



UZ
LEUVEN

KU LEUVEN



Information session of the National Reference Center for Rotavirus

14-12-2023

Jelle Matthijnsens

Lize Cuypers

Recap important information

- **Accreditation** requested: please enter your name (and RIZIV/INAMI if applicable) in the chat box
- **Interactive sessions:** you can speak up by unmuting your microphone to ask questions or raise comments in the chat box
- No recording of the session but slides will be shared
<https://www.uzleuven.be/nl/laboratoriumgeneeskunde/nationale-referentiecentra-en-referentielaboratoria>
<https://www.sciensano.be/nl/nrc-nrl/nationaal-referentiecentrum-nrc-voor-rotavirus>



The screenshot shows a website page with the UZ Leuven logo in the top right corner. A blue navigation bar contains the text 'Laboratoriumgeneeskunde'. Below the navigation bar, there is a breadcrumb trail: 'Home > Diensten, centra en afdelingen > Laboratoriumgeneeskunde'. The main heading of the page is 'Informatiesessies nationale referentiecentra voor humane microbiologie'. Below the heading, there is a list of sessions:

- Streptococcus pneumoniae (invasief) - 30 maart 2023
- Enterovirussen (inclusief poliovirus en parechovirus) en rioolwaterscreening - 27 april 2023
- Mycosis (UZ Leuven en CHU Liège) - 8 Juni
- NRC respiratory pathogens (UZ Leuven en UZA) - 26 oktober

Rotavirus

- RIZIV nomenclature and/or invoice
 - Rotavirus antigen test (EIA): Rotaclone[®]
 - Part of gastro-intestinal panel: detection of 24 pathogens (years 2022 and 2023: PR of 3.1% for rotavirus, with >50% strongly positive)
- NRC budget
 - Typing: RT-PCR and sequencing

Rotavirus
Surveillance
Network
Belgium



Bacteriën:

Campylobacter spp. (Campylobacter jejuni, Campylobacter upsaliensis, Campylobacter coli), Salmonella spp., Clostridium difficile (tcdA/tcdB), Yersinia enterocolitica, Enterotoxinogene E. coli (ETEC), Enteropathogene E. coli (EPEC), Enteroaggregatieve E. coli (EAEC), Shiga-like toxine producerende E. coli (STEC) serotype O157:H7//stx1/stx2, Entero-invasieve E. coli (EIEC)/Shigella, Plesiomonas shigelloides, Vibrio vulnificus, Vibrio parahaemolyticus, Vibrio cholerae

Parasieten:

Entamoeba histolytica, Cryptosporidium spp., Giardia lamblia, Cyclospora cayetanensis,

Virussen:

Humaan adenovirus F40/F41, Norovirus GI, Norovirus GII, **Rotavirus A**, Astrovirus en Sapovirus (GI, GII, GIV en GV).

Nationaal Referentiecentrum (NRC) voor Rotavirus

Nuttige links:

Onderaan deze pagina kan u de **NRC-rapporten** terugvinden.

De bijhorende **epidemiologische surveillance-rapporten** kan u consulteren via:

[Gezondheidsonderwerp Rotavirus](#)

[Gezondheidsonderwerp Vaccineerbare ziekte](#)

Beschikbare testen

1. [Rotavirus Antigeen-ELISA \(RIZIV nomenclatuur\)](#)
2. [Rotavirus RT-PCR en sequentiebepaling \(referentiecentrum activiteit\)](#)

Verantwoordelijke laboratoria

Coördinator

- [UZ Leuven/KU Leuven](#)



Erkend door

- [National Institute for Health and Disability Insurance \(INAMI-RIZIV\)](#)

Aanvraagformulieren

- [Aanvraagformulier Rotavirus](#)

Information on
vaccination status
and in case of
outbreak!

Jaar	Beschrijving
2022	 Rotavirus Report 2021-2022 (English only)
2021	 Rotavirus report 2020-2021

NRC Rotavirus

Jelle Matthijnsens

Marc Van Ranst

Elke Wollants

Mandy Bloemen

Lize Cuypers

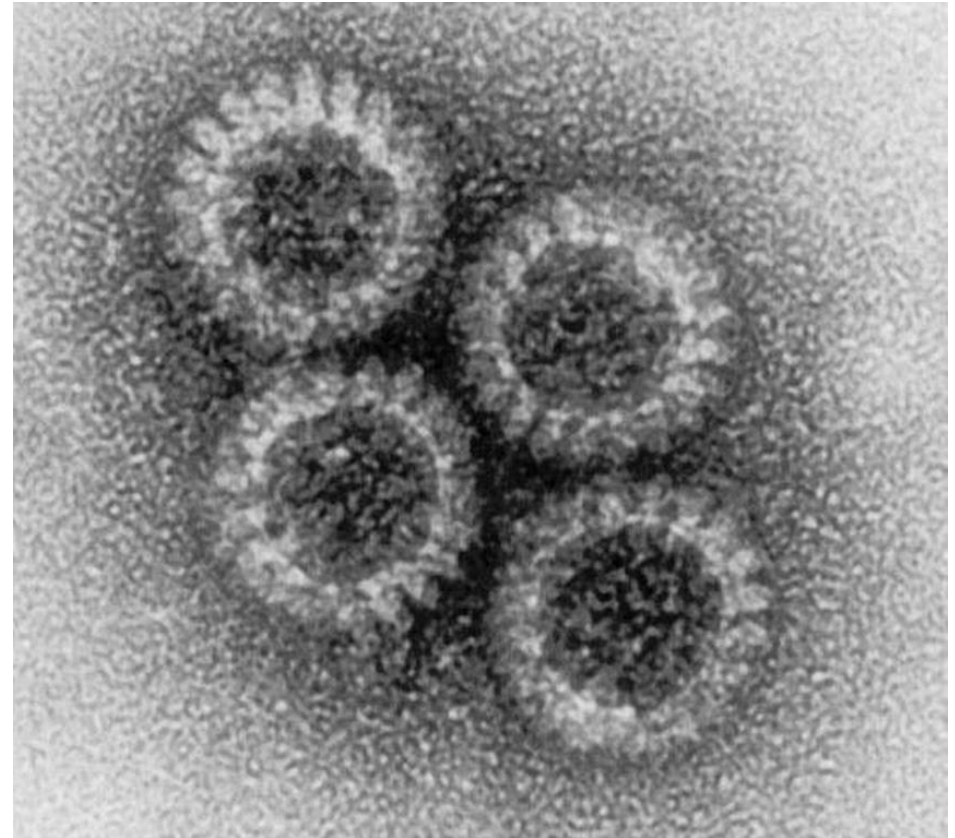
Overview

- Introduction
- Rotavirus surveillance UZ Leuven (1981-2023)
- Rotavirus surveillance NRC (2009-2023)
- Rotavirus co-infections
- Vaccine-derived rotavirus strains

Introduction

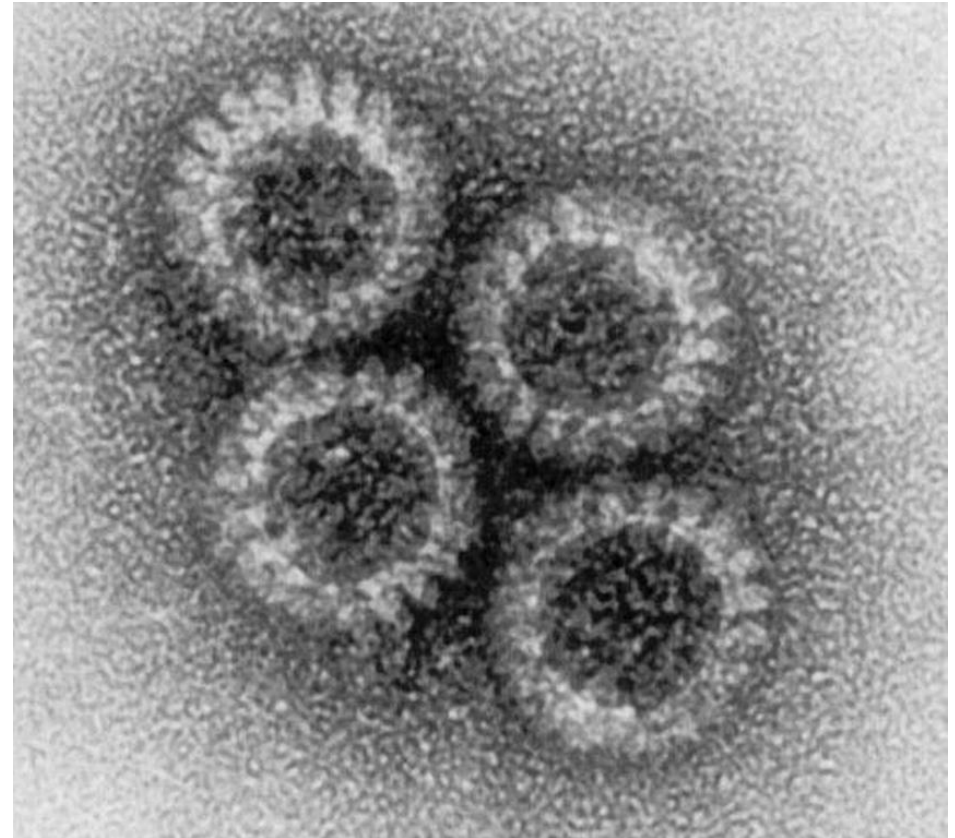
Rotavirus Characteristics

- 'Rotavirus' derived from 'rota' meaning 'wheel' in latin



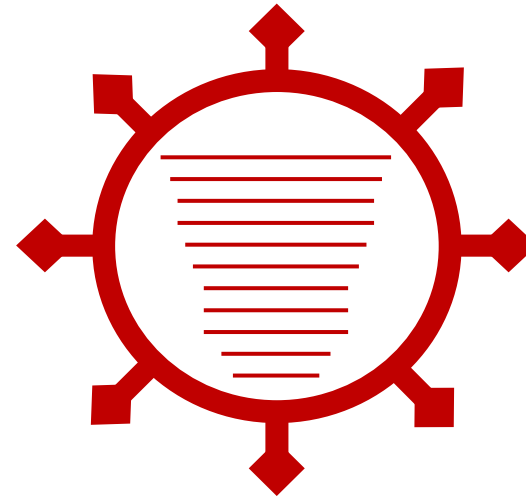
Rotavirus Characteristics

- 'Rotavirus' derived from 'rota' meaning 'wheel' in latin
- **No envelope**



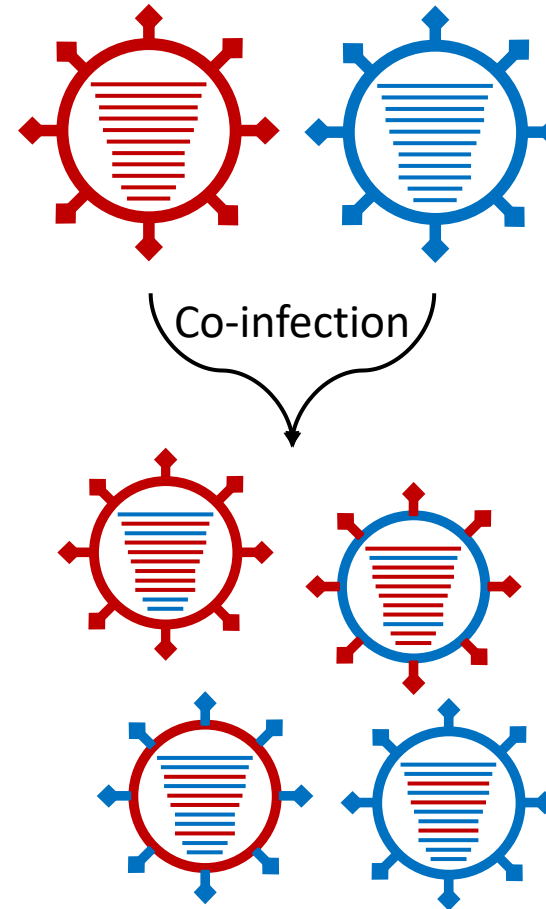
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- **Genome comprised of 11 segments of dsRNA**



Rotavirus Characteristics

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- Genome comprised of 11 segments of dsRNA
- **Reassortment**



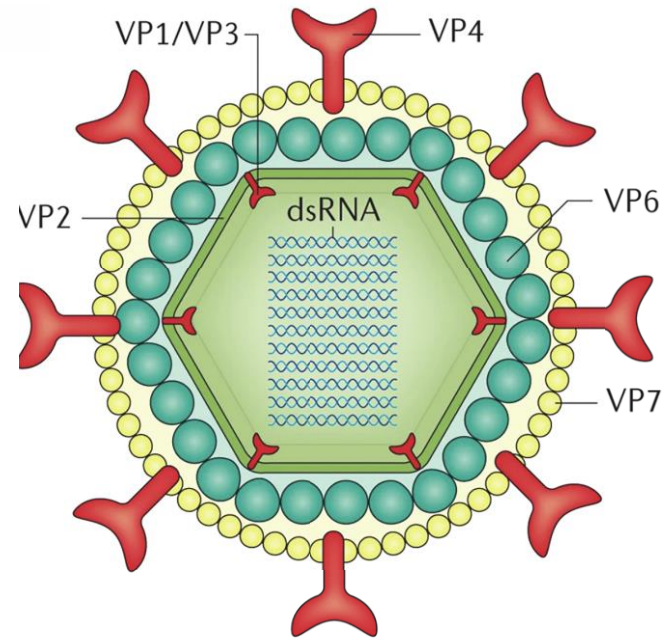
Rotavirus Characteristics

- 'Rotavirus' derived from 'rota' meaning 'wheel' in latin
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- Family *Sedoreoviridae*
- Genus *Rotavirus*
- Species *Rotavirus A-D* and *F-J*



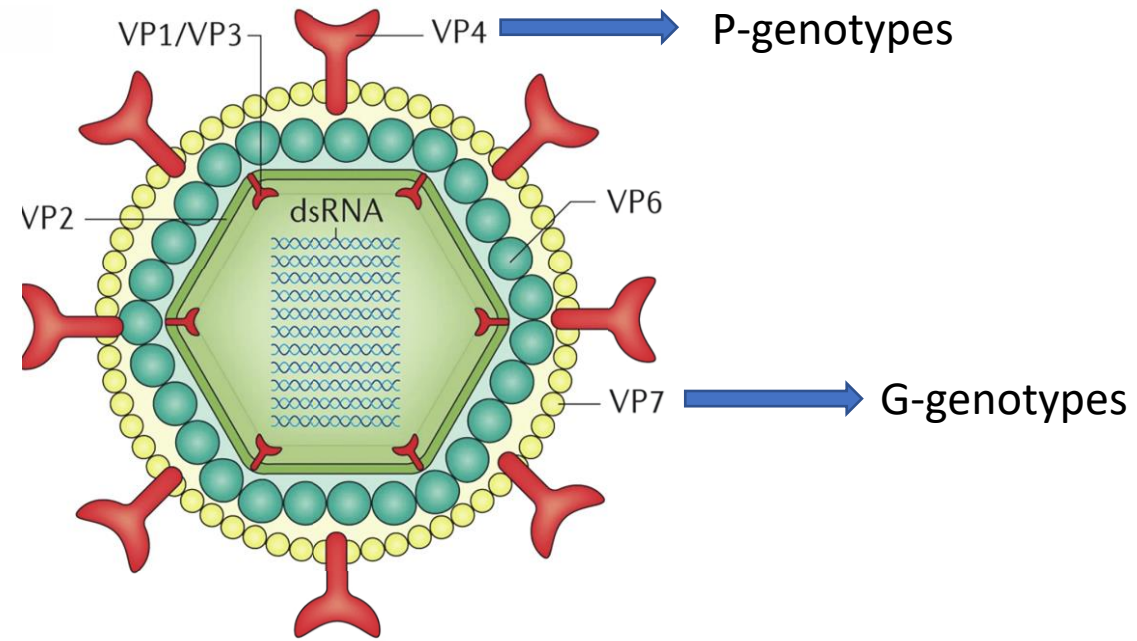
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- **Rotavirus A: G- and P-genotypes**



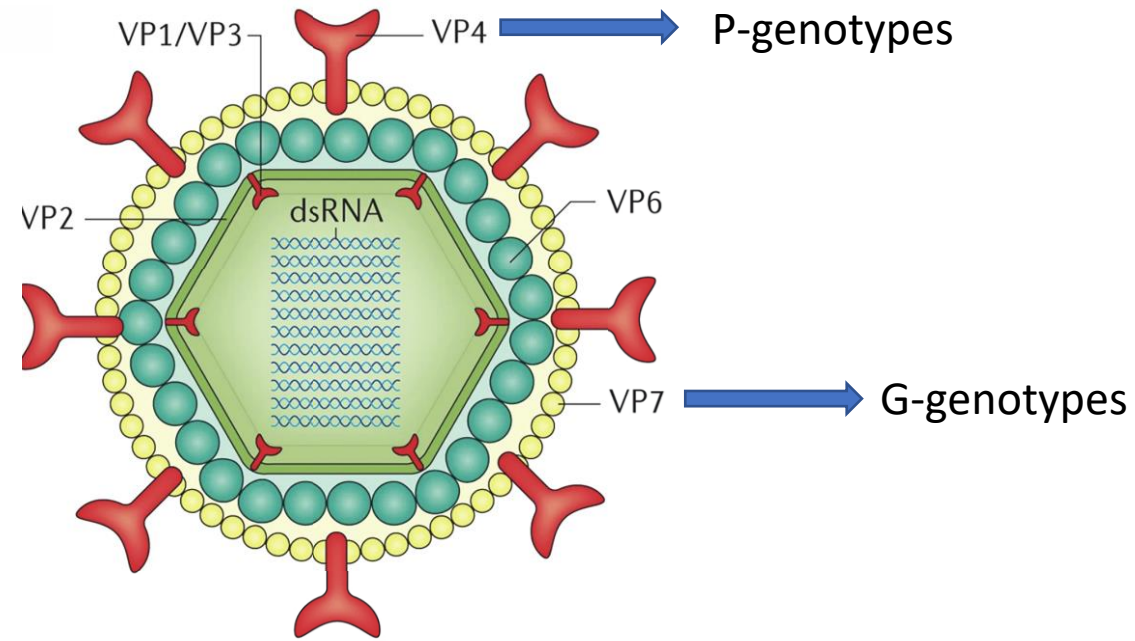
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- **Rotavirus A: G- and P-genotypes**



VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5	
Gx	P[x]	Ix	Rx	Cx	Mx	Ax	Nx	Tx	Ex	Hx	
G1	P[8]	I1	R1	C1	M1	A1	N1	T1	E1	H1	Wa
G2	P[4]	I2	R2	C2	M2	A2	N2	T2	E2	H2	DS-1

Rotavirus Vaccines

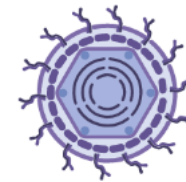
- Live-attenuated / Oral
- Administered @ 2, 4 (6) months
- Safe and effective

Rotavirus Vaccines

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- Administered @ 2, 4 (6) months
- Safe and effective
- Licenced worldwide
 - Rotarix (2 doses): Monovalent



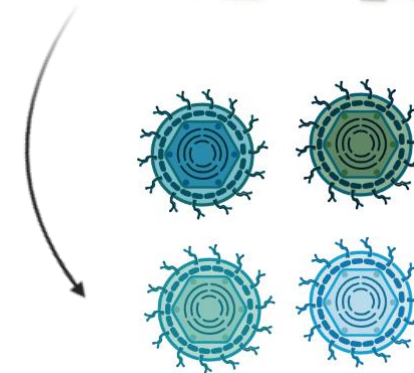
Attenuated
Human RVA



GlaxoSmithKline (GSK)

Rotavirus Vaccines

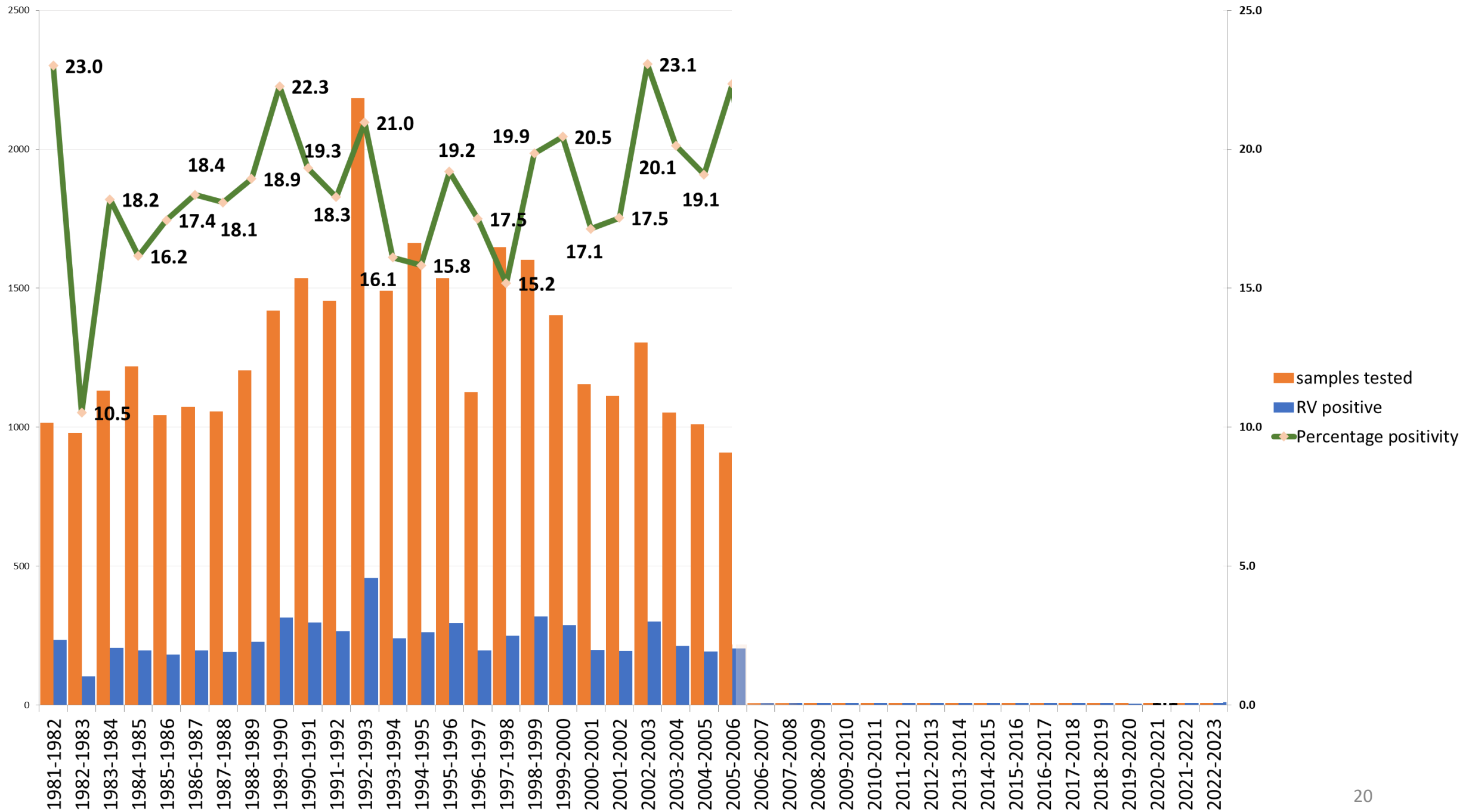
- Live-attenuated / Oral
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- Safe and effective
- Licenced worldwide
 - Rotarix (2 doses): Monovalent
 - RotaTeq (3 doses): Pentavalent

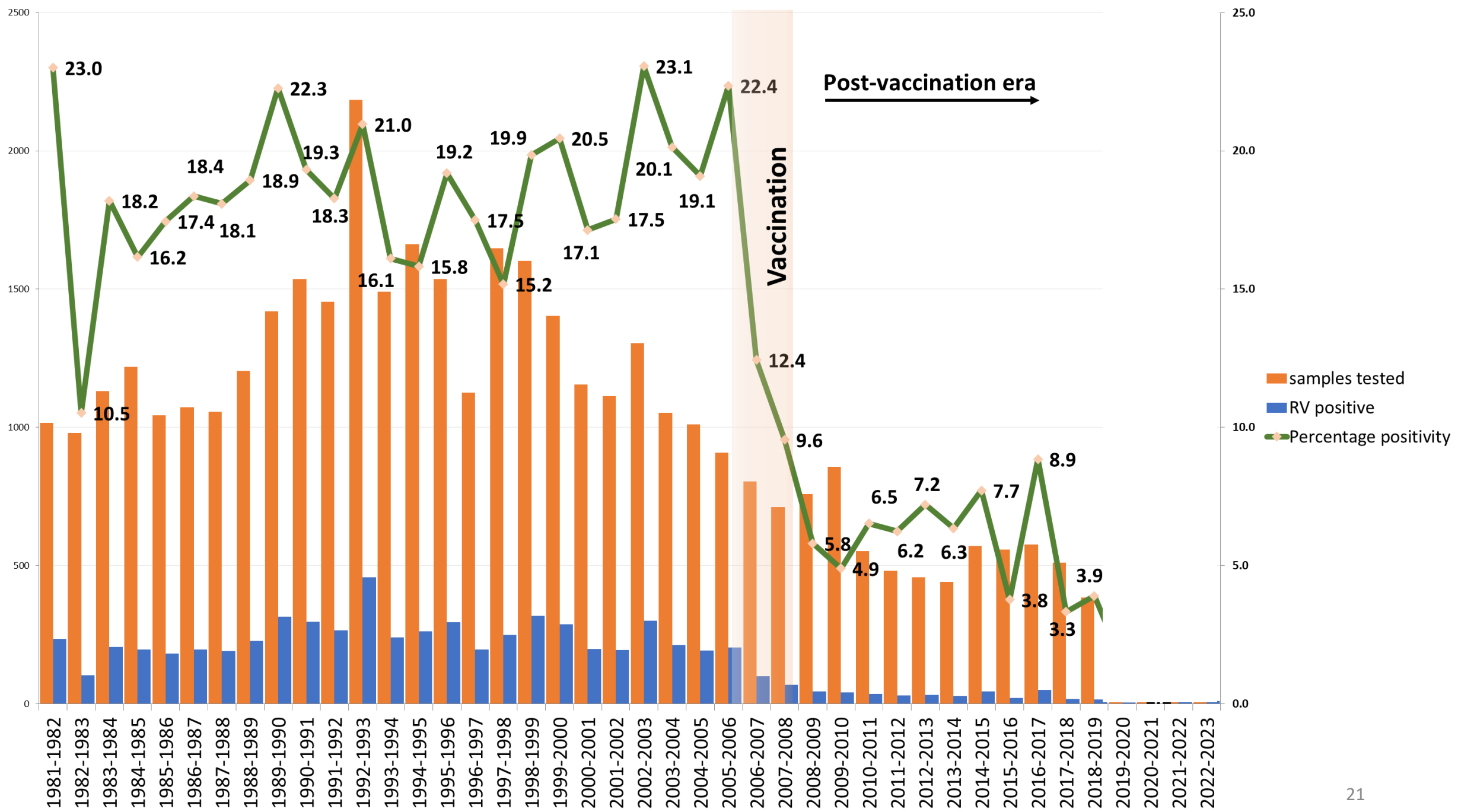


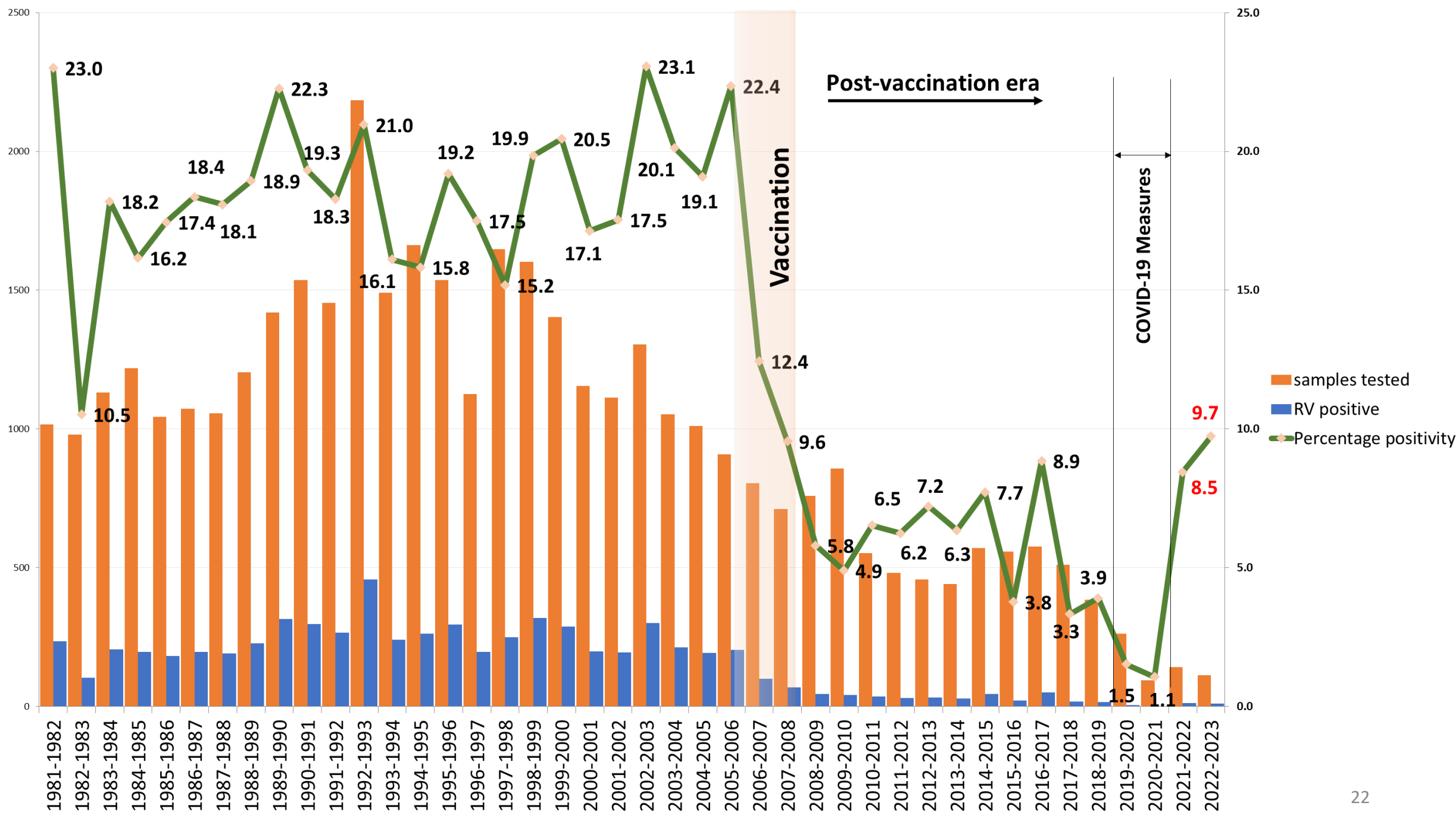
5 reassortant
Bovine x Human RVA

Merck

Rotavirus surveillance UZ Leuven (1981-2023)







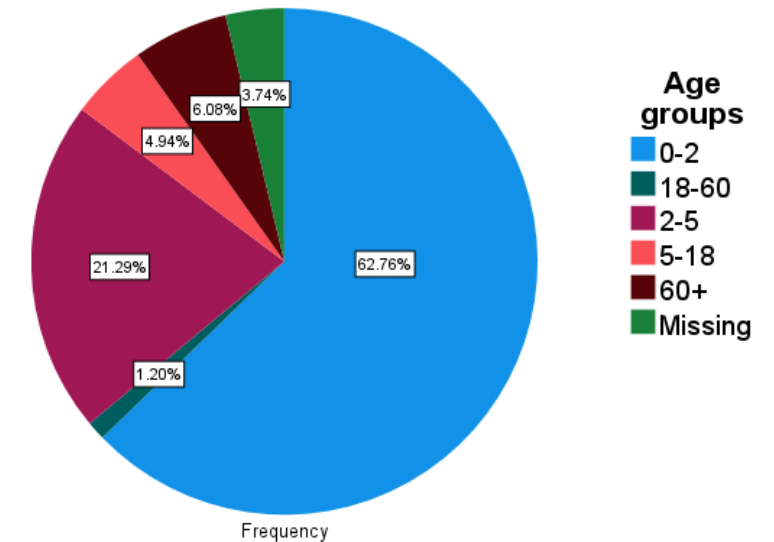
Rotavirus surveillance NRC (2009-2023)

NRC for Rotavirus A, 2009-2023

More than >8000 samples over the course of 14 years

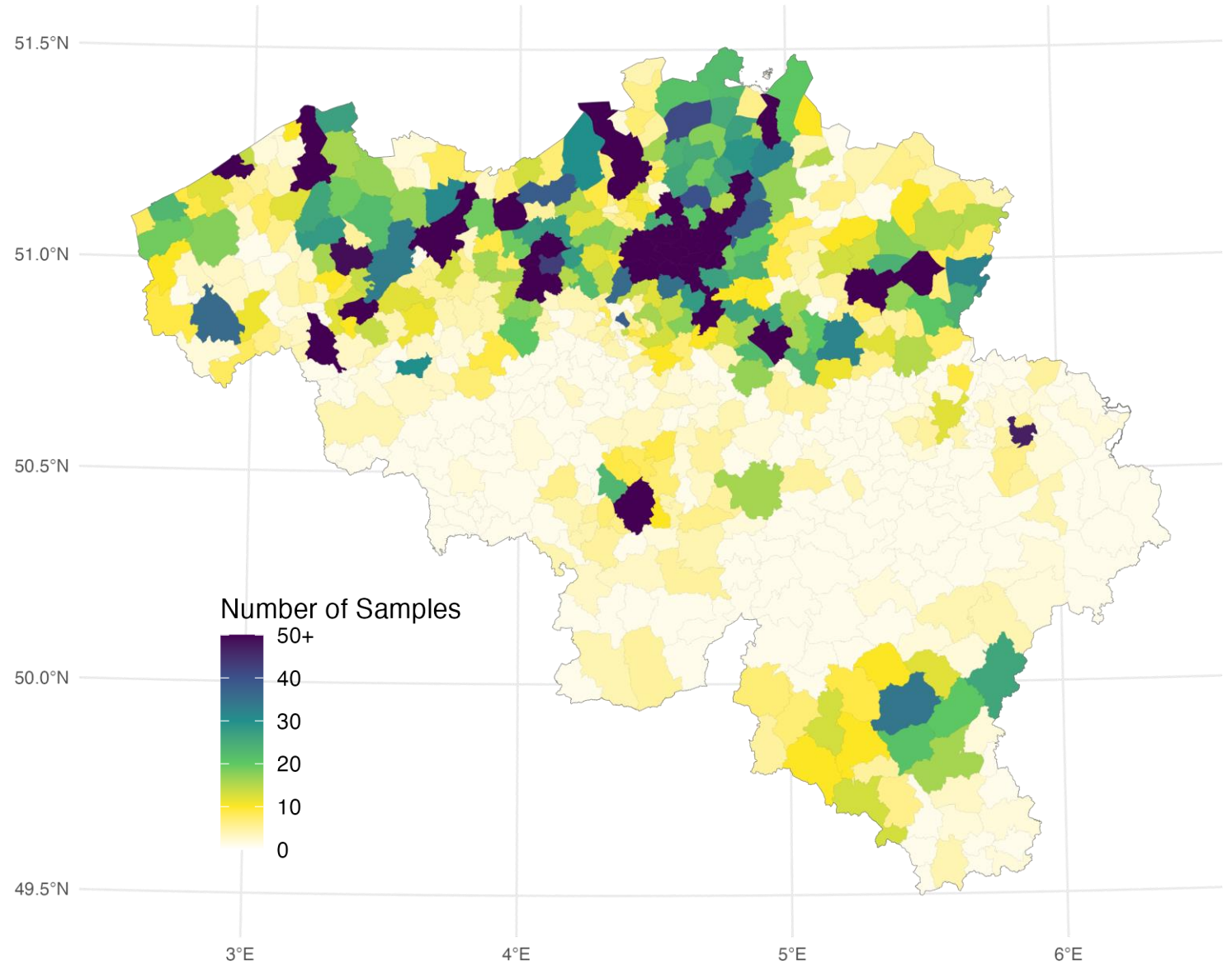
Season: August 1 → July 31

Age information (completeness)

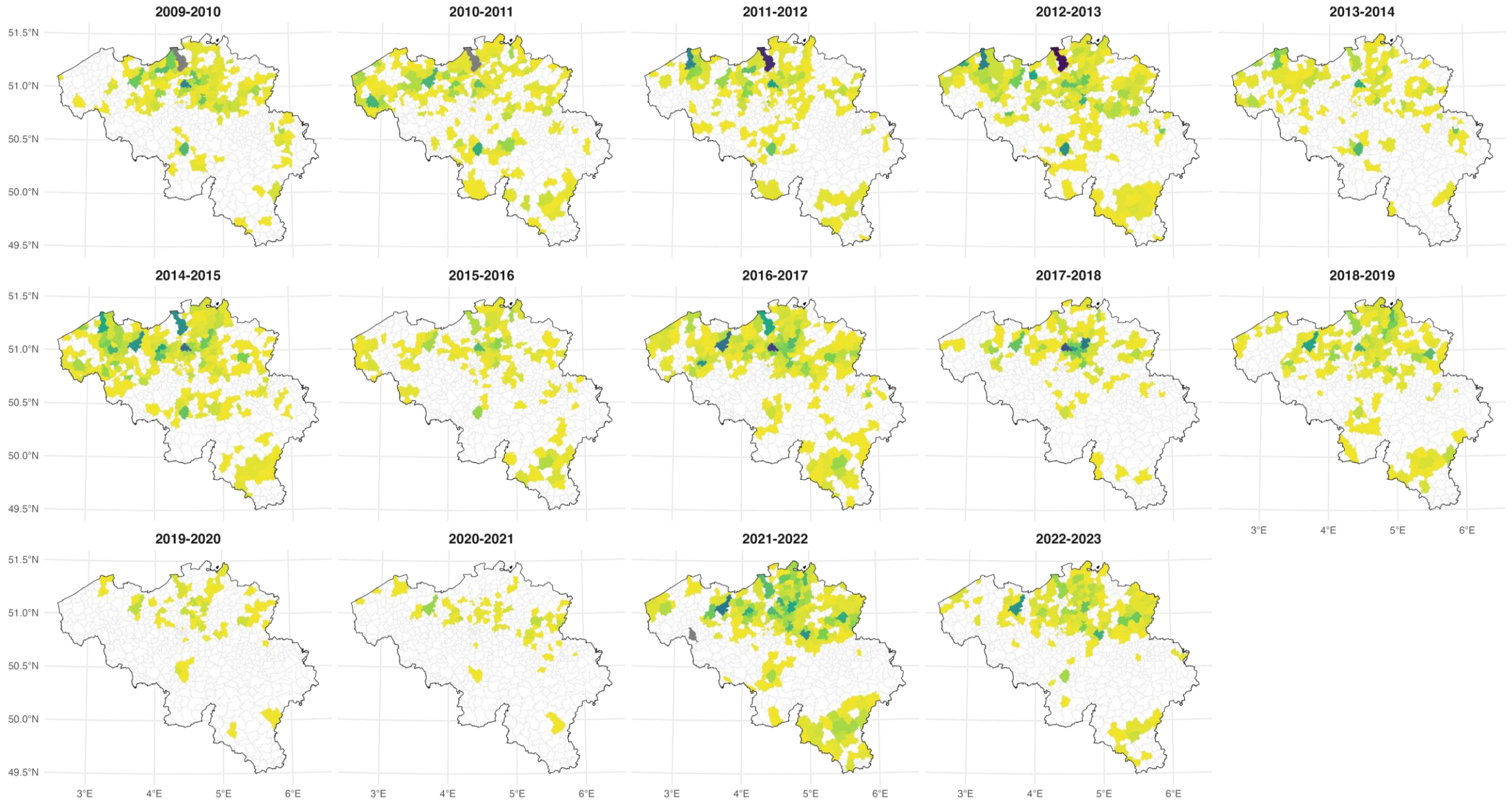


Overall sample distribution

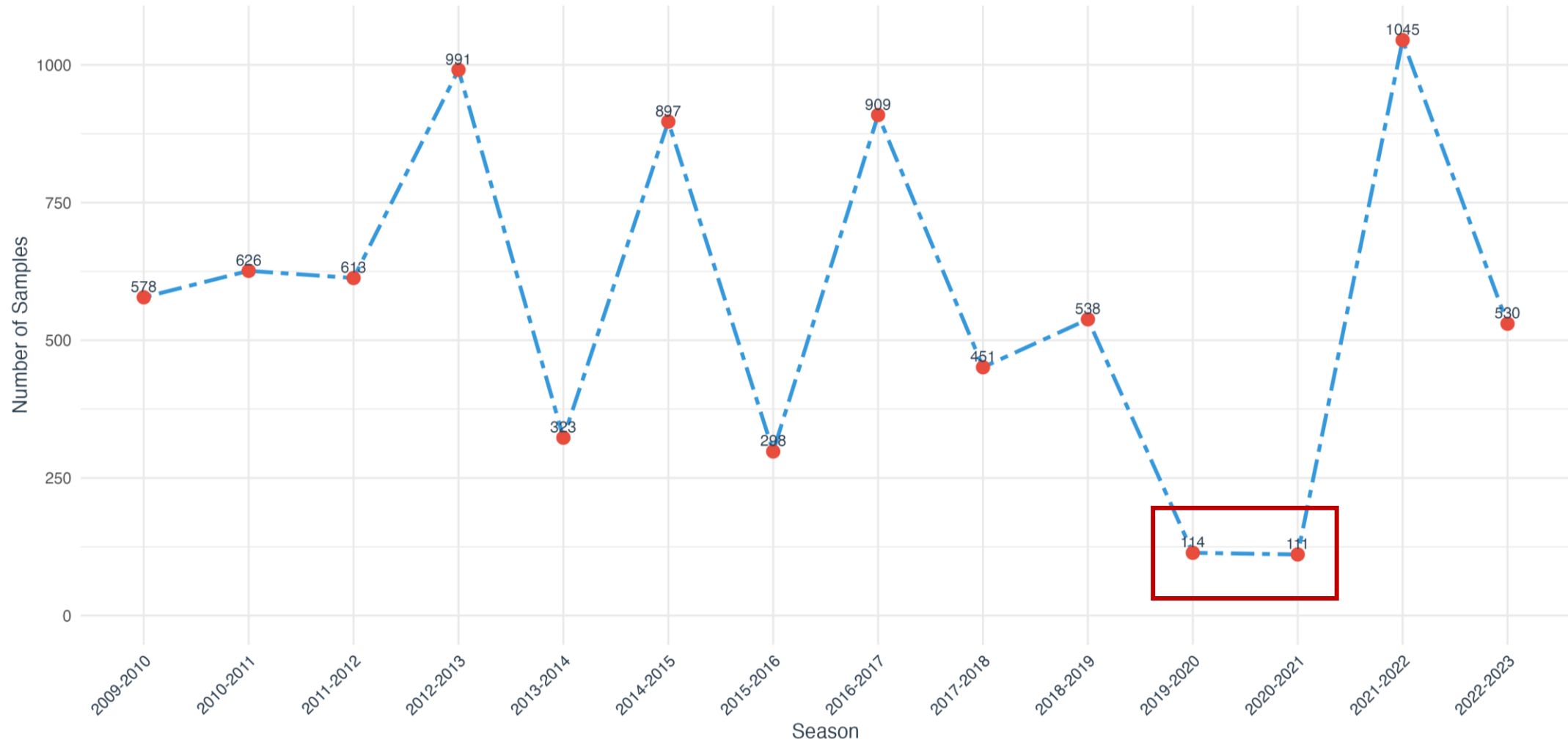
All seasons including 2009-2010 and 2022-2023



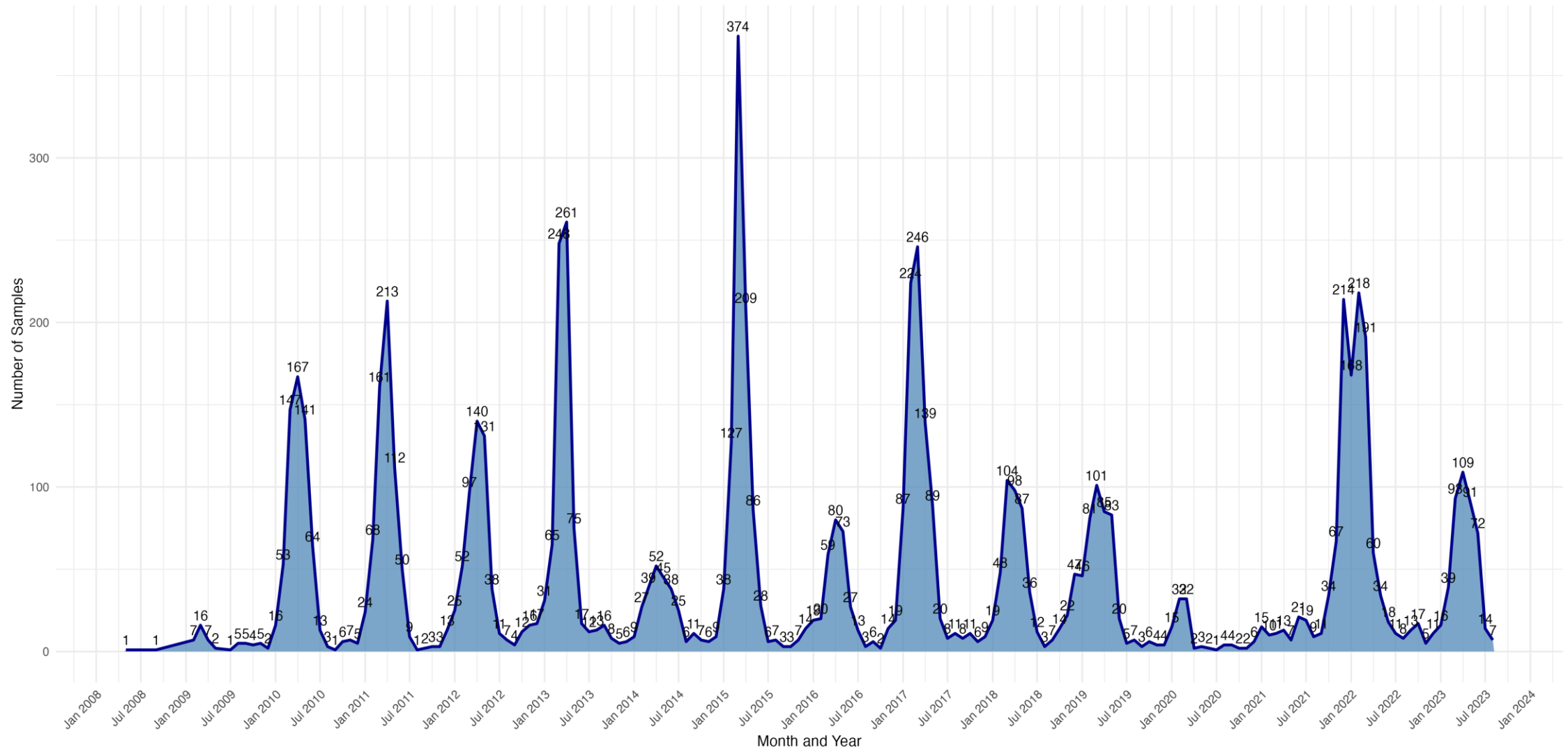
Sample Distribution in Belgium



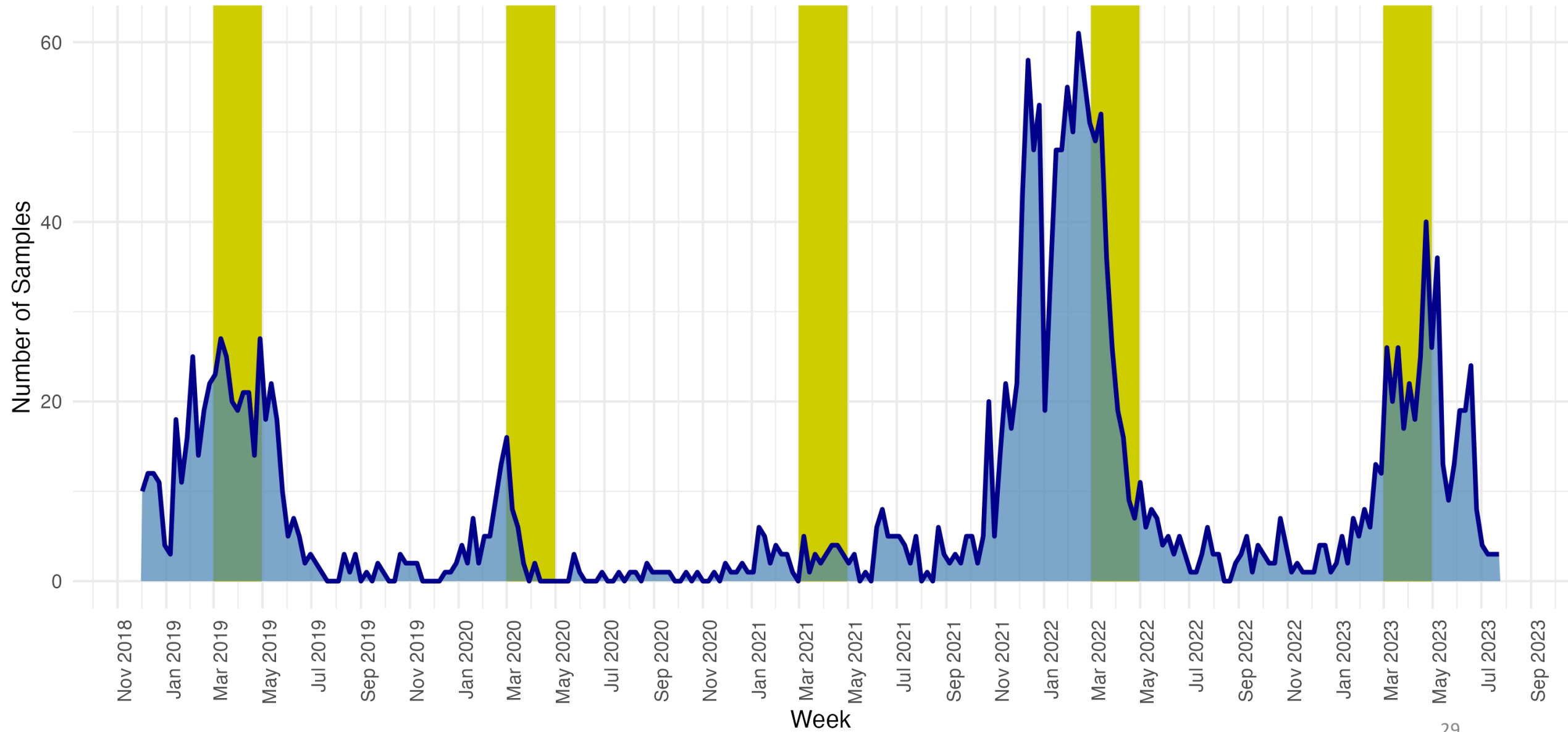
Sample counts per year

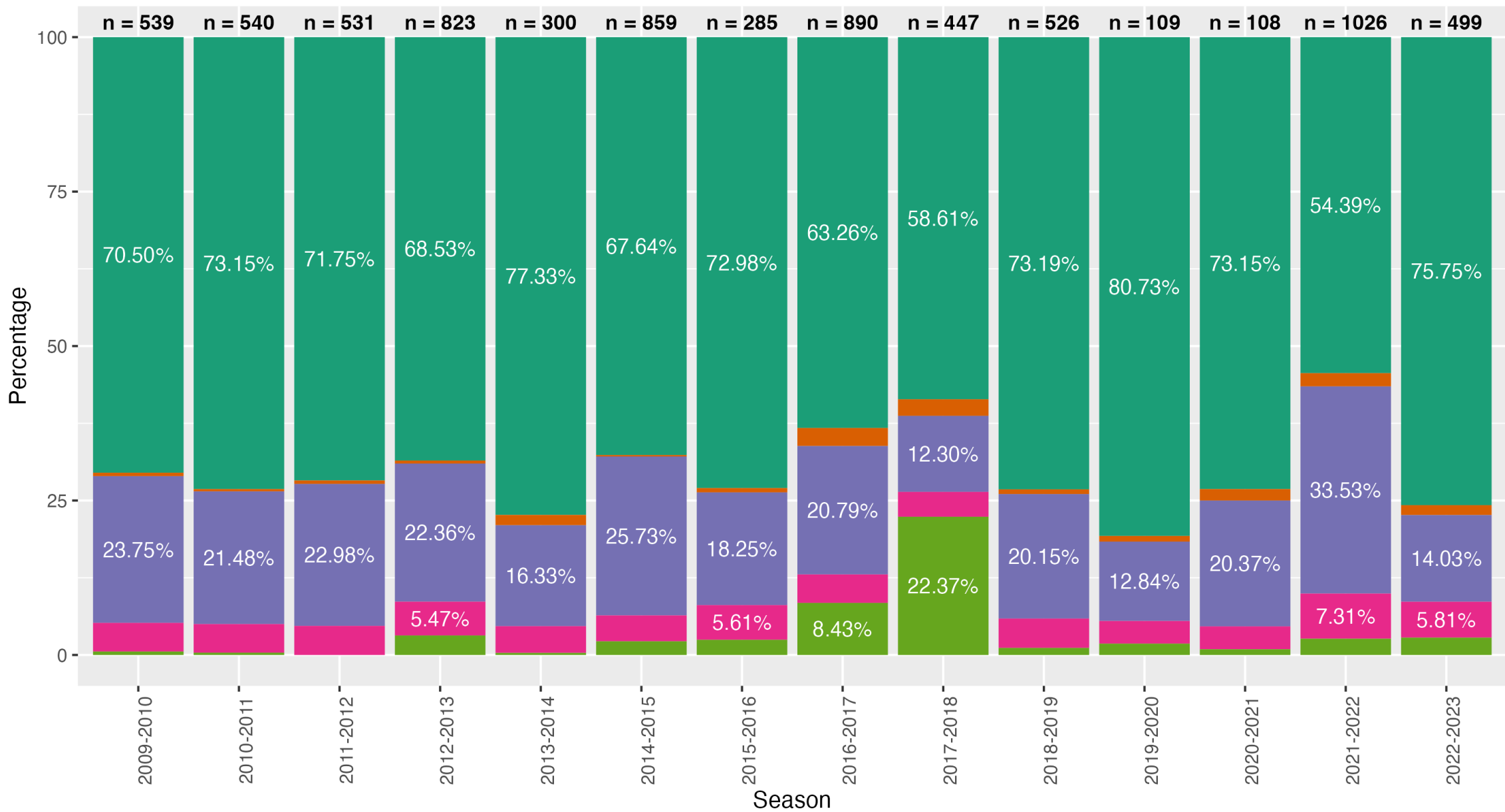


Number of Samples Collected Over Months

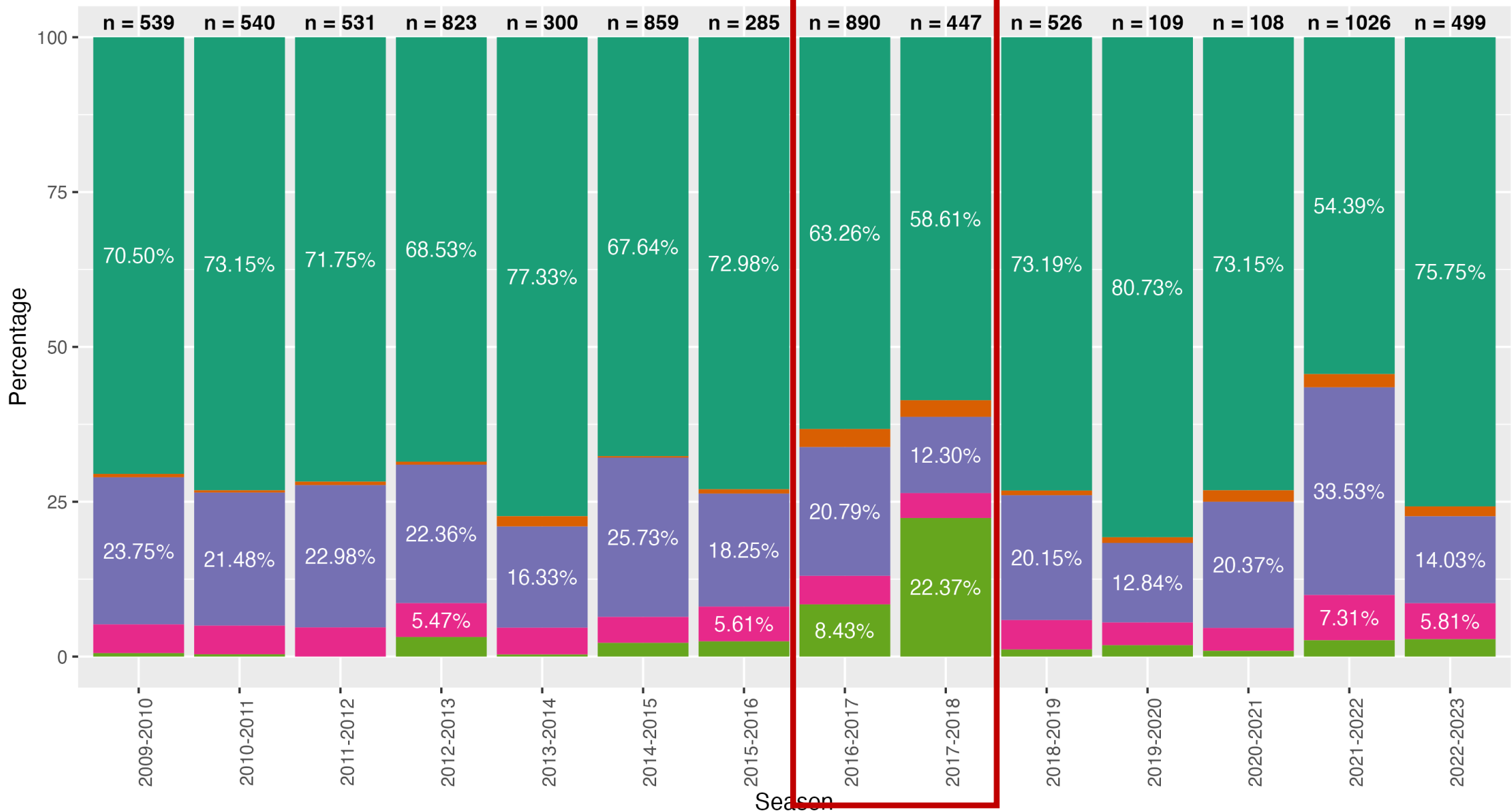


Number of Samples Collected Over Weeks



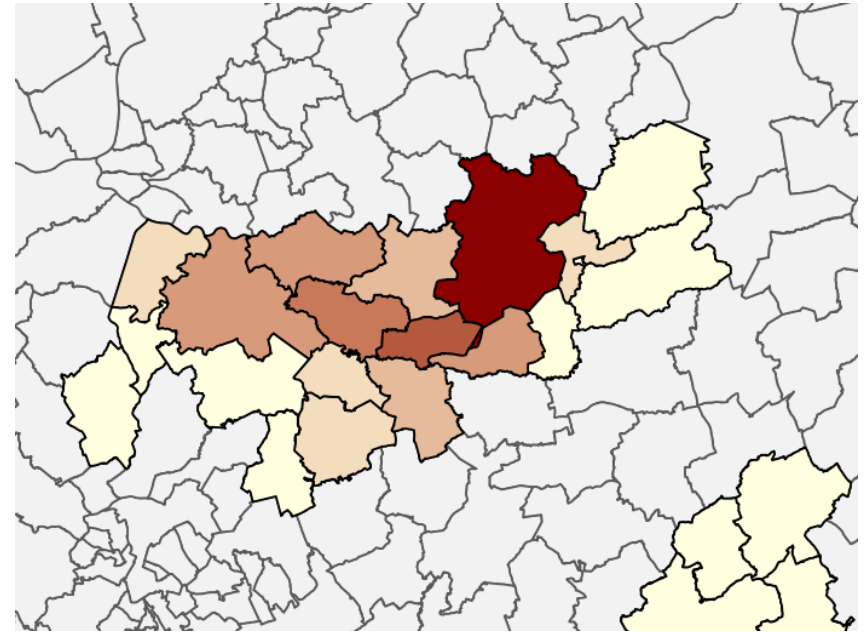
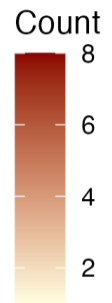
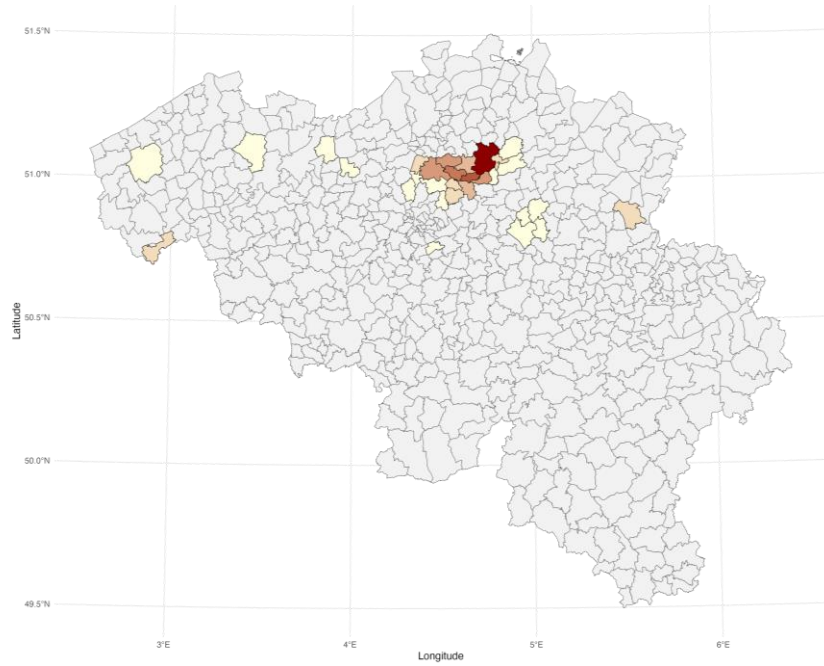


Age Group 0-2 18-60 2-5 5-18 60+

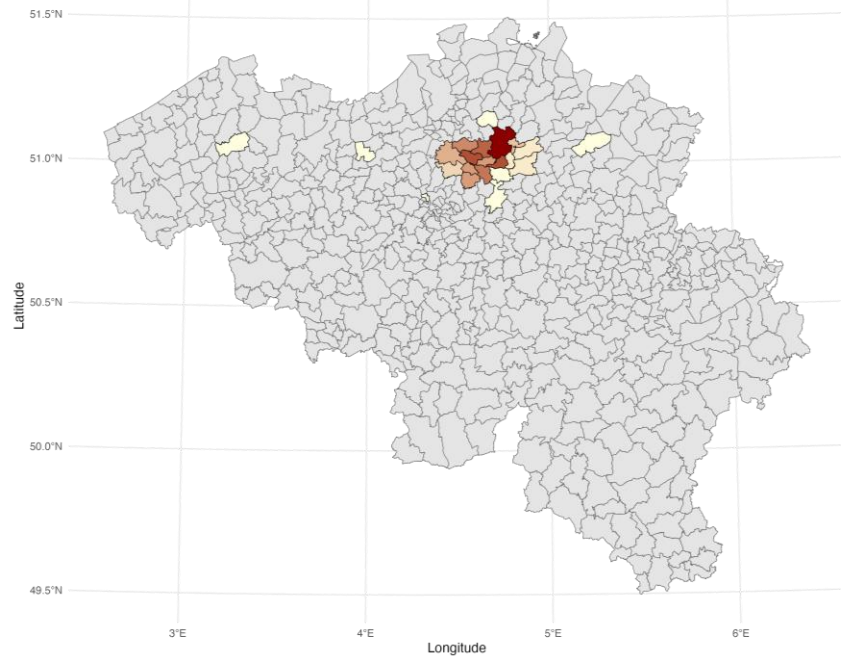


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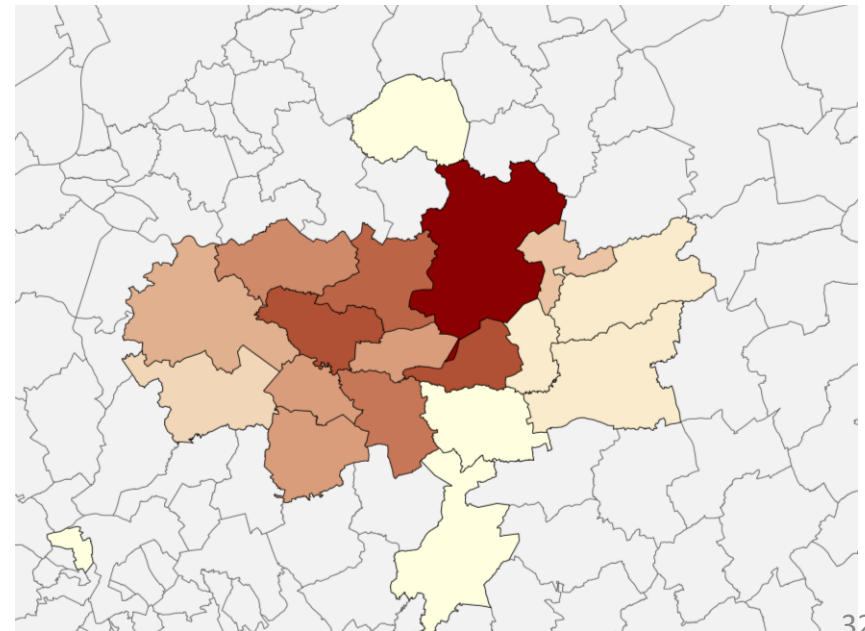
Data for 2016-2017 Season

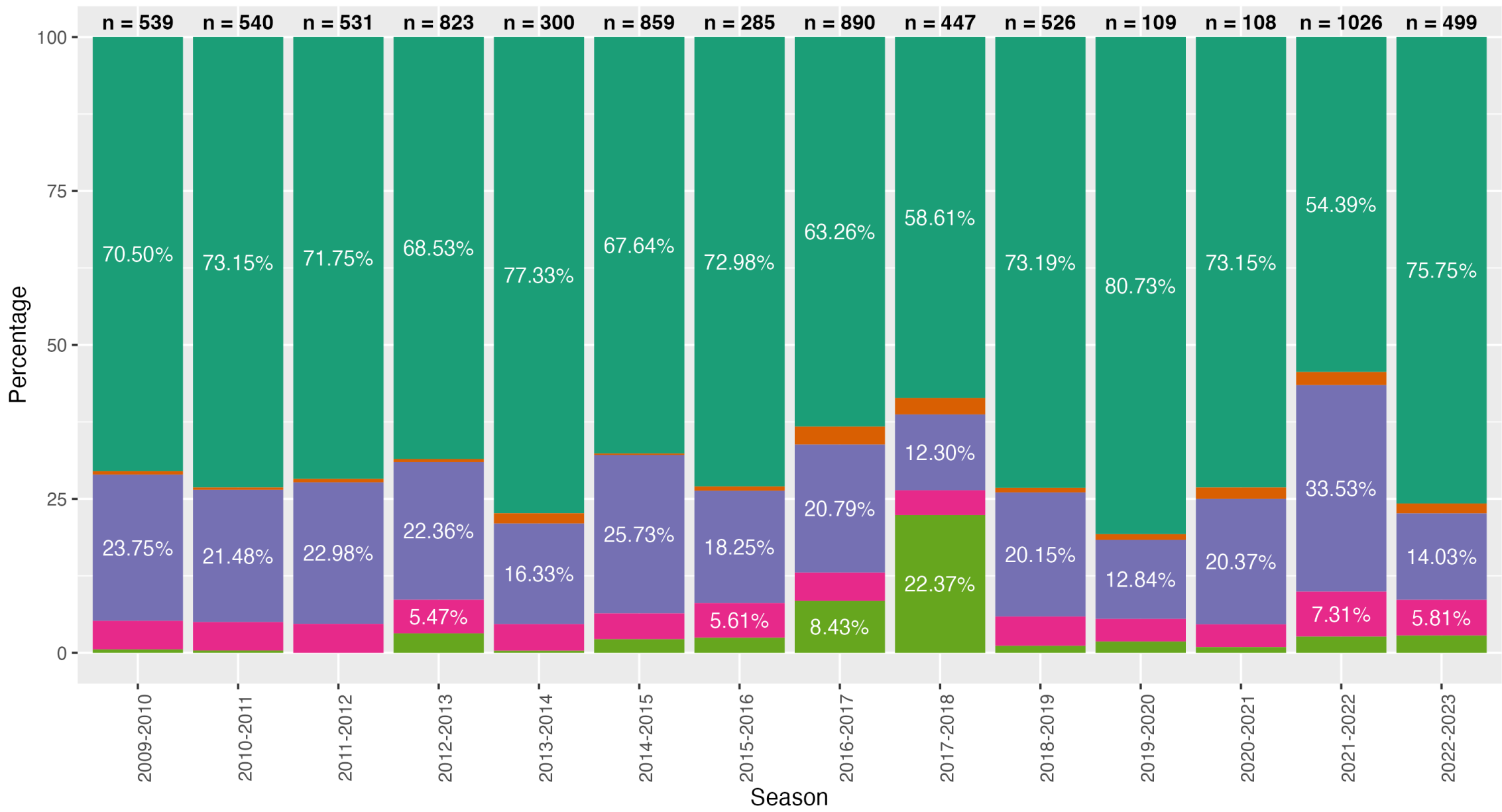


Data for 2017-2018 Season (Age Group 60+)

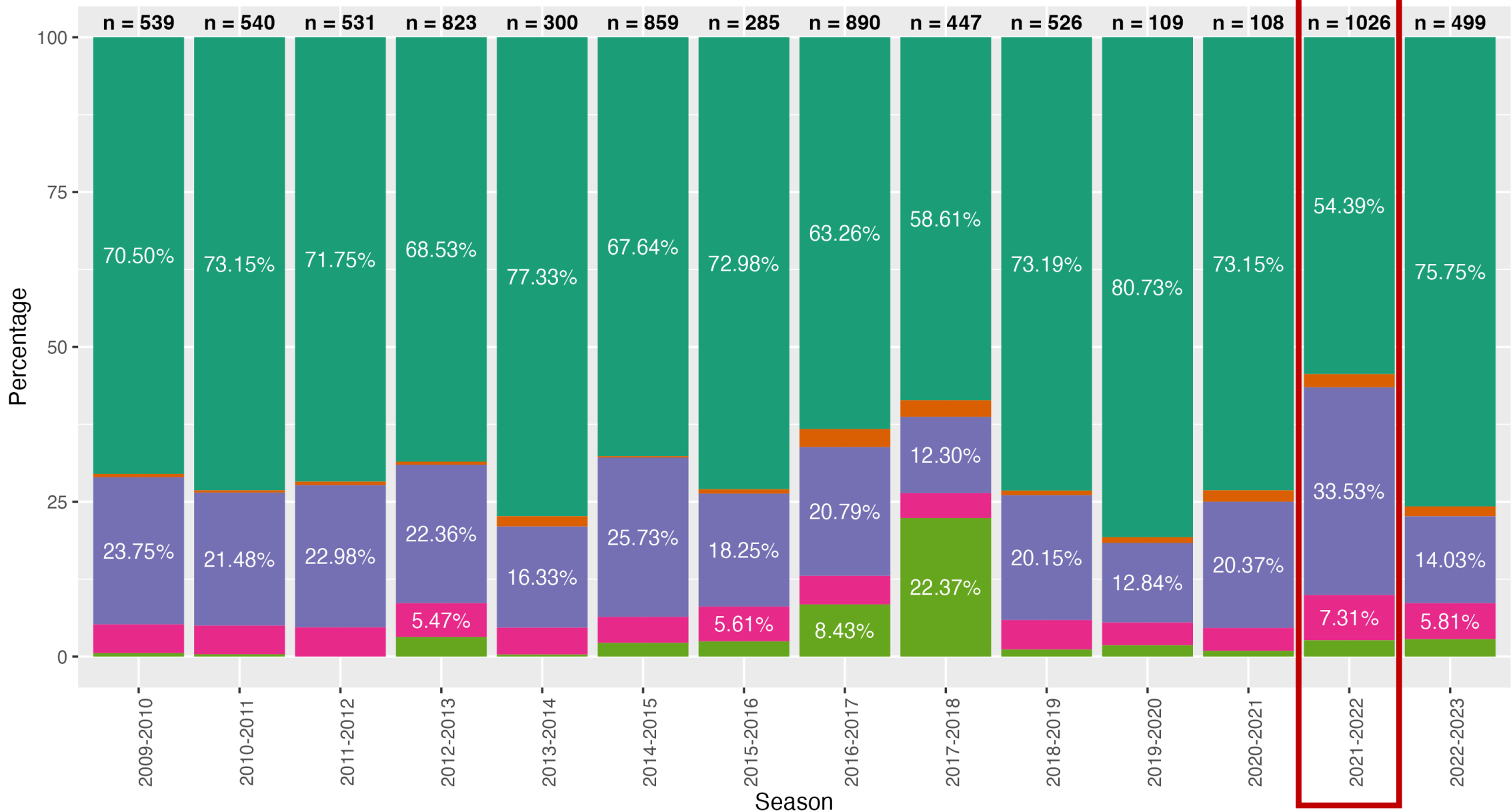


G2P[4]
genotype

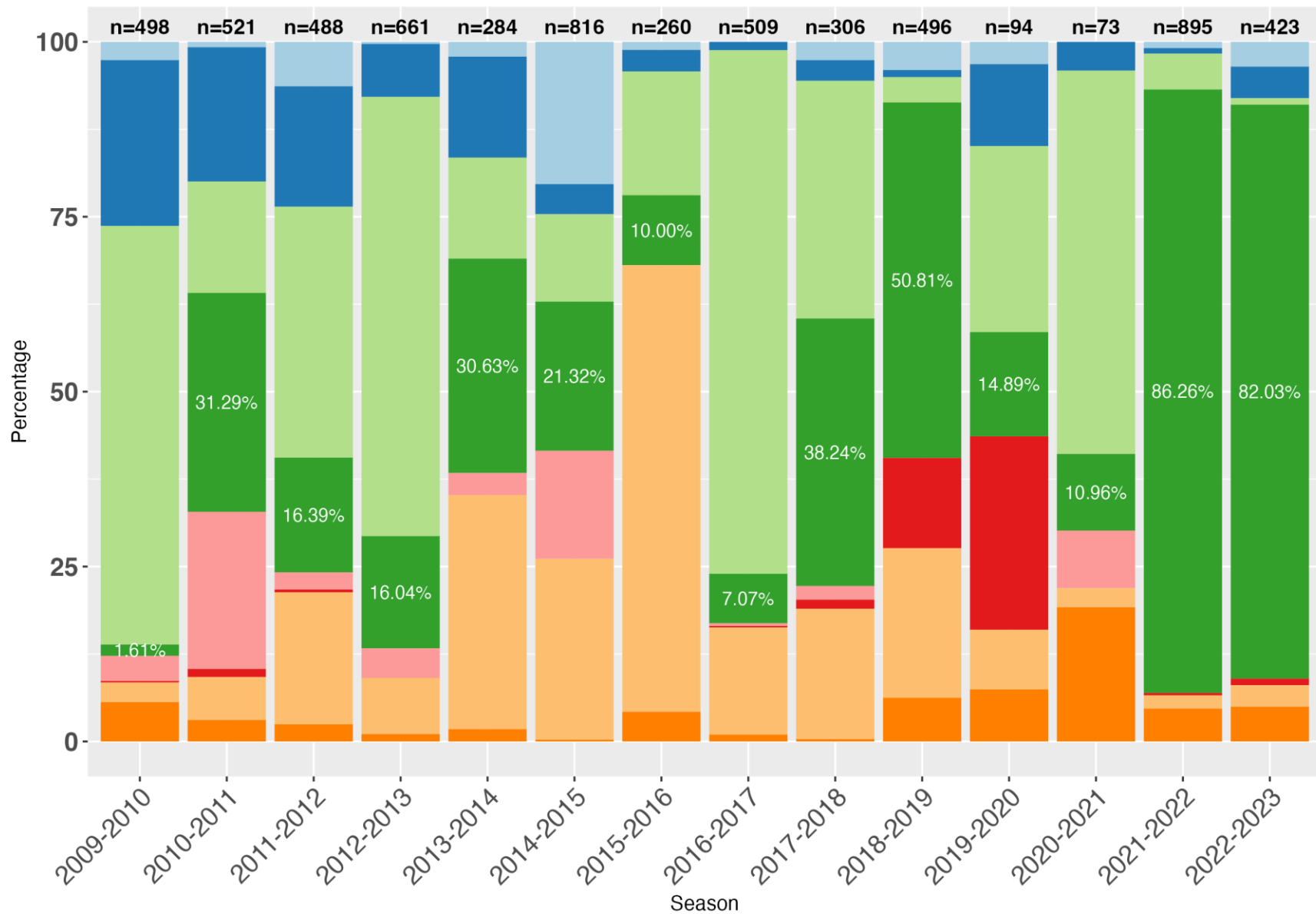


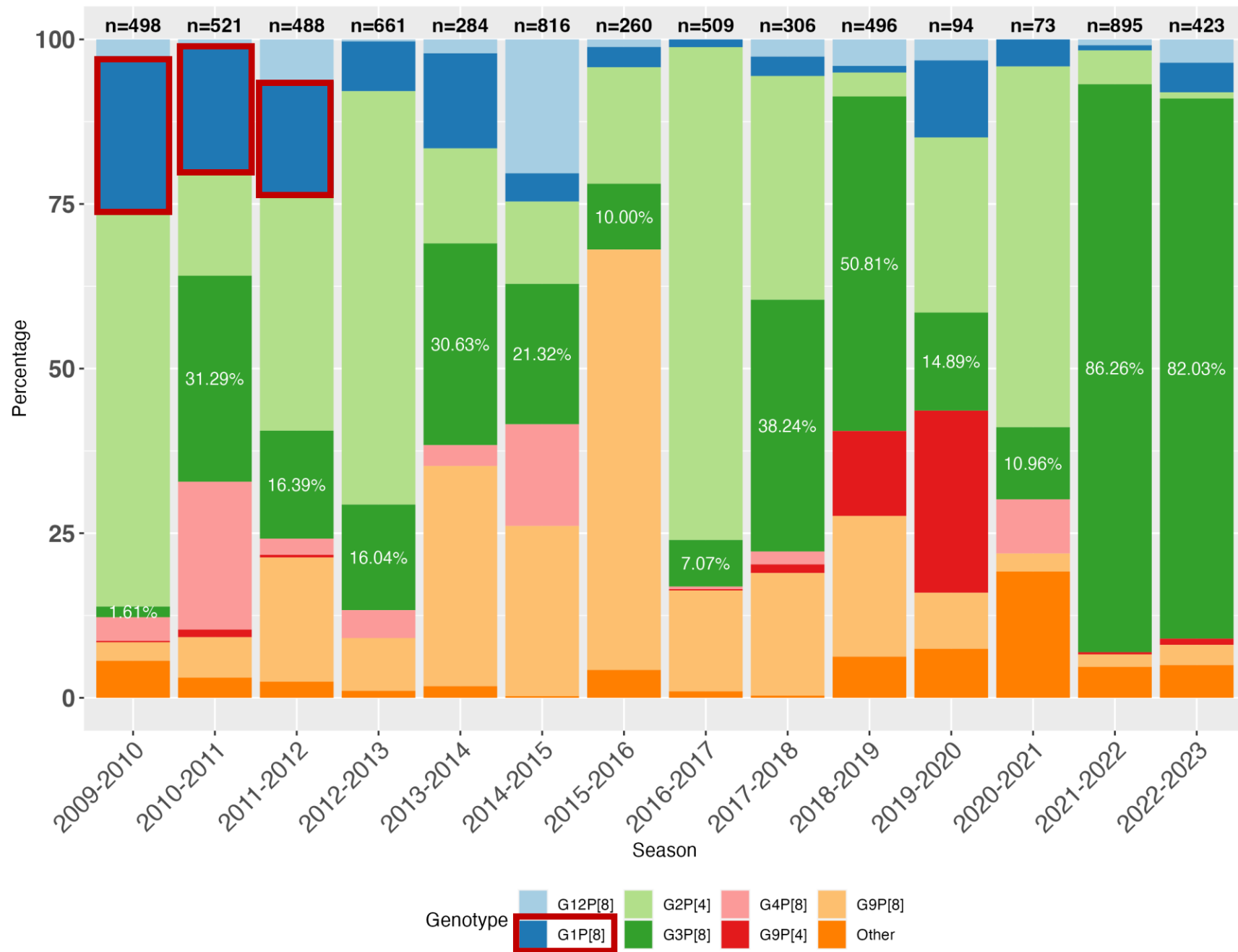


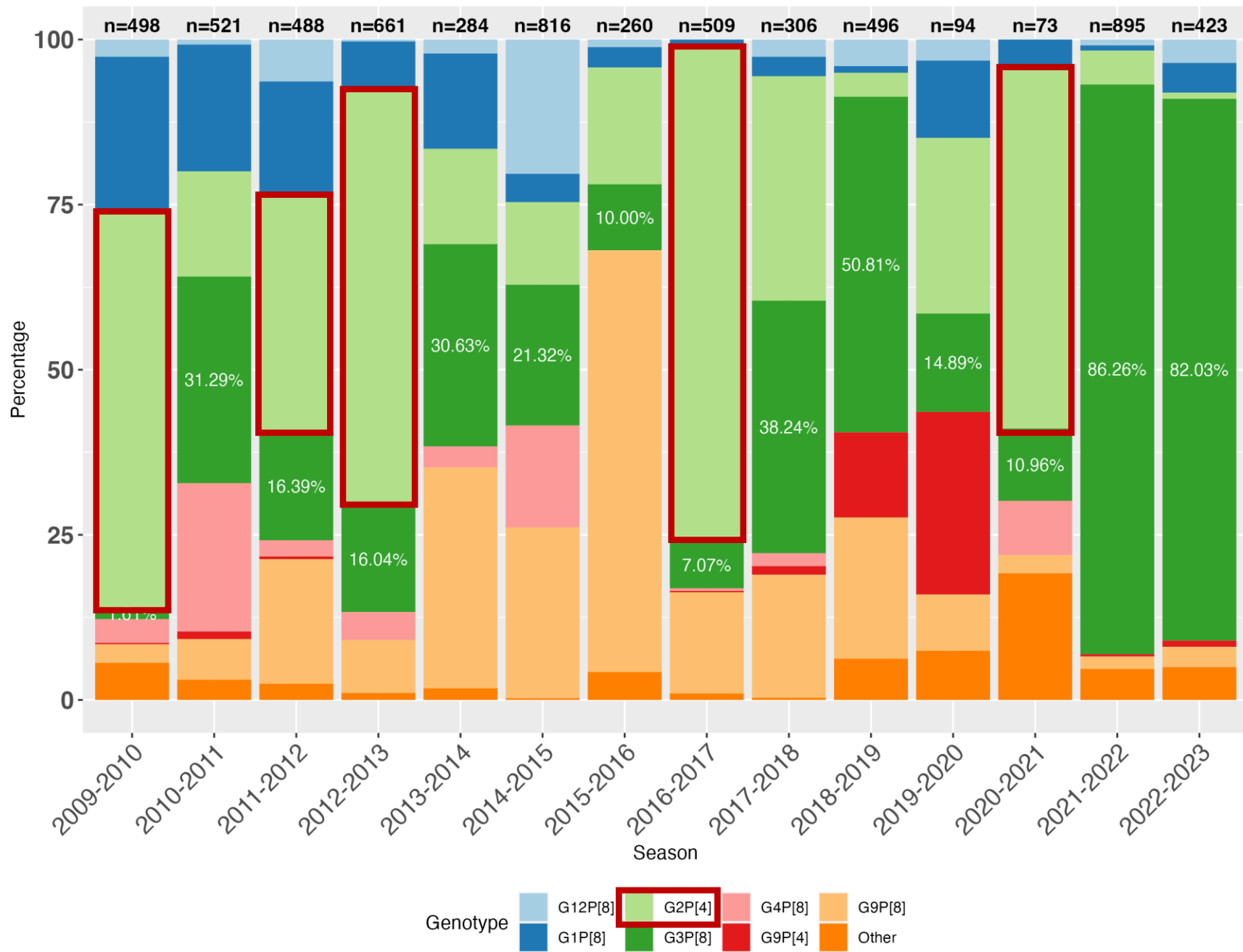
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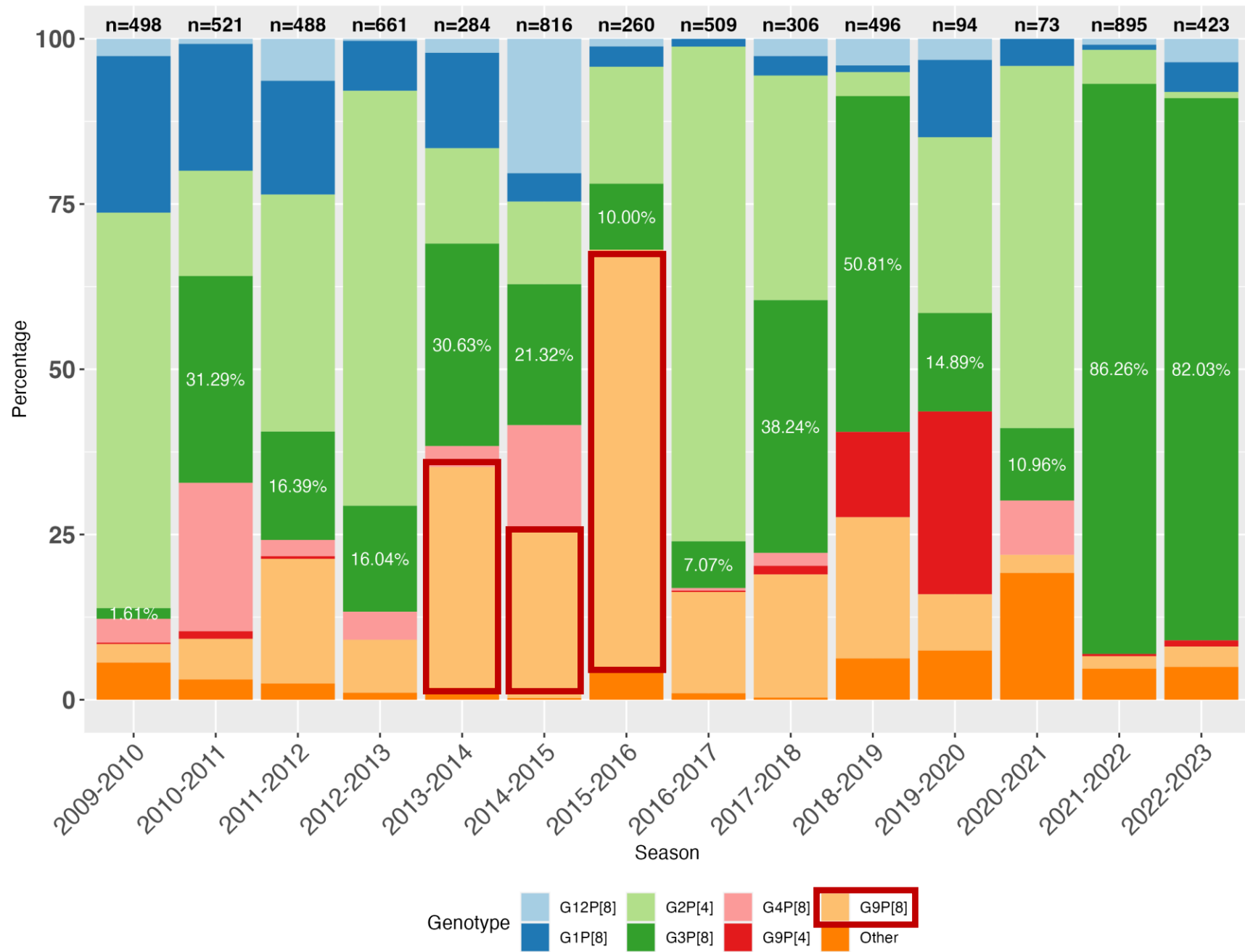


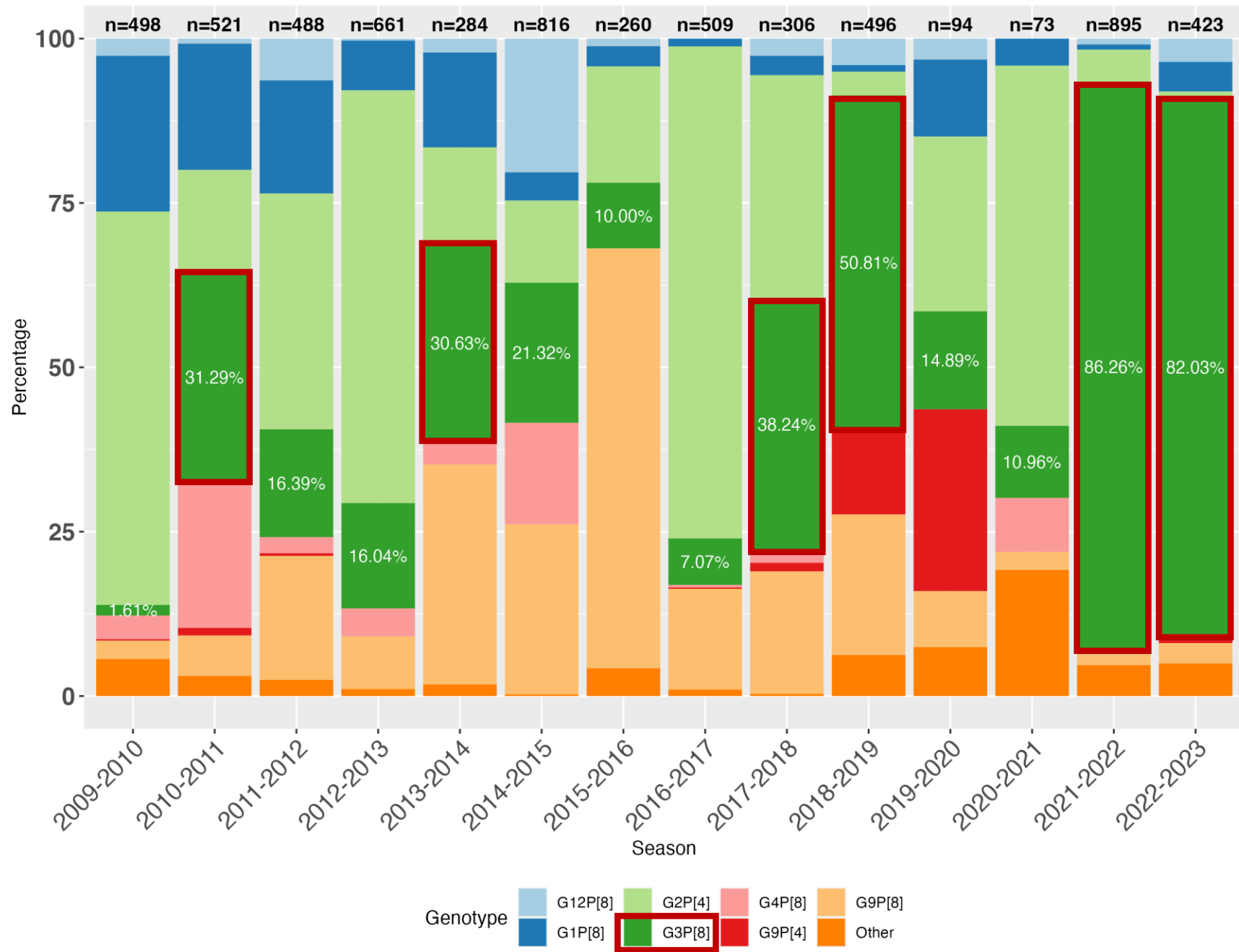
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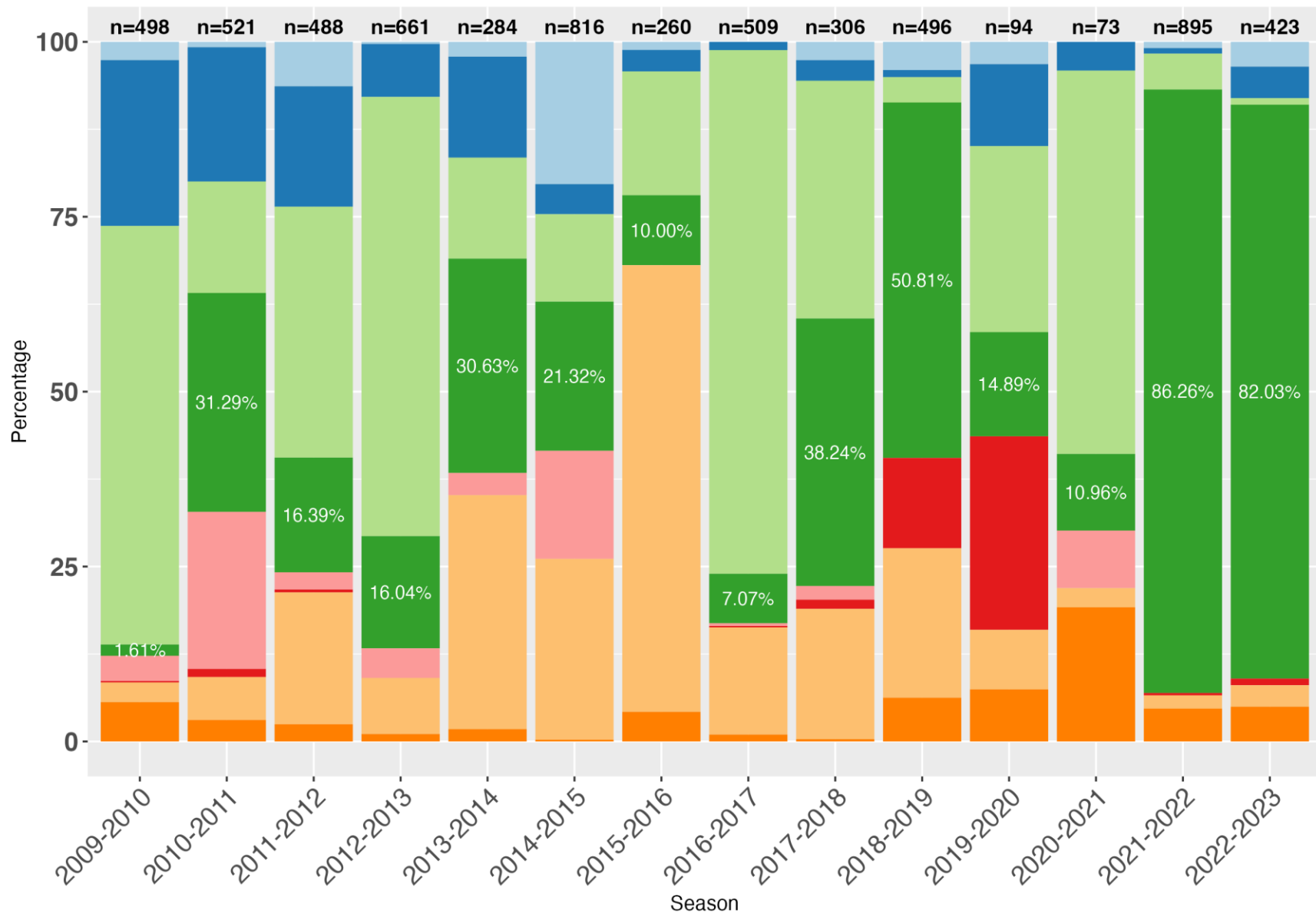






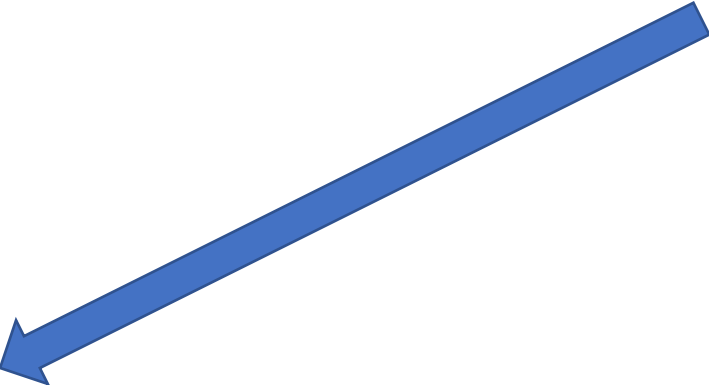






Zoonosis

Zoonosis



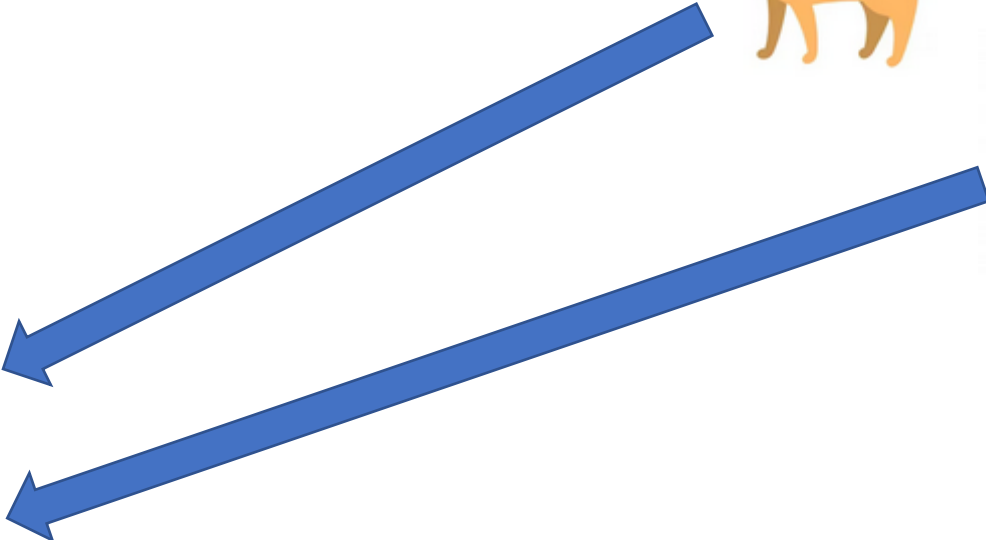
G3P[3]
G3P[9]

1x
1x

Zoonosis



G3P[3] 1x
G3P[9] 1x
G3P[14] 3x



Zoonosis

G3P[3]

1x

G3P[9]

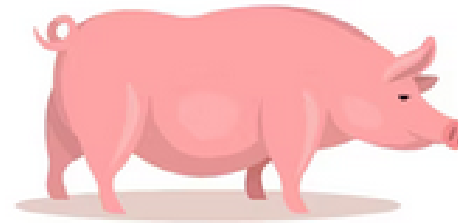
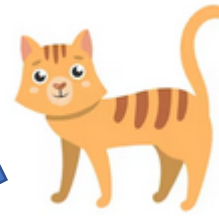
1x

G3P[14]

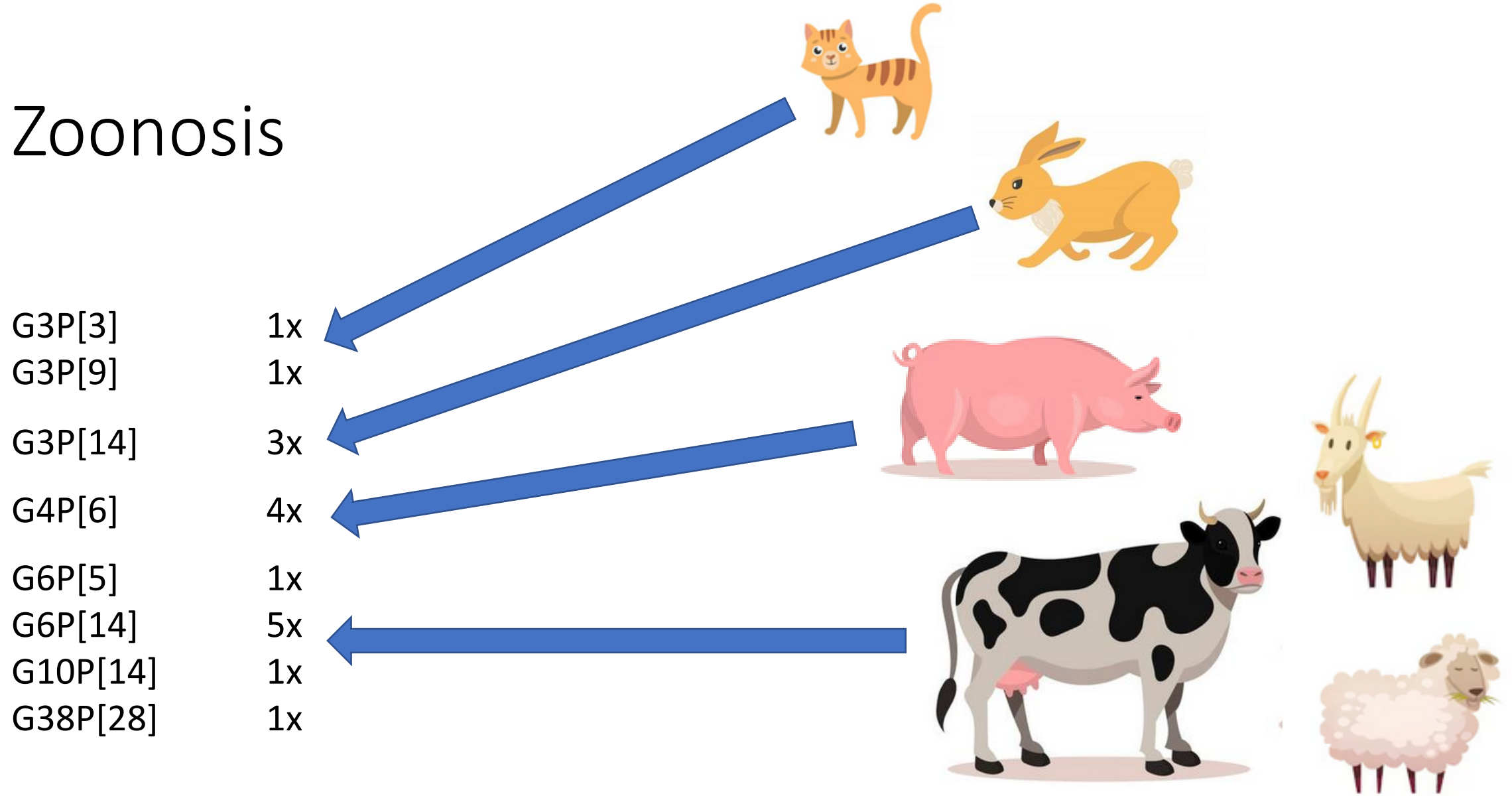
3x

G4P[6]

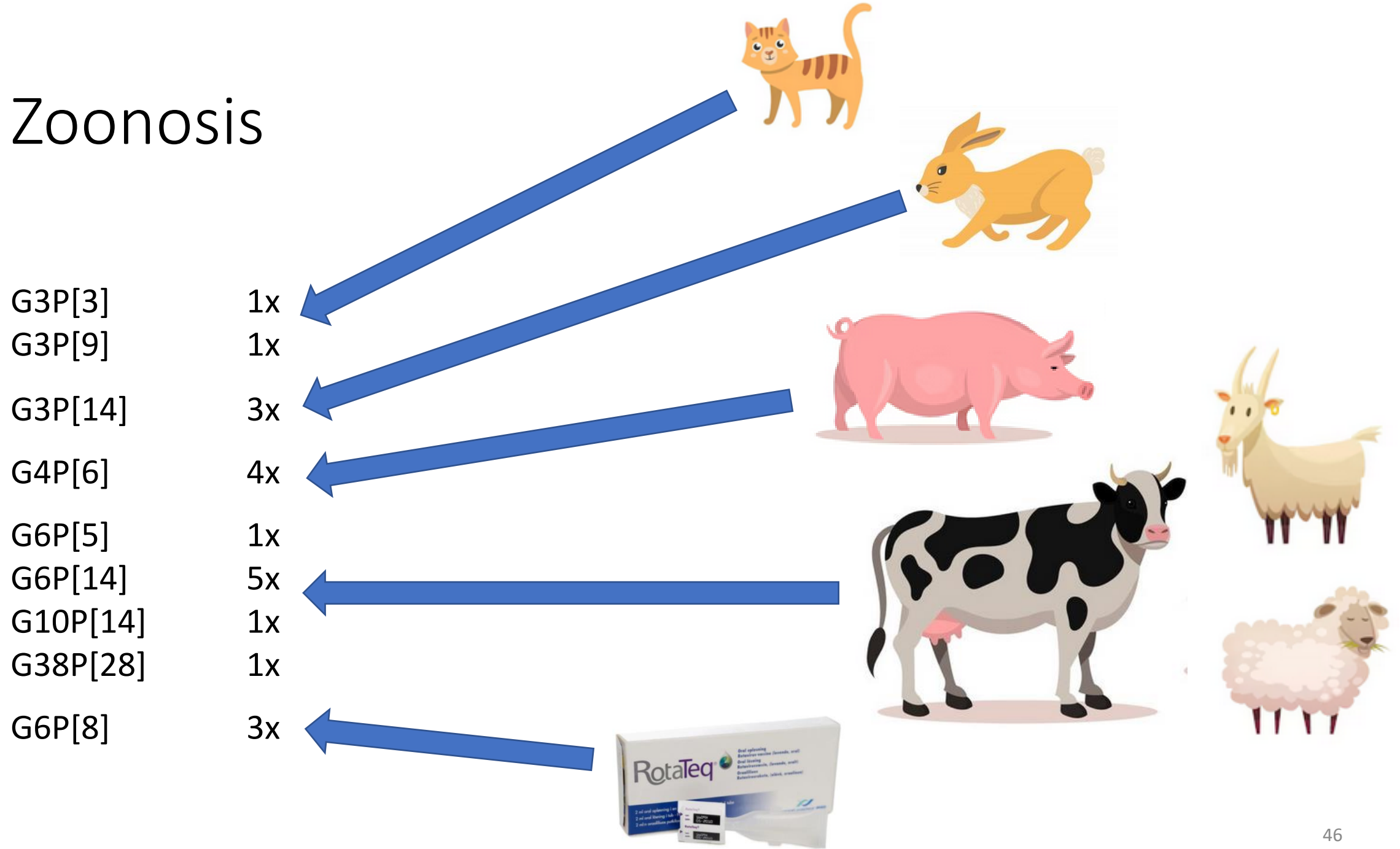
4x



Zoonosis



Zoonosis



Rotavirus co-infections






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MICROBIOLOGY

Journal of
Clinical Microbiology®

EPIDEMIOLOGY

December 2021 Volume 59 Issue 12 10.1128/jcm.01236-21
<https://doi.org/10.1128/jcm.01236-21>

High Prevalence of Coinfecting Enteropathogens in Suspected Rotavirus Vaccine Breakthrough Cases

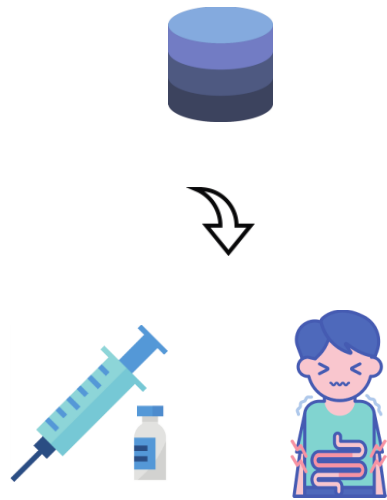
Ceren Simsek ^a, Mandy Bloemen^a, Daan Jansen ^a, Leen Beller^a, Patrick Descheemaeker^b,
Marijke Reynders^b, Marc Van Ranst^a, Jelle Matthijssens ^a

NRC patient database

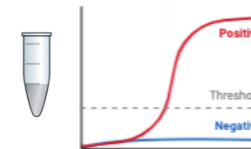


102 samples
from **2007-2008** to **2017-2018**

NRC patient database



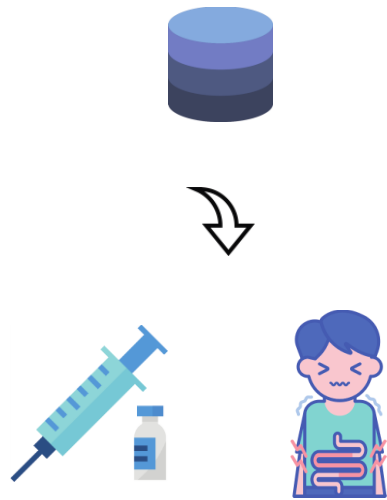
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RT-qPCR



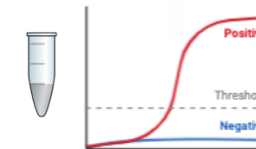
NRC patient database



102 samples
from **2007-2008** to **2017-2018**



NGS



RT-qPCR



NetoVIR protocol

NetoVIR protocol

SCIENTIFIC REPORTS



OPEN

Modular approach to customise sample preparation procedures for viral metagenomics: a reproducible protocol for virome analysis

Received: 19 August 2015

Accepted: 15 October 2015

Published: 12 November 2015

Nádia Conceição-Neto^{1,2}, Mark Zeller¹, Hanne Lefrère¹, Pieter De Bruyn¹, Leen Beller¹, Ward Deboutte¹, Claude Kwe Yinda^{1,2}, Rob Lavigne³, Piet Maes², Marc Van Ranst², Elisabeth Heylen^{1,*} & Jelle Matthijssens^{1,2,*}

NetoVIR protocol

SCIENTIFIC REPORTS

OPEN

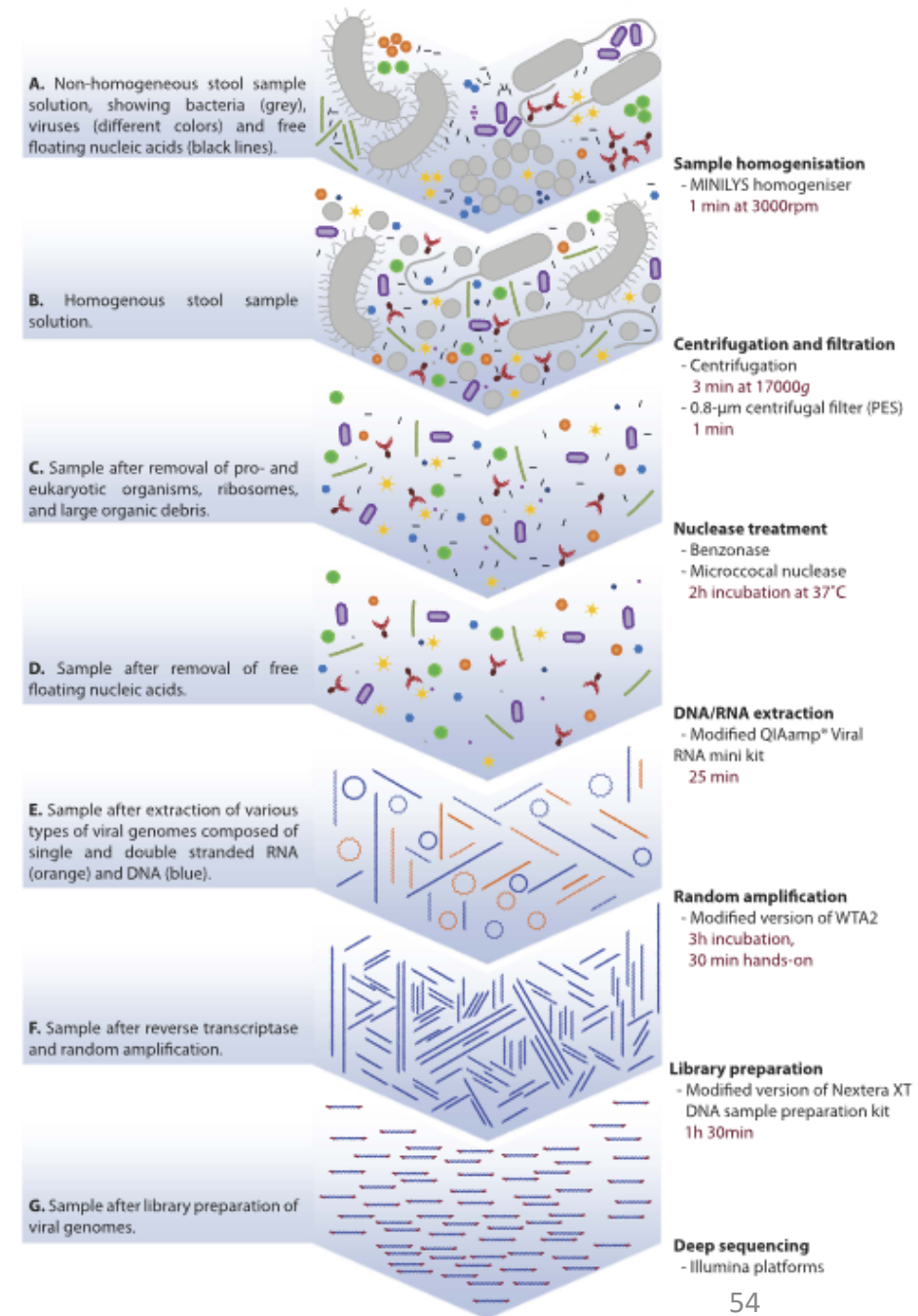
Modular approach to customise sample preparation procedures for viral metagenomics: a reproducible protocol for virome analysis

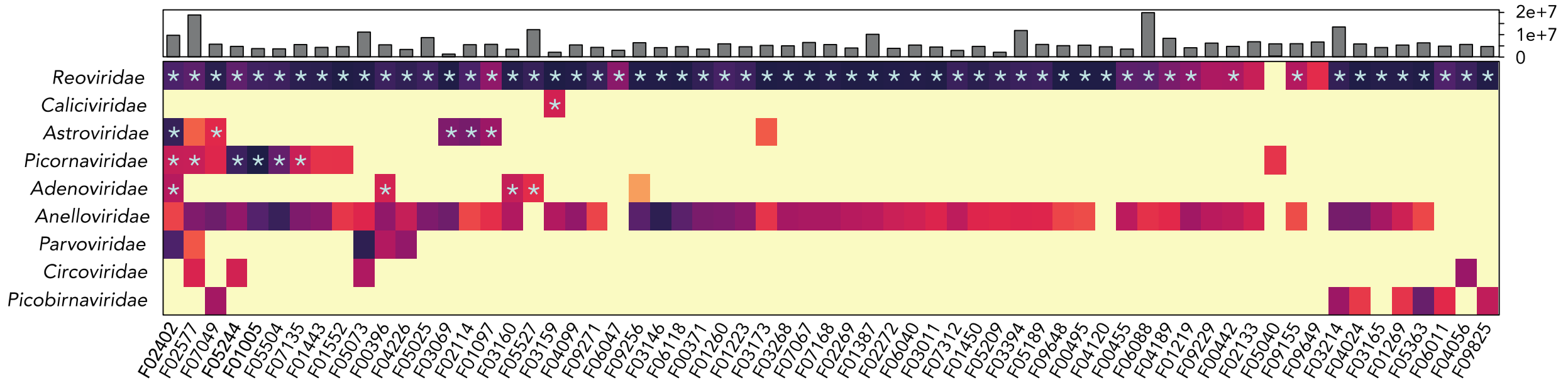
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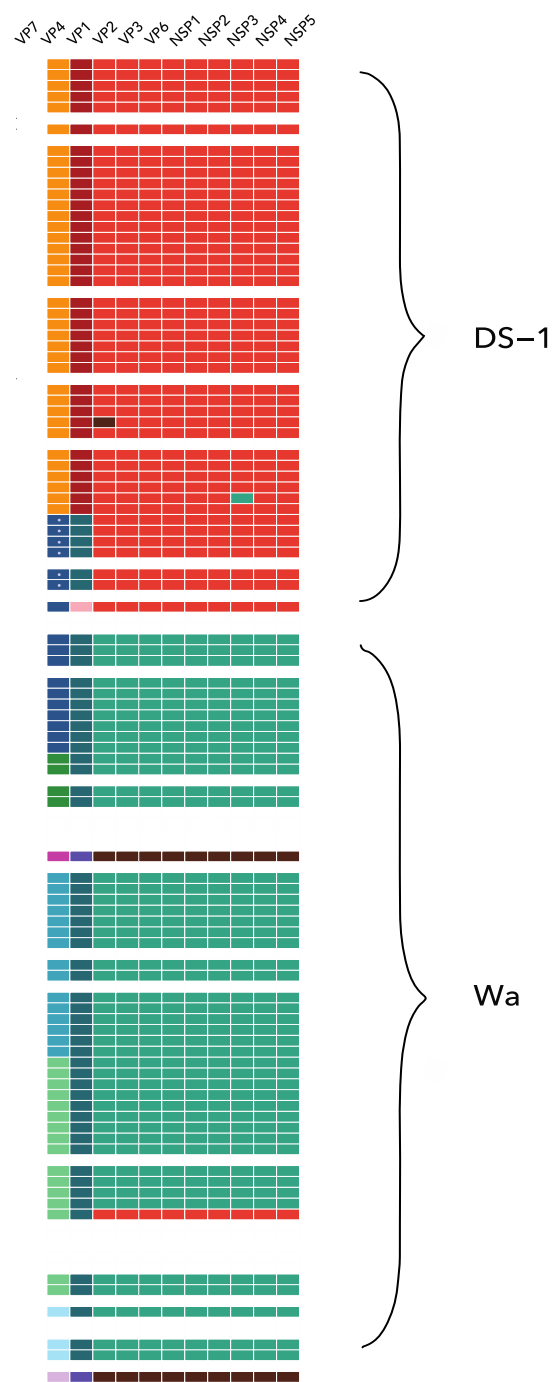
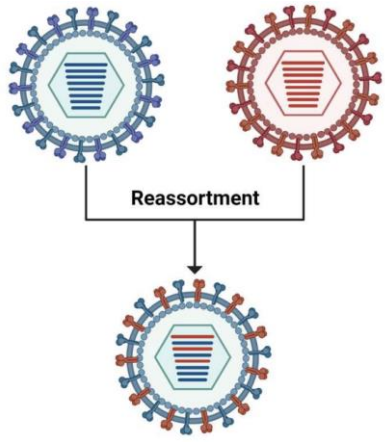
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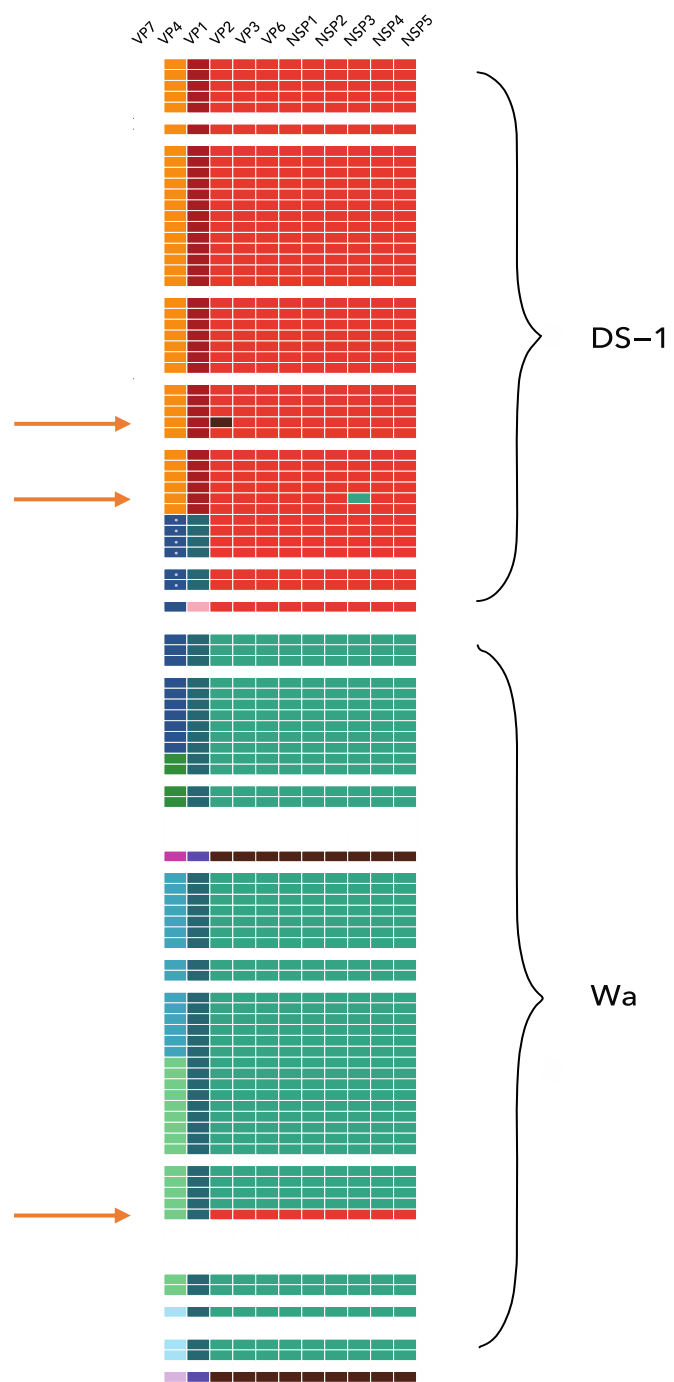
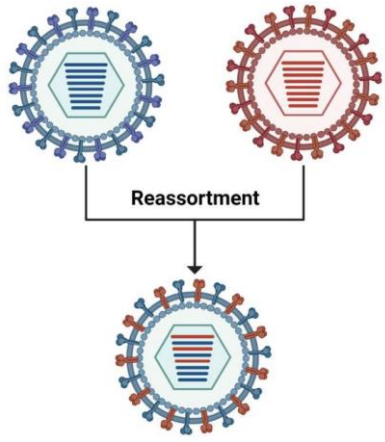
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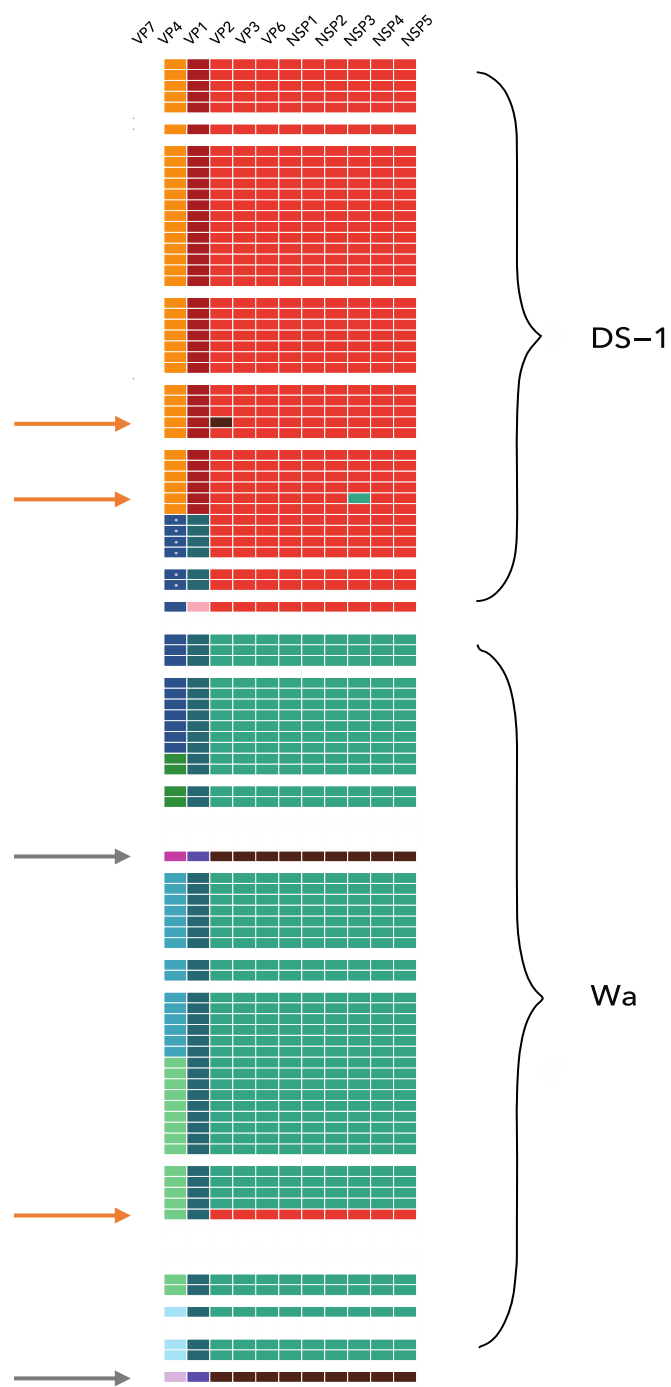
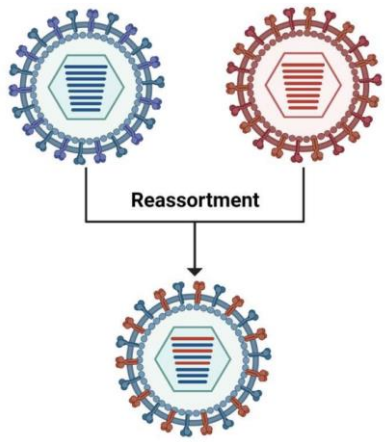




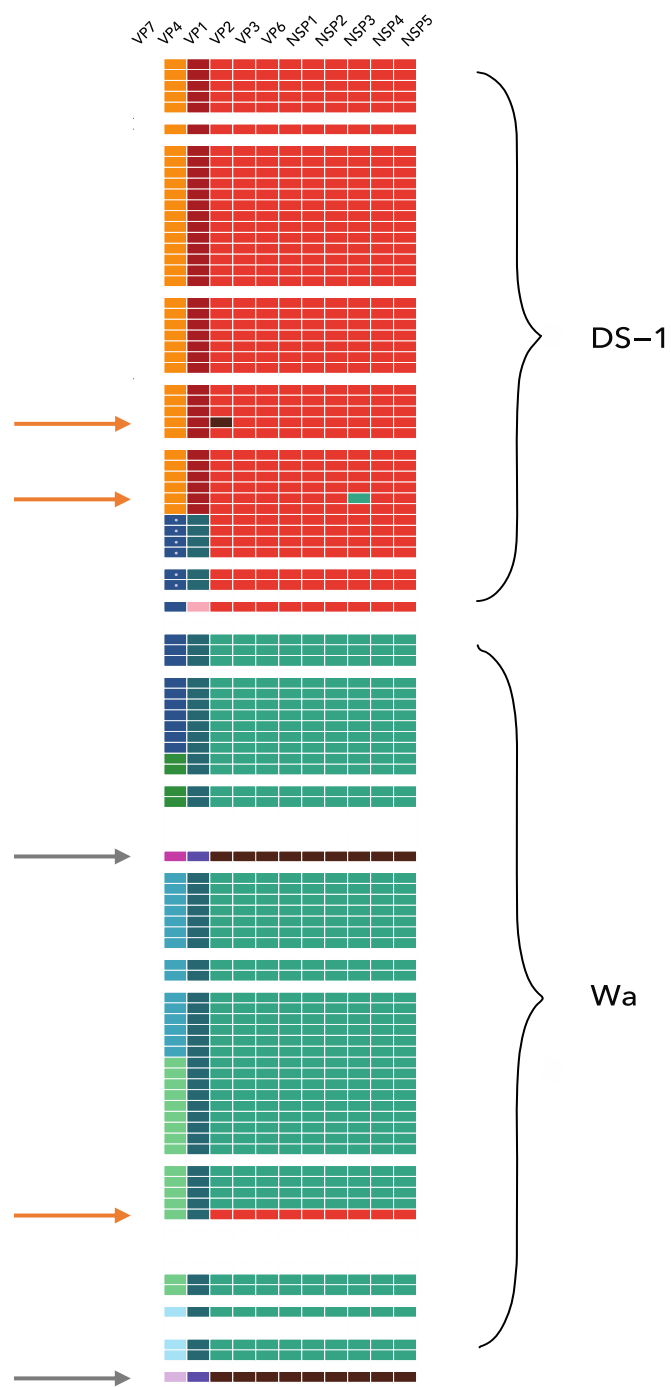
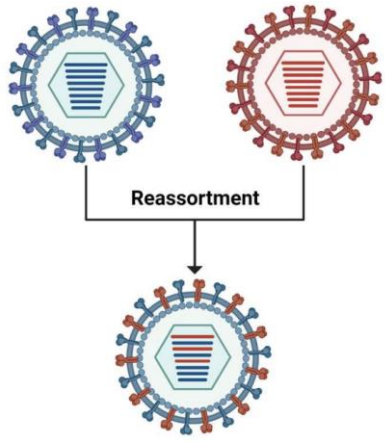




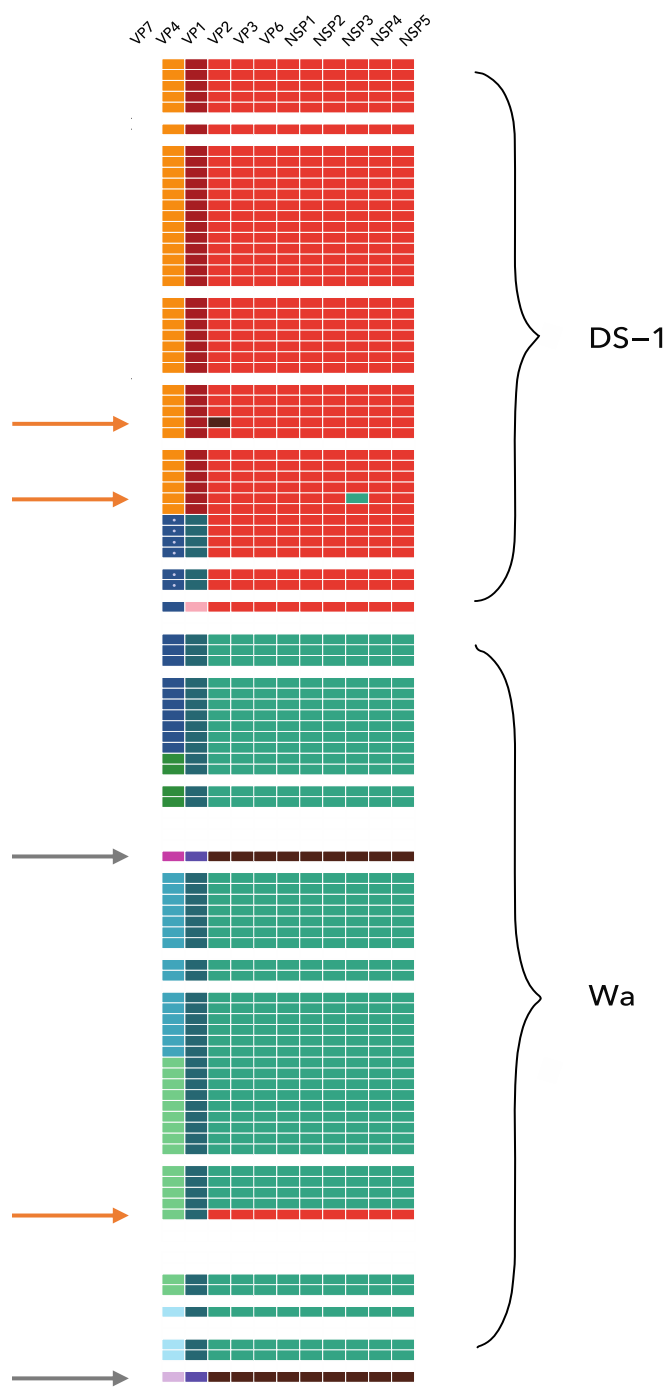
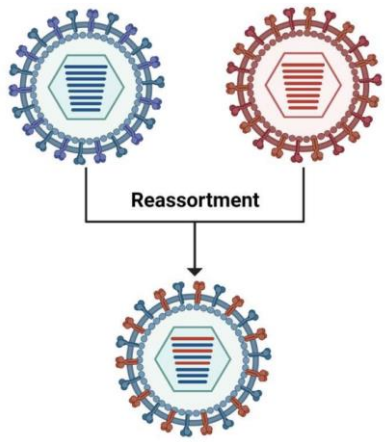
○ Few intergenogroup reassortant



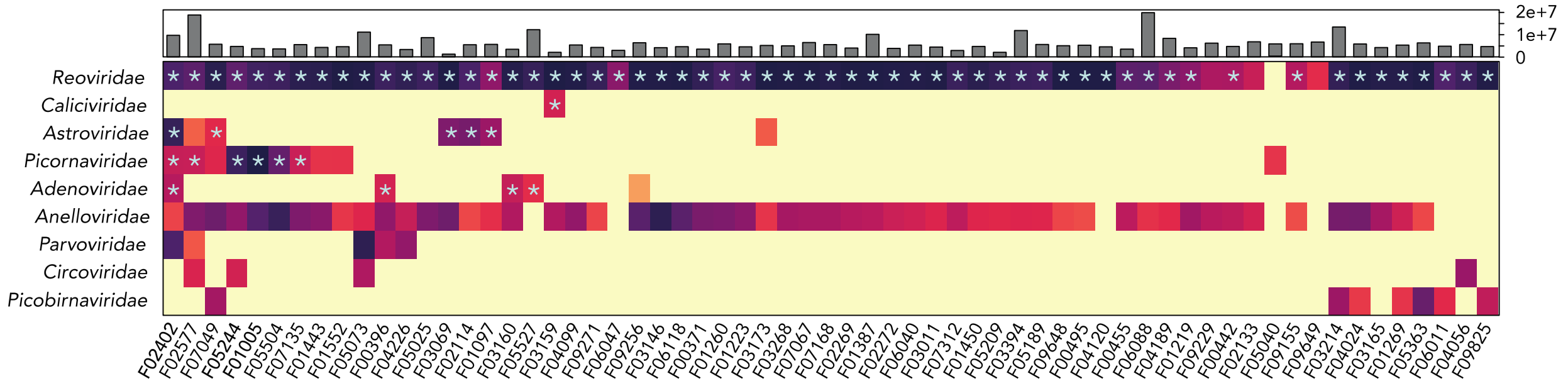
- Few intergenogroup reassortant
- Few zoonotic strains detected

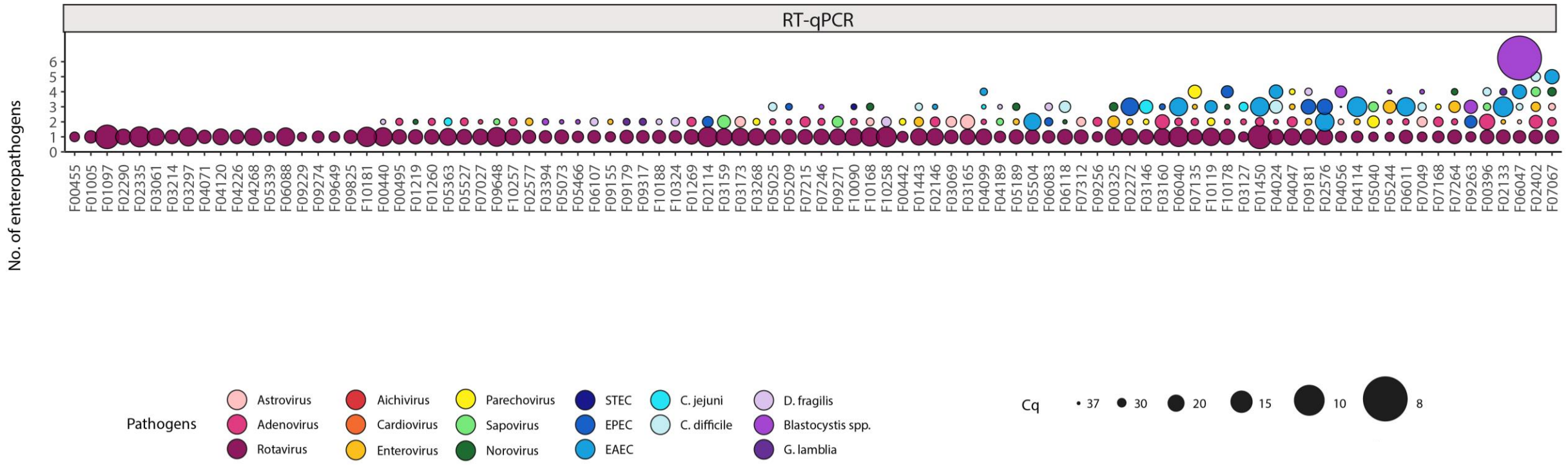


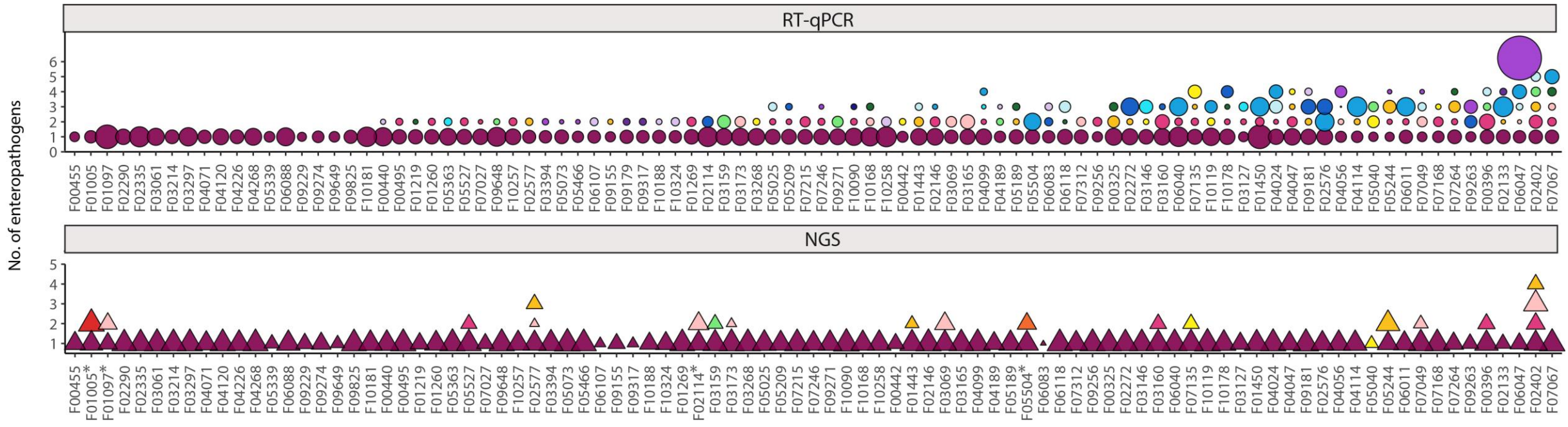
- Few intergenogroup reassortant
- Few zoonotic strains detected
- → Fitness cost

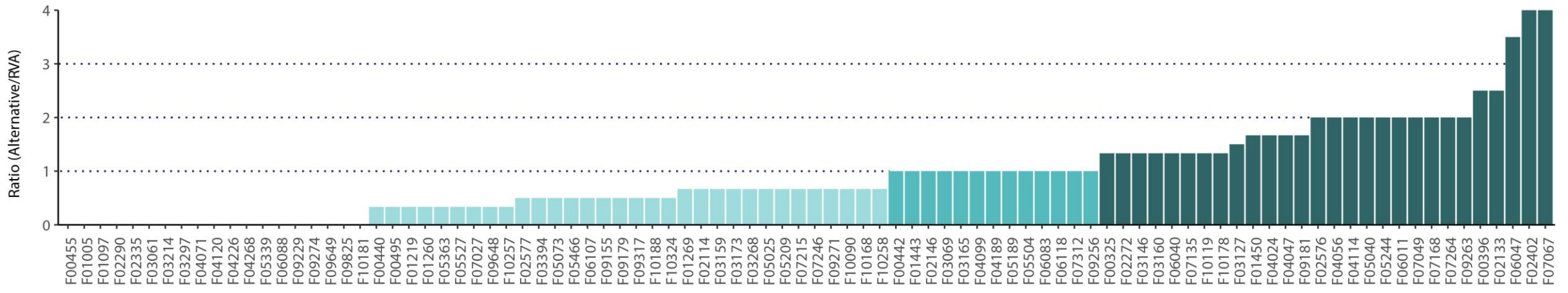
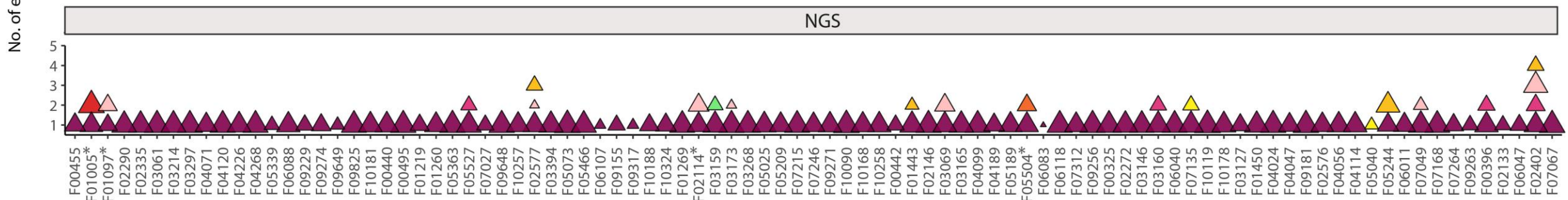
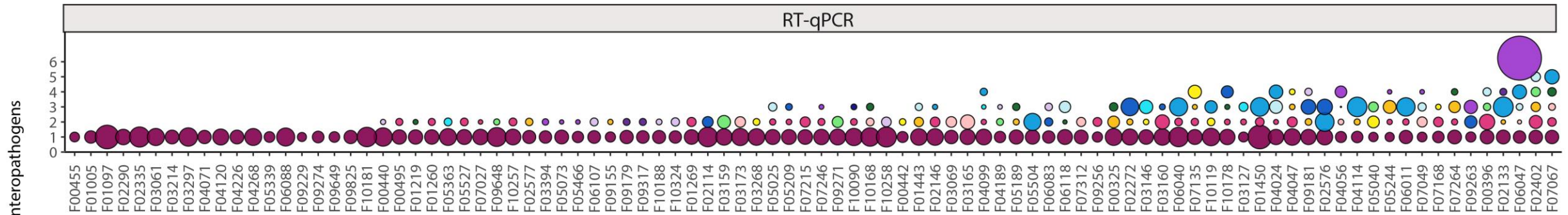


- Few intergenogroup reassortant
- Few zoonotic strains detected
- → Fitness cost
- **No** evidence for unusual genotypes that might suggest escape vaccine-induced immunity









Breakthrough

Equal

Alternative

Summary

- No unusual rotavirus genotypes in breakthrough cases
 - ✓ Few reassortants and few inter species transmissions
- Various other viral, bacterial and parasitic co-infecting pathogens
- Approximately 50% of cases might be explained by other pathogens
- Implications for diagnostics and clinical trials

Vaccine-derived rotavirus strains



ELSEVIER

Vaccine

Volume 40, Issue 35, 19 August 2022, Pages 5114-5125

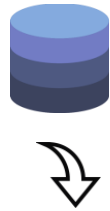


Rotavirus vaccine-derived cases in Belgium: Evidence for reversion of attenuating mutations and alternative causes of gastroenteritis

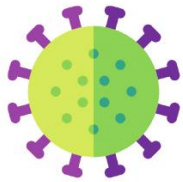
Ceren Simsek^a, Mandy Bloemen^a, Daan Jansen^a, Patrick Descheemaeker^b, Marijke Reynders^b,

Marc Van Ranst^a, Jelle Matthijssens^a  

NRC patient database

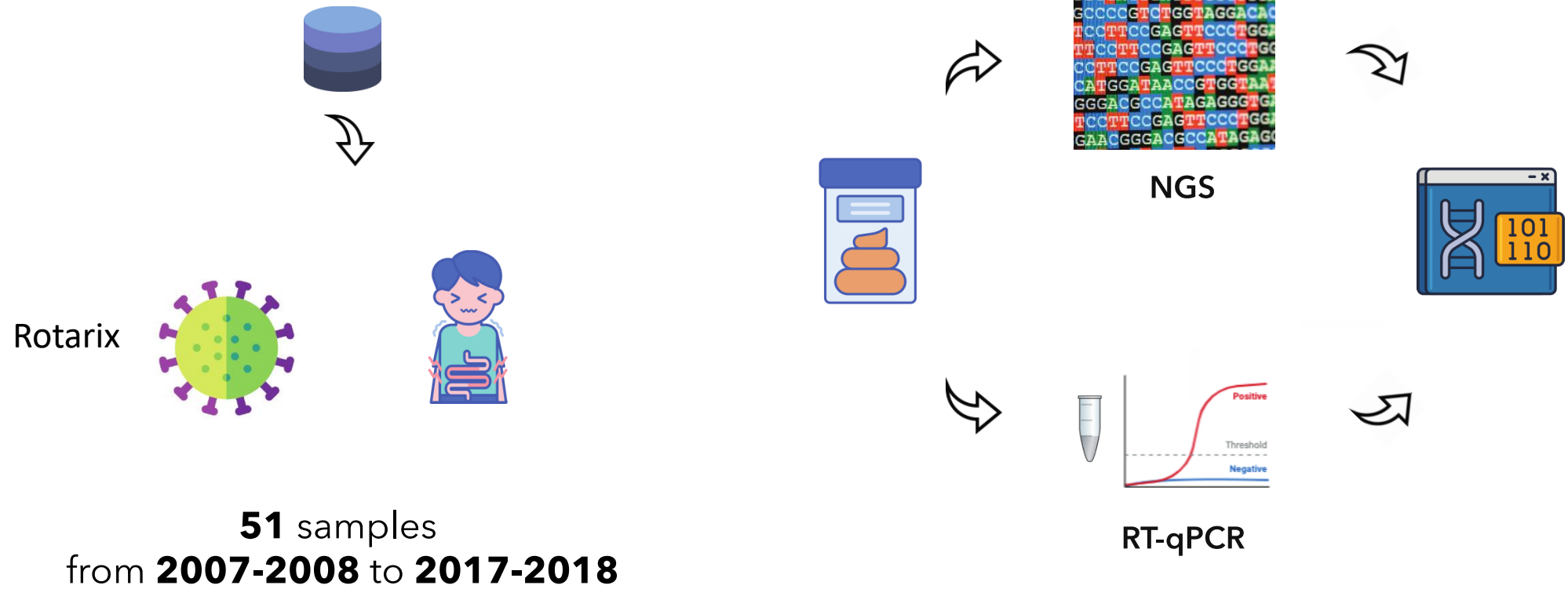


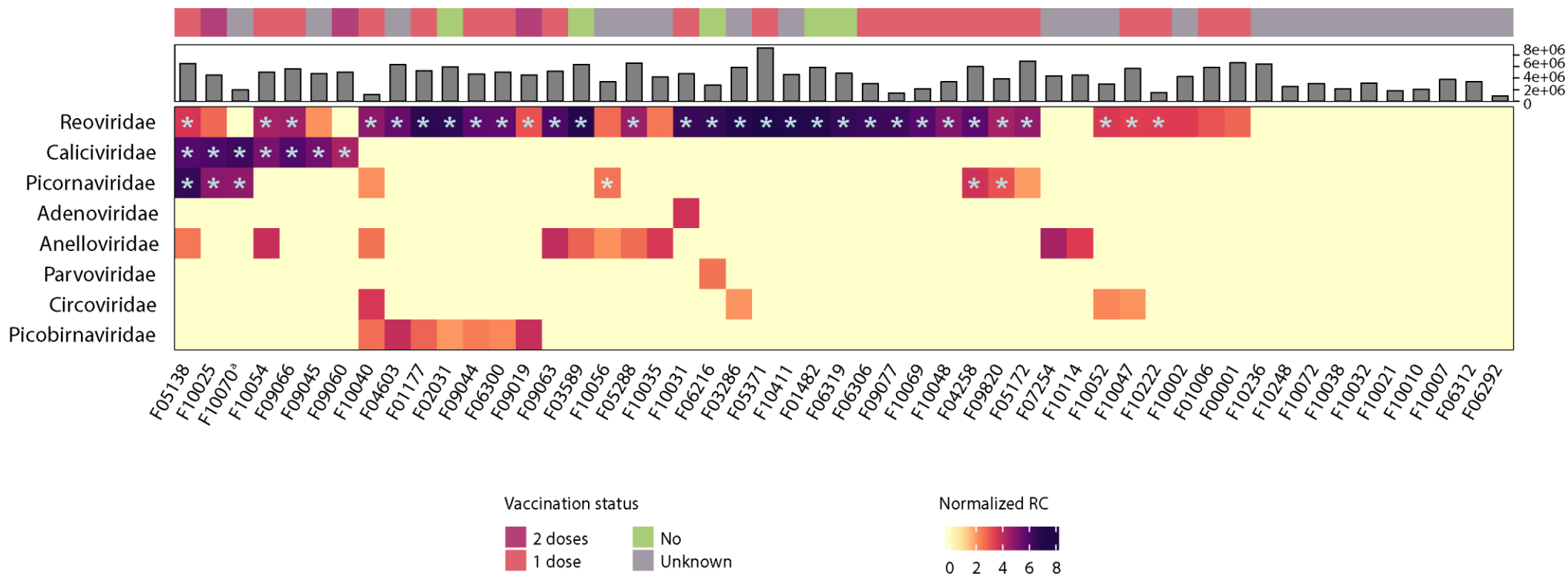
Rotarix

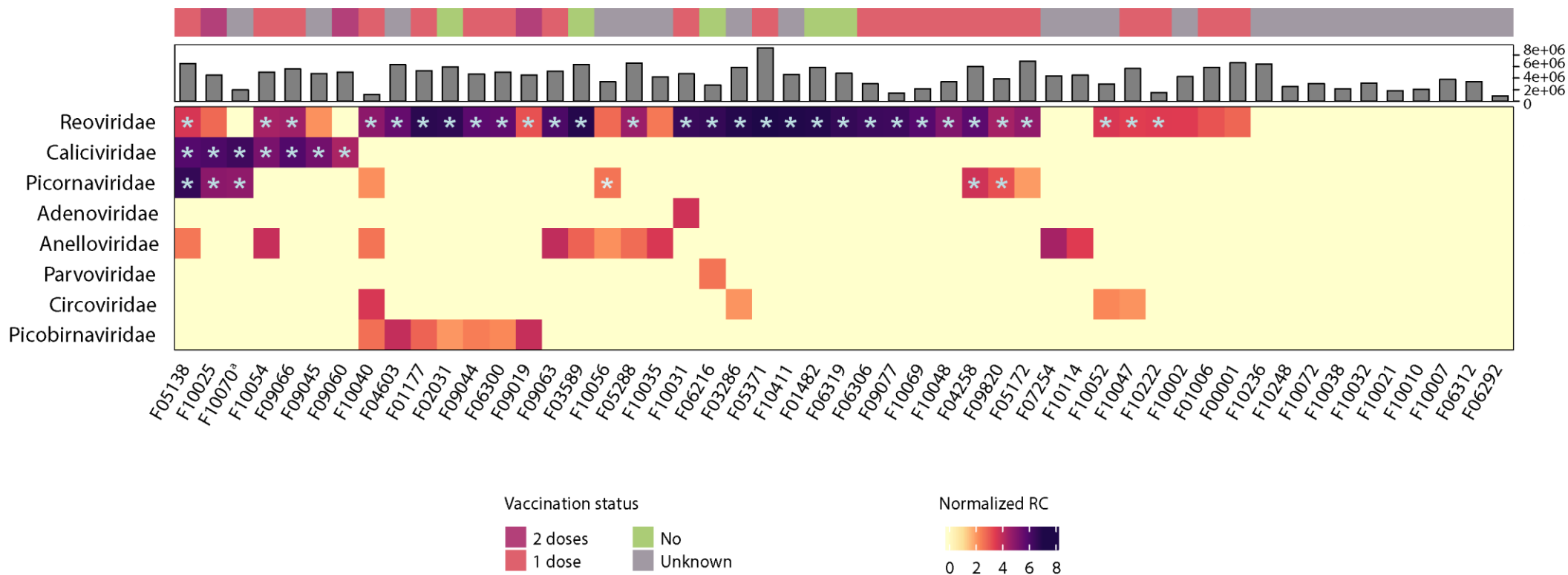


51 samples
from **2007-2008** to **2017-2018**

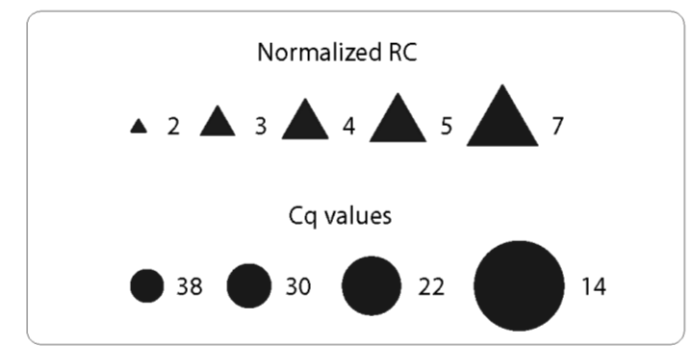
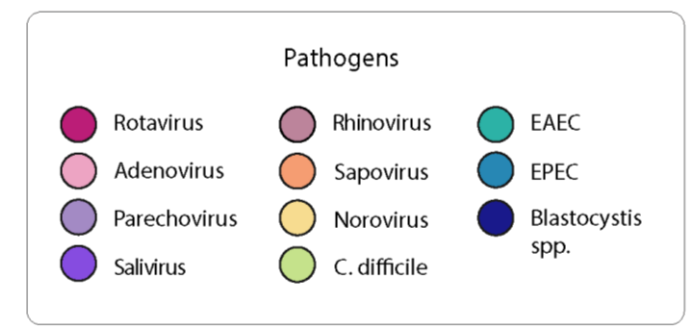
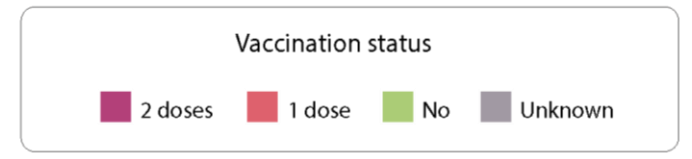
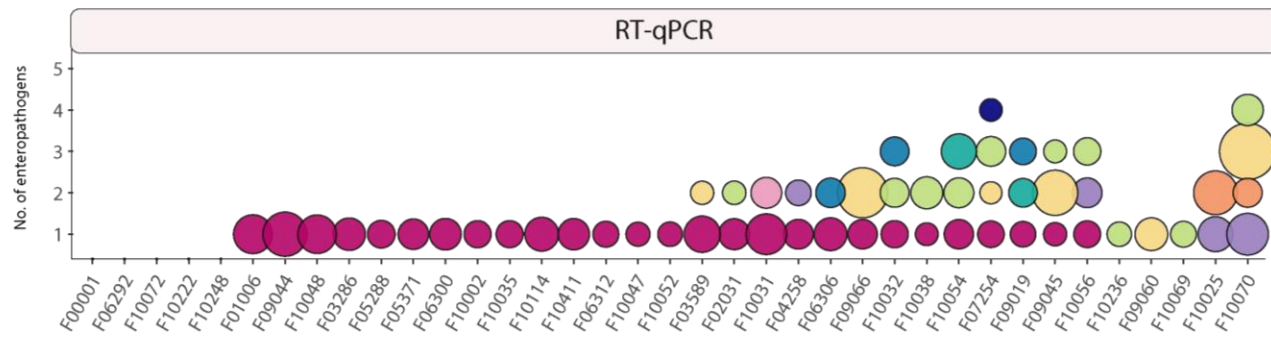
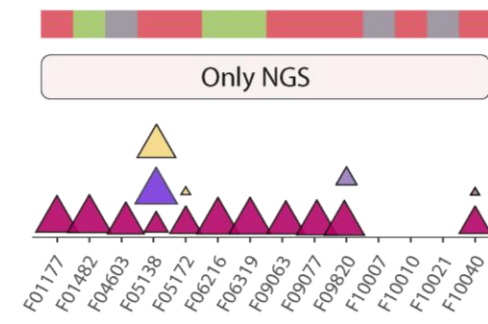
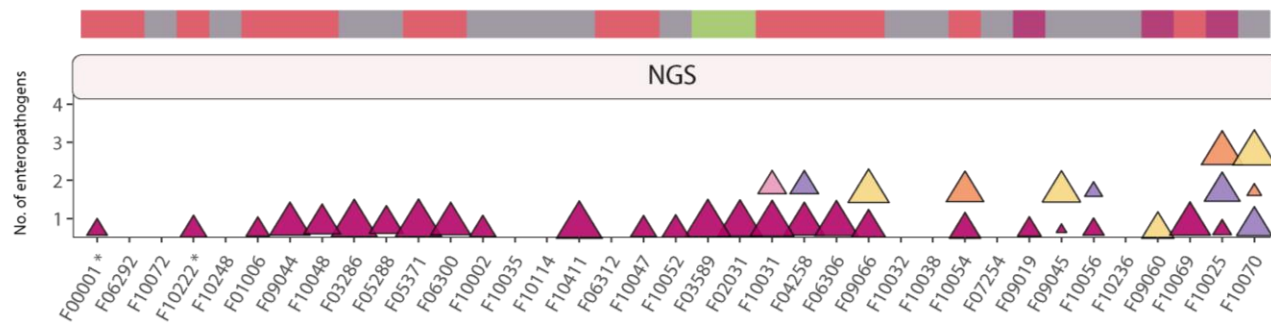
NRC patient database

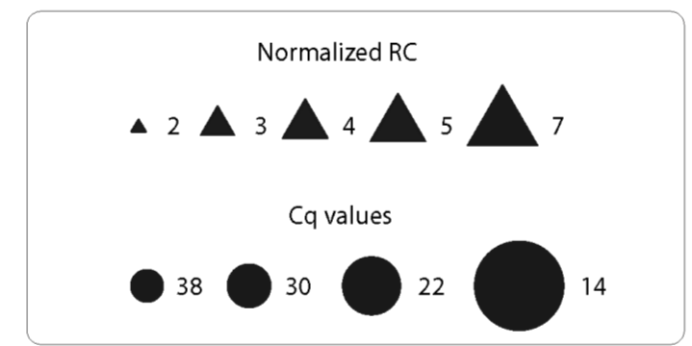
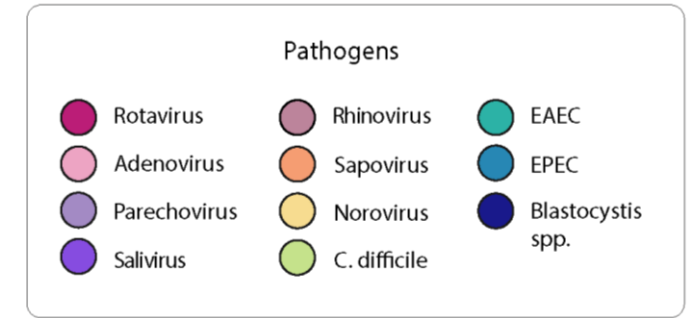
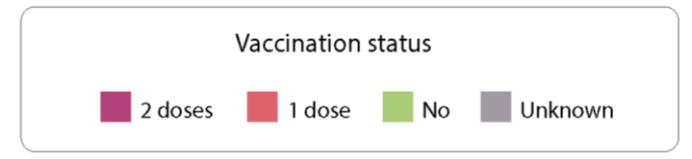
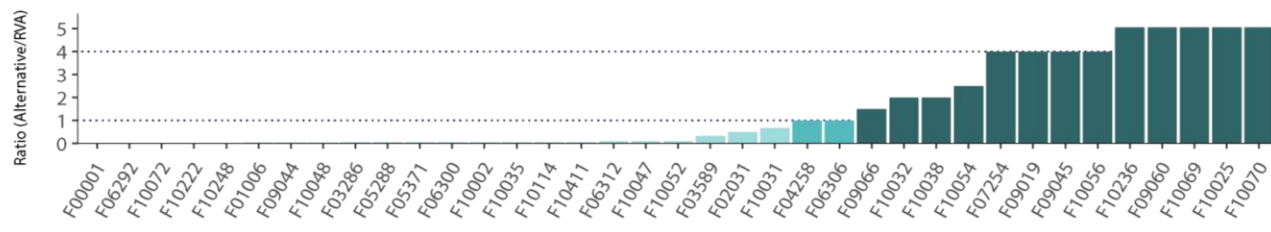
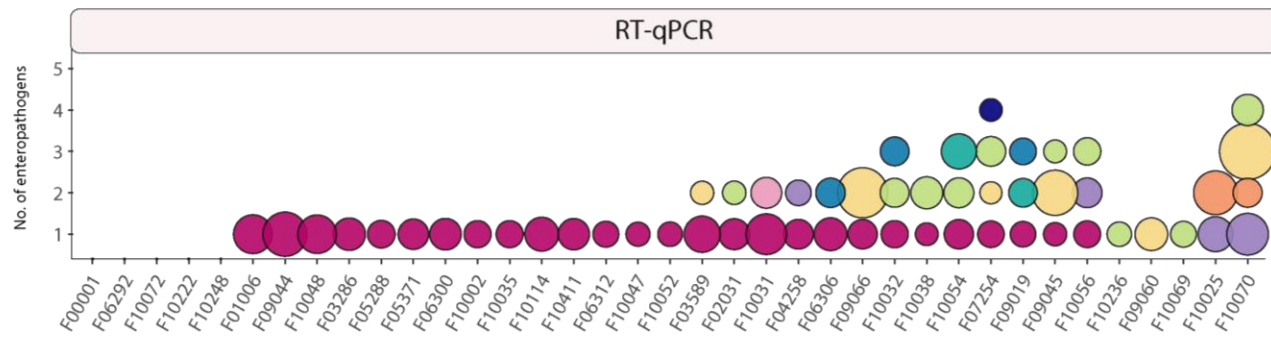
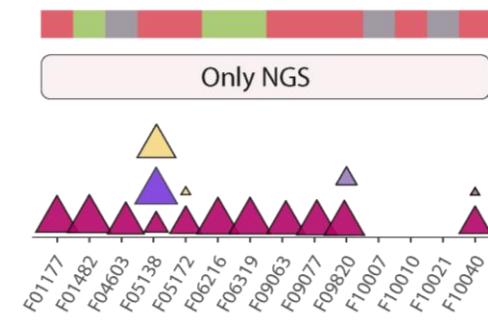
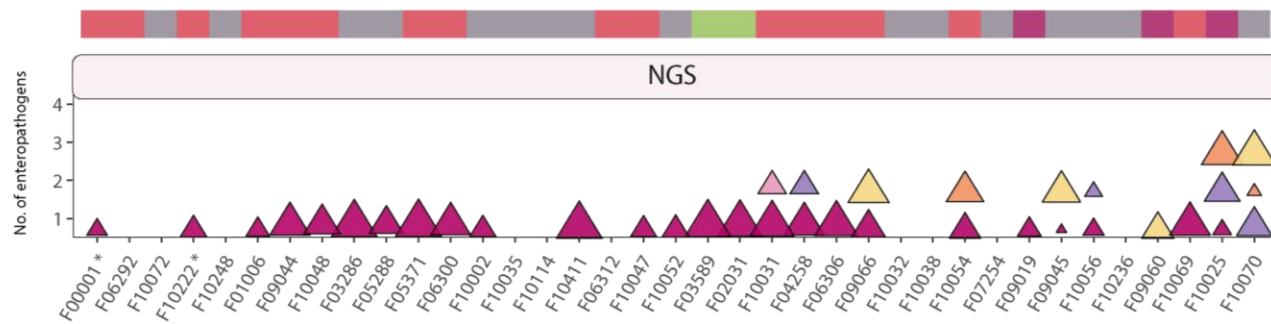






No evidence of reassortment between vaccine strains and wild type strains





Origin of vaccine strains?

Origin of vaccine strains?

Vaccine recipients shedding virus?



Origin of vaccine strains?

Vaccine recipients shedding virus?

Transmission from vaccinated infant?



Origin of vaccine strains?

Vaccine recipients shedding virus?

Transmission from vaccinated infant?

Circulating in the human population?

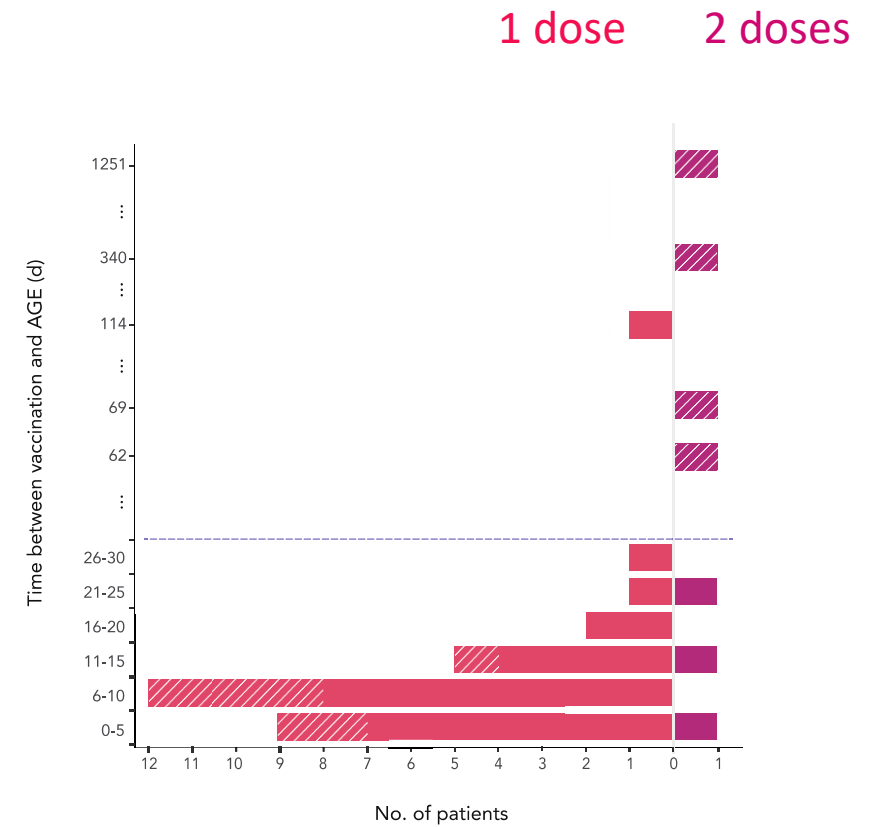


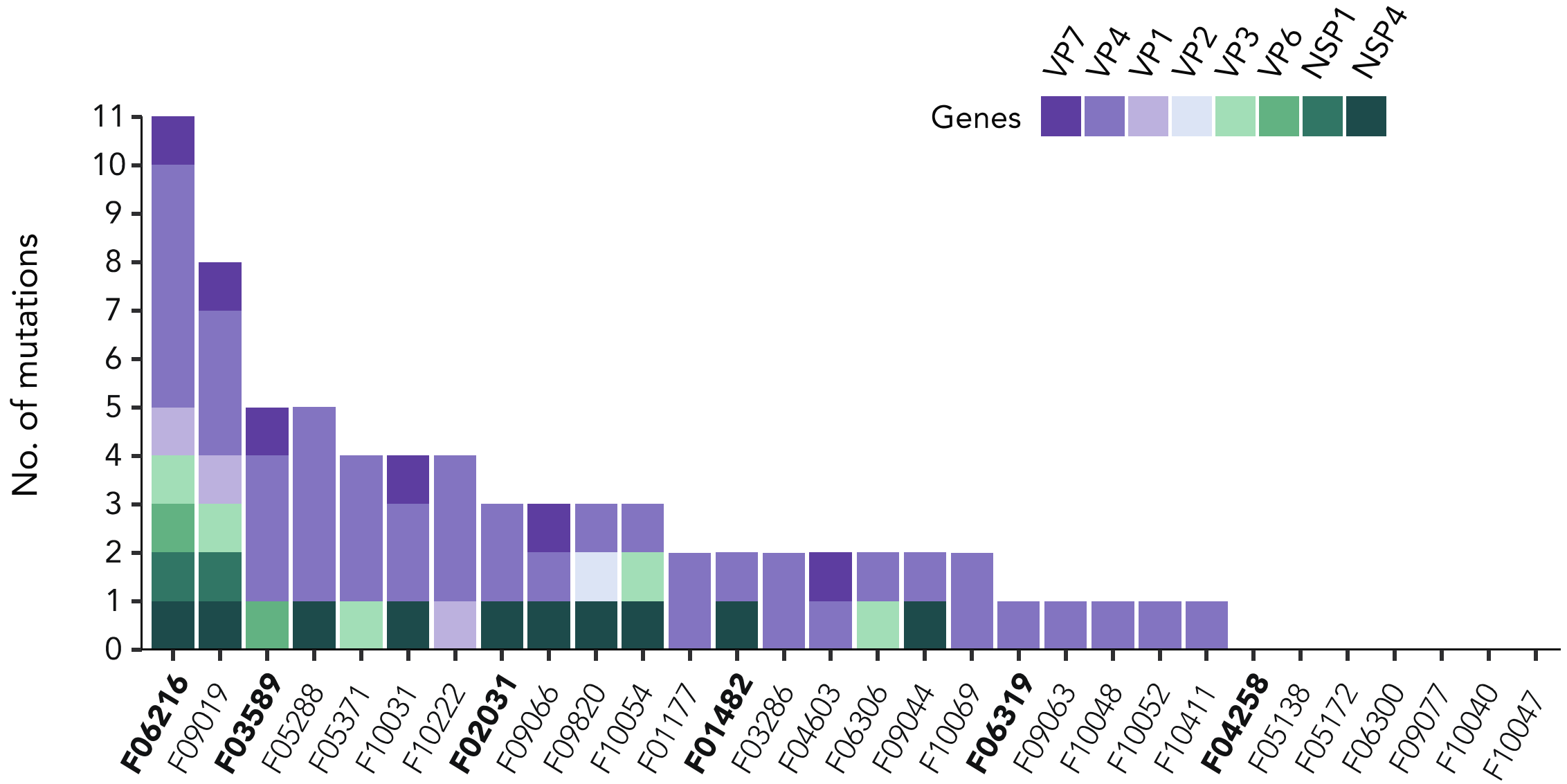
Origin of vaccine strains?

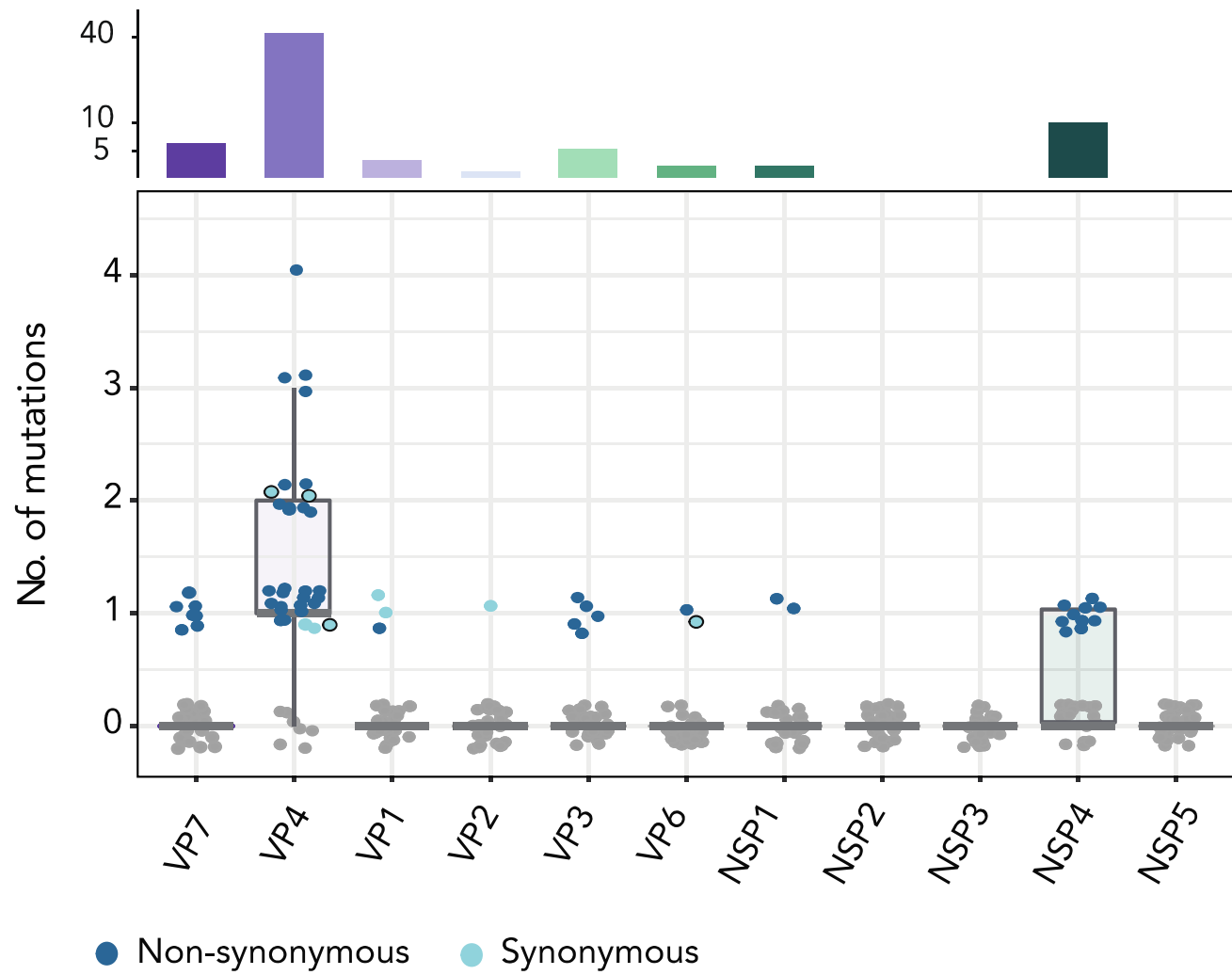
Vaccine recipients shedding virus?

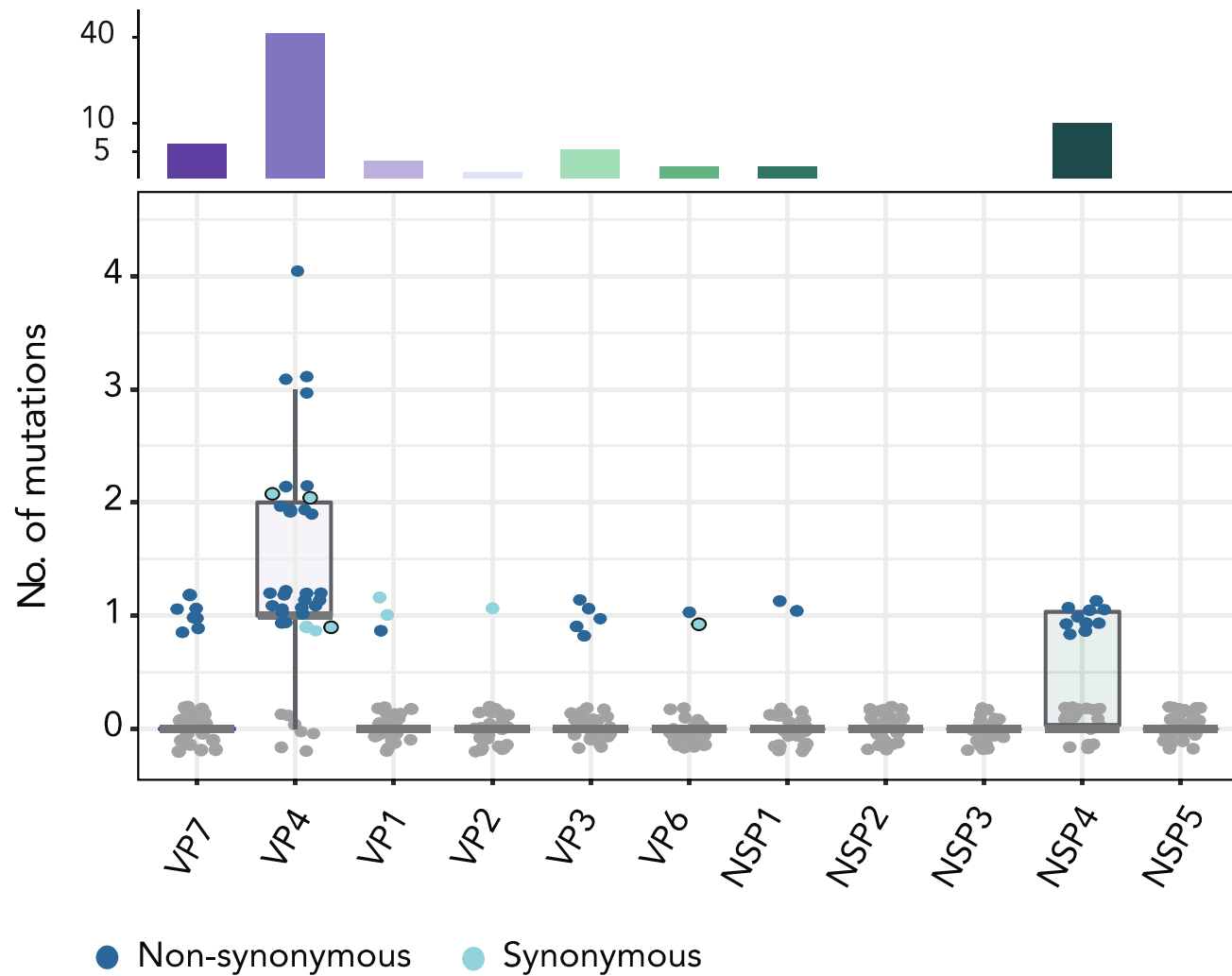
Transmission from vaccinated infant?

Circulating in the human population?

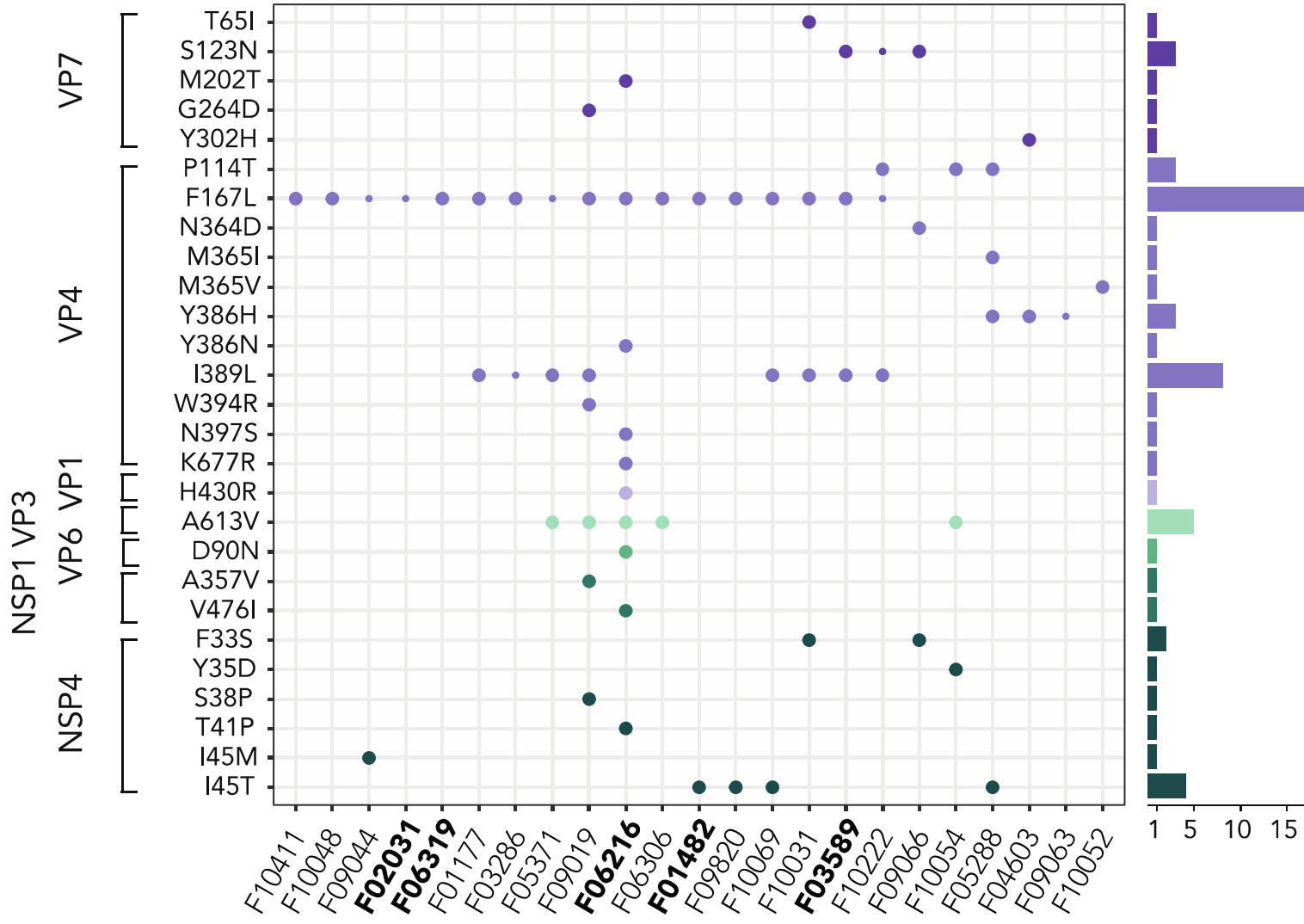


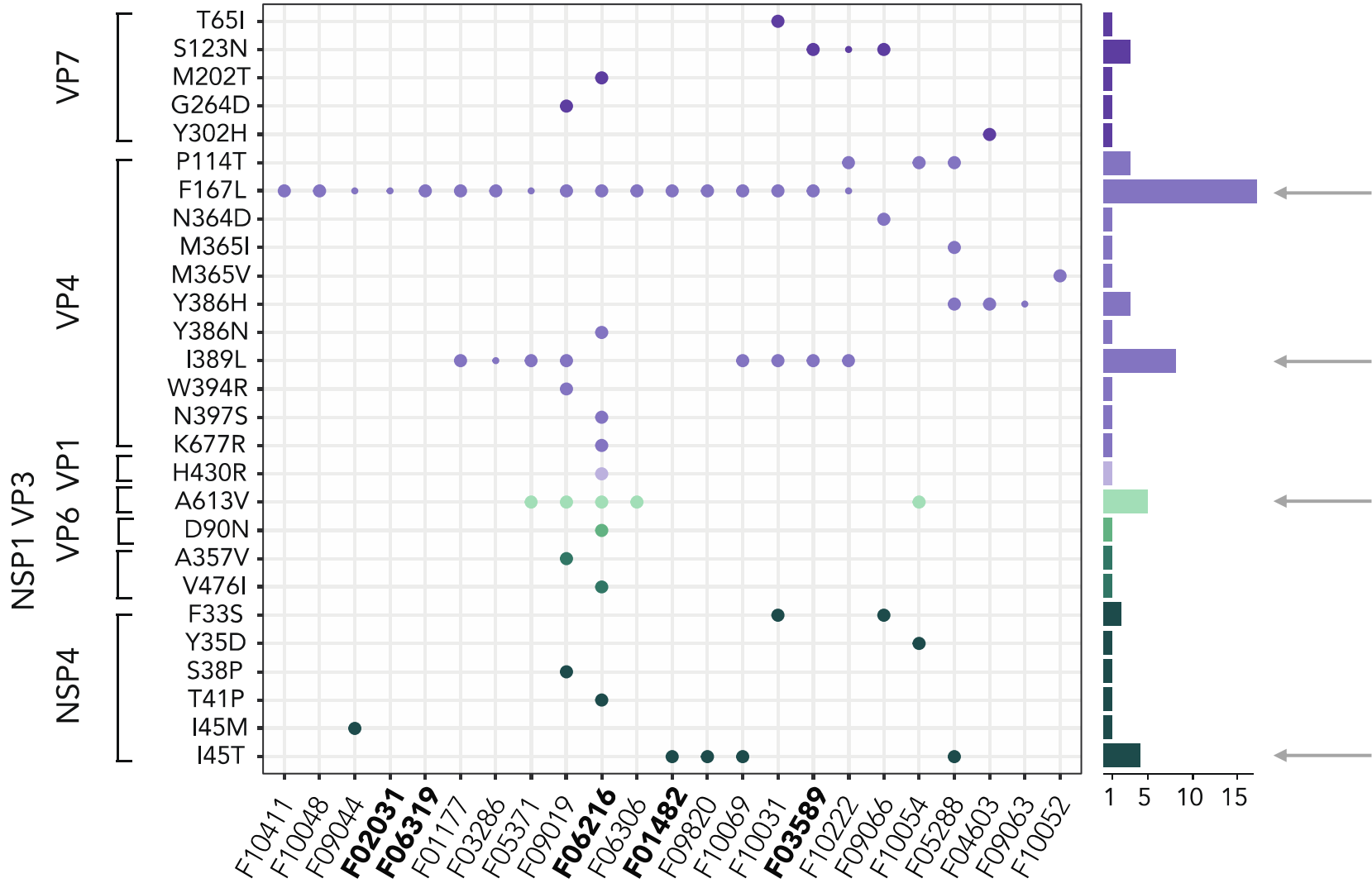


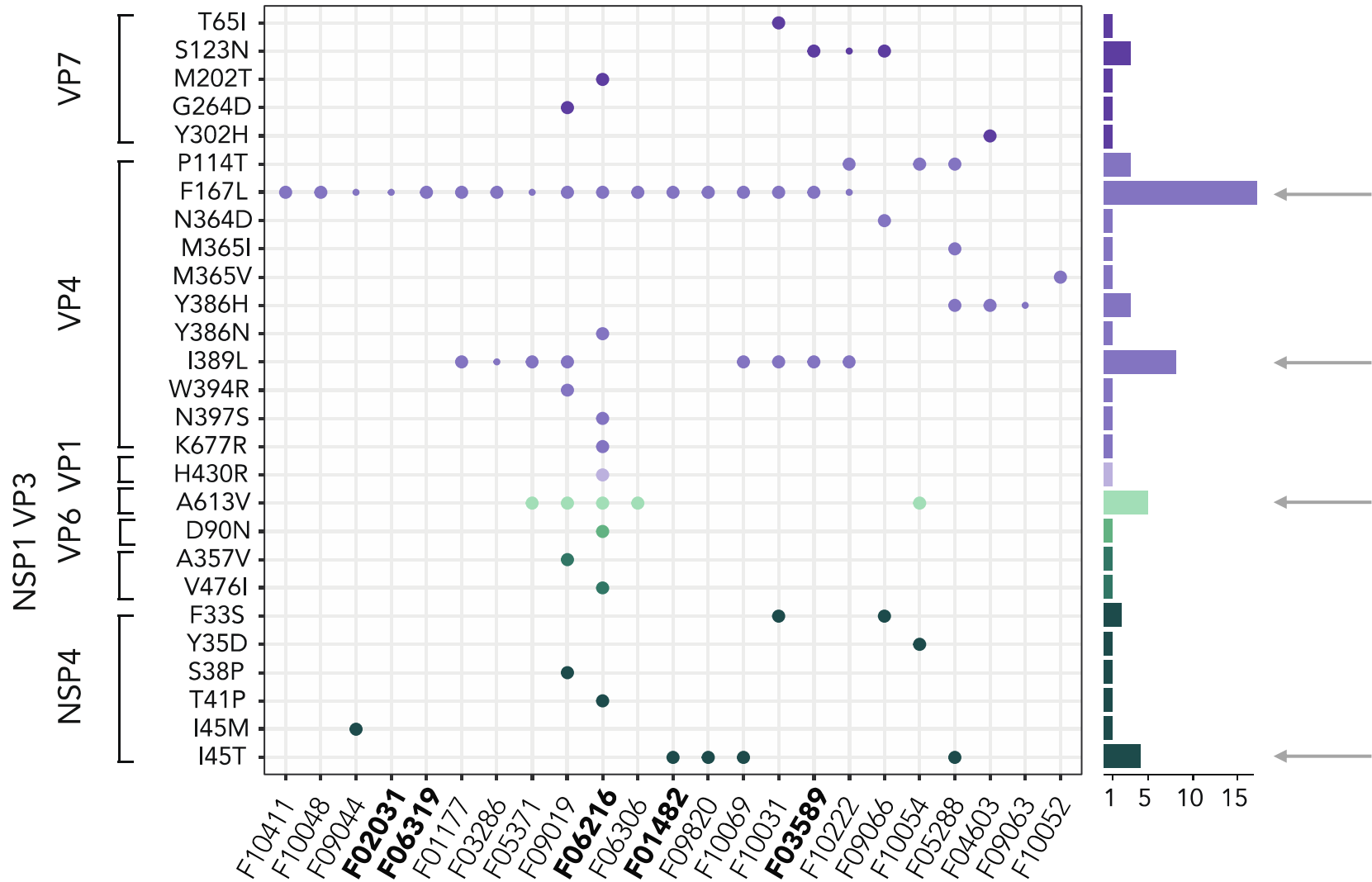




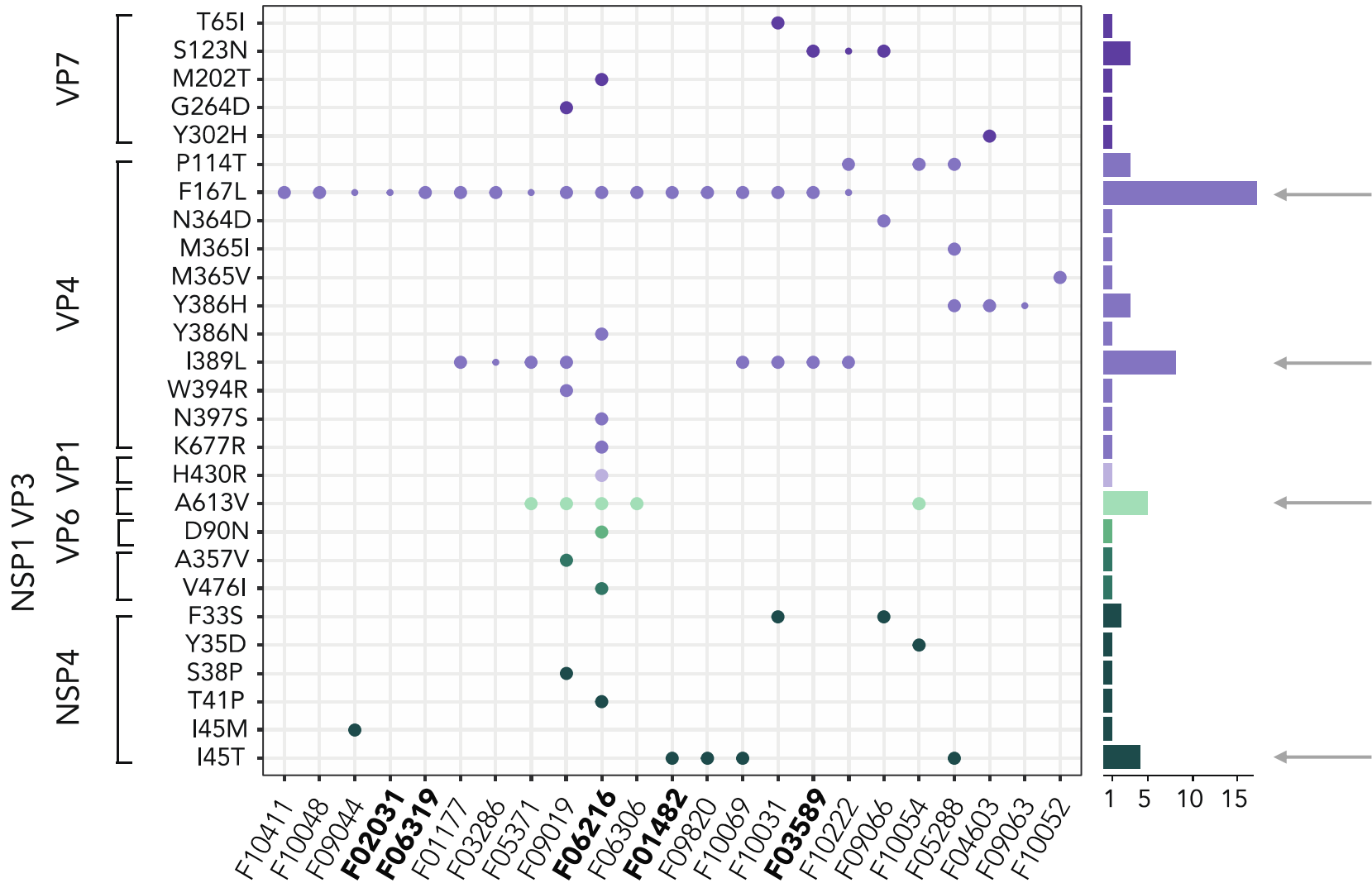
- VP4 harbors >50% mutations
- 88% of the point mutations were non-synonymous and accumulate rapidly







○ Reversion of vaccine strain?



○ Reversion of vaccine strain?

○ According to literature F167L and I45T could be reversions!

Summary

- No evidence of reassortment of vaccine strain with wild type strains
- Approximately 40% of cases might be explained by other pathogens
- Very limited evidence for vaccine circulation in the human population
- Vaccine strains might revert rapidly to parental strains

NRC Rotavirus

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Lize Cuypers