Methodology

1. The National HIV Registry

National surveillance for HIV notifications

HIV is a notifiable disease in each state/territory health jurisdiction in Australia. All new HIV diagnoses are reported by doctors and laboratories to state/territory health authorities. Information sought on the notification forms includes: name code (based on the first two letters of the family name and the first two letters of the given name), gender, date of birth, postcode, country of birth, language spoken at home, Aboriginal and/or Torres Strait Islander status, date of HIV diagnosis, CD4+ cell count at diagnosis, viral load at diagnosis, likely place of HIV acquisition, likely source of HIV exposure, year of arrival in Australia, reason for HIV test, and evidence of newly acquired HIV (see below). If the person was born overseas, language spoken at home and date of arrival in Australia are also recorded. These data are then forwarded to the Kirby Institute for collation and analysis. The database where HIV notifications are stored is referred to as the National HIV Registry.

The procedures used for national HIV surveillance of newly diagnosed HIV are available at www.kirby.unsw.edu.au .

Newly acquired HIV

Newly acquired HIV is defined as newly diagnosed HIV with evidence of a negative or indeterminate HIV antibody test or a diagnosis of primary HIV within the previous 12 months. Information on the date of the last negative or indeterminate test or date of onset of primary HIV has been routinely sought from each state/territory health jurisdiction since 1991.

Late and advanced HIV diagnosis

Advanced HIV diagnosis is defined as newly diagnosed HIV with a CD4+ cell count of less than 200 cells/µL, and late HIV diagnosis was defined as newly diagnosed HIV with a CD4+ cell count of less than 350 cells/µL. HIV notifications classified as newly acquired HIV were categorised as not late or advanced diagnoses irrespective of CD4+ cell count.

High HIV-prevalence countries

Countries recognised by UNAIDS as having a national prevalence above 1% in any of the years in the past 10 years (2009–2018) were considered high-prevalence. The following countries were considered high-prevalence:

Angola
Bahamas
Belize
Benin
Botswana
Burkina Faso
Burundi
Cameroon
Central African Republic
Chad
Congo
Côte d'Ivoire
Democratic Republic of the Congo
Djibouti
Dominican Republic
Equatorial Guinea
Eswatini
Ethiopia
Gabon
Gambia
Ghana
Guinea
Guinea-Bissau
Guyana
Haiti
Jamaica
Kenya
Lesotho
Liberia
Malawi
Mali
Mauritius
Mozambique
Namibia
Nigeria
Panama
Rwanda
Sierra Leone
South Africa
South Sudan
Suriname
Thailand
Togo
Trinidad and Tobago
Uganda
Ukraine
United Republic of Tanzania
Zambia
Zimbabwe

Australian Paediatric Surveillance Unit

Cases of perinatal exposure to HIV were reported to the Kirby Institute by paediatricians through the Australian Paediatric Surveillance Unit (apsu.org.au), and also notified through state and territory health authorities according to national HIV surveillance procedures. Further details of perinatal exposure to HIV data collection are described elsewhere (1,2).

Australian National Notifiable Diseases Surveillance System

The National Notifiable Diseases Surveillance System (NNDSS), established in 1990 under the auspices of the Communicable Diseases Network of Australia. NNDSS coordinates the national surveillance of more than 50 communicable diseases or disease groups. Under this scheme, notifications are made to the state/territory health authorities under the provisions of the public health legislation in the respective jurisdictions. Computerised, de-identified unit records of notifications are supplied to the Australian Government Department of Health on a daily basis for collation, analysis and publication on the NNDSS website, and in the quarterly journal *Communicable Diseases Intelligence*.

Notification data provided include a unique record reference number, state or territory identifier, disease code, date of onset, date of diagnosis to the relevant health authority, sex, age, Aboriginal and Torres Strait Islander status and postcode of residence.

'Diagnosis date' was used to define the case specific occurrence used for rate calculation. This date represents either the onset date or, where the date of onset was not known, the earliest of the specimen collection date, the notification date, and the notification receipt date. As considerable time may have elapsed between the onset and diagnosis dates for syphilis (unspecified), hepatitis B (unspecified) and hepatitis C (unspecified), the earliest of: the specimen collection date, health professional notification date or the public health unit notification receipt date was used

Viral hepatitis

New notifications of viral hepatitis (hepatitis B and C) are notifiable conditions in all state/territory health jurisdictions in Australia. Cases were notified by the diagnosing laboratory, medical practitioner, hospital or a combination of these sources, through state/territory health authorities, to the National Notifiable Diseases Surveillance System (NNDSS). Age-standardised population rates of diagnosis of viral hepatitis were calculated for each state/territory using yearly population estimates provided by the ABS as described above.

Hepatitis B infection and hepatitis C infection were classified as newly acquired if evidence was available of acquisition in the 24 months prior to diagnosis. Newly acquired hepatitis B notification data were available from all health jurisdictions. Newly acquired hepatitis C notifications were available from all health jurisdictions, and in Queensland from 2010 onwards.

Sexually transmissible infections

Diagnoses of sexually transmissible infections were notified by state/territory health authorities to the National Notifiable Disease Surveillance System (NNDSS), maintained by the Australian Government Department of Health. In most health jurisdictions, diagnoses of sexually transmissible infections were notified by the diagnosing laboratory, the medical practitioner, hospital or a combination of these sources (Table M1).

	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Diagnosis								
Gonorrhoea	Doctor Laboratory Hospital	Laboratory	Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory	Doctor Laboratory
Infectious syphilis	Doctor Laboratory Hospital	Doctor Laboratory Hospital	Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory	Doctor Laboratory
Chlamydia	Doctor Laboratory Hospital	Laboratory	Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory	Laboratory	Laboratory	Doctor Laboratory

	Not notifiable		Doctor Laboratory	Doctor Laboratory Hospital	Doctor Laboratory		Doctor Laboratory	Doctor Laboratory
Donovanosis		Laboratory				Laboratory		

Table M1 Source of notification of sexually transmissible infections to the National Notifiable Disease Surveillance System, by state/territory

Age-standardised rates of notification for chlamydia, gonorrhoea and infectious syphilis were calculated using analogous procedures to those described above for HIV notifications (see HIV notifications methodology).

2. Diagnosis and care cascade

HIV diagnosis and care cascade

The approach taken to develop the HIV diagnosis and care cascade was informed by recommendations from a national stakeholder reference group (see Acknowledgments for members of the reference group).

Estimating the number of people with diagnosed HIV

To estimate the number of people living with diagnosed HIV, we performed a simple calculation using annual notifications, estimated mortality rates and emigration rates.

Annual HIV notifications data was provided by Australia's National HIV registry. Notifications are incomplete for several key variables used in the cascade calculations. Using the variables year of diagnosis, jurisdiction, sex, age at diagnosis, country of birth, exposure category, and region of diagnosis (SA4 level) we applied statistical imputation to produce 10 sets of complete notifications for the cascade calculations. A predictive mean matching imputation method was applied using the R package MICE (3). We applied this method to each jurisdiction separately to prevent mismatching of location of diagnosis variables. The calculation method described in the following paragraphs was then applied to each of the 10 imputed sets with the annual mean and range calculated from the sets to produce the final annual estimates for the number of people living with diagnosed HIV.

Due to incomplete or inaccurate recording of name codes the registry contains multiple reports for some individuals especially during the early stages of the epidemic. To estimate the number of duplicates we applied a statistical technique which has previously been applied to Australia's National HIV Registry (4). This calculation estimated the number of duplicate notifications annually up to 2016, resulting in 8.1% duplicate notifications by 2016 with most duplicates occurring early in the epidemic. From 2017, we assumed all notifications were unique.

We combined two estimates for the number of deaths among people diagnosed with HIV. To estimate the number of deaths up to 2003 we used a linkage study conducted between Australia's National Death Index and the National HIV Registry for cases to the end of 2003 (4). This study calculated HIV- and AIDS-related deaths and calculated standardised mortality

ratios for people with HIV during different eras of antiretroviral therapy. It identified 8,519 deaths among people diagnosed with HIV or AIDS to the end of 2003. Of these deaths, 6,900 were recorded in the National HIV Registry, meaning that 19% of all deaths were missing from the registry. Due to the backdating of deaths in the National HIV Registry after 2003, we inflated the number of recorded deaths in the registry until the end of 2003 by 19% (inflating the 7,102 deaths recorded to the end of 2003 to 8,768 deaths overall) and estimated the overall average mortality rate for diagnosed people living with HIV prior to 2003. After 2003 we calculated crude annual mortality rates and their 95% confidence intervals using data from the Australian HIV Observational Database (AHOD)(5). Between 2004 and 2021, similar annual mortality rates were estimated for the AHOD cohort regardless of whether people were retained, lost, or returned to follow-up. We applied the annual mortality rates from AHOD for the period 2003-2021 in our calculations for the number of diagnosed people living with HIV.

We also considered the impact of migration. Some people living with HIV in Australia will have previously received an HIV diagnosis in another country. These people only enter the national HIV registry and become officially notified when they receive a confirmatory diagnosis in Australia. Confirmation of HIV status is routinely performed at point of entry into clinical care and the notification record includes information on previous diagnosis overseas—which is primarily obtained through self-report. We assumed people living with HIV in Australia who have been previously diagnosed overseas are aware of their HIV status and hence part of the diagnosed population (even if they are not in care or have not been notified within Australia). People who enter Australia with undiagnosed HIV are part of the undiagnosed population. We estimated an emigration rate for diagnosed people living with HIV using data from the ABS and follow-up data of people recently diagnosed in New South Wales (6). NSW Health has followed up all people diagnosed with HIV during 2013-2020 and reported up to 5% of people move overseas soon after their diagnosis with most of these movements overseas occurring in people born overseas. Assuming this post diagnosis migration has been constant over time we reduced the number of PLDHIV by a weighted percentage using the cumulative proportion of notifications in Australian born versus overseas born people and the associated percentage from the NSW data.

As there are likely to be people living with HIV who leave temporarily and then return to Australia (some of whom may still receive care and treatment while overseas), we used data on the annual number of people in the overall population who permanently leave Australia (provided by the ABS for 1976–2016 (7) and the estimated resident population from the ABS (8) to calculate an overall annual emigration rate. Since 1981 this rate has risen from around 0.1% to 0.4% of the resident population leaving Australia permanently. From June 2017, permanent removals are no longer recorded by the ABS due to the removal of the green card from customs processes upon leaving Australia. To estimate the permanent removal rate, we used Net Overseas Migration (NOM) emigration data from the ABS (7). A comparison between NOM emigration and permanent removal numbers for the years 2004-2016 shows a relatively stable ratio which we applied to the NOM emigration for the years 2017-2021 to estimate permanent removals and the migration rate for PLDHIV for this period.

The permanent rate of departure is the lower bound of the overall rate at which Australian residents leave Australia for longer than 12 months. However, diagnosed people living with

HIV require ongoing care and treatment which is not subsidised in many countries, so we assume the permanent rate of departure is a reasonable estimate for the population of diagnosed people living with HIV. We adjusted this rate to reflect the different emigration rates for males and females older than 15 years in the general population. Overall, we assumed a range in the annual emigration rate between zero and double the estimated rate of permanent departure.

Our overall estimate of the number of people diagnosed with HIV in Australia each year is obtained by adding the number of unique notifications to the previous year's estimate and subtracting the number of deaths and emigrants using the mortality and migration rates applied to the previous year's estimate.

Subpopulation estimates

We also provided HIV estimates for the number of people living with HIV and the number of people diagnosed for each exposure risk category, region of birth, males, females, and Aboriginal and Torres Strait Islander status.

For each subpopulation, we estimated the proportion of duplicates separately. We also adjusted the death and emigration rates to reflect the differences in these rates in males and females in the general population. Mortality and migration rates were adjusted for the Indigenous and non-Indigenous Australian-born population to reflect the higher overall mortality in Aboriginal and Torres Strait Islanders as reported by the ABS (9) . We also assumed no Indigenous people living with diagnosed HIV move overseas. Finally, we separately estimated the emigration rate for males and females and by region of birth to reflect the large differences in emigration. We did this using net overseas migration departures for 2004–2015 (which were provided to the Kirby Institute by the ABS by age, sex, jurisdiction and age (10) calculating the relative difference between the subpopulation and the overall net overseas migration rates and applying this to the overall migration rate for diagnosed people living with HIV. For years before 2004 and after 2015 we estimated the relative emigration rate using linear regression.

Similarly, we assumed a higher post-diagnosis emigration rate for overseas-born people based on the NSW six-monthly follow-up data for 2013–2020 (which was 0.702% for Australian-born people and 8.57% for overseas-born people).

Estimating the number of people living with HIV

To estimate the overall number of people living with HIV, both diagnosed and undiagnosed, we used the European Centre for Disease Prevention and Control (ECDC) HIV Modelling Tool (version 1.3.0) to estimate the proportion of people with HIV who are undiagnosed (11).

The ECDC tool is a multi-state back-calculation model using notifications data and estimates for the rate of CD4+ cell count decline to fit notification rates over time, producing estimates for HIV incidence, time between infection and diagnosis, and the undiagnosed population by CD4+ cell count strata, using surveillance data on new HIV and AIDS notifications. To run the

model, notifications data is split by CD4+ cell count strata, whether the patient had AIDS at the time of diagnosis, and optional risk of exposure categories. Diagnosis rates can be adjusted to reflect changes over time and whether people with HIV are more likely to be diagnosed at later stages of infection. For the cascade estimates we divided all annual notifications into those attributed to male-to-male sex, heterosexual contact, injecting drug use, and 'other' risk exposures. To estimate the number and proportion undiagnosed we used the ECDC tool with previously diagnosed overseas excluded from diagnoses. As stated previously, we assumed people living with HIV in Australia who have been previously diagnosed overseas are aware of their HIV status and hence part of the diagnosed population (ever since their arrival in Australia).

We ran the ECDC tool for each exposure risk category as well as overall (with all groups combined) and excluding male-to-male sex. Separate models were run for Indigenous and non-Indigenous Australian-born populations, males and females, and for each region of birth. The tool's diagnosis rate options were adjusted to best fit the data on CD4+ cell count at diagnosis. For these estimates we produced a 95% CI using 100 bootstrapped fits produced by the ECDC tool.

For validation we compared the model estimates for undiagnosed gay and bisexual men with empirical data from the COUNT study (12). This study was conducted alongside routine behavioural surveillance surveys in which gay and homosexually active men from Sydney, Melbourne, Canberra and Perth were recruited from a range of gay community sites in 2013–2014. In this study 8.9% of participants were previously undiagnosed with HIV (95% CI 5.8–13.5%). This is closely matched by the ECDC tool estimated percentage undiagnosed in 2014 for gay and bisexual men of 11.3% (range: 10.7–11.9%).

The overall prevalence of HIV in Australia and for each subpopulation was then estimated by inflating the calculated number of people living with diagnosed infection by the estimated level of undiagnosed infection. Because the ECDC model is run and fitted separately for each subpopulation, the sum of the number undiagnosed for each subpopulation can be different from the overall population estimate.

Estimating the number retained in care

To estimate the number of people living with HIV retained in care we used available clinical data on the proportion of HIV-positive people attending a clinic who receive an annual CD4+ or viral load test. An issue with clinic data is that people can appear to be lost to follow-up, and hence not in care, when they have just transferred to another clinic. A study conducted in during 2011-2013 in a network of the six main HIV clinical care sites in Victoria estimated 91.4-98.8% of HIV-positive patents were retained in care (13). A follow-up study was conducted during 2016-2017 and it obtained results agreeing with the earlier study with 96% of people retained in care (14). We assume these results are broadly representative of HIV-positive patients in Australia and assume a best estimate of 96% of people living with HIV retained in care with a range equal to 93% to 99%.

Estimating antiretroviral treatment coverage

We estimated the number of people receiving antiretroviral therapy using a 100% longitudinal dataset of Pharmaceutical Benefits Scheme (PBS) patient-level script claims data provided by the Australian Department of Health. It includes all PBS-listed drugs with HIV indications. A challenge with the PBS data is that five drugs licenced for treating HIV are also used for Hepatitis B, HIV PrEP, and HIV post-exposure prophylaxis (nPEP) which need to be separated from HIV treatment. For our estimate we excluded all patients who only have TDF/FTC, TDF or 3TC. In addition, we excluded patients who are only prescribed DOL or RAL with one of TDF/FTC, TDF or 3TC less than two times per year. Our resulting estimate is the number of unique patients in the remaining PBS data who filled in at least one script for HIV treatment in the 12 months prior to the end of December each year. Given the uncertainty in separating out the number of people using HIV drugs for HIV treatment we estimated a lower bound for the number on ART by also excluding those who had two scripts for HIV drugs < 60 days apart. We adjusted the lower estimate for the number living, diagnosed, and retained in care to be at least the lower range for the number receiving treatment.

To the PBS number we added an estimate for the number of HIV-positive temporary residents taking ART—as temporary residents are ineligible for Medicare and hence are not counted in the in the PBS dataset. A recent report by National Association of People with HIV Australia (NAPWHA) and the Kirby Institute estimated there were 1203 (assumed range: 1146-1260) HIV-positive temporary residents receiving ART in Australia through compassionate access schemes during 2020. We did not have an updated estimate for 2021 so we used the 2020 estimate. We split this estimate into males and females on therapy using the proportions of males and females from the Australian HIV Observational Database Temporary Residents Access Study (ATRAS) (15).

Estimating levels of virological suppression

We define virological suppression as less than 200 viral copies per ml. The proportion of people on antiretroviral therapy with viral suppression is taken to be the proportion of people recorded in the Australian HIV Observational Database (AHOD) who had less than 200 viral copies per ml at their last viral load test. Uncertainty bounds were estimated by calculating the 95% confidence interval for this proportion. We estimated the number of people living with HIV on antiretroviral therapy with viral suppression by multiplying this proportion and range by the estimated number of people receiving antiretroviral therapy.

3. Hepatitis C diagnosis and care cascade

This cascade was developed collaboratively between the Kirby Institute and the Center for Disease Analysis. The approach taken to develop the hepatitis C diagnosis and care cascade was informed by recommendations from an Australian stakeholder reference group (see Acknowledgments for members of the reference group).

Number of people living with hepatitis C

This estimate was derived using a difference equation mathematical model, as described below:

- To determine hepatitis C incidence as a result of injecting drug use, the model used estimates of the number of people who had injected drugs in Australia over the last three decades, the pattern of injecting drug use and estimates of hepatitis C incidence among people who inject drugs derived from cohort studies.
- The relative change in incidence since 2005 was informed by hepatitis C notifications in people aged 15–29 years, reflecting the population most at risk of acquiring infection. As the primary route of transmission is injecting drug use, a practice that primarily starts in late adolescence or early adulthood, trends in the rate of notifications in those aged under 30 years can be interpreted as a surrogate for the incidence of hepatitis C.
- The estimates of hepatitis C incidence due to injecting drug use were then adjusted in accordance with epidemiological data to allow for hepatitis C infections through other transmission routes, including infection in migrants.
- The model also includes the effects of treatment with associated sustained virological response rates reflecting treatment regimen, genotype and access to direct-acting antivirals through compassionate access and clinical trials in 2014–2015 and through generic supply in 2015. From 2016 the sustained response rates were based on antiviral treatment from clinical studies and reflected the disease stage at initiation.
- Estimates of the number of people experiencing long-term sequelae of chronic hepatitis C were then obtained from the estimated pattern of hepatitis C incidence using rates of progression derived from cohort studies. People cured with late stages of disease had a lower progression rate to both decompensated cirrhosis and hepatocellular carcinoma.

To produce the model estimates for the number of people living with HCV and the resulting time trends, we first produced a specific estimate for the year 2015 using cumulative notifications and spontaneous clearance, mortality, and migration rate estimates (16). The estimate of the number of people living with hepatitis C in 2015 is adjusted each year in accordance with updated data. In earlier reports, we assumed there were no duplicate hepatitis C notifications. However, linkage studies being conducted in NSW and Victoria estimate that around 7 to 11% of notifications are duplicates. Given this evidence, we have assumed 9% (range: 7-11%) of all notifications are duplicates nationally (personal communication, Dr Maryam Alavi).

The model also updated morbidity and mortality due to hepatitis C infections. Previously we compared liver-related mortality from the model with the NSW linkage data and found that the model estimated mortality was too low. To improve our estimates of liver-related mortality in the model, we incorporated the higher risk of developing cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and liver-related death among the population with excessive alcohol consumption (defined as > 50g per day). For example, people living with HCV who have excessive alcohol consumption are 2.3 (95% CI 1.7 – 3.3) times more likely to have cirrhosis (17,18). We used available progression rates for those with and without excessive alcohol consumption from published literature and the percentage of HCV infected people with decompensated cirrhosis or hepatocellular carcinoma that have excess alcohol consumption, based on hospital admissions for alcohol use disorder from the NSW linkage study, which increased from 14% to 51% over 2001–2018. We then adjusted the percentage of people with excessive alcohol consumption who do not have decompensated cirrhosis or hepatocellular carcinoma to match the number of liver-related deaths from the NSW linkage study. This resulted in an estimate of 19% which aligns with available data from the NSW linkage and ETHOS studies (19). We assumed the same level of excessive alcohol consumption for Australia overall and in each state and territory.

Further information about modelling methods can be obtained by contacting the Surveillance, Evaluation and Research Program, the Kirby Institute, UNSW.

Number of people diagnosed and living with chronic hepatitis C

This estimate was derived from totalling all hepatitis C notifications from 1991 to 2021 and adjusting for duplicates, spontaneous hepatitis C clearance, mortality, hepatitis C cure through treatment, and overseas migration, with adjustments as follows:

- The percentage of all notifications that are duplicates nationally was estimated at 9% (range: 7-11%).
- The proportion with spontaneous hepatitis C clearance was estimated at 36% (20).
- The annual proportion with mortality among people with a hepatitis C notification in NSW (1993–2020) was extrapolated to the total number of hepatitis C notifications in Australia.
- The estimated number of individuals cured of hepatitis was deducted from the number of total hepatitis C notifications.
- The level of overseas migration was assumed to be small, given the characteristics of the infected population, and given by the annual number of permanent departures for the general population divided by the estimated resident population as estimated by the ABS (7).

Number of people who have received a confirmatory RNA test

To estimate the number of people previously diagnosed with hepatitis C (either antibody-positive or by RNA test) who have received an RNA test (to confirm viraemic infection) we used published data from the ETHOS ENGAGE study (19). Of all people who responded in the survey in 2018-2019 (>1,000 recruited), 75% self-reported HCV confirmatory testing among HCV antibody diagnosed. We assumed this estimate is broadly representative of the chronically infected population. We multiplied this percentage by the number diagnosed and living with chronic hepatitis C to estimate the number diagnosed who have been RNA tested. The range is given by the estimate multiplied by the corresponding lower and upper value for diagnosed with hepatitis C.

Number of people who have ever received hepatitis C treatment

To estimate the numbers of people treated for hepatitis C we totalled the number of prescriptions dispensed to public patients, reported by the Pharmaceutical Benefits Scheme (PBS), since 1997.

- Since 2019, data from a 100% longitudinal PBS dataset provided by the Australian Department of Health were used.
- For estimates in 2013–2018, data from longitudinal tracking of a 10% random sample of PBS prescriptions were used.
- For 2014 and 2015, we included estimates for the number of patients receiving direct-acting antiviral therapies through clinical trials, patient access programs and generic drugs.
- For 2016–2018, we assumed all treated patients received direct-acting antivirals following their listing on the PBS. We estimated the number of people receiving treatment in 2016-2018 using the 10% sample of PBS patient-level script claims data provided by the company Prospection. Our estimate is the number of unique patients in the PBS data who filled in at least one script in the 12 months prior to the end of December 2018 multiplied by 10. We assumed that 10% of the Australian population were sampled to estimate the uncertainty range as a 95% confidence interval (which equates to approximately 5%).
- The numbers of interferon-based hepatitis C treatments dispensed were adjusted for multiple counting considering the duration of treatment for each regimen and the treatment compliance rate.
- For genotype-specific regimens, a distribution of 50% genotype 1 and 50% genotypes 2 or 3 was assumed.
- The total number treated was adjusted for annual mortality and overseas migration (using the same overseas migration rate as for the diagnosed stage).
- People who were cured of chronic hepatitis C were assumed to have reduced rates of disease progression to decompensated cirrhosis (90% reduction (21,22)) and hepatocellular carcinoma (77% reduction (23)). and hepatocellular carcinoma (77% reduction(23)).
- The cured population with decompensated cirrhosis was assumed to have a 50% reduction in liver-related death rate.

- The general population mortality rate was used for those who were successfully cured. The hepatitis C mortality rate from people with a hepatitis C notification in New South Wales was used for patients who did not achieve sustained virological response.

We estimated the proportion of direct-acting antiviral treatments initiated by patients in each fibrosis stage using REACH-C study data and PBS data. The number of people on treatment with cirrhosis, decompensated cirrhosis and hepatocellular carcinoma was estimated from data on planned duration.

4. Hepatitis B diagnosis and care cascade

Cascade estimates were developed by the WHO Collaborating Centre for Viral Hepatitis at the Doherty Institute. The approach taken to develop the hepatitis B diagnosis and care cascade was informed by recommendations from a national stakeholder reference group. This included representatives from: The Kirby Institute; ASHM; Hepatitis Australia; NSW Ministry of Health; Queensland Department of Health; Department of Health and Human Services, Tasmanian Government; Department of Health and Human Services Victoria; WA Health; Australian Government Department of Health; South Australia Health; WHO Collaborating Centre for Viral Hepatitis, The Doherty Institute; Centre for Social Research in Health; Australian Injecting and Illicit Drug Users League; Burnet Institute; Australasian Sexual Health Alliance; Australian Liver Association; Scarlet Alliance.

Number of people living with hepatitis B

The estimate of the number of people living with hepatitis B virus infection and attributable burden of disease in Australia was derived using a deterministic compartmental mathematical model of hepatitis B virus infection in the Australian population from 1951 to 2050. The model was parameterised using a wide range of data sources including the Australian Bureau of Statistics (ABS), existing mathematical models, surveillance notifications, epidemiological research and clinical studies. Important factors such as migration, attributable and all-cause mortality, the ageing of the population, the variable natural history of chronic hepatitis B infection, the impact of treatment and vaccination were all incorporated. The changing prevalence over time, due predominately to increases in infant vaccination in migration source countries, was accounted for in this updated model, with prevalence estimates across different time periods applied to migration data according to age group and year of arrival. Model construction included sensitivity analyses around critical parameters such as the force of infection (FoI) and migration estimates.

Diagnosis

The proportion of people living with chronic hepatitis B who have been diagnosed was estimated using model-derived estimates of the total number of people who have ever had chronic hepatitis B in Australia as the denominator and the cumulative number of notifications of hepatitis B from 1971 to 2020 as the numerator. Mortality is not included in

this aspect of the analysis and therefore the proportion derived represents those ever having lived with chronic hepatitis B that have ever been diagnosed.

Monitoring

The number of people who received monitoring each year for chronic hepatitis B in 2016–2021 was determined using Department of Human Services data regarding rebates for an annual hepatitis B viral load test, which is recommended for all people living with chronic hepatitis B. This item is specific to people living with chronic hepatitis B who are not receiving treatment and is limited to one test per year. The number of viral load tests was adjusted to account for the use of the on-treatment Medicare Benefit Schedule item in those not on treatment for billing purposes.

Treatment

The number of people receiving treatment for chronic hepatitis B in 2016–2020 was derived using pharmaceutical dispensing data from the Department of Human Services Australia regarding the number of individuals prescribed treatment indicated for hepatitis B virus infection (adefovir, entecavir, lamivudine, tenofovir and pegylated interferon).

Detailed methodology and source references can be found in the published paper which described the derivation of these estimates (24) and in the methods of the National Hepatitis B Mapping Project Reports (http://www.ashm.org.au/HBV/more-about/hepatitis-b-mapping-project).

A combined estimate of people in care for chronic hepatitis B was derived by combining the number who received monitoring while not on treatment and those on treatment. Each of these estimates is expressed as a proportion of the total number living with chronic hepatitis B as derived using the prevalence methodology outlined above.

Hepatitis B prevalence according to population

The proportion of people living with chronic hepatitis B in each population group and the relative prevalence in each was determined using the Census method, attributing prevalence of chronic hepatitis B by country of birth, Aboriginal and Torres Strait Islander status, and other risk status applied to Australian population data provided in the 2016 Census.

The estimated prevalence of chronic hepatitis B according to country of birth was derived from combining multiple published sources into an average point estimate. The estimates used comprised Australian antenatal seroprevalence studies(25–27), the estimates from which were then adjusted upwards to account for the disparity in prevalence between men and women(28); a study of hepatitis B prevalence in migrants to the United States(29); and the most recent global seroprevalence study conducted as part of the Global Burden of Disease Project(30). The Australian prevalence figure was obtained from local modelled estimates as described above. Detailed methodology and sources, including individual

seroprevalence estimates and population figures, can be obtained from the published paper(24).

5. The chlamydia diagnosis and care cascade

Chlamydia notifications

We obtained the number of chlamydia notifications for 15-29-year-old males and females in Australia directly from the National Notifiable Diseases Surveillance System (NNDSS).

Estimating new infections

New Chlamydia infections were estimated using the modelling approach described elsewhere (31). This method uses a Bayesian statistical approach to calibrate model parameters to the notifications data from NNDSS, the number of tests for chlamydia obtained by Medicare (item numbers 69316, 69317, and 69319), and annual population estimates for each sex and age group published by the Australian Bureau of Statistics (ABS) over 2001-2020. Model outcomes were validated through comparison against chlamydia prevalence among 16-29-year-olds measured in 2011 by the Australian Chlamydia Control Effectiveness Pilot (ACCEPt).

The model outputs 95% credible intervals for the annual number of incident chlamydia cases in 15-19-year, 20-24-year, and 25-29-year-old males and females. We summed the incident chlamydia cases for each age group to estimate the number of new infections. The range corresponds to the lower and upper bound of the credible intervals with the midpoint corresponding to our best estimate.

Estimating treatment and re-testing

We estimated chlamydia treatment following diagnosis and retesting after treatment using multiple sources describing chlamydia infection and care across urban, regional, and remote areas and multiple service contexts.

From the NNDSS notifications data we calculated the percentage notifications in 15-29-year-olds occurring in urban, regional, and remote areas. Based on a previous published study in 2013, 11% of these notifications occurred in sexual health clinics (32). We divided the remainder of notifications into those made in general practice (80%) and other contexts (9%) using data from the second Australian Study of Health and Relationships data published in 2014 (33).

Treatment following diagnosis

Based on data from NSW sexual health clinics almost all people diagnosed with chlamydia in urban and regional areas were treated (ranging from 99-100% of those diagnosed) in 2013 (34). In NSW remote areas the percentage diagnosed is a little lower at 96% (34). A published study in 2014 produced a lower estimate of 85% for remotes areas in the Northern Territory (35). Data from Western Australian general practices suggest a much lower rate of treatment with 92% receiving a script for treatment after diagnosis (36). Based on this data we assumed 92% of patients attending urban and regional general practice clinics receive treatment with 99% of patients in other clinical settings receiving treatment.

In remote areas, we assumed 90% of those diagnosed were treated. Taking a weighted average by multiplying the notifications breakdown across regions by the estimated percentage treated, we estimated the percentage of people diagnosed with chlamydia each year. We assumed a range from 90% (corresponding to the percentage treated in remote areas) to 100%. Assuming the same treatment proportion and range for males and females and multiplying by the number of notifications we estimated the number of 15-29-year-old males and females who received treatment after diagnosis.

Re-testing after treatment

From the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of STIs and BBVs (ACCESS) and the ACCEPT study, we obtained the percentage of 15-29-year-olds diagnosed with chlamydia nationally who were re-tested for chlamydia within 1.5 to 6 months after treatment in sexual health clinics and general practice, respectively, in urban, regional and remote settings. We regional and remote GP clinics had the same re-testing rate due to limited data for remote areas. Taking a weighted average by multiplying the notifications breakdown across regions by the notification breakdown across contexts, we estimated the percentage re-tested after treatment. We assumed a range corresponding to the range in percentage re-tested across all estimates.. Applying these re-testing percentages and range for males and females and multiplying by the number of notifications we estimated the number of 15-29-year-old males and females who re-tested for chlamydia after treatment.

6. The gonorrhoea diagnosis and care cascade

Estimating new infections

The number of new gonorrhoea infections was calculated by applying an incidence estimate from ACCESS sexual health clinic data weighted by HIV-positive status to a population estimate of sexually active gay and bisexual men in Australia. The population estimate was derived by multiplying the ABS estimate for males aged 16-69 years to estimates of the proportion of gay and bisexual identified men (3.2%) with same-sex experience in the last

12 months (68%) taken from the second Australian Study of Health and Relationships (37) with an assumed range of +/- 10%.

Notifications

We obtained the number of gonorrhoea notifications for gay and bisexual men in Australia by first calculating the proportion of annual notifications in males in major cities and other areas of residence attributable to male-to-male sex, in jurisdictions (Australian Capital Territory, New South Wales, Victoria, Western Australia, South Australia, Tasmania) which collect enhanced data. These proportions were then applied to gonorrhoea notifications among men in major cities and other areas of residence in jurisdictions which do not collect enhanced data (Queensland and Northern Territory) to derive a national estimate of notifications among gay and bisexual men.

Treatment and re-testing after treatment

We obtained the percentage of all gay and bisexual men diagnosed with gonorrhoea who received treatment and were retested within 1.5 to 6 months after treatment using data from sexual health clinics from the ACCESS network. These percentages were then applied to the number of notifications to estimate the overall number who received treatment and who were retested.

7. The gonorrhoea and infectious syphilis diagnosis and care cascade

The gonorrhoea and syphilis cascade estimates for gay and bisexual men in Australia are calculated separately using the same methods and data sources.

Estimating new infections

The number of new gonorrhoea and syphilis infections was calculated by applying an incidence estimate from ACCESS sexual health clinic data weighted by HIV-positive status to a population estimate of sexually active gay and bisexual men in Australia (38). For gonorrhoea, incidence includes an infection at any anatomical site. The population estimate was derived by multiplying the ABS estimate for males aged 16-69 years and estimates of the proportion of men who are gay and bisexual identified men (3.56%) (39) and then multiplying by a weighted average for the proportion of gay and bisexual men with same-sex experience in the last 12 months (71.6%) taken from the second Australian Study of Health and Relationships with an assumed range of +/- 10%.

Notifications

We obtained the number of infectious syphilis and gonorrhoea notifications for gay and bisexual men in Australia by first calculating the proportion of 2018 notifications in males in major cities and other areas of residence attributable to male-to-male sex, in states and territories which collect enhanced data (Australian Capital Territory, New South Wales, Victoria, Western Australia, South Australia, Tasmania). These proportions were then applied to gonorrhoea notifications among men in major cities and other areas of residence in states and territories which do not collect enhanced data (Queensland and Northern Territory) to derive a national estimate of notifications among gay and bisexual men in 2017.

Treatment and re-testing after treatment

We obtained the percentage of all gay and bisexual men diagnosed with gonorrhoea or syphilis who received treatment and were retested within 1.5 to 6 months after treatment using data from sexual health clinics from the ACCESS network. These percentages were then applied to the number of notifications to estimate the overall number who received treatment and who were retested.

8. Notification rates

Age-standardised notification rates were calculated using population denominators obtained from the Australian Bureau of Statistics (ABS) estimated residential population by state, year, gender, and age (ABS series 3101051-3101058) and were standardised using ABS Standard Population data (31010DO003_200106 Standard Population for Use in Age-

Standardisation). Population denominators by country/region of birth were based on the Standard Australian Classification of Countries (SACC) (ABS series 1269.0). Population denominators by year, sex, age and state for Aboriginal and Torres Strait Islander people were obtained from ABS catalogue 32380 estimated and projected population. ABS regional population denominators by age, sex, Aboriginal and Torres Strait Islander status, and state were obtained from the ABS and from the 2016 Census-based Aboriginal and Torres Strait Islander Population Projections by Age, Sex and Remoteness Area (2011–2026). Remoteness area categories for these data were 'metropolitan', 'regional' and 'remote' and based on the Australian Statistical Geography Standard (ASGS) Remoteness Structure. Proportion of estimated residential population by age, sex, Aboriginal and Torres Strait Islander status, country of birth, state and remoteness region were ascertained from ABS 2011 & 2016 Census data. Counts of notifications missing Aboriginal and Torres Strait Islander status were added to the numerator in the notification rate calculations for non-Indigenous people. Rates of HIV in Aboriginal and Torres Strait Islander populations were also compared with Australian-born non-Indigenous populations. This allows for a focus on HIV infection endemic to Australia and without direct fluctuation in trend according to changes in immigration patterns. All notification rate calculations exclude HIV cases with a first ever diagnosis outside Australia unless otherwise stated.

9. The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS)

Briefly, ACCESS is a national surveillance network monitoring blood borne viruses and sexually transmissible infections using routinely collected de-identified demographic, testing, diagnosis and treatment data from health services and laboratories across Australia to monitor the sexual health of high-risk population groups including gay and bisexual men, people who inject drugs, Aboriginal and Torres Strait Islander people, sex workers and young people. ACCESS has been described in more detail elsewhere (31). The project is managed collaboratively between the Kirby Institute, the Burnet Institute and the National Reference Laboratory. In total, ACCESS collects data from over 110 health services and laboratories.

10. The Australian Gonococcal Surveillance Program (AGSP)

The AGSP is a collaborative project involving gonococcal reference laboratories in each state/territory and is coordinated by the NSW Gonococcal Reference Laboratory at the Prince of Wales Hospital, Sydney. The primary objective of the program is to monitor antibiotic susceptibility of isolates of *Neisseria gonorrhoeae* to assist in the effective treatment of gonorrhoea. Information on sex and site of isolation of gonococcal strains was also collected (AGSP 2014). The proportion of gonococcal referred isolates with decreased susceptibility to ceftriaxone (minimum inhibitory concentration or MIC 0.06–0.125 mg/L) was obtained from the AGSP.

11. The Australian HIV Observational Database (AHOD)

The Australian HIV Observational Database (AHOD) is a collaborative study that records observational data on the natural history of HIV and its treatment. The primary objective of AHOD is to monitor the pattern of antiretroviral treatment use by demographic factors and markers of HIV stage. Other objectives are to monitor how often people with HIV change antiretroviral treatments and the reasons for treatment change. Methodology associated with AHOD has been described in detail elsewhere (5).

Information is collected from hospitals, general practitioner sites and sexual health clinics throughout Australia. Participating sites contribute data biannually from established computerised patient management systems. Core variables from these patient management systems are transferred electronically to the Kirby Institute, where the data are collated and analysed. By March 2021, 30 participating clinical sites had been enrolled into AHOD, including data on over 4557 people.

AHOD data were used for the result of the last viral load test among HIV-positive patients.

12. The Australian Needle Syringe Program Survey (ANSPS)

The ANSPS is conducted annually at needle syringe programs (NSPs) over a one- to two-week period and provides serial point prevalence estimates of HIV and hepatitis C and monitors injecting behaviour among people who inject drugs. All clients attending NSPs during survey implementation were asked to complete a brief self−administered questionnaire and provide a finger prick blood spot sample for HIV and hepatitis C antibody testing and hepatitis C RNA testing. Between 2011-2020, the number of participating NSP ranged from 54 (in 2019) to 38 (in 2020), the number of ANSPS participants ranged from 2742 (in 2018) to 1324 (in 2020) and the response rate ranged from 48% (in 2014) to 35% (In 2020). In 2020, COVID-19 related restrictions meant the ANSPS was not conducted in VIC and overall (all other jurisdictions combined), recruitment was approximately 30% less than previous years. The ANSPS methodology has been described in detail elsewhere (40).

13. The Australian and New Zealand Liver and Intestinal Transplant Registry (ANZLITR)

ANZLITR is a network of liver transplant centres in Australia and New Zealand which has collected information on the characteristics of people undergoing liver and intestinal transplantation. People undergoing liver transplantation have been routinely tested for hepatitis B and hepatitis C since antibody testing became available in 1990. Information was sought on the primary and secondary causes of liver disease including the results of tests for hepatitis B and hepatitis C. The information was forwarded to the Liver Transplant Registry located at Austin Hospital in Melbourne. The number of liver transplants by primary cause of liver disease and hepatitis status where the primary diagnosis was hepatocellular carcinoma was obtained from the ANZLITR.

14. The Gay Community Periodic Surveys (GCPS)

The Gay Community Periodic Surveys are conducted annually using time and location convenience samples of men at gay community venues and events in capital cities (Sydney, Melbourne, Brisbane, Adelaide, Perth and Canberra). The report is prepared by the Centre for Social Research in Health, UNSW Sydney. The methodology associated with the Gay Community Periodic Surveys has been described in detail elsewhere (41).

15. Medicare

Medicare is delivered by the Australian Government Department of Human Services and pays rebates on specified services and procedures. Publicly available Medicare online data on number of tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* as identified by item numbers 69316, 69317 and 69319 were obtained by sex, age, state, and quarter.

16. National Centre for Immunisation Research and Surveillance (NCIRS)

The primary function of NCIRS is to perform research aimed at reducing the incidence of vaccine-preventable diseases and improving vaccine uptake, in children and adults, including surveillance. Hepatitis B vaccine and HPV vaccine coverage were estimated using data from the NCIRS surveillance of immunisation coverage and the Australian Immunisation Register. For HPV vaccine coverage estimates prior to 2019, estimates were generated using data from the HPV Register.

17. Pharmaceutical Benefits Scheme

Deidentified linked PBS data for all dispensed subsidised prescriptions were obtained from the Australian Government department of Health. Each record contains an anonymised patient code (linking prescriptions in the same patient) as well as patient age, sex, and

postal district of residence (postcode), an anonymised prescriber code (linking prescriptions from the same prescriber) as well as prescriber postal district of practice (postcode), medication date-of-supply, quantity dispensed and level of co-payment.

Medical and epidemiological terms

age-standardised rate of infection: The proportion of infected people in a particular population, adjusted mathematically to account for the age structure of the population so that comparisons can be made between populations with different age structures (i.e. with more or fewer younger people).

AIDS: Acquired immunodeficiency syndrome, the spectrum of conditions caused by damage to the immune system in advanced HIV infection.

area of residence: Locations of residence, indicated by postcode, are classified into one of three categories: major cities, inner or outer regional areas, and remote or very remote areas (i.e. areas with relatively unrestricted, partially restricted and restricted access to goods and services).

bacterium: A type of single-celled micro-organism. Some bacteria cause illness in humans, and most can be treated with antibiotics.

chlamydia: A sexually transmissible infection caused by a bacterium (*Chlamydia trachomatis*). The infection causes no symptoms in about 80% of cases. In people with symptoms, the infection causes inflammation of the urethra (the tube through which urine passes out of the body), leading to some pain and penile discharge in men, and to painful urination and bleeding between menstrual periods in women. Complications of chlamydia can be serious for women, including pelvic inflammatory disease, ectopic pregnancy and infertility. Throat and anal infections do not usually cause symptoms. Chlamydia is curable by antibiotics.

congenital: A condition (disease or physical abnormality) present from birth. Congenital conditions may be inherited; or acquired during foetal development or at birth.

diagnosis: A labelling or categorisation of a condition, usually by a doctor or other healthcare professional, on the basis of testing, observable signs and symptoms reported by the patient. 'Newly diagnosed infection' means that a person previously not known to have the infection has been tested and now found to have the infection.

deoxyribonucleic acid (DNA): is an acid in the chromosomes in the centre of the cells of living things. DNA determines the particular structure and functions of every cell and is responsible for characteristics being passed on from parents to their children.

donovanosis: A sexually transmissible infection caused by a bacterium, *Klebsiella granulomatis*. The most common symptom is the presence of one or more painless ulcers or lesions in the genital or anal regions. If not treated, the ulcers or lesions can progress and become complicated by other bacterial infections, ultimately resulting in damage to the affected part of the body. Donovanosis is curable by antibiotics. Donovanosis was once common in central and northern Australia and is now very rare.

endemic: A disease is endemic if it is common in a region or local area, or in a group of people

gonorrhoea: A sexually transmissible infection caused by a bacterium (Neisseria gonorrhoeae). Gonorrhoea has no symptoms in about 80% of women and 50% of men. Symptoms are similar to those of chlamydia, as are the complications.

Most men with urethral gonorrhoea will eventually develop symptoms. Throat and anal infections do not usually cause symptoms. Gonorrhoea can be cured with antibiotics.

hepatitis B virus infection: A viral infection transmissible by blood and sexual contact and from mother to child at birth. Most healthy adults will not have any symptoms and are able to get rid of the virus without any problems. Some adults are unable to get rid of the virus, leading to chronic infection. The focus of this report is chronic hepatitis B infection. 'Newly diagnosed' hepatitis B infection means that a person previously not known to have the infection has been tested and now found to have the infection. 'Newly acquired' infections are those that have been acquired within the past two years.

hepatitis C virus infection: A viral infection transmissible by blood contact as well as from mother to new-born. Some people get rid of the virus, but the majority develop ongoing chronic infection. The focus of this report is chronic hepatitis C infection. 'Newly diagnosed' hepatitis C infection means that a person previously not known to have the infection has been tested and now found to have the infection. 'Newly acquired' infections are those that have been acquired within the past two years.

human immunodeficiency virus (HIV): HIV is transmissible by sexual and blood contact as well as from mother to child. If untreated, HIV can progress to AIDS.

human papillomavirus (HPV) infection: Of over 140 types of HPV that infect humans, about 40 affect the anal and genital area, mostly without causing any disease. This subset of HPV types is sexually transmissible and is occasionally transmitted from mother to child. Two HPV types (6 and 11) cause most genital warts. Two other HPV types (16 and 18) cause most cervical and anal cancers, and an increasing proportion of mouth and throat cancers. Many less common HPV types also occasionally cause cancers. Most people acquire at least one genital HPV infection through their lives, but the great majority clear the infection.

incidence: The rate at which a condition occurs in a population, usually expressed as the number of diagnoses (or pregnancies, injuries etc.) over a period of time during which people are exposed to risk (see person-years). Incidence is an important indicator of new transmissions, reflecting the impact of current prevention programs, whereas prevalence reflects the burden of disease

infection: The condition of having bacteria or viruses multiplying in the body. Many infections cause no symptoms, so the person may be unaware they have an infection unless they are tested.

newly acquired HIV: This means the person has become infected within the past year.

newly diagnosed HIV: This means that a person previously not known to have the virus has been tested and now found to have the virus.

notifiable disease: A disease is notifiable if doctors and/or laboratories are required to report cases to the authorities for disease surveillance, i.e. monitoring of disease at population level.

person-years: A measure of the incidence of a condition (e.g. a disease or pregnancy) over variable time periods. If 100 people are exposed to the risk of an infection for a year, or 50 people are exposed for two years, the number of infections can be reported 'per 100 person-years'.

prevalence: The number of cases of a condition at a single time, usually expressed as a proportion (percentage, or per 100 000 people) of the population. Prevalence decreases if people with the condition die or are cured, and increases as new cases occur.

primary HIV infection (or seroconversion illness): A flu-like illness that occurs soon after infection with HIV.

ribonucleic acid: is a polymeric molecule essential in various biological roles in coding, decoding, regulation, and expression of genes.

symptom: A physical or mental indication of a disease or condition experienced by the patient.

syphilis: An infection caused by the bacterium *Treponema pallidum*. It is transmissible by sexual contact as well as from mother to child. Congenital syphilis occurs when the foetus is infected during pregnancy. Infectious syphilis is defined as infection of less than two years' duration. The main symptoms include a painless ulcer at the site of infection within the first few weeks of infection, followed by other symptoms (e.g., rash) a couple of months later. Often symptoms are not detected. In the absence of treatment, there will then be a period of several years without any symptoms, with a chance of a range of complications over decades that can involve the skin, bone, central nervous system and cardiovascular system. Infectious syphilis is fully curable with a single injection of long-acting penicillin.

virus: A very small, microscopic infectious agent that multiplies inside living cells. Antibiotics are not effective against viral infections, so treatment requires antiviral drugs.

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