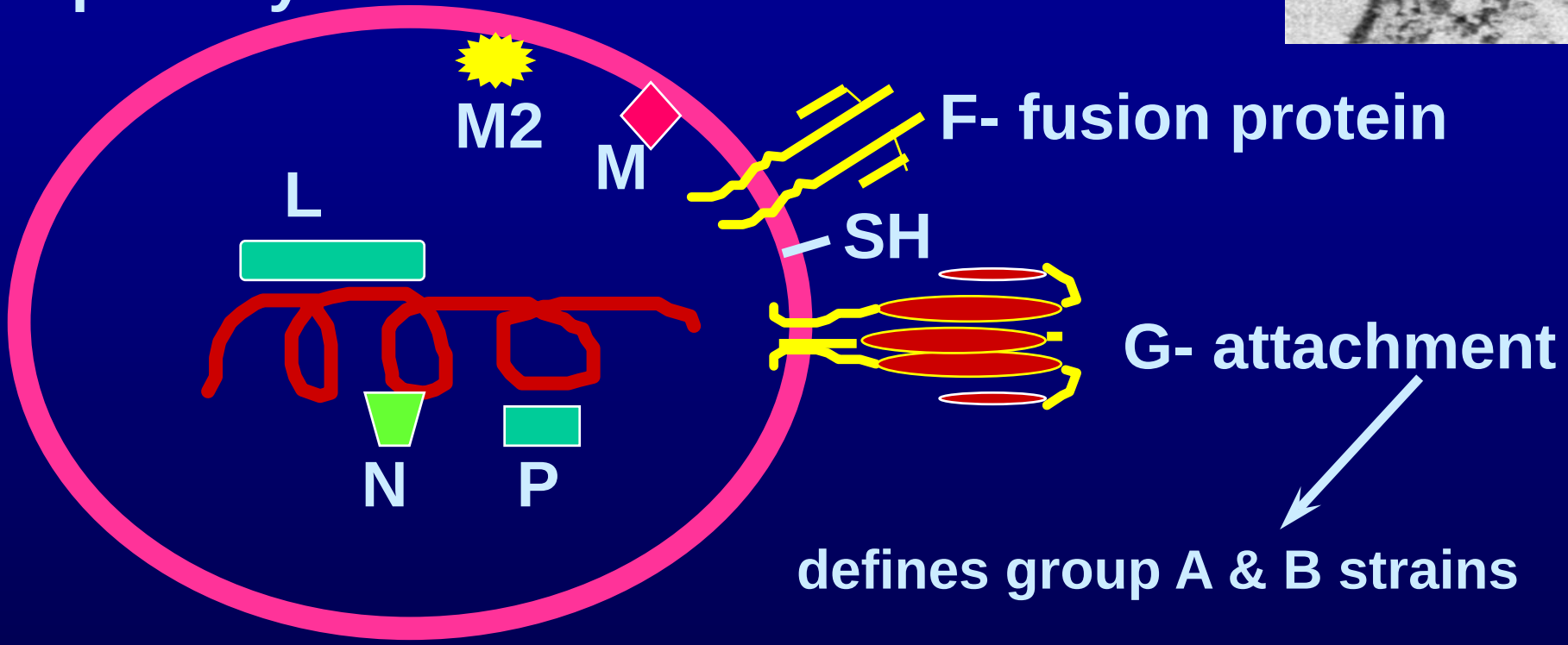
Epidemiology and Impact of RSV in Older Adults

Ann R. Falsey, M.D.
University of Rochester

Brief History of RSV

1956	RSV first named “Chimpanzee Coryza Agent” CCA
1957	RSV recovered from infants
1958-98	Defined as the most important cause of LRTI in infants - 90-100,000 hospitalizations a year in the US
1966	Formalin-inactivated vaccine disaster
1980-98	Re-infection in adults

10 genes
8 structural proteins
ss - polarity RNA



defines group A & B strains

RSV Adult Studies

- Case reports and outbreaks
- Indirect evidence and modeling studies
- Illness based studies

  Visits to GP, ER, hospitalizations

- Prospective studies

Attack rates 12-89% in outbreaks

1-15% in prospective studies

Reported severity is highly variable

Pneumonia	(0-55%)
Death	(0-53%)

RSV is an Important cause of Community Acquired LRTI among Hospitalized Adults

Dowell SF. J Infect Dis 1996; 174:456

Organism	(%)*
S. pneumoniae	6.2
Influenza A & B	5.4
RSV	4.4
M. pneumoniae	4.1
Total confirmed	21

* 1195 cases evaluated, 2 winters

Mathematically derived estimates of RSV disease burden in elderly and high-risk adults

$$Y = \alpha \, exp(\beta_0 + \beta_1[t] + \beta_2[t^2] + \beta_3[\sin(2\pi/52)] + \beta_4[\cos(2\pi/52)] + \beta_5[A(H1N1)] + \beta_6[A(H3N2)] + \beta_7[B] + \beta_8[RSV]$$

Thompson et al JAMA 2003

Age Specific Annual Deaths in US
P & I and Circulatory & Respiratory
1976-1997

Age	All Flu	RSV
<1	**39**	**335**
1-4	**91**	**32**
5-49	**1061**	**641**
50-64	**3084**	**1816**
≥65	**39977**	**11199**
Total	**44252**	**14028**

Thompson et al JAMA 2003

Influenza A and RSV Mortality in US 1997-2009

	Age	Flu A	RSV	Rate per 100,000
P & I	0-4	29	92	0.5
	50-64	578	381	0.8
	65-74	873	805	4.3
	>75	6057	4714	27.4
Cardiorespiratory	0-4	52	146	0.7
	50-64	1847	1888	4
	65-74	3022	2483	13.2
	>75	14765	11753	68.1

Matias et al IORV 2014

Modeling Estimates of the Burden of RSV Infection in Adults & Elderly in UK

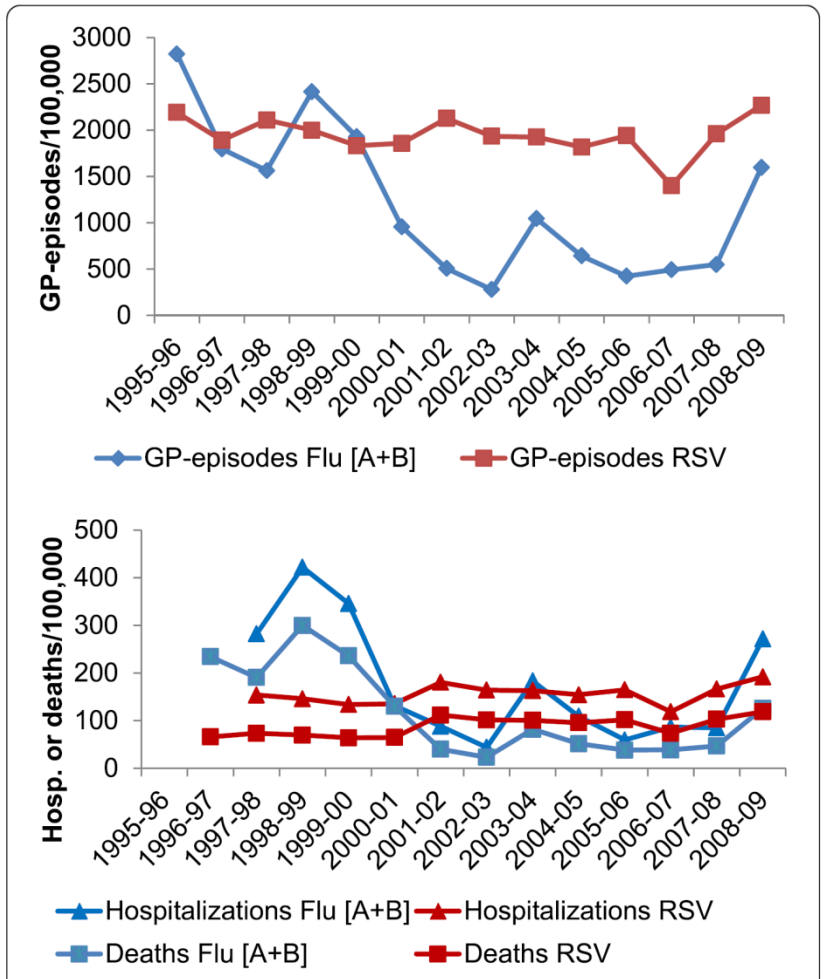


Fig. 1 Incidence (per 100,000) of respiratory GP episodes, hospitalizations and deaths among 65+ year olds attributed to RSV or Influenza [A + B] in the seasons studied

Fleming DM et al BMC 2015

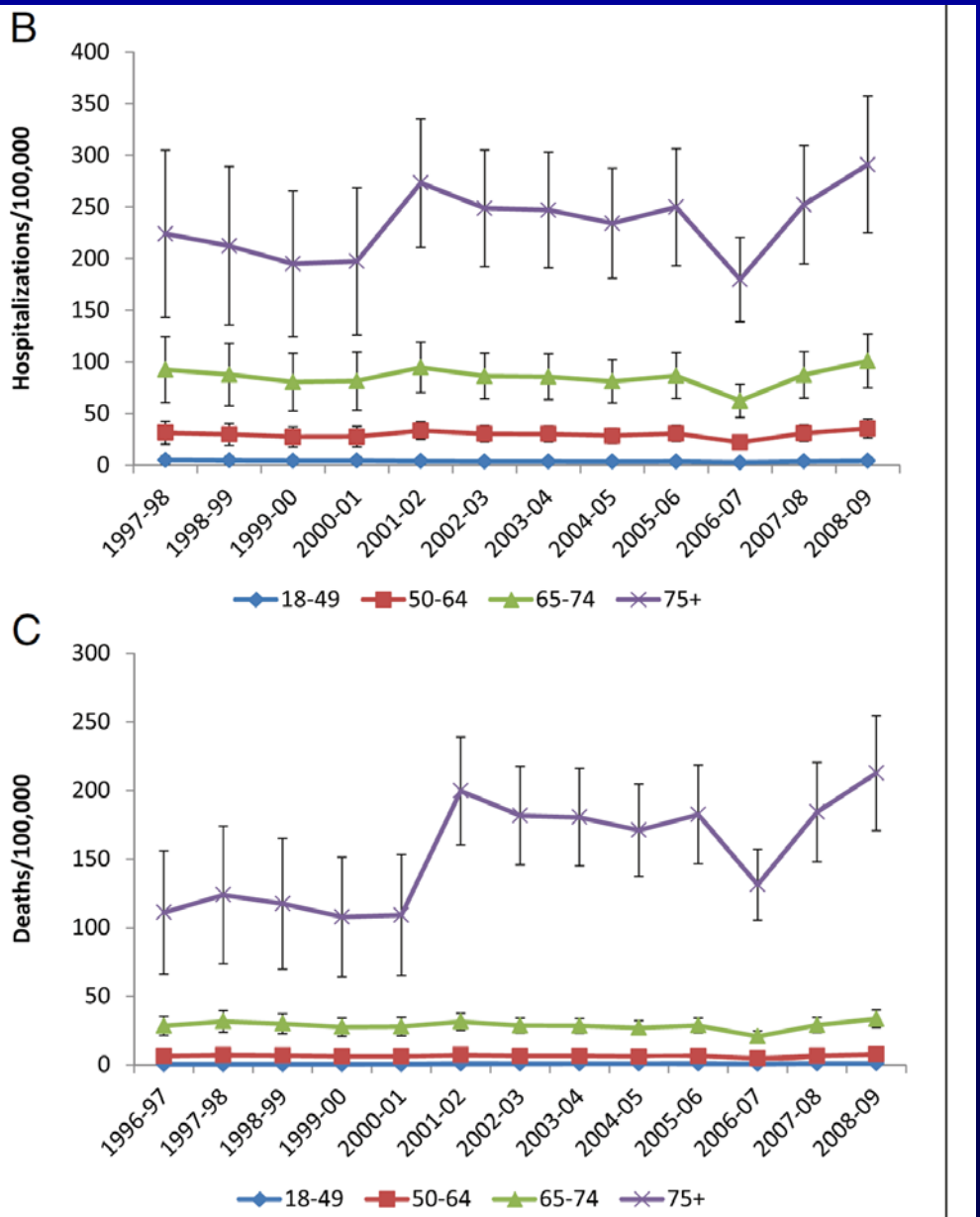


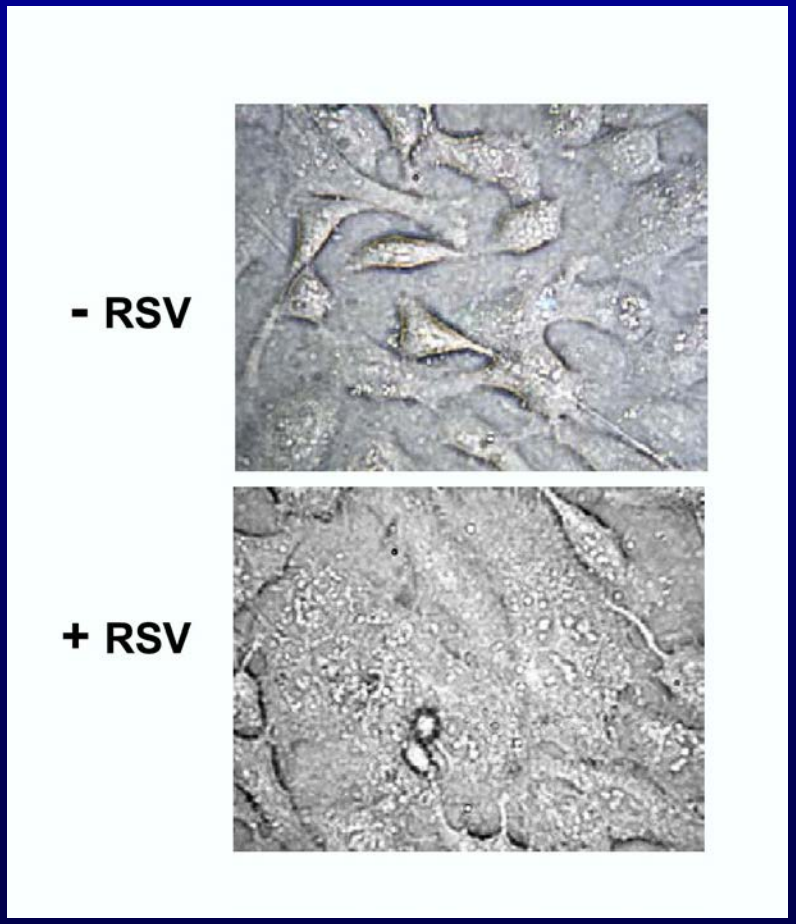
Fig. 2 Seasonal incidence (per 100,000) of GP episodes (**a**) hospitalisations (**b**) and deaths (**c**) due to RSV-attributable respiratory disease. Vertical lines = 95 confidence intervals

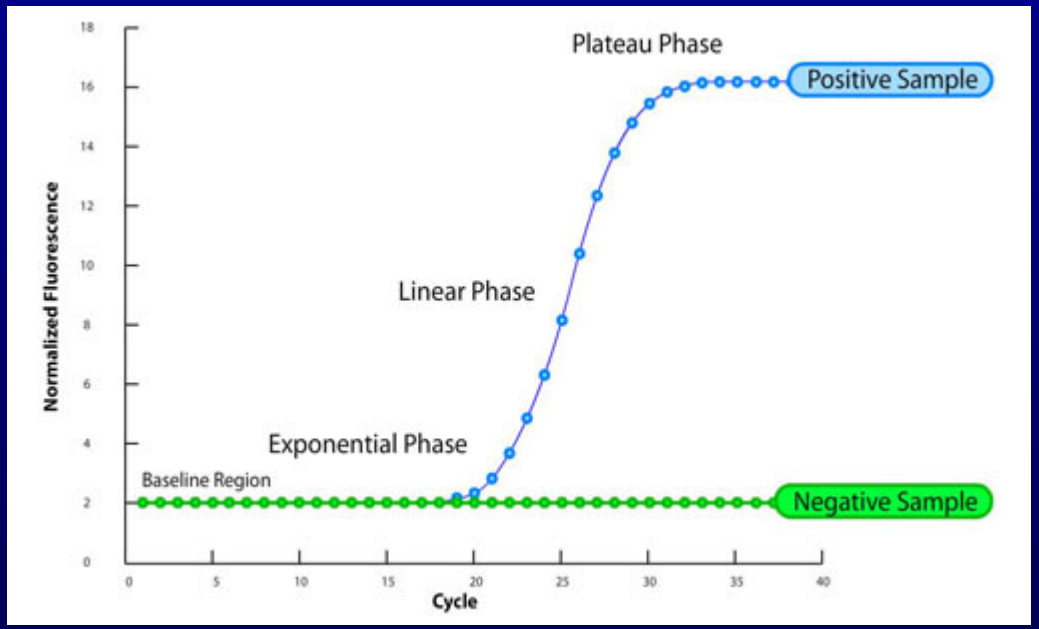
Fleming DM et al BMC 2015

Diagnosis

RSV

Diagnosis of RSV in Adults





Diagnostic Challenges in Older Adults

- Lack of distinctive syndromes (croup, bronchiolitis)
- Diminished febrile response
- Exacerbations of comorbid conditions
- Diagnosis not commonly considered
- Adults shed lower titers of virus in the nose than infants ($<10^{2\text{-}3}$ vs. $>10^{6}$ pfu/ml)

Total RSV Testing in all Subjects

	Positive	Number Tested	Percent
Culture	47	1134	4.1
PCR	102	1135	9.0
Serology	138	1114	12.4
RSV by any method	166	1495	11.1

Diagnostic testing in illnesses with all 3 tests available (N =1114)

	Culture	PCR	Serology	# Subjects
	+	+	+	37
	+	+	0	6
	0	+	+	37
	0	0	+	30
	0	+	0	7
	0	0	0	995
Total	43	87	104	1112

Not all had convalescent sera

117 RSV +

Diagnostic testing in illnesses with all 3 tests available (N =1114)

	Culture	PCR	Serology	# Subjects
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	+	+	0	6
	0	+	+	37
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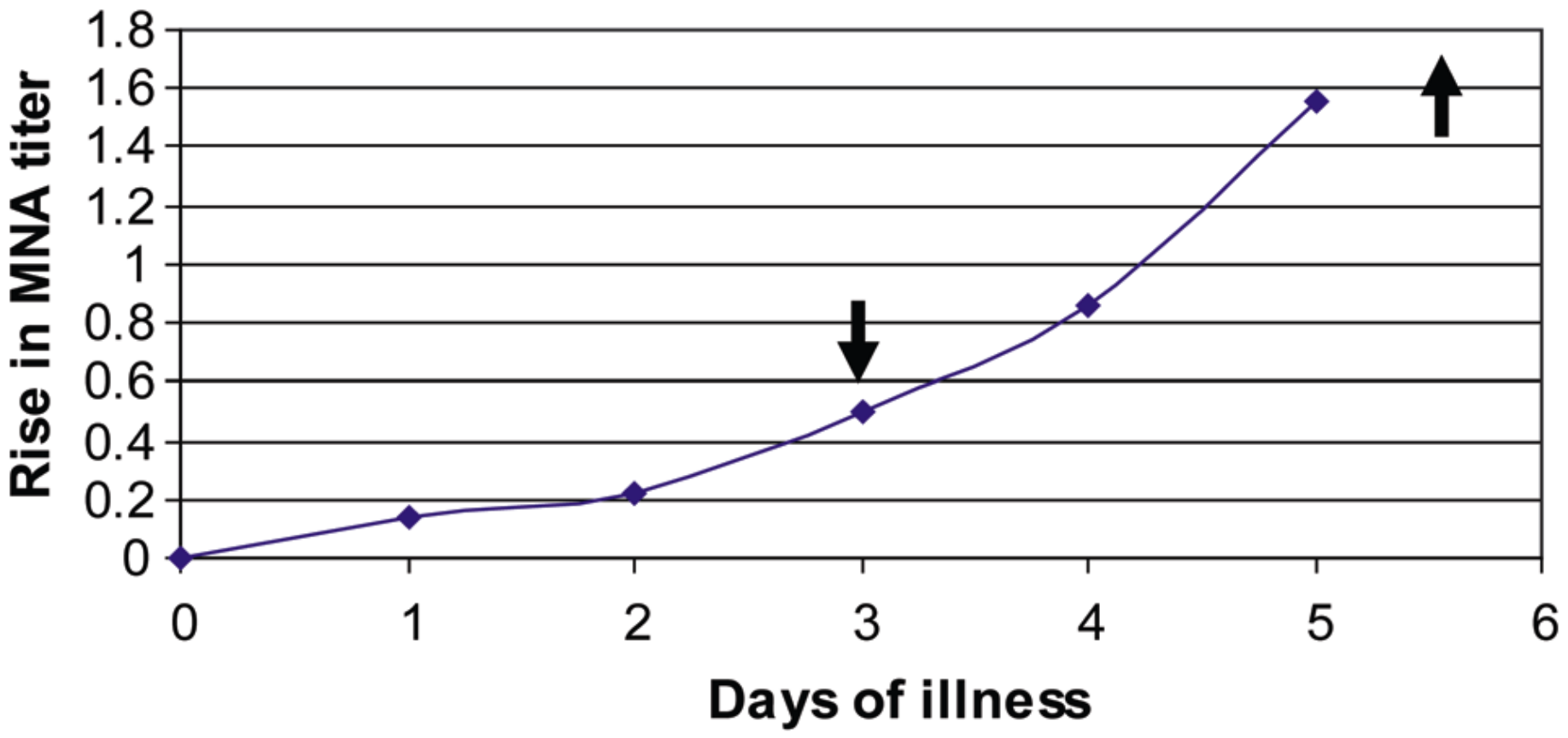
Rapid amnestic antibody rise



Is sample important of location?

Improved Diagnostic Yield of Sputum

	Total	Both Spt NPS	NPS only	Spt only
Flu A	59	36%	30%	34%
RSV	63	46%	32%	22%
HMPV	48	52%	17%	31%

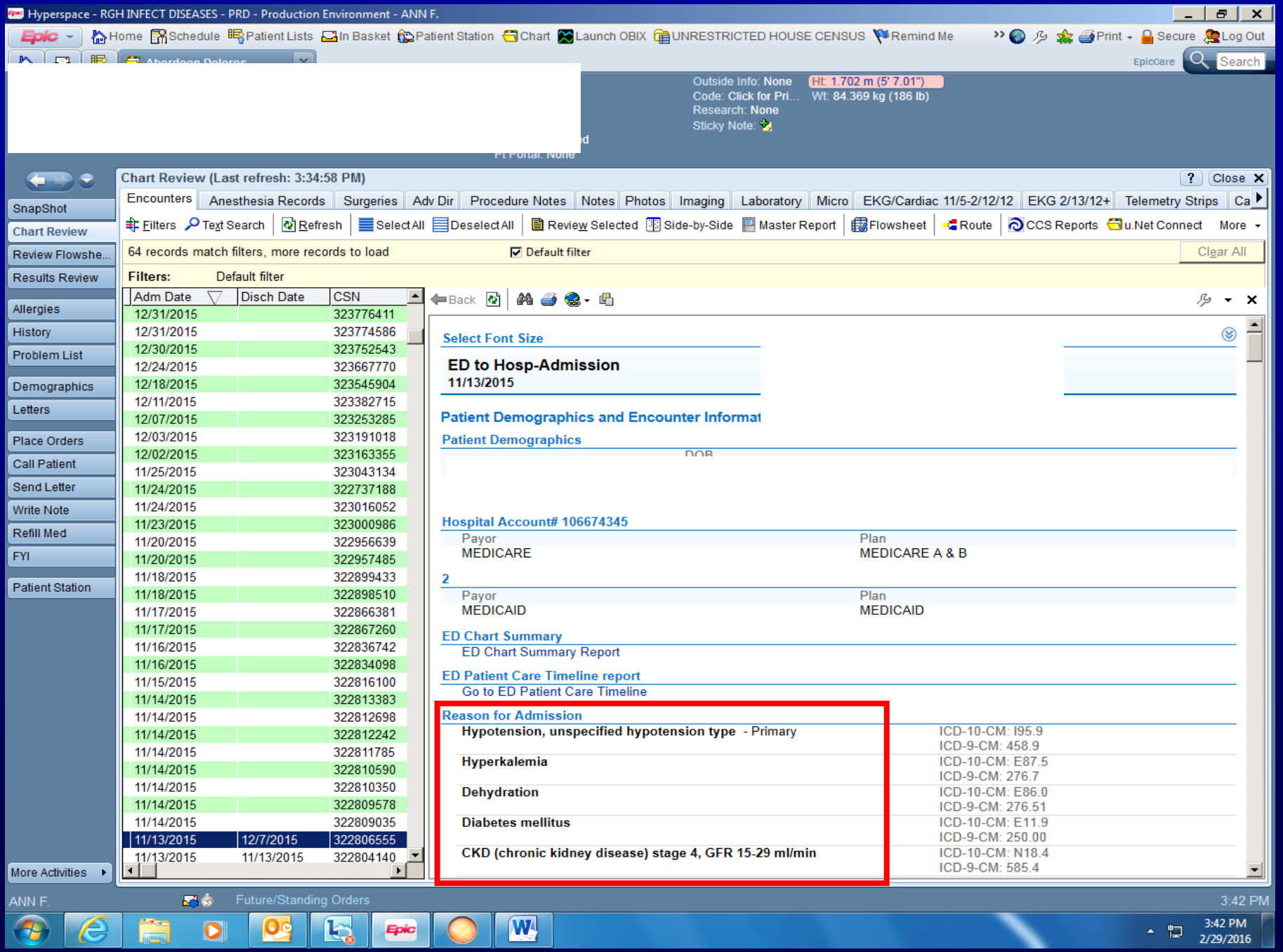
Branche et al JMC 2014

Sensitivity of RT-PCR vs. Serology

- Timing of samples for PCR and serology
- Early in illness nasal swab for PCR is very sensitive
- Later in illness may be negative, sputum may be of value
- Well timed serology is very sensitive in older adults (pre illness and 4-6 weeks later)
- Rapid amnestic response may obscure antibody rise if “acute” is 5-6 days into illness

Diagnostic Methods in the Elderly

Standard culture	5 - 40%
Antigen detection	0 – 24 %
RT-PCR	75 - 82%
Serology - EIA	85 - 90%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Reason for Admission
Hypotension, unspecified hypotension type - Primary
ICD-10-CM: I95.9
ICD-9-CM: 458.9
Hyperkalemia
ICD-10-CM: E87.5
ICD-9-CM: 276.7
Dehydration
ICD-10-CM: E86.0
ICD-9-CM: 276.51
Diabetes mellitus
ICD-10-CM: E11.9
ICD-9-CM: 250.00
CKD (chronic kidney disease) stage 4, GFR 15-29 ml/min
ICD-10-CM: N18.4
ICD-9-CM: 585.4
ANN F.
Future/Standing Orders
3:42 PM
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2/29/2016

Epidemiology and Impact of RSV in Elderly Adults

- 4 winter seasons 1999-2003
- Prospective surveillance of healthy elderly, adults with cardiopulmonary disease
- Adults hospitalized with acute cardiopulmonary conditions
- Diagnosis of influenza and RSV by culture, one tube nested RT-PCR, serology.

Falsey et al NEJM 2005;352:1749

1999-2003

Group	Enrolled	Illnesses
Healthy Old	622	535
High Risk	528	502
Hospitalized	1481	1569

Incidence in Older Adults

	99-00	00-01	01-02	02-03
	N=420	N=553	N=375	N=467
Flu A	2.4	0.2	4.3	1.5
RSV	7.6	6.9	3.2	4.1

RSV 5.5 per 100 / season (3.2 - 7.6)

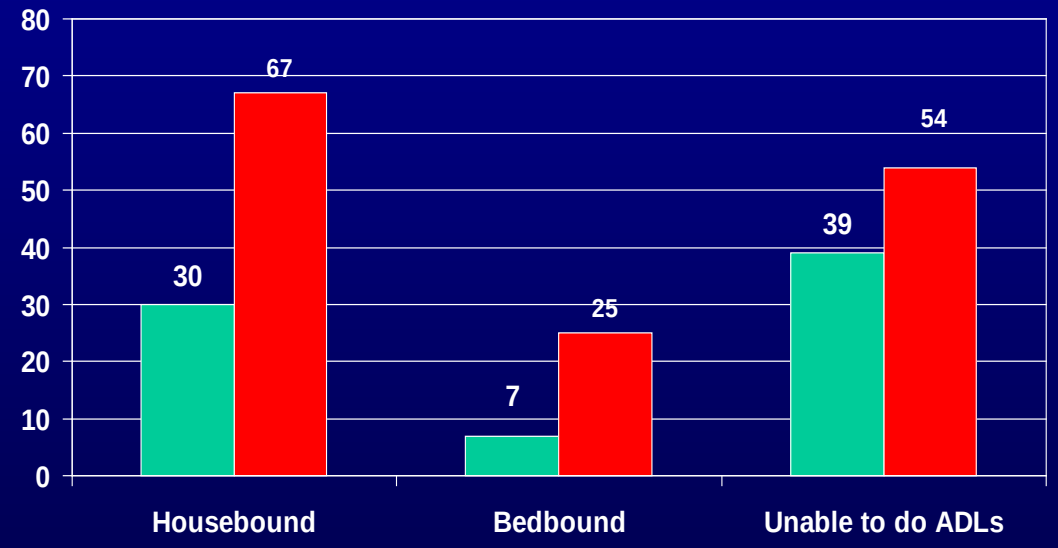
Flu A 2.1 per 100 / season (0.2 - 4.3)

10% infection were asymptomatic

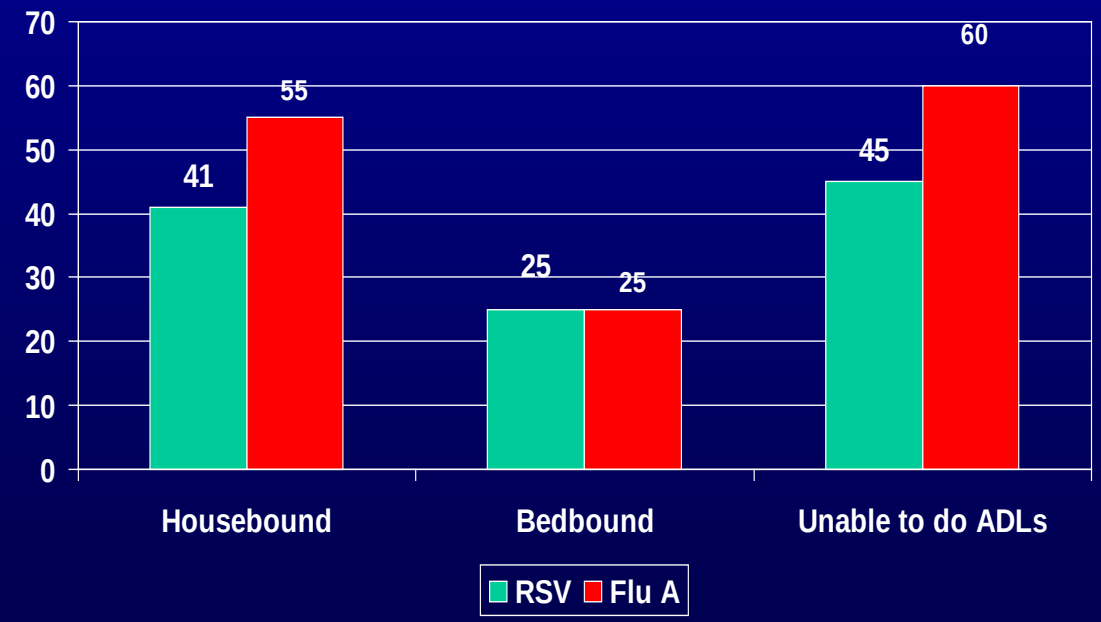
Falsey et al NEJM 2005;352:1749

Functional Impact RSV

Healthy



High Risk



Impact of RSV in Community Elderly

	RSV	
%	Healthy N=48	High-risk N=54
Office visit	17	29
ER	0	9
Hospitalized	0	16
Death	0	5

Incidence of MARI:

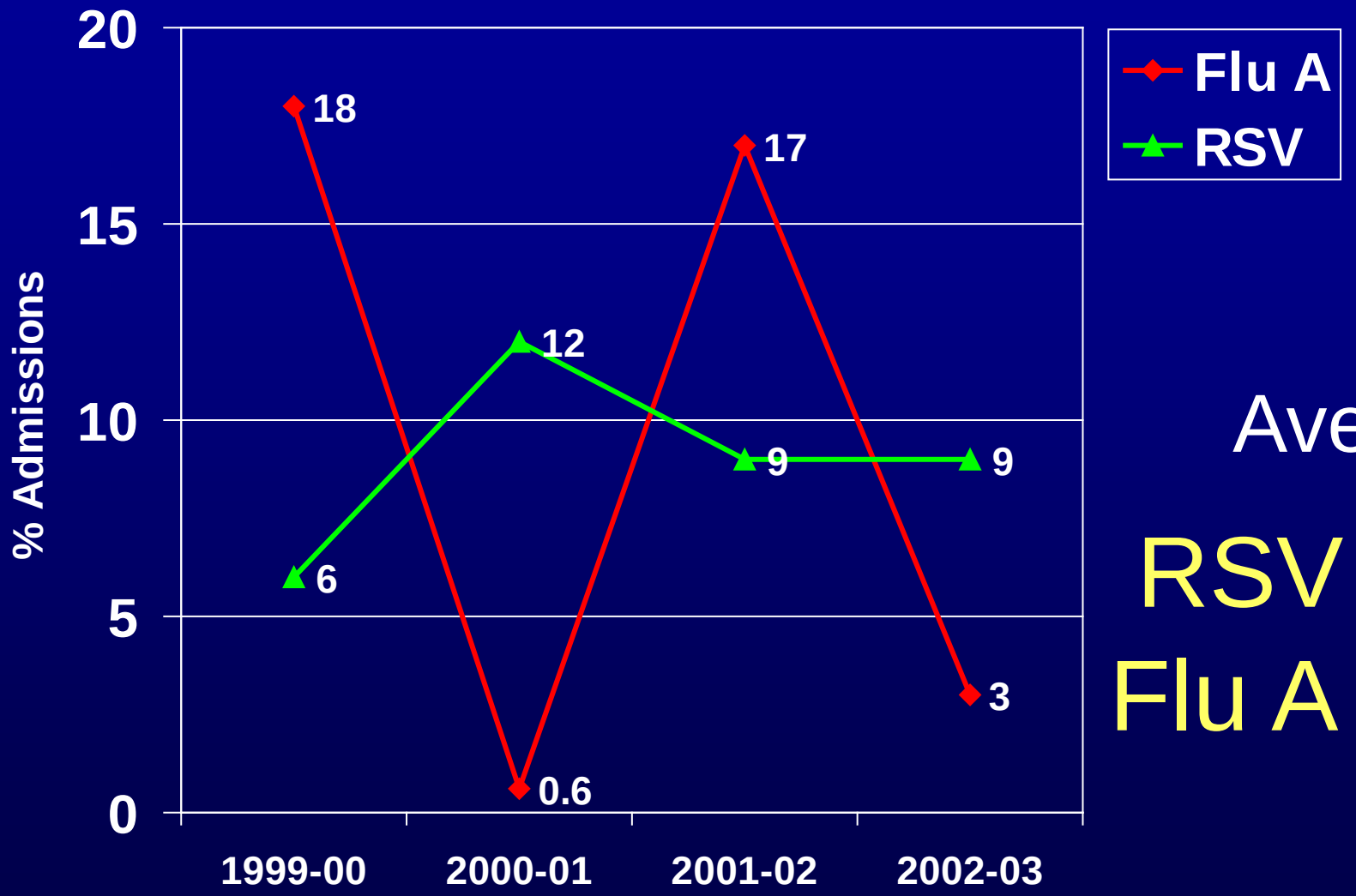
Healthy 0.50 - 1.20/100

High Risk 1.8 - 4.4/100

Hospitalization ~1/1000

Falsey et al NEJM 2005;352:1749

Percent Admissions due to RSV and Flu A



Average

RSV - 9.0 %

Flu A - 9.5 %

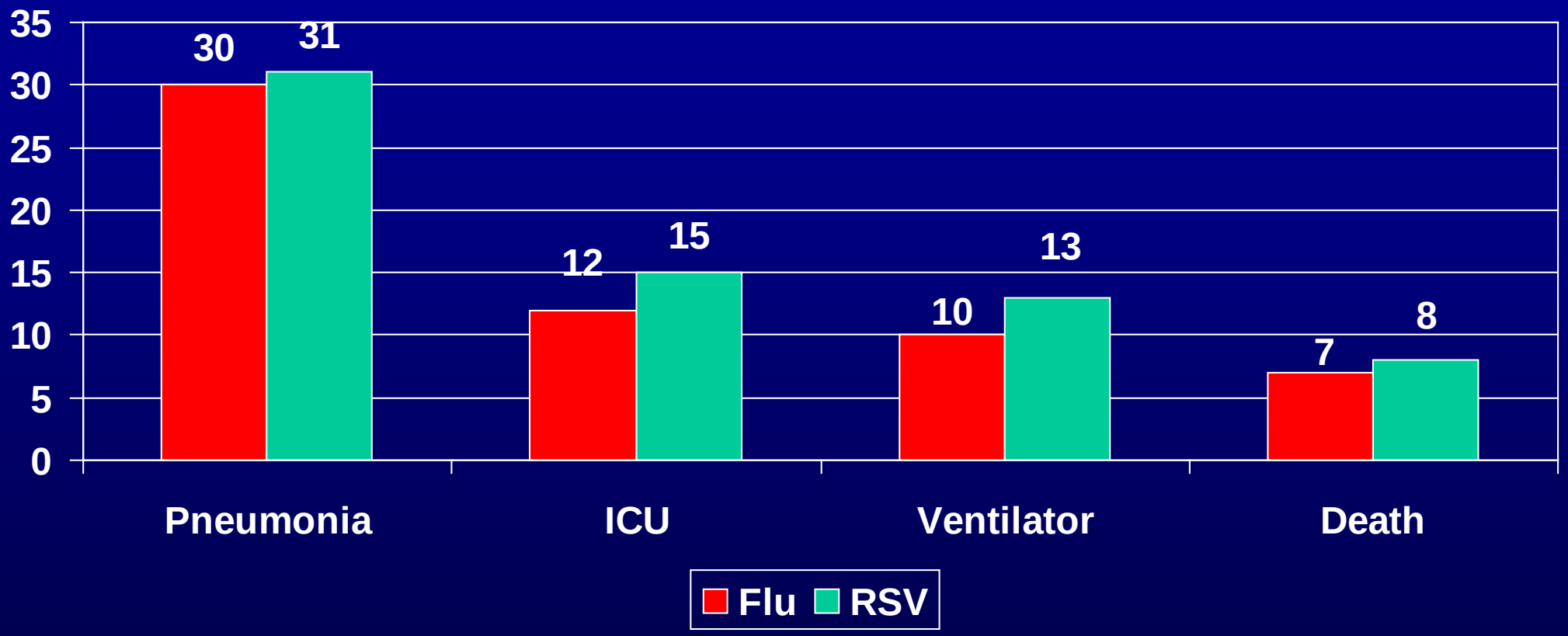
Characteristics of Hospitalized RSV and Flu A Patients

	RSV N=132	Flu A N=144
Age	76 ± 13	76 ± 12
IADL score (1-12)	4.1 ± 4.1	3.3 ± 4.0
Heart or lung disease	80	78
Diabetes	26	22
Smokers	67	68
Steroids	15	9
Home Oxygen	21	16

Symptoms of RSV and Flu A in hospitalized patients are nearly indistinguishable except fever is more common with influenza

	RSV	Flu A
Nasal	+++	+
Dyspnea	+++	++
Wheezing	++++	++
Fever	+	+++

Outcome of Hospitalized Subjects



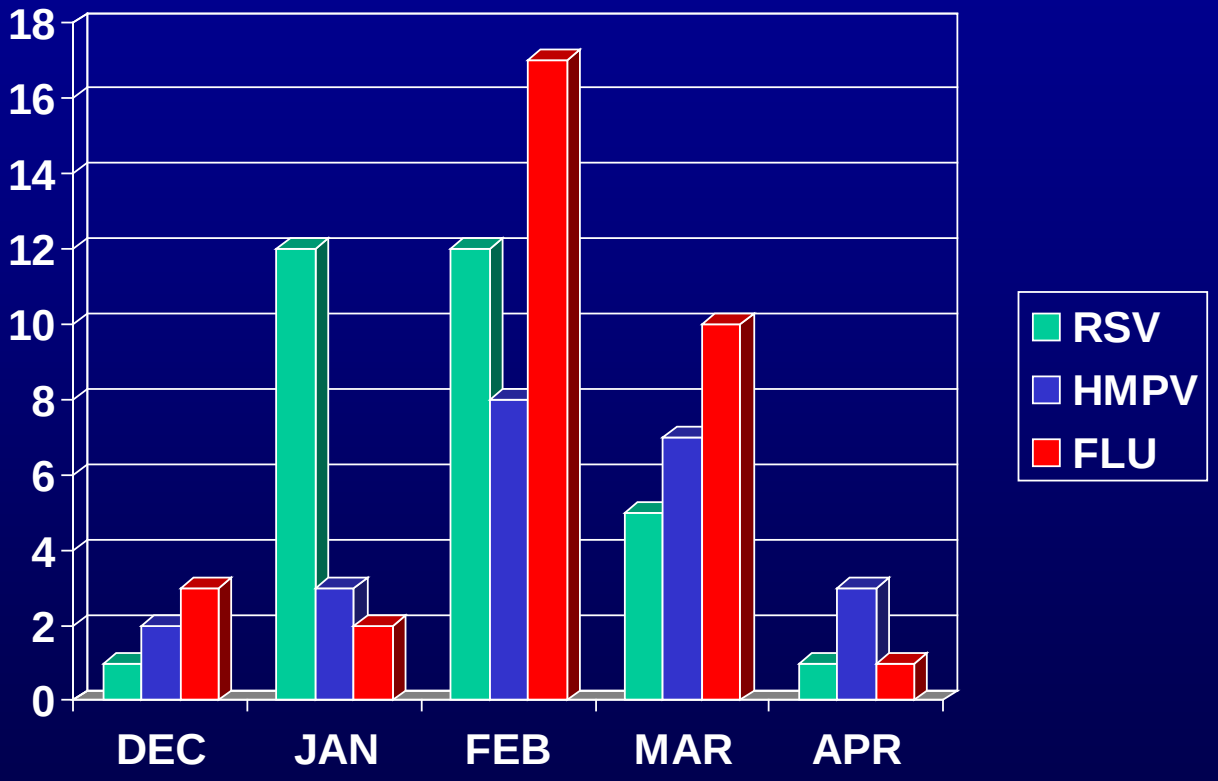
Projection of Elderly & High-Risk infections & hospitalizations in U.S.

Source	Method	Hospitalized	Deaths
Falsey (Rochester, NY) NEJM 352:1749, 2005	RSV+ illnesses	177,525	14,000
Thompson (CDC-U.S. data) JAMA 289:179, 2003	Attributable Excess Events	Not calculated	11,000

RSV, HMPV, Flu Hospitalizations

Widmer et al JID 2012

6.1% due to RSV

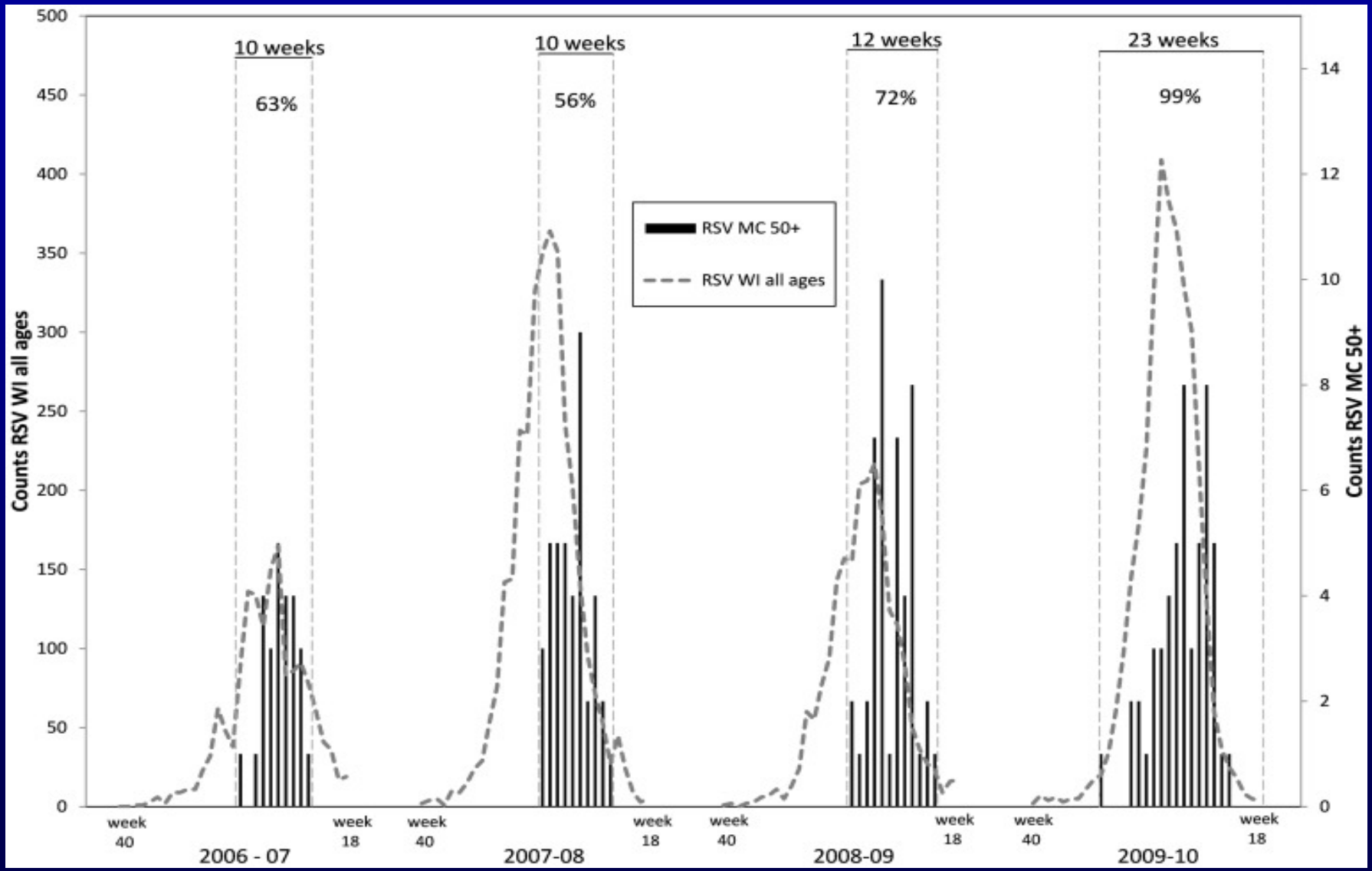


Rate /10,000

	RSV	Flu
50-64	1.8	11.5
>65	25.4	12.3
Overall	15.0	11.8

(1.5/1000~ similar to Rochester data)

Seasonal Incidence of RSV Related MARI in Adults > 50 yo



1.54/100 persons

Rochester

Healthy
0.50 - 1.20/100

High Risk
1.8 - 4.4/100

McClure et al Plos One July 2014 ;9:e102586

Rochester Prospective Cohort Studies

Year	Population		RSV	Flu A
89-90	LTCF		6.8	0.3
92-93	Senior Daycare	1	6.0	10.9
		2	6.0	7.2
93-94	Healthy Old		4.7	NA
96-98	High Risk Adults	1	7.4	5.9
		2	2.5	7.6
99-03	Elderly	1	7.6	2.4
		2	6.9	0.2
		3	3.2	4.3
		4	4.1	1.5
03-04	COPD		10.7	NA
04-05	All Adults		3.8	NA

Rochester Illness Based Data

Year	Population	RSV	Flu A
		% Illness	% Illness
89-92	Hospital upstate NY	10	11
95-96	Hospital Canada	13	NA
99-03	Hospital Rochester 1	6	18
	2	12	0.6
	3	9	17
	4	9	3
03-04	ED – COPD Boston, Minn	8	3
08-12	Hospital Rochester 1	7	9
	2	9	8
	3	4	14

Viral Specific Studies From Other Centers

Author	DX	Population	RSV	Flu A
Nicholson ‘99	S,C	Elderly Outpatient	3%	4%
Zambon ‘01	PCR	Elderly Outpatient	15%	28%
Rohde ‘03	PCR	AE-COPD	25%	22%
De Roux ‘04	S	CAP	1.4%	8%
Van de Hoogen	S,C	Elderly Hospital	0	
Carret ’06	PCR	ICU	5%	7%
Ong ‘14	PCR	ICU	4%	15%

More Recent Studies with Multiplex PCR

Author	Years	Population	Country	RSV
Ren	05-07	5808 Adults	China	<1%
Puzellis	04-07	580 adults ILI	Italy	1.7%
Boivin	07-08	108 COPD	Canada	7%
Bellei	01-03	420 adults ILI	Brazil	2.5%
Jennings	99-00	225 Hosp CAP	N Zealand	3.6%
Nolte	05-06	354 Adults ARI	US	3.7%
Marcus	1 winter	198 Adults ARI	Spain	2.5%
Creer	1 year	80 adults GP	UK	2.5%
Dia	09-11	Adults >50yo	Senegal	3%

Season vs. year round, method of diagnosis, illness definition

RSV Infection in Adults in China

3 years – Adults diagnosed during routine care (IFA)

	RSV N=607	Flu A N=547	P- value
Age	75 ± 16	75 ± 17	NS
Nursing Home Resident	33%	30%	NS
Chronic lung disease	36%	42%	<.001
Other medical condition	74%	66%	.003
Days of symptoms	2.6± 2.2	2.0 ± 1.7	<.001
Pneumonia	42%	37%	.006
Respiratory Failure	11%	6%	.003
30 day mortality	9%	8%	NS

Nelson Lee et al CID 2013;57 1069

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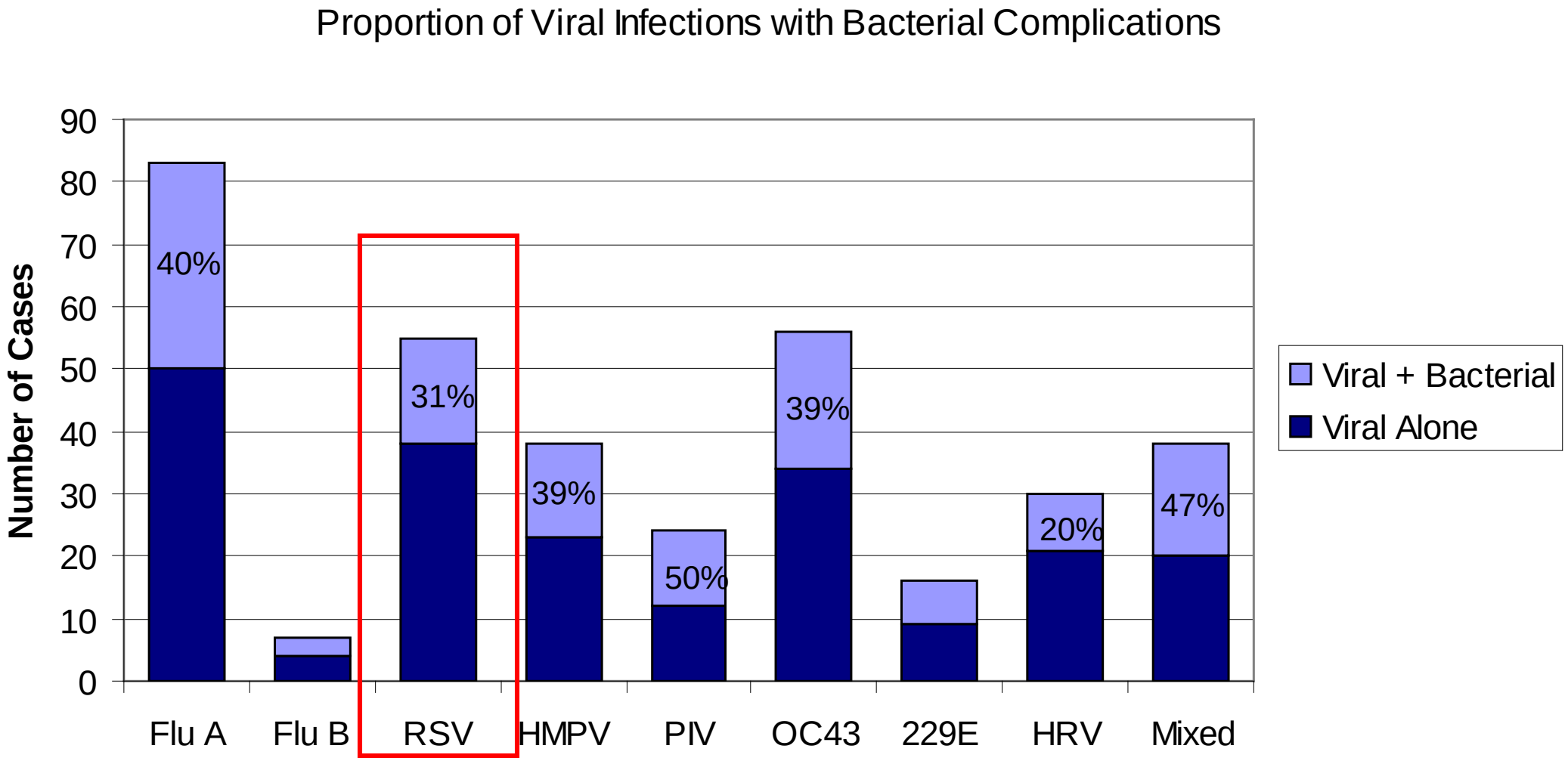
Complications



Using comprehensive bacterial testing + High Procalcitonin

Falsey et al JID 2013

RSV Hospitalization in Toronto, 2012-2013

Table 2 Complications and outcomes of 86 patients hospitalized with RSV infection, 2012/13 winter season

Complication/outcome	Number (%)
Lower respiratory tract complications[1]	45 (52%)
Cardiovascular complications[2]	19 (22%)
Pneumonia[3]	34 (40%)
Confirmed radiologically	26 (30%)
Unifocal infiltrate	18 (21%)
Multifocal infiltrates	8 (9%)
Lobar consolidation	11 (13%)
Co-pathogen identified[4]	11 (13%)
Viral[5]	2 (2%)
Bacterial[6]	9 (11%)
Need for intensive care	13 (15%)
Need for invasive mechanical ventilation	8 (9%)
In hospital mortality	5 (6%)
Median time to death (range)	6 days (2–52 days)
Median hospital length of stay (range)	6 days (1–140 days)

Volling BMC 2104

Summary Rates

Infection	2 - 6 per 100
MARI	0.5 - 4 per 100
Hospitalization	1 - 1.5 per 1,000
Death	0.4 - 7 per 10,000
Secondary Complications	????

Thank you
Questions