Surveillance and data to help understand endemic, epidemic and pandemic viruses

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About me…

Associate Professor in Statistics for Infectious Disease Epidemiology at LSHTM

Interdisciplinary: biology / statistics / epidemiology

Interests:

- Making best use of surveillance data
- Statistical methods
- Sewage surveillance
- Polio eradication (10+ years, WHO polio SAGE member)
- Norovirus infection dynamics
- COVID-19

If you want to contact me, please do!

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Outline

Case data and contacts applied to norovirus

- Using the COVID-19 pandemic to understand norovirus transmission

Sewage surveillance applied to detection of poliovirus in London

- Early warning for an epidemic

Closing remarks

Norovirus

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Key facts

- Viral infection, endemic in all countries, a 'winter' virus
- Many genotypes and serotypes – GII.4 variant is my focus
- Infects children early in life, results in vomiting and diarrhoea
- In old and vulnerable people, disease can be more serious, requiring hospitalisation
- No licenced vaccine

Questions

- What or who drives norovirus transmission?
- Why has GII.4 remained the dominant variant
- Should vaccination target transmission or disease?

Source: https://www.otsuka.co.jp

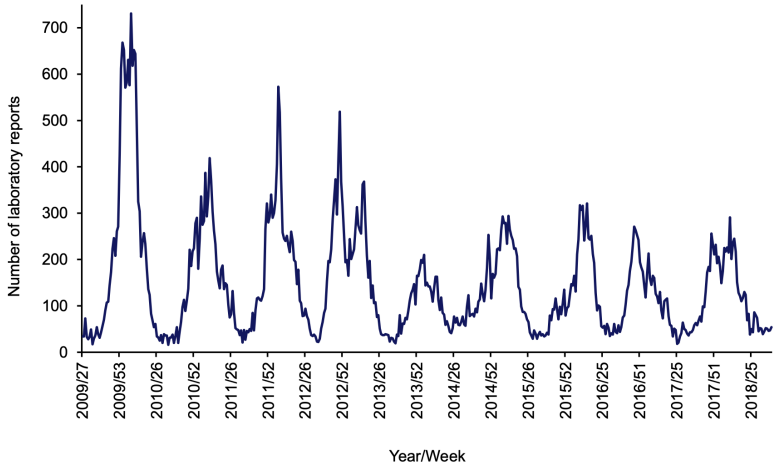
Norovirus Surveillance in the UK

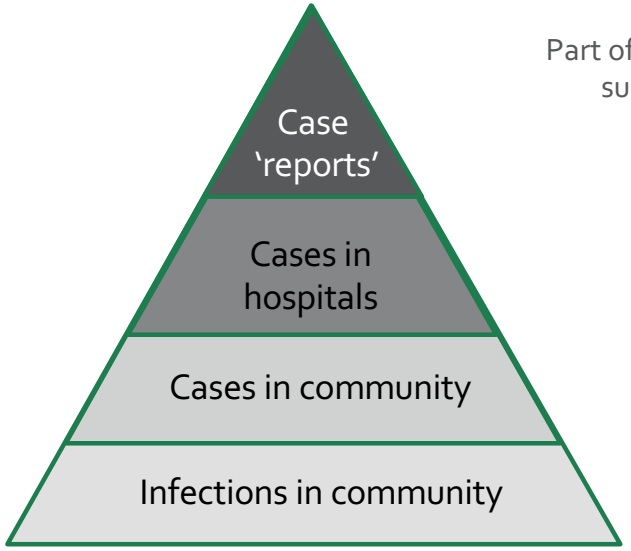
National surveillance by UKHSA of reported outbreaks from key settings (hospitals, schools, care homes)

No compulsory reporting – only 'outbreaks' enter the system

- Large under-reporting of the general population
- Hospital outbreaks are likely well represented, but no age data available

Figure 4: Laboratory reports of norovirus by week 2009-2018 (England and Wales)





	Part of UK norovirus surveillance	Importance in understanding transmission
Case 'reports'	✓✓✓	○○○
Cases in hospitals	✓✓○	✓○○
Cases in community	✓○○	✓✓○
Infections in community	○○○	✓✓✓

Contact Data to Understand Transmission

- Infection transmission relies on an infected person having 'enough' contact with a susceptible person
- For infections with no immunity, if age-specific contact patterns are not important:
    - The age distribution of infection would be the same as the age distribution of the population
- If age-specific contact patterns are important:
    - Age distribution of infection differs from distribution of population
- Immunity will affect age-specific infection rates:
    - Young often have less immunity
- Both contact patterns and immunity mean that most infections are driven by children

The basic reproduction number:

Ro = **p** x **c** x **D**

Duration of infection (days)

Probability of transmission if a contact

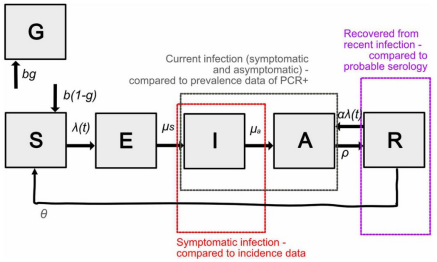
Contacts (per day)

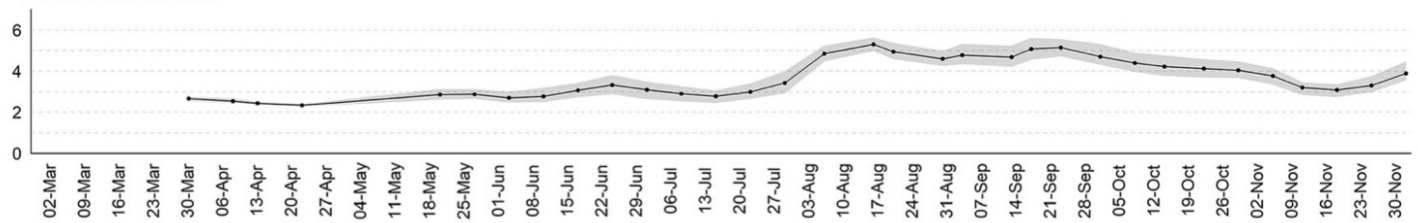
Will be affected by age

Using the COVID-19 Pandemic to Test our Argument

- We fitted an age-structured norovirus transmission model to infection rates from a UK cohort study (Harris et al. 2017)
  - This gave us the 'pre-COVID' infection rate and surveillance under-reporting
- We then fed weekly contact rates into the model and outputted the infection and disease incidence
- If children drive norovirus transmission
  - Estimated disease rates should match those reported
- If children don't drive transmission
  - Estimated disease rates will look wrong

Age-structured infection model





Average number daily contacts in UK in 2020, from Jarvis (2021) https://doi.org/10.1186/s12916-021-01924-7
Pre covid-19 avg. contacts were ~10

See O'Reilly et al. 2021 https://doi.org/10.1186/s12916-021-02153-8 for further information

What we found out

A) During COVID-19 (winter 2020)

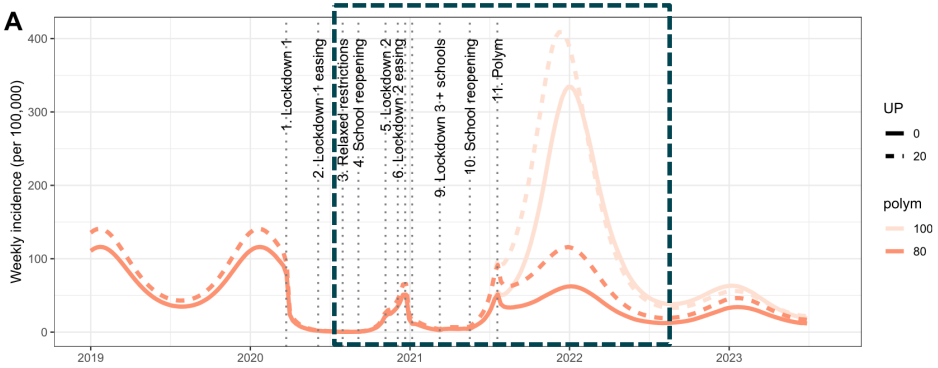
- Model predicted a rapid winter resurgence
- Not seen in surveillance, but UKHSA surveillance was very biased towards COVID-19 (esp. in hospitals)

B) During COVID-19 (2021-2022)

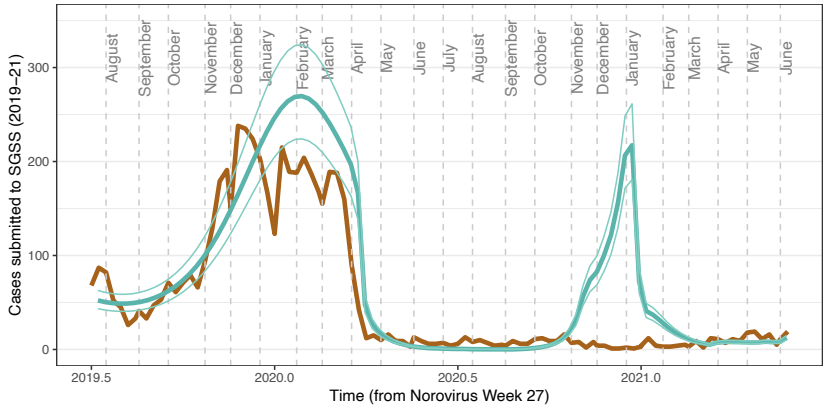
- Summer norovirus resurgence (2021) was likely and future cases depended heavily what contacts people have

C) Winter 2021 resurgence happened & quick summer comeback

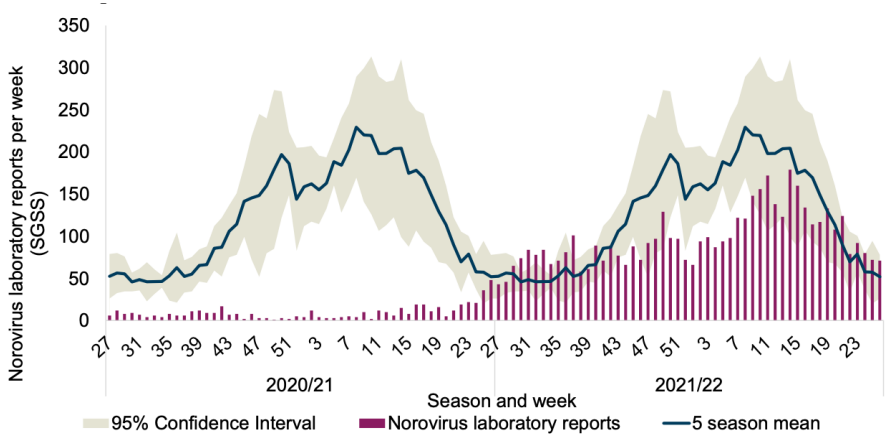
B) Projections into 2022-23 (made in 2022)



A) Simulations (green lines) and cases reported to SGSS (brown line) between July 2019 to June 2021.



C) Weekly reports from UKHSA (red bars)



What is a better surveillance system for norovirus?

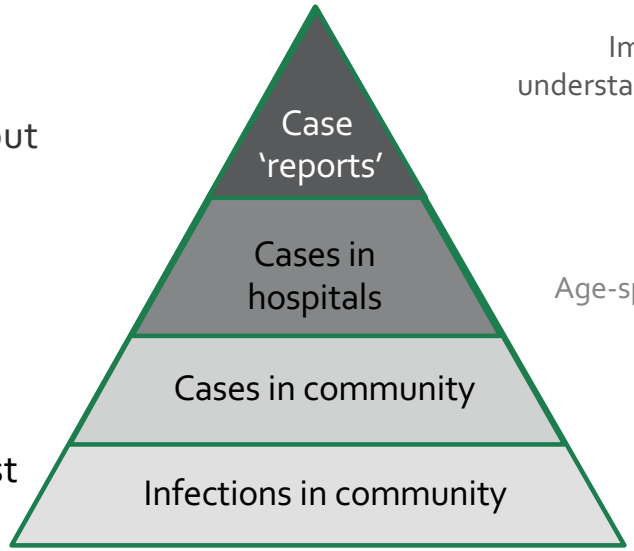
Most 'surveillance' is not designed for the purpose of surveillance, but to summarise what illnesses people are reporting with

Community testing for infection is the most useful

- Community SARS-CoV-2 ('Covid infection survey') is good example
- Rarely done for other pathogens due to low prevalence, cost

What would be realistic surveillance data?

- Age-specific norovirus cases from hospitals and community clinics
- Combining these data with physical contact data, would be even better!
- <u>Prefectures within Japan may have this data, and further analysis could very valuable</u>
- Example: Nakamura et al (20216) DOI: 10.1002/jmv.24445



Sewage Surveillance* for Infectious Diseases

Context

Humans shed many pathogens and genetic fragments in stool

- Part of transmission or life-cycle, can be infectious
- Excreted after infection, (typically) not infectious

Sewage surveillance has been useful in public health

- Polio (1930s in USA), and now used in many countries
- Plans to use sewage testing to assess typhoid vaccine, and other applications

Increasing interest after COVID-19

- Many countries saw sewage surveillance as a useful measure
- Cheaper PCR based tools enables testing for multiple pathogens in 1 sample
- Bioinformatics pipelines for variant detection

* Sometimes also called 'environmental surveillance'

Early Warning for an Epidemic – Poliovirus in London

Poliovirus was first detected* in Feb-2022 from a large north London sewage treatment works

- First detected as 'vaccine-like'

Poliovirus continues to be isolated…(as of late Aug-2022),

- The viruses isolated have acquired mutations that have the potential to cause paralysis
- In an unvaccinated population, for every 2000 infections 1 case is probable
- The UK vaccinates using the IPV (up to 5 doses), which protects against paralysis, north London coverage 71% (PSB)

No clinical cases have been detected so far, but…

- Polio case in NY, USA is genetically linked to virus in London sewage samples

Rotary London pledge on the Tower of London

* Using WHO approved culture and extraction

Actions Taken in Response

Vaccination 'catchups'

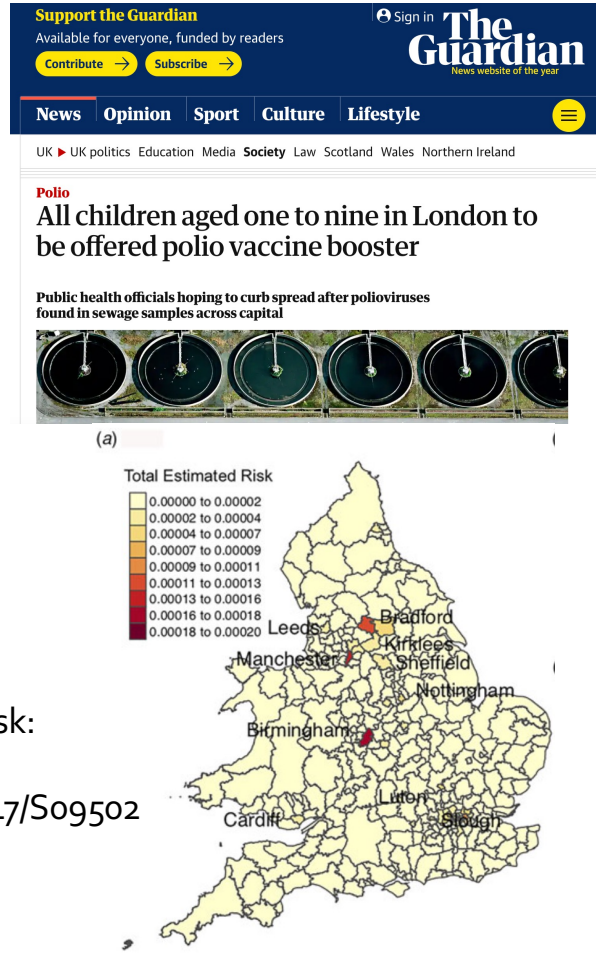
- 'call and recall' to complete vaccination schedule (May 2022)

Vaccination booster for all children in north London

- ~900,000 children
- Concern about vaccine interference from maternal pertussis (dTaP/IPV used)

Improve surveillance further

- National sewage surveillance
- Enhanced enterovirus surveillance



National poliovirus risk:
O'Reilly et al (2020)
https://doi.org/10.1017/S0950268820001004

Closing remarks

Many considerations when aspiring to understand and prevent disease burden

- Data that you have
- Information that you want!
- Resource available

Role of research is to balance these challenges

- For norovirus, age-specific clinical data and contacts may be more valuable than clinical data alone
- For polio, sewage sampling is essential for early warning of poliovirus until eradication

Role of sewage sampling in general

- Huge interest because of potential
- Validation of methods (sampling, lab testing & interpretation) is essential to improve the technology