Communication of vaccine benefit beyond the infection prevented

Scientific and policy momentum to support active and healthy ageing ?

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Disclosure of interest

As consultant, speaker, workshop and advisory boards : Pfizer/ BioMérieux/ Sanofi-Pasteur MSD/ Astellas /AstraZeneca/Sanofi / MSD

Invitation for congress : Eisai, Pfizer, Sanofi Pasteur, Novartis, Pfizer, MSD

Preambule : Vaccination as Individual / Collective issues

- Diseases and complications of the diseases
- Vaccine : Efficacy- effectiveness / Adverse drug reaction ratio
- Cost /Effectivness ratio

  Incidence and prevalence of the disease

  Cost (dis+complications) versus cost (Vaccine /ADR)

Individual perception of

Efficacy- effectiveness / Adverse drug reaction ratio

Collective vaccine policies (PH institution)

Individual interest / Collective interest

Cost /Effectivness ratio

Balinska MA 2004, **Salgado CD** 2004

Summary

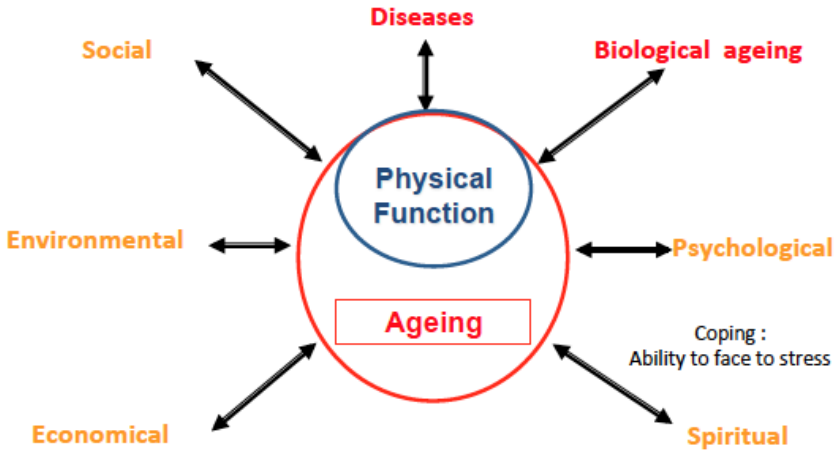
- What is « healthy ageing » / Active ?
- Scientific evidence of ID (VPD) impact on ageing - role of vaccine ?
- Vaccine Policies , Evidences?

Healthy Ageing

General Concept

Result of the individual perception of his own ageing throught the definition of well-being and Health

« *Healthy ageing is the process of optimising opportunities for physical, social and mental health to enable older people to take an active part in society without discrimination and to enjoy an independent and good quality of life.* »



Adapted from Guralnik JM Am J Prev Med 2003

EU definition for EIT/EIP Healthy ageing projects

AGEING,
heterogeneous older population

From healthy

Frailty

to Pathologic
DISABLE

Ageing

The older persons

One trigger = several complications

Numerous unexpected complications

Iatrogenic events,
Health care Associated Infection
Falls
Malnutrition
Immobilisation / pressure sores
Delirium /behavioural disorders
Complications of Chronic Diseases
(known or unknown)

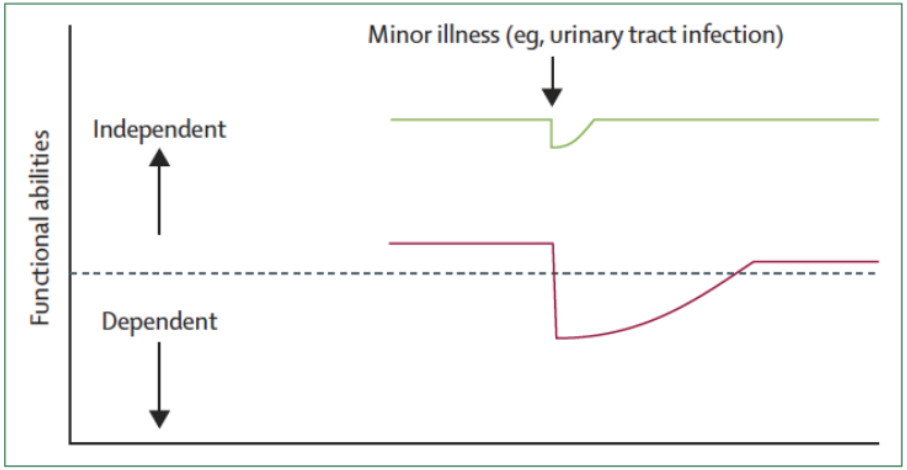


Figure 1: Vulnerability of frail elderly people to a sudden change in health status after a minor illness

Disability

↗↗ in hosptal length of stay and ↗↗↗ cost

THOM 1 Healthy Ageing : biological and medical factors

- Less acute diseases (severe)
- Less Chronic diseases (severe)
- Less disability associated Diseases/Ageing
- Less frailty associated Diseases/Ageing

Summary

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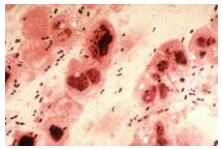


VPD
Pneumococcus
Influenza
Zoster

- Vaccine Policies , evidences?

Overview

VPD : Pneumococcal disease in EU

20,785 confirmed cases of Invasive Pneumococcal Disease were in 27 EU/EEA countries in 2012, **> 50% in 65+.**

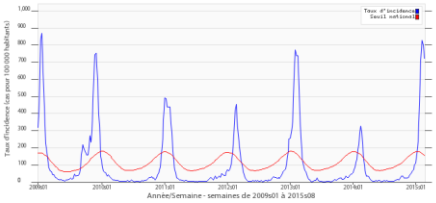
Pneumococcal diseases = 12 – 68% of the cause of community acquired pneumonia (CAP) in 13 European countries

400,000 – 2.3 million out of 3.37 million cases of CAP.

20-50% of CAP cases are hospitalized : 1 M. hospitalizations

- **Mortality rates** ranging **from 6.4 - 40%** in different settings, 26,000 – 920,000 deaths in the 400,000 – 2.3 million cases expected in the population of the EU and **Long term Mortality >1 y**
- **Disability** : (CAP/ HCAP): occurrence and Increasing

Kaplan V et al. Arch Intern Med. 2003;163(3):317-23. • Ewig S et al. Thorax. 2012;67(2):132-8.



Influenza

Saisons épidémiques de grippe	Durée en semaines	Tous âges confondus: Effectif Observé	Excès[2] (Sur 1000 communes)		Excès extrapolé à la France entière[3]	65 ans ou plus: Effectif Observé	Excès[2] (Sur 1000 communes)		Excès extrapolé à la France entière[3]
2006-2007	7	52 077	1 286	+3%	1 919	41 657	1 385	+3%	2 068
2007-2008	9	68 644	3 020	+5%	4 508	55 194	2 966	+6%	4 427
2008-2009	10	83 601	10 166	+14%	15 173	67 988	9 339	+16%	13 939
2009-2010	10	71 346	-286	0%	-427	56 146	-388	-1%	-579
2010-2011	9	71 032	3 829	+6%	5 715	57 203	3 162	+6%	4 719
2011-2012	8	66 388	6 995	+12%	10 440	54 959	6 788	+14%	10 132
2012-2013	13	107 777	10 206	+10%	15 234	88 607	8 950	+11%	13 359
2013-2014	5	38 491	700	+2%	1 045	31 593	428	+1%	638
2014-2015	**9**	**80 514**	**12 272**	**+18%**	**18 317**	**67 875**	**11 127**	**+20%**	**16 608**

2016/17 Influenza season

France : **+ 24 000 additional Deaths**

Direct and Indirect

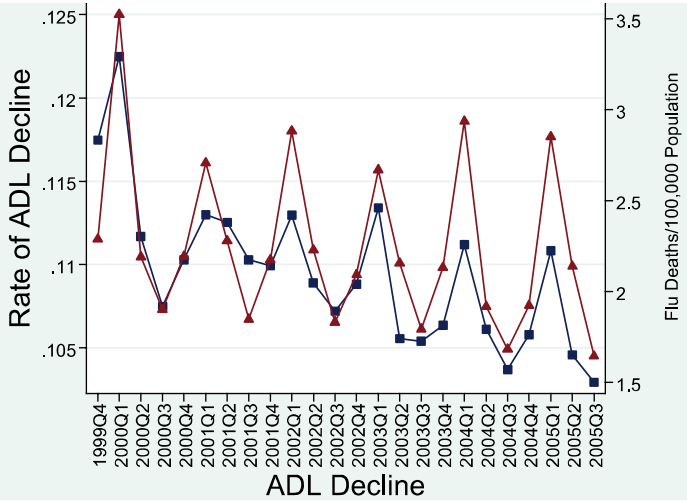
Europe : **> 90 000 additional Deaths 90% > 65 y**

http://www.invs.sante.fr/Actualites/Publications

Table 4. Case and Comparison Subjects Experiencing Worsening in ≥1 Functions From Before Outbreak (Baseline) and 3 to 4 Months After Outbreak*

No. of Worsening Functions	Case Subjects (n = 116)		Comparison Subjects (n = 127)	
0	87		107	
1	16	29 (25.0%)	15	20 (15.7%)
2	7		4	
3	2		0	
≥4	4		1	

William H. Barker Arch Intern Med 1998

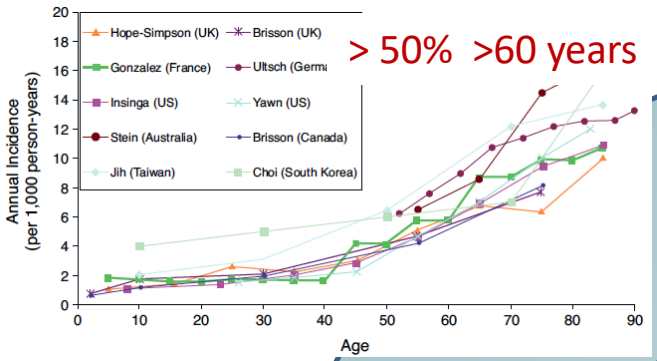


Gozalo PL JAGS 2013

Flu Increasing Disability (impact on ADL)

Zoster : does it Harm ?

Greater pain burden, associated with poorer physical functioning, increased emotional distress, and decreased role and social functioning



> 50% >60 years

Physical impact
Chronic fatigue
Anorexia
Weight loss,
Physical inactivity
Insomnia

1 out of 4/5 individual will experiment Zoster over his life

Psychological impact
Depression
Anxiety
Difficulty concentrating

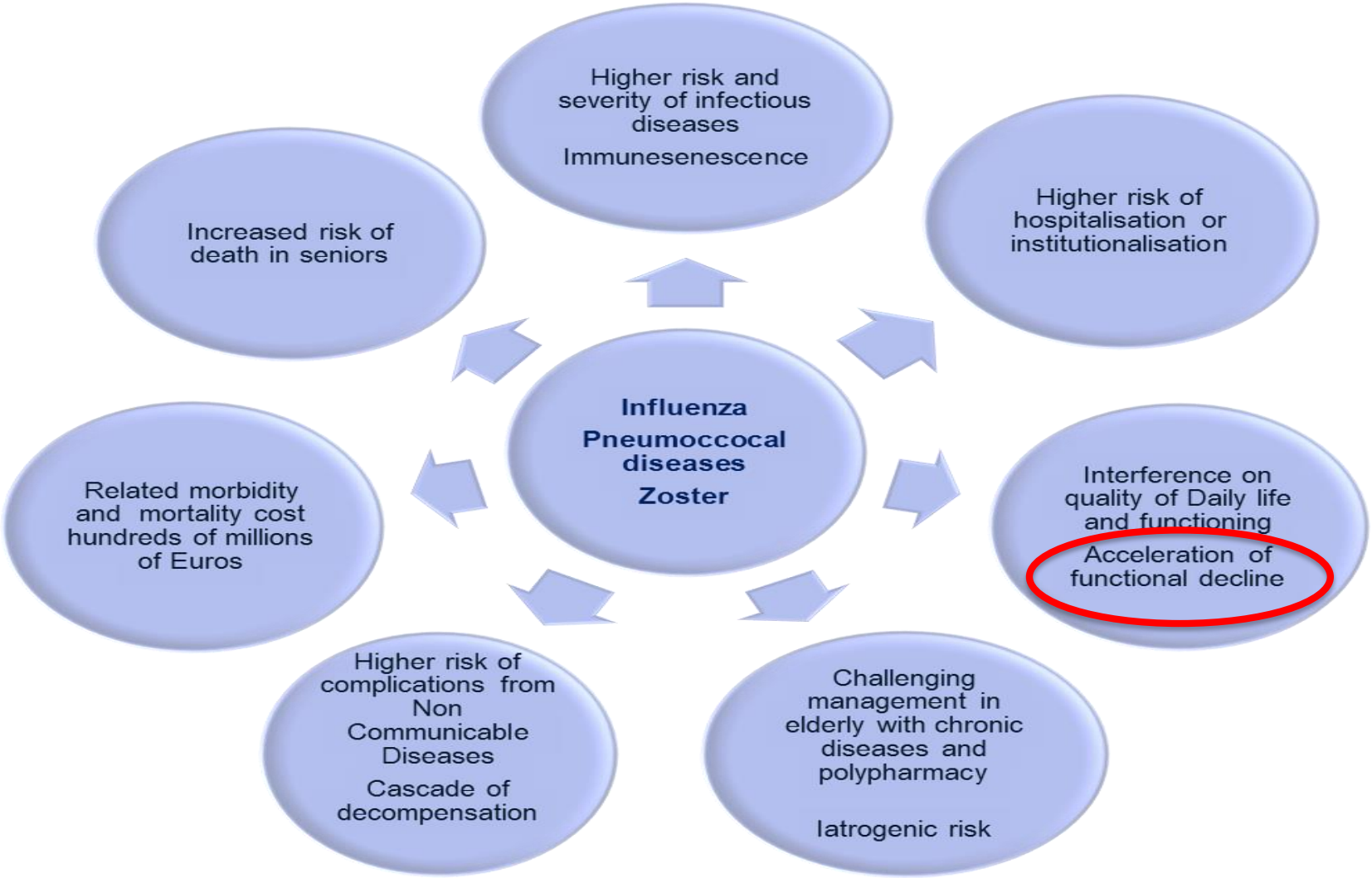
HZ-related pain
The magnitude of suffering is directly related to pain intensity & duration

Functional impact
Interfere with basic and instrumental activities of daily living:
- Dressing, bathing, eating, mobility,
- Ttravelling, cooking, housework, shopping

Social impact
Decreased social gatherings
Change in social role

Schmader CID (2001).

Take home message 2



+ Relationship between VPD and Frailty syndrom

Influenza European vaccination Guidance (ESCMID/EUGMS/WAIDID)

Meta analysis (ss) : Efficiency of inactivated influenza vaccine

Despite low Immunological Efficacy <50 %

- Letal and non letal Complications, - 30 %
- Reduced ILI onset - 40 %
- Virologically Confirmed flu - 50 %

Beyer WE, Vaccine 2013

Respiratory causes (pneumonia, COPD exacerbation)

Cardiovascular causes (strokes and Myocardal Infarction)

The Risk Benefit ratio is largely high to promote flu vaccination in older populations

Largely use in all EU member states

But Prevention of disability ???

Esposito S et al Human Vac Immun 2016

PPV23 and PCV 13 in adults

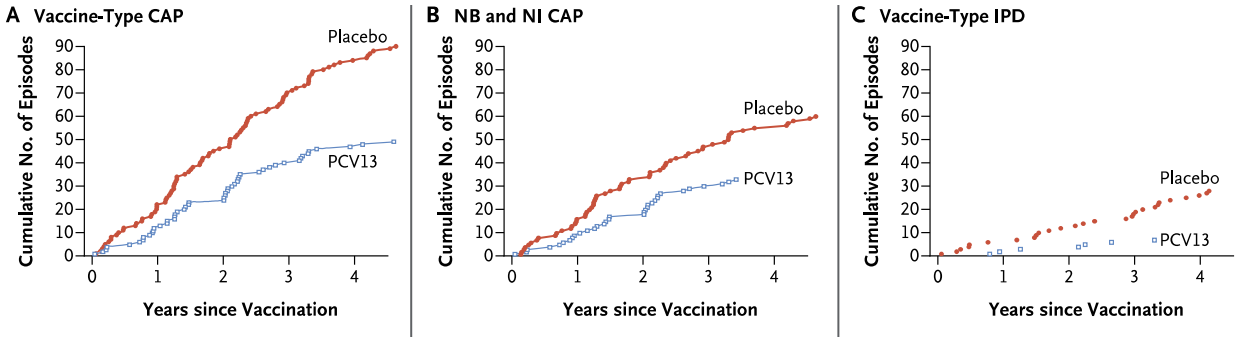
PPV23

- Included **18 RCTs** (n=64,852) and **7 non-RCTs** (for IPD only; n=62,294)
- **Meta-analysis**:
  - Prevention of IPD: OR **0.26** [0.14; 0.45
  - **Prevention of all cause pneumonia**
    - in low income countries, general population: OR **0.54** [0.43; 0.67]*
    - In high income countries, general population: OR **0.71** [0.45; 1.12]
    - High income countries, chronic illness: OR **0.93** [0.73; 1.19

*African goldminers (Austrian,1976; Smit 1977); AR 90 / 1,000 person years; PPV6, PPV12, PPV13; Community dwelling adults in highlands of Papua New Guinea (1977); PPV14

Moberly et al. Cochrane analysis 2013

PCV 13



45.00% (95.2% CI14.21%-65.31%;1st non bacteremic and non invasive CAP

75.00% (95% CI 41.43%-90.78%;) for preventing VT invasive pneumococcal disease.

Durability of vaccine efficacy through 4 years Very few side effects

But

Prevention of disability ???

Bonten MJM et al N Engl J Med 2015

Age-related efficacy response to 1st live-attenuated VZV vaccine

Efficacy of zoster vaccine. HZ indicates herpes zoster; PHN indicates postherpetic neuralgia. Data for these outcomes were adapted from reference [25••]. 'Preserving activity' indicates maintenance of activities of daily living.

Clinical endpoint	Efficacy (%)			
	All ages (years)	60–69	70–79	≥80
HZ incidence	51	64	41	18
PHN incidence	67	66	74	42
Preserving activity*	66	70	61	59

Real decrease efficacy to reduce shingles incidence after 80 years old

Still a large efficay regarding, PHN and impact on DISABILITY

Levin MJ , *Current op Immunol* 2012, ***Schmader K** *JAGS* 2010

Take Home Messages 3

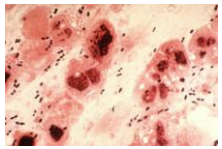
ID (VPD) decreases dramatically "Healthy Ageing"

Vaccines decreases direct and indirect short /long term mortality associated with VPD in ageing population

Zoster vaccine only prove an impact to prevent Disability associated Zoster.

Summary

- What is « healthy ageing » / Active ?
- Scientific evidence of ID (VPD) impact on ageing - role of vaccine ?



VPD
Pneumococcus
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- Vaccine Policies , evidences?

Overview

European vaccination Guidance for older adult (ESCMID/EUGMS/WAIDID)

Dt Pertussis vaccine >65 y (Pertussis according outbreak)

Flu vaccine >65 y

PCV13 and before giving PPV23 after 1 year >65 y

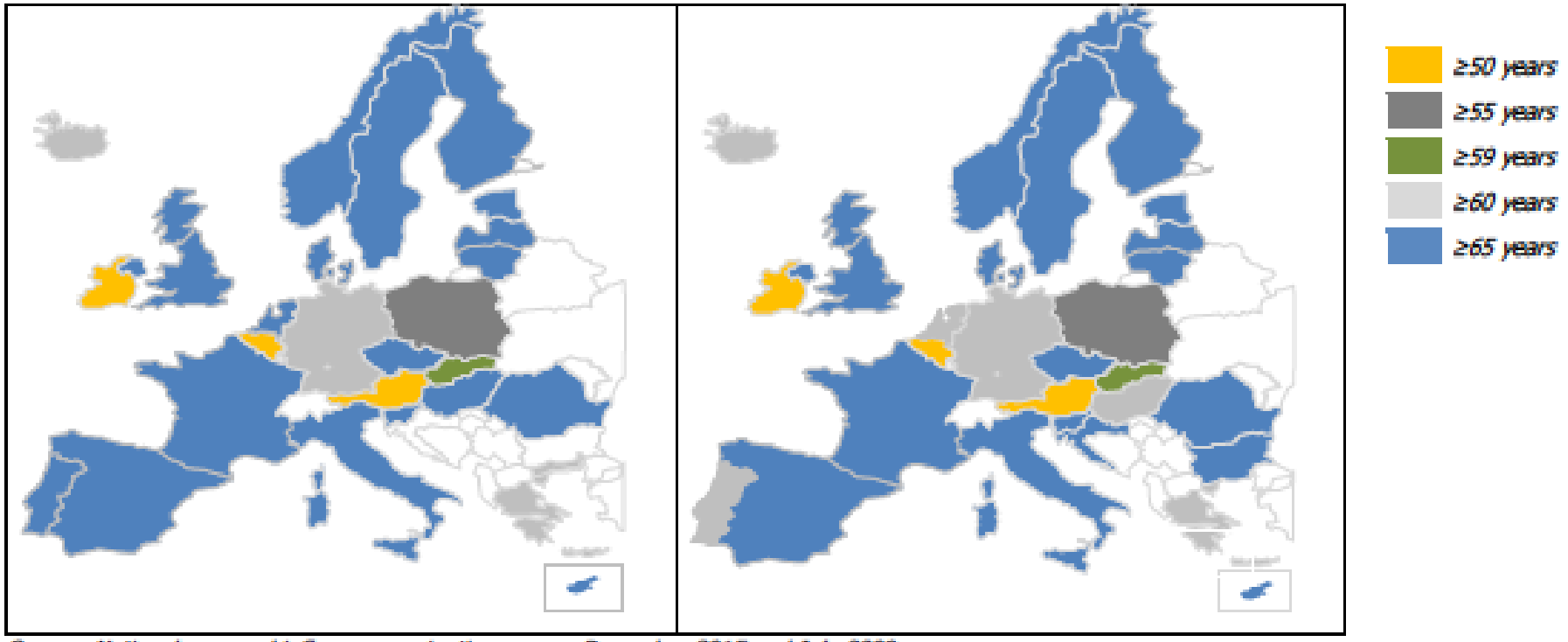
HZV vaccine All > 50 y

But

Very different recommandations in EU member states

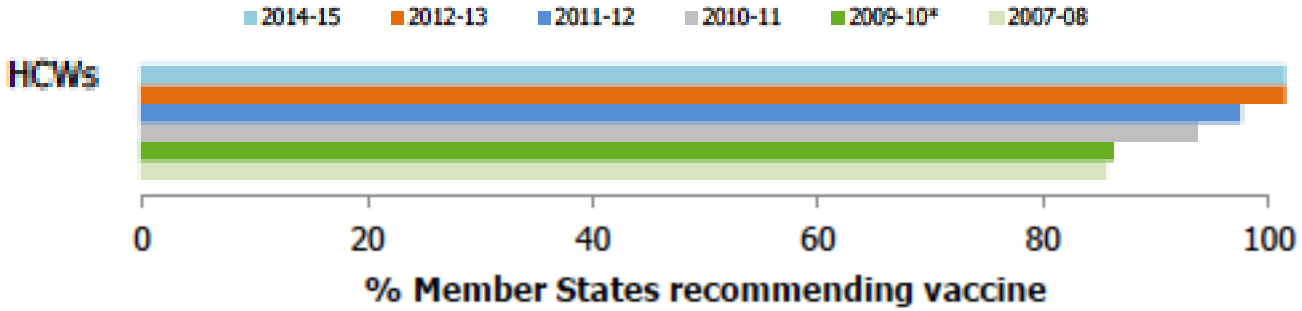
Esposito S et al Human Vac Immun 2016

Vaccine Policies , Evidences for flu ?



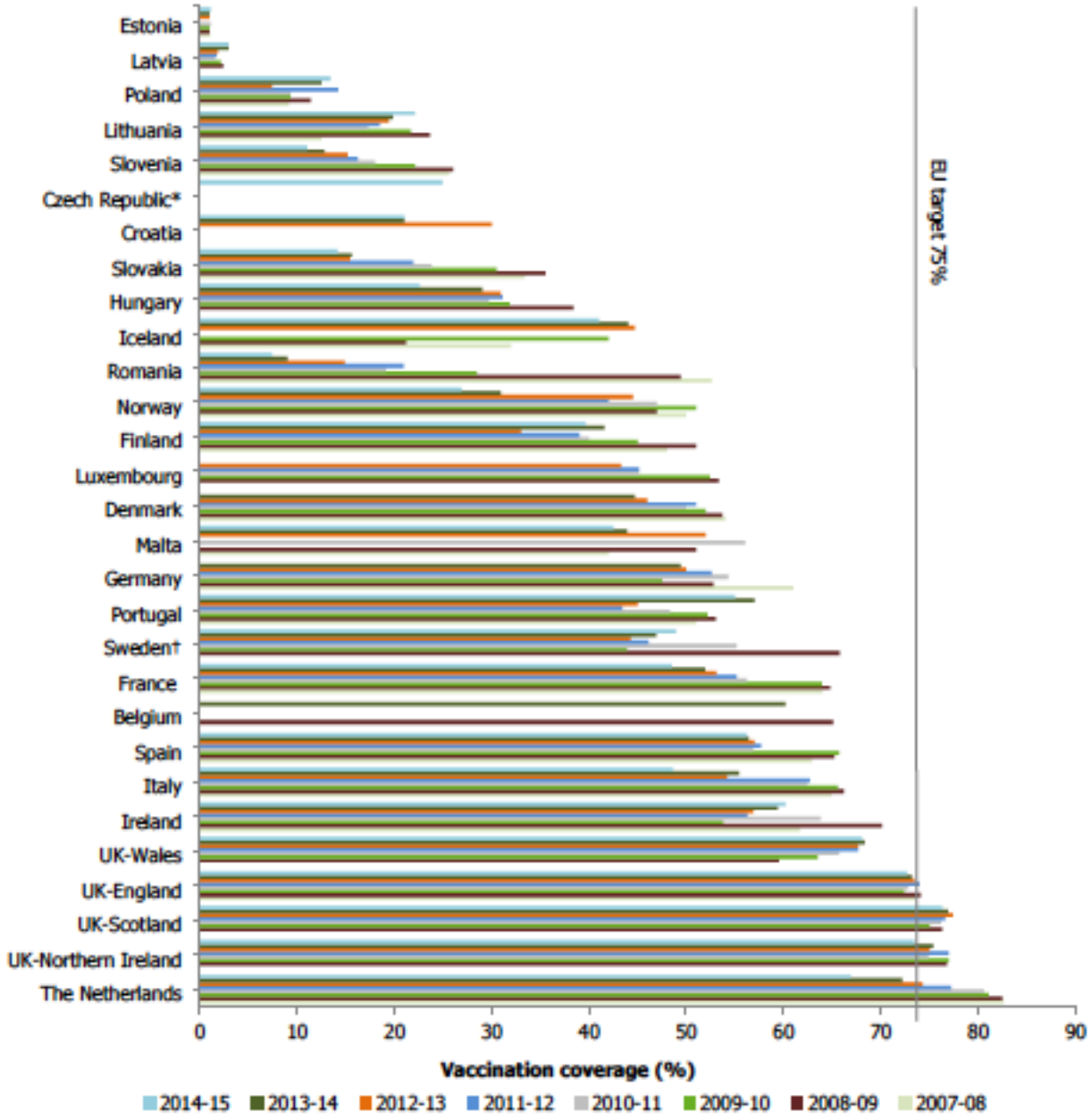
Source: National seasonal influenza vaccination survey, December 2015 and July 2009

Flu European recommandations / nation from 2008 to 2014



https://ecdc.europa.eu/sites/portal/files/documents/influenza-vaccination-2007–2008-to-2014–2015.pdf

Flu Vaccine coverage EU (2008-2015)

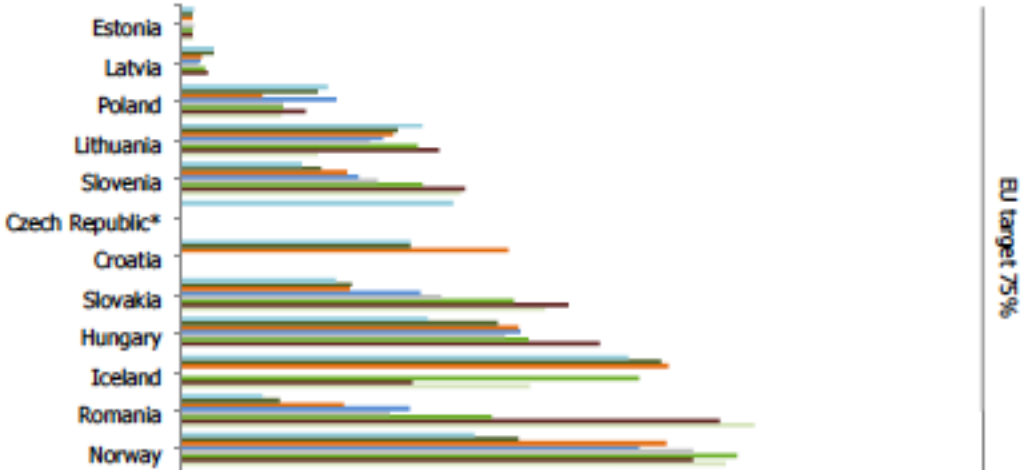


Dramatic decreases Everywhere…

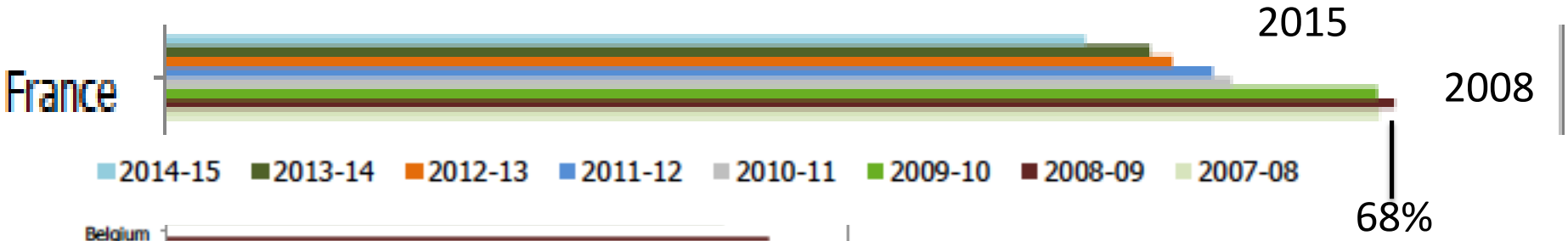
…

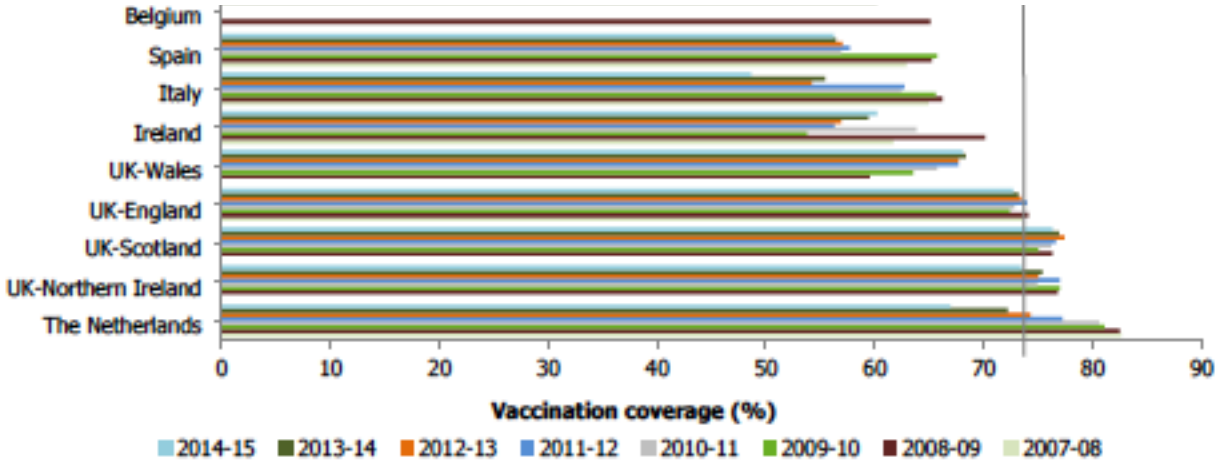
Out of UK

Flu Vaccine coverage EU (2008-2015)



Dramatic decreases
Out of UK





The impact of European vaccination policies on seasonal influenza vaccination coverage rates in the elderly

Human Vaccines & Immunotherapeutics 8:3, 328–335; March 2012

Patricia R. Blank,[1,2,*] Matthias Schwenkglenks[1,2] and Thomas D. Szucs[1]

No
Yes

	GBR	NLD	FRA	ESP	ITA	IRL	BEL	DEU	CHE	FIN	SWE	PRT	CZE	SVK	POL	BRG
Recommendation for all people aged 65+																
Recommendation for all people aged 50-55 or 60 to 64				a)			b)									
National object per year for flu for elderly or underlying conditions?																
Monitoring VCR each year by target (By HA and/or NVIG)				a)		*c)*										
HCW have objective to achieve in high risk groups (GP and/or Specialist)	d)		d)		a)											
HCW financial incentive (yes/no)			e)								a)					
Reimbursement of vaccine (90-100%)											a)				d)	
Letter for free flu vaccine (from HA/ GP/ HC)				a)		d)		d)			a)					
Awareness campaigns: Radio and tv			f)													
Awareness campaigns: press adverts				a)	a)											
Awareness campaigns: Flyers in medical waiting rooms																
Awareness campaigns: Website for public				a)												
Awareness campaigns: Press / media conference for public?	d)								d)							

The impact of European vaccination policies on seasonal influenza vaccination coverage rates in the elderly

Patricia R. Blank,[1,2,*] Matthias Schwenkglenks[1,2] and Thomas D. Szucs[1]

Stand alone policy element:

Variable	Parameter Estimate	Pr > |t|
Monitoring VCR (By HA and/or NVIG)	0.194	0.111
Patients receive personal letter/voucher for free flu vaccine	0.131	0.050
National objectives	0.195	0.096
National objectives adopted for risk-groups	-0.122	0.420
90–100% reimbursement of vaccine	0.201	0.105

Best = association of several reommandations :

	Objectives	Monitoring	Incentive	Reimbursement	Letter /voucher	Flyers
Objectives AND monitoring			0.607	0.631	0.607	0.558
Incentive AND reimbursement	0.734	0.734			0.721	
Letter /voucher AND reimbursement						0.820

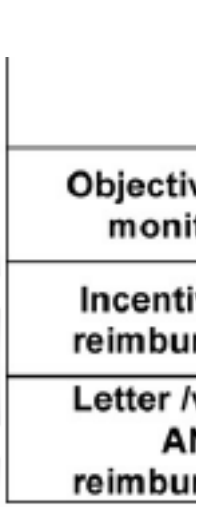
The impact of European vaccination policies on sea

Be

However,

the best association in France and

flu vaccine coverages decrease



Cost effectiveness analysis VZV vaccine in elderly population : recommandation ?

Study reference	Year of publication	Country	Perspective	Age of vaccination	Incremental cost effectiveness/QALY
Van Hoek *et al.* [2009]	2006	England and Wales	Provider	65 years	£20,412
Moore *et al.* [2010]	2006	United Kingdom	Society	⩾50 years	£11,417
				⩾65–69 years	£10,033
			Provider	⩾50 years	£13,077
				⩾65–69 years	£10,275
Annemans *et al.* [2010]	2007	Belgium	Society	⩾50 years	€7137
			Provider	⩾60 years	€6799
Van Lier *et al.* [2010]	2008	The Netherlands	Society	60 years	€38,519
			Provider	70 years	€21,716
Szucs *et al.* [2011]	2011	Switzerland	Society	70–79 years	CHF28,544
			Provider	70–79 years	CHF25,528
De Boer *et al.* [2013]	2013	The Netherlands	Society	60 years	€35,555
				70 years	€29,664
Ultsch *et al.* [2013b]	2013	Germany	Society	60 years	€30,212
			Provider	60 years	€28,146
Bresse *et al.* [2013]	2013	France	Provider	70–79 years	€14,198

QALY, quality-adjusted life year.

Johnson, *Adv therap* 2016

Cost effective in <80 y old population and less after 80….

BUT High variability according which variables….

Missing data impact of medication use, Impact on functional status, nutritional status

Is there any problem for flu HCW vaccination : HCW In USA?

SA.... 2013 / 2014
Flu season

	No. in sample	Weighted %†	Weighted % vaccinated
Influenza vaccination			
Required	738	35.5	97.8
Hospital	520	58.2	97.7
Ambulatory care/ Physician office§	252	33.6	96.4
Long-term care	88	20.1	98.4
Other clinical setting**	88	29.3	99.5

Black CL et al

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 63 / No. 37
September 19, 2014

Is there any problem for HCW in France ?

Vaccination	Vacccination Policy	Vac coverage %
B Hepatitis	Mandatory	97.8
Diph/Tetan/Pol	Mandatory	95.5
BCG	Mandatory	94.9
Measles	Recommended	49.7
Pertussis	Recommended	11.4
Varicella	Recommended	29.9
Influenza	Recommended	25.6

Guthmann JP *Vaccine* 2014

Take Home Messages 3

Enough Policies ?

Heterogeneity of Policies drive to No Policies

Main recommandations to improve VC are known

Need for Strong Political willingness

To put together…all stakeholders…

Risk/benefit / Surveillance / Feed back

Media

Thank you for your Attention

Winter ….not so far

« **What's natural** is the **microbe**. **All** the rest - **health**, **integrity**, purity (**if you like**) - is a product of the human will, of a vigilance that **must never** falter ».

in « the PLAGUE » Albert Camus

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