

Österreich – Masernland: Erkenntnisse am Nationalen Referenzlabor

Assoc.Prof.Priv.Doiz.Dr. Lukas Weseslindtner

Dr. David Springer

Dr. Jeremy Camp

Christian Borsodi

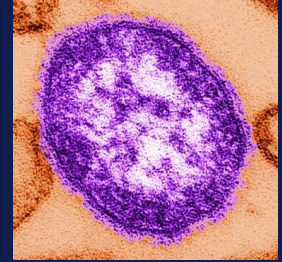
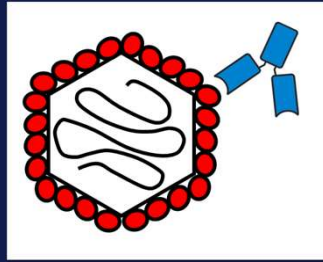


Image: CDC/ Cynthia S.
Goldsmith; William
Bellini, PhD)

Center for Virology

Medical University of Vienna

NRL for Measles, Mumps & Rubella

Participant for Austria of the WHO European Regional

Measles / Rubella Laboratory Network

EUVAC.NET (EU)



Lukas Weseslindtner
Zentrum für Virologie

Das Virus Die Erkrankung

Lukas Weseslindtner
Zentrum für Virologie

Measles Virus: Pathogenesis

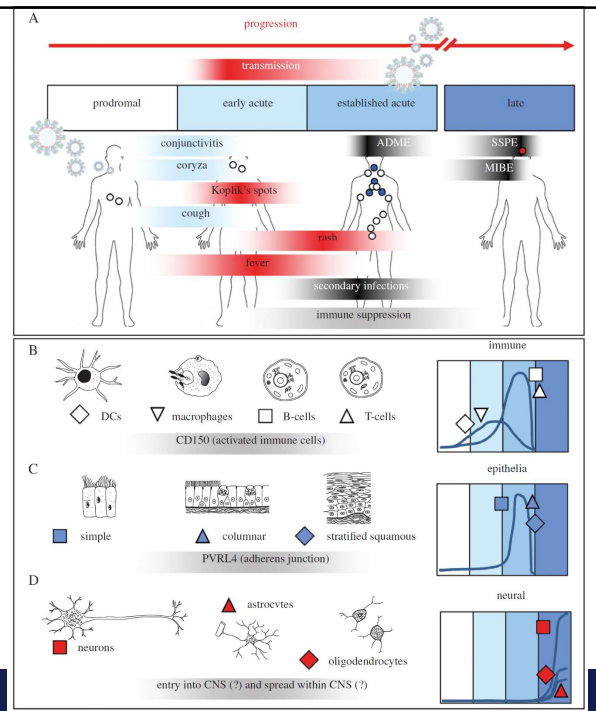
J Pathol 2015; **235**: 253–265
www.thejournalofpathology.com



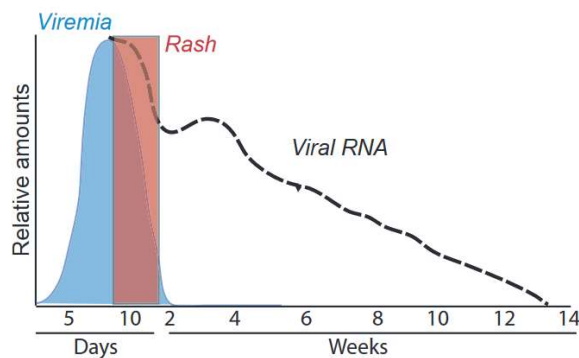
Immune cells

Epithelial cells

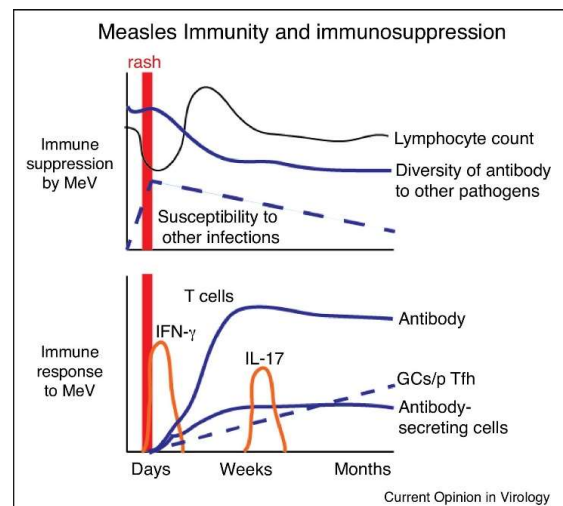
Cells in the Central Nervous System



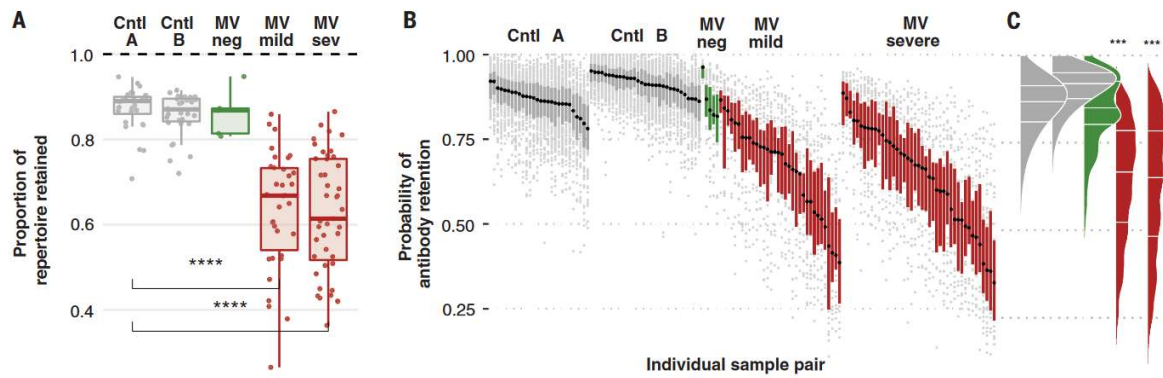
Measles Virus: Virus persistence and Immunosuppression



FEMS Microbiol Rev **36** (2012) 649–662



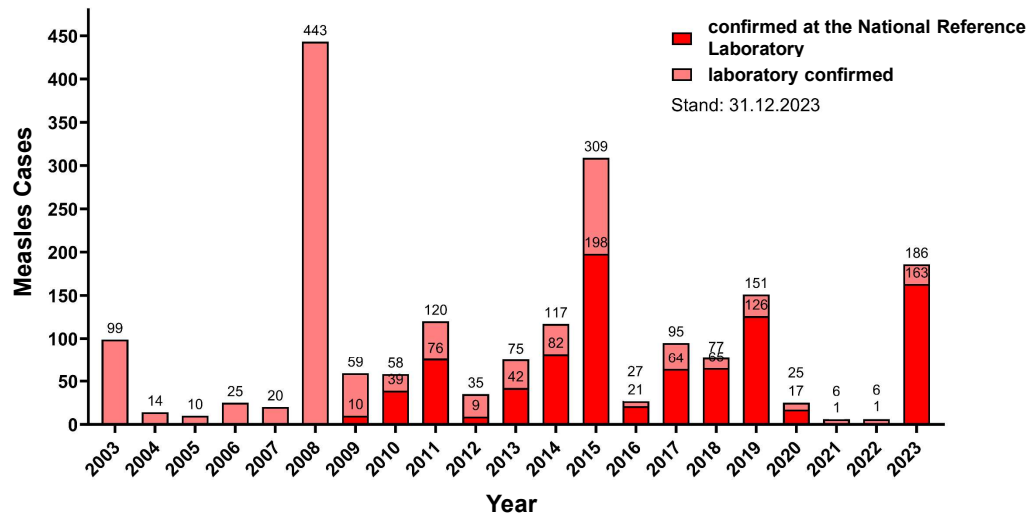
Measles Virus: Reduction of antibody diversity



Mina *et al.*, *Science* **366**, 599–606 (2019)

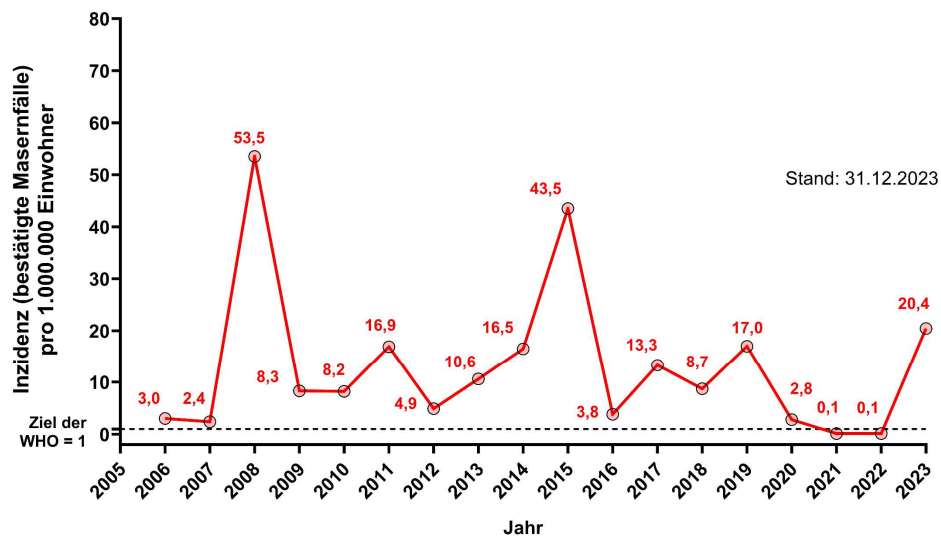
2023: Prolog für die aktuelle Situation

Measles Cases in Austria 2023



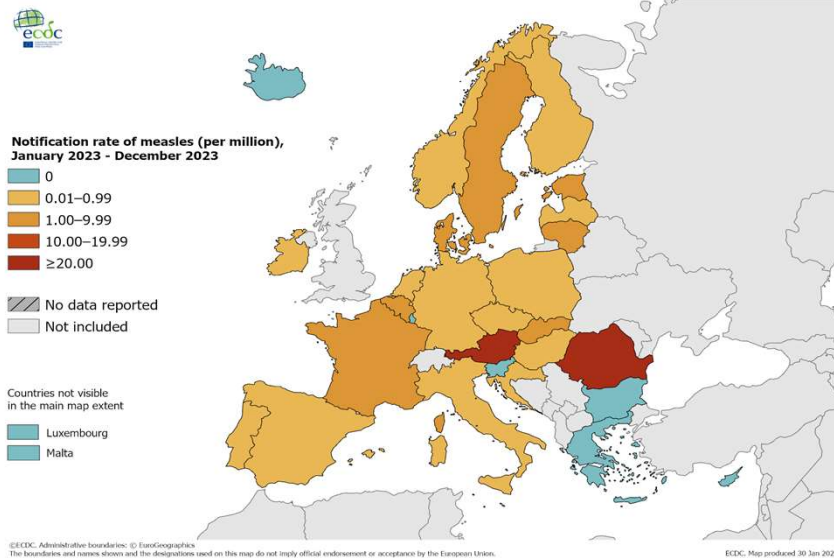
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Measles Incidence in Austria 2023



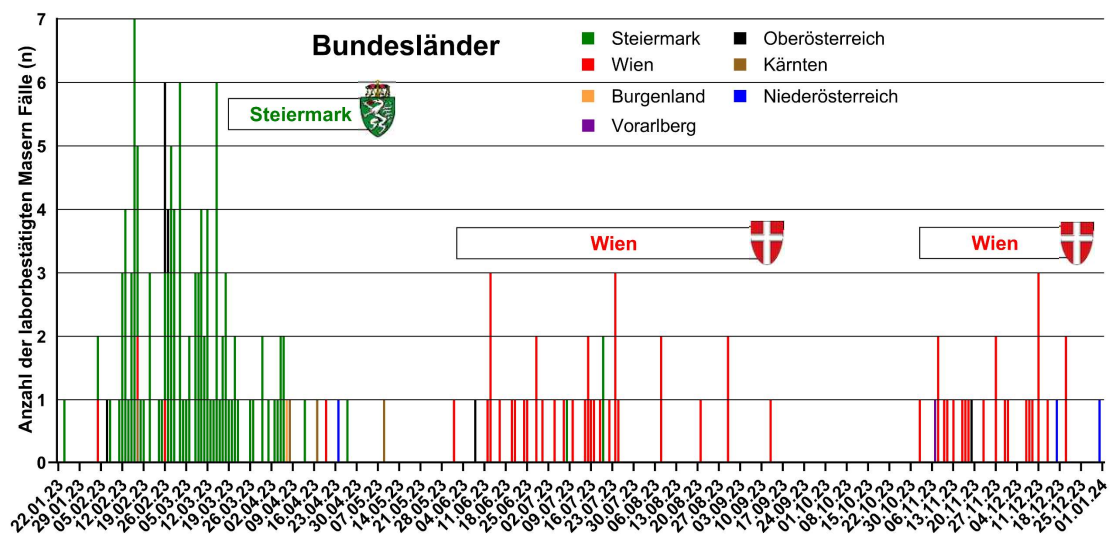
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Measles Incidence in Europe 2023



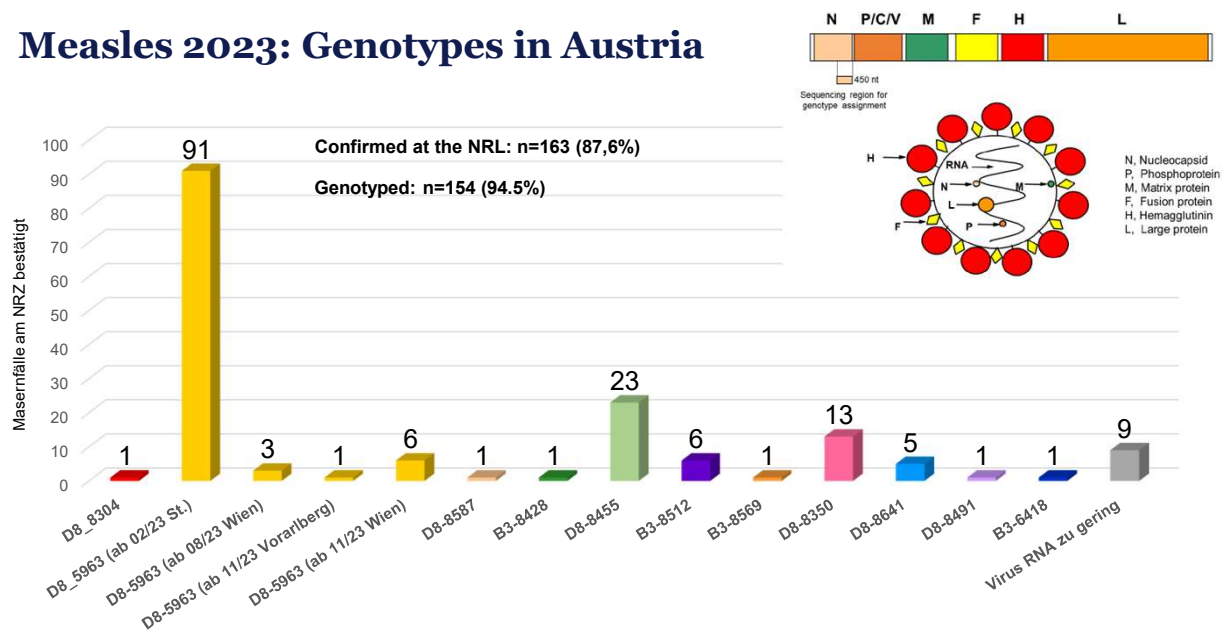
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Measles Cases 2023 in different districts (Bundesländer)

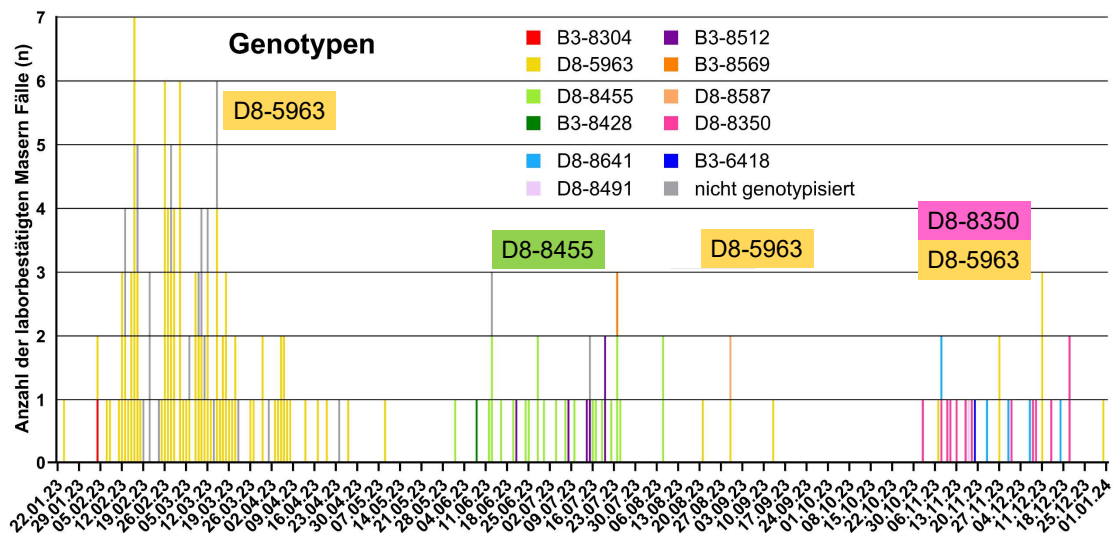


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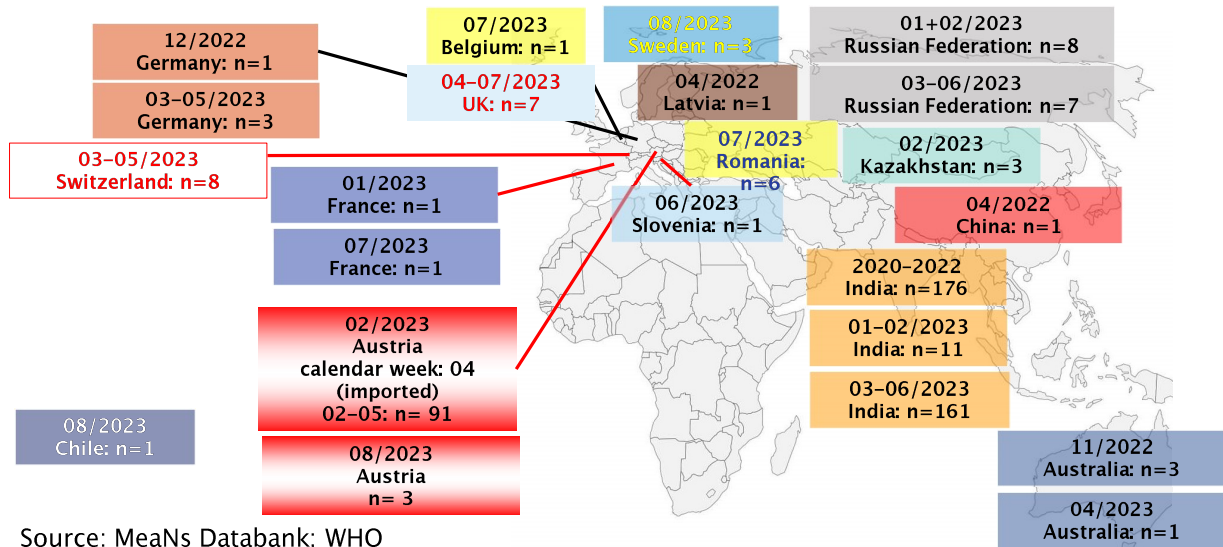
Measles 2023: Genotypes in Austria



Measles Cases 2023: Genotypes



Measles Virus Genotype D8-5963: pre- and post-arrival in Austria



Measles Virus Genotype D8-5963






Country	Date received	Country	Date received
Romania	2023-07-13	Romania	2023-08-21
Romania	2023-07-13	Romania	2023-08-22
Romania	2023-07-17	UK	2023-08-23
France	2023-07-18	Sweden	2023-08-23
Romania	2023-07-18	Germany	2023-08-29
Maldives	2023-07-23	Austria	2023-08-29
Ukraine	2023-07-26	Sweden	2023-08-29
Ukraine	2023-07-26	Sweden	2023-08-30
Ukraine	2023-07-26	Netherlands	2023-08-31
Belgium	2023-08-03	Ukraine	2023-09-01
Romania	2023-08-03	Romania	2023-09-01
Denmark	2023-08-03	Austria	2023-09-01
Kazakhstan	2023-08-04	Uzbekistan	2023-09-13
India	2023-08-04	Germany	2023-09-14
India	2023-08-05	Austria	2023-09-18
Sweden	2023-08-10	New Zealand	2023-09-27
India	2023-08-11	Switzerland	2023-10-05
Chile	2023-08-11	Oman	2023-10-08
Denmark	2023-08-14	Croatia	2023-10-16
UK	2023-08-15	Romania	2023-10-19

Measles Virus Genotype D8-8455



Source: MeaNs Databank; WHO

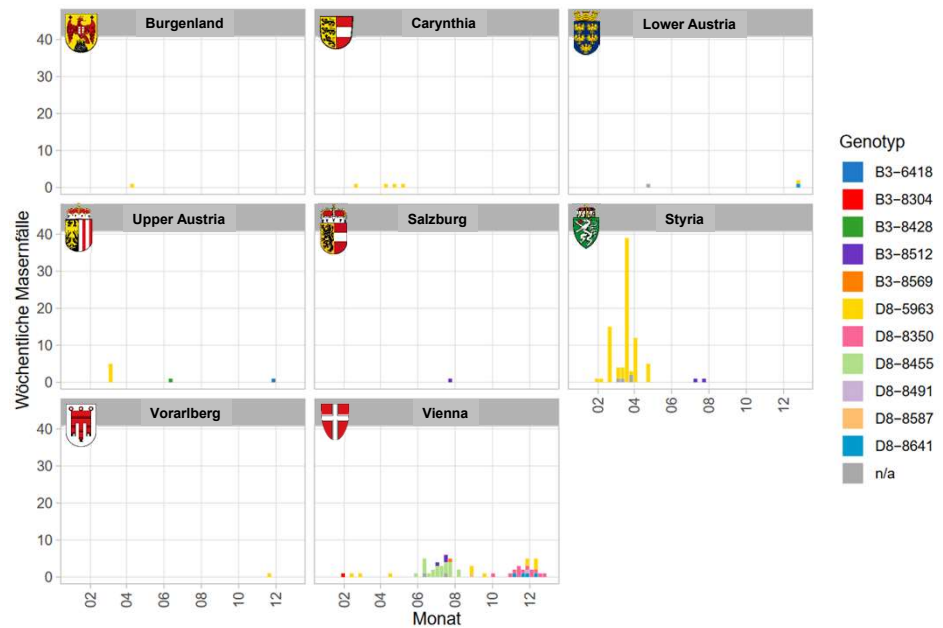
Measles Virus
Genotype D8-
8350

Country		Date received	Country		Date received
Romania		2023-08-07	Spain		2023-09-12
Romania		2023-08-07	Romania		2023-09-13
Romania		2023-08-07	Spain		2023-09-15
Romania		2023-08-18	Romania		2023-09-22
Switzerland		2023-08-20	Romania		2023-09-22
Romania		2023-08-22	Romania		2023-09-25
Romania		2023-08-24	Romania		2023-09-26
Romania		2023-08-25	France		2023-09-28
Romania		2023-08-27	Romania		2023-10-03
Romania		2023-08-28	Romania		2023-10-04
Romania		2023-08-28	Romania		2023-10-04
Romania		2023-08-29	Romania		2023-10-06
Romania		2023-08-29	Romania		2023-10-12
Romania		2023-08-30	Romania		2023-10-16
Germany		2023-08-31	Romania		2023-10-20
Romania		2023-09-01	Romania		2023-10-22
Romania		2023-09-05	Austria		2023-11-02
Romania		2023-09-05	Austria		2023-11-12
UK		2023-09-07	Austria		2023-11-12
Romania		2023-09-11	Austria		2023-11-12

Measles Cases 2023 Districts and genotypes

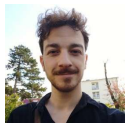


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Measles Cases 2023 Districts and genotypes

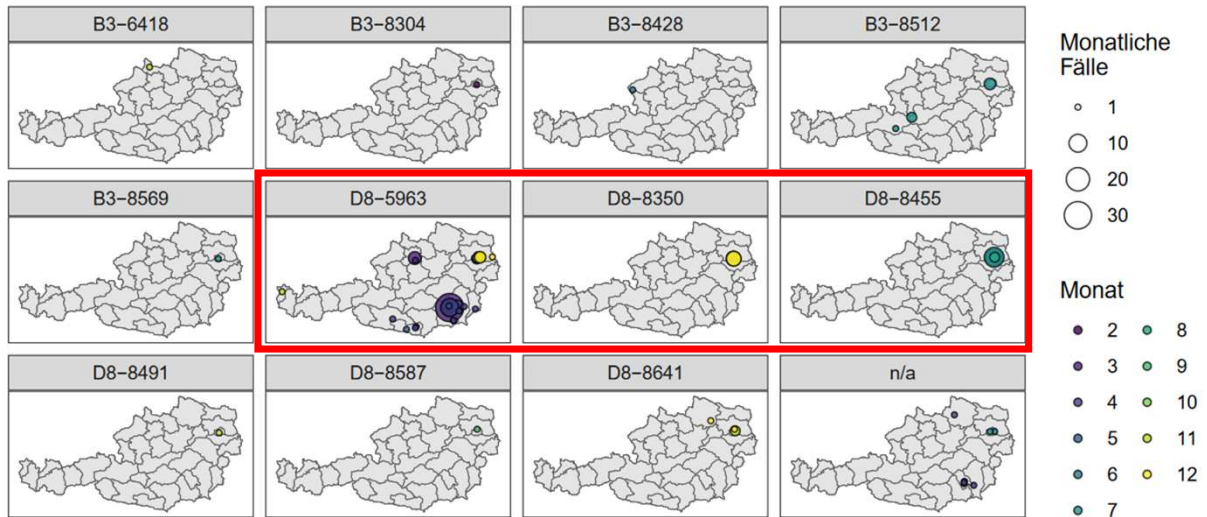


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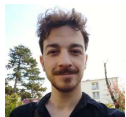


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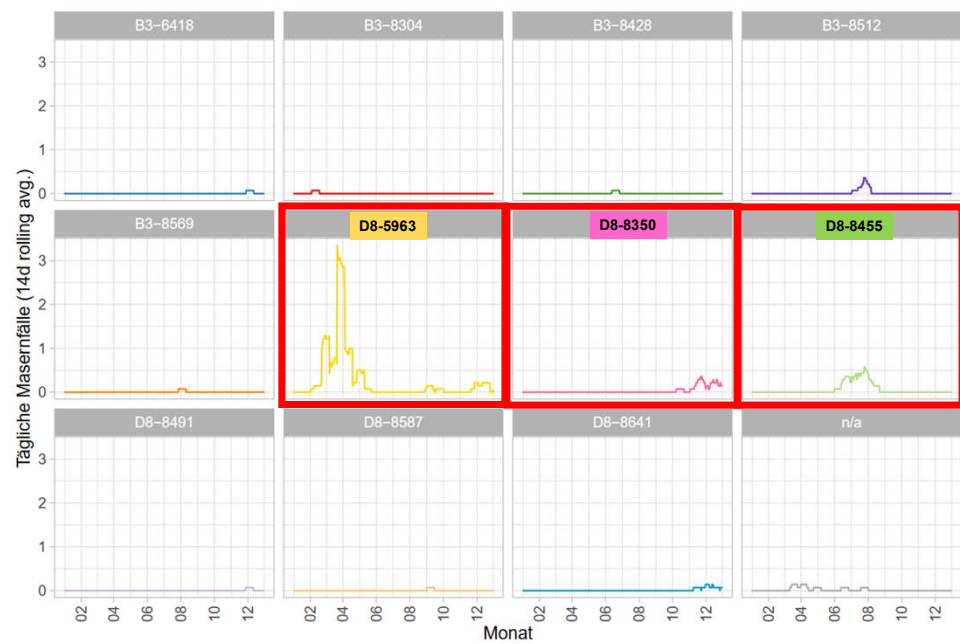
Measles Cases 2023: Spread of genotypes in different parts of Austria



Measles 2023: Most genotypes could be controlled

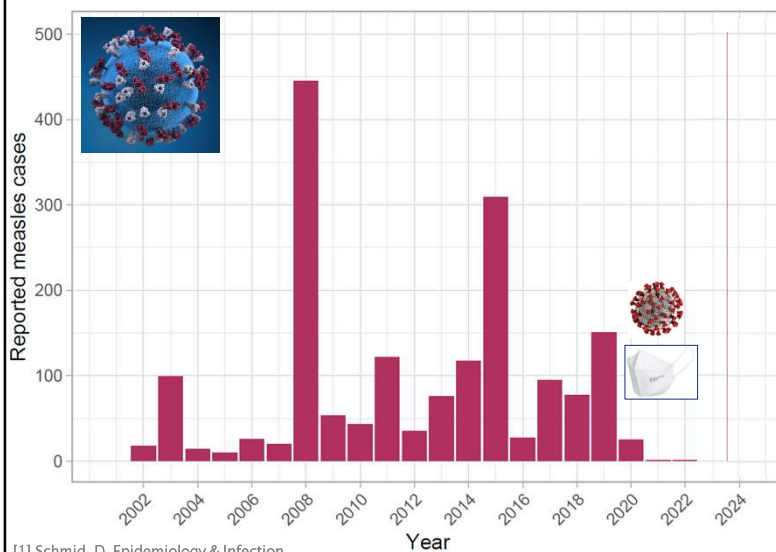


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2024: Österreich wird Masernland

Masern in Österreich, 2000 – 2024



2023: 186 Fälle (20.4 / Mio)

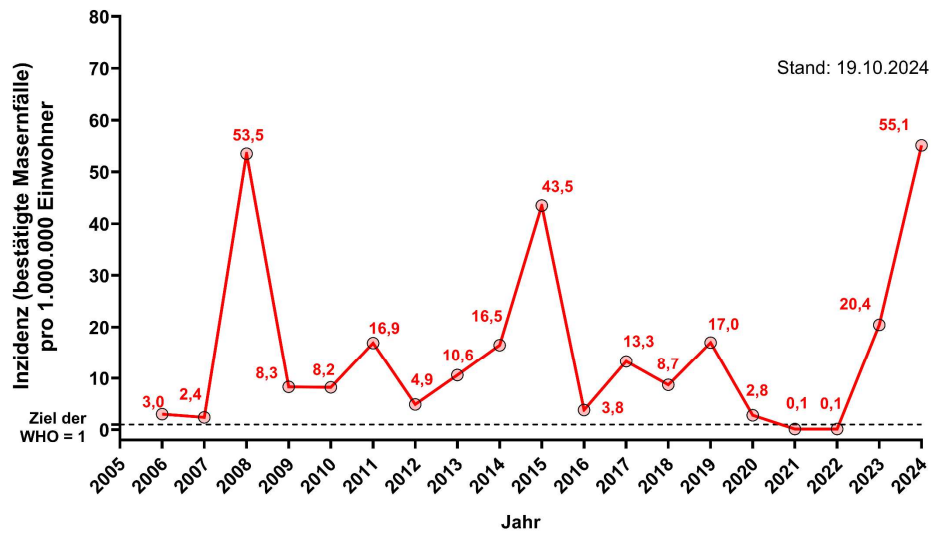
2024: > 500 Fälle (~55 / Mio)

[1] Schmid, D. Epidemiology & Infection

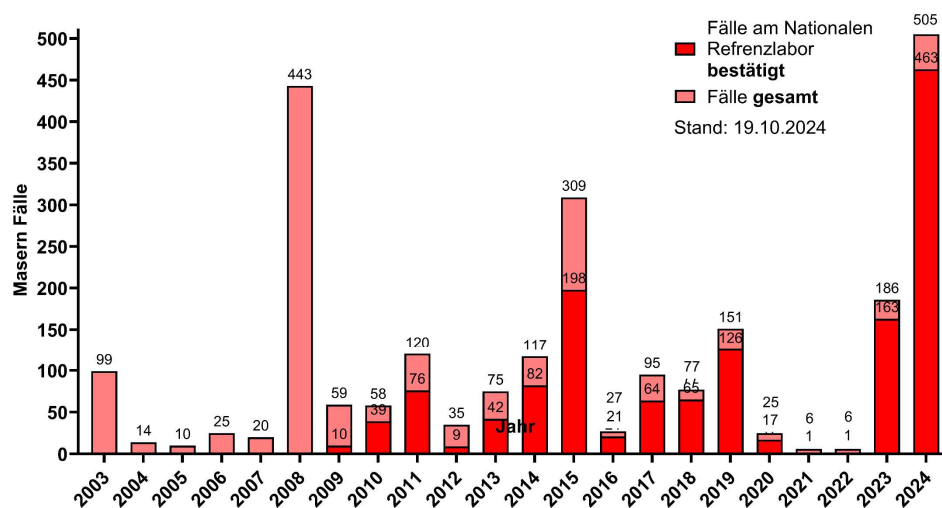
Dr. David Springer



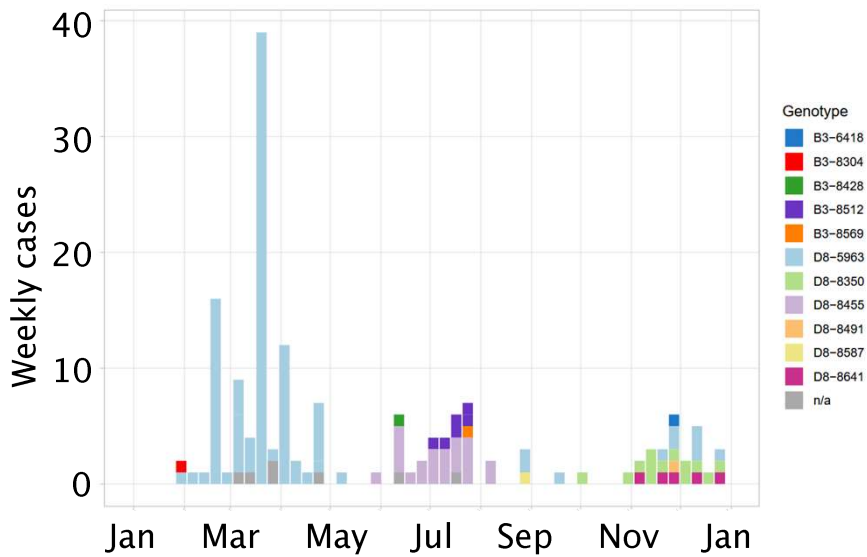
Measles Cases in Austria 2024



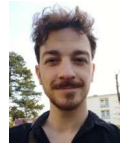
Measles Incidence in Austria 2024



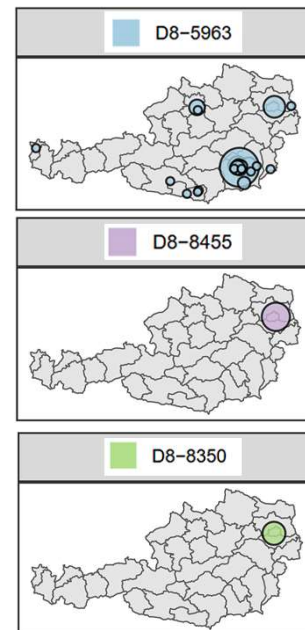
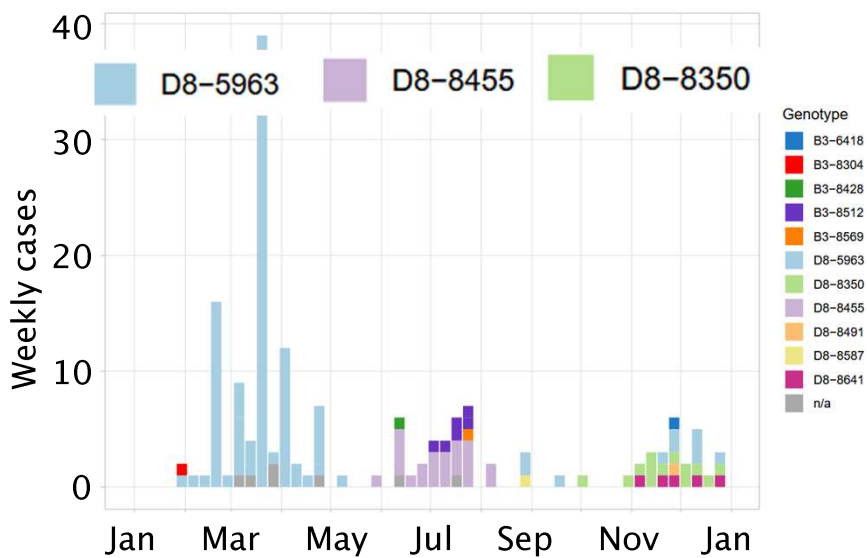
2023: Große regionale Ausbrüche



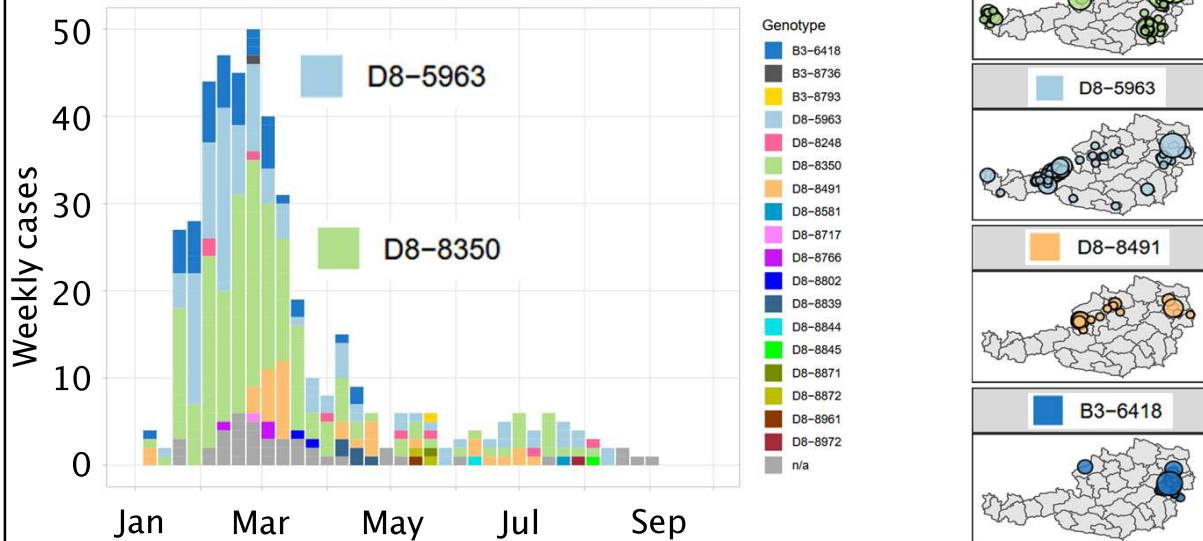
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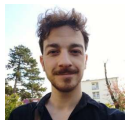
2023: Große regionale Ausbrüche



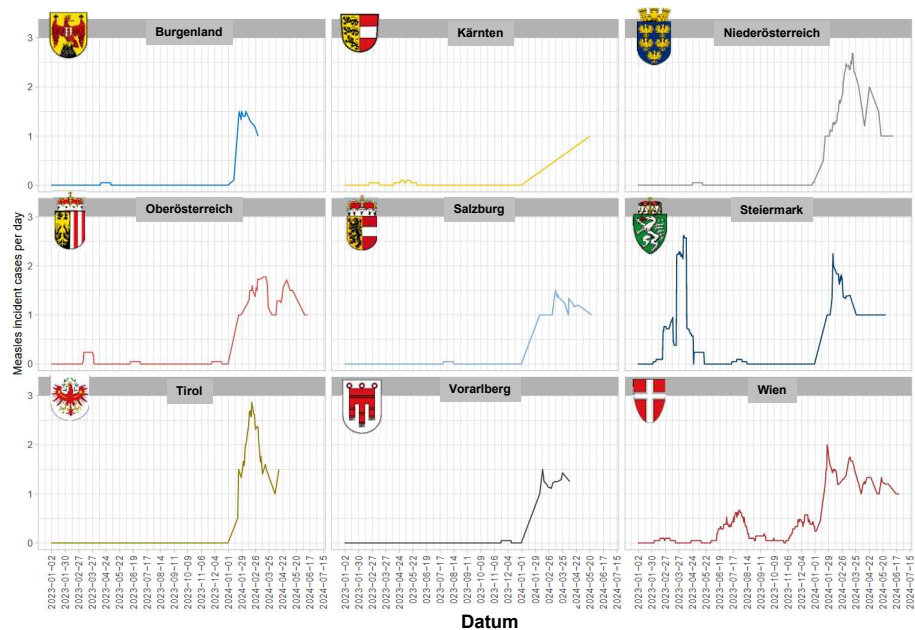
2024: Masern überall in Österreich



Measles Incidence (cases per day) in Austria 2024: districts



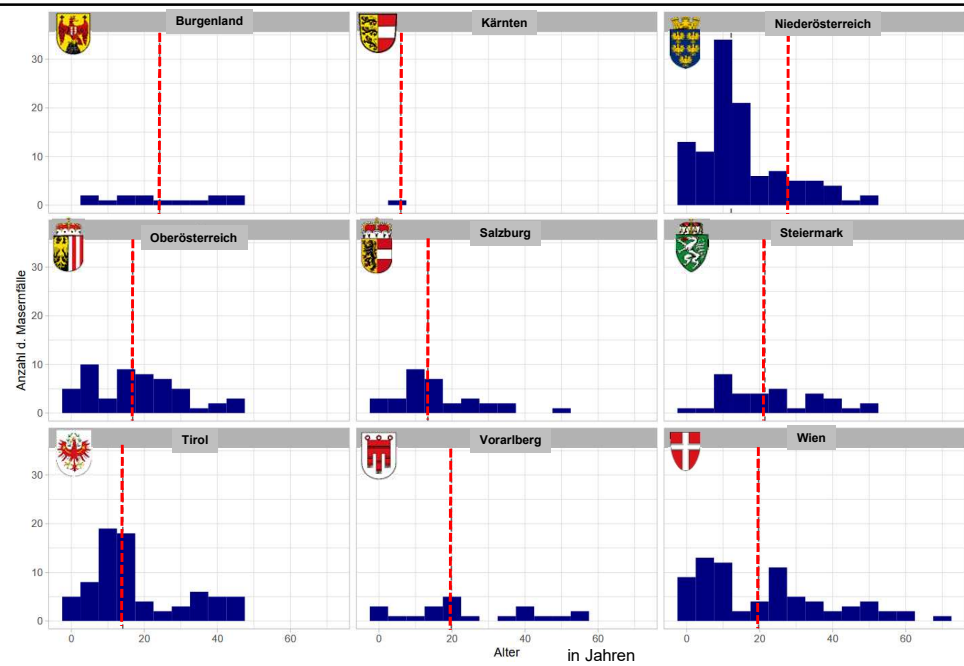
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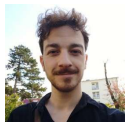
Age of at the NRL confirmed cases: districts



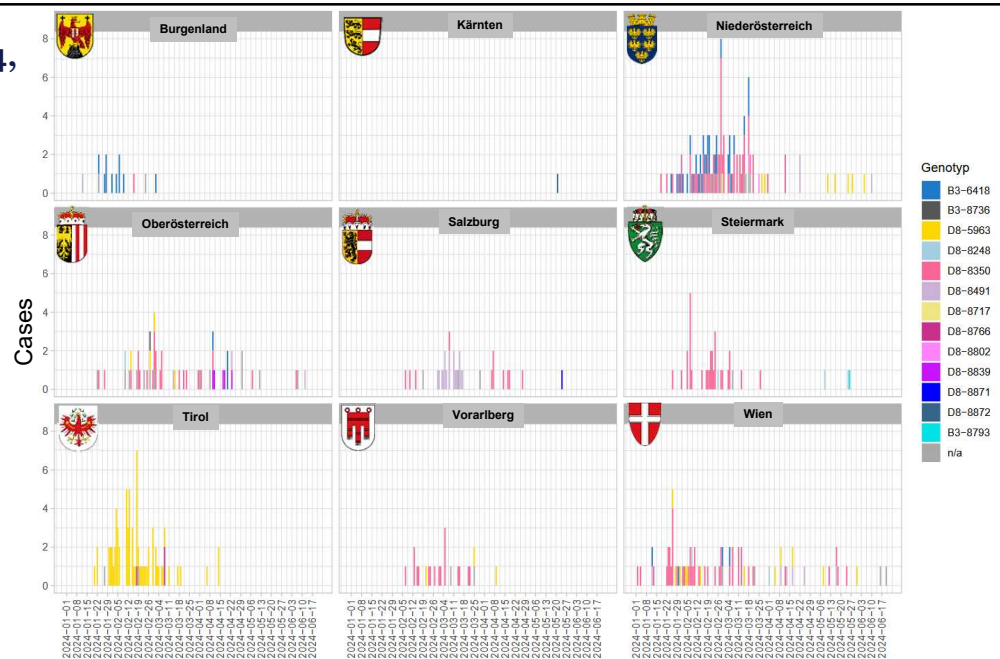
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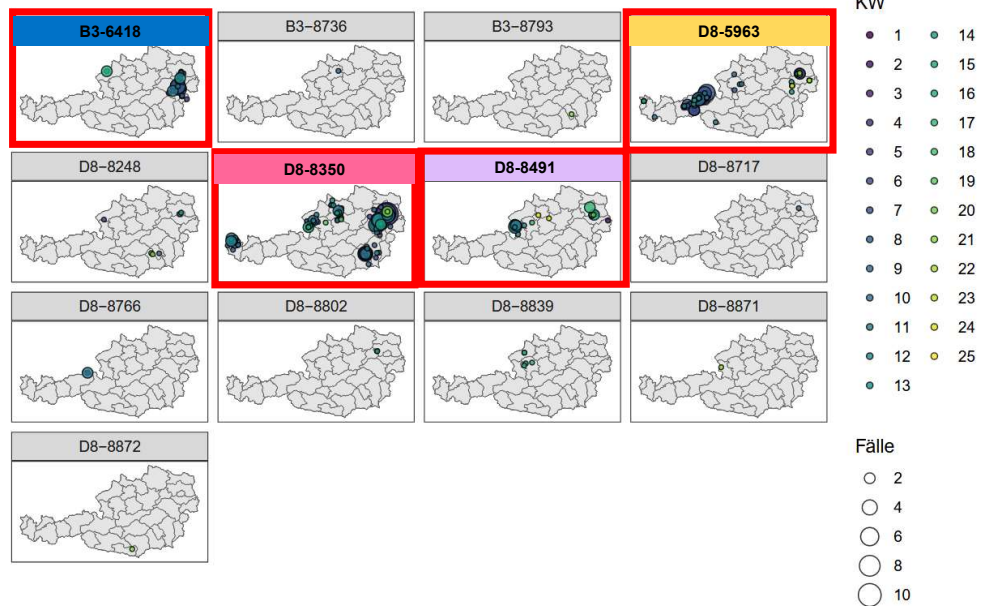
Measles 2024, Genotypes in Austria: districts



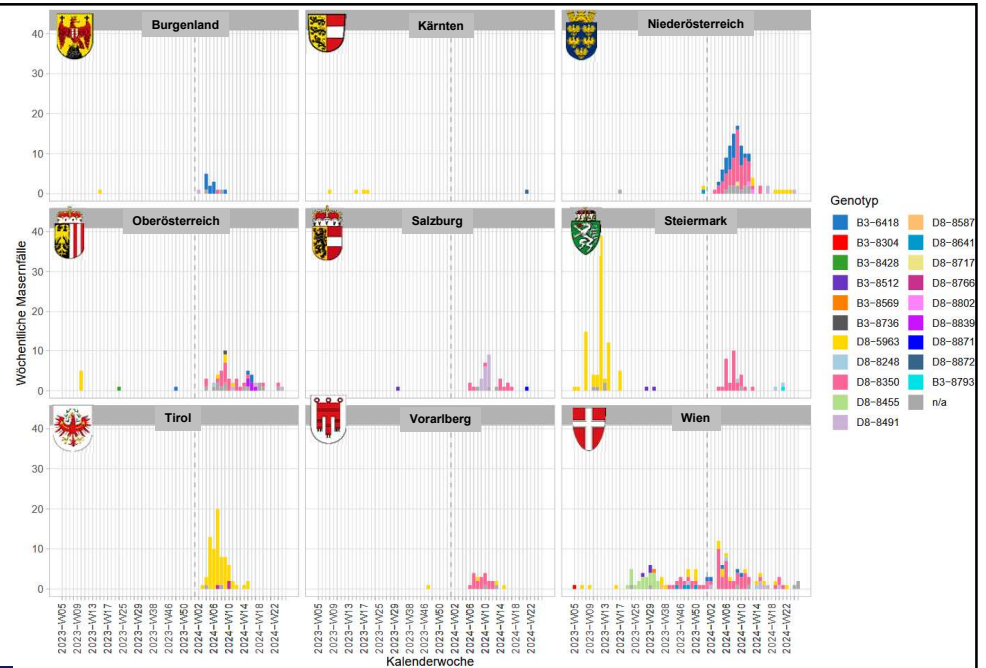
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Masern 2024: Genotypes in Austria, Spread in different districts



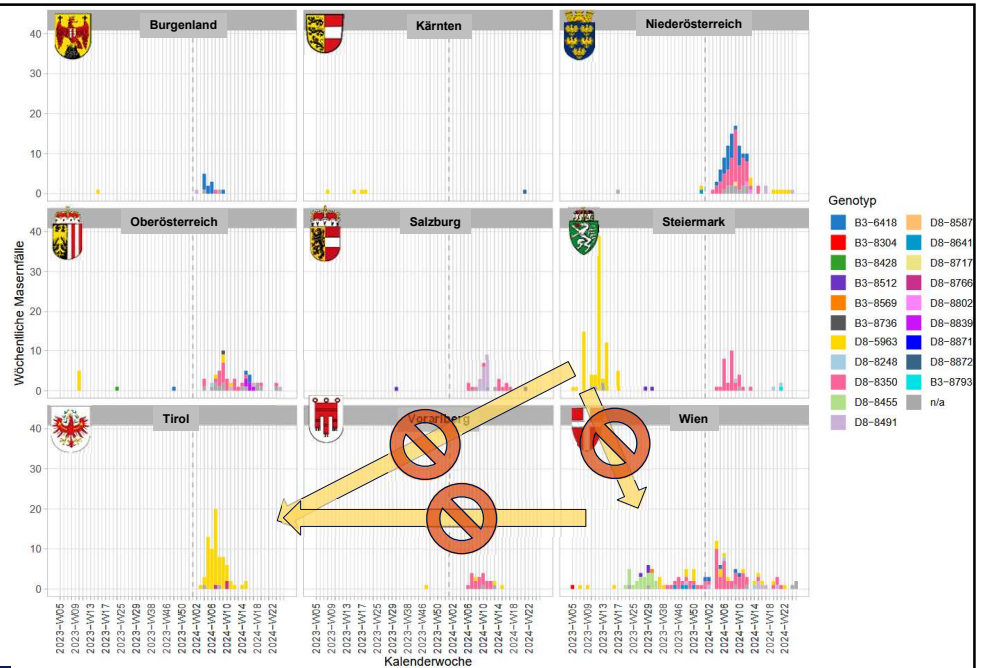
Measles 2023-2024: Genotypes in Austria, districts



Measles 2023-2024: Genotypes in Austria, districts

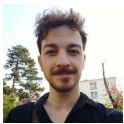


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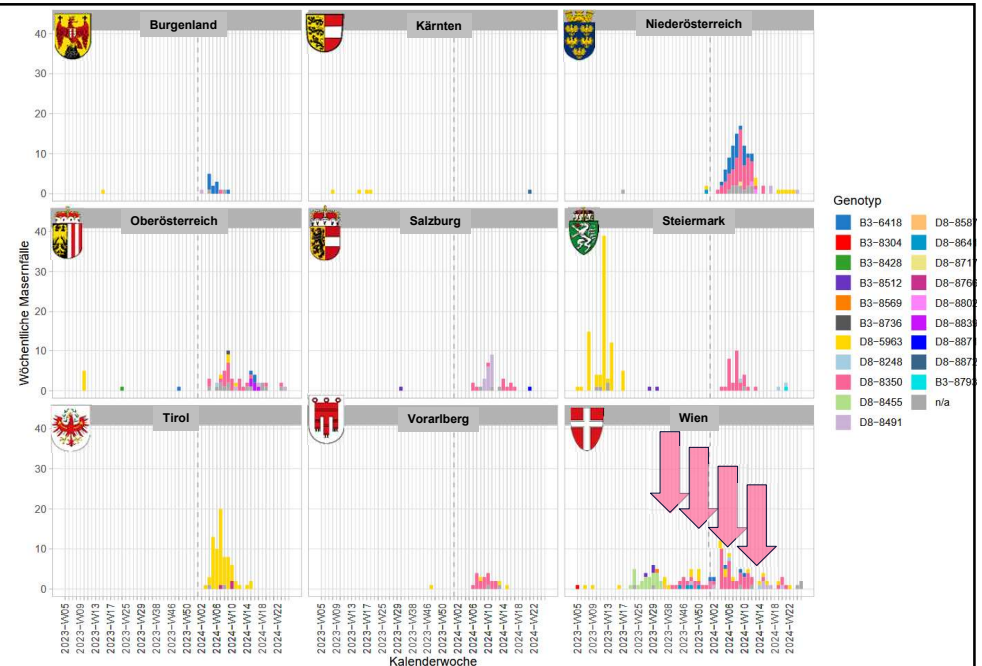


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Measles 2023-2024: Genotypes in Austria, districts



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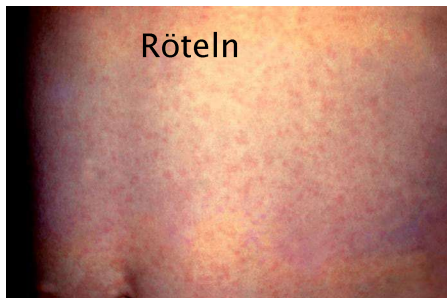
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Erkenntnisse für die Diagnostik

Masern



Röteln



Ringelröteln



Arzneimittel-
exanthem



Masern

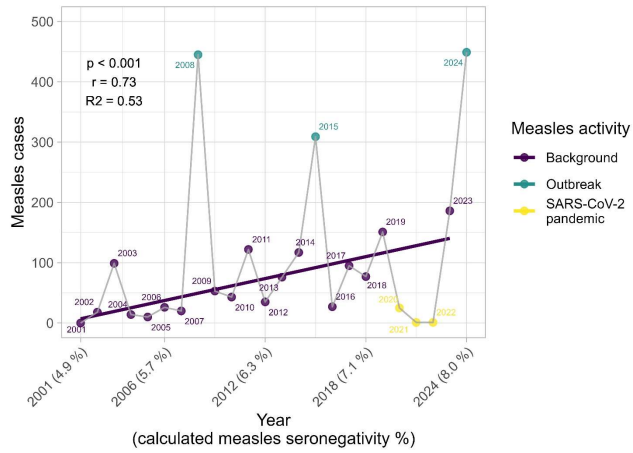


Scharlach

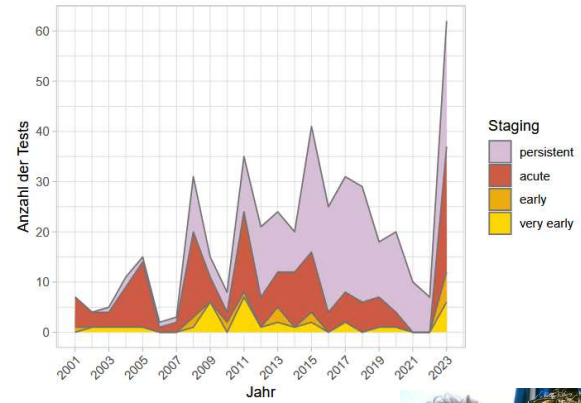


Papularisch-
Purpurnes-Gloves-and-Socks
Syndrome bei Ringelröteln

Masernfälle in Österreich



Parvovirus B19 bei Schwangeren

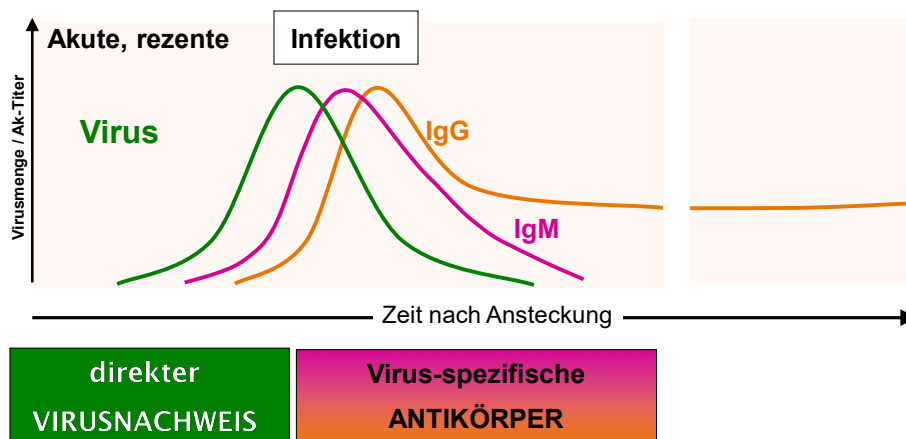


Dr. David Springer
c.m. Annabarbara Seebrecht

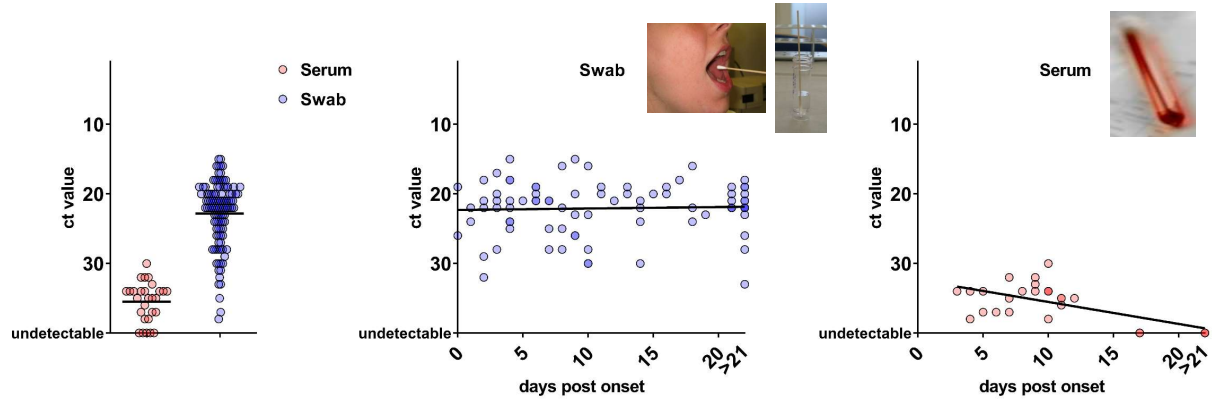


Diagnostik

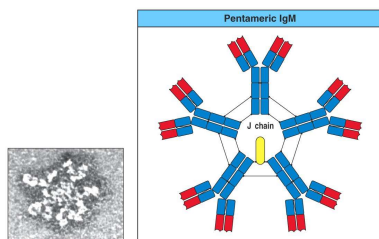
Symptome



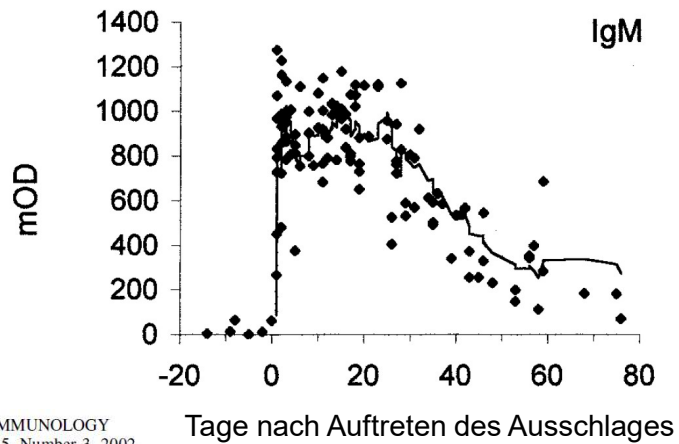
CT Values Swab, Serum Measles Cases 2023



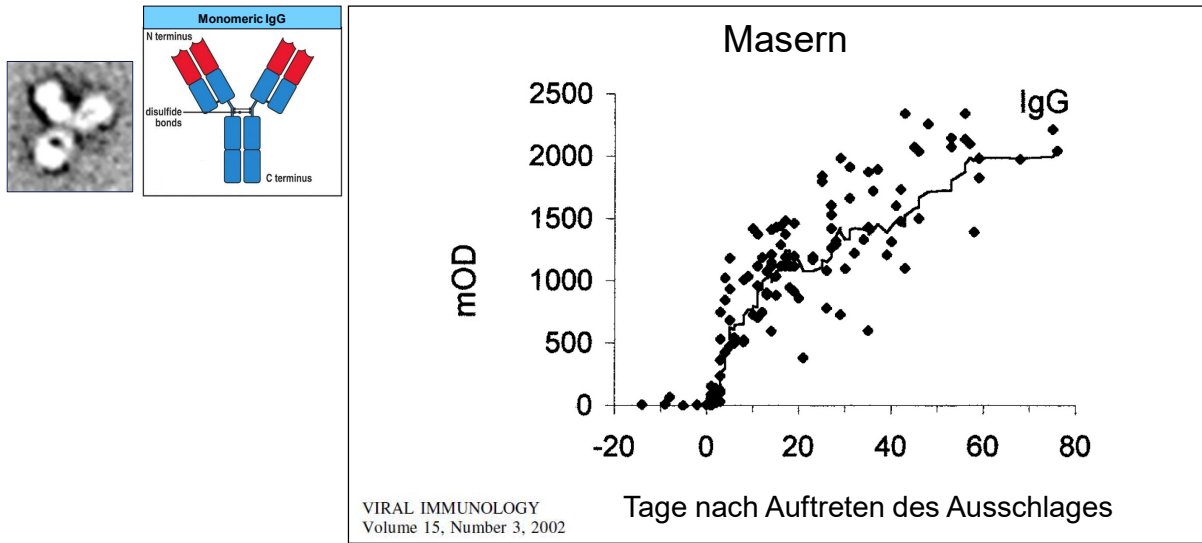
Virusspezifische IgM Antikörper nach Primärinfektion



Masern



IgG Antikörper nach Primärinfektion



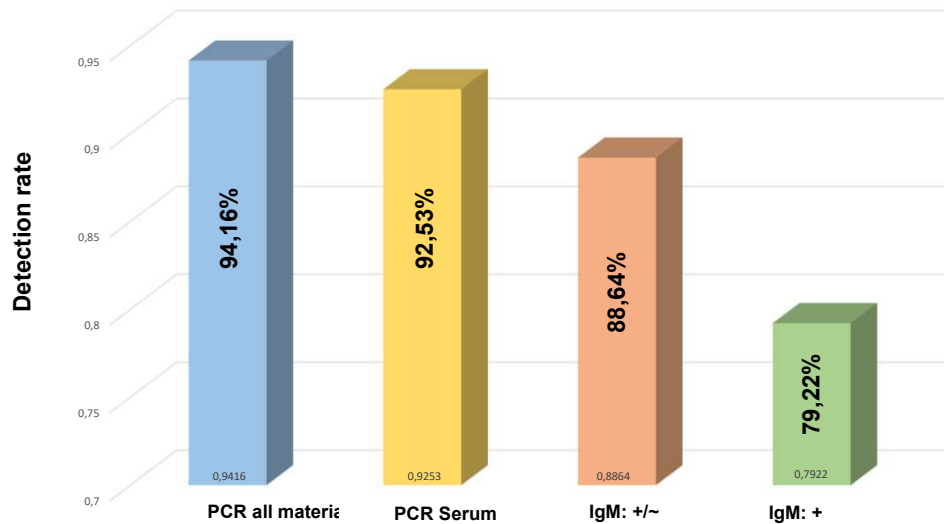
Measles Cases 2023/2024 at NRL with Serum available

PCR (Serum / Urine/ Swab)	IgM Serum (Euroimmun)	IgG Serum (Euroimmun)	IgG Avidity (Euroimmun)	Interpretation	n (308)
+	- / ~	- / ~	n.d.	very early	51
+	+	- / ~	n.d.	early	162
+	+	+	low	acute	37
+	-	+	low	late	1
+	+ / ~	+	borderline	late? / reinfection?	3
+	+	+	high	reinfection after vaccination	13
+	- / ~	+	high	reinfection after vaccination	11
+	+	+	IgG too low for avidity / no material for avidity / ongoing analysis	inconclusive	12
-	+	+	low	acute, serology only	13
-	+	+	high	NT titer indicating reinfection	5

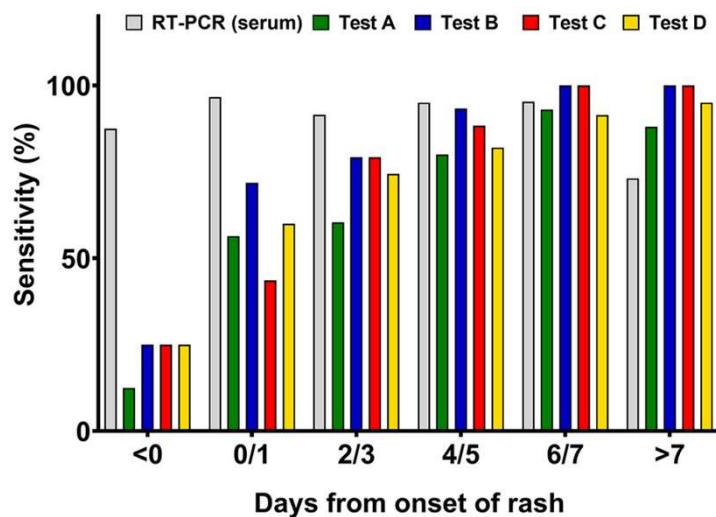
21% nicht
eindeutig
IgM-positiv

Sensitivity of PCR and Measles IgM-Tests: 2023-2024, n=308 samples

Sensitivität PCR - IgM 2023/24 n=308

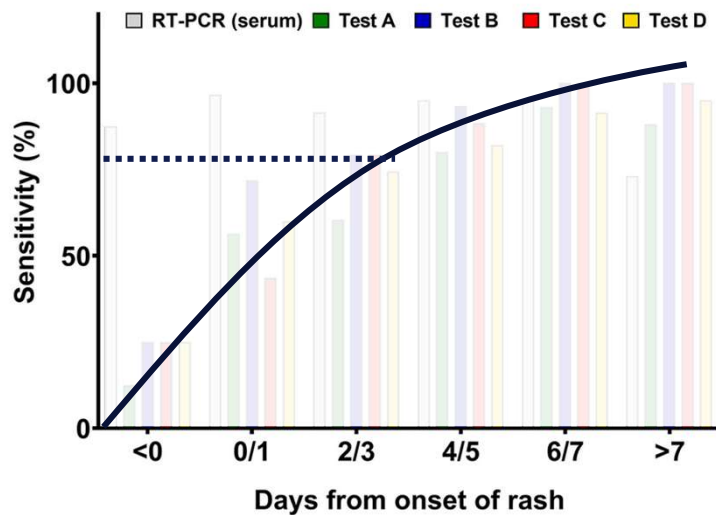


Sensitivität von Masern-IgM-Tests nach Exanthembeginn



Semmler G., [...], Weseslindtner L, J Clin Microbiol. 2021

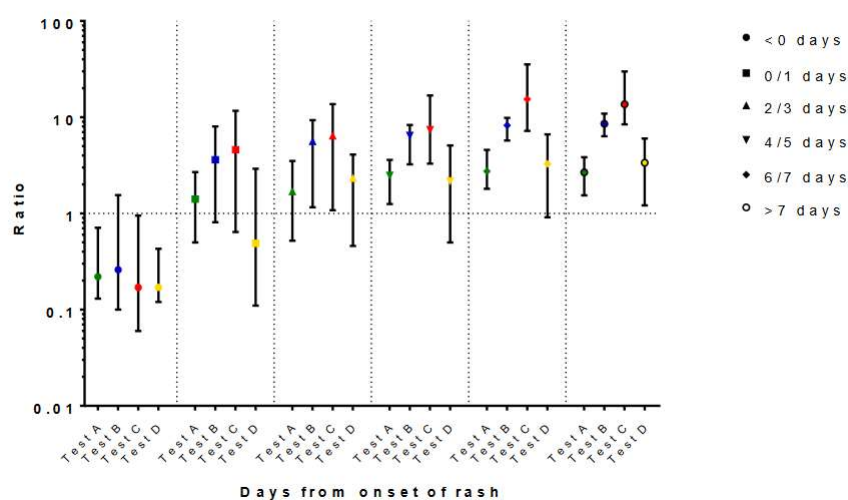
Sensitivität von Masern-IgM-Tests nach Exanthembeginn



IgM-Tests
erreichen erst
ca. 4–5 Tage nach
Exanthembeginn
hohe Sensitivität!

Semmler G., [...], Weseslindtner L, J Clin Microbiol. 2021

Sensitivität von Masern-IgM-Tests: Hersteller-spezifische Unterschiede

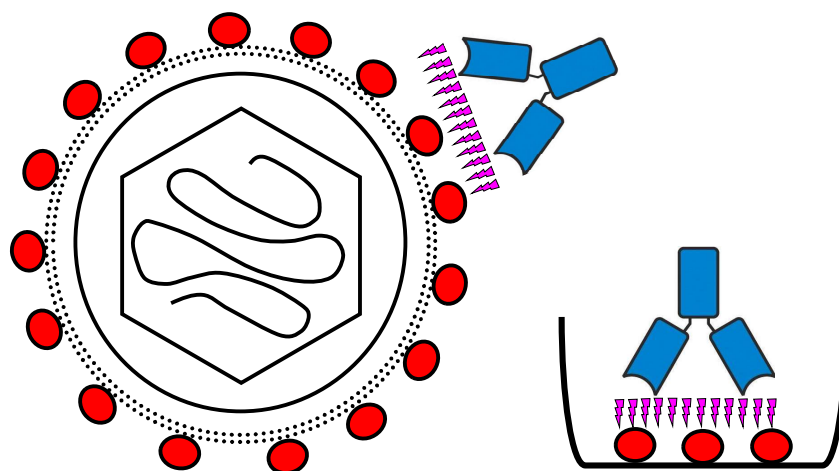


Semmler G., [...], Weseslindtner L, J Clin Microbiol. 2021

Klaus Hedman: Entwickler des Aviditätstests



IgG Avidität



IgG Avidität =
Bindungsstärke, mit der polyklonale IgGAntikörper an ihre antigenen Epitope binden

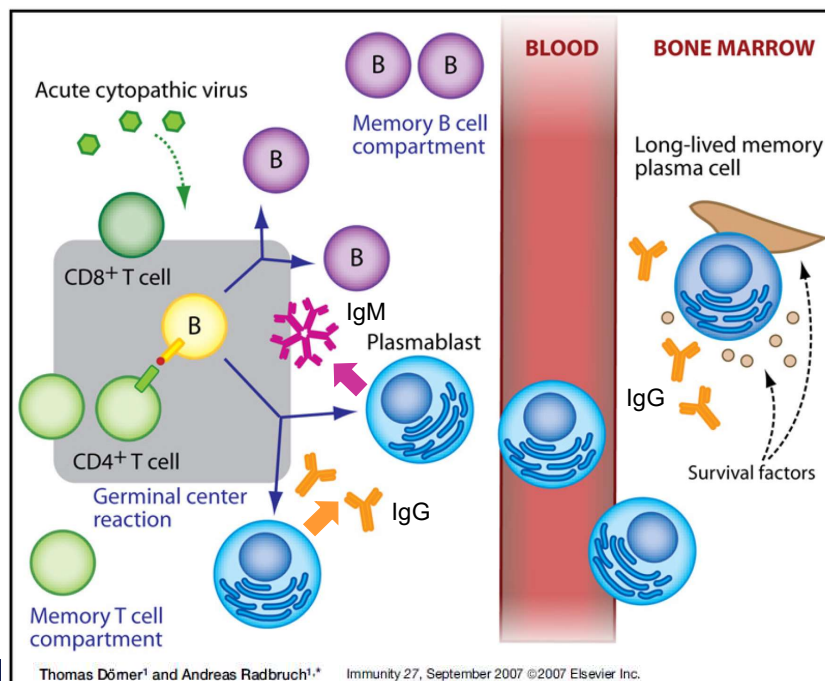
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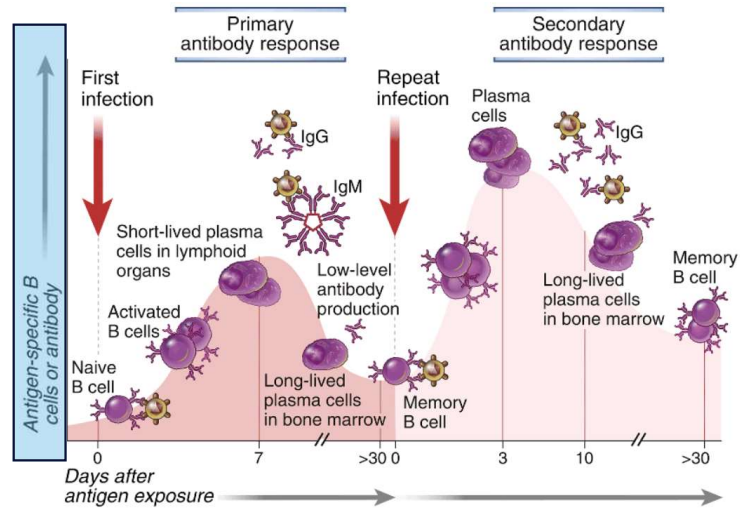
21% nicht
eindeutig
IgM-positiv

9%
Reinfektionen
nach Impfung

Bildung von IgM und IgG Antikörpern

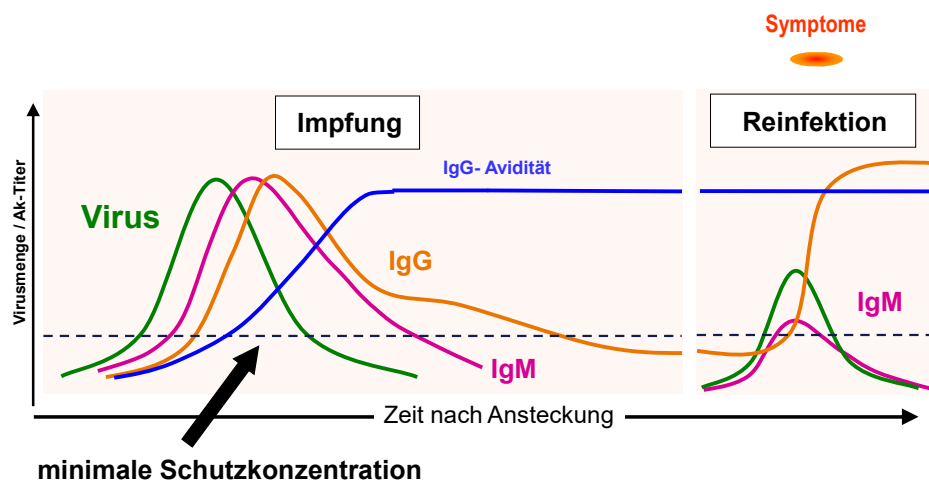


Humorale Immunantwort bei Virusinfektionen (primär & sekundär)



Abbas AK et al. Cellular and Molecular Immunology, Elsevier

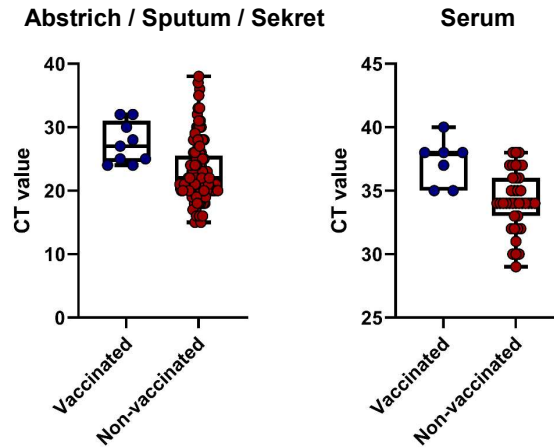
Reinfektion mit Gedächtnisreaktionen: “Impfdurchbruch”



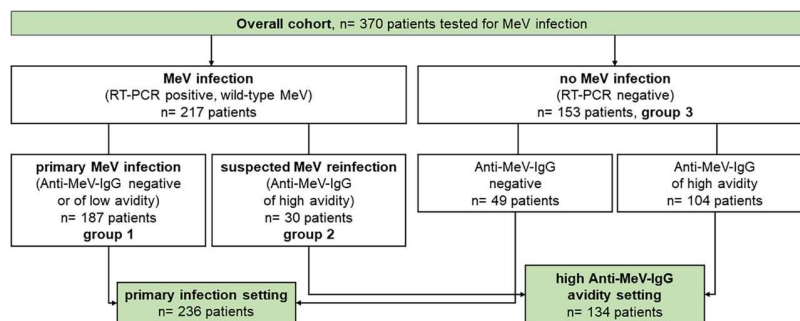
Reinfections after vaccination: lower virus concentration



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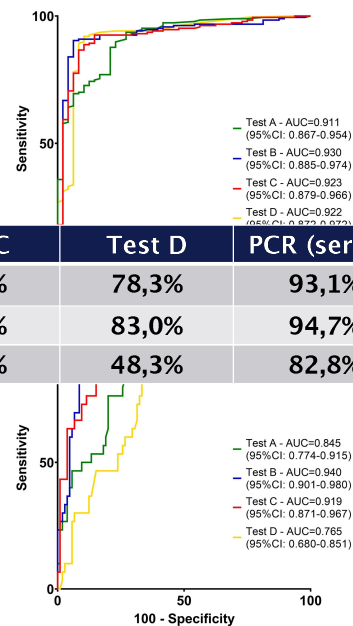
Sensitivität von Masern-IgM-Tests



Semmler G., [...], Weseslindtner L, J Clin Microbiol. 2021

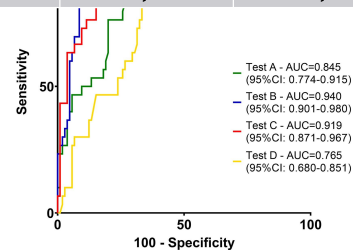
Sensitivität von Masern-IgM-Tests bei Impfdurchbrüchen

Primärinfektion



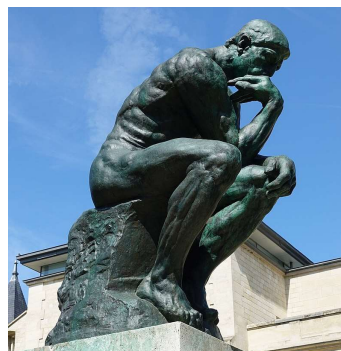
	Test A	Test B	Test C	Test D	PCR (serum)
Gesamt	69,6%	86,6%	84,8%	78,3%	93,1%
Primärinfektion	72,3%	87,2%	86,2%	83,0%	94,7%
Reinfektion	51,7%	82,8%	75,9%	48,3%	82,8%

Reinfektion nach Impfung



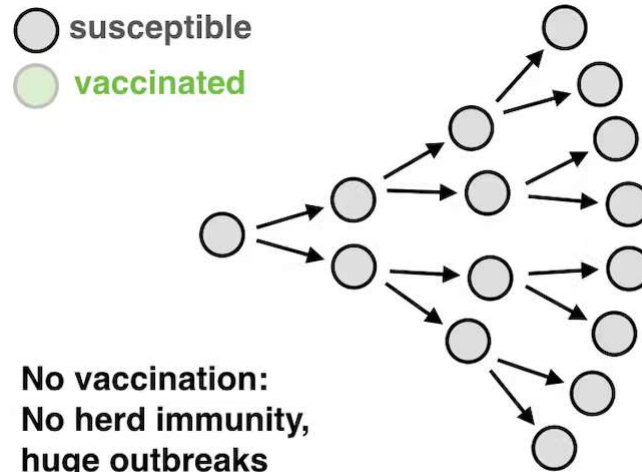
Semmler G., [...], Weseslindtner L, J Clin Microbiol. 2021

Wie konnte es zu so vielen Masernfällen in Österreich kommen?



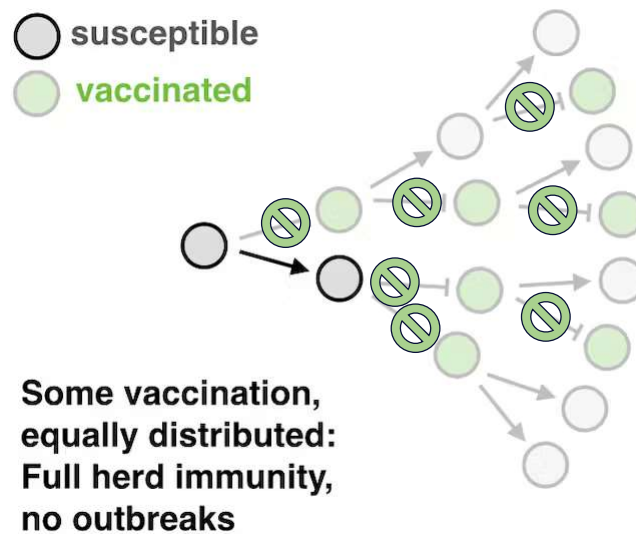
Der Denker vor dem Musée Rodin in Paris

Die Ursache für Masernausbrüche im Modell



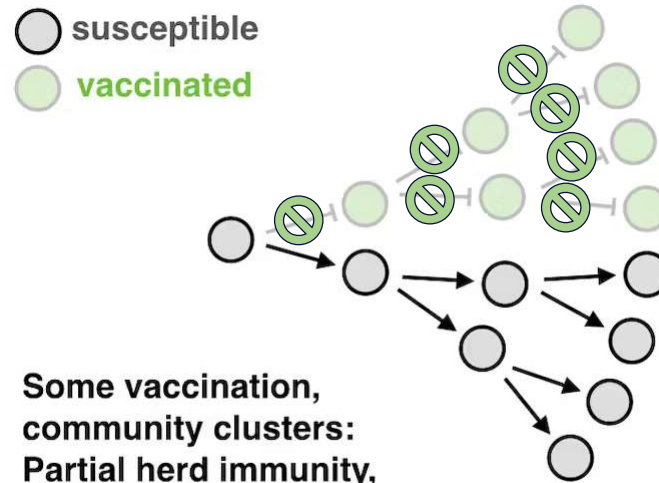
www.theconversation.com; by Marcel Salathé

Die Ursache für Masernausbrüche im Modell



www.theconversation.com; by Marcel Salathé

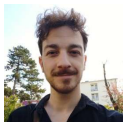
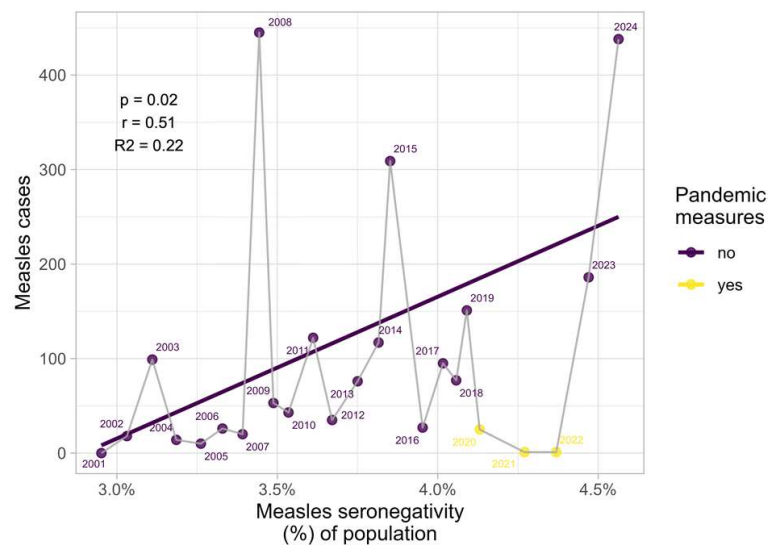
Die Ursache für Masernausbrüche im Modell



**Some vaccination,
community clusters:
Partial herd immunity,
large outbreaks**

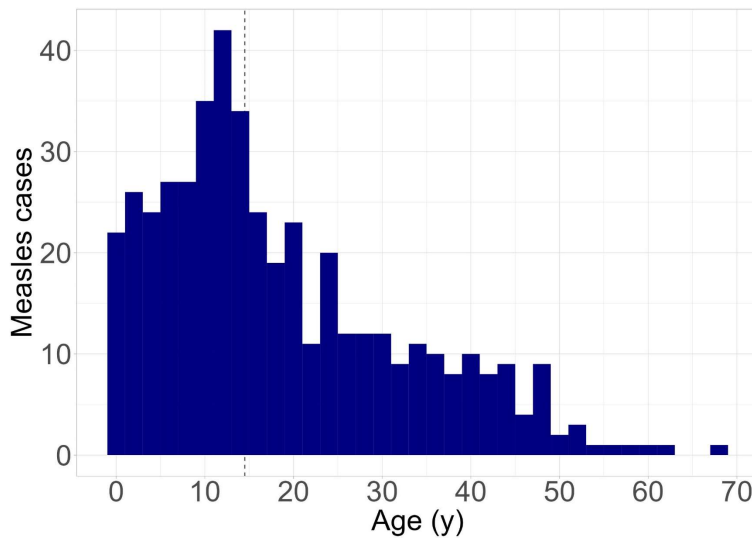
www.theconversation.com; by Marcel Salathé

Masernfälle in Österreich: Sie nehmen zu!



David Springer
Zentrum für Virologie

Measles in Austria: 2023 + 2024 (n = 622 at NRL)



- Median: 14 years (0–68a)
- < 1 a: n = 14 (4 %)
- < 4 a: n = 85 (14 %)
- > 30 a: n = 120 (24 %)

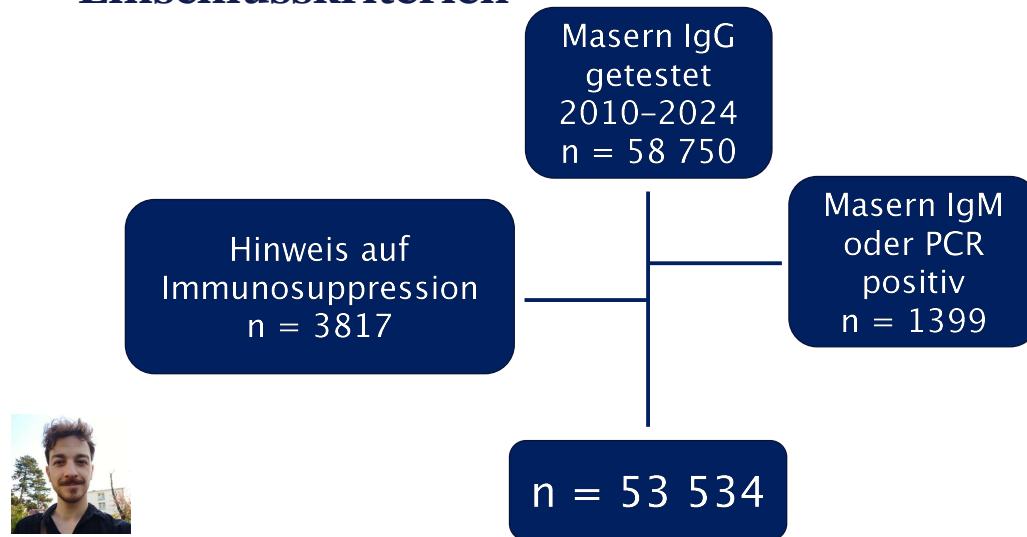
Mehrere Ausbrüche, Zirkulation in weiten Teilen der Bevölkerung

1) *Impflücken durch die COVID-Pandemie?*

2) *Antikörper „Waning“ nach der Impfung?*

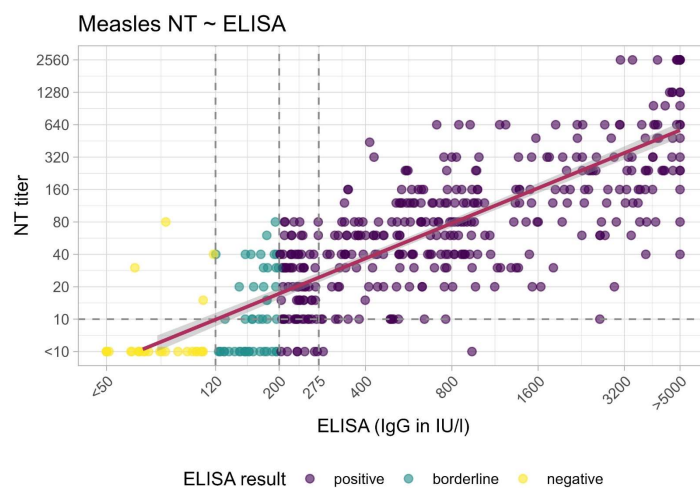
3) *Immunitätslücken breiten Teilen der Bevölkerung?*

Einschlusskriterien



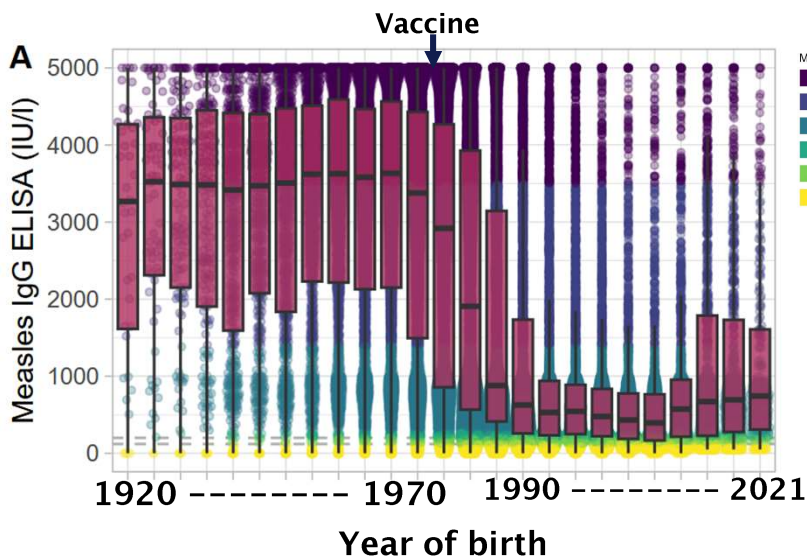
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Korrelation: Masern IgG ELISA-Neutralisationstest



Karin Stiasny
David Springer
Zentrum für Virologie

Estimating measles seroprevalence (n = 50,754)

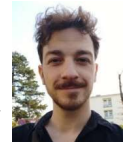


Wildvirus circulation

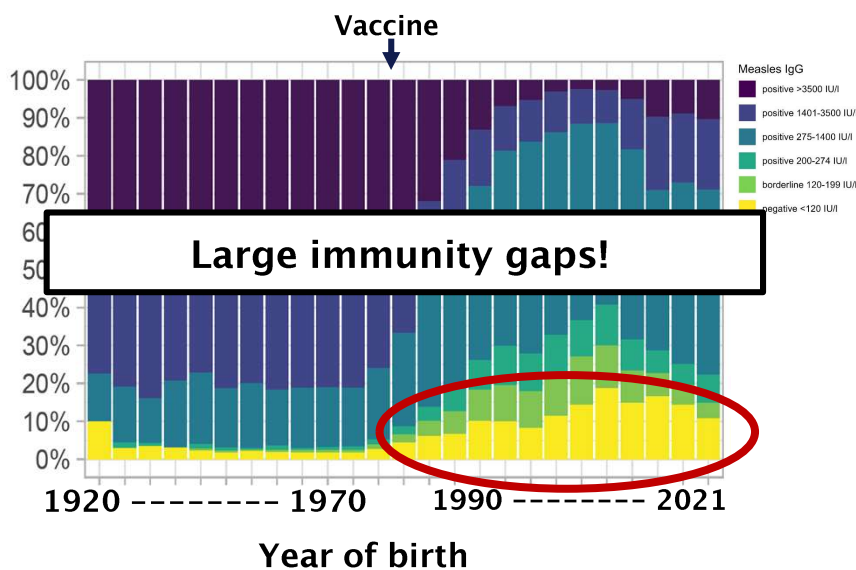
vs.

vaccination

Dr. David Springer



Estimating measles seroprevalence (n = 50,754)

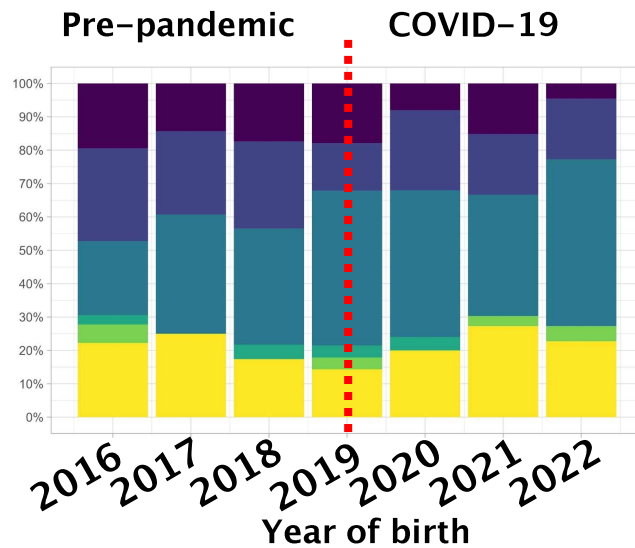


Individuals
born since 1990:
12.5 % negative
(<120 IU/ml)

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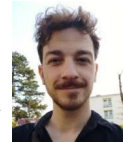


Children aged 12-24 months (n = 195)

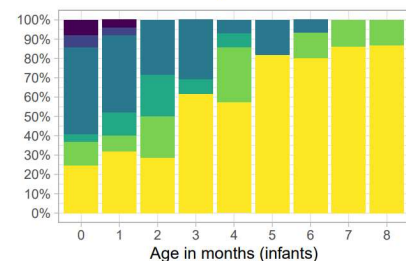
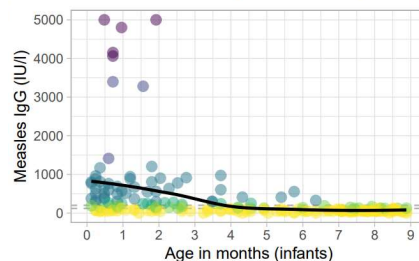
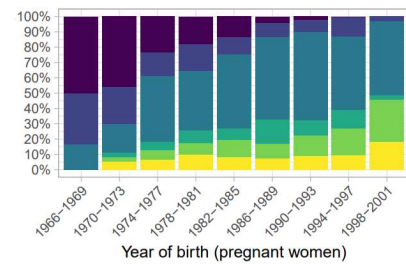
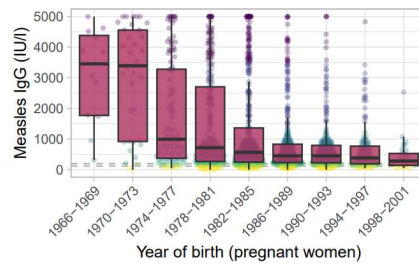


Low impact of the
CopVID19 pandemic on
immunization rates!

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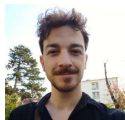


Pregnant women and infants



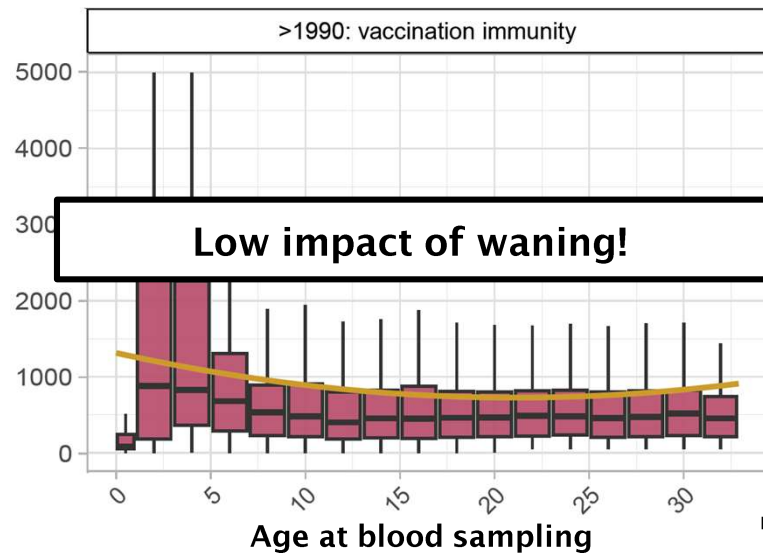
Measles IgG

- positive >3500 IU/l
- positive 1401-3500 IU/l
- positive 275-1400 IU/l
- positive 200-274 IU/l
- borderline 120-199 IU/l
- negative <120 IU/l

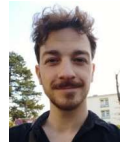


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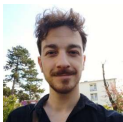
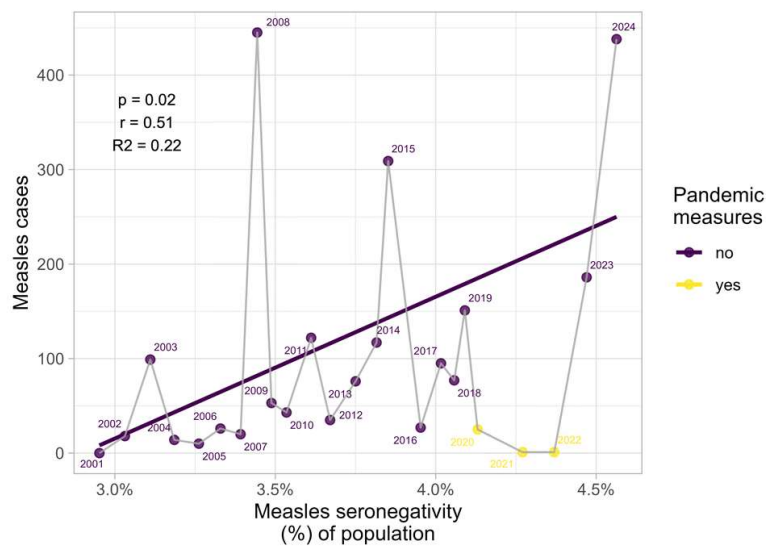
Waning immunity after vaccination? (n = 12,502)



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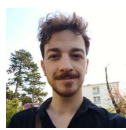
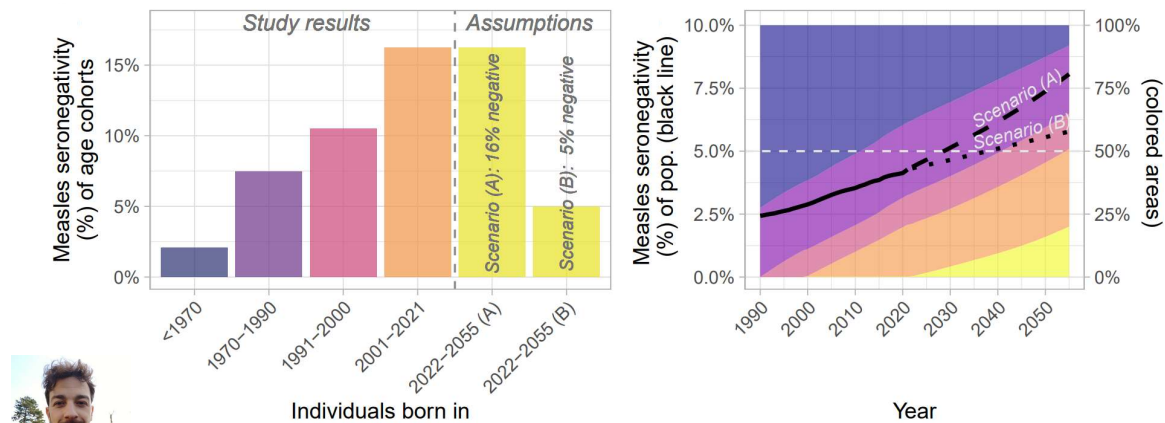


Future Perspective: Measles Seroprevalence



David Springer
Zentrum für Virologie

Future Perspective: Measles Seroprevalence



David Springer
Zentrum für Virologie

Conclusio

- seit 2023: kontinuierlich Importe neuer Maserngenotypen nach Österreich
 - die meisten: erfolgreich eingedämmt
 - gleichzeitiger Import desselben Genotyps: Ganzgenomanalyse
 - ca. 9% Reinfektionen nach (einer) früher durchgeführten Masernimpfung(en) („Impfdurchbrüche“): Labordiagnostik unterschiedlich
 - 2024: in mehreren Bundesländern mehrere Genotypen gleichzeitig, mehrere „Brandherde“
 - Immunität in der Gesamtbevölkerung reicht nicht aus, um eine (kurzdauernde) Masernzirkulation zu unterbinden
 - Lücken v.a. in Geburtsjahrgängen nach 1970: Masern sind KEINE Kinderkrankheit!
 - „Waning“ der Antikörper und CoVID-Pandemie: untergeordnete Rolle
- D. Springers Modell „The measles will return big in the future!“



Vielen Dank für
die
Aufmerksamkeit!