VACCINE-PREVENTABLE OUTBREAKS IN PORTUGAL: HEPATITIS A AND MEASLES

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FARO, PORTUGAL

OUTBREAKS IN PORTUGAL

HEPATITIS A

- Introduction – the virus and the disease
- National and european prevalence data
- Outbreak in Portugal and EU countries 2016-2017
- Management by National Health Authorities
- Discussion

MEASLES

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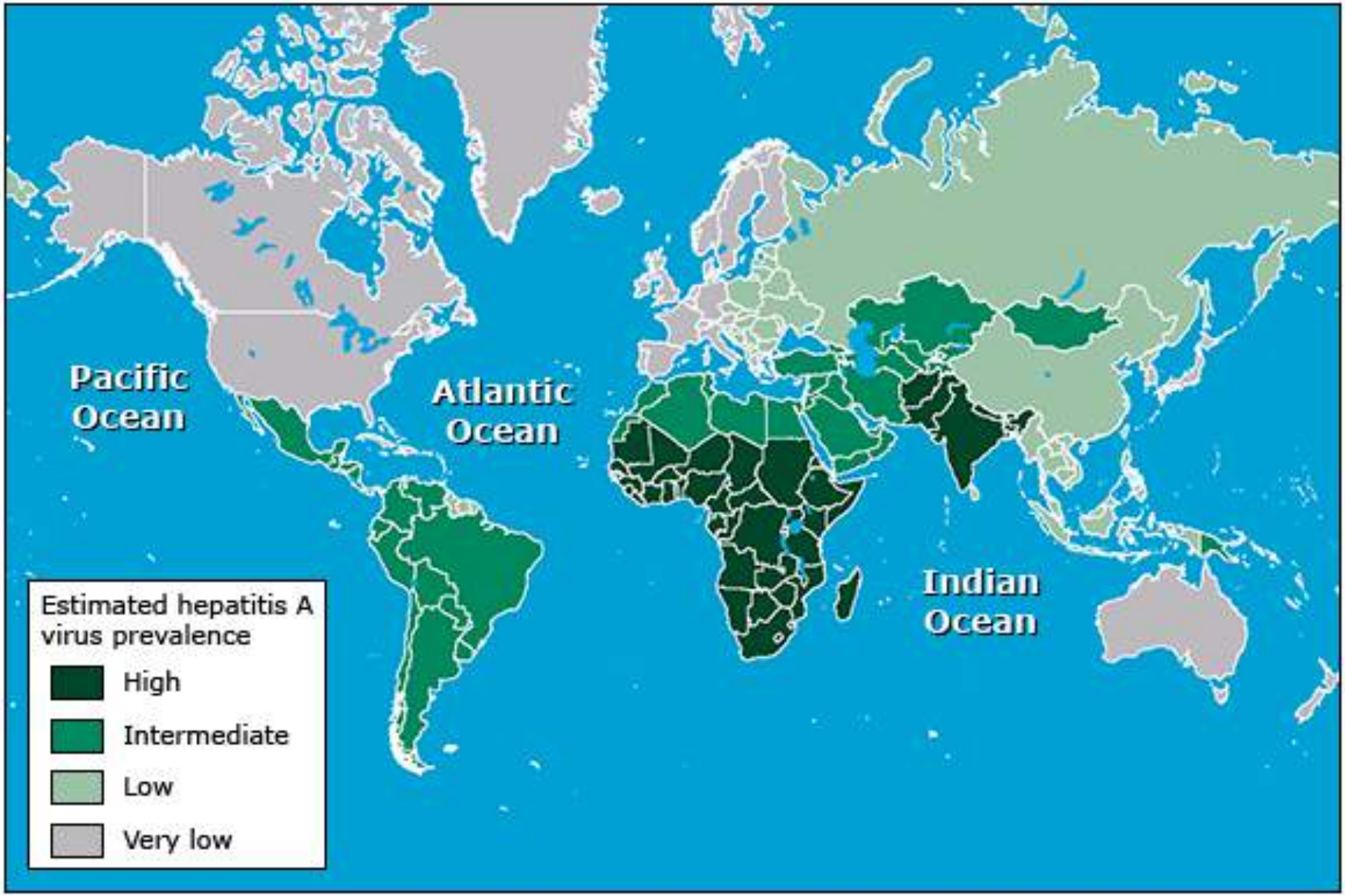
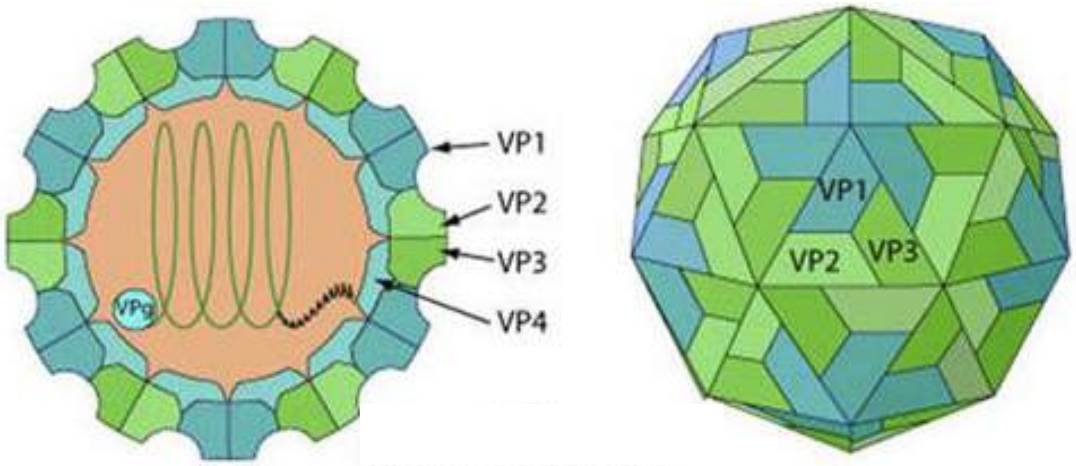
HEPATITIS A – GLOBAL SEROPREVALENCE



http://wwwnc.cdc.gov/travel/yellowbook/2012/

HEPATITIS A

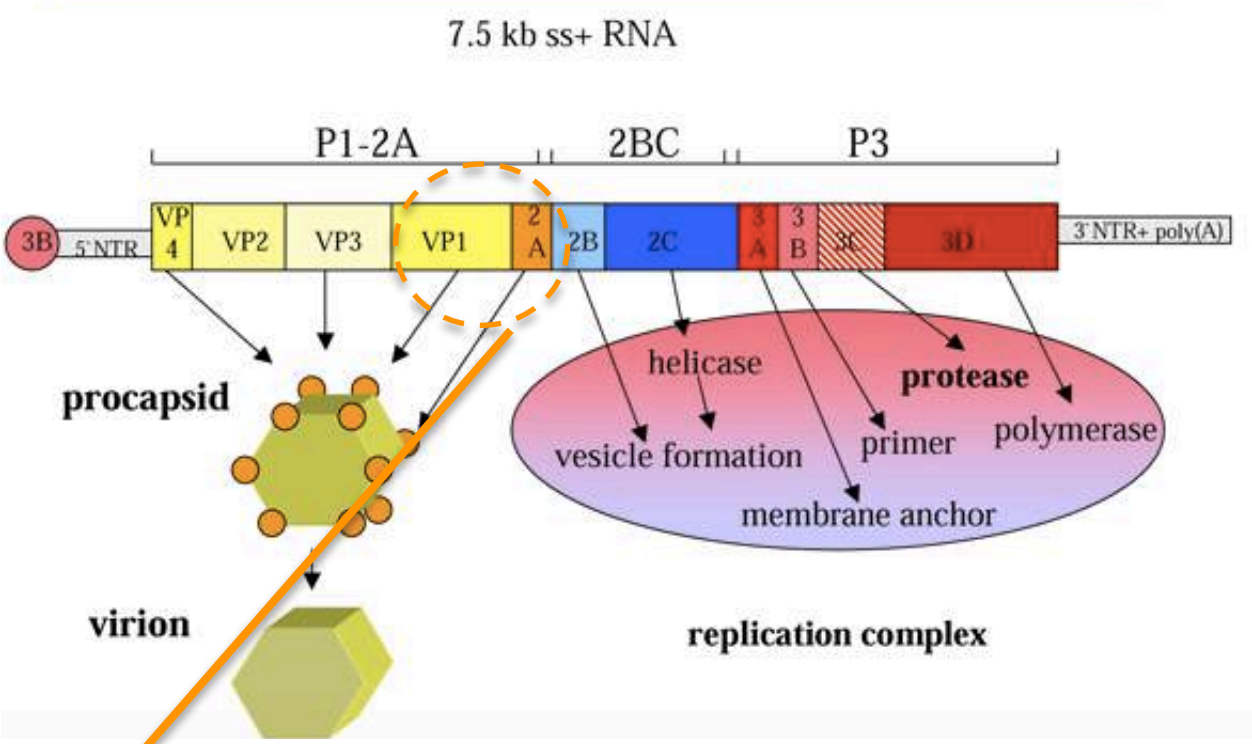
- Non-enveloped RNA hepatovirus (*Picornaviridae*) - 1975
- 1 serotype, several genotypes
- Resistant to inactivation (Temp.60°c or ≤4°c, eter, acid, anionic substances)



Vaughan G et al, Infect Genet Evol 2014, 227-43

Pinto RM, Future Microbiol 2012, 331-46

HEPATITIS A



GENOTYPES	**I a VI** (I - III – human infection)
SUBTYPES	**A e B**
CLUSTERS	**Variable**

IA: worldwide

80% of human infections

IIIA: Asia

Vaughan G et al, Infect Genet Evol 2014, 227-43

Pinto RM, Future Microbiol 2012, 331-46

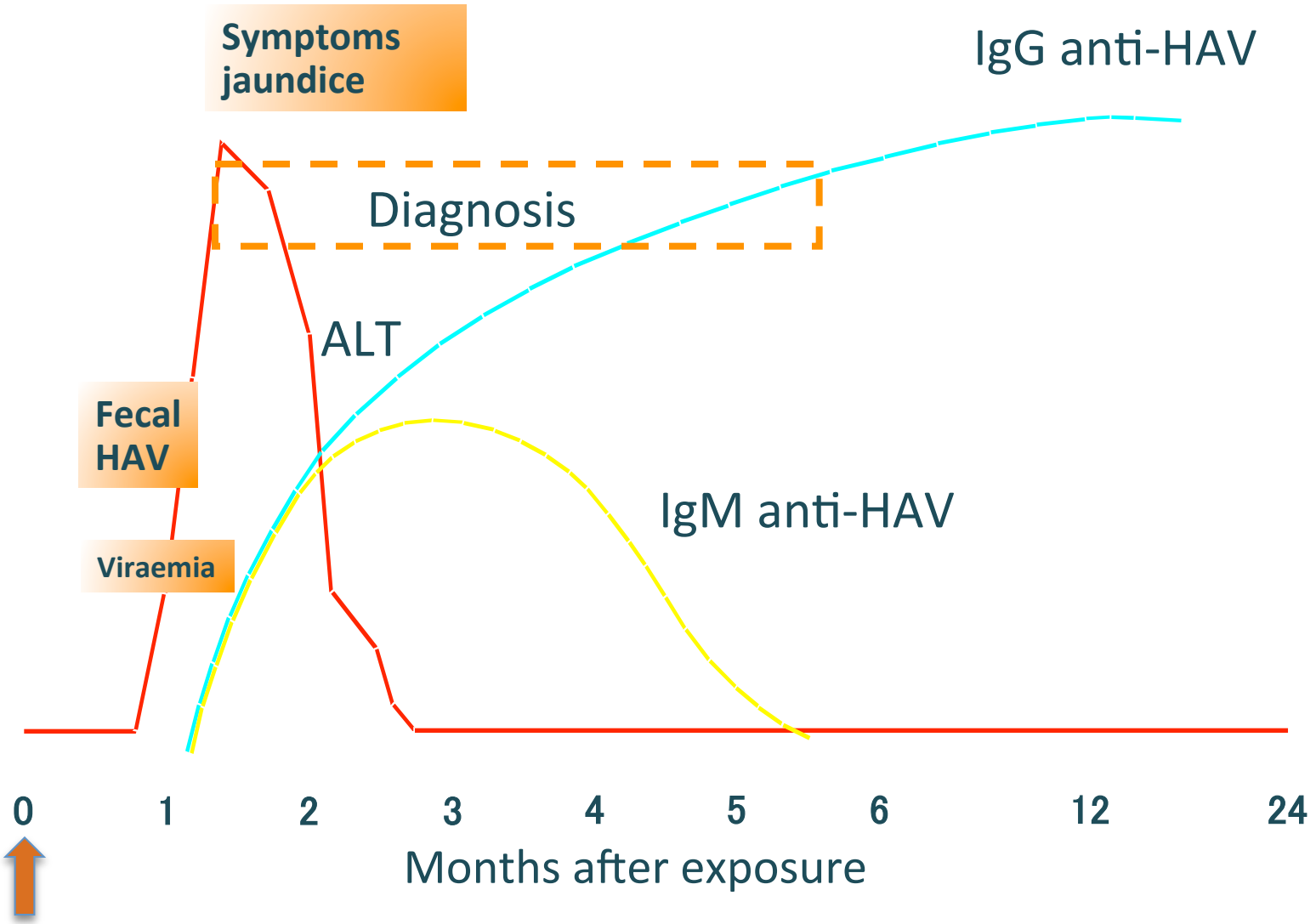
HEPATITIS A PRESENTATION

Transmission route	**Fecal-oral:** - Water / food contaminated - Interpersonal contact **Parenteral**
Incubation **Infectious period**	30 days (15-50 days) incubation (2 Wks) ➔ 1 Wk after symptoms begin
Presentation	Asymptomatic (children) Fever, vomiting, abdominal pain, astenia, jaundice, choluria
Age variation	Adolescent and adult: ↑symptoms (70% Vs 30% by 6yrs) and complications; ↑ mortality (>50A: 1,8%)
Complications	Recurrent Hepatitis, prolonged Fulminant Hepatitis <1%, Mortality (0,1-0,6%)
Diagnosis	IgM anti-HAV; RNA HAV (*PCR*: *clusters*)
Treatment	Supportive; ⊘ toxic drugs and alcohol

Christenson JC, Pediatr Rev 2016, 426-438

http://www.uptodate.com

HEPATITIS A PRESENTATION



Christenson JC, Pediatr Rev 2016, 426-438

http://www.uptodate.com

HEPATITIS A PREVENTION: VACCINES

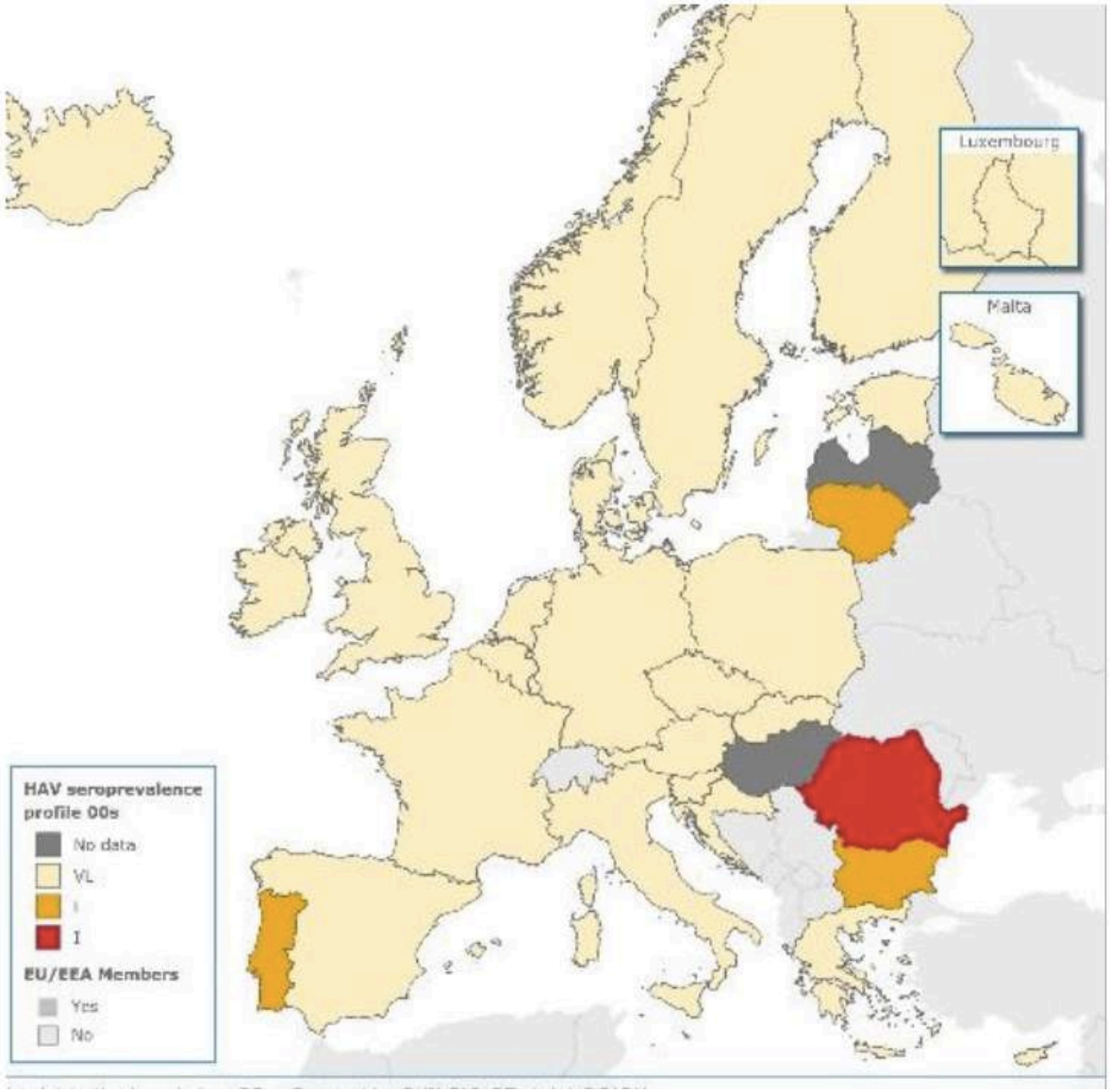
- Available since 1998 (extra-National Immunisation Programme)
- Inactivated vaccines
- Imunogenic, safe, effective (comparable), interchangeable

	HAVRIX® (Glaxo)	VAQTA® (Merck)
Type	adsorved, inactivated	adsorved, inactivated
Presentation	ped® 720 EL.U/ 0,5mL adult® 1440 EL.U/ 1mL	25U/ 0,5mL 50U/ 1mL
Age	1yr to 15yr (<18A) >16yr	1yr a 18yr >18yr
Dosis	2 dosis (0, 6 a 12M)	2 dosis (0, 6 a 18M)
Seroconversion	1 dose: 88% (2 Wks) 96-100% (4-6 wks)• 2 dosis: >95% after 25yrs	1 dose: 88% (2 Wks) 96-100% (4-6 wks)• 2 dosis: >95% after 25yrs

Immunisation, Vaccines and Biologicals. WHO, II series, 2011

* RCM Vaqta: 99% às 4sem; • RCM Havrix: 99% às 4sem

HEPATITIS A SEROPREVALENCE: EU (2000-13)



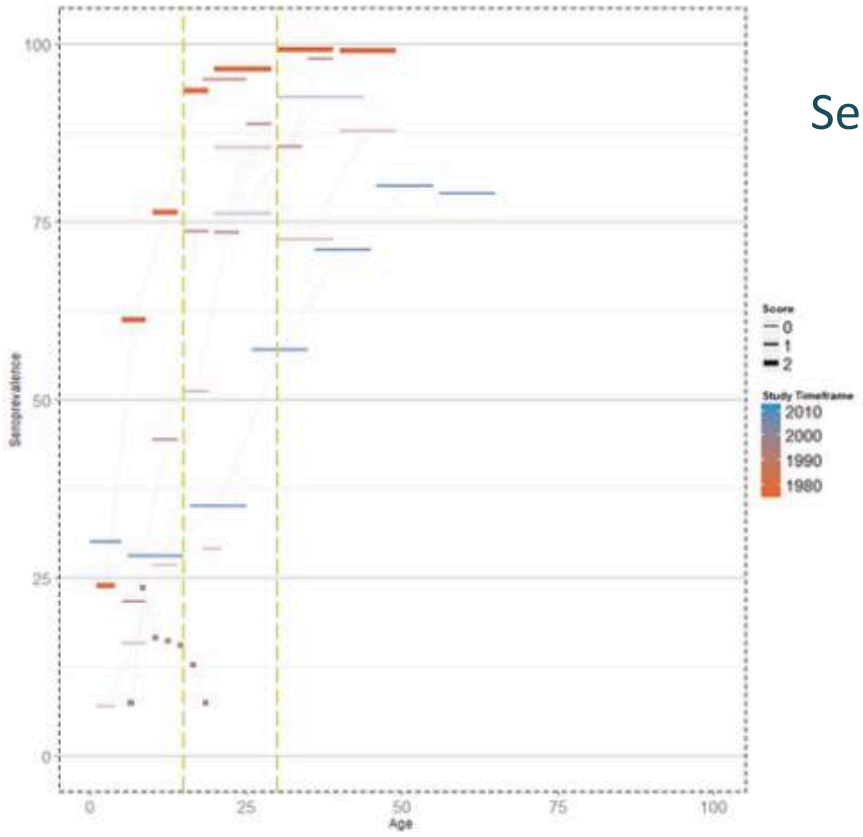
http://ecdc.europa.eu/en/publications/Publications/hepatitis-a-virus-EU-EEA-1975-2014.pdf

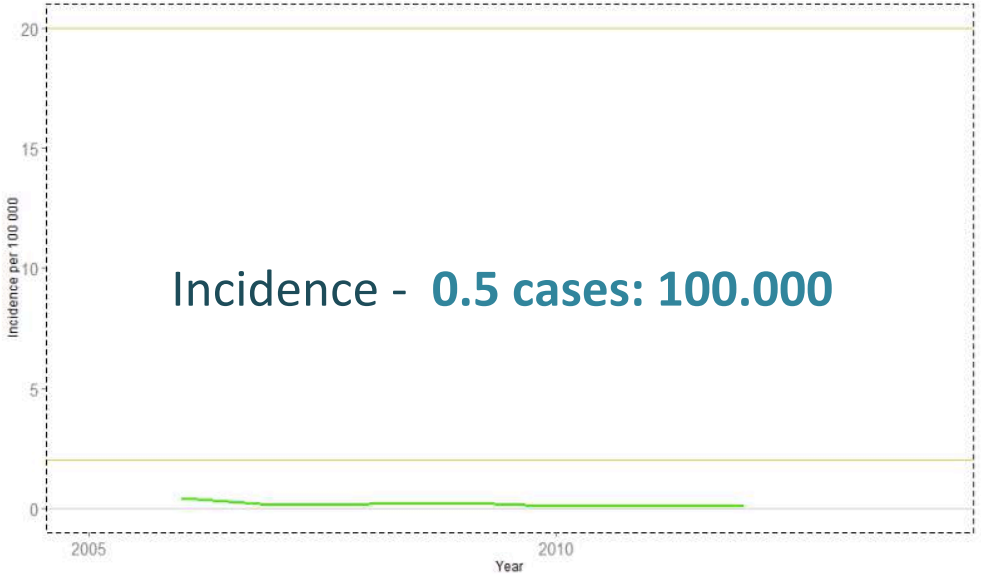
HEPATITIS A IN PORTUGAL: LOW ENDEMICITY

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Seroprevalence 2000-2013: **93%, ≥55yrs**

Seroprevalence 2016, Lx*: **30%, 20-29 A**
88% aos ≥55A





Incidence - **0.5 cases: 100.000**

*Palminha P et al, J Clin Virol 2016 (82), S79-80

http://ecdc.europa.eu/ EU-EEA-1975-2014

HEPATITIS A: CURRENT EU OUTBREAK (JUL/16 – FEV/17)

- Reported cases in 13 EU countries (287*)
- Affect MSM
  - Sexual transmission (anal and oro-anal route)
  - High local and regional interconectivity (MSM)

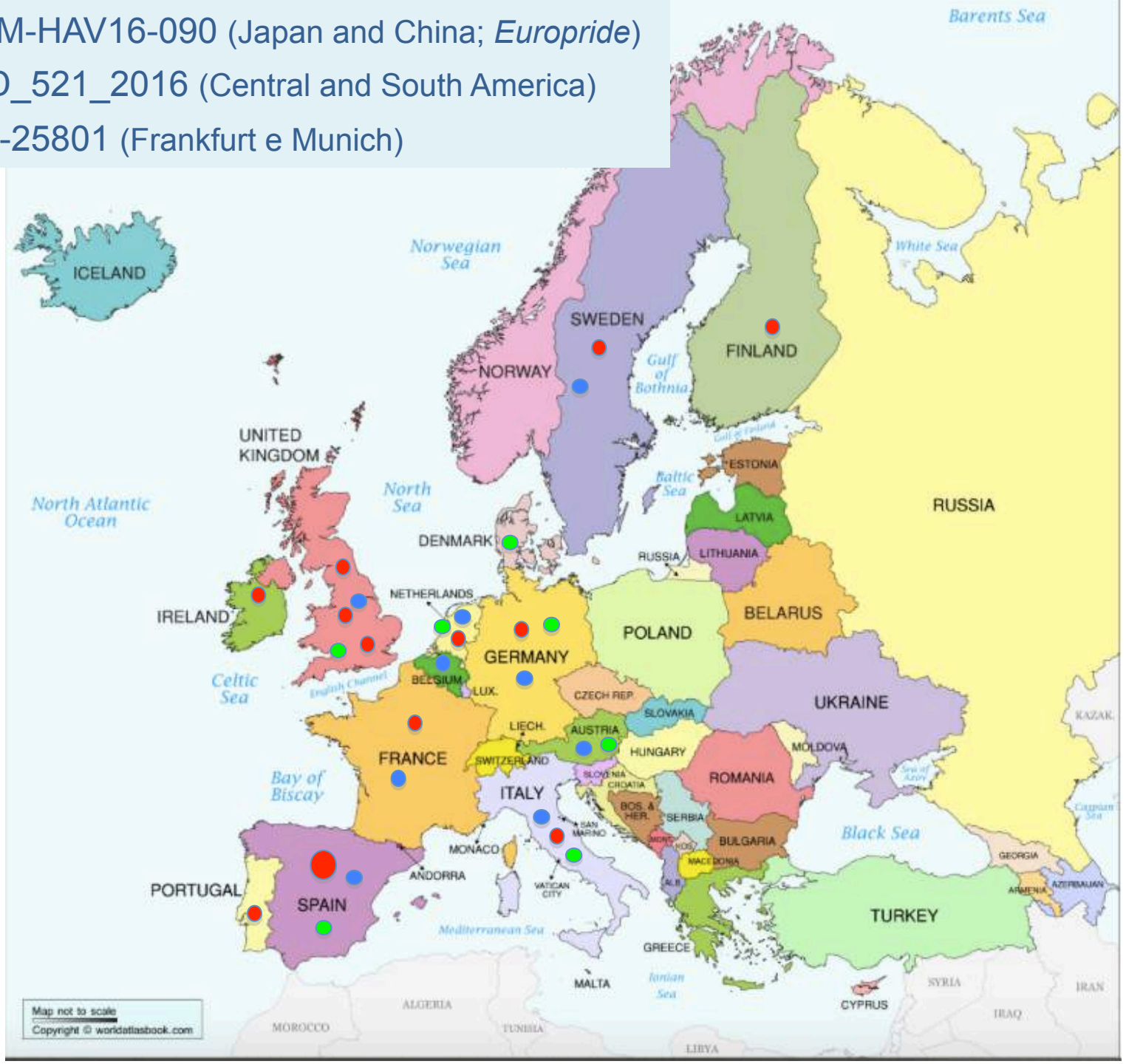
Risk factors – epidemiological questionnaires

✓**UK**: - activities in group (saunas, clubs), use of meeting *apps* (LGBT)
- multiple sexual partners, anonimous contacts
- sexual activity as subsistence

✓**Germany**: - travelling (national and international) and group events

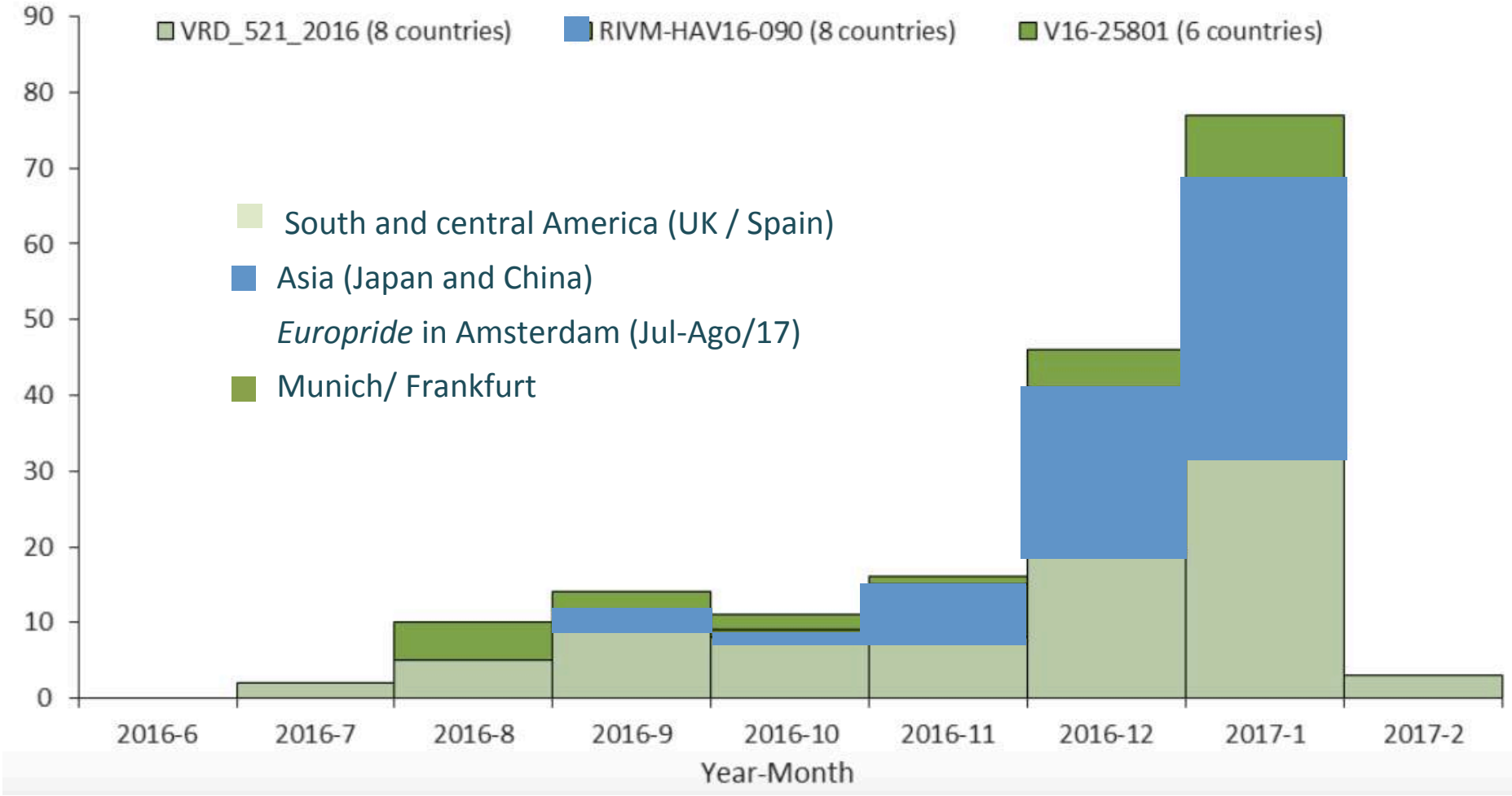
http://ecdc.europa.eu/ EU-EEA-1975-2014

- RIVM-HAV16-090 (Japan and China; *Europride*)
- VRD_521_2016 (Central and South America)
- V16-25801 (Frankfurt e Munich)



HEPATITIS A: CLUSTERS IN EU OUTBREAK

- 3 *clusters* of HAV subgenotype IA
- Independent transmission chains



ECDC. Hepatitis A outbreaks in the EU/EEA – first update, 23 February 2017. Stockholm: ECDC; 2017

HEPATITIS A: CLUSTER VRD_521_2016 (Portugal)

- 1/Jan through 24/Apr/2017: **242 cases*** notified
- 93% are young adult men°
- 79% live in Lisbon°
- 50% admitted to hospital°

National Guidelines for Outbreak Control - DGS (09-04-17)

Outbreak in Portugal / EU

Global vaccine restrictions (EU)

° Source: Hepatitis A, National Guidelines, 08/05/2017, National Health Direction

* Source: DGS

HEPATITIS A OUTBREAK: MANAGEMENT IN PORTUGAL

- **OUTBREAK CONTROL:**
  - **IMMUNISATION is the main control measure**
  - Alert about hygiene and sanitary preventive measures
  - Education and communication (LGBT community)

- Vaccination: **pre and post-exposure** conditions
  - ✓ **Target: MSM**; identification of contacts
  - ✓ **1 dose of anti-HAV vaccine: free of charge**
  - ✓ **Those who have 1 dose of vaccine are considered protected**

Travelers ???

- Control of vaccines by National Health Authorities
- Specific locations for vaccine administration

Hepatite A, Norma no 003/2017 de 09/04/2017, Direção Geral de Saúde

HEPATITIS A PREVENTION: IMMUNOGLOBULIN

- **Immunoglobulin: post-exposure (2 wks)**
  - ✓ IG IM 0,02mL/kg; protection in 80-90% through 3M
    - Immunodeficiency with vaccine failure
    - Children <12M of age
    - Chronic hepatic disease
    - Vaccine contraindications

- IG IM pre-exposure: 0,02mL/Kg IM (duration <3M)

  0,06mL/Kg IM (duration 3-5M)

Hepatite A, Norma no 003/2017 de 09/04/2017, Direção Geral de Saúde

HEPATITIS A OUTBREAK: DISCUSSION

- Outbreak activity:
  - ✓ Number of cases / week? Severity?

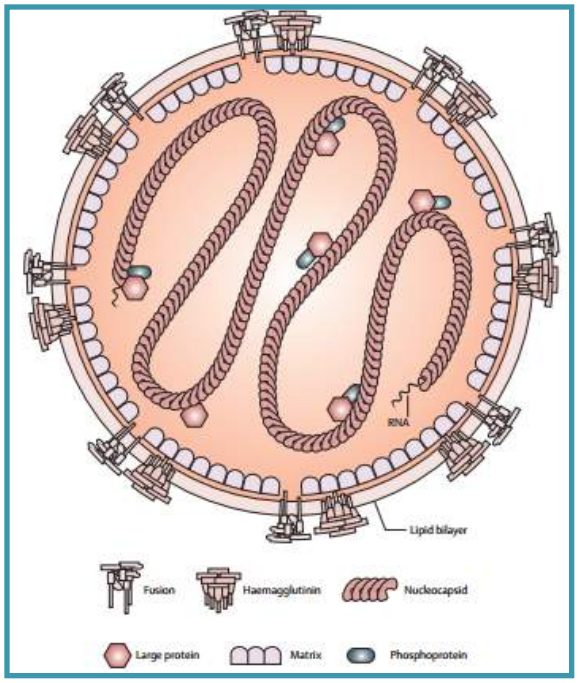
- Management guidelines:
  - ✓ Nº of administered vaccines in 1 month ? **(1149)**
  - ✓ Nº of secondary cases / contacts? Pediatric cases?
  - ✓ Nº of available vaccines?

- Controversies about National Health Authorithies guidelines:
  - ✓ Travelers and other risk groups neglected
  - ✓ Efficacy of health education efforts?
  - ✓ Pediatric vaccine in pre-exposure prophylaxis? Evidence?

MEASLES

MEASLES VIRUS (MeV)

- RNA virus, morbilivirus, paramyxoviridae
- 1 serotype, 24 genotypes compiled in 8 clades (A-H) and clusters

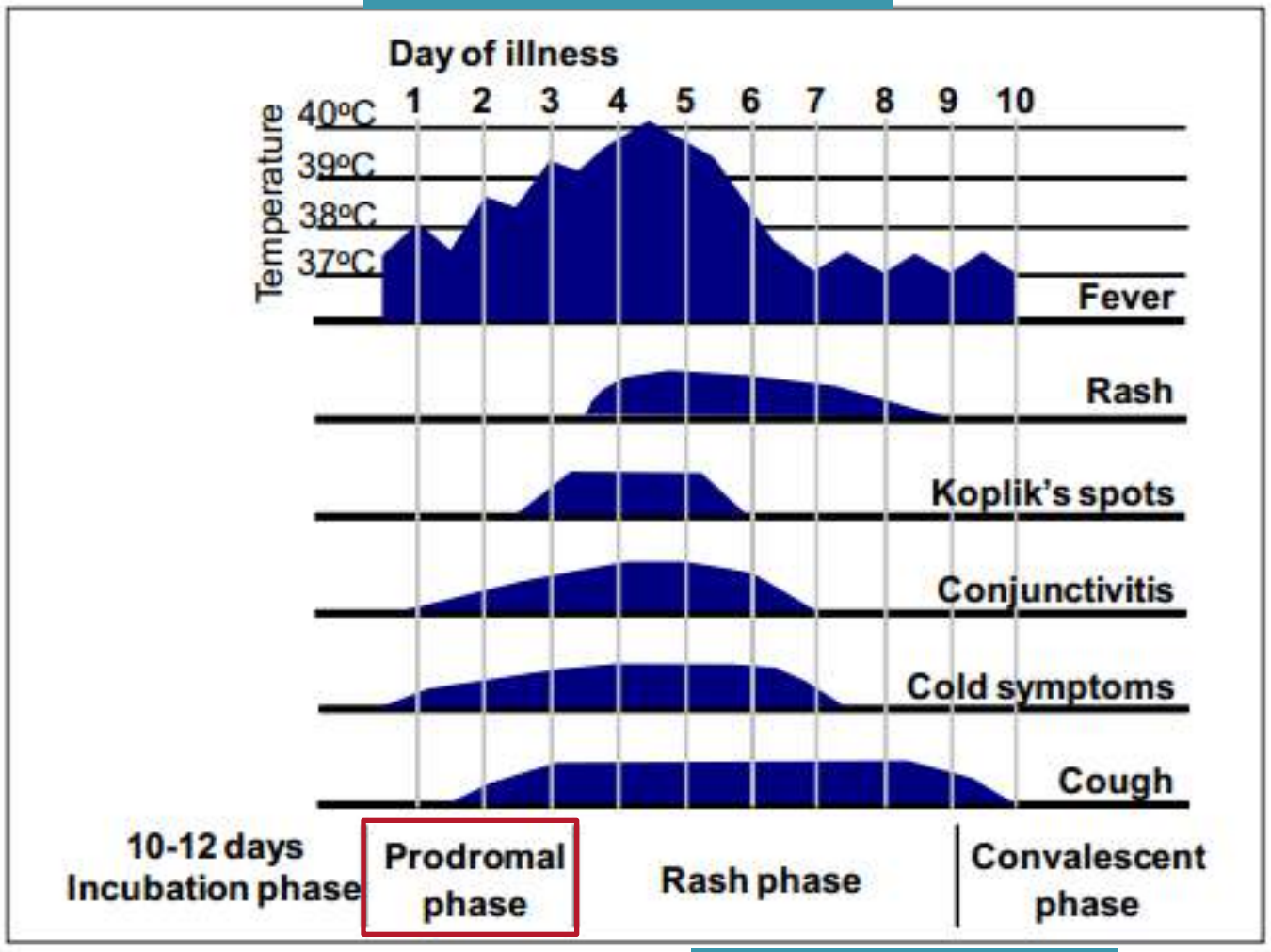


- Human reservoir
- Transmission: droplets and airborne
- Highly infectious (Ro 12-18)
- Infective period: 4d before/4d after exanthem

Moss WJ, Griffin DE. Lancet, 2012
Griffin DE (2013) Measles, in Fields Virology. Wolters Kluwer/Lippincott, Williams & Wilkins, Philadelphia
Feigin and Cherry's. TEXTBOOK OF PEDIATRIC INFECTIOUS DISEASES. Seventh Edition

TYPICAL MEASLES - PRESENTATION

CONTAGIOUNESS



COMPLICATIONS

Source: DGS, WHO

RISK FACTORS FOR SEVERE MEASLES

- Pregnancy
- Imunodeficiency
- Poor nutrition
- Vit. A deficiency
- Infants / Adults

Measles keratitis + Vit A deficiency: blindness

MEASLES COMPLICATIONS

- ≈ 30% of measles cases
- Induces T imunosupression: >risk of secondary infection

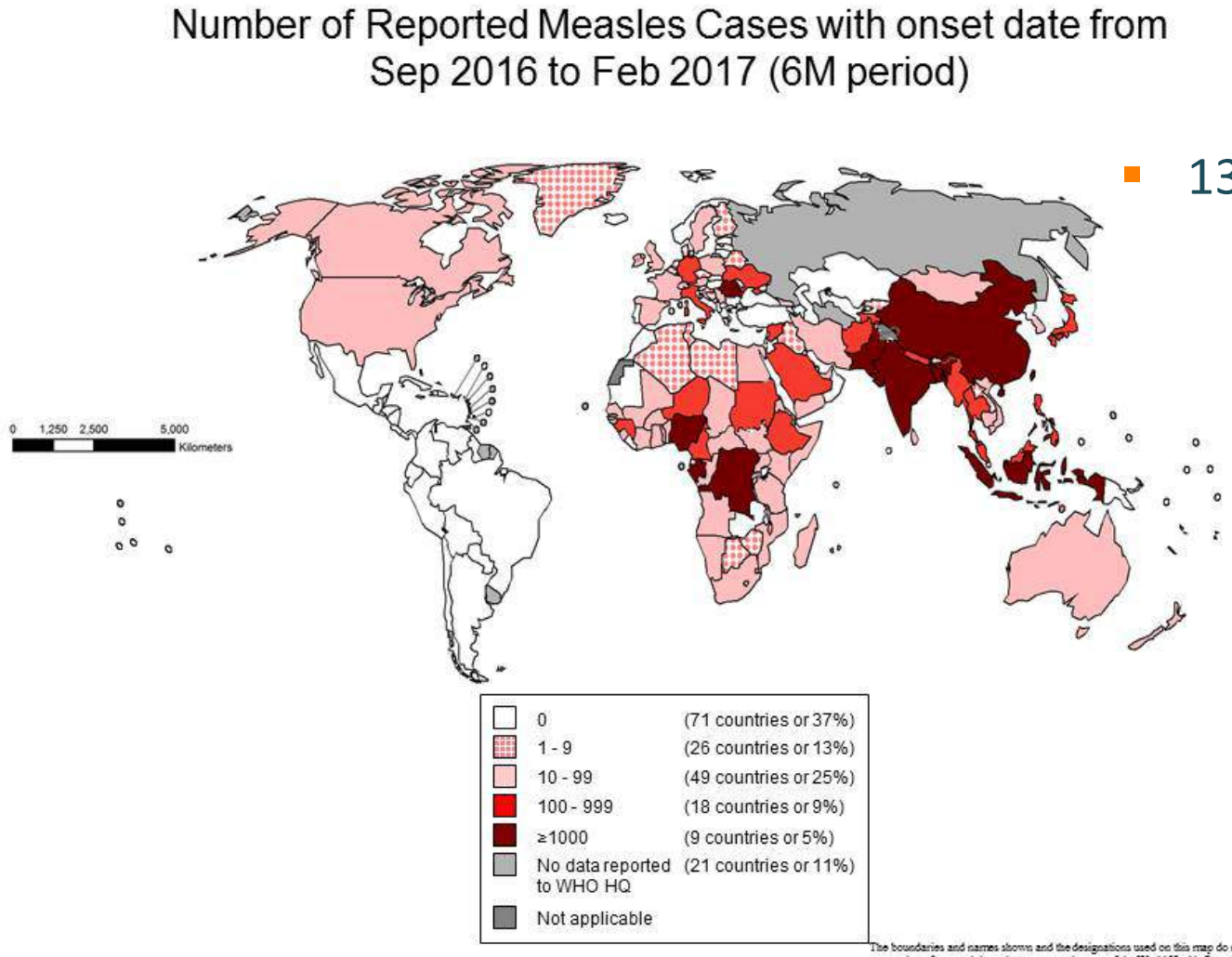
Persistent fever > 3 days after the begining of the exanthem: **alert sign**

Table. Complications of Measles[1,12,29]

Complication	Approximate Rate per No. of Cases
Diarrhea	1/12
Otitis media	1/14
Pneumonia	1/20
Seizures (febrile and nonfebrile)	6-7/1000
Death	2/1000
Primary measles encephalitis	1-3/1000
Acute postinfectious encephalomyelitis	1/1000
Subacute sclerosing panencephalitis	4-11/100 000

Bester JC .JAMA Pediatr, 2016

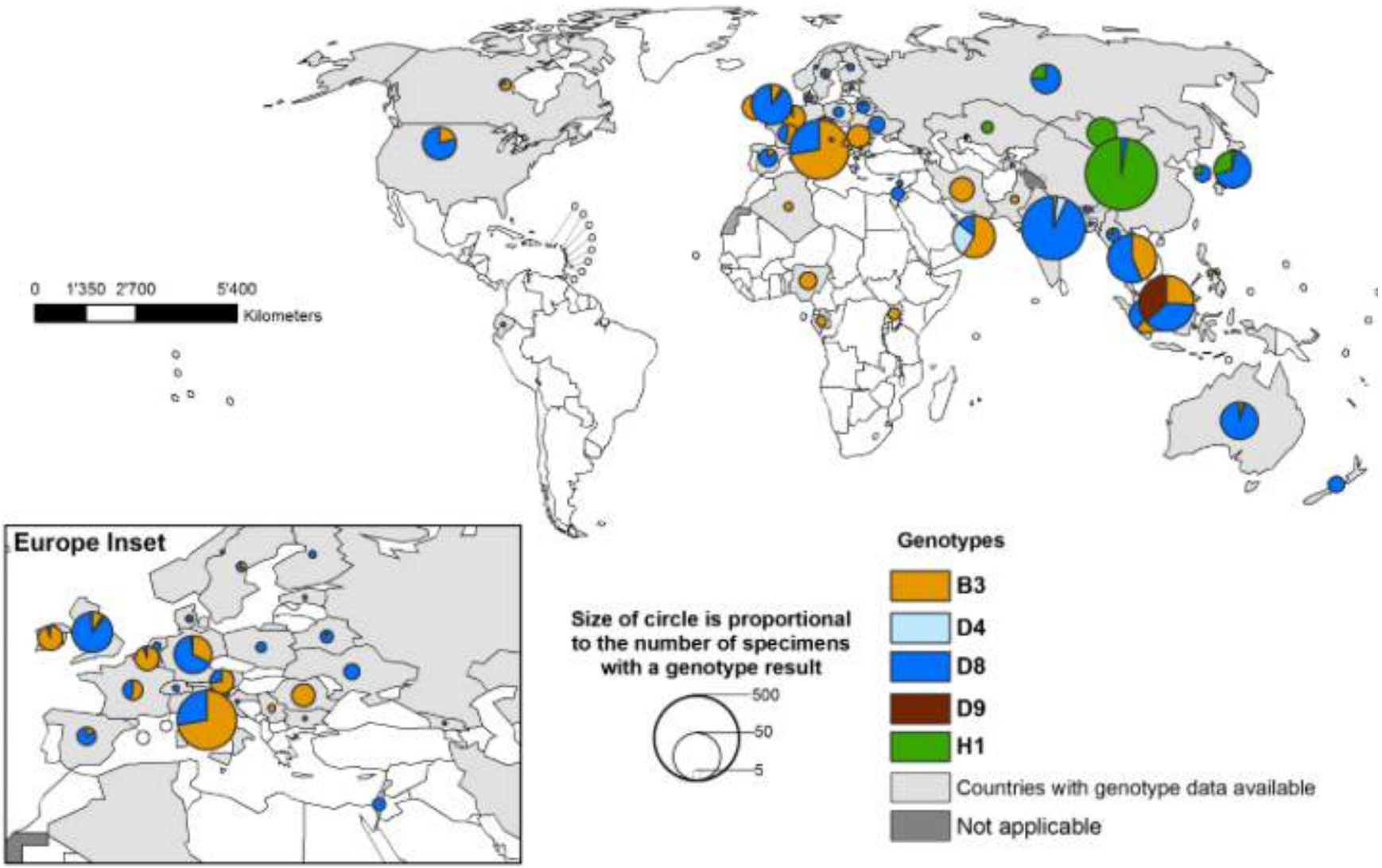
MEASLES – WORLDWIDE PREVALENCE



- 134.200 deaths/2016

SOURCE: WHO 2017

MeV GENOTYPE GEOGRAPHICAL DISTRIBUTION 2016-2017

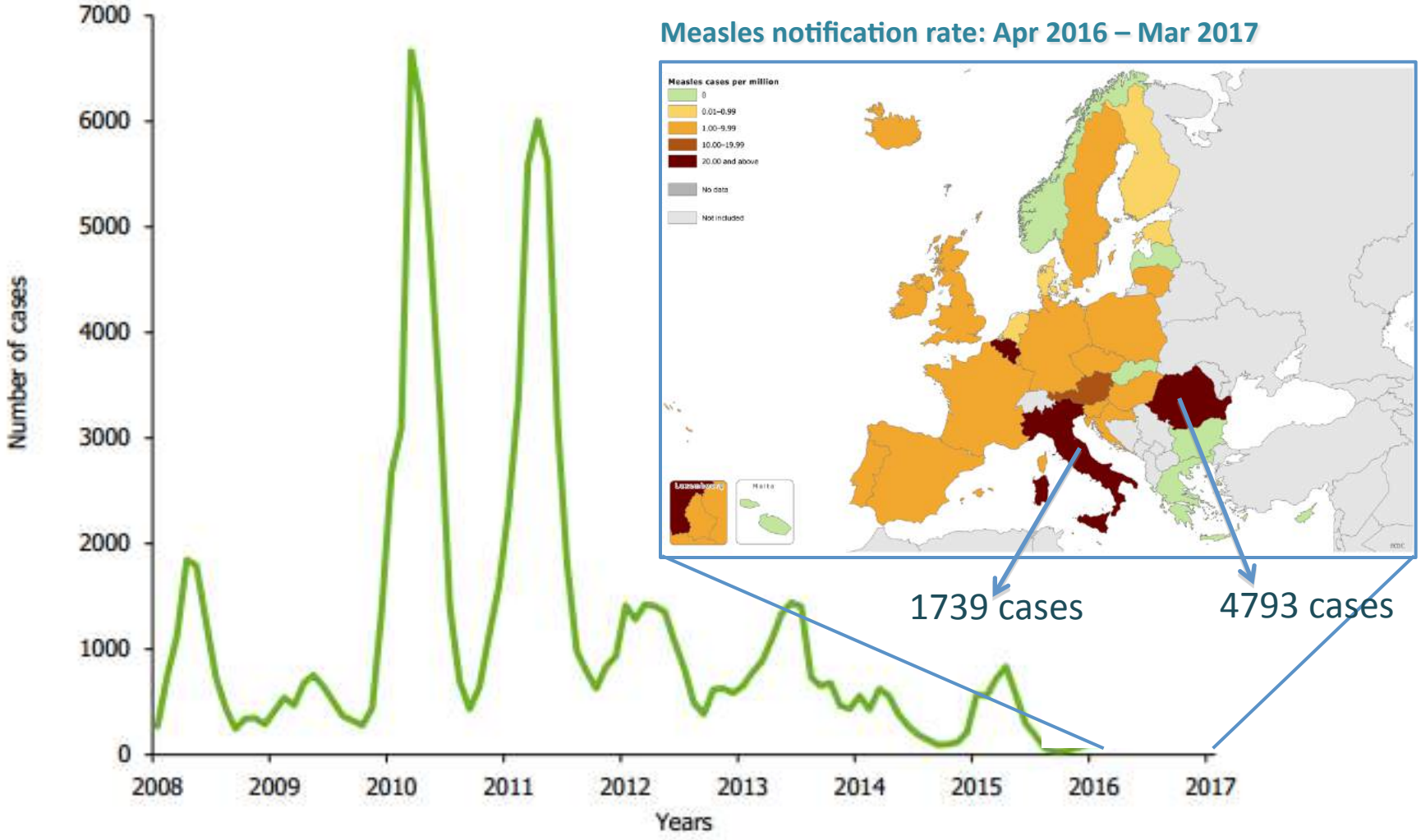


. www.who-measles.org

EUROPEAN PREVALENCE 2016-2017

- EU: 6597 cases/yr – 30 countries (1st Apr/2016 ➔31st Mar/2017)

Figure 4. Number of measles cases by month, EU/EEA countries, 1 January 2008–31 January 2017



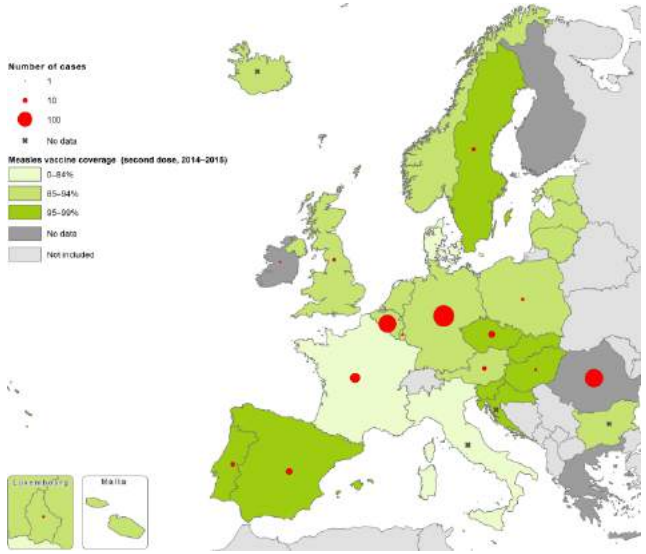
SOURCE: WHO 2017

EUROPEAN VACCINATION COVERAGE

Vaccination coverage with the first and second dose of MMR (2014–2015, WHO*), EU/EEA countries

	MCV1		MCV2	
Country	2015	2014	2015	2014
Austria	-	96	-	87
Belgium	96	96	85	85
Bulgaria	92	93	87	89
Croatia	93	94	96	97
Cyprus	90	86	-	-
Czech Republic	-	99	99	96
Denmark	91	90	80	84
Estonia	93	93	92	93
Finland	95	-	-	-
France	-	90	-	74
Germany	97	97	93	93
Greece	97	97	-	-
Hungary	99	99	99	99
Iceland	93	90	94	93
Ireland	93	93	-	-
Italy	85	87	83	83
Latvia	96	95	92	89
Lithuania	94	93	92	92
Luxembourg	99	99	86	86
Malta	89	98	91	94
Netherlands	95	96	92	93
Norway	95	94	91	92
Poland	96	97	94	95
Portugal	98	98	95	96
Romania	86	89	-	-
Slovakia	95	97	98	98
Slovenia	94	94	96	94
Spain	96	96	95	93
Sweden	98	97	95	95
United Kingdom	95	93	91	89

Measles vaccination coverage (2nd dose) Jan 2014 April 2017



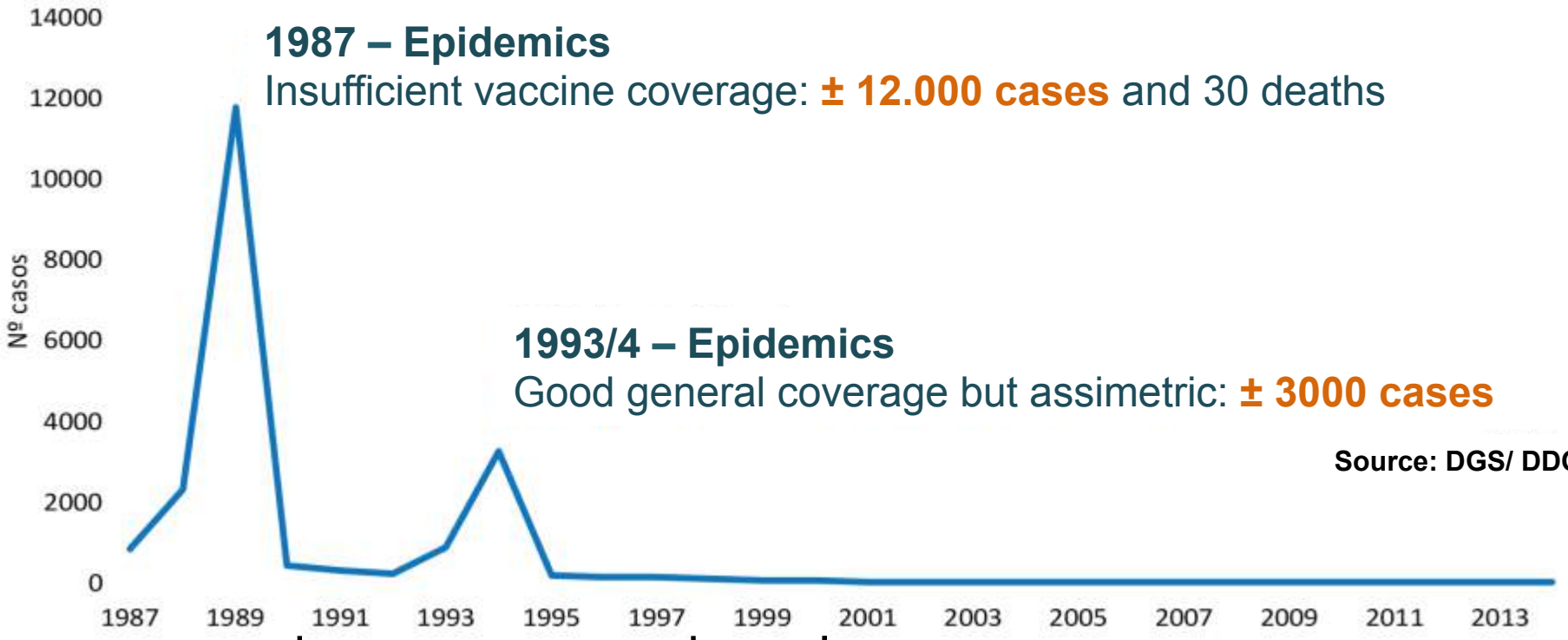
ECDC; WHO 2017

NATIONAL IMMUNISATION SCHEDULE 1965-2017

1965	1973/4	1980	1984	1987	1990	1993/5	2000	2006	2008/9	2012	2015	2017
smallpox	smallpox											
Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria	Diphteria
Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus	Tetanus
pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis	pertussis .	pertussis **pregnant**
BCG	BCG	BCG	BCG	BCG	BCG	BCG	BCG	BCG	BCG	BCG	BCG	**Risk groups**
Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio	Polio
	Measles	**Measles**	**Measles**									
			Measles Adol. F	Measles Adol. F								
				MMR 15 M	**MMR** 15 M **11-13 A**	MMR 15 M 11-13 A	**MMR** 15 M **5 – 6 A**	MMR 15 M 5 – 6 A	MMR 15 M 5 – 6 A	**MMR 12 M** 5 – 6 A	MMR 12 M 5 – 6 A	MMR 12 M **5 A**
						Hep B	Hep B	Hep B	Hep B	Hep B	Hep B	Hep B
							Hib	Hib	Hib	Hib	Hib	Hib
								MenC	MenC	MenC	MenC	MenC
									HPV	HPV	HPV	HPV
											PCV13	PCV13

Campaign VAS
1973-77
Children 1–4 A

MEASLES PREVALENCE - PORTUGAL



1987 – Epidemics
Insufficient vaccine coverage: **± 12.000 cases** and 30 deaths

1993/4 – Epidemics
Good general coverage but assimetric: **± 3000 cases**

Source: DGS/ DDO

1974 Measles vaccine

1990
2ªdose: 11-13yrs

2000
2ªdose: 5-6 yrs

2012
1ªdose: 12 M

MEASLES CASES IN PORTUGAL – 2004/16

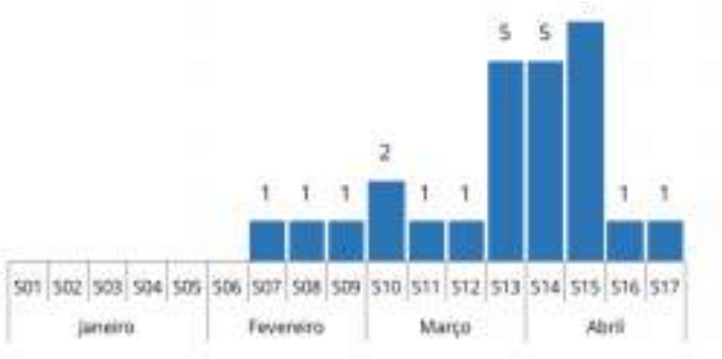
YEAR	Nº OF CASES	CONFIRMED CASES	DATA
2004	1	0	
2005	7	6	- 1 case from Romenia + 5 secondary cases (migrant community)
2006	0	0	
2007	0	0	
2008	1	1	- 1 case from UK
2009	3	3	- Outbreak 2 cases: 1 case from Etiopia + 1 secondary - 1 case from France
2010	5	5	- Outbreak 4 cases: 1 from África do Sul + 3 secondary (healthcare worker) - 1 case from UK
2011	7	2	- 1 case from France (genotype D4) - 1 case from Angola (genotype B3.1)
2012	21	5	- Outbreak of 4 cases: 1 from China + 2 secondary + 1 terciary (gen H1) - 1 case from UK (genotype D4) - 1 case from Angola (genotype ?)
2013	6	1	- 1 case from Germany (genotype D8)
2014	**?**	**0**	
2015	**?**	**0**	
2016	**?**	**0**	

SOURCE: DGS Palminha P *et al*. Diagnóstico laboratorial do sarampo em Portugal, 2011-2013. Observações_ Boletim Epidemiológico

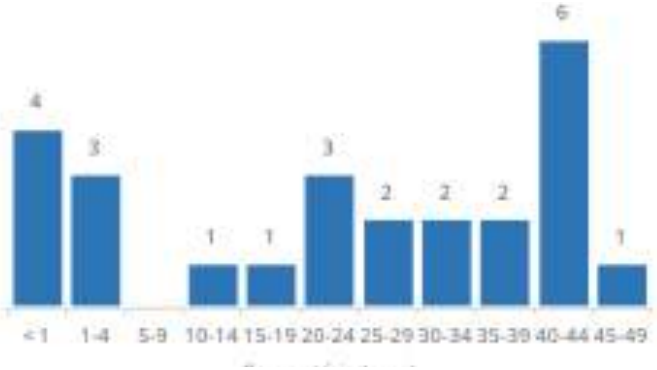
MEASLES CASES IN PORTUGAL – 2017

Cases on 2nd may/2017: week 18 (1 – 6th may/2017)

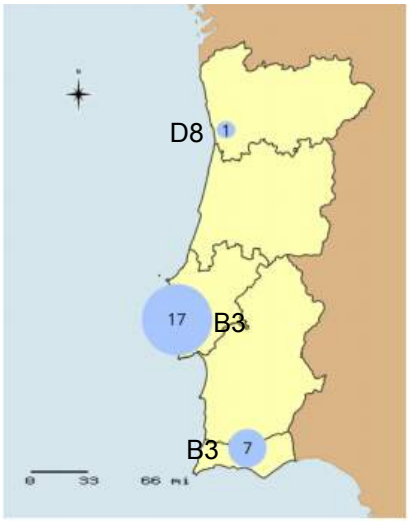
Confirmed cases by week of symptoms



Confirmed cases by age



Cases by Region



114 notifications since 1st jan/2017

27 confirmed cases

64% age ≥18yrs

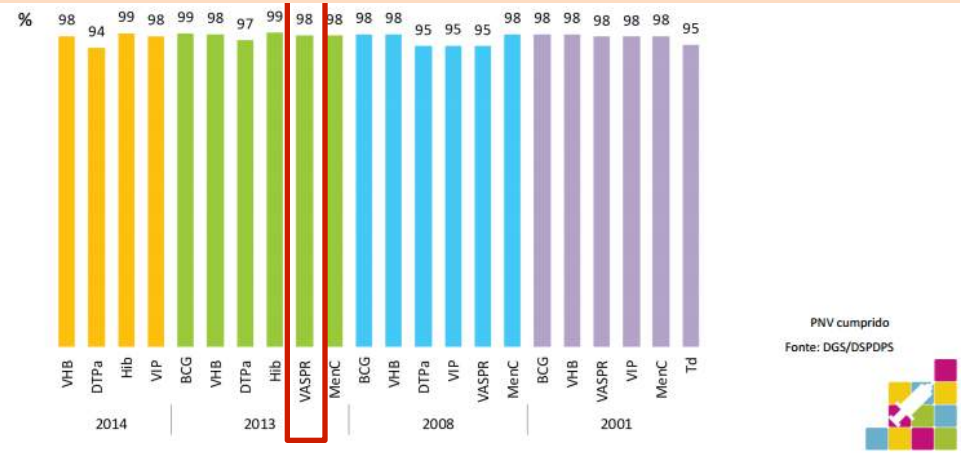
60% non-vaccinated

48% in healthcareworkers

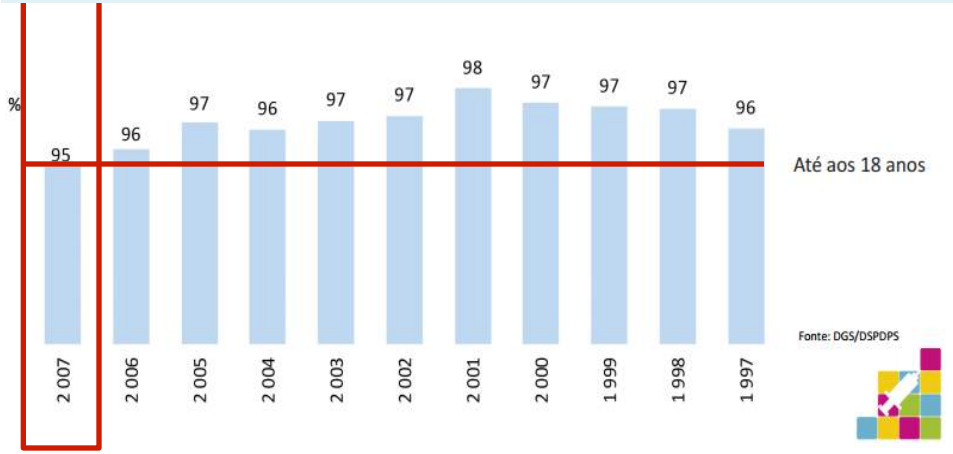
1 death

MMR VACCINE COVERAGE IN PORTUGAL

VACCINE COVERAGE BY BIRTH DATE



VACCINE COVERAGE MMR2 BY BIRTH DATE

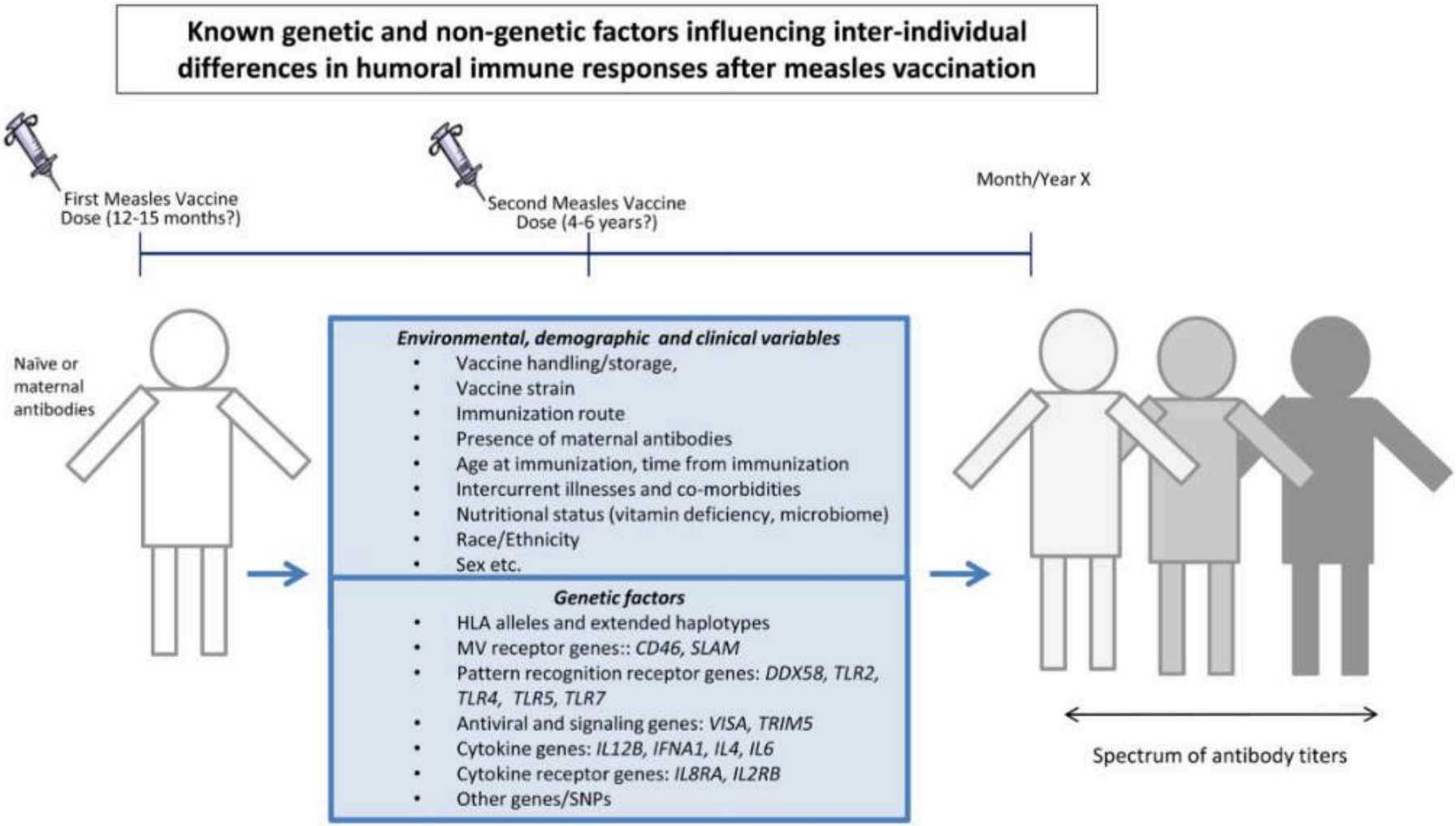


IMPORTANT TO CONSIDER:

- Seroprevalence – national data
- Vaccine coverage – local and regional
- Immunisation delay
- Vaccine failure

SOURCE: DGS

MMR VACCINE FAILURE – TYPE I AND II



Haralambieva IH et al..Trends Mol Med, 2015

MEASLES OUTBREAK – CASE DEFINITION

- **Possible case** (clinical criteria)
- **Probable case** (clinical and epidemiological criteria)
- **Confirmed case** (clinical and lab criteria)

CLINICAL CRITERIA	LAB CRITERIA	EPIDEMIOLOGICAL CRITERIA
Fever **and** Exanthem **and** **1 of:** Cough Rhinitis Conjunctivitis	**At least one of:** - MeV isolation (sample) - MeV RNA detection (sample) - Specific serum IgM detected - Seroconversion in 2 samples	Epidemiological link identified

DGS 2017. Norma SARAMPO: Procedimentos em unidades de saúde - Programa Nacional Eliminação Sarampo

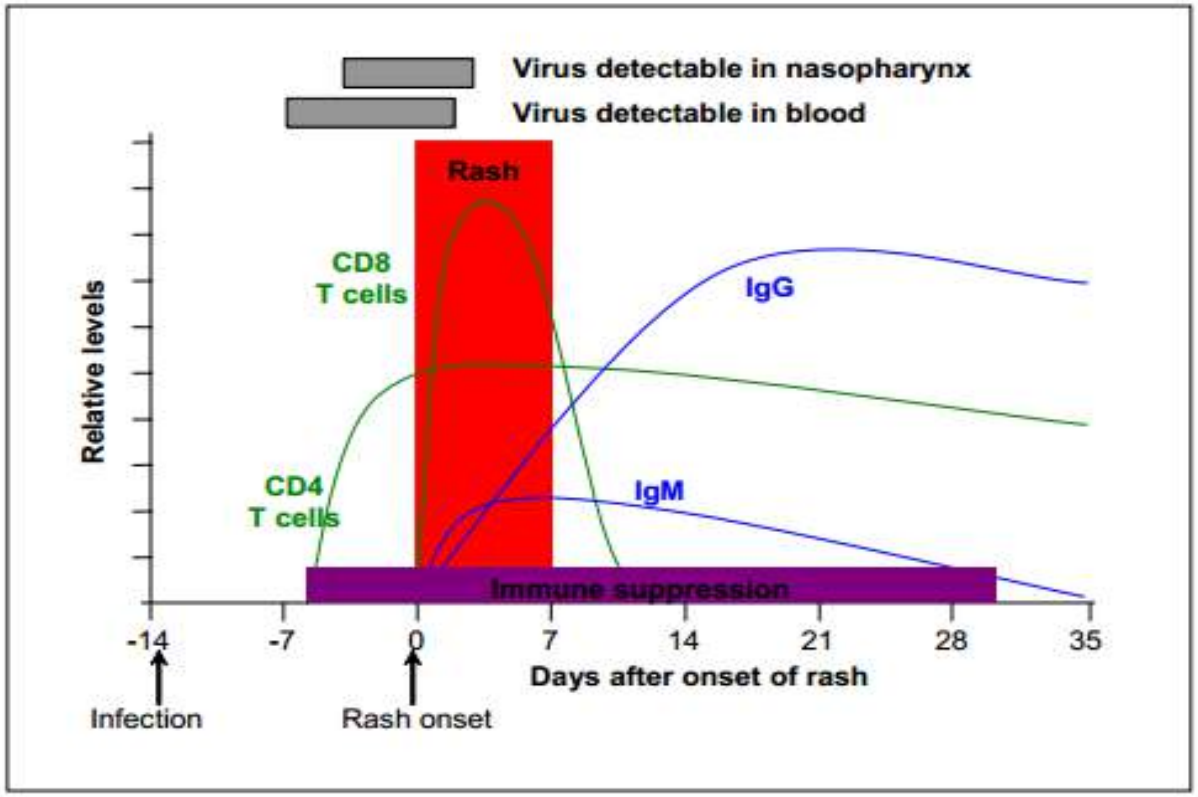
MEASLES OUTBREAK – LAB DIAGNOSIS

National reference laboratory – INSA

Samples sent free of charge

1. Serology
2. RT-PCR
3. Viral isolation

   Genetic analysis



Exanthem < 3 wks → Blood, Oral fluids / Oropharynx exudate, Urine

Exanthem > 3 wks → Blood

SOURCE: www.who.int/immunization_monitoring/LabManualFinal.pdf

MEASLES OUTBREAK: MANAGEMENT IN PORTUGAL

1. **Isolation of suspected cases**
2. **Identification and follow-up of contacts**
3. **Post-exposure vaccination (<72h) and IG**

CONTACT:

Any person who has shared the same space for any period of time, or being in the same location 30 mins after the patient has exited the location (during the infectious period)

- Cohabitants
- Healthworkers
- Patients in the same space
- Working or school colleagues
- Contacts during trips / transportation

DGS 2017. Norma SARAMPO: Procedimentos em unidades de saúde. Programa Nacional Eliminação Sarampo

MEASLES OUTBREAK: MANAGEMENT IN PORTUGAL

1. **Isolation**
2. **Identification and follow-up of contacts**
3. **Post-exposure vaccination (<72h) and IG**

AGE / CONDITION	REQUIRED MMR DOSIS
≥6M and <12M	1 dose (“*zero dose*”)
≥12M and <18yrs	2 dosis
≥18 yrs and bornt ≥1970	2 dosis
≥18 yrs and bornt <1970*	1 dose
Healthcare workers	2 dosis
HIV infection without immunosupression	In accordance with age and condition
Others	In accordance with age/condition

*National Serological Inquiry 2001-2002, >97% of protection

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MEASLES OUTBREAK: MANAGEMENT IN PORTUGAL

1. **Isolation**
2. **Identification and contacts follow-up**
3. **Post-exposure vaccination (<72h) and IG**

INDICATIONS FOR POST-EXPOSURE IG ADMINISTRATION	
Until 6 days post-exposure, when MMR is contraindicated or has risk of complications	Children <6M old Pregnant women HIV infection with immunosupression Severe Imunosupression
Until 6 days post-exposure, when MMR period of administration was overcomed	Children aged 6M–12M, without vaccine HIV infection without immunosupression Others

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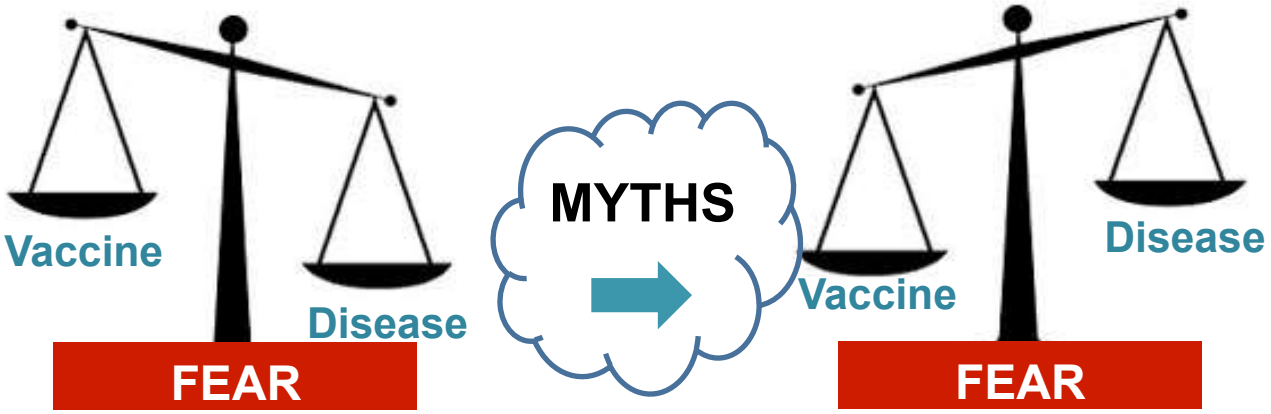
ERADICATION OF MEASLES: REMAINING CHALLENGES

- Fight vaccine coverage asymmetries
- Vaccine delay and false contraindications
- Anti-vaccine movements



Among 1 Million Children Infected With Measles

- 300 000 Children would have some form of complication, including:
- 50 000 Cases of pneumonia
- 80 000 Cases of diarrhea
- 70 000 Cases of otitis media
- 1000-3000 Cases of primary measles encephalitis
- 1000 Cases of acute postinfectious encephalomyelitis
- 110 Cases of subacute sclerosing panencephalitis
- 2000 Deaths

Among 1 Million Children Who Are Vaccinated and Do Not Develop Measles

- 999 966 Children would not experience a serious adverse effect
- 33 Cases of transient thrombocytopenia
- 1 Significant allergic reaction
- <1 (0.22) Case of encephalitis

Unmask

ERADICATION OF MEASLES: REMAINING CHALLENGES

- Elimination / Eradication is possible
  - ✓ Exclusive human transmission
  - ✓ Effective vaccine
- Management plan: transmission interrupted (south) and ↓ (Lisbon) in 2 months
- Fight vaccine hesitancy: teaching (not coercion / obligation)

HEPATITIS A NAD MEASLES OUTBREAK: DISCUSSION

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Thank you☺!