Differences – COVID and Flu, SARS and Influenzaviruses

Prof William Rawlinson

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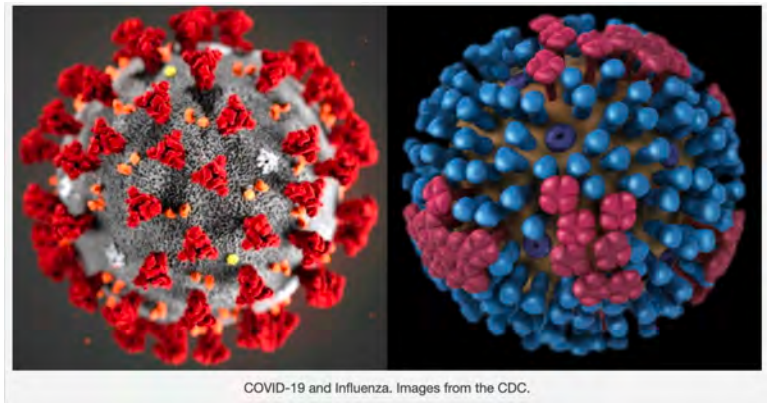


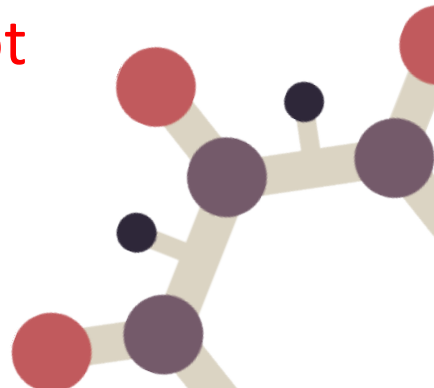
COVID-19 and Influenza. Images from the CDC.

IMMUNISATION COALITION

- Case definitions
- Presentation
- Virology
- Outcomes

A pandemic is defined as “an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people”. The classical definition includes nothing about population immunity, virology or disease severity.

By this definition, pandemics can be said to occur annually in each of the temperate southern and northern hemispheres, given that seasonal epidemics cross international boundaries and affect a large number of people. However, seasonal epidemics are not considered pandemics



To the thinking person nothing is more remarkable in this life than the way in which Humanity adjusts itself to conditions which at their outset might well have appeared intolerable.

P.G. Wodehouse, London 1926

SARS Case Definitions

Version: 1
Authorisation: PHLN
Consensus Date: 17 November 2014

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1 PHLN Summary Laboratory Definition

1.1 Condition:

Severe acute respiratory syndrome coronavirus (SARS-CoV) infection

1.1.1 Definitive Criteria (1)

- *Virus isolation in cell culture of SARS-CoV from any specimen, with PCR confirmation using a validated method.*
- *Positive on a validated NAD test specific for SARS Co-V*
  - on at least 2 different clinical specimens (e.g., nasopharyngeal swab and stool)
    OR
  - the 2 or more samples from the same site collected on 2 or more days during the course of the illness
    OR
  - 2 different assays or repeat NAD tests using a new RNA extract from the original clinical sample on each occasion of testing.
- *Seroconversion or a four-fold or greater rise in antibody by neutralization, enzyme-linked immunosorbent assay (ELISA*) or immunofluorescence assay (IFA)**

*Virus antibody detected by EIA or IFA should be confirmed by neutralization to exclude serological cross-reactions with other circulating coronaviruses.

SARS CoV2 Case Definition

5. Communications

Public Health Units (PHU) should, within one working day, notify the central state/territory communicable diseases unit of confirmed cases and COVID-19 deaths upon receipt of a notification/report.

As much information regarding the case's age, sex, comorbidities, place of residence, Indigenous status, any culturally/linguistically diverse background, date of onset, travel history, laboratory results, clinical status, likely place of acquisition, identification of close contacts and follow-up action taken should be included in the initial report, with additional information being followed up as soon as possible.

Central state/territory communicable diseases units will notify confirmed COVID-19 cases and COVID-19 deaths as soon as practicable to the Australian Government Department of Health via both transmission of data to the National Notifiable Diseases Surveillance System (NNDSS) and via email or telephone notification to the National Incident Room.

6. Data management

Initial information on confirmed and probable cases of COVID-19 should be entered onto the jurisdictional notifiable diseases database, for transmission to the NNDSS, within one working day of the notification/report. Enhanced surveillance data should be entered shortly after case follow-up.

7. Case definition

The case definition is based on what is currently known about the clinical and epidemiological profile of cases of COVID-19 presenting in Australia and internationally. Health authorities are constantly monitoring the spectrum of clinical symptoms and nature of illness. Using a 14 day exposure period will cover the duration of the incubation period in the vast majority of cases.

Confirmed case

A person who:

i. tests positive to a validated specific SARS-CoV-2 nucleic acid test;

OR

ii. has the virus isolated in cell culture, with PCR confirmation using a validated method;

OR

iii. undergoes a seroconversion to or has a significant rise in SARS-CoV-2 neutralising or IgG antibody level (e.g. four-fold or greater rise in titre).[1]

Probable case

A person who has detection of SARS-CoV-2 neutralising or IgG antibody[1] **AND** has had a compatible clinical illness **AND** meets one or more of the epidemiological criteria outlined in the suspect case definition (see below).

Suspect case

Clinical and public health judgement should be used in assessing if hospitalised patients with non-specific signs of infection and patients who do not meet the clinical or epidemiological criteria should be considered suspect cases.

A person who meets the following clinical **AND** epidemiological criteria:

Clinical criteria:

Fever (≥37.5°C)[2] or history of fever (e.g. night sweats, chills) **OR** acute respiratory infection (e.g. cough, shortness of breath, sore throat)[4] **OR** loss of smell or loss of taste.

Epidemiological criteria:

In the 14 days prior to illness onset:

- Close contact[5,6] (refer to Contact definition below) with a confirmed or probable case
- International travel
- Passengers or crew who have travelled on a cruise ship
- Healthcare, aged or residential care workers and staff with direct patient contact
- People who have lived in or travelled through a geographically localised area with elevated risk of community transmission, as defined by public health authorities[7]

Notes:

[1] Antibody detection must be by a validated assay and included in an external quality assurance program.

[2] It is recommended that temperature is measured using a tympanic, oral or other thermometer proven to consistently and accurately represent peripheral body temperature.

[3] If the person is a close contact of a probable case, at least one person in the chain of transmission must be a confirmed case.

[4] Other reported symptoms of COVID-19 include: fatigue, runny nose, muscle pain, joint pain, diarrhoea, nausea/vomiting and loss of appetite. Clinical and public health judgement should be used to determine if individuals with sudden and unexplained onset of one or more of these other symptoms should be considered suspect cases.

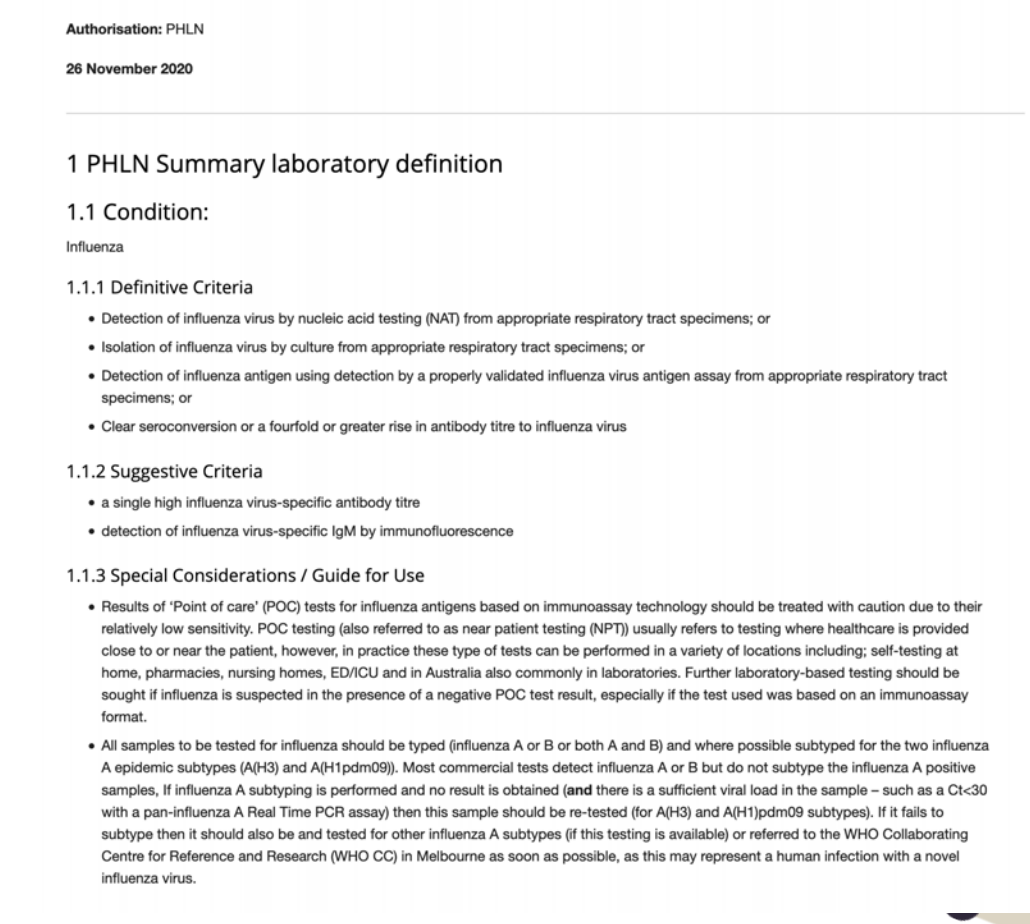
[5] Testing household contacts of confirmed or probable cases of COVID-19 may not be indicated where resources are constrained. These cases would be considered 'probable cases' (refer to definition above).

[6] In certain high risk outbreak settings, PHU may consider testing asymptomatic contacts to inform management of the outbreak. For further information, refer to outbreak investigation and management in high-risk settings.

[7] For further information on geographically localised areas with elevated risk of community transmission, refer to the Department of Health website: (https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm)

Influenza Case Definitions

- Case definition assessments suggest high sensitivity but lower specificity
- Variation with season
- Cough + Fever
  - Sensitivity 87%
  - Specificity 70% (Gupta 2012)
- Headache + Myalgia
  - Sensitivity 86%, 73%
  - Specificity 10%, 26% (Hirve 2012)



Authorisation: PHLN

26 November 2020

1 PHLN Summary laboratory definition

1.1 Condition:

Influenza

1.1.1 Definitive Criteria

- Detection of influenza virus by nucleic acid testing (NAT) from appropriate respiratory tract specimens; or
- Isolation of influenza virus by culture from appropriate respiratory tract specimens; or
- Detection of influenza antigen using detection by a properly validated influenza virus antigen assay from appropriate respiratory tract specimens; or
- Clear seroconversion or a fourfold or greater rise in antibody titre to influenza virus

1.1.2 Suggestive Criteria

- a single high influenza virus-specific antibody titre
- detection of influenza virus-specific IgM by immunofluorescence

1.1.3 Special Considerations / Guide for Use

- Results of 'Point of care' (POC) tests for influenza antigens based on immunoassay technology should be treated with caution due to their relatively low sensitivity. POC testing (also referred to as near patient testing (NPT)) usually refers to testing where healthcare is provided close to or near the patient, however, in practice these type of tests can be performed in a variety of locations including; self-testing at home, pharmacies, nursing homes, ED/ICU and in Australia also commonly in laboratories. Further laboratory-based testing should be sought if influenza is suspected in the presence of a negative POC test result, especially if the test used was based on an immunoassay format.
- All samples to be tested for influenza should be typed (influenza A or B or both A and B) and where possible subtyped for the two influenza A epidemic subtypes (A(H3) and A(H1pdm09)). Most commercial tests detect influenza A or B but do not subtype the influenza A positive samples, If influenza A subtyping is performed and no result is obtained (**and** there is a sufficient viral load in the sample – such as a Ct<30 with a pan-influenza A Real Time PCR assay) then this sample should be re-tested (for A(H3) and A(H1)pdm09 subtypes). If it fails to subtype then it should also be and tested for other influenza A subtypes (if this testing is available) or referred to the WHO Collaborating Centre for Reference and Research (WHO CC) in Melbourne as soon as possible, as this may represent a human infection with a novel influenza virus.

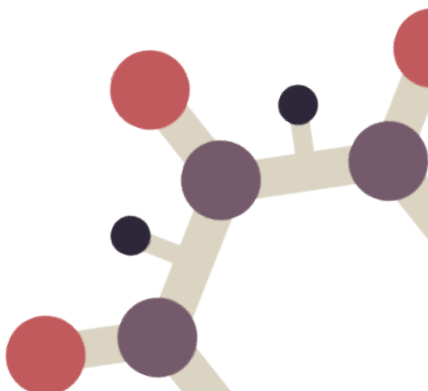
Epidemiology

Influenza

- Yearly epidemics
- Well established monitoring methods
  - GP surveillance
  - Laboratory surveillance
  - ED surveillance
  - Specific projects
- Affected populations

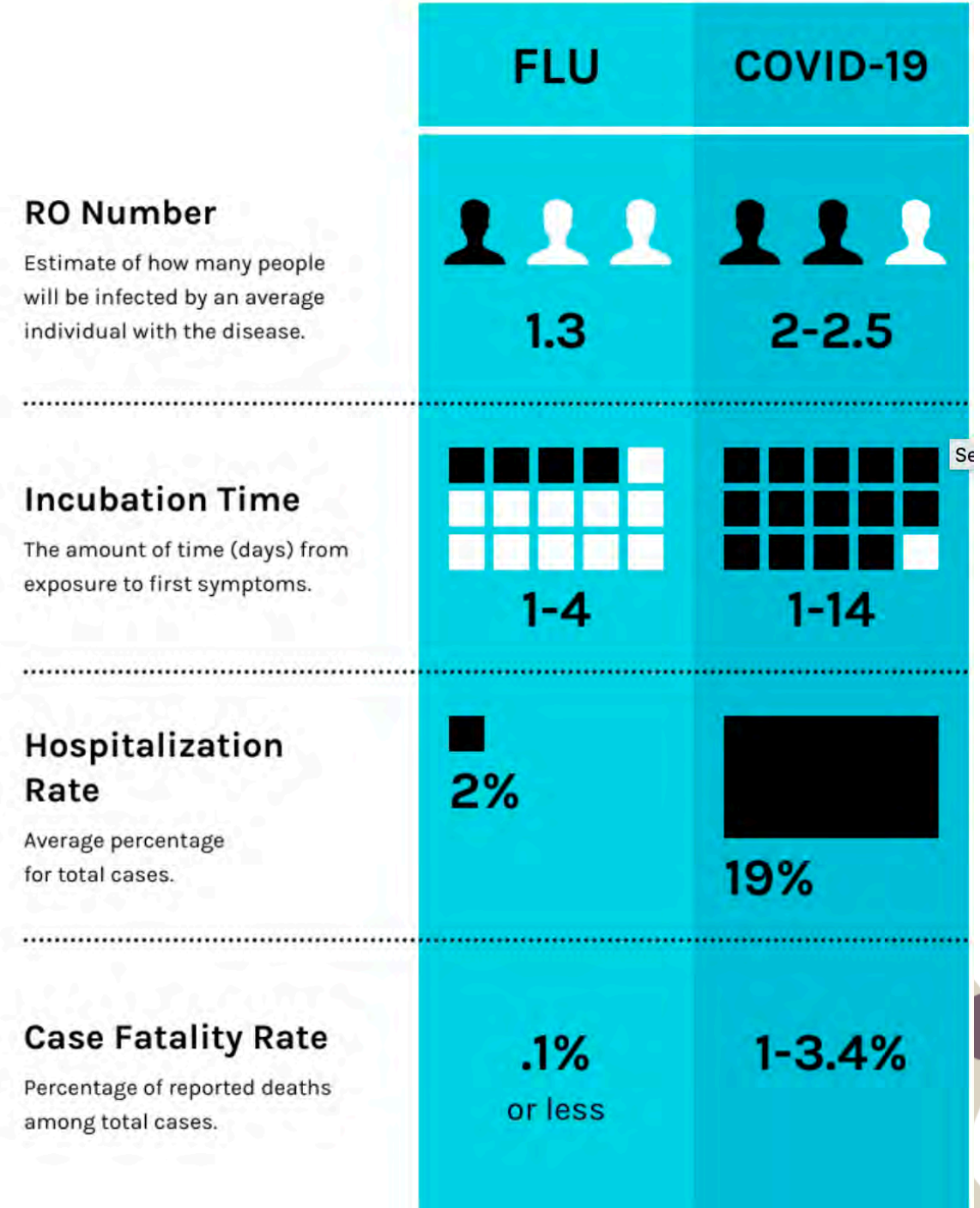
Coronaviruses

- Established infections
  - Recurrent betacoronavirus outbreaks
  - OC43 established in the population ?1890
  - HKU1 found 2005 (Woo 2005)
- Recent pandemic
- Asymptomatic infection
- Affected populations
  - Children 2.8% severe

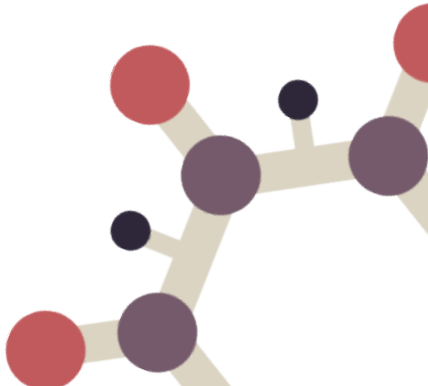


Overall comparison

IP COVID29 11.5 d in 97.5%
101/10,000 symptoms >14 d (Lauer 2020)



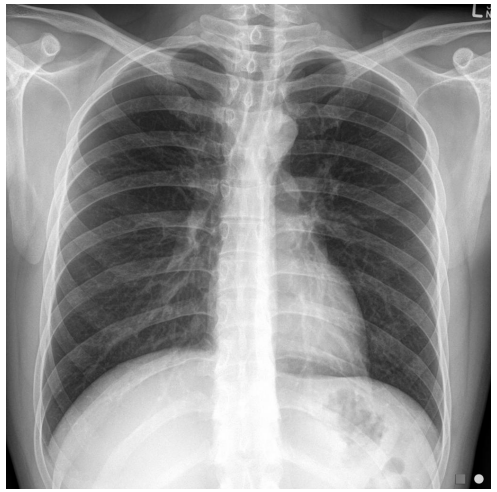
Many different viruses cause infections similar to COVID19

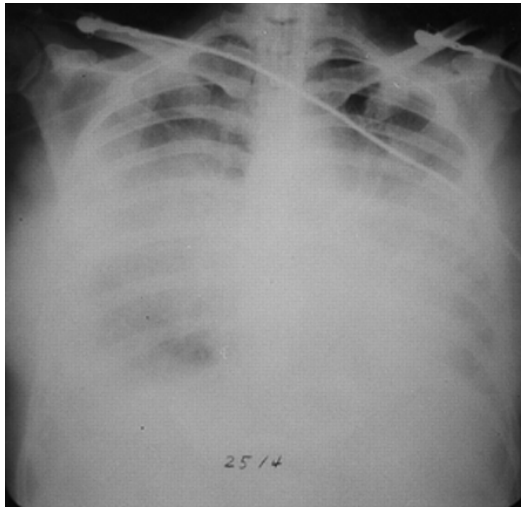


Viruses causing respiratory infections

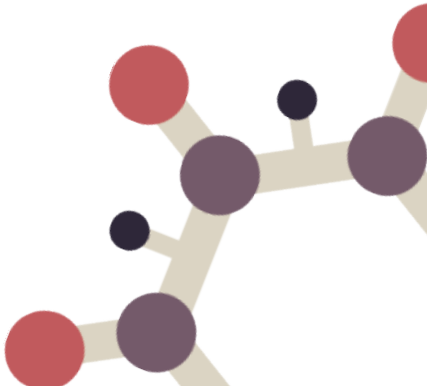
- Rhinoviruses
- Coronaviruses ~12%
  - Coronavirus NL63
  - Coronavirus 229E
  - Coronavirus OC43
  - Coronavirus HKU1
- Adenoviruses
- Human respiratory syncytial virus
- Influenza A & B
- Parainfluenza 1,2,3,4
- Human metapneumovirus
- Enteroviruses

- HSV/VZV
- EBV/CMV
- Measles

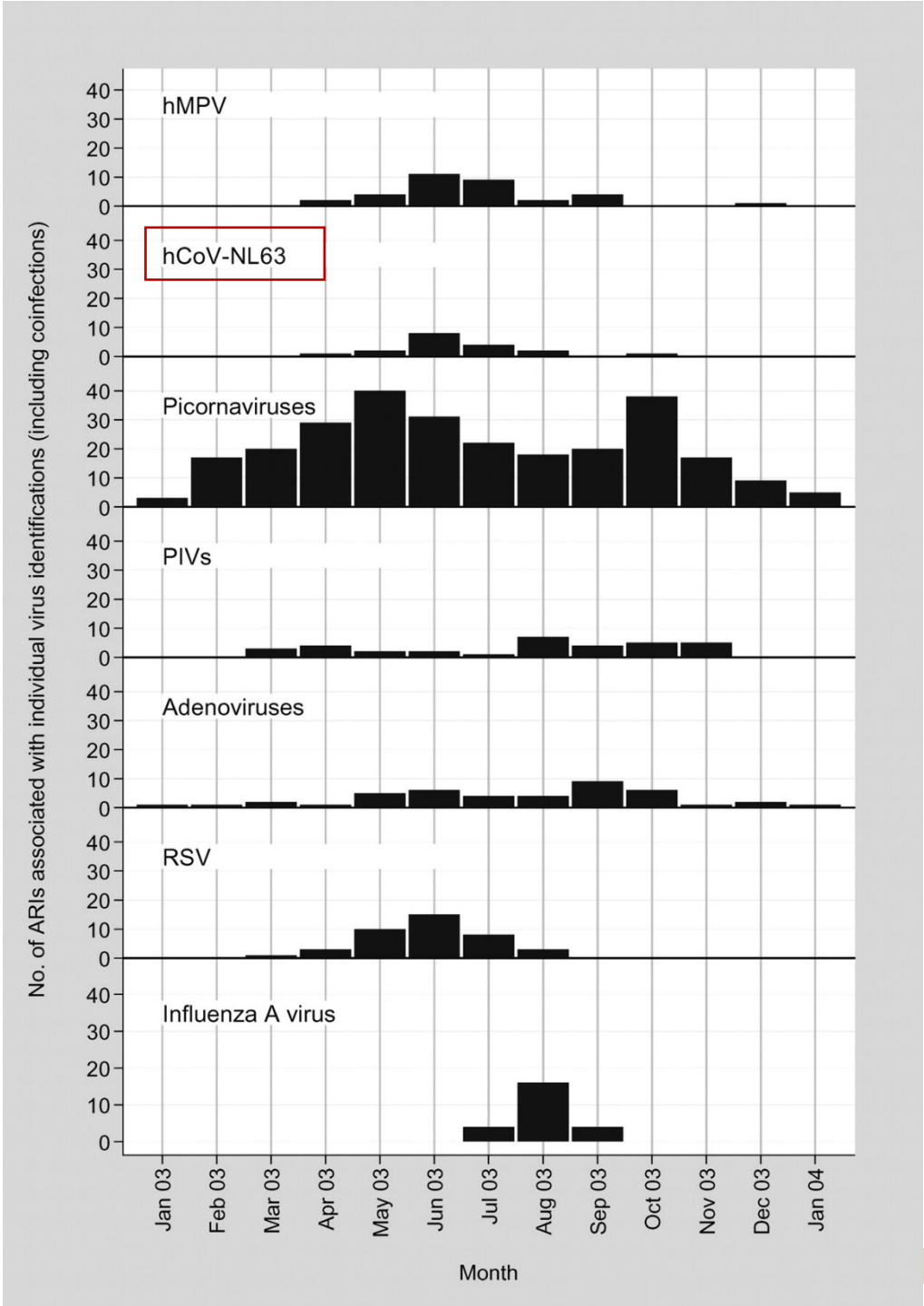




- Emerging Viruses
  - Human Coronaviruses
    - SARS CoV (2003)
    - MERS CoV (2012)
    - COVID-19
  - Influenza



Other (non SARS) coronaviruses mainly occur in winter every year



[Lambert 2007]

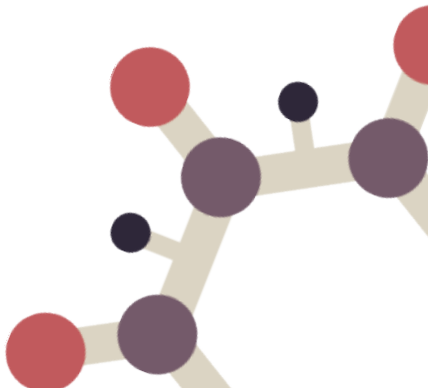
Clinical presentation

COVID19 and Influenza

- Respiratory transmission
- Clinical presentation with fever, respiratory symptoms
- Similar complications of pneumonia, inflammation, mortality, neurological effects
  - Higher with pandemic 2009? 92% vs 3.8-50% (Chacko 2012)
- Effects on inflammatory and coagulation pathways (Madjid 2004)
- Neurological syndromes
  - Flu Encephalitis, GBS, Cerebellar ataxia

COVID19

- Inflammation higher
  - Associated higher mortality
  - Myocarditis associated with death (93% with myocarditis, 38% without) (Khan 2020)
  - Intravascular clotting
- Neurological syndromes
  - Dysgeusia
  - Anosmia
  - Encephalitis, Seizures
  - Stroke
  - ADEM



Patient characteristics in hospitalized

COVID19 and Influenza

- Median age similar

(68, 71 yrs)

- Coinfections

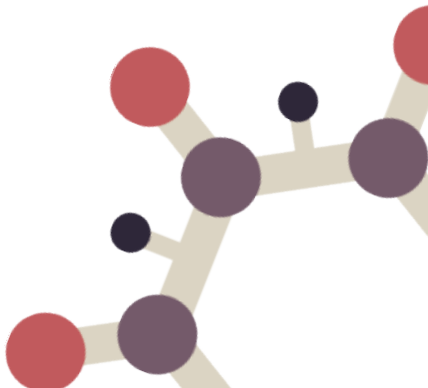
COVID19

- More frequently
  - Obese
  - Diabetes
  - Hypertension
  - Dyslipidaemia
- In hospital more
  - Respiratory failure
  - PTE
  - Septic shock
  - Haem stroke

Influenza

- More frequently
  - Heart failure
  - Chronic respiratory disease
  - Cirrhosis
  - Anaemia
- In hospital more
  - AMI
  - AF
  - Children hospitalized, lower mortality

(Piroth 2020)



Mortality

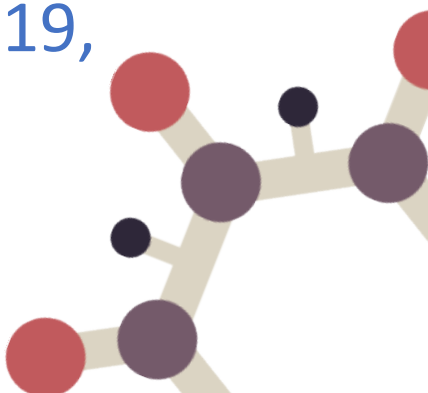
SARS CoV2/COVID19

- In hospital mortality higher with
  - Older
  - Male
  - Chronic cardiac disease
  - Biomarkers higher IL6, higher D-dimer
  - Biomarkers possibly higher ALT, LDH, CK, Ferritin, Creatine, Procalcitonin

(Khan MS 2020)

Influenza

- Acute influenza
  - Hospitalised mortality 3.8-50%
  - Hospitalised 2009 pandemic 92% (Chacko 2012)
- Uncertain association of mortality with pre existing cardiac disease (Harris 2019, Fagnoul 2013)



Mortality

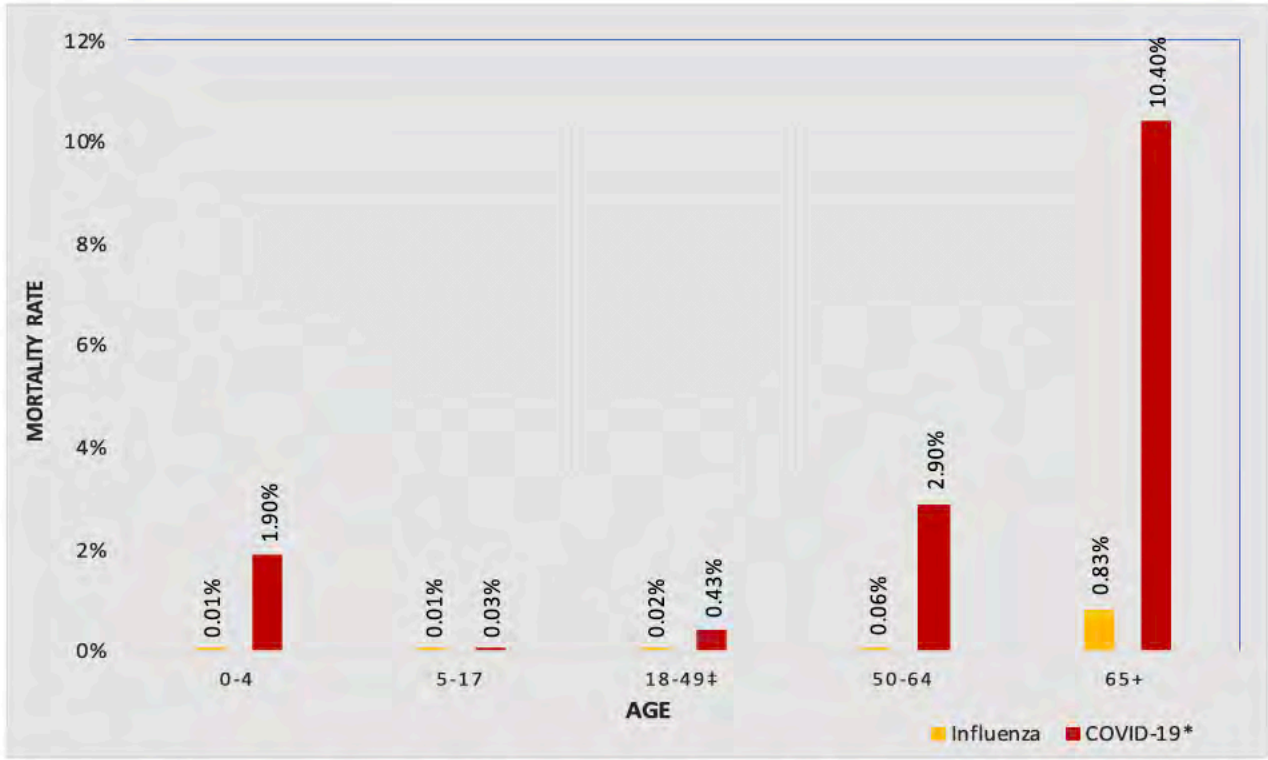


Fig. 1 Comparison of estimated influenza vs confirmed COVID-19 death rate by age. *CDC confirmed COVID-19 death rate as of June 23, 2020. ‡Average of COVID-19 death rate obtained for age group 18–29, 30–39, and 40–49

Cardiovascular complications

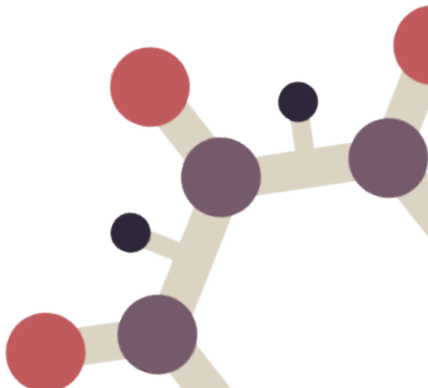
SARS CoV2/COVID19

- COVID19 deaths 15-70% underlying cardiovascular disease
  - 1.38% case fatality
- Higher DVT, PTE
- Reduced cardiac hospitalization
  - Most likely deferred admission
  - 50% decrease
- Higher numbers with increased troponin levels

(Khan MS 2020)

Influenza

- Cardiac excess mortality
  - 0.0962% case fatality
- Vascular thrombosis uncommon
- Increased cardiac hospitalization
  - 24% increase at peak
  - Increased risk of AMI after influenza



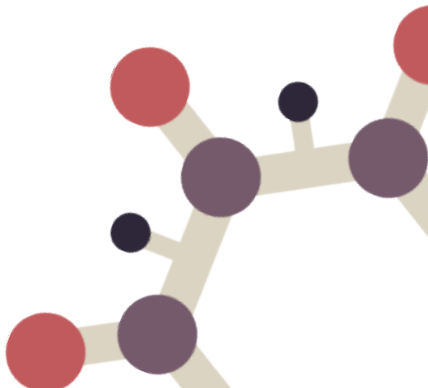
Virus Properties

SARS CoV2

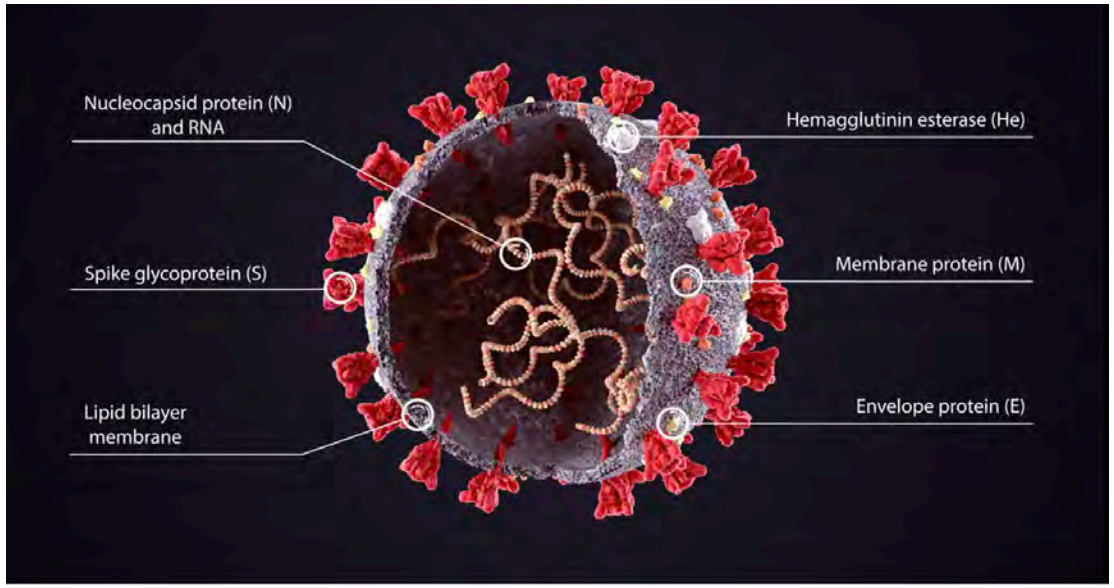
- 1 strain
  - Multiple emerging variants
  - VoC B.1.1.7, B.1.351/501Y, P1, B.1.1.316
- +ve stranded, non segmented RNA
- 30 kb length
- Surface Spike protein
- Enveloped
- Incubation 2-14 d (up to ~2 months outliers)

INFLUENZAVIRUS

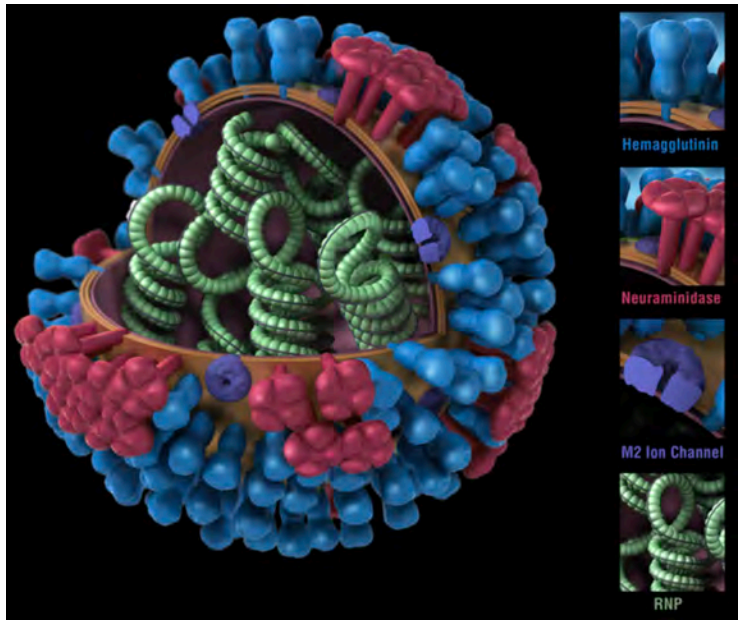
- Human 3 (4) main strains
  - Multiple subtypes
- -ve stranded, segmented RNA
- 13.5 kb length
- Surface NA, HA proteins
- Enveloped
- Incubation 1-4 d



Virus structure

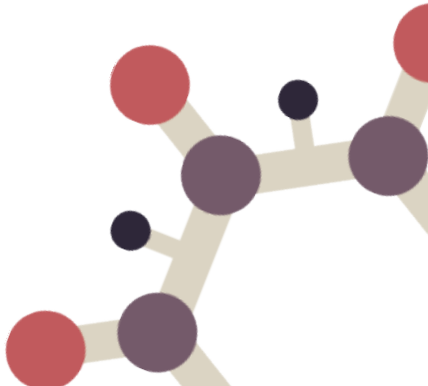


- Binds ACE 2 receptor
- Requires TMPRSS enzyme

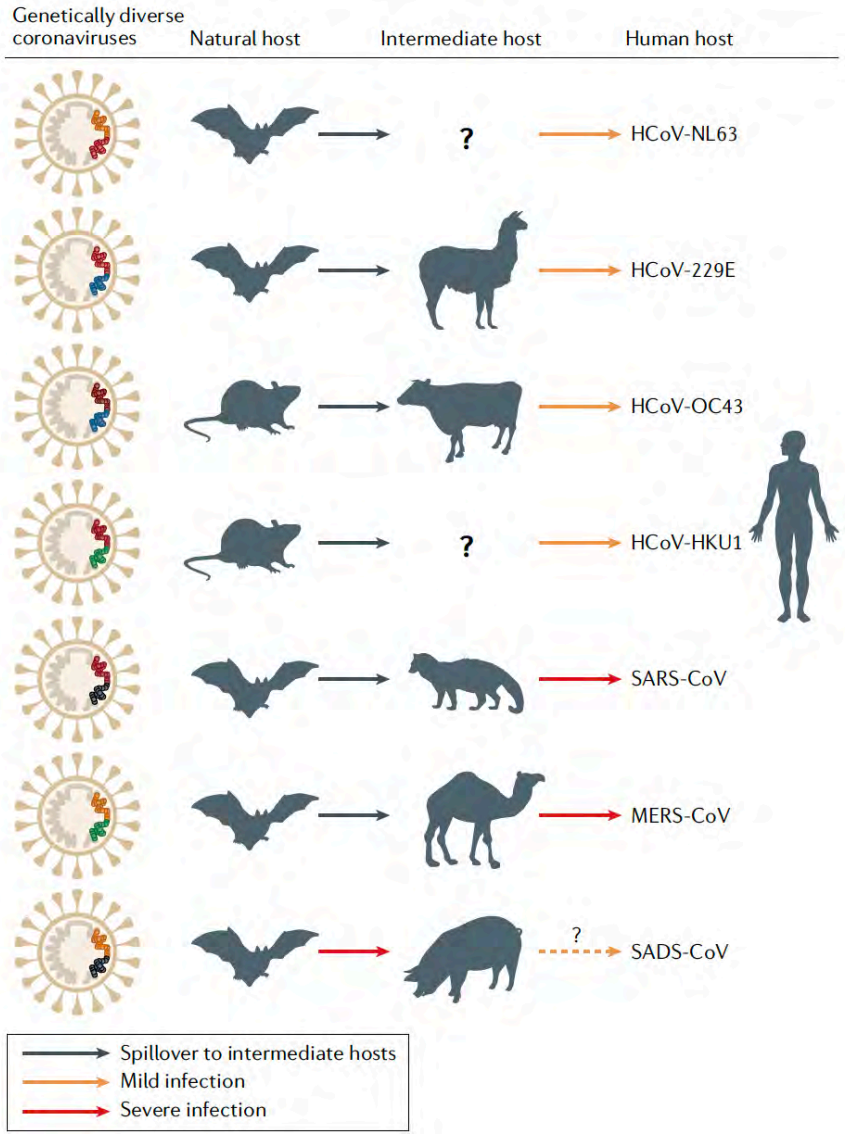


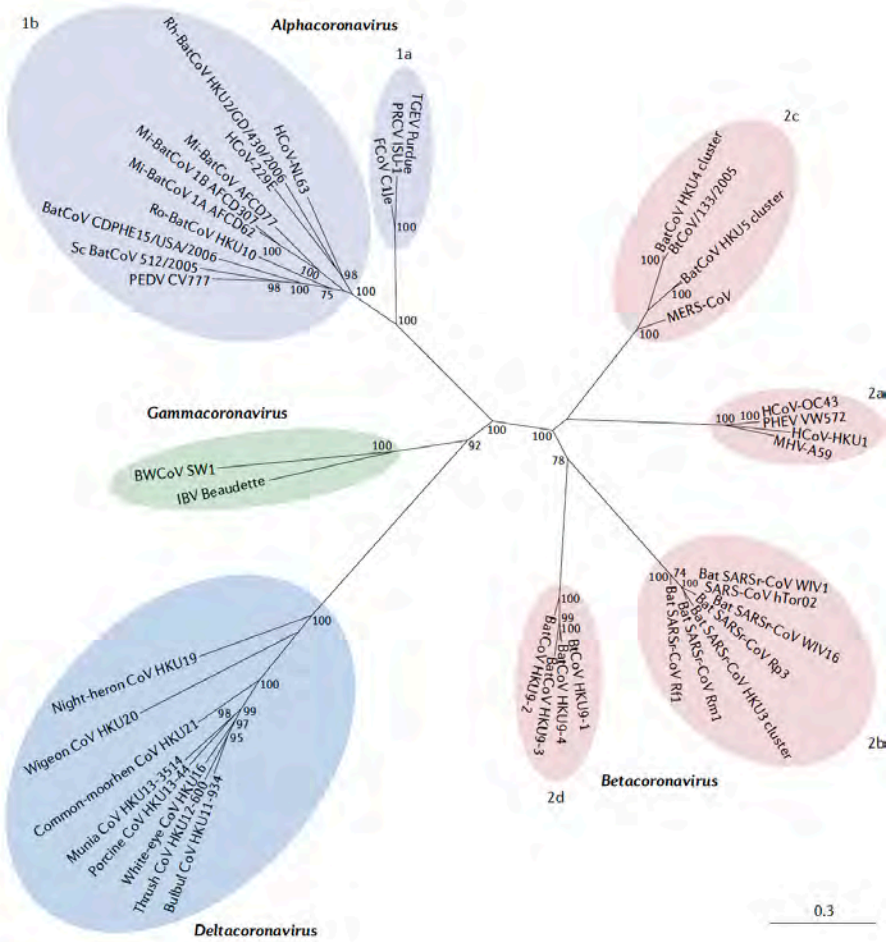
- Binds Glycans with terminal sialic residues as
  - α2,3-linked SA humans
  - α2,6-linked SA birds
- Requires HA, NA enzyme

SARS CoV2 closely resembles coronaviruses found in bats, and SARS CoV that caused infections in humans during 2003

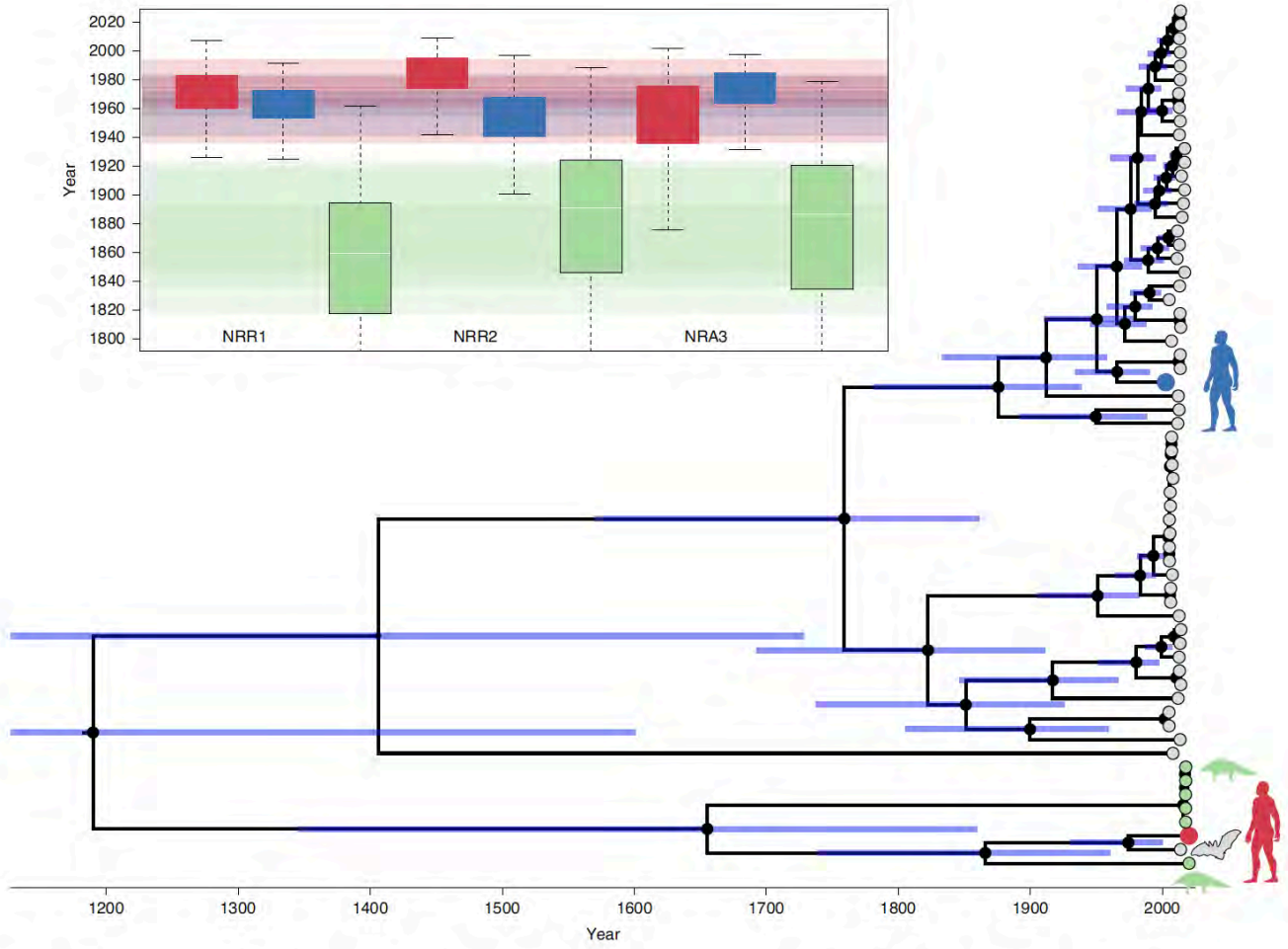


Coronaviruses are spread from animals (Zoonoses)





Coronavirus Diversity



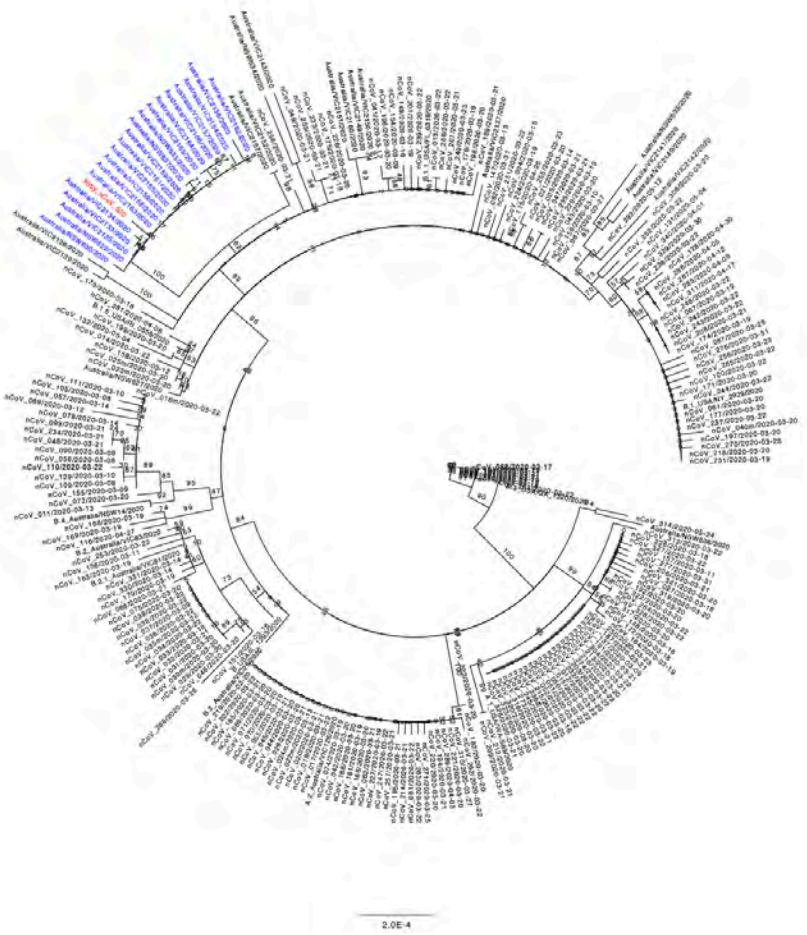


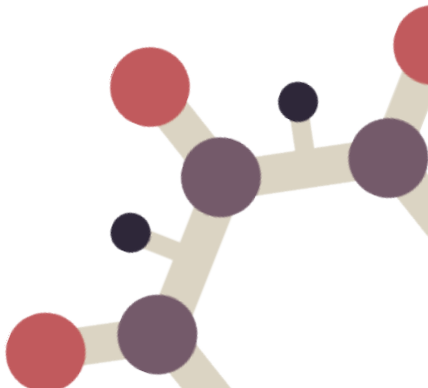
Fig. 5 | Time-measured phylogenetic estimates and divergence times for sarbecovirus lineages using an HCoV-OC43-centred rate prior. The time-calibrated phylogeny represents a maximum clade credibility tree inferred for NRR1. Grey tips correspond to bat viruses, green to pangolin, blue to SARS-CoV and red to SARS-CoV-2. The sizes of the black internal node circles are proportional to the posterior node support. 95% credible interval bars

(Boni 2020)

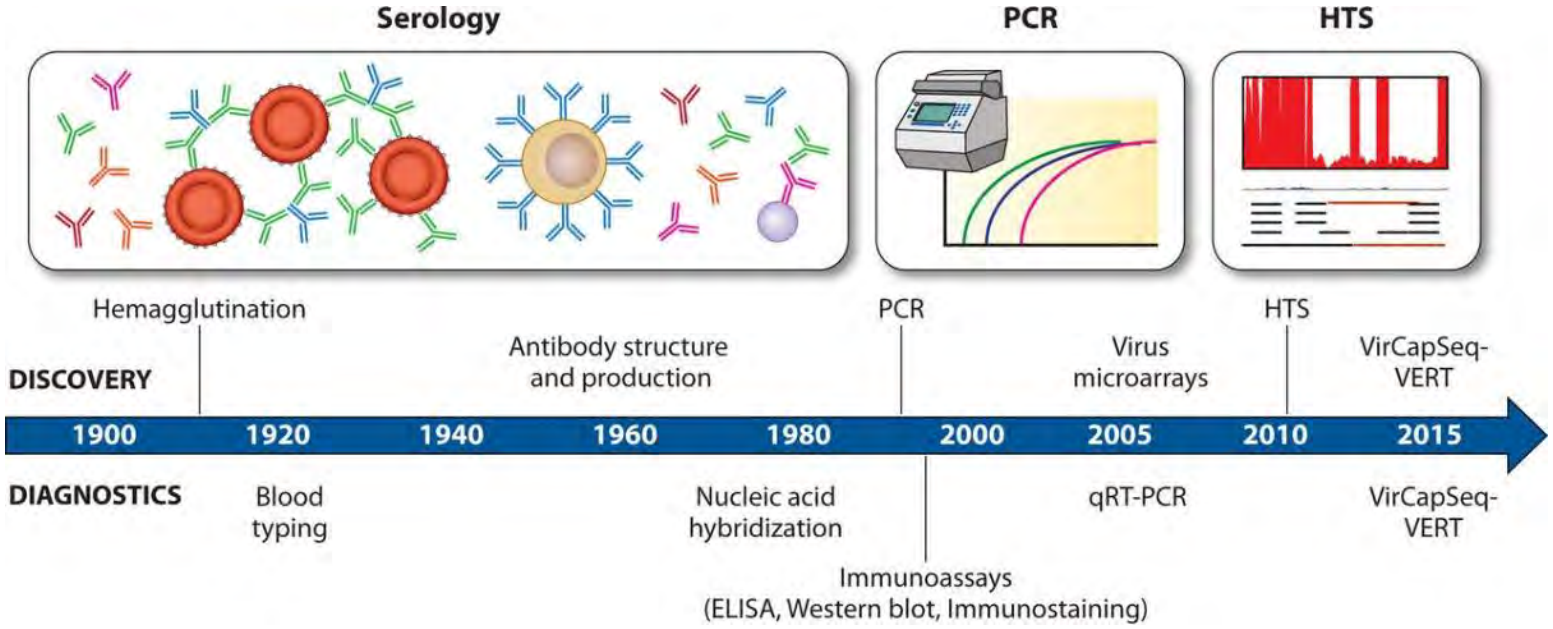
Responses to winter – circulating flu & SARS

- Enhanced testing
- Distinguish because of
  - Different spread, clinical progress
  - Differing prognosis
  - Vaccination
  - Therapy for influenza with antivirals (NI), steroids contraindicated
  - Therapy for SARS with antivirals (remdesivir), dexamethasone
- Clinical effects on availability of ICU and ED resources
- Coinfection
  - Variable studies, flu + SARS in 12% (Zeng 2020) or 2% (Kim 2021)
- Vaccination for flu associated with reduced COVID19 mortality (Marchionni 2020)

(Rubin 2020)



Evolution of virus detection

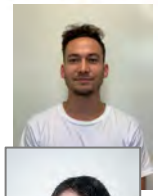


Rasmussen *mBio* 2015

Through art and science in their broadest senses it is possible to make a permanent contribution towards the improvement and enrichment of human life and it is these pursuits that we students are engaged in.

Fred Sanger, Cambridge 1980



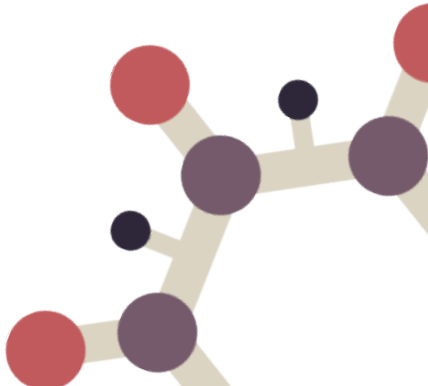





Acknowledgements

- Commonwealth Health
- NSW Ministry of Health
- NSW Health Pathology, SEALS Randwick SAViD

We diagnose SARS CoV2 with molecular tests (PCR) and serology



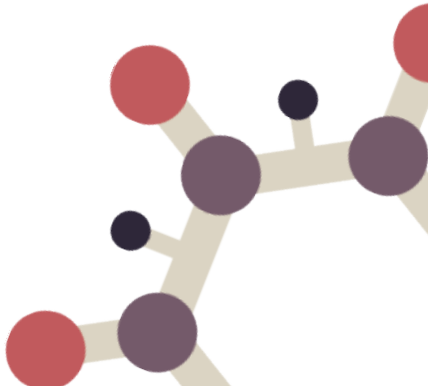
The process of diagnosis of SARS CoV2

Diagnosis at SAViD

- Commenced early February 2020
- Utilised standard PCR testing
  - In house assays based around E, N, Orf 1b genes
  - In house assays from HKU, CDC, WHO
  - Based on overseas sequences, local verification
- Rapid development of commercial assays
  - Roche 6800 automated PCR platform
  - Seegene multiplex platform
  - Genetic Signatures automated PCR platform
  - Pooling to improve workflow and reduce reagent use
- Ongoing issues
  - Reagent shortages
  - Equipment MTBF
  - Staff stressors, illness
  - Team plans for infection of laboratory scientists

How we diagnose SARS CoV2

- Swabs taken
- Rapid development of commercial assays
  - Roche 6800 automated PCR platform
  - Seegene multiplex platform
  - Genetic Signatures automated PCR platform
  - Pooling to improve workflow and reduce reagent use
- Ongoing issues
  - Reagent shortages
  - Equipment MTBF
  - Staff stressors, illness
  - Team plans for infection of laboratory scientists



Molecular Tests used in Australian Laboratories

ABBOTT REALTIME SARS-COV-2	RDRP, N	17 APRIL 2020
AUSDIAGNOSTICS (AUSTRALIA) RESPIRATORY VIRUS PANEL (INCL SARS-COV-2)	ORF 1a, ORF 8	19 March 2020
BECTON DICKINSON (USA) BD SARS-COV-2 FOR BD MAX™ SYSTEM	N1, N2	17 April 2020
BIOFIRE RESPIRATORY PANEL 2.1 PLUS	M, S	27 July 2020
CEPHEID (USA) XPERT® XPRESS SARS-COV-2	E, N2	22 March 2020
CERTEST BIOTC SL (SPAIN) VIASURE SARS-COV-2 S GENE REAL TIME PCR DETECTION KIT	S	21 March 2020
CERTEST BIOTC SL (SPAIN) VIASURE SARS-COV-2 REAL TIME PCR DETECTION KIT		31 March 2020
GENETIC SIGNATURES (AUSTRALIA) EASYSCREEN™ SARS-COV-2 DETECTION KIT	N, E	13 APRIL 2020
HOLOGIC (USA) PANTHER FUSION® SARS-COV-2 ASSAY	ORF 1ab (Region 1 & 2)	20 May 2020
HOLOGIC (USA) APTIMA® SARS-COV-2 ASSAY		29 June 2020
ROCHE (SWITZERLAND) COBAS® SARS-COV-2	ORF1ab, E	20 March 2020
SEEGENE (KOREA) ALLPLEX™ 2019-NCOV ASSAY	E, N, RdRp	27 March 2020
SEEGENE (KOREA) ALLPLEX™ SARS-COV-2 ASSAY	RdRp, E, N	17 June 2020

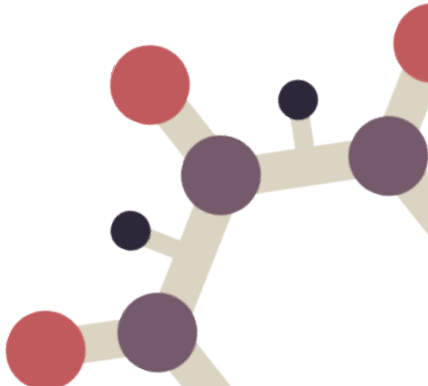
[Guilholm 2020, Pathology]

Serology Tests used in Australian Laboratories

ABBOTT (IRELAND) SARS-COV-2 IGG KIT	28 JULY 2020
BECKMAN COULTER (USA) ACCESS SARS-COV-2 IGG ANTIBODY TEST	24 July 2020
BIOMERIEUX (FRANCE) VIDAS® SARS-COV-2 IGM	3 August 2020
BIOMERIEUX (FRANCE) VIDAS® SARS-COV-2 IGG	3 August 2020
BIO-RAD (FRANCE) PLATELIA SARS-COV-2 TOTAL AB	23 June 2020
DIASORIN SPA (ITALY) LIAISON® SARS-COV-2 S1/S2 IGG AND IGM	31 July 2020
EUROIMMUN MEDIZINISCHE LABORDIAGNOSTIKA AG (GERMANY) ANTI-SARS-COV-2 ELISA (IGG)	18 May 2020
EUROIMMUN MEDIZINISCHE LABORDIAGNOSTIKA AG (GERMANY) ANTI-SARS-COV-2 ELISA (IGA)	18 May 2020
EUROIMMUN MEDIZINISCHE LABORDIAGNOSTIKA AG (GERMANY) ANTI-SARS-COV-2 NCP ELISA (IGG) (IGM)	5 August 2020
ORTHO-CLINICAL DIAGNOSTICS (UNITED KINGDOM) VITROS IMMUNODIAGNOSTIC PRODUCTS ANTI-SARS-COV-2 TOTAL	19 June 2020
ROCHE'S ELECSYS ANTI-SARS-COV-2	20 May 2020
SIEMENS (USA) ADVIA CENTAUR® SARS-COV-2 TOTAL (COV2T) ASSAY	5 June 2020
SIEMENS (USA) ATELLICA® IM SARS-COV-2 TOTAL (COV2T) ASSAY	5 June 2020
SIEMENS (USA) DIMENSIONS EXL SARS-COV-2 TOTAL ANTIBODY ASSAY	5 JUNE 2020
SHENZHEN YHLO BIOTECH (CHINA) IFLASH-SARS-COV-2 IGG AND IGM	31 July 2020

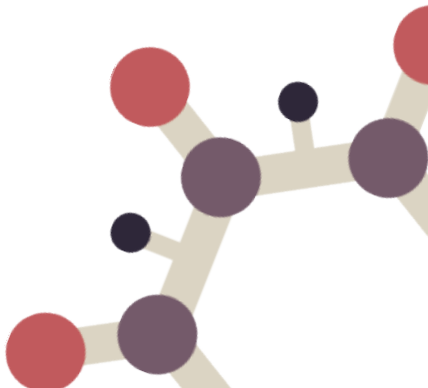
[Guilholm 2020, Pathology]

How we diagnose Influenza and other Respiratory Viruses



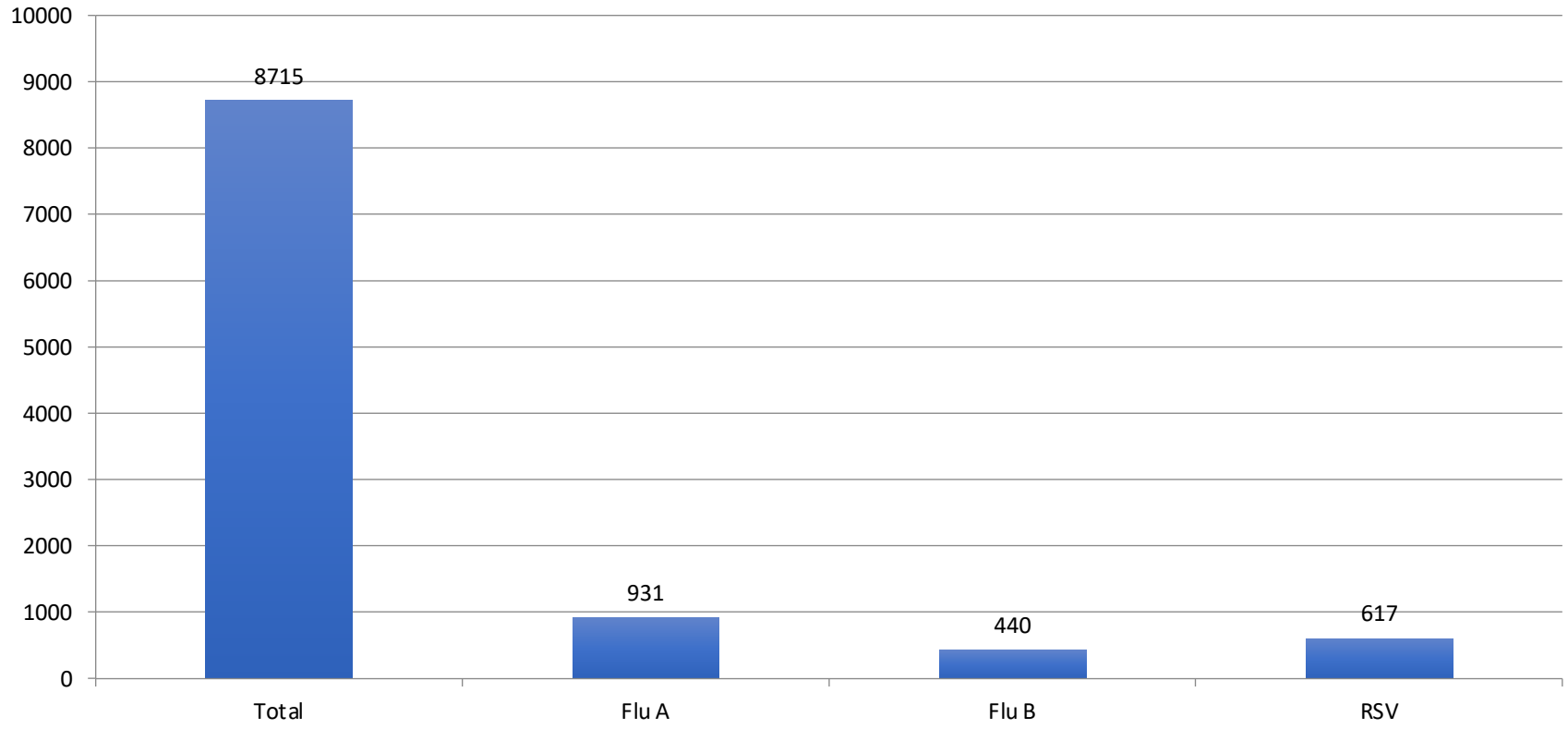
NSWHP RANDWICK RESPIRATORY ASSAYS

- Respiratory testing assays
  - **NAT/PCR**
    - Rapid Influenza/RSV NAT (Cepheid GeneXpert)
    - Respiratory Multiplex NAT (Seegene Allplex Respiratory panels 1. 2 & 3)
      - 19 targets:
        - Panel 1: Flu A, Flu B, RSV A, RSV B, Flu A-H1, Flu A-H1pdm09 & Flu A-H3
        - Panel 2: AdV, HEV, PIV1, PIV2, PIV3, PIV4 & MPV
        - Panel 3: HBoV, HRV, CoV NL63, CoV 229E & CoV OC43
  - **Serology**
    - **CFT:** Flu A, Flu B, RSV, AdV, PIV1, PIV2, PIV3, HEV
    - **EIA**: Bordetella pertussis, M pneumoniae
    - **IFA**: Legionella pneumophila & Legionella longbeachae



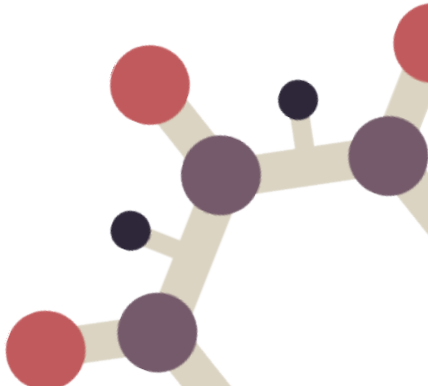
FLU & RSV, NSWHP RANDWICK 2017

- **N= 7714 (In-house Multiplex, Flu & RSV inclusive only)**
- **N = 1001 (Rapid, Flu & RSV)**



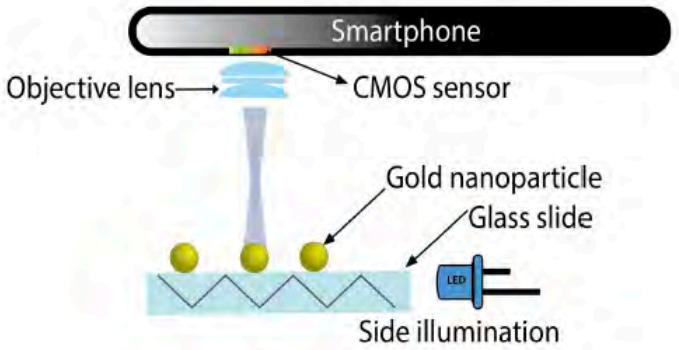
Neuraminidase Inhibitor Susceptibility Analysis, WHO Report 2017

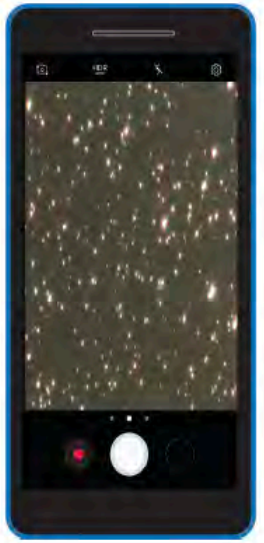
- 50/99 sample submitted to WHO cultured
- **Case study:**
- 85 yro female
- NPA Specimen collected on 21/08/2017
- Flu A & RSV Positive
- 30mg Oseltamivir for total 15 days
- Subtype: A/Sydney/521/2017
- Inhibition:
  - Highly reduced inhibition: Oseltamivir (IC50:2862.02)
  - Reduced Inhibition: Peramivir (IC50: 13.77)



Studies going forwa

- Newer diagnostics
  - Rapid near patient sensing
  - Mass Spectrometry, laboratory based
- Serology
  - Commercial Assays
  - In house purified protein targets
- Ophthalmology
  - Ocular tropism
- Cohorts
  - Phylogeography
  - Infection of surfaces
  - Spread, children





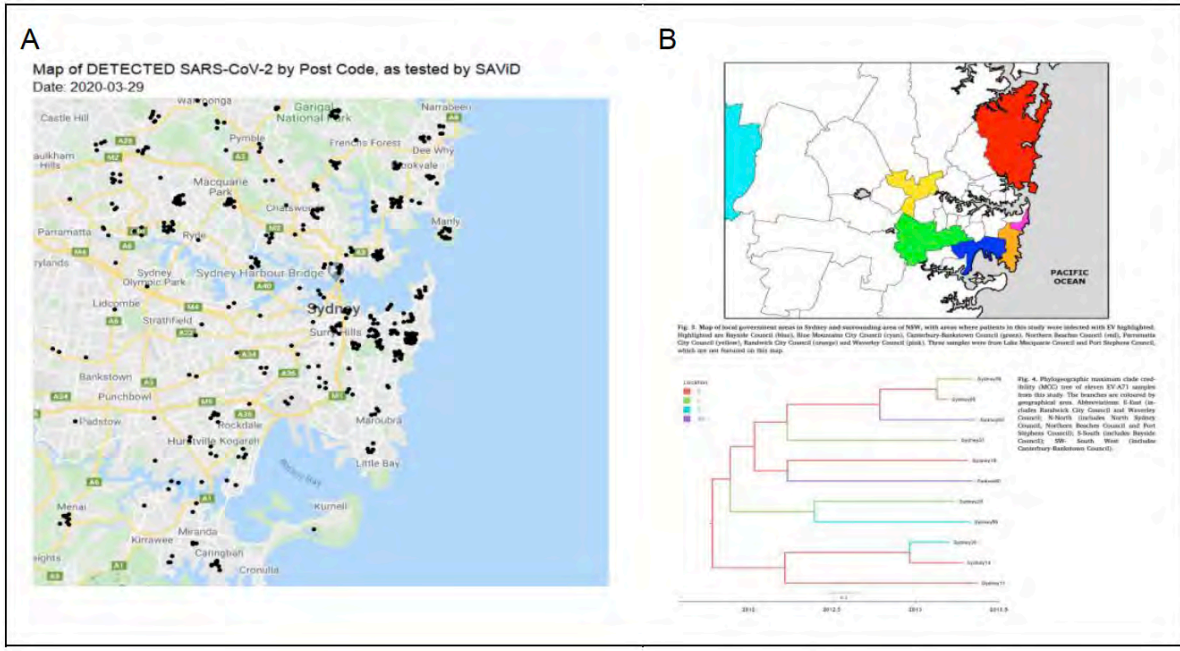
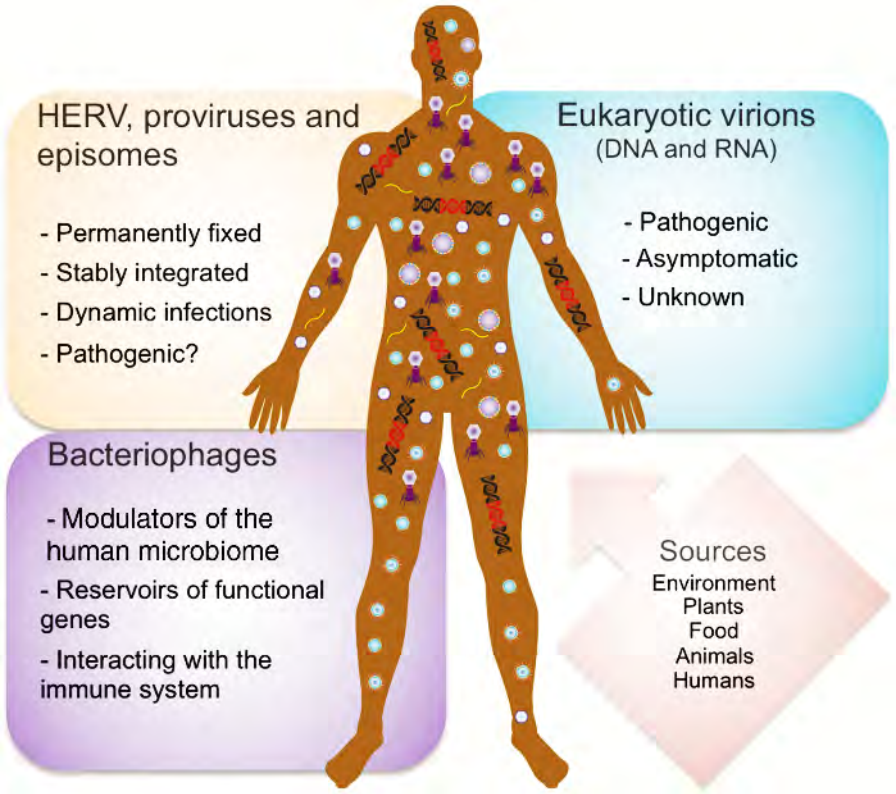


Figure 1: A) *Plot of the number of cases, each represented by dots, in the metropolitan/eastern part of Sydney* ***B)*** *Example of phylogeographic data (Ref 2), that took ~12 months to accumulate using standard methods* [2]

Human virome

- Vertebrate-infecting viruses most relevant to disease pathogenesis

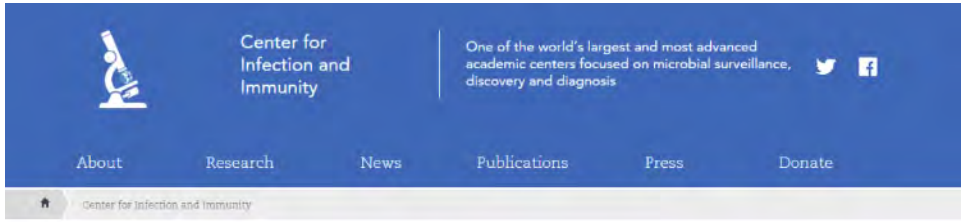


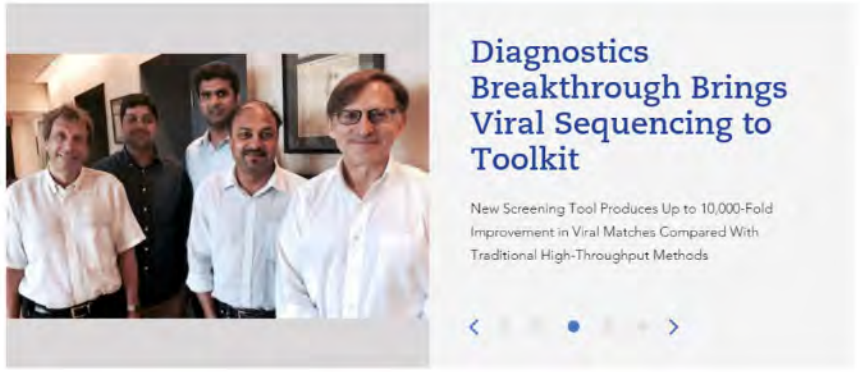
Forterre, *Clin Infect Dis.* 2017

Virome Capture Sequencing for vertebrate-infecting viruses (VirCapSeq-VERT)

~2 million probes (avg. 70 mer)

complete genomes of all known vertebrate-infectious viruses
(207 viral taxa)





RESEARCH ARTICLE

Virome Analysis of Transfusion Recipients Reveals a Novel Human Virus That Shares Genomic Features with Hepaciviruses and Pegiviruses

Amit Kapoor,[a] Arvind Kumar,[a] Peter Simmonds,[b] Nishit Bhuva,[a] Lokendra Singh Chauhan,[a] Bohyun Lee,[a] Amadou Alpha Sall,[c] Zhezhen Jin,[d] Stephen S. Morse,[e] Beth Shaz,[f] Peter D. Burbelo,[g] W. Ian Lipkin[a]

ABSTRACT To investigate the transmission of novel infectious agents by blood transfusion, we studied changes in the virome composition of blood transfusion recipients pre- and posttransfusion. Using this approach, we detected and genetically characterized a novel human virus, human hepegivirus 1 (HHpgV-1), that shares features with hepatitis C virus (HCV) and human pegivirus (HPgV; formerly called GB virus C or hepatitis G virus). HCV and HPgV belong to the genera *Hepacivirus* and *Pegivirus* of the family *Flaviviridae*. HHpgV-1 was found in serum samples from two blood transfusion recipients and two hemophilia patients who had received plasma-derived clotting factor concentrates. In the former, the virus was detected only in the post-transfusion samples, indicating blood-borne transmission. Both hemophiliacs were persistently viremic over periods of at least 201 and 1,981 days. The 5′ untranslated region (UTR) of HHpgV-1 contained a type IV internal ribosome entry site (IRES), structurally similar to although highly divergent in sequence from that of HCV and other hepaciviruses. However, phylogenetic analysis of nonstructural genes (NS3 and NS5B) showed that HHpgV-1 forms a branch within the pegivirus clade distinct from HPgV and homologs infecting other mammalian species. In common with some pegivirus variants infecting rodents and bats, the HHpgV-1 genome encodes a short, highly basic protein upstream of E1, potentially possessing a core-like function in packaging RNA during assembly. Identification of this new human virus, HHpgV-1, expands our knowledge of the range of genome configurations of these viruses and may lead to a reevaluation of the original criteria by which the genera *Hepacivirus* and *Pegivirus* are defined.

IMPORTANCE More than 30 million blood components are transfused annually in the United States alone. Surveillance for infectious agents in the blood supply is key to ensuring the safety of this critical resource for medicine and public health. Here, we report the identification of a new and highly diverse HCV/GB virus (GBV)-like virus from human serum samples. This new virus, human hepegivirus 1 (HHpgV-1), was found in serum samples from blood transfusion recipients, indicating its potential for transmission via transfusion products. We also found persistent long-term HHpgV-1 viremia in two hemophilia patients. HHpgV-1 is unique because it shares genetic similarity with both highly pathogenic HCV and the apparently nonpathogenic HPgV (GBV-C). Our results add to the list of human viruses and provide data to develop reagents to study virus transmission and disease association and for interrupting virus transmission and new human infections.

Received 2 September 2015 Accepted 9 September 2015 Published 22 September 2015

Citation Kapoor A, Kumar A, Simmonds P, Bhuva N, Singh Chauhan L, Lee B, Jin Z, Morse SS, Shaz B, Burbelo PD, Lipkin WI. 2015. Virome analysis of transfusion recipients reveals a novel human virus that shares genomic features with hepaciviruses and pegiviruses. mBio 6(5):e01466-15. doi:10.1128/mBio.01466-15.

WGS to identify SARS CoV2 variation – National genomics for viral pandemic

Objectives:

- Coordinated Australian national program of SARS-CoV-2 genomics
- Public health understanding and response improved
- Understanding behaviour, spread, evolution of the virus
- National coverage of sequencing, analysis, ensure national equity

Specific aims

(1) What are the optimal approaches to SARS-CoV-2 whole genome sequencing and analysis that will yield high-resolution, high-quality characterisation and bioinformatics analysis of the virus?

(2) What is the best-practice method for integration of national genomics and epidemiological data to identify transmission clusters and events?

(3) How can phylodynamics (genomic modelling) be used retrospectively and in real-time, to further improve understanding of the reproductive rate of SARS-CoV-2 across states and territories, and nationally?

(4) What is the impact of pathogen genomics in this COVID-19 pandemic and how will it impact future outbreak responses?

Team

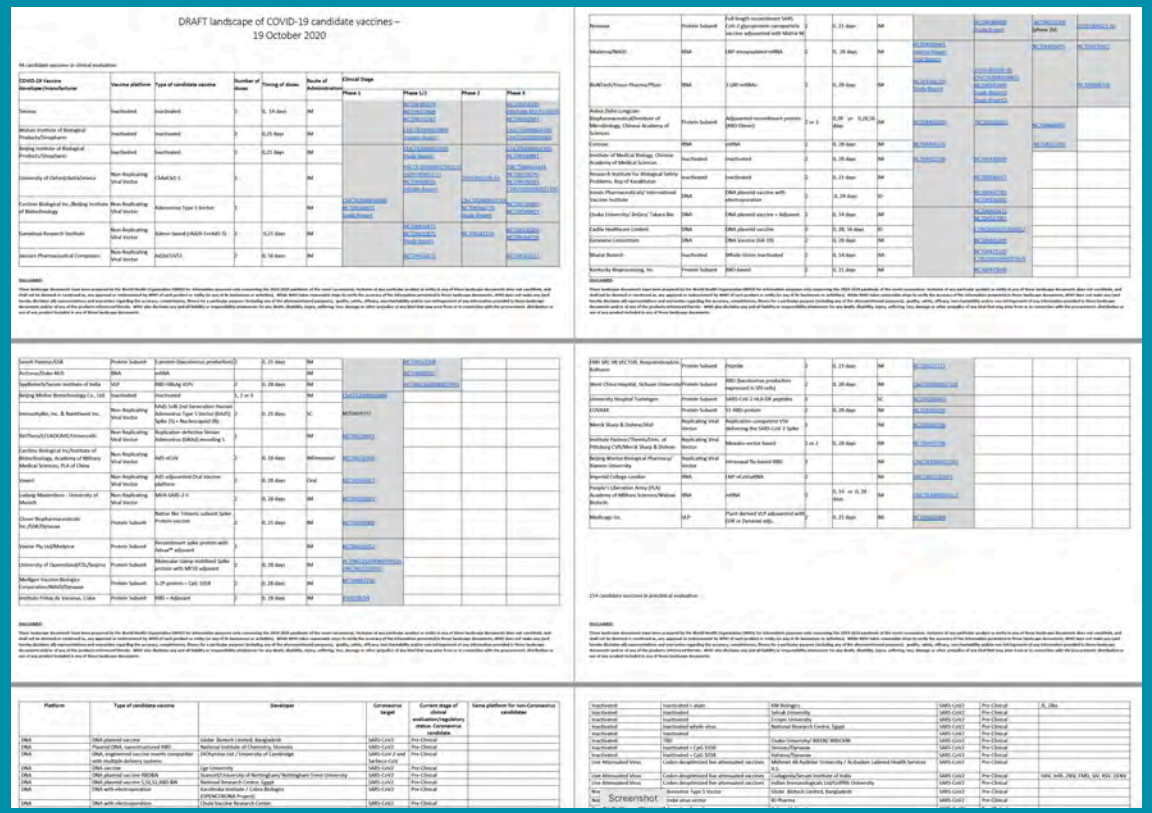
CIs Rawlinson (UNSW), Howden (UMelb), Sintchenko (USyd), Jennison (QldHealth), Williamson, Seeman, Duchene, Kelaher (UMelb), and AIs Caly, Lane, Da Silva, Kirk, Schlebusch, Moore, Bull Rockett, Leong, Smith

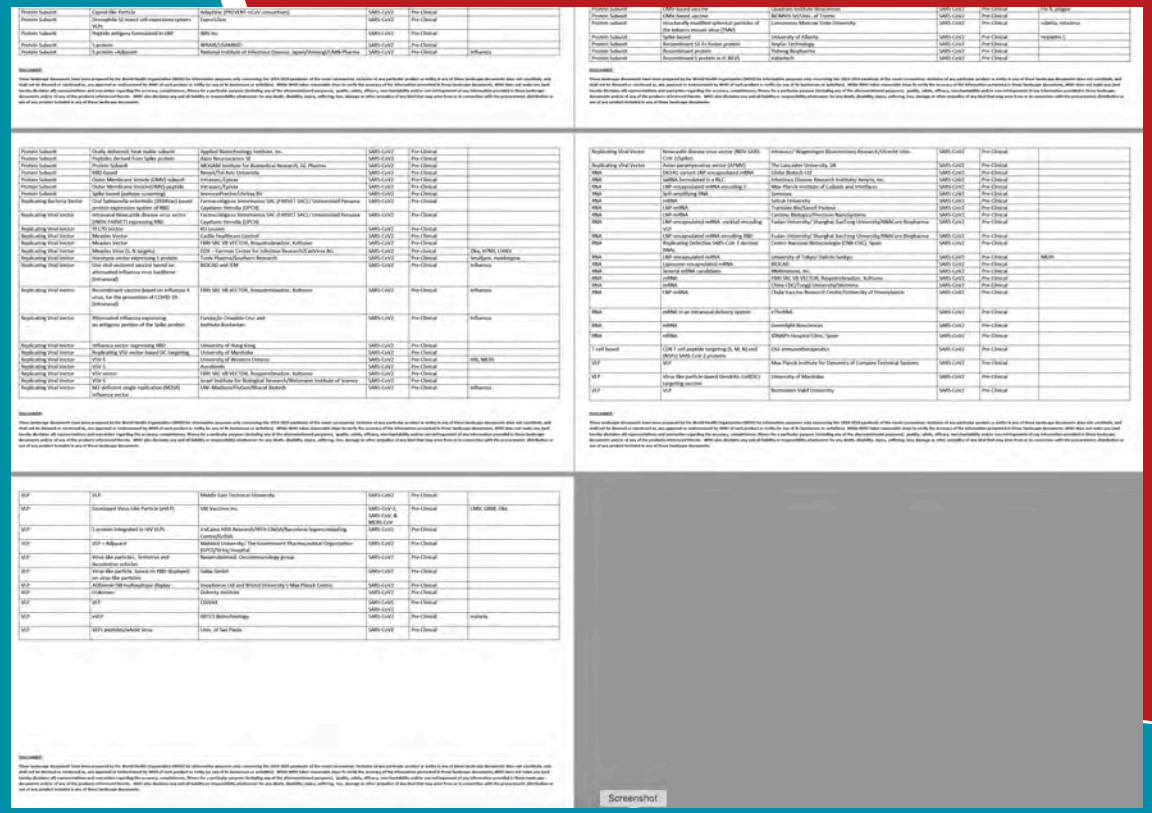
Outcomes to date:

- ***Initial technical studies***
  - Platforms (Bull et al Nature Comms)
  - Low viral load sample assessments for WGS
  - AusTrakka use in WGS assessments
- ***Identify blocks***
  - Low template amounts
  - Resourcing remote and rural
  - Multi institutional agreements/approaches
- ***Opportunities***
  - National data with metadata
  - Mutation analysis of individual strains
  - Transmission nationally and internationally
- ***Longer term plans***
  - Continuing studies/infrastructure after grant finished
  - Continued support of regional and remote
  - Better preparedness

Speaker: William Rawlinson AM FAHMS

Vaccine Candidates


DRAFT landscape of COVID-19 candidate vaccines – 19 October 2020



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SYDNEY ADVENTIST HOSPITAL

Vaccine Candidates

- 187 Candidates
- Most pre clinical
  - Phase 1/2 safety, dosage, side effects, efficacy
- 38/187 human trials

Vaccine Candidates

- Uni Oxford/AstraZeneca
  - ChAdox1
  - Phase3, 30K in US, 5K Brazil, 10.5K UK
  - Adeno spike
- Moderna, NIAID
  - mRNA-1273
  - Phase1 NEJM, side effects
  - Spike protein
- Pfizer/BioNTech/Fosun
  - mRNA
  - Phase2,3 30K USA
  - RBD spike
- J&J Janssen
  - Ad26
  - Phase3, 60K USA
  - Adeno vector, Spike
- Novavax
  - NVX-CoV2373
  - Phase1/2 NEJM
  - Spike protein

Vaccine Candidates

- Sinovac Biotech
  - Inactivated SARS CoV2
  - Phase2 results unpublished
- CanSino
  - Adeno
  - Phase2, Lancet
- Sinopharm
  - Inactivated SARS CoV2
  - Phase1,2 JAMA
  - Abu Dhabi 15K