



Surveillance of Viral Hepatitis in Germany – An analysis

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Disclosures

- No conflict of interest

Country context: Germany



- Federal Republic with ~83 million inhabitants
- National level
 - Emission of national guidelines, case definitions
 - Advice and support
 - Data collation and quality assurance
- 16 federal states
 - Decisions and implementation
- Local level - rural and urban districts (n = 401)
 - Measures implementation, case/outbreak investigation
 - Contact tracing
 - Data collection & entry



→ 1st response always by local public health authorities

Know your epidemic!



| | HBsAg, % (N studies) | Hepatitis C, % (N studies) |
|---|--------------------------------------|--|
| General population | 0,3-0,7% (12) <i>*0,14</i> | Anti-HCV 0,2-1,9% (8) HCV-RNA 0,2-0,4% (2) |
| Migrants <i>(limited data)</i> | 2,3%-3,6% (4) | Anti-HCV 0,4-1,9% (4) HCV-RNA 0,7% (1) |
| PWID + people on OAT | 1,1-1,3% (3) | Anti-HCV 63-73% (3) HCV-RNA 27-44% (3) |
| Homeless people <i>(limited data)</i> | 1,9% (1) | Anti-HCV 24% (1) HCV-RNA 16% (1) |
| People in prison <i>(limited data)</i> | ? | ? |

Sperle, et al. (2020). Frontiers in Public Health 8(424).

2013 Data (Workbook method, RKI)

Total N HBsAg+ among adults
228,000 [179,000–291,000]

- 41% General population
- 58% Migrants (1st gen.)
- 2% People who inject opioids

Kremer et al, Frontiers in Public Health 2024, in review

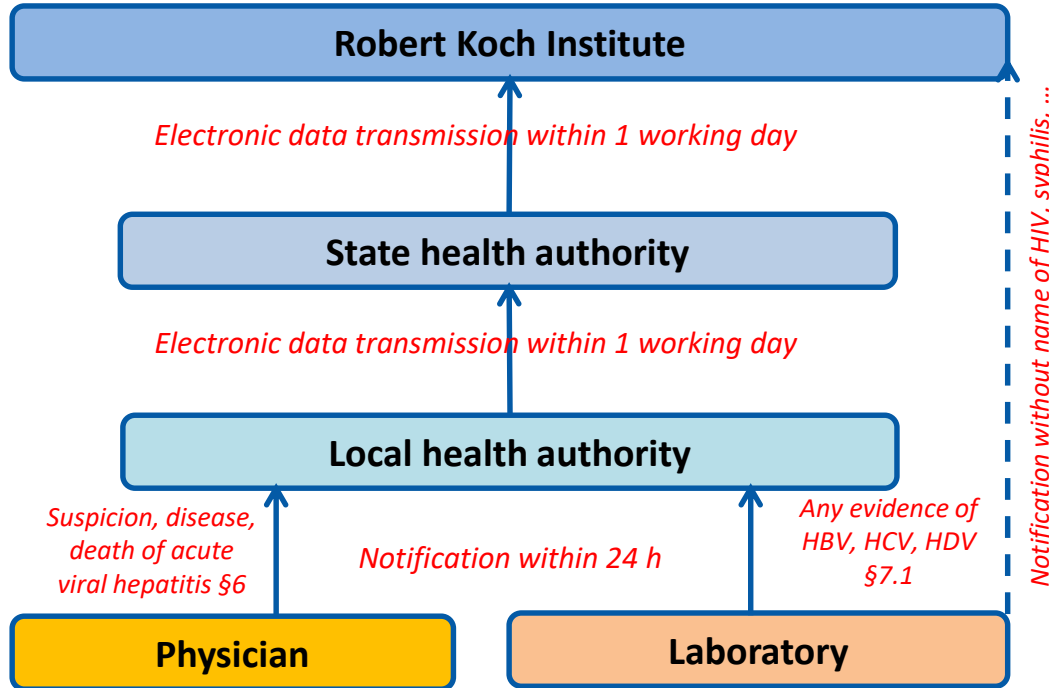
2019 Data (ECDC MPES project)

Total N HCV-RNA+ among adults
196,671 [137,555-279,639]

- 50% current or previous injecting drug use

Thomadakis et al, The Lancet Regional Health – Europe 2024

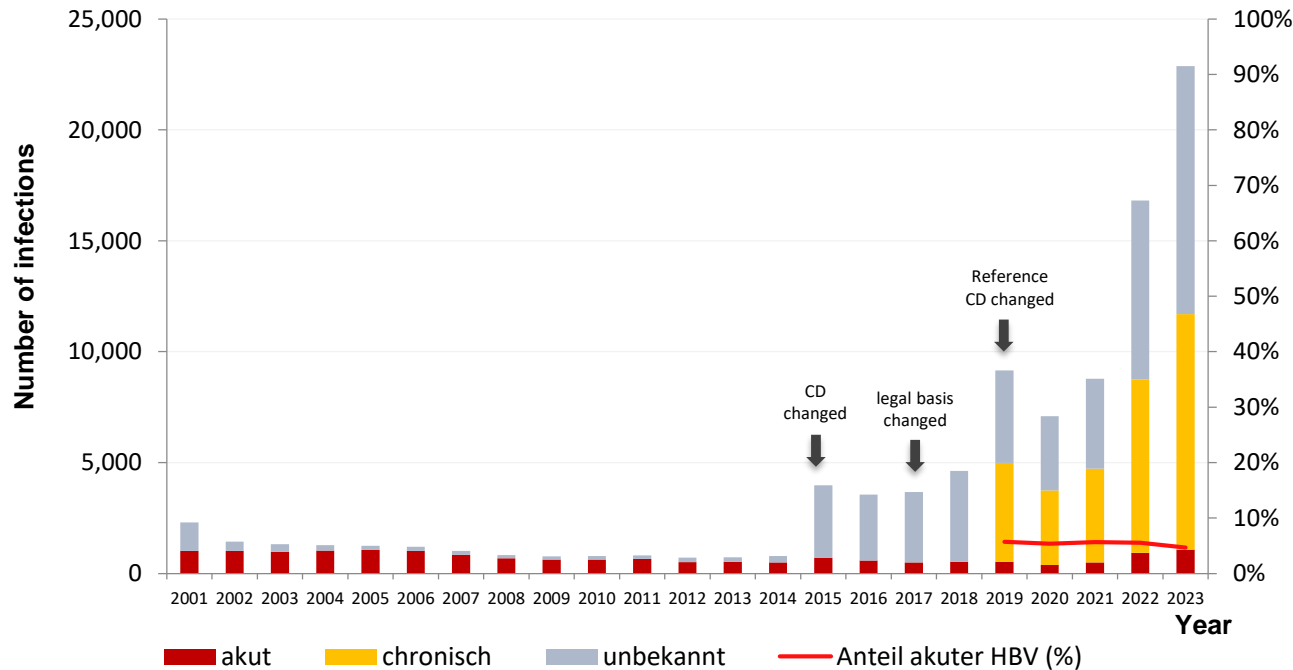
How is the surveillance system organized?



Infection protection act

- Which diseases are notifiable
- Who is required to report
- How reporting should be carried out and which information passed on (e.g., local, state, national level)
- Deadlines for reporting

Hepatitis B cases 2001-2023, Germany



2015

- change of case definition: clinical symptoms not required

2017

- change of legal basis: all laboratory evidence to be notified (regardless of clinical stage /symptoms)

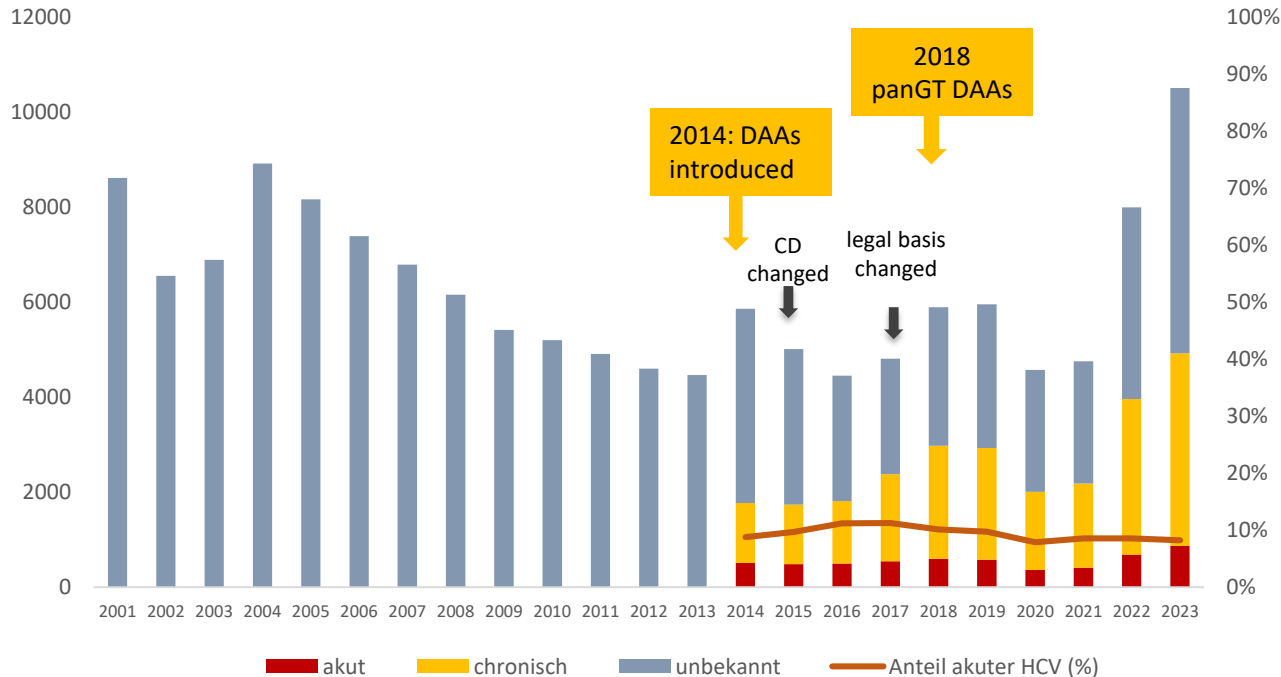
2019

- chronic cases included in official RKI publications

Méndez-Brito A, et al, Epid Bull 2024 DOI 10.25646/12295



Hepatitis C cases 2001-2023, Germany



2015

- change of case definition: direct evidence (PCR/cAg) needed

2017

- legal basis officially adapted: all laboratory evidence to be notified (regardless of clinical stage and symptoms)



Case definitions of viral hepatitis B and C

HBV

HCV

All laboratory-confirmed infections (direct evidence)
regardless of clinical symptoms are published at national level

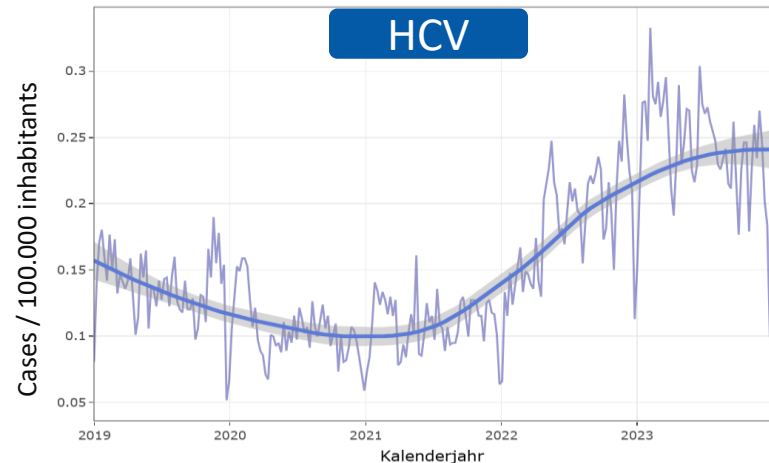
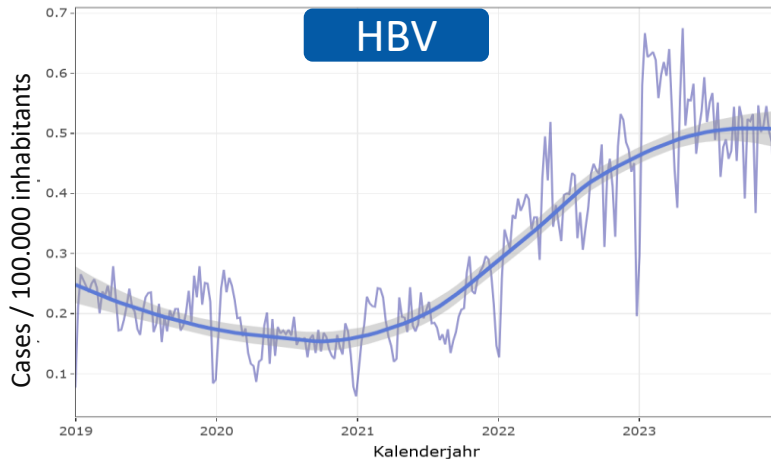
- ▶ HBV-DNA by NAT (PCR)
or HBs-Ag (ELISA), confirmed by
- additional HBsAg test or
 - Anti HBc or HBe Ag

- ▶ HCV-RNA by NAT (PCR)
or HCV core Ag (Immunoblot)



Hepatitis B and C in Germany, weekly incidence

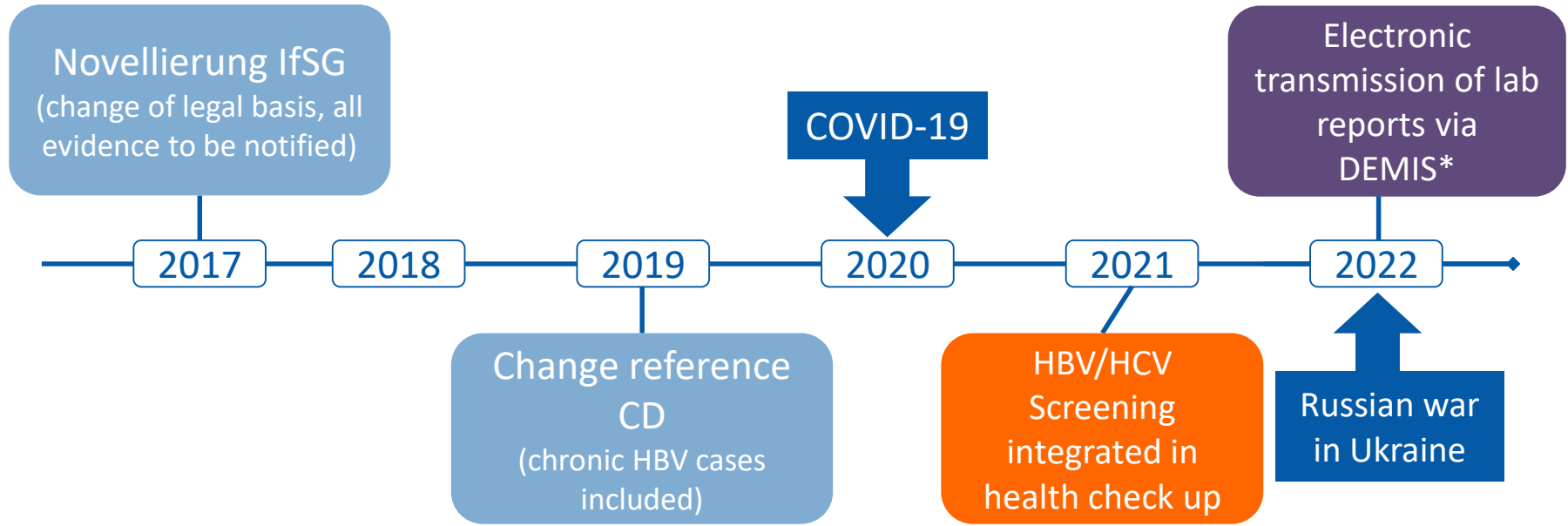
- In 2023, 22,875 HBV- and 10,512 HCV cases were transmitted to RKI
 - Increase by 35% and 32% since 2022
 - Increase 2022 by 90 % and 70 % since 2021
 - Increase 2022 by 80 % and 30 % in comparison to 2019.



LOESS shown as coloured line and corresponding 95 % confidence interval in grey.



Timeline of relevant events since 2017





Hypotheses

- 1 The change to electronic transmission of lab notifications to the LPHA since January 2022 has impacted case numbers.
- 2 Refugee migration from Ukraine since February 2022 and testing /screening has increased case notifications in Germany.
- 3 The introduction of the HBV /HCV Screening in persons aged 35+ years in October 2021 has led to an increase of case notifications.



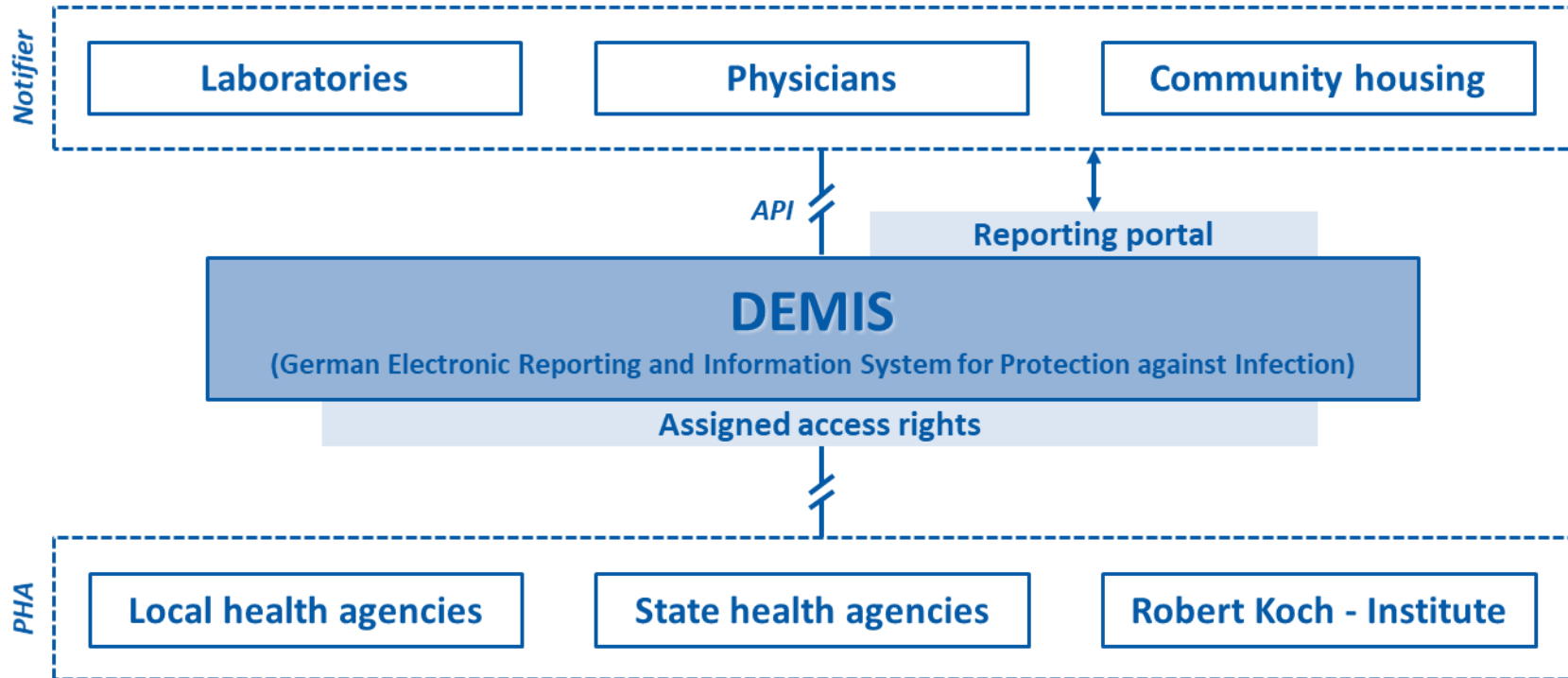
Methods

- Descriptive analyses of HBV/HCV surveillance data (2019-2023)
 - changes in proportions (percentage points) of selected characteristics over time (2023 vs. mean 2019–2021)
 - changes in weekly and monthly incidences (cases/100.000 inhabitants) over time (2019-2022) by selected characteristics + trend description using LOESS
- Matching of electronic laboratory notifications 2022 with associated HBV|HCV surveillance data (using information regarding **birthdate**, **gender**, **district**)
 - Identification of **potential duplicates** (proportion)

LOESS-Locally estimated scatterplot smoothing



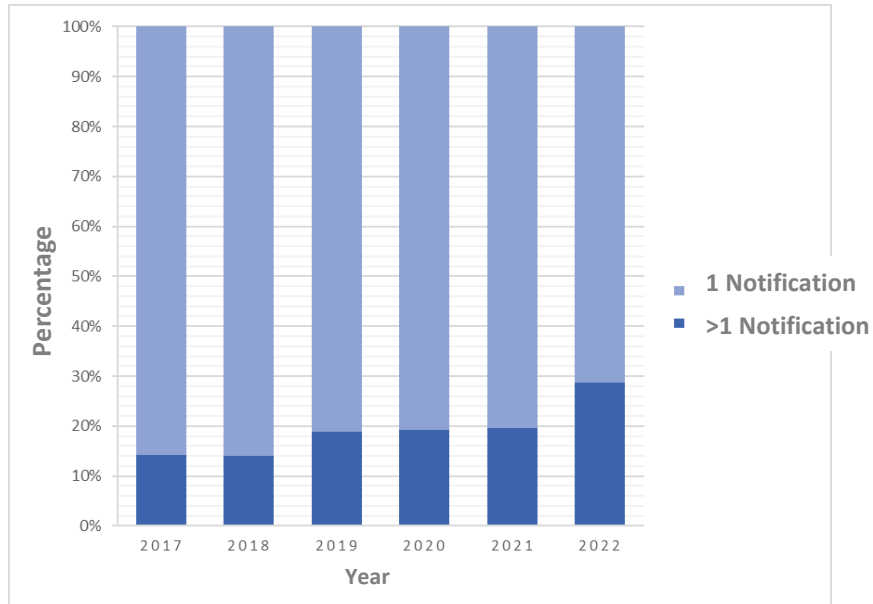
Electronic reporting system in Germany



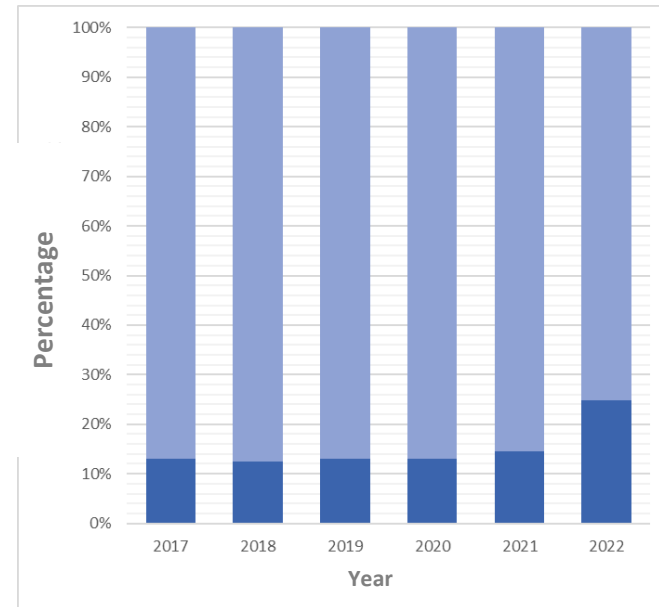


Hepatitis B & C notifications per case

HBV



HCV





Notifications via DEMIS

- For 2022, potential duplicates in 6% of HBV and 3% of HCV cases
 - associated notifications were not merged

A proportion of cases seems to be re-transmitted when newly tested

- Retransmission probable due to...
 - software changes without transfer of personal data;
 - short deletion periods of person data at local level.

Finding through dialogue



Hypotheses

1

The change to electronic transmission of lab notifications to the LPHA since January 2022 has impacted case numbers.

2

Refugee migration from Ukraine since February 2022 and testing /screening has increased case notifications in Germany.

3

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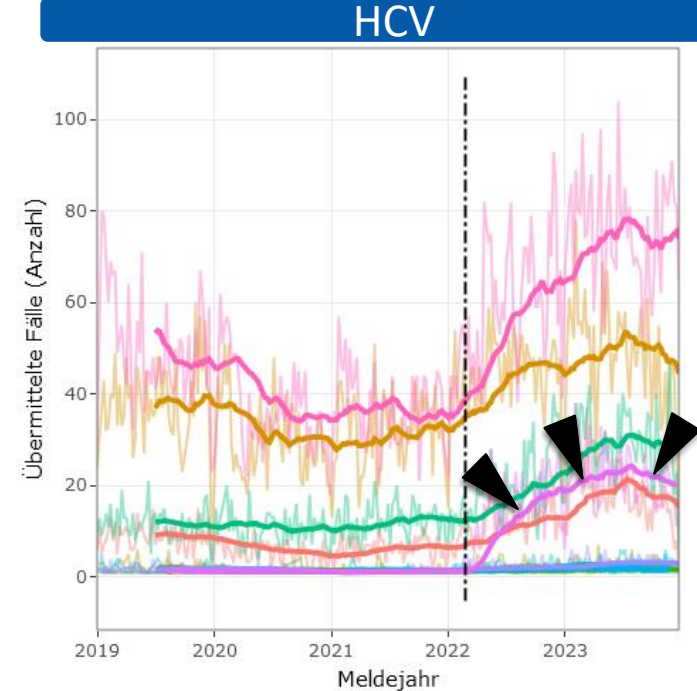
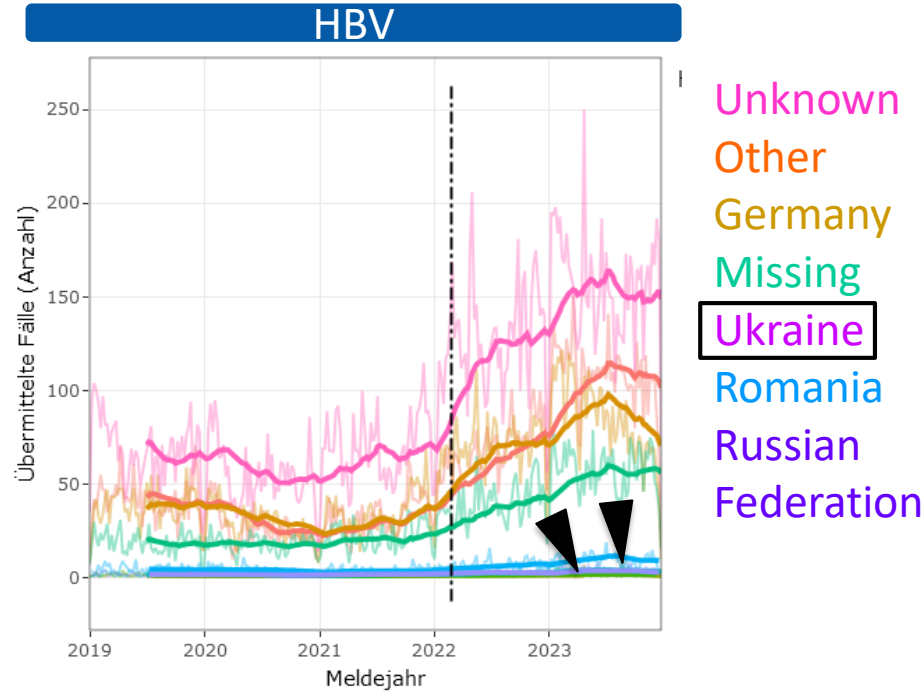
Impact of refugee migration on HBV /HCV case numbers

- Since 24 Febr 2022, >1.2 million registered refugees from Ukraine
- Prevalence of viral hepatitis in Ukraine
 - HCV-RNA/cAg: 2.7 [2.2 - 3.4]
 - HBsAg: 1.4 [1.2 - 1.6]
- Refugees from Ukraine have access to the German health care system:
 - people with already diagnosed HBV or HCV infection can be treated
 - medical check-up including hepatitis for undiagnosed

<https://www.globalhep.org/countryregions-data-dashboards>



Number of HBV and HCV cases per week by country of origin, 2019-2023



Moving average (26 weeks) bold line

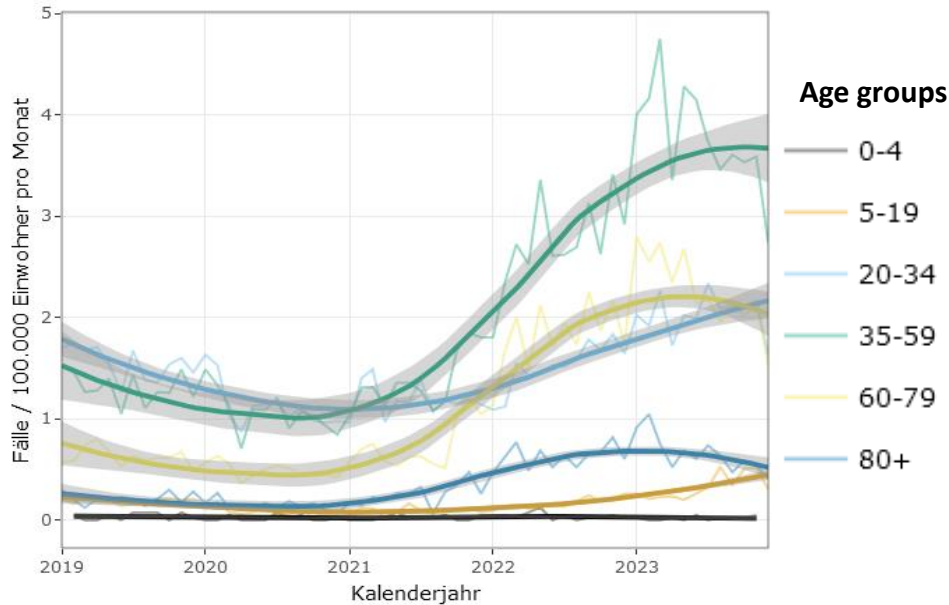


Hypotheses

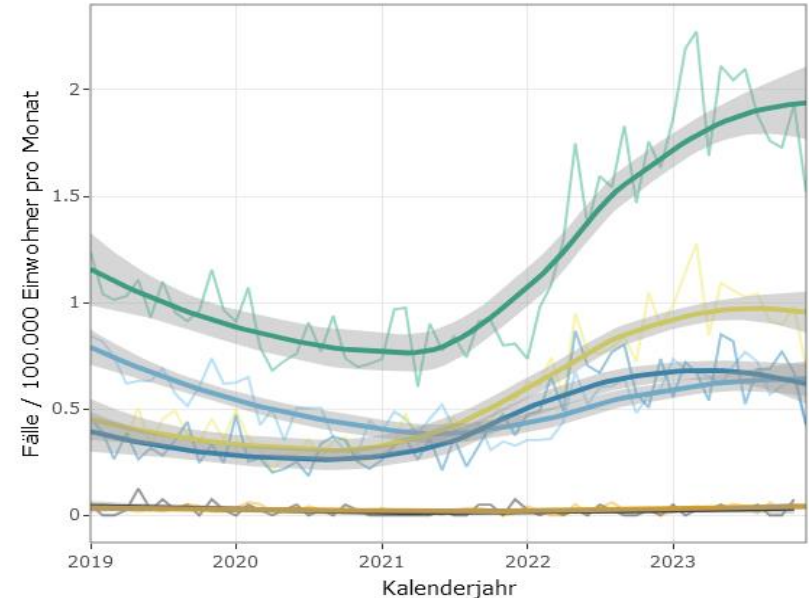
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Hepatitis B & C cases by age groups, 2019 - 2023

HBV



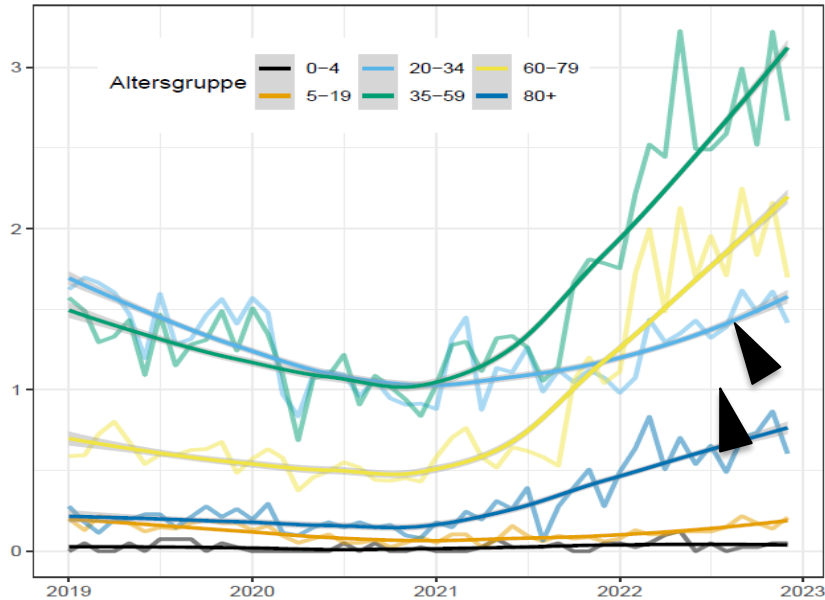
HCV



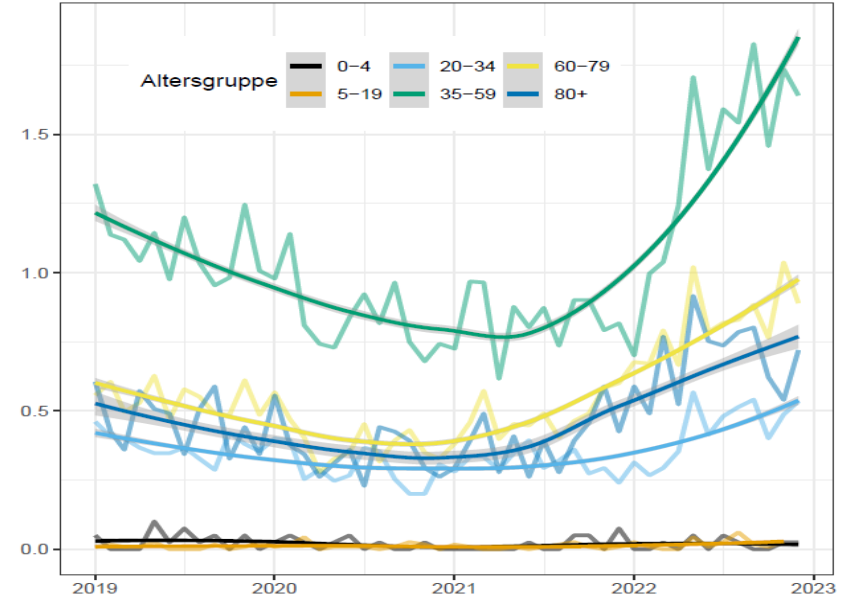


Hepatitis B & C cases by age groups, 2019 - 2022

HBV



HCV



Kalenderjahr

Biallas R, et al, *Epid Bull* 2023; DOI 10.25646/11669



Hepatitis B & C changes in proportions, 2023 vs. 2019-2021

| HBV | | Observed, n (2023) | Observed proportion | Expected proportion* | Difference, percentage point |
|-----|---------|-----------------------|------------------------|-------------------------|---------------------------------|
| | Total | 22,875 | | | |
| | AG 35+ | 18,351 | 80% | 66% | + 14 |
| | Ukraine | 593 | 2.6% | 0.2% | + 2.4 |



| HCV | | Observed, n (2023) | Observed proportion | Expected proportion* | Difference, percentage point |
|-----|---------|-----------------------|------------------------|-------------------------|---------------------------------|
| | Total | 10,512 | | | |
| | AG 35+ | 7,968 | 76% | 88% | -12 |
| | Ukraine | 1,178 | 11.2% | 0.5% | +10.7 |



*Mean of proportions 2019-2021



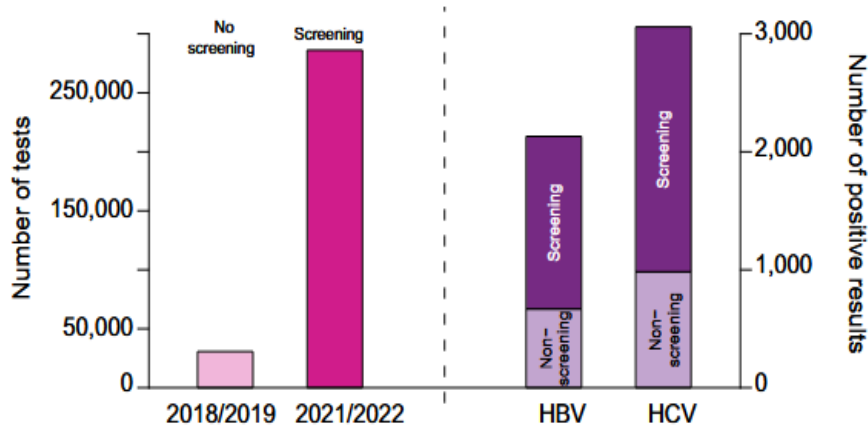
In summary

- Surveillance data is influenced by numerous effects
 - changes of surveillance system
 - screening/treatment strategies
 - other external factors
- Main increase of notifications since 2022 in age groups 35+,
 - Increase stronger in 2022 than 2023
 - Major effect of new screening for HBV, smaller effect on HCV
- Increase of HCV notifications also due to cases from Ukraine since 2022
 - Smaller effect on HBV
- Quantitative attribution of reasons with surveillance data alone not possible



What else do we know on the impact of the new screening?

- Substantial increase of laboratory tests and of the number of positive results



*HBsAg und anti HCV

Bätz et al, 2024, <https://doi.org/10.1016/j.jhepr.2024.101122>

- Of N= 5,603,337 Screenings from Q4/2021-Q3/2023) in KBV billing data
 - HBsAg + n=24,733 (0.44 %)
 - anti HCV + n=39,137 (0.70 %)
- Confirmation of viremia (from Bätz et al, 2024) in
 - 72.7% of HBsAg+ cases
 - 16.3% of anti HCV positive cases

→ Approximation of

17,980 viremic HBV cases

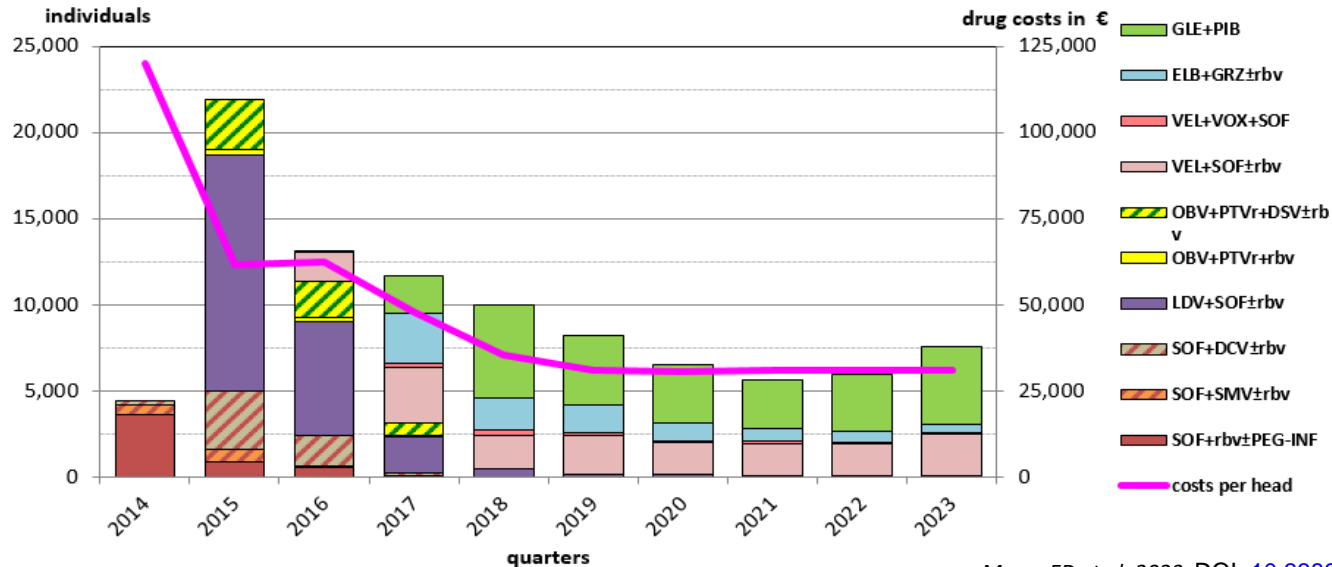
6,379 viremic HCV cases

Hüppe et al., Zeitschrift für Gastroenterologie 2024
10.1055/a-2435-5069



HCV antiviral treatment re-increases

- Numbers treated from Pharmacy sales data among patients with Social health insurance [DAA packages*treatment duration per regimen]



Meyer ED et al, 2023; DOI: [10.3389/fpubh.2023.1149694](https://doi.org/10.3389/fpubh.2023.1149694)
 Bull Epid Bull 2022;38:7-25 | DOI 10.25646/10582;
 Unpublished data



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- H Wedemeyer
- M Cornberg

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