

-To travel is to live -



NECTM9

European Meeting on Immune Compromised Travellers



Measles, mumps, Rubella (MMR) vaccination in the immune compromised traveller and host

Micha Loebermann, Universitätsmedizin Rostock

Department of Tropical Medicine and Infectious Diseases

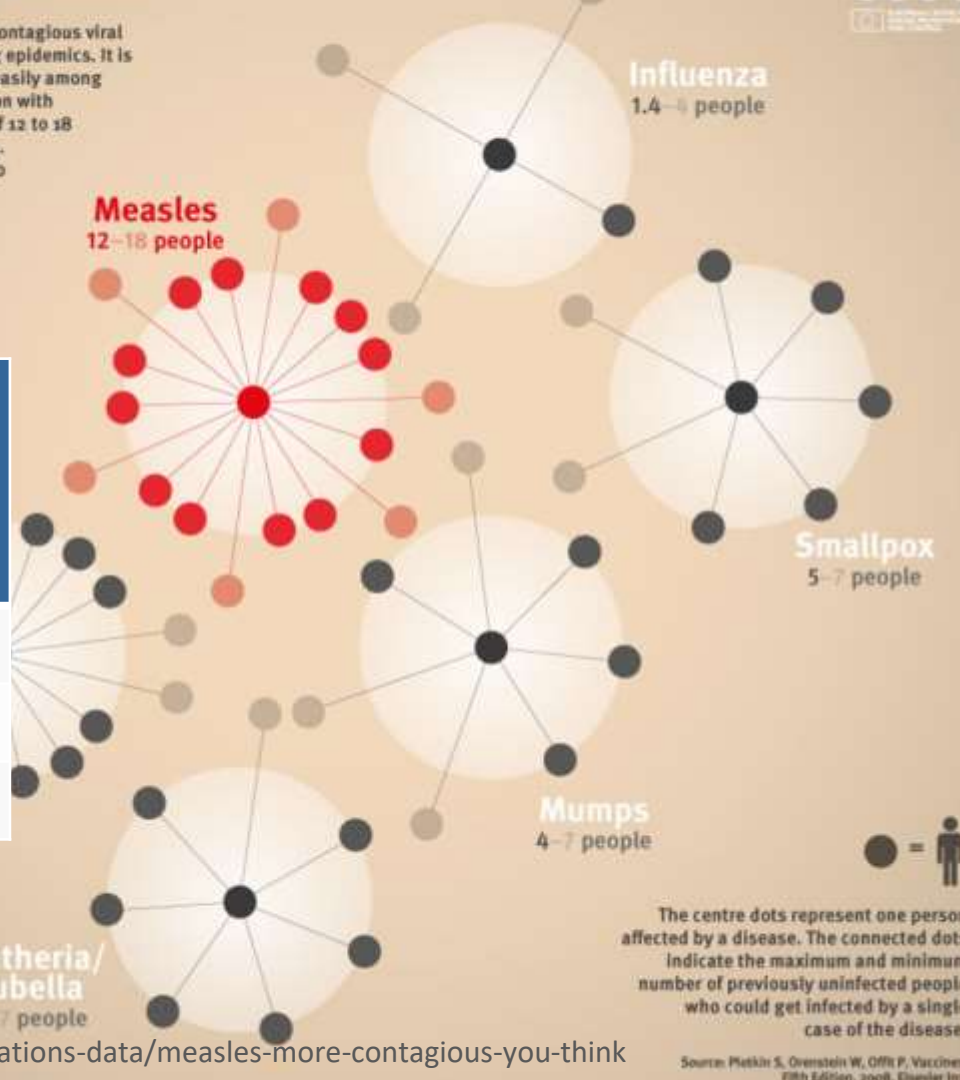
Disclosures

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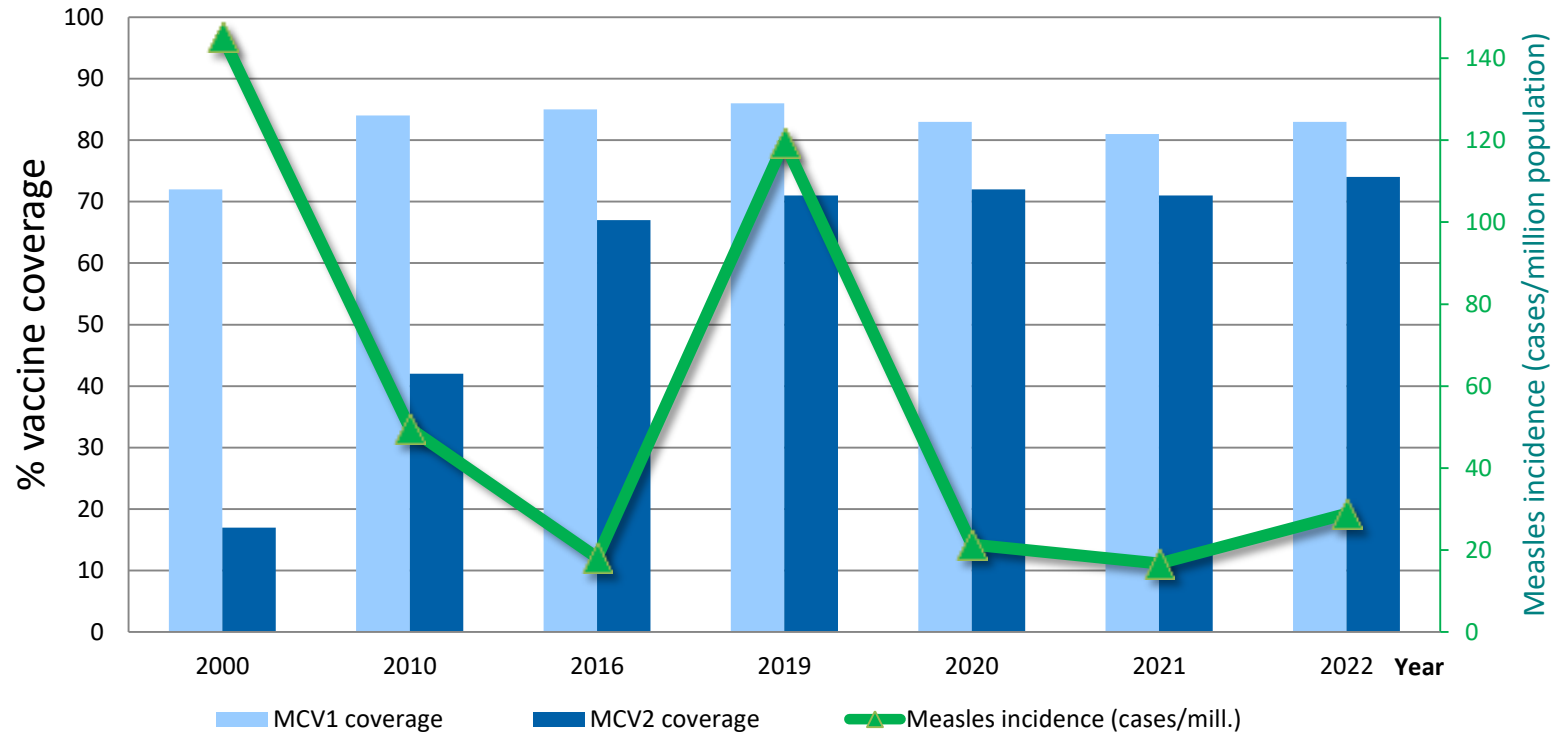
- Epidemiology of measles in travel
- Vaccination coverage in travellers
- MMR vaccine safety in immunosuppression
- Options for travellers at risk

Measles is an acute, highly contagious viral disease capable of producing epidemics. It is very infectious and spreads easily among unvaccinated people. A person with measles infects an average of 12 to 18 previously uninfected people. Vaccination is the best way to protect yourself and others against measles.

	Basic reproductive number (unprotected)	Vaccination Efficacy (1-2 doses)
Measles	12-18	95 - >99%
Mumps	4-7	78-88%
Rubella	6-7	98%

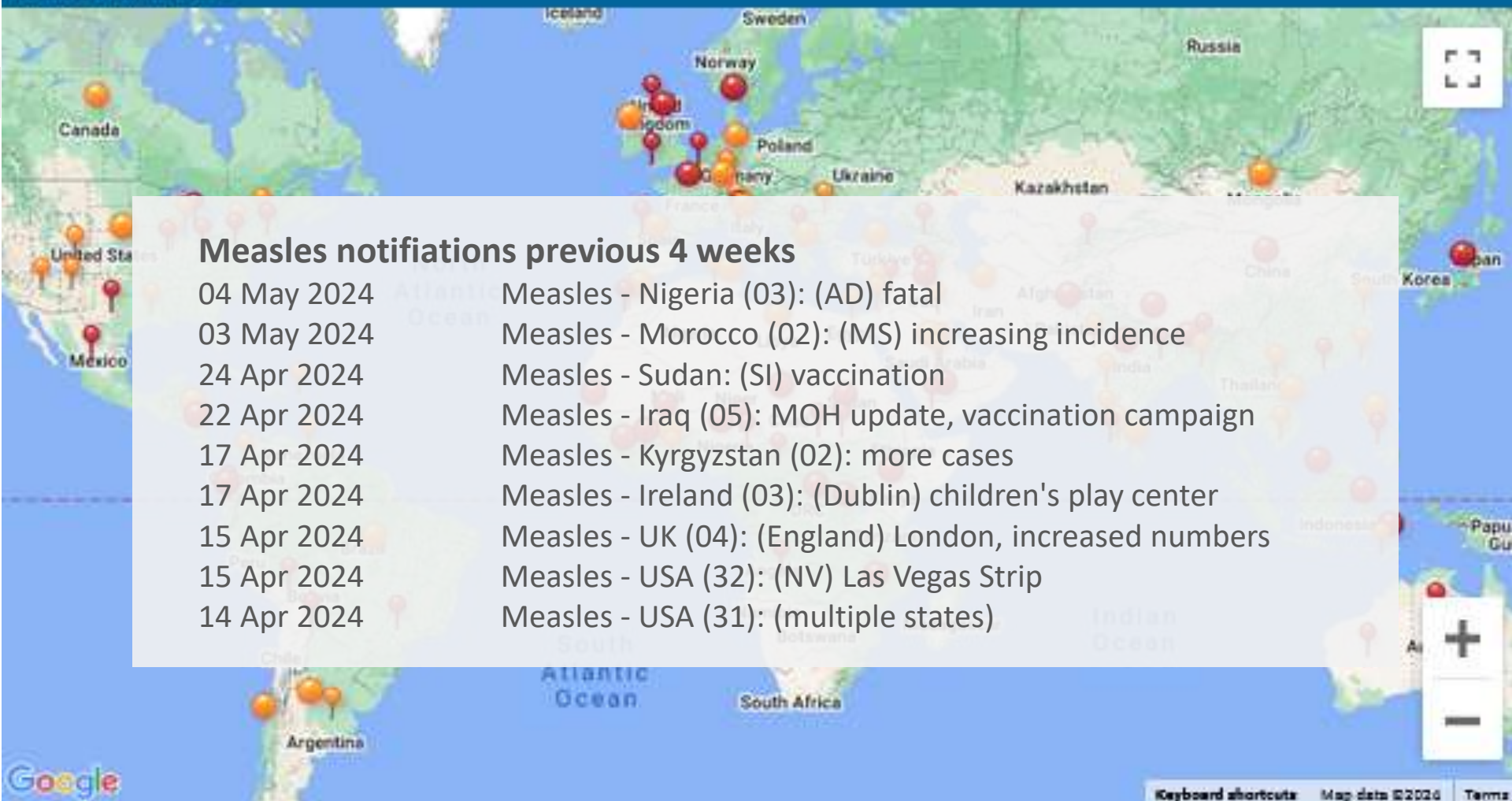


Measles vaccine coverage worldwide



Measles Outbrakes 2023

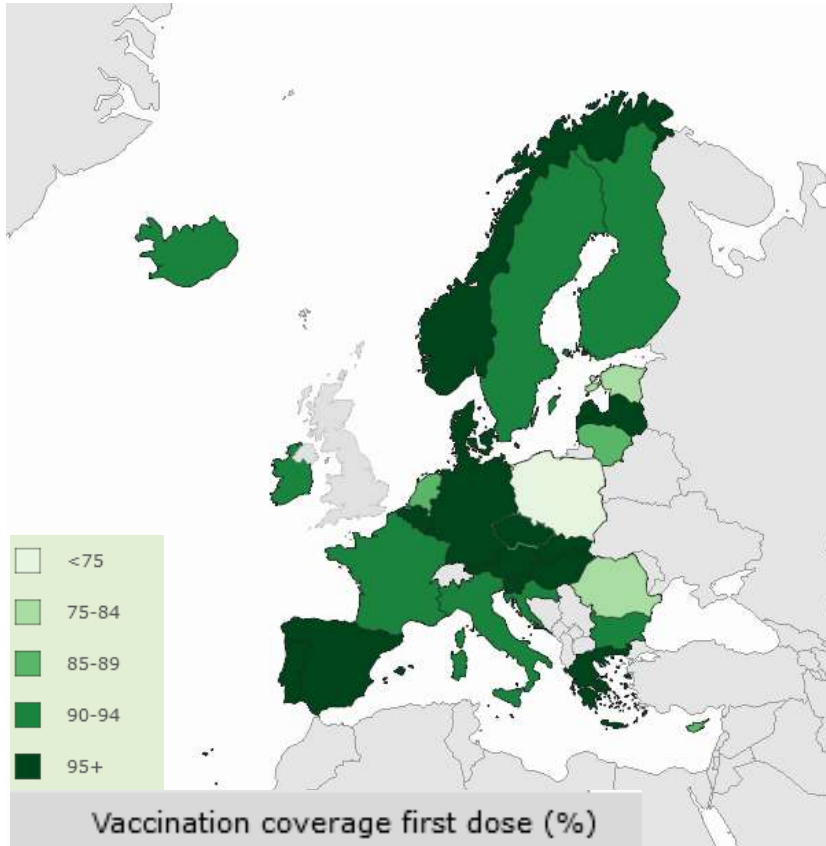




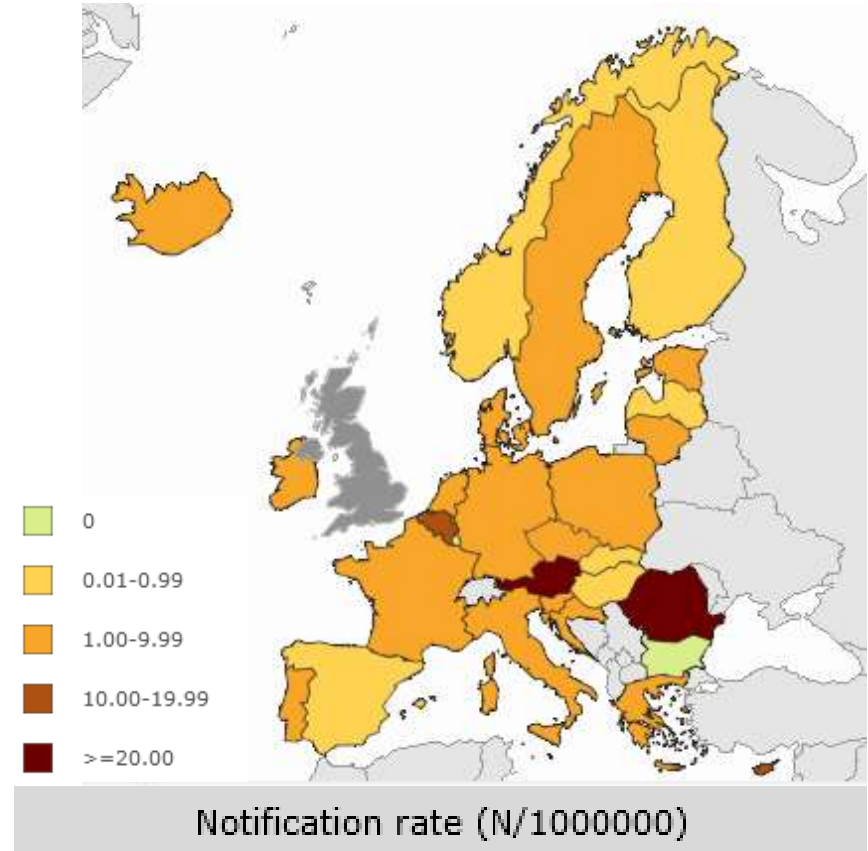
Measles notifications previous 4 weeks

- 04 May 2024 Measles - Nigeria (03): (AD) fatal
- 03 May 2024 Measles - Morocco (02): (MS) increasing incidence
- 24 Apr 2024 Measles - Sudan: (SI) vaccination
- 22 Apr 2024 Measles - Iraq (05): MOH update, vaccination campaign
- 17 Apr 2024 Measles - Kyrgyzstan (02): more cases
- 17 Apr 2024 Measles - Ireland (03): (Dublin) children's play center
- 15 Apr 2024 Measles - UK (04): (England) London, increased numbers
- 15 Apr 2024 Measles - USA (32): (NV) Las Vegas Strip
- 14 Apr 2024 Measles - USA (31): (multiple states)

MMR Vaccine coverage



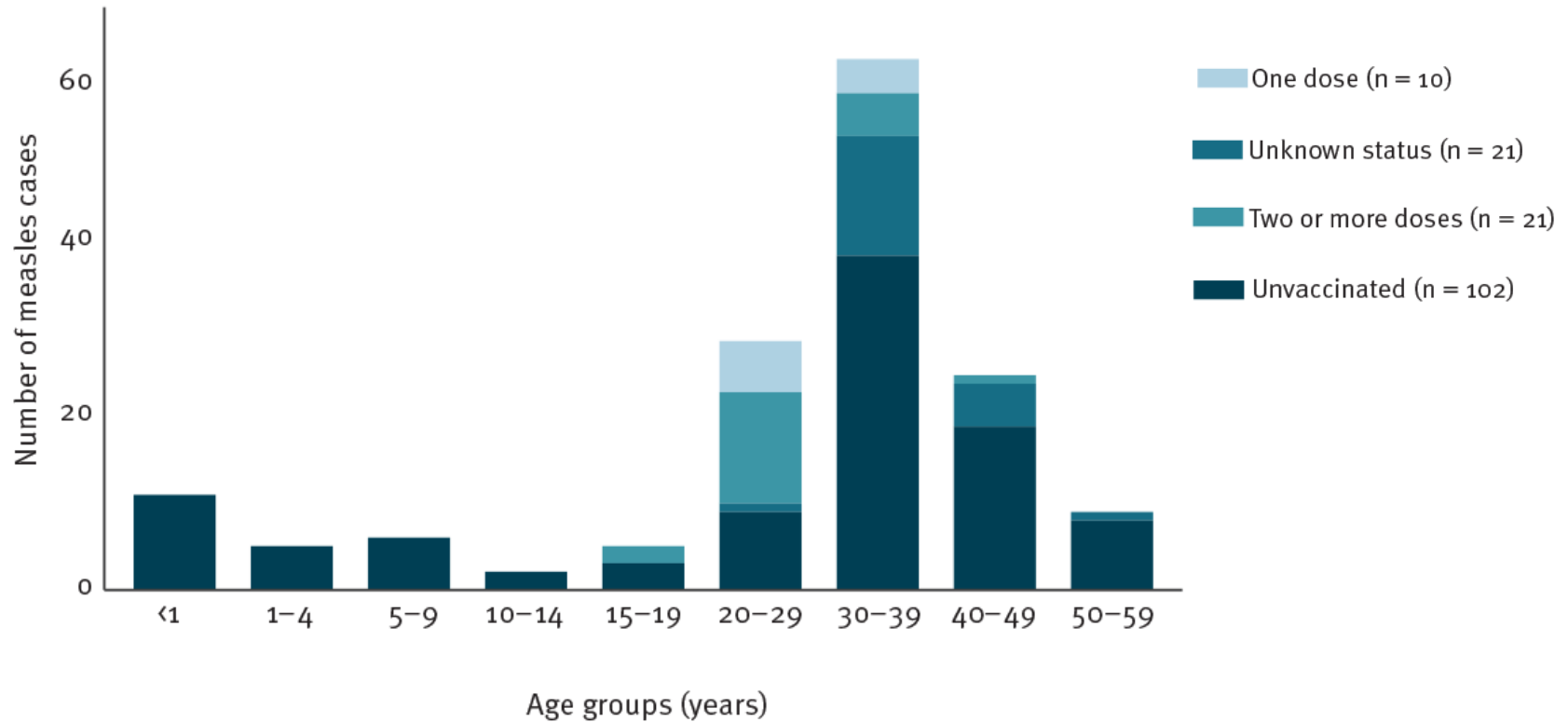
Measles rates (recent 12 months)



Measles following a trip to Italy

- d3: Nausea
- d7: fever, diarrhoea
- d9: exanthema, arthralgia, hypotension
- splenomegaly, Koplik spots, fever: 39°C, thrombo-/leukocytopenia
 - Measles PCR positive
 - Measles IgM and IgG positive
- Measles vaccinations in childhood

Interregional measles outbreak, Spain, November 2017 – July 2018



Travel associated measles (GeoSentinel 2000-2014)

94 cases (63% male; 87% aged 18-45 years)

Exposure:

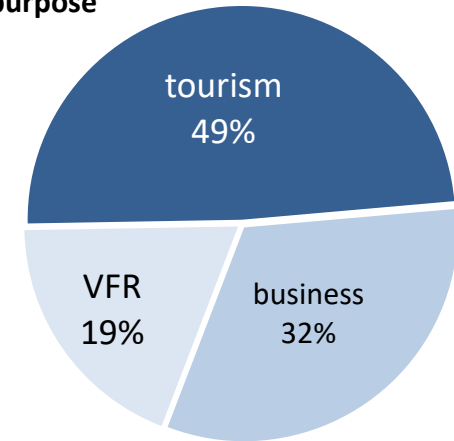
66% Asia

17% Africa

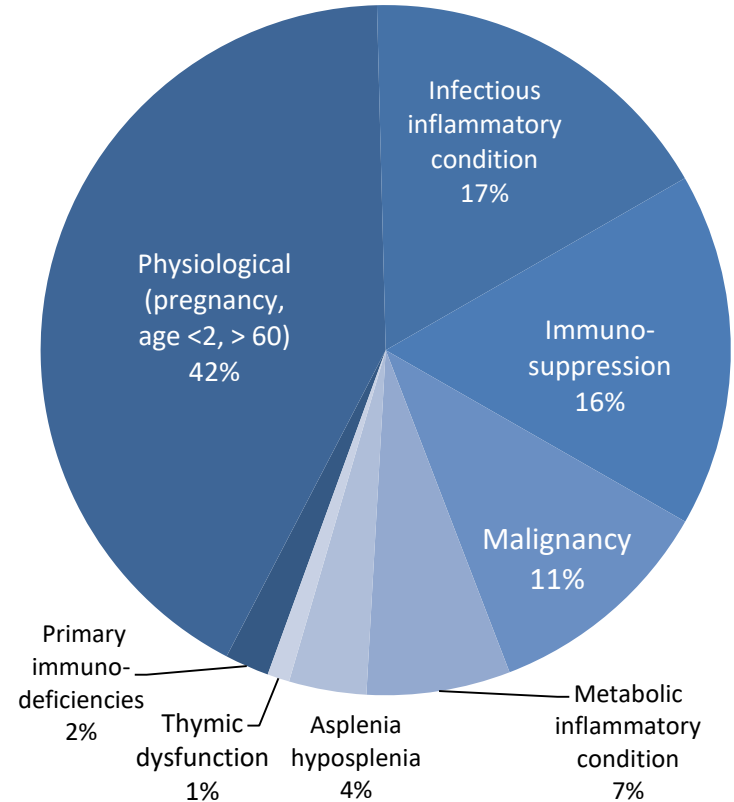
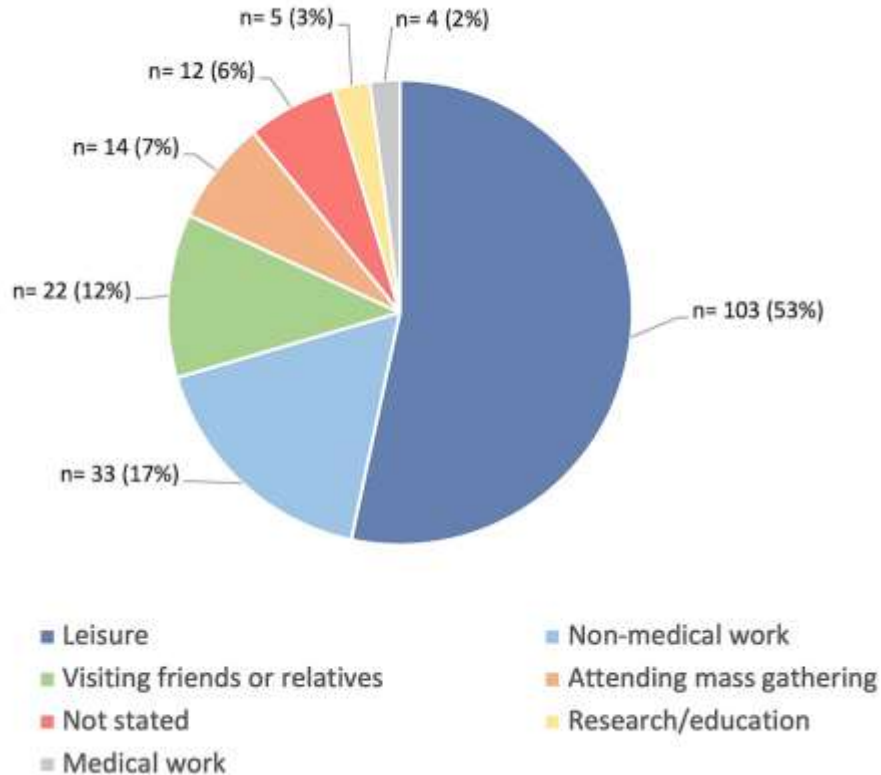
13% Europe

2%: Caribbean, Middle East, during flight

Travel purpose



Pre-travel advice for immunosuppressive conditions



RESEARCH

Open Access

Advising the immunocompromised traveller:
a review of immunocompromise at The
London Hospital for Tropical Diseases Travel
Clinic between 1st April 2019 and 30th April
2020

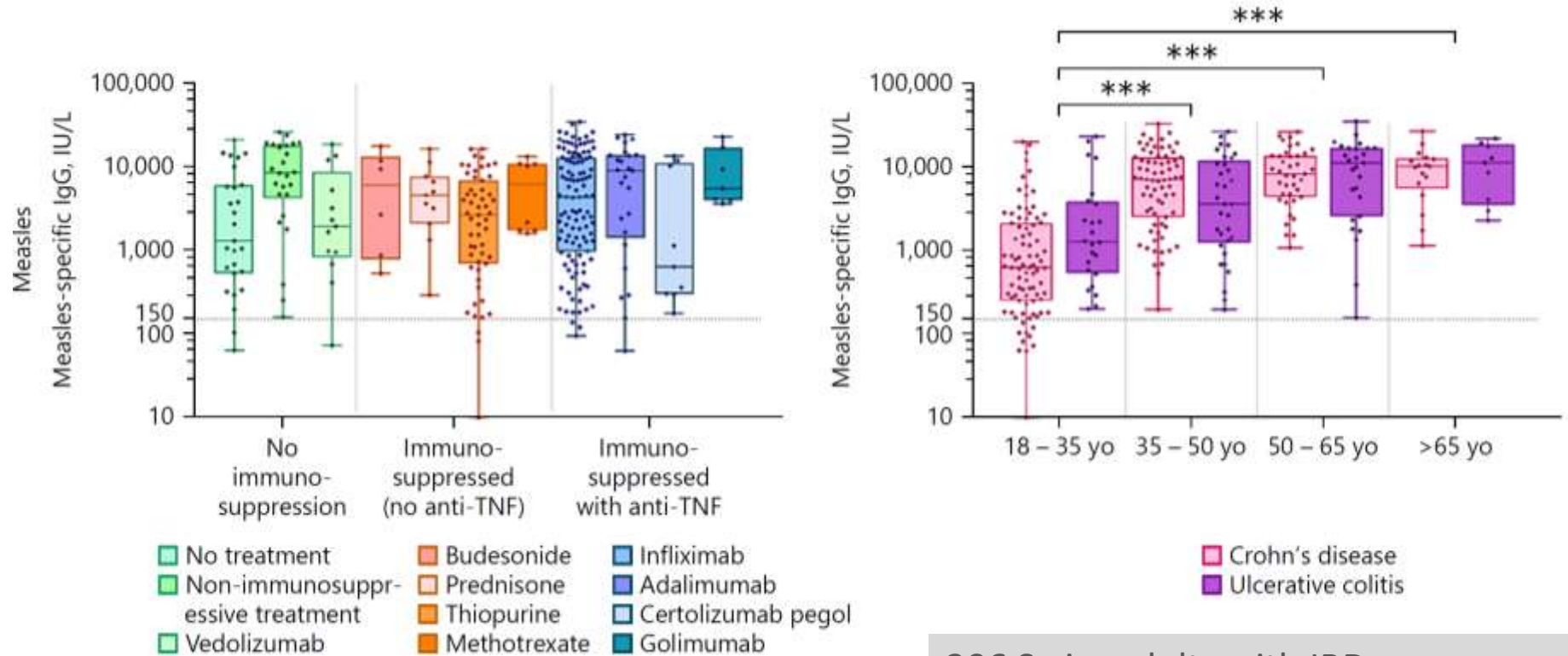


Ellen Beer^{1*}, Humayra Chowdhury², Bernadette Carroll³, Akish Luintel¹, Christoffer van Tulieken² and Nicky Longley^{2,3}

13/193 (6.7%): MMR vaccine was indicated for travel

- 7 vaccinated
- 5 MMR vaccine contraindicated (hematological malignancy, < 2y post HSCT, < 2y post CAR-T therapy, rituximab, current TNF-inhibitor)
3/5 residual measles antibodies

Measles antibodies in Inflammatory Bowel Disease



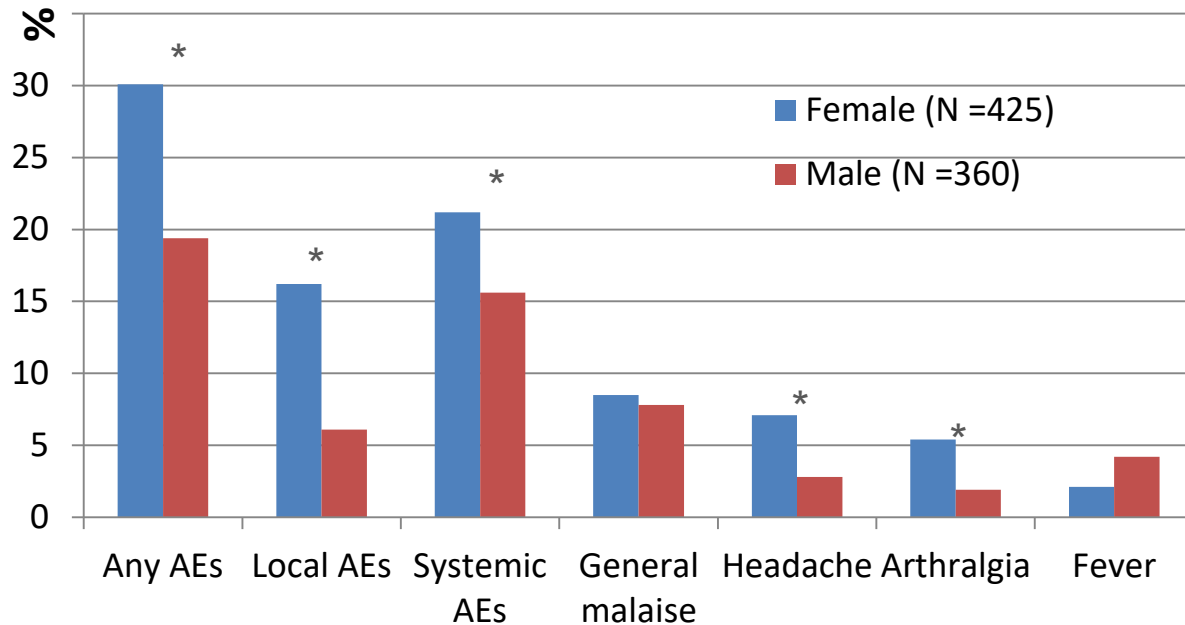
306 Swiss adults with IBD
 immunization record available in 33%
 3% not seroprotected (all < 30 years)

Humoral vaccine derived immunity under chemotherapy for malignancy

	Negative during and after chemotherapy	Negative during and positive after chemotherapy	Positive during and negative after chemotherapy	Positive during and after chemotherapy
Measles	2.9%	2.9%	16.8%	77.4%
Mumps	9%	12.8%	24.8%	53.4%
Rubella	8.6%	20%	12.4%	59%
Varicella	14.3%	25.7%	14%	49.5%

195 children/adolescents (< 21 years) with chemotherapy due to malignancies, ALL vs AML/Hodgkin/other neoplasia had significantly more loss of pre-existing immunity

Safety of MMR/V vaccine in adults



Travellers to high-risk regions with < 2 measles vaccines:

No difference between MMR vs. MMRV

More AEs in younger adults

Measles vaccine safety

Until 2024: 80 vaccine derived measles (laboratory confirmed)

- 5 deaths (3x primary immunodeficiency disorders; 1 ALL/chemotherapy <2 weeks; 1 AML/HCT < 2weeks; undiagnosed Hodgkin lymphoma at vaccination)
- 6 cases in adults (HIV, ALL/HCT, MS/natalizumab, postpartum, none/not specified) - all recovered

Symptoms 7-14 d post vaccination: fever, rash, cough, conjunctivitis, myalgia, giant cell pneumonitis

Chang SY et al. Open Forum Infect Dis. 2021;8(8):ofab326; Emerg Infect Dis. 2022;28(4):906-8; Ther Adv Vaccines Immunother. 2022;10:25151355221115016; Infect Med. 2023;2(1):57-62; Miauton A et al. BMC Infect Dis. 2020;20(1):753; Stokke JL et al. N Engl J Med. 2021;385(13):1246-8

Measles (MMR) vaccine in immunodeficiency conditions (ID)

condition	Interval from vaccination to ID	Vaccination during ID condition advised	Interval following ID to vaccination
Primary immunodeficiency		No	
Age > 60 years	none	Generally not needed when born before 1970	
Pregnancy	4 weeks	No	none
Chronic liver/renal disease	none	Yes	
Asplenia	none	Yes	
Blood transfusion/immunoglobulins			3 months
HIV		> 200 CD4/ μ l, VL negative (asymptomatic disease)	
Autoimmune disease (immunomodulatory tx)	> 4 weeks	No (booster vaccination may be safe)*	2 - > 12 months*
Stem cell transplant	> 4 weeks	No	> 2 years*
Solid Organ transplant	> 4 weeks	No*	

Measles (MMR) vaccine in immunomodulatory tx

Mechanism of action	Drug	Interval from vaccine to treatment (weeks)		Live vaccine during therapy permitted	Interval from treatment to live vaccine
		Inactivated vaccine	Live vaccine		
Direct depletion or cytotoxicity	Ocrelizumab	>6	>6	No	>18 months + normal B cell count
	Rituximab	>4	>4	No	>12 months + normal B cell count
	Ofatumumab	2-4	>4	No	Not studied; after B cell repletion (>40 weeks)
	Inebilizumab	>4	>4	No	After B cell repletion
	Alemtuzumab	6	6	No	>12 months + normal B cell count
Impairment of cell proliferation	Teriflunomide	2-4*	4	No	>6 months
	Azathioprine	2-4*	4	No	>3 months
	Cladribine	2-4*	4-6	No	4-6 weeks + normal lymphocyte count
	Cyclophosphamide	2-4*	4	No	>3 months
	Mitoxantrone	2-4*	4	No	>3 months
	Mycophenolate mofetil	2-4*	>4-6	No	>2 months
Inhibition of cell migration	Natalizumab	2-4*	4	No	>3 months
	Fingolimod	2-4*	4	No	>2 months
	Ozanimod	4*	>4	No	3 months
	Ponesimod	4*	>4	No	2 weeks
Pleiotropic effects	Siponimod	4	4	No	4 weeks
	IFNβ	0	0	Individual risk assessment	None
	Glatiramer acetate	2-4*	2-4*	Individual risk assessment (avoid YF vaccine)	None
	Dimethyl fumarate	2-4*	4	No (when lymphopenic)	After normalization of lymphocyte count

TABEL 1. Duur van het effect van immunosuppressieve medicatie na staken.

Medicatie	Farmacologische eliminatie	Duur van immunosuppressief effect na staken
Corticosteroiden >10 mg prednisolon of equivalent	weken tot maanden, afhankelijk van de dosis en behandelduur	1 maand
Calcineurineremmers		1-3 maanden
Ciclosporine	55 uur	
Tacrolimus	42-78 uur	
mTOR-remmers		3 maanden
Sirolimus	310 uur	
Everolimus	250-350 uur	
Azathioprine en andere thiopurines	25 dagen	3 maanden
Mycofenolzuur	90-90 uur	1 maand
Methotrexaat	20-40 uur	1 maand
Lymfocytenremmers		
Fingolimod	100 dagen	12 maanden
Alemtuzumab	afhankelijk van dosis	28 maanden
Abatacept	65 dagen	3 maanden
Dimethylfumarate/fumaraatzuur	5 uur	3 maanden
TNF-alfa-remmers		
Infliximab	90 dagen	3-6 maanden
Adalimumab, golimumab, certolizumab	70-90 dagen	3 maanden
Etanercept	350 uur	1 maand
Cytokineremmers		
IL-1 remmers, IL-2 basilicimab, IL-6 tocilizumab		
IL12/23 ustekinumab, IL-23 guselkumab, JAK-STAT inhibitori, IL-17A secukinumab, belimumab, brodalumab	30 uur t/m 135 dagen	Minimaal 3 maanden

Medicatie	Wiskundig	Latenstijd (dagen) na therapie*	Nieuwste therapie na latenstijd
Calcineurineremmers	Uitkomst: Niet	Uitkomst: Niet	Niet
Ciclosporine	Uitkomst: Niet	Uitkomst: Niet	Niet
Tacrolimus	Uitkomst: Niet	Uitkomst: Niet	Niet
Sirolimus	Uitkomst: Niet	Uitkomst: Niet	Niet
Everolimus	Uitkomst: Niet	Uitkomst: Niet	Niet
Azathioprine	Uitkomst: Niet	Uitkomst: Niet	Niet
Mycofenolzuur	Uitkomst: Niet	Uitkomst: Niet	Niet
Methotrexaat	Uitkomst: Niet	Uitkomst: Niet	Niet
Fingolimod	Uitkomst: Niet	Uitkomst: Niet	Niet
Ozanimod	Uitkomst: Niet	Uitkomst: Niet	Niet
Ponesimod	Uitkomst: Niet	Uitkomst: Niet	Niet
Siponimod	Uitkomst: Niet	Uitkomst: Niet	Niet
IFNβ	Uitkomst: Niet	Uitkomst: Niet	Niet
Glatiramer acetate	Uitkomst: Niet	Uitkomst: Niet	Niet
Dimethyl fumarate	Uitkomst: Niet	Uitkomst: Niet	Niet

MMR vaccine in immunosuppression

- MMR booster vaccine in juvenile idiopathic arthritis
 - (MTX or DMARDs) booster vaccine was safe, no measles during follow-up
- Children with autoimmune-inflammatory rheumatic disease
 - MMR/V booster vaccine safe and immunogenic (n= 234)
 - antibody response lower than in control group
- 716 Children with liver-transplantation: 833 measles vaccines safe (review)
- Seroconversion in post-transplant vaccination (various publications):
 - measles 44-100%, rubella 70-100%, mumps 48-100%

MMR vaccine in immunosuppression

- MMR primary vaccine in 2 patients with juvenile idiopathic arthritis
 - one (MTX and glucocorticosteroids) had fever+rash following vaccination
- 22 Patients (1-25 y.) with immunosuppressive tx (CsA, Tac, MMF, MZR, AZP, EVR, MTX):
 - no relevant AE after vaccination
 - all had negative or borderline measles antibody; normal CD4 count and IgG levels before vaccination
- No increased AE in travellers with immunosuppressive therapy
 - 21 of 197 travellers had MMR vaccination (mesalazine, methotrexate, adalimumab, IFN-beta, sulfasalazine), no relevant AE reported

Conclusions

- Measles may pose a risk in travel for those unprotected
- Need for protection with MMR should be evaluated prior to immunosuppression whenever possible
- MMR booster vaccination seems safe and effective in some immunosuppressive conditions (methotrexate, low dose glucocorticosteroids)
- missing evidence for primary MMR vaccination in immunosuppression
- If unprotected: other means of risk reduction (avoid regions with outbreaks, avoid mass gatherings, postpone travel ...)

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