

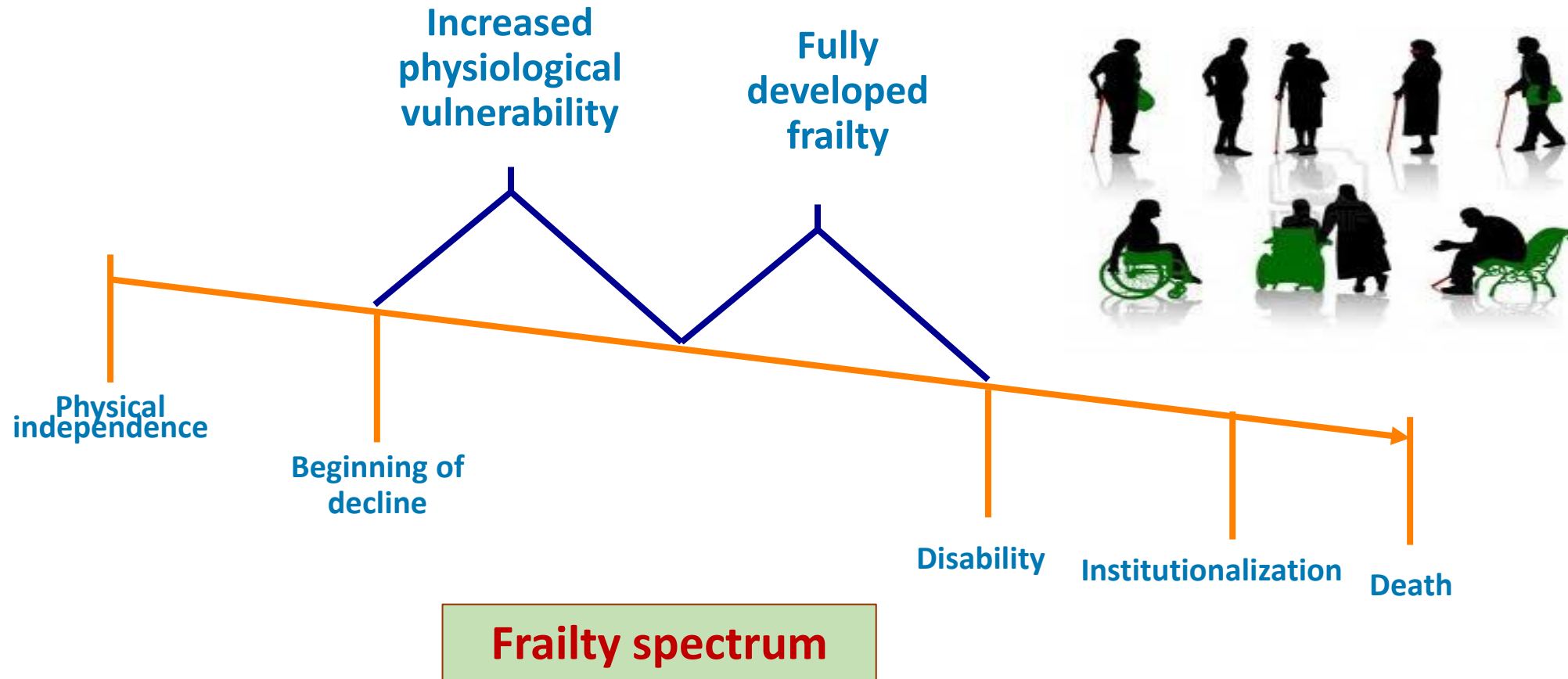
RSV/Influenza example

Stefania Maggi

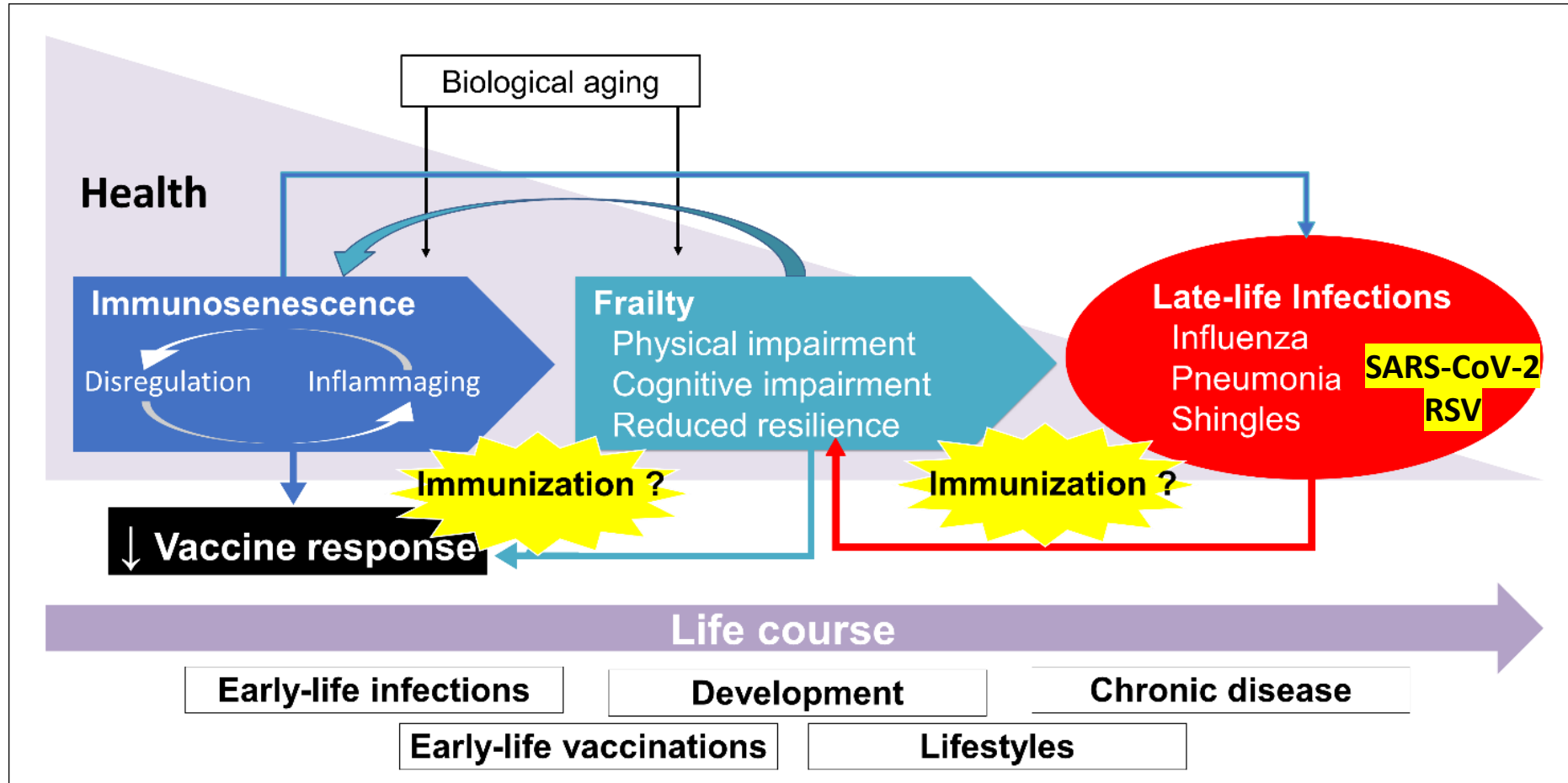
CNR Aging Branch-NI

Padova

The heterogeneity of older individuals



Unifying framework about the relationship between immunosenescence, frailty and late-life infections



Clinical signs and symptoms: risk of underestimated rates of ILI



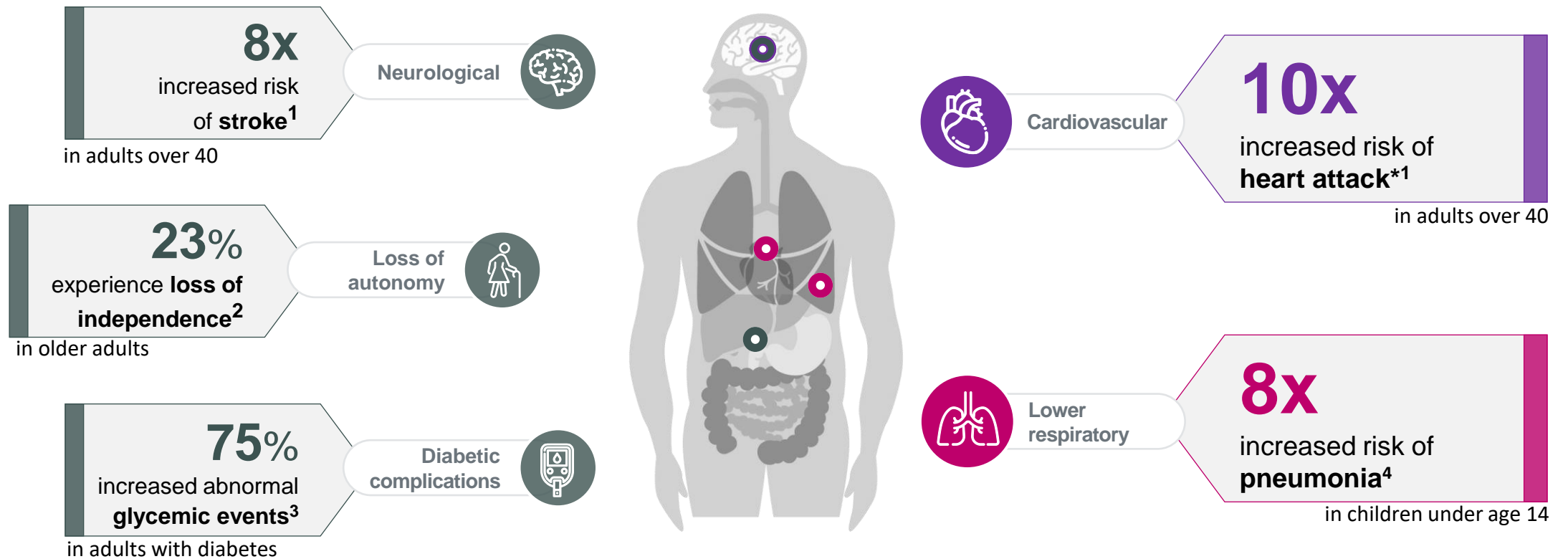
Older frail patients often have atypical presentations:

- Blunted or no fever
- Unexplained hypoxia
- Tachycardia, tachypnea
- Delirium
- Fatigue, functional decline or falls

Is there any difference
between the burden of RSV vs
influenza?

Influenza is associated with severe outcomes, not only limited to the respiratory system

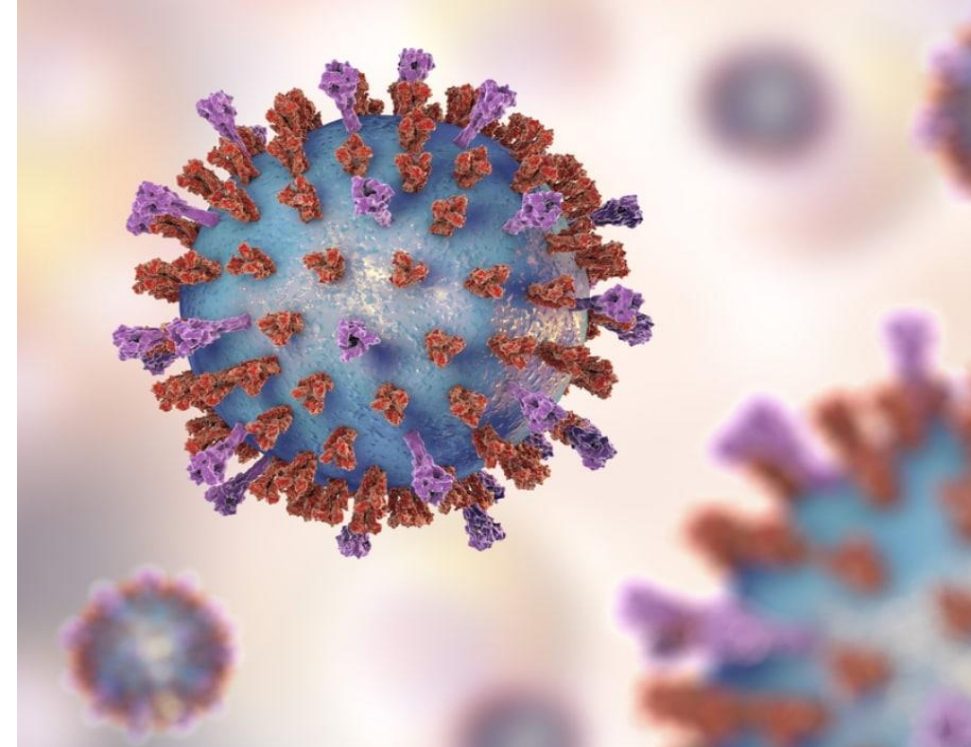
A heavy, multidimensional impact



1. Warren-Gash C, et al. Eur respir J. 2018
2. Andrew MK, et al. J Am Geriatr Soc. 2021.
3. Samson SI, et al. J Diabetes Sci Technol. 2019
4. Kubale J et al., Clin Inf Dis. 2021

RSV in adults – general remarks

- Paucity of data available for adult RSV disease compared to infants. There has not been as much research into this area
- Individuals are susceptible to re-infection with RSV throughout life
- There are no recommended specific treatments for RSV associated illness in older adults, and no vaccine currently



RSV is associated with severe outcomes, not only limited to the respiratory system

- ✓ Responsible for a significant burden of disease among adults:
 - Majority of RSV mortality in industrialized countries is in those >65 years old
- ✓ Often milder in the elderly vs primary childhood infections but can still cause severe respiratory disease
- ✓ Severe respiratory disease occurs in those with:
 - Increased frailty and immunosenescence
 - Underlying comorbidities (chronic cardiac or pulmonary disease, diabetes, severe immunosuppression)
 - Significant increase in healthcare utilization following hospitalization

Disease burden estimates of RSV in adults with comorbidities:

A systematic review and meta-analysis

	Older Adults	OA with comorbidities
Annual incidence rates/1000	6.7	37.6
Hospitalisation rates/1000	4.8	13.2 (with COPD or HF)
In-hospital case fatality rate/100	1.6	11.7

Four-fold increase of experiencing RSV-ARI among patients with any comorbidity compared to those without, **RSV affects the most vulnerable**

- Adults age 65 and older, primarily institutionalised
- People of any age with underlying medical conditions, including: chronic lung disease or moderate to severe asthma, previous pneumonia, serious heart conditions, compromised immune function

The burden of RSV in the community is similar to influenza, as shown by recent RESCEU data¹

An international, prospective, observational cohort study identified the incidence of RSV illness through RT-PCR and serology in 1,040 community-dwelling adults aged ≥ 60 years (median 75) during two RSV seasons (2017–2018 and 2018–2019) in the United Kingdom, Belgium and Netherlands:

RSV was identified in 59 (**5.7%**) participants (season 1: 4.2%; season 2: 7.2%)

Illness duration was **19 days** (equal to influenza)

31% of RSV cases were **medically attended** illnesses

RSV-ARTI could not be clinically differentiated from all other ARTI based on symptoms

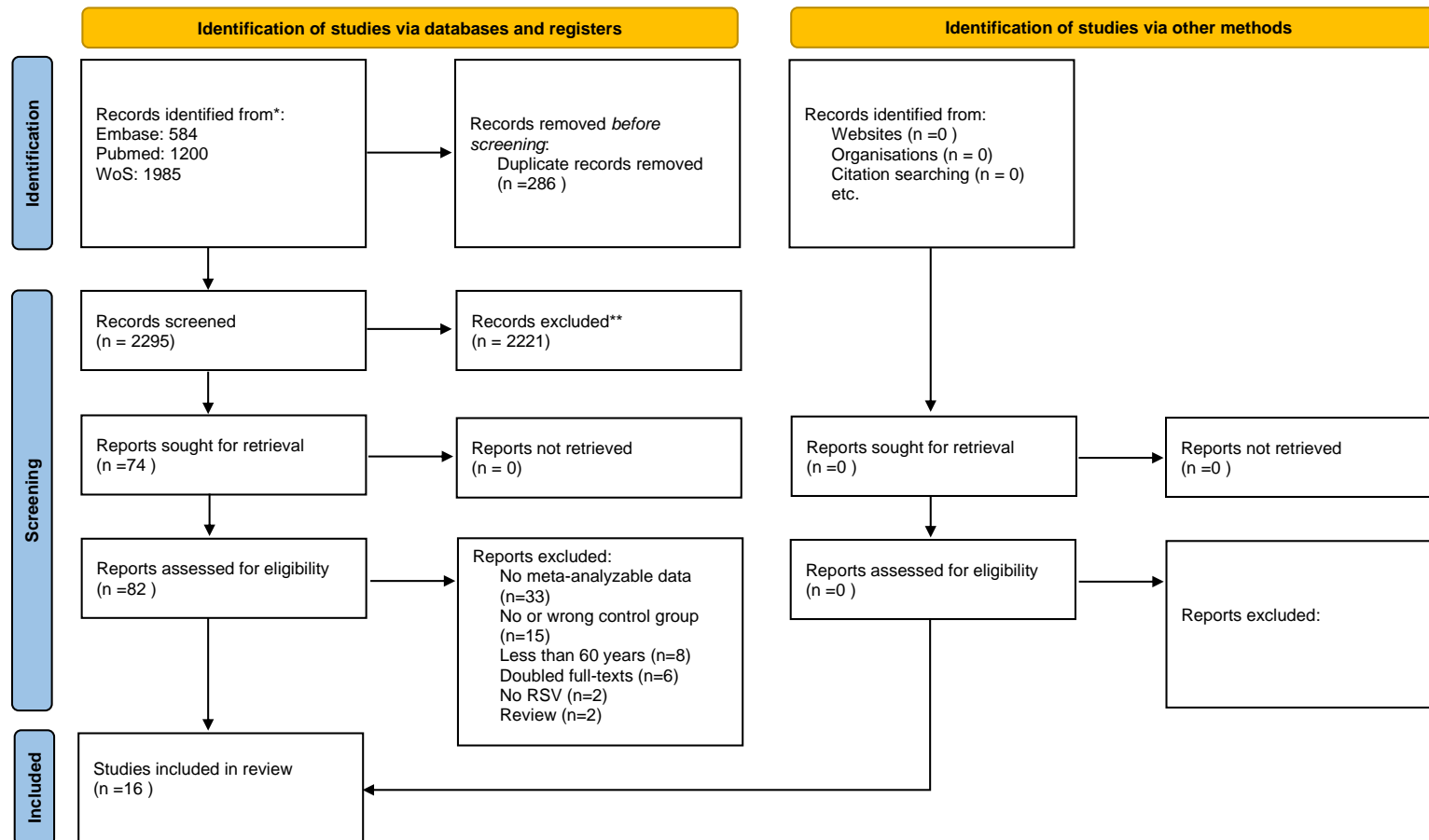
	2017–2018 N=527		2018–2019 N=513	
	Cases	% (95% CI)	Cases	% (95% CI)
RSV-illness*	22	4.2% (2.6–6.3)	37	7.2% (5.5–10.2)
PCR positive [†]	11	2.1% (1.0–3.7)	25	4.9% (3.2–7.1)
Seroconversion [‡]	15	2.8% (1.6–4.7)	24	4.7% (3.0–6.9)

These results were similar to Rochester, NY data in healthy older adults²

ARTI = acute respiratory tract infection; RSV = respiratory syncytial virus; RT-PCR = reverse transcription-polymerase chain reaction.

1. Korsten K et al. Eur Respir J. 2021;57(4):2002688. 2. Falsey AR et al. N Engl J Med. 2005;352(17):1749-1759.

Rates of hospitalizations and Mortality in RSV Infection compared to Influenza in older people: A systematic review and meta-analysis



Prisma Flow-chart

Descriptive characteristics of studies included

Author, year	Type of study	Sample size	Mean age	Diagnosis of RSV and influenza	Follow-up (months)	NOS
Ackerson, 2019	Retrospective	2523	78	PCR and culture	12	8
Auvinen, 2021	Prospective	974	76	PCR	48	8
Ellis, 2003	Retrospective	10581	65+	Antigen tests and cultures	48	7
Falsey, 2005	Prospective	146	72	RT-PCR, Serologic test, viral culture	48	8
Falsey, 2021	Prospective	604	65.6	PCR	3	8
Gilca, 2014	Prospective	210		Luminex RVP FAST assay	48	7
Gonçalo Matias, 2017	Retrospective	64456	65+	Weekly influenza update	144	7
Korsten, 2020	Prospective	1040	75	PCR	48	8
Loubet, 2016	Prospective	1452	74	PCR	12	8
Malosh, 2017	Prospective	426		PCR	24	8
Muller-Pebody, 2006	Prospective	551633	65+	ICD-10	36	7
Rabarison, 2019	Retrospective	375		PCR	60	8
Schanzer., 2008	Retrospective	103262		Hospitalization Morbidity Database (HMDB)14	60	7
Sharp, 2021	Retrospective	21787	65-74	Antigen detection, culture, and genomic/pcr/lcr detection	84	8
Tseng, 2017	Prospective	2586	60+	PCR	48	8
Widemer 2012	Prospective	29	65+	PCR	36	8
Total	9 studies: prospective; 7 studies: retrospective	762,084	73.4	9 studies: PCR; 7 studies: others	48 (range: 3-84)	

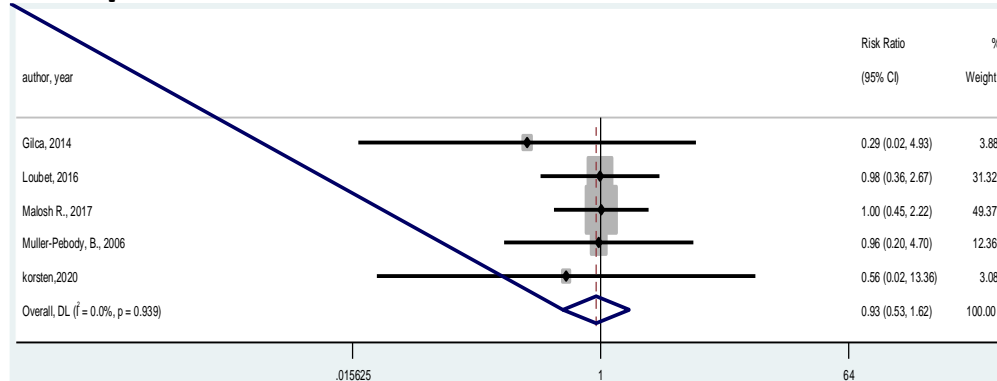
Meta-analysis of hospitalization and mortality rates comparing RSV and influenza



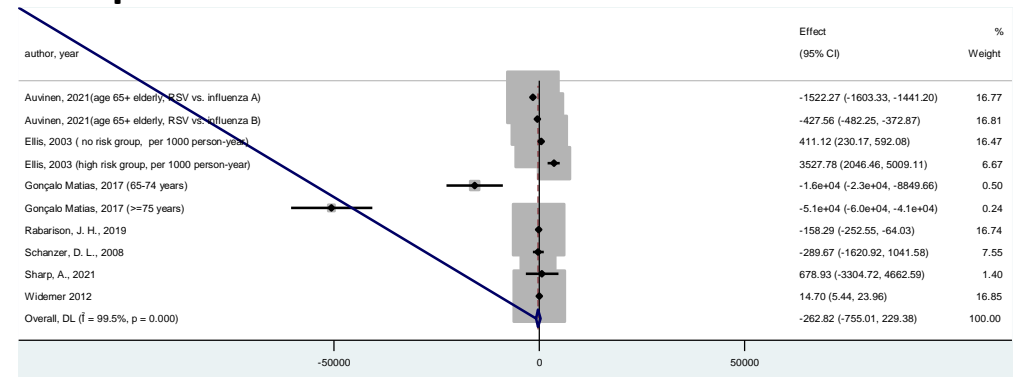
Outcome	Cumulative incidence						Incidence rate (per 100,000 persons-year)					
	N of studies (participants)	RR	95%CI	p-value	I ²	Egger's test (p-value)	N of studies	MD	95%CI	p-value	I ²	Egger's test (p-value)
Hospitalization	5	0.93	0.53-1.62	0.80	0	-0.73 (p=0.08)	10	-262	-755; 229	0.30	99	-6.57 (p=0.20)
Mortality	4	1.19	0.98-1.45	0.08	0	0.57 (p=0.10)	2	15	-133; 162	0.85	0	Not possible

Comparison of cumulative incidence and incidence rates

Hospitalization cumulative incidence between RSV and influenza

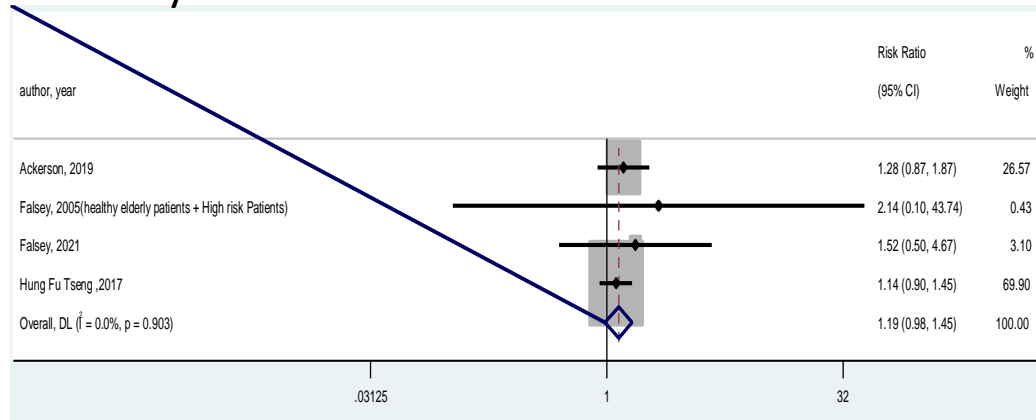


Hospitalization incidence rate (per 100,000 persons-year) Comparison between RSV and influenza

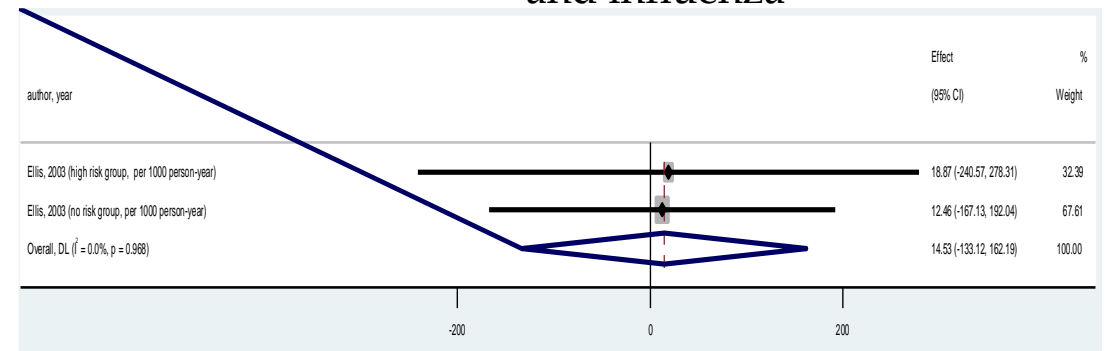


Comparison of cumulative mortality and mortality rates

Mortality cumulative incidence between RSV and influenza



Mortality incidence rate (per100,000 persons-year) comparison between RSV and influenza



RSV as a cause of hospital admissions

Hospitalisation rates for RSV are similar to those for Influenza¹

RSV+ patients hospitalized, have higher odds of comorbidity and of experiencing and extended LOS>8 days and a need for mechanical ventilation compared to influenza+ patients in a recent prospective US study of 10311 ARI cases across 3 seasons²

Current Issues in RSV diagnosis in older adults:

- Clinical diagnosis is not possible due to similarities with other viral diseases
- Lack of incentive to diagnose RSV as no dedicated treatment exists
- Many cases, especially in primary care, currently go undiagnosed
- Relatively high cost of polymerase chain reaction (PCR) analysis
- Research on RSV in older adults is important to get a full understanding of the prevalence, the risk of spread in NHs and other facilities, the risk of poor outcomes and the potential impact of soon available vaccines

Conclusions

RSV and influenza are important pathogens in older adults worldwide

The disease burden is large and increases with an aging population

The highest risk of severe disease is for frail patients, mostly with underlying cardiopulmonary disease