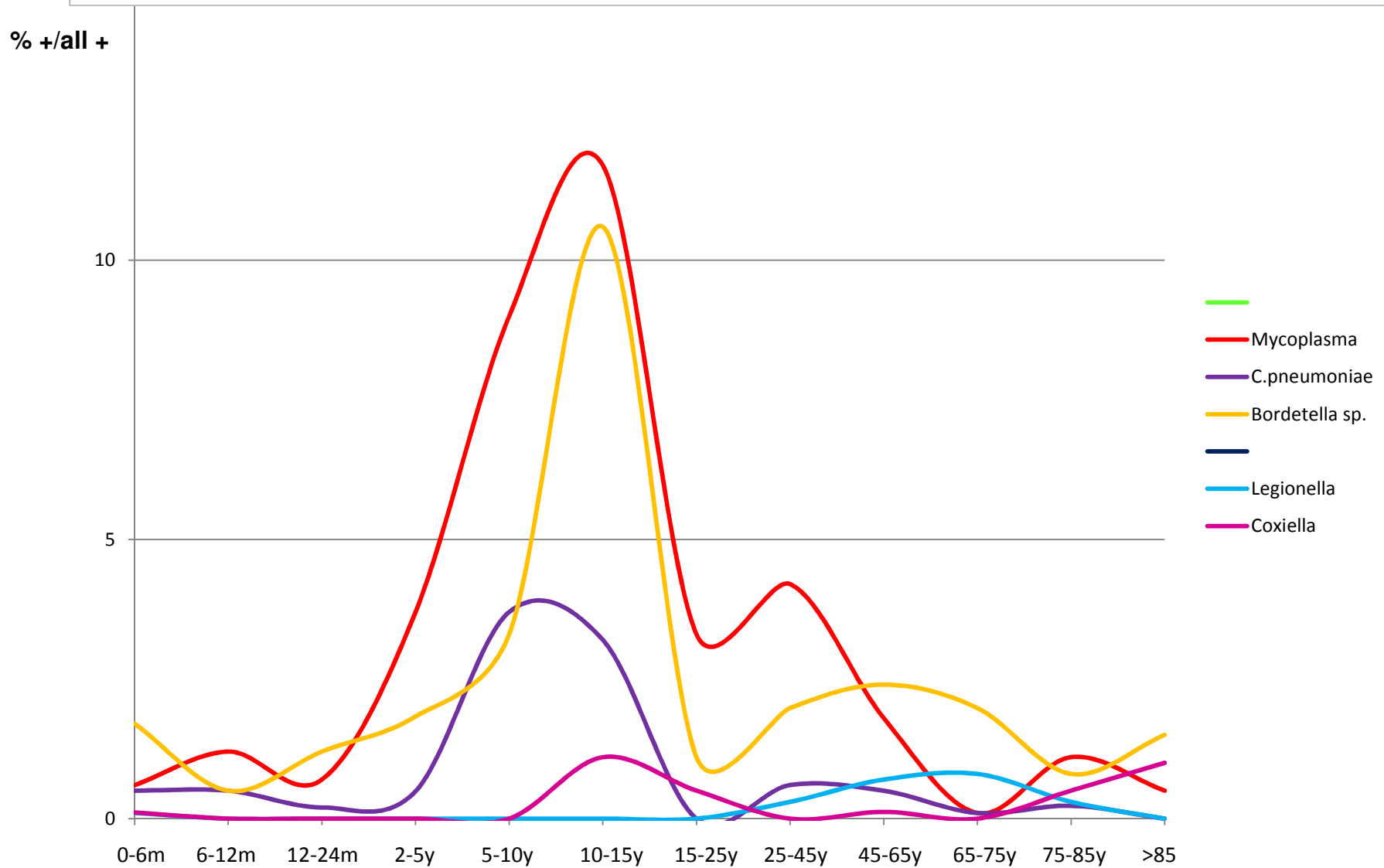
Atypical pathogens (+Pneumocystis) over the ages

% +/all +

Age

- Pneumocystis
- Mycoplasma
- C.pneumoniae
- Bordetella sp.
- Legionella
- Coxiella

0-6m 6-12m 12-24m 2-5y 5-10y 10-15y 15-25y 25-45y 45-65y 65-75y 75-85y >85
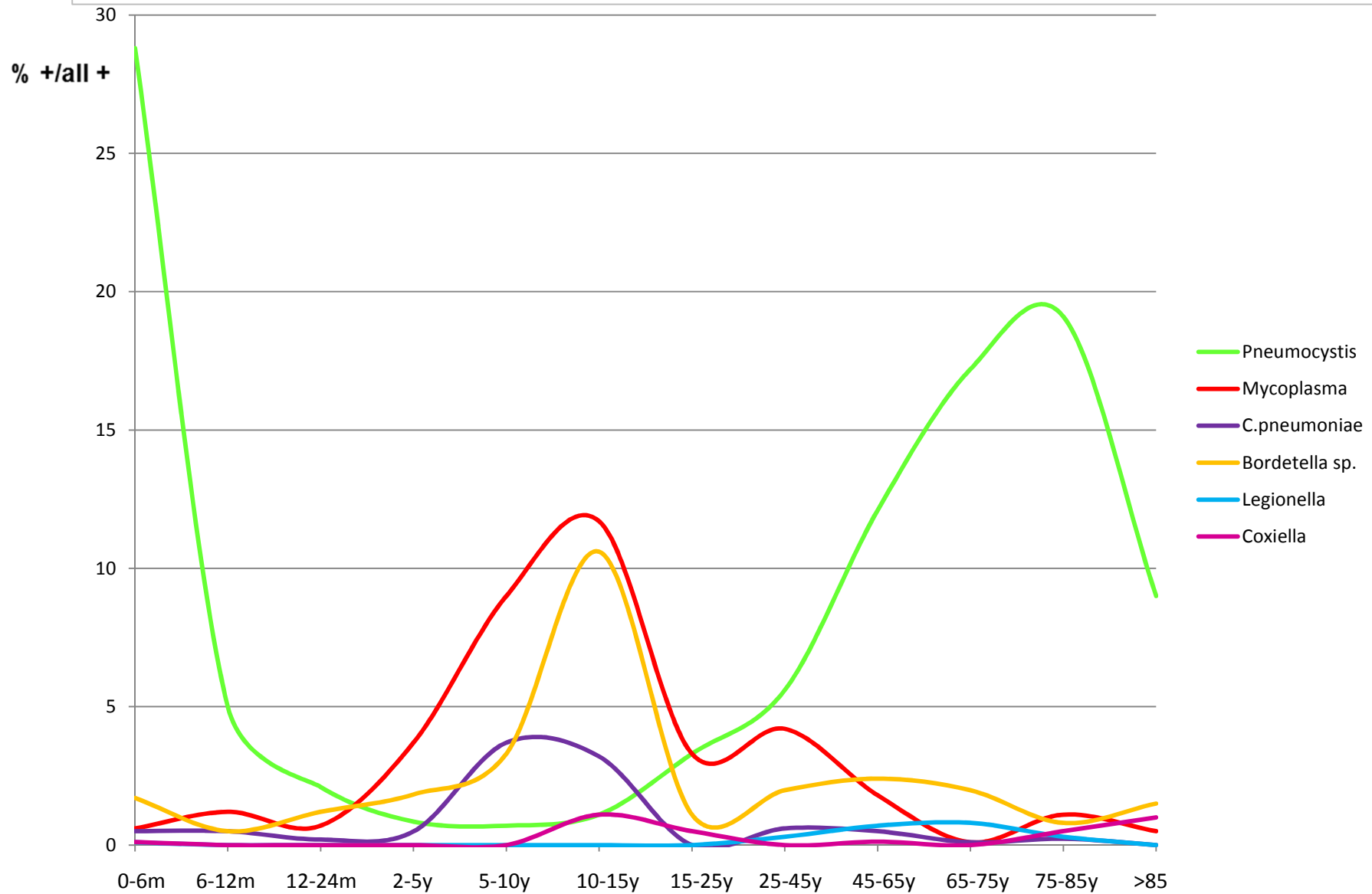
Atypical pathogens (+CMV) over the ages

% +/all +

Pneumocystis
Mycoplasma
C.pneumoniae
Bordetella sp.
CMV
Legionella
Coxiella

Age

0-6m 6-12m 12-24m 2-5y 5-10y 10-15y 15-25y 25-45y 45-65y 65-75y 75-85y >85
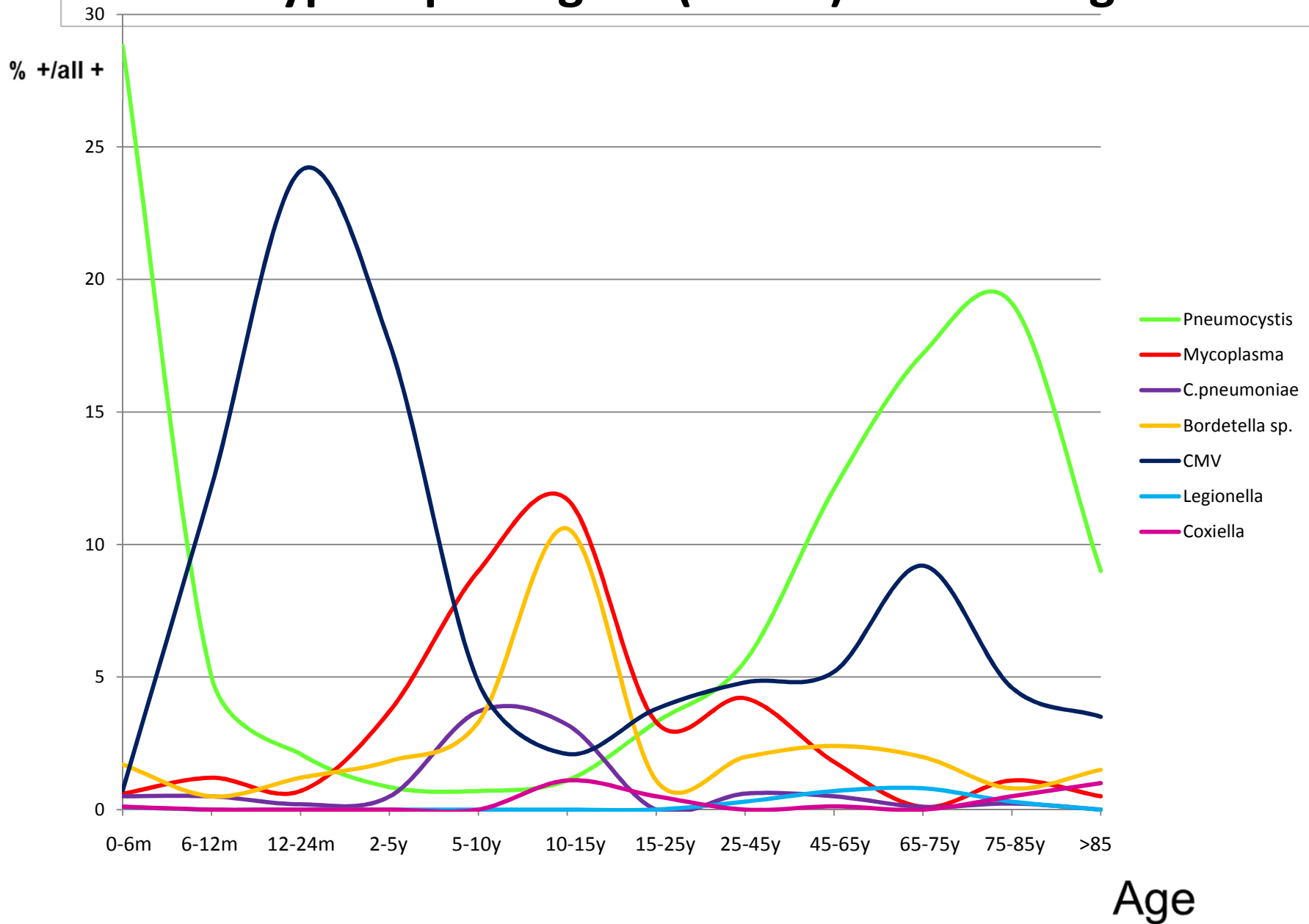
EPIC-Study
Epidemiology of Pneumonia in Community

- January 2010-June 2012; 3 hospitals USA
- 2358 children with radiographic evidence of pneumonia
- Median age: 2years
- Exclusion: recent hospitalization or immunosuppression

- Blood & respiratory specimen (NPA-BRAS-BAL-pleural fluid)
- PCR for viruses & atypical bacteria on NPA; bacterial PCR's on pleural fluid; PCR *Strep pyogenes & S.pneumoniae* on blood; bacterial culture; viral serology on paired sera
- 497 (21%) on ICU; 166 (7%) mechanical ventilation; 3 died
- 81% of samples positive for bacteria or virus
  - 66%: ≥1 virus
  - 8%: bacteria
  - 7%: mixed viral/bacterial

EPIC-Study

Pathogens Detected in U.S. Children with CAP Requiring Hospitalization

- Annual incidence pneumonia: 15,7 cases/10000 children

- Highest rate among children <2y of age (62,2 cases/10000)

- RSV, adeno, hMPV: more common beneath 5y of age

  RSV 37% vs. 8%

  Adeno 15% vs. 3%

  hMPV 15% vs. 8%

- *Mycoplasma pneumoniae*: more common above 5y of age (19% vs.3%)
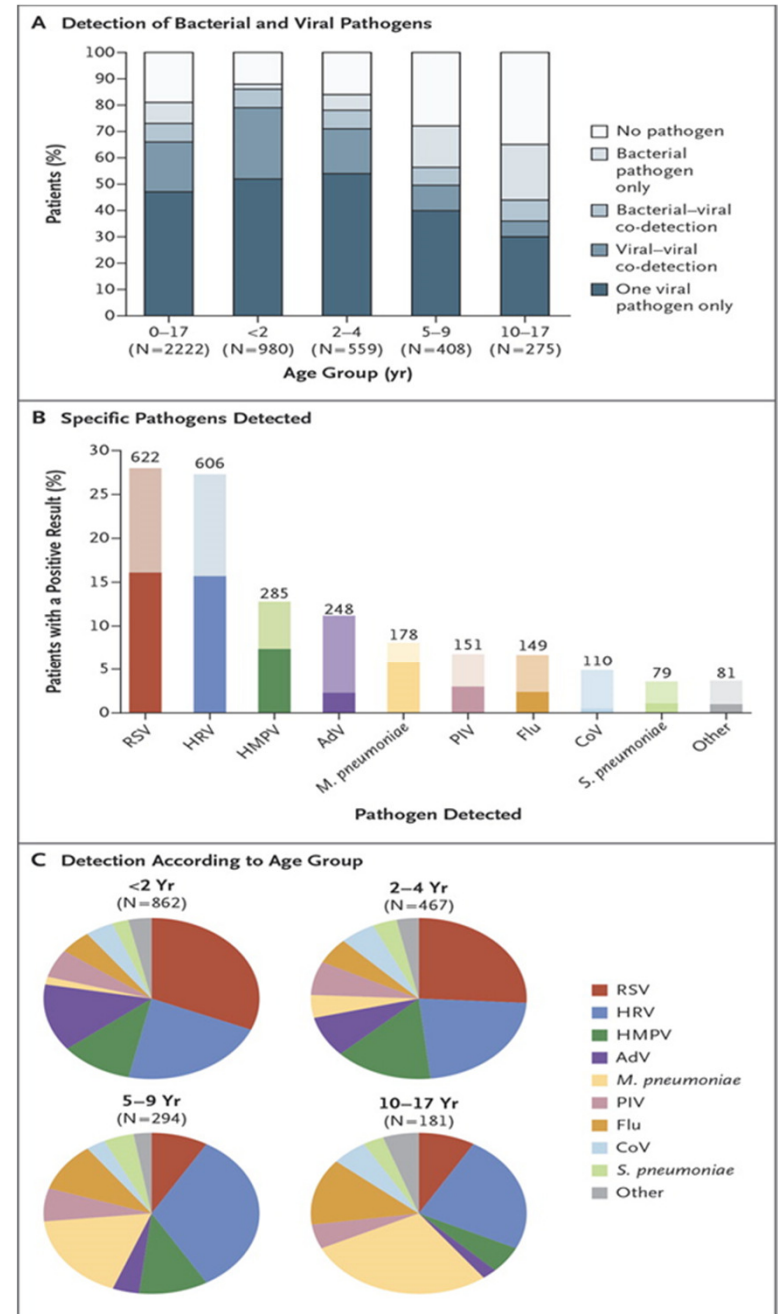
Jain S et al. N Engl J Med 2015;372:835-845

Respiratory Viral Detection in Children & Adults: comparing Asymptomatic controls & CAP patients
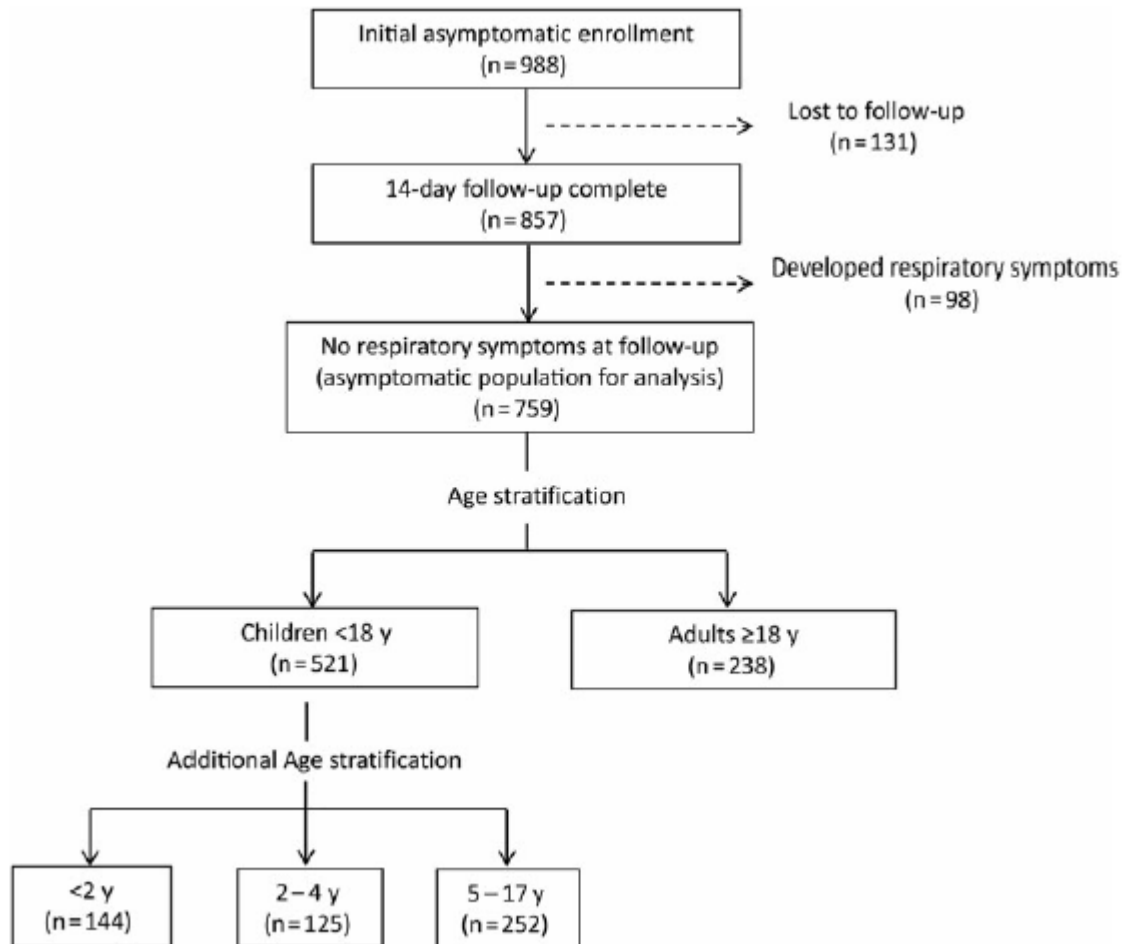
- 1024 CAP patients
  - < EPIC-criteria
    - -->832 children
- 759 controls
  - --->521children
- NP/OP flocked swab, analysis within 72h
- rRT PCR for 13 viruses using CDC protocols
- Ct-value <40 → pos

Self WH et al. J Infect Dis 2015 July 14

Respiratory Viral Detection in Children & Adults: comparing Asymptomatic controls & CAP patients

Table 2. Prevalence of Respiratory Virus Detection With rRT-PCR in Asymptomatic Controls and Patients With CAP <18 Years Old

Virus	Asymptomatic Children, No. (%) (n = 521)	Children With CAP, No. (%) (n = 832)	P Value[a]	aOR (95% CI)[b]	AF (95% CI)
Any virus[c]	127 (24.4)	572 (68.8)	<.01	NC[d]	NC
hRV	90 (17.3)	182 (21.9)	.04	1.13 (.84–1.51)	0.12 (−.18–.34)
RSV	10 (1.9)	221 (26.6)	<.01	15.2 (7.92–29.2)	0.93 (.87–.97)
hMPV	8 (1.5)	126 (15.1)	<.01	10.4 (5.02–21.6)	0.90 (.80–.95)
AdV	16 (3.1)	53 (6.4)	<.01	1.77 (.99–3.17)	0.44 (−.01 to .68)
Influenza (A and B)	0	28 (3.4)	<.01	NC	NC
PIV (types 1–3)	10 (1.9)	39 (4.7)	.01	2.29 (1.11–4.69)	0.56 (.10–.79)
CoV (229E, HKU1, NL63, OC43)	8 (1.5)	37 (4.5)	<.01	3.17 (1.44–6.99)	0.68 (.31–.86)

Self WH et al. J Infect Dis 2015 July 14

Respiratory Viral Detection in Children & Adults: comparing Asymptomatic controls & CAP patients

Table 3. Prevalence of Respiratory Virus Detection With rRT-PCR in Asymptomatic Controls and Patients With CAP ≥18 Years Old
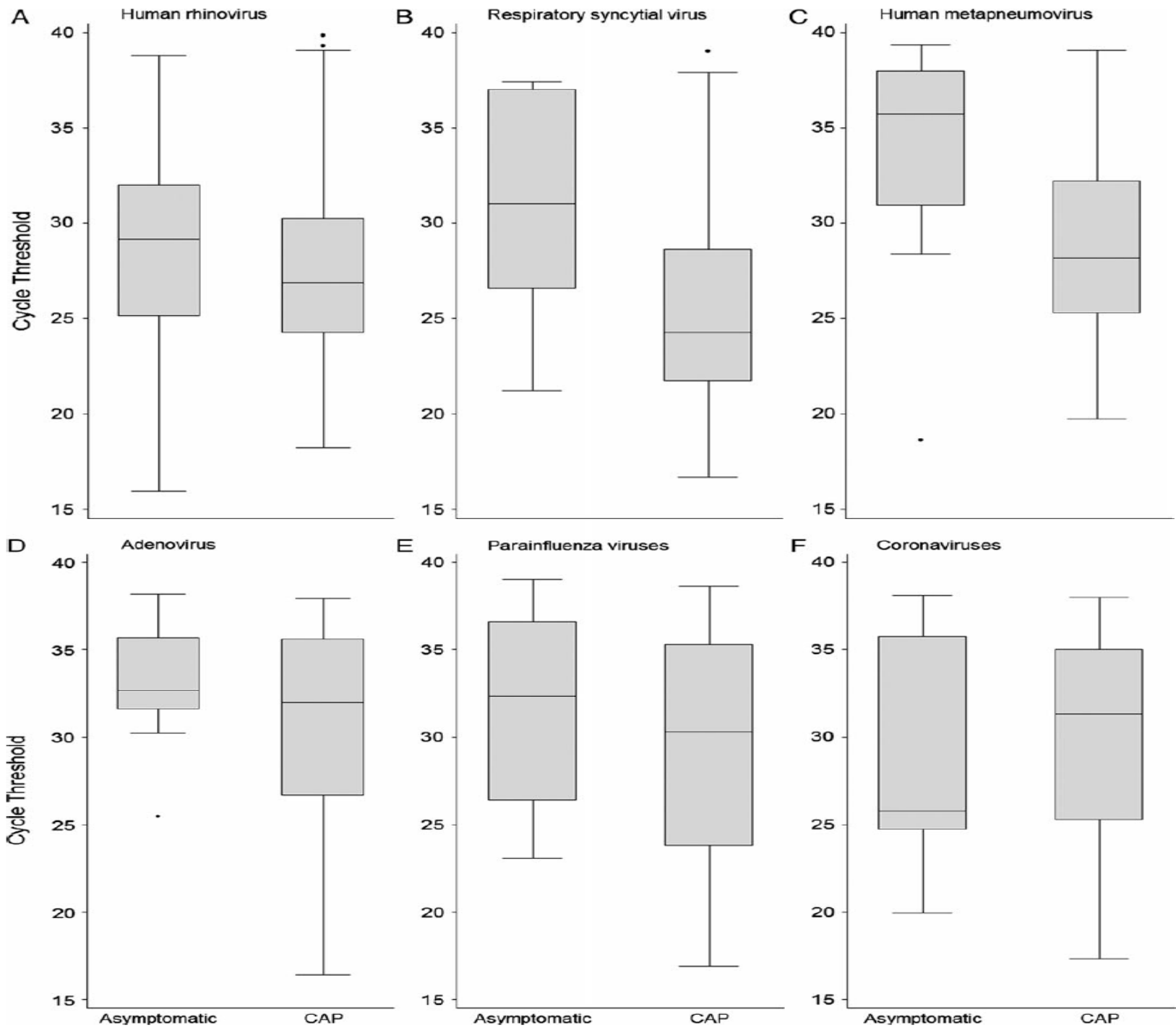
Virus	Asymptomatic Adults, No. (%) (n = 238)	Adults With CAP, n (%) (n = 192)	P Value[a]	aOR (95% CI)[b]	AF (95% CI)
Any virus[c]	5 (2.1)	47 (24.5)	<.01	NC[d]	NC[d]
hRV	2 (0.8)	21 (10.9)	<.01	13.4 (3.04–59.1)	0.93 (.67–.98)
RSV	0	3 (1.6)	.09	NC[d]	NC
hMPV	1 (0.4)	8 (4.2)	.01	13.5 (1.65–110)	0.93 (.39–.99)
AdV	0	3 (1.6)	.09	NC	NC
Influenza (A and B)	0	5 (2.6)	.02	NC	NC
PIV (types 1–3)	0	3 (1.6)	.09	NC	NC
CoV (229E, HKU1, NL63, OC43)	2 (0.8)	6 (3.1)	.14	3.19 (.59–17.1)	0.69 (−.69 to .94)

Self WH et al. J Infect Dis 2015 July 14

Respiratory Viral Detection in Children & Adults: comparing Asymptomatic controls & CAP patients

- **RESULTS:** Detections of influenza, RSV & hMPV were significantly more common in patients with CAP of all ages than in controls (AFs near 1.0). PIV & hCoV were also more common among patients with CAP (AF 0.5-0.75). Rhinovirus was associated with CAP among adults (AF 0.93) but not children (AF 0.02). Adenovirus was associated with CAP only among children <2 years old (AF 0.77).

- **CONCLUSIONS**: The **probability that a virus detected with rRT PCR in patients with CAP contributed to symptomatic disease varied by age group & specific virus**. Detections of influenza, RSV & hMPV among patients with CAP of all ages probably indicate an etiologic role, whereas detections of PIV, hCoV, rhinovirus, & adenovirus, especially in children, require further studies

Significance of Rhino and Corona positives?

Pathogen	ILI (n = 166)		ARTI (n = 376)		Control subjects (n = 541)	
	Crude prevalence	Adjusted prevalence[a]	Crude prevalence	Adjusted prevalence[a]	Crude prevalence	Adjusted prevalence[a]
Adenovirus	0 (0)	0 (0)	7 (1.9)	12 (3.2)	0 (0)	0 (0)
Coronavirus	6 (3.6)	5 (3.0)	29 (7.7)	30 (8.0)	21 (3.9)	30 (5.5)
Enterovirus	2 (1.2)	2 (1.2)	13 (3.5)	12 (3.2)	7 (1.3)	12 (2.2)
hMPV	5 (3.0)	4 (2.4)	6 (1.6)	6 (1.6)	0 (0)	0 (0)
Influenza virus						
Type A	49 (29.5)	69 (41.6)	18 (4.8)	17 (4.5)	3 (0.6)	3 (0.6)
Type B	15 (9.0)	14 (8.4)	10 (2.7)	13 (3.5)	0 (0)	0 (0)
Parainfluenza virus	0 (0)	0 (0)	14 (3.7)	17 (4.5)	0 (0)	0 (0)
Rhinovirus	30 (18.1)	50 (30.1)	89 (23.7)	93 (24.7)	60 (11.1)	90 (16.6)
Respiratory syncytial virus	3 (1.8)	3 (1.8)	12 (3.2)	18 (4.8)	3 (0.6)	3 (0.6)
M. pneumoniae	5 (3.0)	4 (2.4)	9 (2.4)	11 (2.9)	3 (0.6)	2 (0.4)
C. pneumoniae/Chlamydophila psittaci	2 (1.2)	2 (1.2)	4 (1.1)	3 (0.8)	10 (1.8)	25 (4.6)
No virus	57 (34.3)	46 (27.7)	191 (50.8)	176 (46.8)	438 (81.0)	385 (71.2)

No. (%) of subjects, by presentation

Van Gageldonk-Lafeber et al. CID 2005; 41: 493

Virus shedding after human rhinovirus infection in children, adults and patients with hypogammaglobulinaemia
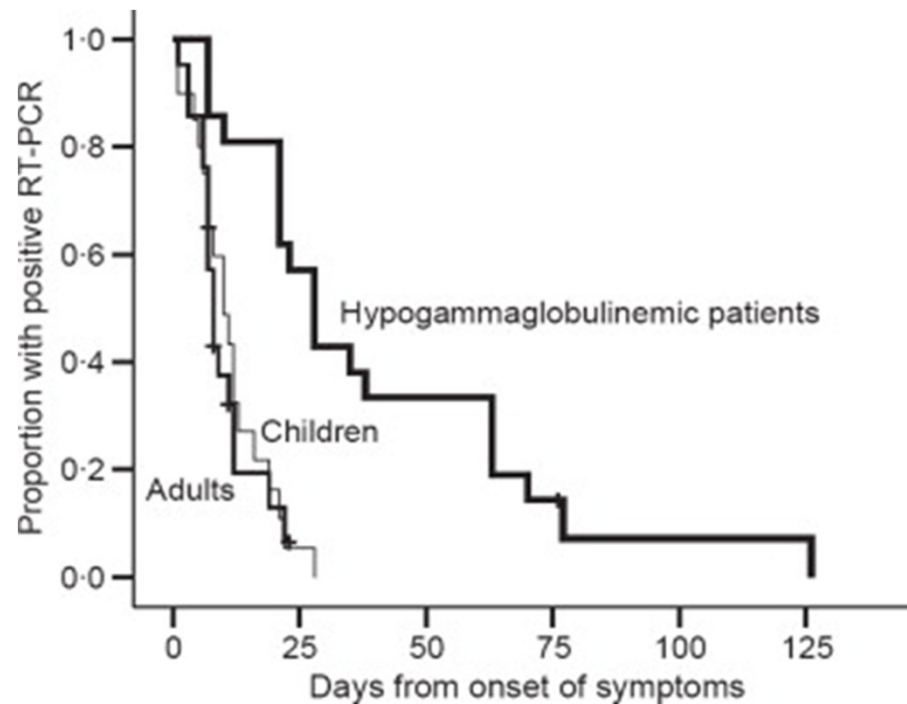

FIG. 1. Proportion of subjects positive for human rhinovirus (HRV) by RT-PCR in relation to days from onset of symptoms. The duration of HRV shedding was longer in patients with hypogammaglobulinaemia than in children or adults without hypogammaglobulinaemia.

Conclusions

- All epidemiological studies illustrate a fundamental limitation of pathogen-based diagnosis
  → detection of a pathogen does not prove it's the cause of patient's illness

- Rhinovirus is especially problematic
  ~ increasingly respected as a legitimate pathogen causing LRTI & URTI
  ~ frequently detected in asymptomatic young children/adults

- An appealing approach to escape from this conundrum is to query **host responses**

⟹ host gene expression in peripheral blood leucocytes showed differences in response to viral vs bacterial OR in response to symptomatic vs asymptomatic infection

Conclusions (2)

- **Proteomics & metabolomics** provide alternative pathways to evaluate host responses
- An approach combining pathogen detection & characterization of host response

  → <u>ultimate goal</u>:

a test that informs clinicians regarding the need for AB

withhold AB when bacterial infection is unlikely

= the key to lessening the current overuse of antibiotics in viral RTI

Acknowledgment

Questions?

Prevalence of hMPV & importance of viral co-infection in respiratory samples of febrile pediatric patients in Belgium

Objective: determination prevalence of hMPV, Coronavirus 229E, NL63, OC43, Bocavirus and viral coinfection in paediatric patients with fever (>38°C) & symptoms of URTI or LRTI

Study design: prospective study from January-March 2008 in 407 infants < 7 years of age admitted for 416 acute respiratory episodes in 2 university hospitals, for which an initial rapid virological screening for InflA/B, RSV, Adeno by immunochromatography didn't reveal a causal agent.

Material & Methods:

Virological diagnosis was made by classical viral cell culture on 3 cell lines (Vero, LLC-MK2, MRC-5), completed by multiple multiplex real time PCR's for 15 viruses

Prevalence of hMPV & importance of viral co-infection in respiratory samples of febrile pediatric patients in Belgium

Results:

- 65.1% (n=271) of samples contained viruses
- Viral coinfection in 67 samples = 24.7% of all the ⊕ viral samples, viro-bacterial in 9 samples (2%)
- Prevalences:
  - hMPV: 3.8% (25% viral coinfection)   1%
  - PIV-1-4: 4,1% (38% coinfection)   1,9%
  - Bocavirus: 8.9% (60.5% coinfection)   1%
  - Corona NL63: 7.7% (47% coinfection)   4,3%
  - Corona OC43: 4.6% (32% coinfection)   0%
  - Corona E229: 1.9% (50% coinfection)   1%
  - Rhino: 14,6% (36% coinfection)   5,4%
- Control group (n=92) apyretic children without fever

Results

Table 2. Virus in function of age

	< 1 month n = 26 (6%)	1- < 6 months n = 130 (31%)	6- < 12 months n = 100 (24%)	1-2 years n = 68 (16%)	3-4 years n = 71 (17%)	≥ 4 years n = 21 (5%)	Total
Influenza	2 (7.6%)	14 (10.8%)	7 (7%)	11(16.2%)	21(29.6%)	10 (47.6%)	65
Inf A	2	12	6	10	15	5	50
Inf B		2	1	1	6	5	15
Parainfluenza	0	6 (4.6%)	6 (6%)	3 (4.4%)	2 (2.8%)	0	17
type I		3	1	1			5
type II			1				1
type III		2	1		1		4
type IV		1	3	2	1		7
hMPV	1 (3.8%)	3 (2.3%)	9 (9%)	1 (1.5%)	2 (2.8%)	0	16
RSV	0	13 (10%)	6 (6%)	4 (5.9%)	1 (1.4%)	0	24
A		10	5	1	1		17
B		3	1	3			7
Coronaviruses	3 (1.1%)	18 (13.8%)	12 (12%)	15 (22%)	8 (11,3%)	2 (9.5%)	58
NL63	1	6	8	8	7	2	32
OC43	1	10	2	5	1		19
229E	1	3	2	2			8
Rhinoviruses	5 (19,2%)	27(20.7%)	10 (10%)	11 (16.2%)	8 (11.3%)	0	61
Bocavirus	1(3.8%)	7 (5.4%)	13 (13%)	12 (17.6%)	5 (7%)	0	38
Adenoviruses	1 (3.8%)	4 (3.1%)	17 (17%)	10 (14.7%)	3 (4.2%)	0	35
	13	92	80	67	50	12	314