MEDICINEINSIGHT

Disease Surveillance Report

Herpes Zoster – Phase 1

June 2017

Suggested citation

NPS MedicineWise. MedicineInsight Disease Surveillance Report: Herpes zoster – phase 1. Sydney: NPS MedicineWise, June 2017.

Contents

1. EXECUTIVE SUMMARY

1.1. Purpose

The purpose of this report is to inform disease surveillance activities using MedicineInsight data by describing patients with herpes zoster (HZ), including complications and their management.

1.2. Data and focus

This report for the Department of Health Office of Health Protection (OHP) addresses specific questions on the following topics for HZ: patient profile, complications, laboratory testing, medicines used and related adverse events.

1.3. Methods

The information presented in this report is based on general practice clinical information system (CIS) data collected from participating practices recruited to the MedicineInsight program. Data were extracted from 420 clinically representative practices, 4203 active GPs and 2,075,157 patients aged 35 years or over with at least 3 clinical encounters during the 5-year study time period (1 March 2012 to 28 February 2017 inclusive) – the "*total study population*".

A patient was defined as having a history of HZ if they had a recorded diagnosis (coded or free-text) of herpes zoster, varicella zoster, shingles, post-herpetic neuralgia, or Ramsay Hunt syndrome in a relevant diagnosis fields (diagnosis, reason for encounter or reason for prescription) when they were aged 35 years or over. To define patients with a new (incident) diagnosis of HZ during the study time period, the recorded onset date of HZ or inferred date of diagnosis (ie, the first record of HZ for the patient) were used.

1.4. Results

1.4.1. Patient profile with HZ

Of the 2.08 million MedicineInsight patients in the *total study population,* 41,426 patients had their first ever (incident) recorded diagnosis of HZ during the study period and were included in the "*incident HZ population*".

The average annual incidence of new HZ cases per year was estimated to be 6.2 per 1000 patients among individuals aged 35+ years and 7.8 per 1000 patients among individuals aged 50+ years.

The 5-year cumulative incidence increased with age, from 7 per 1000 patients aged 35–44 years, to 39 per 1000 patients aged 80–84 years, before decreasing to 25 per 1000 persons aged 95 years and above. The 5-year incidence of HZ was greater in females than males at 22 per 1000 females aged 35+ compared with 17 per 1000 males aged 35+.

Among the *incident HZ population,* 11% were at risk of being immunocompromised (n=4593) prior to their diagnosis: 10% had been prescribed a potentially immunosuppressive therapy 12 months before their HZ diagnosis, and 1% had an immunocompromising condition recorded at any time before their HZ diagnosis.

1.4.2. Laboratory testing for HZ

HZ is usually diagnosed by clinical assessment, with laboratory tests reserved for more atypical cases. To distinguish HZ from other skin conditions, laboratory confirmation of a skin sample using DNA testing by polymerase chain reaction (PCR) is considered the gold standard test and can be requested in primary care.

Since 1 March 2015 (when the first HZ PCR test was recorded in MedicineInsight) a total of 931 HZ PCR tests were recorded for the *total study population:* a minority of tests results were positive for the varicella zoster virus (13.1%). The estimated rate of testing for HZ virus was higher in females than males, although not statistically significant (0.6 versus 0.3 respectively, per 1000 patients in the *study population*).

Among the *incident HZ population*, 196 (0.5%) had an HZ PCR test recorded. The rate of testing for HZ virus was similar for females and males (5.1 versus 4.2, respectively, per 1000 patients; no significant difference*)*.

1.4.3. HZ-related complications

Among the *incident HZ population*, 23% (n=9466) had one or more potentially HZ-related complications recorded in the 12 months after their HZ diagnosis. Post-herpetic neuralgia was the most common complication, reported in 18.1% of the *incident HZ population*, followed by herpes ophthalmicus (2.9%).

1.4.4. Prescribing patterns

Among the *incident HZ population* 26,944 patients (65%) were prescribed a total of 31,010 prescriptions for HZ-specific pack sizes of the antivirals during the study period. The most commonly prescribed medicine for the treatment of HZ was famciclovir (53%), followed by valaciclovir (38%) and aciclovir (8%). The annual prescribing rates for the *incident HZ population* were similar across the five years.

There were 13,614 patients in the *total study population* with prescriptions for HZ-specific pack sizes of antivirals recorded during the study period who didn't have a diagnosis of HZ recorded in MedicineInsight.

1.4.5. Adverse events

In the entire MedicineInsight database, a total of 909 adverse events were recorded for the antiviral medicines of interest (famciclovir, valaciclovir, aciclovir), regardless of the indication for therapy. The most common adverse events recorded in MedicineInsight were rash (n=151), nausea (n=69) and vomiting (n=57).

1.5. Discussion

This is the first report to provide insights into HZ in the primary care setting using MedicineInsight data, including the incidence of new cases, complications, laboratory testing, medicine utilisation and adverse events.

The average annual incidence in MedicineInsight was 6.2 new HZ cases recorded (excluding episodes of recurrent HZ) per 1000 patients among individuals aged 35+ years. This aligns with other Australian studies that report from 5.6 to 7 new cases per 1000 people across all ages. The average annual incidence in people aged 50+ years was 7.8 per 1000 patients in MedicineInsight. As expected the incidence of HZ recoded in MedicineInsight increased with age, peaking in patients aged 80 to 84 years.

There was a proportion of patients in MedicineInsight who, despite not having a recorded diagnosis of HZ, were prescribed a pack-size for one of the antiviral medicines that is only reimbursed on the Pharmaceutical Benefit Scheme (PBS) for treating HZ. While these medicines are used to treat other herpes infections, because of the specific pack size prescribed, it is likely the majority of these prescriptions were for people who had HZ but their diagnosis was either not recorded by the GP or was entered in the progress notes which are not collected by MedicineInsight. While this finding needs further investigation, based on prescribing information, the total number of patients with HZ could be up to a third higher than the total number of patients with a *recorded* diagnosis of HZ.

Around 11% of patients with HZ were considered at risk of being immunocompromised in the year prior to their diagnosis, the majority of whom had record(s) of potentially immunosuppressive therapies which could increase the risk of herpes zoster, particularly in older patients.

In this study, one in four patients had a potentially HZ-related complication recorded within 12 months of their HZ diagnosis; as expected, post-herpetic neuralgia was the most common complication affecting 18% of the population and 2.5% of patients developed herpes ophthalmicus.

The low number of total PCR tests ordered for suspected HZ events (n=931) was not surprising, given that HZ is routinely diagnosed clinically through the observation of the distinctive rash and symptoms. Only 13.1% of tests ordered were positive for the varicella zoster virus. Of the PCR tests in MedicineInsight, a fifth (n=196) were among patients with a recorded diagnosis of HZ. Interestingly, nearly all HZ PCR tests were ordered for patients in WA, the reasons for which need further exploration.

Among the incident HZ population (35+ years), 65% had at least one prescription for an antiviral, compared to an Australian study using the Bettering the Evaluation and Care of Health (BEACH) database, which found that antivirals were prescribed for 73.5% of new HZ problems managed in patients aged 50+ years. The lower prescribing rate in MedicineInsight could be explained in part by the different age groups studied. For example, if younger patients were less likely to be prescribed antivirals versus older patients (perhaps due to more uncertainty in the diagnosis in this age group); or if younger patients were to present less frequently within 72 hours of the rash versus older patients 50+ years. Another factor to consider is the proportion of patients in MedicineInsight who, despite not having a recorded diagnosis of HZ, were prescribed one of the HZ-specific antiviral medicines, as described earlier. If further investigation reveals that the majority of these patients did indeed have HZ, despite the diagnosis not being recorded, the prescribing rate in MedicineInsight could be underestimated.

The proportions of medicines prescribed were similar between MedicineInsight (8% acyclovir, 53% famciclovir, and 38% valaciclovir) and the BEACH study (9% aciclovir, 51% famciclovir and 40% valaciclovir). As expected, famciclovir and valaciclovir were the preferred medicines, given their greater bioavailability and less frequent dosing in comparison to aciclovir. The most common adverse events for these medicines were rash, nausea and vomiting.

This report provides an introduction to the use of MedicineInsight data for HZ disease surveillance and will be expanded upon in Phase 2 to include information on vaccine surveillance.

The MedicineInsight resource provides the opportunity to better understand HZ within the Australian primary care setting. Based on these initial findings, some recommendations for further analyses include:

- Refining definitions, eg,
  - reviewing the definition of an HZ diagnosis, in consultation with experts, to understand the impact of including patients without a recorded diagnosis of HZ but with a relevant prescription and/or a positive test result for HZ
  - conducting a validation study with contributing practices on HZ case ascertainment.
- Enhancing the statistical analyses, eg,
  - with age-standardisation.
- Exploring the findings in more detail, eg,
  - further analysis of prescribing rates by age-group
  - understanding the relationship between age, being immunocompromised, and the risk of HZ
  - understanding recurrences of HZ
  - qualitative research on the HZ PCR testing rates.

With further detailed exploration of the findings in this report, the MedicineInsight resource is a valuable source of routinely collected data for surveillance.

2. INTRODUCTION

2.1. About the report

The purpose of this report is to inform the disease surveillance activities of the Department of Health, Office of Health Protection (OHP) by describing patients with HZ and their management in primary care, using MedicineInsight data.

The investigation focuses on:

- the profile of the MedicineInsight patient cohort with HZ
- laboratory testing for HZ
- antiviral medicines used for HZ
- adverse events and allergies related to antiviral medicines.

Section 3 presents a summary of the methods, and Section 4 the results of the investigations.

2.2. MedicineInsight data used in this report

The information presented in this report is based on general practice clinical information system (CIS) data collected from participating practices recruited to the MedicineInsight program. Data were used from 420 clinically representative practices (see Appendix B, 6.2.3), 4203 active GPs and 2,075,157 patients aged 35 years and over, with at least three clinical encounters during the study time period (1 March 2012 to 28 February 2017, inclusive) – the "*study population*".

This report uses the following information from the CIS data:

- patient demographics (including age [derived from year of birth], gender, State/Territory of residence, Aboriginal and Torres Strait Islander status)
- medicines prescribed (including ATC classification,[1] generic names, trade names, reason for prescription)
- encounters (including reason for encounters)
- diagnoses or conditions
- pathology test results
- allergy or adverse events.

For more information about MedicineInsight see:

- Appendix B: About MedicineInsight
- The NPS MedicineWise Using *MedicineInsight data* web page where you can access the *MedicineInsight Databook* (https://www.nps.org.au/medicine-insight/using-medicineinsight-data)

2.3. Report background

2.3.1. Clinical features and epidemiology of HZ

Herpes zoster (also referred to as shingles) is caused by a reactivation of the same varicella zoster virus that causes chickenpox. Over 90% of Australians have been infected with, and have antibodies to varicella zoster virus, meaning almost all adults are at risk of developing HZ. HZ commonly presents as a painful, unilateral, self-limiting rash in a dermatomal distribution. The majority of cases involve a prodromal phase including itching, tingling or severe pain, followed by the characteristic rash within 48–72 hours.[2]

While usually self-limiting, it is estimated that 13% to 26% of those who experience HZ develop complications associated with the disease,[3,4] usually occurring soon after the onset of HZ. The most common complication is chronic neuropathic pain, known as post-herpetic neuralgia, generally considered as pain persisting beyond 90 days from onset of the rash.[5] Other HZ-related complications include:[2]

- secondary bacterial infection of the rash
- herpes zoster ophthalmicus
- neurological complications
- Ramsay Hunt syndrome
- pneumonia
- meningitis.

HZ occurs most commonly in elderly people (particularly rising in incidence after the age of 50 years), with risk factors including:[2]

- age
- physical trauma
- malignancy
- immunocompromising conditions
- immunosuppressive therapies
- chronic lung or kidney disease
- a history of varicella (chickenpox) in the first year of life.

The lifetime risk of varicella zoster reactivation causing HZ is estimated to be about 20% to 30%, with the condition affecting half of people who live to 85 years.[2] Incidence of shingles is greater in females than males. One study reports that women aged 45 to 64 years have a 48% greater incidence of HZ than men of the same age.[6]

Based on recent Australian studies the annual HZ incidence has been estimated to range from:

- 5.6 to 7.0 per 1000 persons across all age groups[2,7]
- 9.7 to 11.7 per 1000 persons aged 50+ years.[7,8]

2.3.2. Vaccinations for HZ

A herpes zoster vaccine, ZostaVax®, is a live attenuated vaccine for the prevention of shingles that became freely available to people aged 70 years in Australia from 1 November 2016, with catch-up vaccinations at present for those aged 71–79 years. Though the vaccine has had a good safety profile in clinical trials, with fever and rash occurring rarely, rare adverse events have been reported, particularly in immunocompromised and immunosuppressed people and, as such, disease surveillance and vaccine surveillance are important.[2]

2.3.3. Treatment for HZ (antivirals)

Treatment for HZ mainly consists of the administration of antiviral medicines – aciclovir, famciclovir and valaciclovir – and analgesics. If started within 72 hours of onset of the rash, antivirals reduce the severity and duration of the illness.[9] Many of these medicines can be used to treat other herpes-related infections; however, only specific pack sizes are reimbursed on the Pharmaceutical Benefits Scheme (PBS) for the treatment of HZ (PBS authority required).[9] Both the dosage and duration of antiviral treatment are greater for herpes zoster than for herpes simplex.[10]

An Australian study using the BEACH (Bettering the Evaluation and Care of Health) database found that antivirals were prescribed for 73.5% of new HZ problems managed in patients aged 50+ years; 9% were aciclovir, 51% famciclovir and 40% valaciclovir. Most prescribing was by GPs with specialists prescribing only 4.7% of antivirals.[4] Famciclovir and valaciclovir are the preferred medicines, given their greater bioavailability and less frequent dosing in comparison to aciclovir.

3. METHODS

In this section, we present a summary of the methods used for this HZ report. This section contains the following subsections:

3.1. Report questions

These report questions were agreed with the Office of Health Protection and present a preliminary analysis of the MedicineInsight data for HZ.

Objectives	Questions
1. The profile of the patient cohort with HZ (Section 4.1)	1. What was the incidence of HZ in MedicineInsight patients over the last 5 years, overall and including: a. the age-specific incidence b. the gender-specific incidence c. the region-specific incidence (State) d. the indigenous-specific incidence. 2. How many patients with HZ were potentially immunocompromised due to: a. comorbidities: - HIV - leukaemia - lymphoma b. immunosuppressive therapies - chemotherapy - radiotherapy - corticosteroids - disease-modifying anti-rheumatic drugs (DMARDs) - anti-rejection/transplant medication.
2. Laboratory testing for HZ (Section 4.2)	1. How many MedicineInsight patients had a HZ polymerase chain reaction (PCR) test result recorded? 2. What was the rate of HZ PCR testing, by age, gender, State and indigenous status? 3. Of those patients diagnosed with HZ, how many had a HZ PCR test result recorded?
3. HZ-related complications (Section 4.3)	For people with HZ, how many developed the following potentially HZ-related complications (within 12 months of their diagnosis): a. post-herpetic neuralgia b. pneumonia c. pneumonitis d. herpes meningitis e. secondary skin bacterial infection

	f. hearing problems g. blindness h. encephalitis i. Ramsay Hunt syndrome (facial paralysis) j. herpes zoster ophthalmicus k. stroke.
3. Patterns of HZ drug utilisation (Section 4.4)	1. What medicines of interest were prescribed for people with a recorded diagnosis of HZ? 2. What medicines of interest were prescribed for people without a recorded diagnosis of HZ? 3. What were the patterns of HZ drug utilisation over 5 years? 4. What were the number of prescriptions of medicines of interest between 1 March 2016 and 28 February 2017?
4. Adverse events of treatments (Section 4.5)	1. What were the 10 most common adverse events for medicines used to treat HZ in MedicineInsight? 2. How do the 10 most common adverse events compare with the numbers reported in the Therapeutic Goods Administration database of adverse event notifications (TGA-DAEN)?

3.2. Methods

3.2.1. Study type/design

This was a descriptive analysis of data collected from Australian national general practice clinical information systems (CIS). Analyses were cross-sectional.

3.2.2. Study time period

Five years from 1 March 2012 to 28 February 2017, inclusive, unless otherwise specified.

3.2.3. Study population

Patients were included if they met the following criteria:

- ≥ 35 years of age at data extract (including patients currently marked as deceased or inactive in the CIS)
- had three or more clinical encounters at a clinically representative practice (see Appendix B, 6.2.3) in the 5 years before 28 February 2017.

Patients < 35 years of age at data extract were excluded because, although they may (rarely) have a diagnosis of HZ, there is more uncertainty about whether the condition is HZ or chickenpox.

A clinical encounter, or any professional exchange between a patient and a healthcare professional, was defined as all those encounters at the general practice that were: a) not identified as administrator entries nor encounters that had been transferred/imported from another practice and b) were not identified by predefined ‘administration-type’ terms found in the ‘reason for encounter’ field such as “administrative reasons”, “forms”, “recall”, etc.

Patients with at least three clinical encounters during the study period were selected for this report, to exclude temporary patients and to ensure that patients included in the study had sufficient opportunities for diagnoses, tests and prescriptions to be recorded.

Patients currently marked as deceased or inactive in the CIS, with three or more clinical encounters during the study period, were included because they were alive and active for at least some of the study period. Excluding them would introduce selection bias and could lead to an under or overestimate of the incidence of HZ, and complications.

Where additional restrictions were applied for specific objectives, these are described under the relevant sections in Chapter 4.

3.2.4. Diseases and conditions

Depending on the CIS at their practice, clinicians use code systems such as 'Docle', 'Pyefinch' or 'ICPC' to enter medical terms into their system. However it is not mandatory to use a code and clinicians can enter terms as free-text.

This report uses data from both coded and free text fields which can be entered into the following areas of the CIS:

- Medical history (diagnosis)
- Encounter (reason for encounter)
- Prescription (reason for prescription).

3.2.4.1. Definition of HZ

A patient was defined as having a history of HZ if they had a recorded diagnosis (coded or free-text) of herpes zoster, varicella zoster, shingles, post-herpetic neuralgia, or Ramsay Hunt syndrome in a relevant diagnosis fields (diagnosis, reason for encounter or reason for prescription) when they were ≥ 35 years of age. Table D3 in Appendix D details codes and free text used to identify patients with HZ.

Varicella zoster was included because, although most often used to describe chickenpox, this study was restricted to patients aged 35+ years when a diagnosis of zoster at these ages is most likely to be herpes zoster. We recognise there is potential for misclassification of chickenpox as HZ with this method but expect this would be minimal, considering up to 95% of the population have already been infected with the varicella zoster virus by the time they are 30 years of age.[10]

3.2.4.2. Definition of incident HZ cases

To define patients with a first ever 'incident' diagnosis of HZ during the study time period we used the recorded or inferred date of diagnosis. The flow diagram for defining patients with incident HZ is provided in Figure 1.

The date of diagnosis of HZ was based on the first 'date of onset' recorded in the clinical information system. If 'date of onset' was not recorded, the date of the earliest record of HZ in one of the three diagnosis fields was used as the proxy for the date of HZ diagnosis (the inferred date of diagnosis).

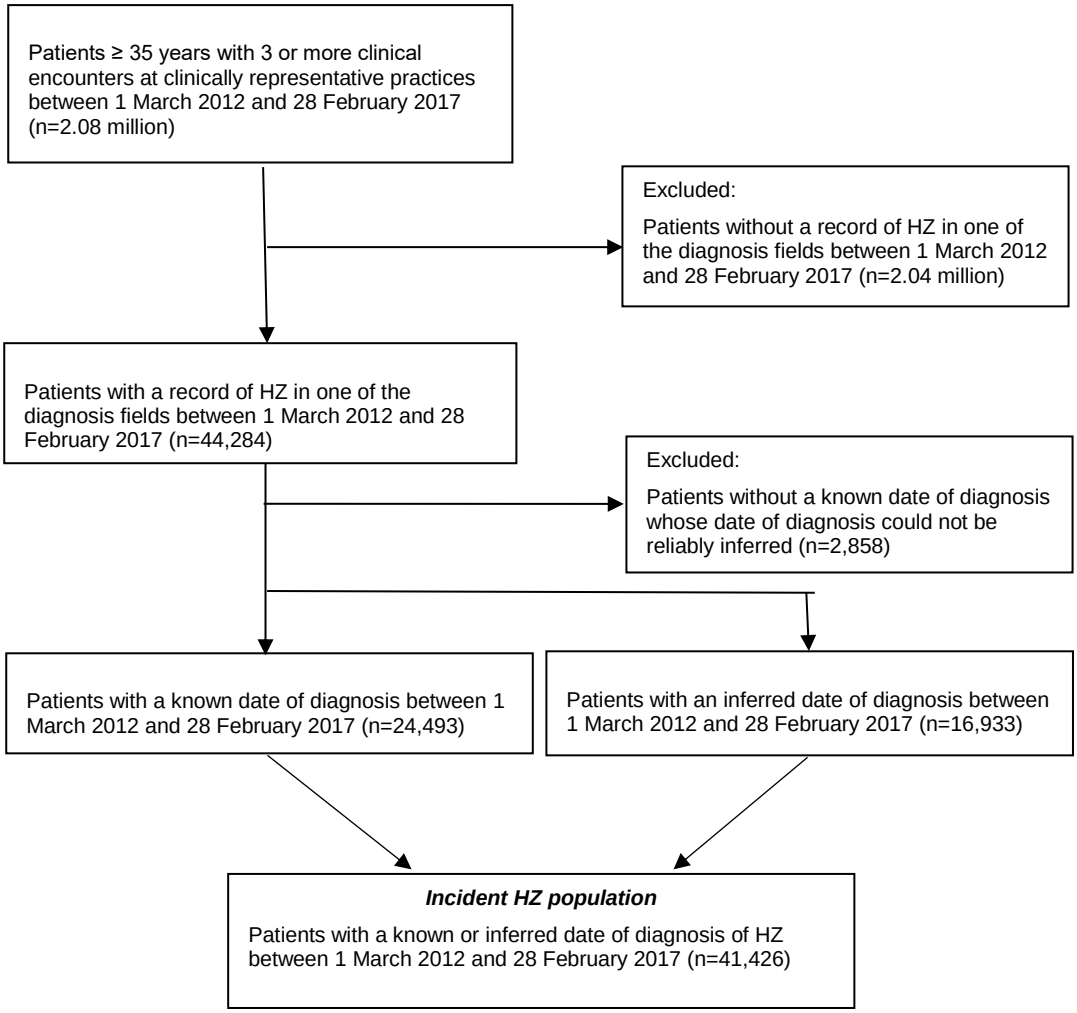
However, if the first HZ record was within 12 months of the patient's start date at the practice (defined as the first encounter) this may have been a condition that was first diagnosed at another practice before visiting this practice. For these patients the date of diagnosis could not be reliably inferred and they were not included in the *incident HZ population*.

3.2.4.3. Definition of potentially HZ-related complications

A patient was considered to have a potentially HZ-related complication if they had a recorded diagnosis (coded or free-text) of post-herpetic neuralgia, Ramsay Hunt syndrome (facial paralysis), herpes zoster ophthalmicus, herpes meningitis, pneumonia, pneumonitis, secondary skin bacterial infection, hearing problems, blindness, encephalitis, or stroke in a relevant diagnosis field (diagnosis, reason for encounter or reason for prescription) in the 12 months after the date of diagnosis of HZ.

Note, some conditions included in this definition, such as pneumonia or stroke, occur commonly in the general population and may not be related to HZ. It is difficult to ascertain definitely HZ-related complications using routinely collected general practice health records. Assuring there is a temporal association between the HZ diagnosis and the secondary condition (within 12 months of diagnosis in this report) goes some way in addressing this limitation of the data source, however, we recognise there will be some remaining misclassification of conditions as HZ-related.

FIGURE 1: FLOW DIAGRAM FOR THE IDENTIFICATION OF PATIENTS WITH AN INCIDENT (NEW) DIAGNOSIS OF HZ DURING THE STUDY PERIOD



3.2.4.4. Definition of potentially immunocompromised

A patient was considered to be potentially immunocompromised before their diagnosis of HZ if they met one or more of the following criteria:

- Immunocompromising condition:
  - had a recorded diagnosis of HIV, leukaemia or lymphoma at any time before their first diagnosis of HZ. Refer to Appendix D, 6.4.2 for the definition of immunocompromising conditions. Autoimmune diseases (eg, inflammatory bowel disease, rheumatoid arthritis) and transplant recipients weren't included in this definition, however many of these patients will be included in the immunosuppressive therapy group based on the medicines used to manage them (eg, DMARDs, anti-rejection/transplant medicines).
- Immunosuppressive therapy:
  - had undergone radiation therapy or chemotherapy within the 12 months before their first diagnosis of HZ. Refer to Appendix D, 6.4.1 for the definitions of radiotherapy and chemotherapy.
  - had a prescription for one or more of the potentially immunosuppressing medicines listed in Appendix D, 6.4.1 within the 12 months before their first diagnosis of HZ.

The methodology used in this report provides an estimate of the proportion of patients who were 'potentially immunocompromised', rather than 'definitely immunocompromised', the latter being more difficult to ascertain using routinely collected health data. The reasons for this are described below.

- According to the definition used, immunocompromising conditions could occur at any time before the HZ diagnosis and may not have been immunocompromising at the time of the diagnosis of HZ.
- Radiation therapy and chemotherapy are markers of, but do not always cause, immunosuppression.
- All prescriptions for oral corticosteroid medicines (prednisone and prednisolone) were included in the definition of immunosuppressive therapies, however not all dosage schedules definitely lead to immunosuppression (particularly short courses and low doses). It was not possible in the timeframe for delivery of this report to use the daily dose and duration information recorded in MedicineInsight to categorise prescriptions as potentially immunosuppressive versus low risk. Dosage instructions can be missing, or recorded by GPs as free text, requiring extensive data cleaning and coding.

3.2.5. Pathology test results

Most Australian general practices now receive pathology test results electronically, transferred directly into the CIS from the pathology providers. Pathology test results include those ordered by the GP and those where the results from other requestors are copied to the GP.

There are three potential sources of information about tests within the CIS:

- The first and largest source contains individual records for each test with a test result. Information includes the test name, the result, the test units, if it was within or outside normal limits, and a relevant Logical Observation Identifiers Names and Codes (LOINC) (an international test classification system). This data source is referred to as **'atomic test results'** and most pathology test results appear in this table.
- The second data source contains a summary record describing the name of the test(s) and does not include any information on the results. This is referred to as 'notification of test results'. These are generally tests for which the results did not transfer successfully into the CIS and are called the **'non-atomic tests'**.
- The third data source is a collection of PDF documents that have been transferred or scanned into the CIS, containing detailed information about test results for an individual patient. These records are not available to MedicineInsight.

Currently MedicineInsight accesses the first two sources of information on pathology tests.

3.2.5.1. Definition of HZ polymerase chain reaction (PCR) tests

Shingles is usually diagnosed by clinical assessment, especially once the characteristic rash appears. However, to distinguish HZ from other skin conditions, laboratory confirmation can be obtained by ordering a nucleic acid detection test (such as PCR), direct-fluorescent antibody test (DFA) or viral culture of a sample (swab) taken from the affected skin.[2] PCR tests are considered the gold standard for HZ detection (being the most sensitive test with a fast turn-around of 1 day[10]), and were the only test considered in this report.

A patient was defined as having an HZ PCR test recorded within the study time period if they had a relevant LOINC code and test name, as listed in Appendix C (Table C1), recorded in the atomic or non-atomic pathology test results.

3.2.6. Medicines and medicine classes

Table 1: lists the antiviral medicines used for the treatment of HZ. Only prescriptions for the medicine pack sizes (strength and quantity) described in Table 1 were included in this study; these pack sizes are reimbursed on the Pharmaceutical Benefits Scheme (PBS) only for the treatment of HZ (PBS authority required). Prescriptions with repeats were excluded because the PBS restriction is for one course only with no repeats. All PBS/Repatriation Pharmaceutical Benefits Scheme (RPBS) prescriptions for the HZ medicines were extracted for the study time period.

TABLE 1: MEDICINES USED FOR THE TREATMENT OF HZ

ATC class[1]	ATC code	Generic name	PBS restricted pack size for HZ[9]	Dosage and duration for HZ[9]
J05AB	J05AB01	aciclovir	800 mg × 35	800 mg 5 times a day for 7 days
J05AB	J05AB09	famciclovir	Immunocompetent: 250 mg × 21 Immunocompromised: 500 mg × 30	Immunocompetent: 250 mg 3 times a day for 7 days, Immunocompromised: 500 mg 3 times a day for 10 days
J05AB	J05AB11	valaciclovir	500 mg × 42	1 g 3 times a day for 7 days

Prescriptions for the medicines of interest were identified by an Anatomical Therapeutic Chemical (ATC) code, generic name and/or by brand name (as assigned by the CIS), and using strength and quantity information. Appendix D, 0 lists the generic and brand names of the medicines investigated.

Data were extracted both from the prescription transaction file (which contains all information about prescriptions ordered) and the prescription history table (which contains information about current medicines, including those prescribed elsewhere, over-the-counter medicines, and medicines that have been stopped). Multiple prescriptions for the same medicine prescribed on the same day were considered duplicates (in error) and were counted as a single prescription.

3.2.7. Analysis plan

Analysis of the data was conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Definitions of the measures (proportions and rates) calculated for this report are detailed in Section 4.

To indicate the reliability of the estimated prevalence rates and proportions, 95% confidence intervals were calculated (a range of values that should contain the actual rate 95% of the time). Comparisons within categories were made by comparing the degree of overlap of the corresponding 95% confidence intervals. Cluster-corrected 95% confidence intervals were calculated using the general practice as the unit of clustering. The analyses used the SAS PROC SURVEYFREQ procedure.

4. RESULTS

In this section, we present a summary of results found from our investigations with additional notes on the methods used, where required.

4.1. Profile of the HZ patient cohort

Question 1

Among the 2.08 million patients in the *total study population* – aged 35 years or over with at least 3 clinical encounters during the 5-year study period – 44,284 had a diagnosis of HZ recorded. Of these, 41,426 had a known (59%) or inferred (41%) diagnosis date for HZ during the study period and were included in the *incident HZ population* (see Figure 1Figure 1:). The cumulative incidence of new HZ cases over the 5-year period was 20.0 per 1000 patients among individuals aged 35+ years.

Annual incidence of HZ (per 1000 patients)

The average annual incidence of new HZ cases per year was estimated to be:

- 6.2 per 1000 patients among individuals aged 35+ years (95% CI: 6.0 – 6.4)
- 7.8 per 1000 patients among individuals aged 50+ years (95% CI: 7.6 – 8.1)

Table 2: the 5-year study period in patients aged 35+ years and 50+ years, respectively.

TABLE 2: ANNUAL INCIDENCE OF HZ PER 1000 PATIENTS IN THE STUDY POPULATION AGED 35+ YEARS, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

			Incidence per 1000 patients / year	
Time period	New HZ diagnoses	Patients 35+ in the study population†	Incidence	95% confidence limits
1 March 2012 – 28 February 2013	7,692	1,245,800	6.17	(5.88,6.47)
1 March 2013 – 28 February 2014	7,943	1,327,970	5.98	(5.73,6.23)
1 March 2014 – 28 February 2015	8,299	1,357,639	6.11	(5.86,6.36)
1 March 2015 – 29 February 2016	8,649	1,378,566	6.27	(6.03,6.52)
1 March 2016 – 28 February 2017	8,843	1,337,347	6.61	(6.37,6.85)

† *Patients were also required to have at least one clinical encounter at the practice during that year to be included in the denominator*

TABLE 3: ANNUAL INCIDENCE OF HZ PER 1000 PATIENTS IN THE STUDY POPULATION AGED 50+ YEARS, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

			Incidence per 1000 patients / year	
Time period	New HZ diagnoses	Patients 50+ in the study population†	Incidence	95% confidence limits

1 March 2012 – 28 February 2013	6,536	844,827	7.74	(7.39,8.09)
1 March 2013 – 28 February 2014	6,722	886,750	7.58	(7.27,7.89)
1 March 2014 – 28 February 2015	6,945	898,551	7.73	(7.43,8.03)
1 March 2015 – 29 February 2016	7,151	904,214	7.91	(7.62,8.20)
1 March 2016 – 28 February 2017	7,258	877,083	8.28	(7.99,8.55)

† *Patients were also required to have at least one clinical encounter at the practice during that year to be included in the denominator*

Five-year cumulative incidence of HZ, by demographic factors (per 100 patients)

Both Figure 2 and Table 4 demonstrate how the incidence of HZ changed with age in the *total study population*.

The incidence of HZ increased with age, from 0.7 per 100 MedicineInsight patients aged 35–44 years, to 3.5 per 100 patients aged 70–74 years, peaking at 3.9 per 100 patients aged 80–84 years, before decreasing to 2.5 per 100 patients aged 95 years and above.

FIGURE 2: AGE GROUP-SPECIFIC CUMULATIVE INCIDENCE OF HZ OVER 5 YEARS, MEDICINEINSIGHT, 1 MARCH 2012 – 28 FEBRUARY 2017 (N=41,426).

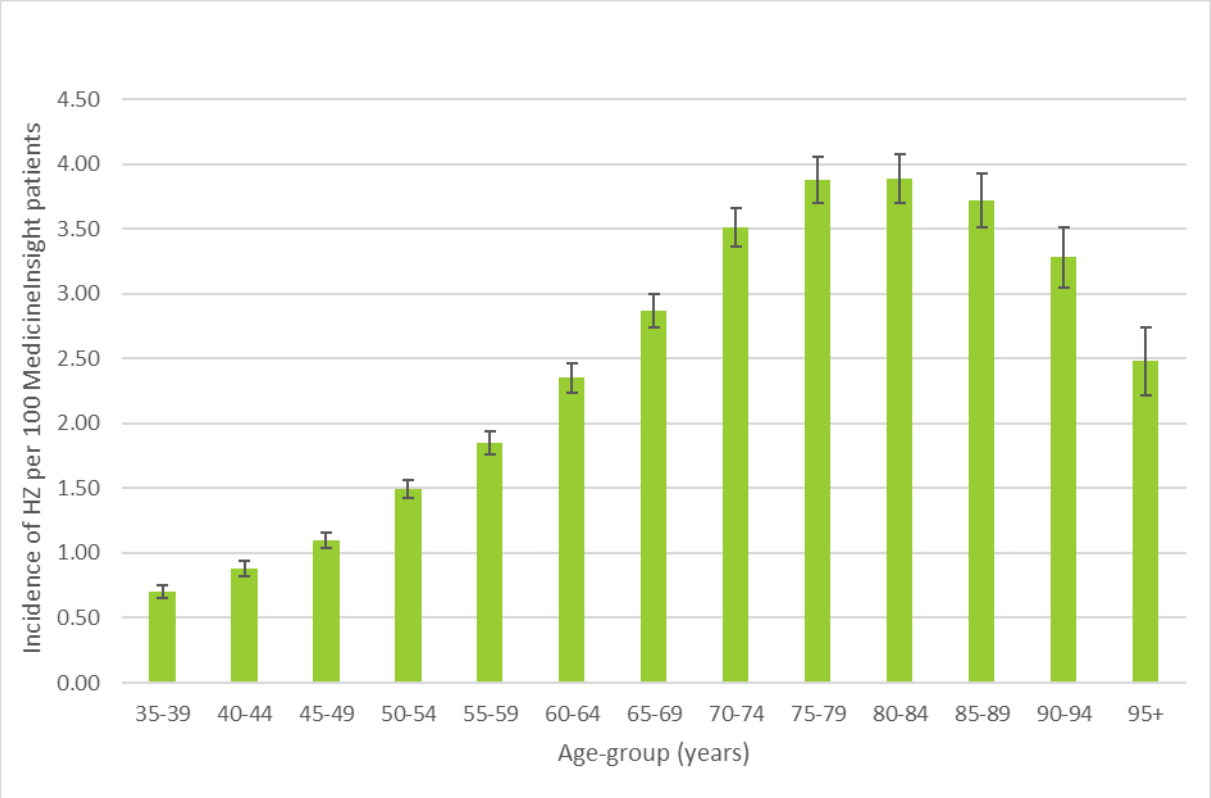


TABLE 4: AGE GROUP-SPECIFIC CUMULATIVE INCIDENCE OF HZ OVER 5 YEARS, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017 (N=41,426)

		Cumulative incidence per 100 patients	
Age group	New HZ diagnoses	Incidence	95% confidence limits
35–39	1,865	0.70	(0.66, 0.75)
40–44	2,224	0.88	(0.83, 0.94)
45–49	2,725	1.10	(1.04, 1.16)
50–54	3,447	1.49	(1.4, 1.56)
55–59	4,158	1.85	(1.76, 1.94)
60–64	4,776	2.35	(2.24, 2.46)
65–69	5,458	2.87	(2.74, 3.00)
70–74	5,268	3.51	(3.36, 3.66)
75–79	4,306	3.88	(3.69, 4.06)
80–84	3,231	3.89	(3.69, 4.08)
85–89	2,382	3.72	(3.51, 3.93)
90–94	1,218	3.28	(3.04, 3.51)
95+	368	2.48	(2.21, 2.74)
All ages	41,426	2.00	(1.91,2.08)

Table 5 presents the unadjusted cumulative incidence of HZ by gender, State and indigenous status. The incidence of HZ was greater in females, at 2.2 new cases of HZ per 100 females compared with 1.7 per 100 males.

The incidence of HZ in MedicineInsight practices was highest in (and not significantly different between) New South Wales, Victoria, Queensland, South Australia, Tasmania and the Australian Capital Territory (ranging from 1.8 to 2.5 per 100 patients). There was some evidence to suggest that HZ incidence was lower in MedicineInsight practices in Western Australia (1.6 per 100 patients, respectively). Patients in MedicineInsight practices in the Northern Territory were significantly less likely to be diagnosed with HZ, with an incidence of 0.9 per 100 patients.

In non-indigenous Australians the incidence of HZ was 2.2 per 100 non-indigenous patients compared with 1.4 per 100 indigenous patients (although the 95% confidence interval was comparatively wide, at 0.9 to 1.7 per 100 indigenous patients, indicating lower precision with this estimate).

TABLE 5: SOCIODEMOGRAPHIC-SPECIFIC CUMULATIVE INCIDENCE OF HZ IN THE PAST 5 YEARS, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017 (N=41,426)

		Cumulative incidence per 100 patients	
	New HZ diagnoses	Incidence	95% confidence limits
Gender			
Male	15,775	1.69	(1.61, 1.77)
Female	25,642	2.25	(2.16, 2.35)
Missing/indeterminate	9		
State			
ACT	1073	2.28	(1.85, 2.71)
NSW	14,042	2.12	(1.97, 2.27)
NT	404	0.89	(0.64, 1.14)
Qld	7,691	1.88	(1.73, 2.03)
SA	1,371	2.51	(2.19, 2.83)

	New HZ diagnoses	Cumulative incidence per 100 patients	
		Incidence	95% confidence limits
Tas	3,501	2.43	(2.23, 2.64)
Vic	8,811	2.02	(1.80, 2.23)
WA	4,533	1.65	(1.41, 1.89)
Indigenous status			
Indigenous	422	1.43	(0.91, 1.71)
Non-indigenous	31,359	2.23	(2.13, 2.32)
Not stated	9,641	1.51	(1.39, 1.63)
Missing	<5		

Question 2

Potentially immunocompromised patients with HZ

Among the 41,426 patients who made up the *incident HZ population*, 4593 (11.1%) had an immunocompromising condition (diagnosed at any time before their HZ diagnosis) and/or had been prescribed immunosuppressive medications in the 12 months preceding their diagnosis of HZ. Refer to Table 6 for the breakdown of patients with either an immunocompromising condition or prescribed immunosuppressive medication.

TABLE 6: PROPORTION OF PATIENTS WITH HZ AND AN IMMUNOCOMPROMISING CONDITION AND/OR ON IMMUNOSUPPRESSIVE MEDICATION 12 MONTHS BEFORE DIAGNOSIS OF HZ, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017 (N=41,426)

Comorbidity	Number of patients with HZ	Proportion of patients with HZ	
		%	95% confidence limits
Immunocompromising conditions	549	1.33	(1.01, 1.64)
Immunosuppressive medications	4,127	9.96	(9.50, 10.43)
Immunocompromised and/or immunosuppressed	4,593	11.09	(10.57, 11.61)

4.2. Laboratory testing for HZ

Table 7: details the rate of HZ PCR tests recorded by demographic factors for the *total study population* and its subset, the *incident HZ population* between 1 March 2015, when the first HZ PCR test was recorded in MedicineInsight, and 28 February 2017 (the end of the study period).

A total of 930 HZ PCR tests were recorded for the *total study population:* a minority of tests results were positive for the varicella zoster virus (13.1%). The estimated rate of testing for HZ virus was higher in females than males, although not statistically significant (0.6 versus 0.3 respectively, per 1000 patients in the *study population*).

Among the *incident HZ population*, 196 (0.5%) had an HZ PCR test recorded, of which 50% were positive for the varicella zoster virus. The rate of testing for HZ virus was similar in females and males (5.1 versus 4.2, respectively, per 1000 patients; no significant difference).

Analysis by State revealed most HZ tests were recorded for patients in Western Australia (n=864) and the Northern Territory (n=54). All other States and Territories, together, accounted for less than 1% of tests recorded in MedicineInsight.

TABLE 7: CHARACTERISTIC-SPECIFIC RATES OF HZ PCR TESTING, MEDICINEINSIGHT, BETWEEN 1 MARCH 2015 AND 28 FEBRUARY 2017

		Total study population			Incident HZ population		
Category	Demographic	Number of patients with a test (n)	Testing rate per 100 patients	95% confidence limits	Number of patients with a test (n)	Testing rate per 100 patients (%)	95% confidence limits
Gender							
	Male	283	0.03	(0.01,0.05)	66	0.42	(0.17,0.67)
	Female	646	0.06	(0.02,0.09)	130	0.51	(0.14,0.88)
	Missing/indeterminate	<5	-	-	0	0.00	(0.00,0.00)
Age group							
	35–39	118	0.04	(0.02,0.07)	11	0.59	(0.03,1.15)
	40–44	103	0.04	(0.01,0.07)	13	0.58	(0.10,1.07)
	45–49	114	0.05	(0.02,0.08)	16	0.59	(0.03,1.14)
	50–54	116	0.05	(0.01,0.09)	10	0.29	(0.00,0.66)
	55–59	121	0.05	(0.02,0.09)	30	0.72	(0.22,1.23)
	60–64	103	0.05	(0.02,0.08)	31	0.65	(0.17,1.13)
	65–69	84	0.04	(0.02,0.07)	22	0.40	(0.13,0.68)
	70–74	66	0.04	(0.02,0.07)	26	0.49	(0.14,0.85)
	75–79	40	0.04	(0.02,0.05)	10	0.23	(0.03,0.44)
	80–84	34	0.04	(0.01,0.07)	13	0.40	(0.08,0.72)
	85–89	17	0.03	(0.01,0.05)	9	0.38	(0.06,0.69)
	90–94	9	0.02	(0.00,0.05)	<5	-	-
	95+	5	0.03	(0.00,0.06)	<5	-	-
Indigenous status							
	Indigenous	13	0.04	(0.01,0.08)	0	0	(0.00,0.00)
	Non-indigenous	917	0.04	(0.02,0.07)	196	0.48	(0.15,0.80)
State							
	ACT	0	0.00	(0.00,0.00)	0	0	(0.00,0.00)

		Total study population			Incident HZ population		
Category	**Demographic**	**Number of patients with a test (n)**	**Testing rate per 100 patients**	**95% confidence limits**	**Number of patients with a test (n)**	**Testing rate per 100 patients (%)**	**95% confidence limits**
	NSW	<5	-	-	0	0	(0.00,0.00)
	NT	54	0.13	(0.00,0.27)	15	3.92	(0.83,7.00)
	Qld	<5	-	-	0	0	(0.00,0.00)
	SA	<5	-	-	0	0	(0.00,0.00)
	Vic	0	0.00	(0.00,0.00)	0	0	(0.00,0.00)
	WA	869	0.32	(0.13,0.50)	180	3.99	(1.49,6.49)
	Tas	0	0.00	(0.00,0.01)	0	0	(0.00,0.00)
Rurality							
	Inner regional Australia	131	0.03	(0.00,0.07)	8	0.07	(0.00,0.15)
	Major cities of Australia	562	0.04	(0.01,0.08)	133	0.52	(0.07,0.97)
	Outer regional Australia	162	0.07	(0.00,0.15)	41	1.02	(0.00,2.19)
	Remote	52	0.16	(0.00,0.33)	8	1.81	(0.00,4.46)
	Very remote	<5	-	-	<5	-	-

4.3. HZ-related complications

Among the *incident HZ population*, 9,466 (22.8%) had one or more potentially HZ-related complications recorded in the 12 months after their HZ diagnosis.

The proportion of the *incident HZ population* who experienced each complication is presented in Table 8: . As expected, post-herpetic neuralgia was the most common complication, reported in 18.1% of the incident HZ population, and accounting for 78.7% of all reported HZ-related complications, followed by herpes ophthalmicus (reported in 2.9% of patients). The least common complication was pneumonitis, reported in only 0.04% of the *incident HZ population*.

TABLE 8: PROPORTION OF PATIENTS WITH HZ-RELATED COMPLICATIONS WITHIN 12 MONTHS OF HZ DIAGNOSIS BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017, MEDICINEINSIGHT (N=41,426)

HZ complications	Number of patients (n)	Proportion with complication (%)
Post-herpetic neuralgia	7,449	18.14
Herpes ophthalmicus	1,201	2.92
Pneumonia	525	1.28
Stroke	251	0.61
Ramsay Hunt syndrome	209	0.51
Hearing problems	174	0.42
Blindness	39	0.10
Herpes meningitis	33	0.08
Encephalitis	32	0.08
Skin infection	27	0.07
Pneumonitis	15	0.04

4.4. Patterns of HZ drug utilisation

Question 1

Prescriptions for the incident HZ population

Among the *incident HZ population*, 26,944 patients (65.0%) had a total of 31,010 prescriptions for HZ-specific medicine recorded during the study period. Of these, the most commonly prescribed medicine for HZ treatment was famciclovir (53.4%), followed by valaciclovir (38.2%) and aciclovir at (8.5%) (Table 9). Multiple prescriptions for the same patient were included in the tally of prescriptions by class (Table 9).

TABLE 9: MEDICINES OF INTEREST PRESCRIBED FOR PATIENTS WITH INCIDENT HZ, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

ATC code	Generic name	Number of prescriptions (n)	Proportion of HZ prescriptions (%)	95% confidence limits
J05AB09	famciclovir	16,544	53.35	(50.74,55.96)
J05AB11	valaciclovir	11,842	38.19	(35.73,40.65)
J05AB01	aciclovir	2,624	8.46	(7.16, 9.76)
Total		31,010	100	

Question 2

Prescriptions *for patients without a recorded diagnosis of HZ*

Of the 2.03 million patients in the *total study population* without a diagnosis of HZ recorded, a total of 13,614 patients were prescribed 16,193 HZ-specific medicine presentations between 1 March 2012 and 28 February 2017. Of these, the most commonly prescribed medicines were famciclovir and valaciclovir (48.1% and 44.8%, respectively), with the least prescribed being aciclovir at 7.1% (Table 10). Multiple prescriptions for the same patient were included in the tally of prescriptions by class (Table 10).

TABLE 10: MEDICINES OF INTEREST PRESCRIBED FOR PATIENTS WITHOUT A RECORDED DIAGNOSIS OF HZ, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

ATC code	Generic name	Number of prescriptions (n)	Proportion of all HZ prescriptions (%)	95% confidence limits
J05AB09	famciclovir	7,787	48.09	(47.32, 48.86)
J05AB11	valaciclovir	7,258	44.82	(44.06, 45.59)
J05AB01	aciclovir	1,148	7.09	(6.69, 7.48)
Total		16,193	100	

Question 3

Annual prescribing rates over 5 years for the incident HZ population

We defined the annual rate of prescribing for the incident HZ population as:

$$\frac{\text{\# of newly diagnosed HZ patients that year prescribed HZ-specific medicines}}{\text{\# of patients newly diagnosed with HZ that year}} \times 100$$

The annual prescribing rates for the incident HZ population were similar across the five years and ranged from 63.1 to 66.5 people prescribed HZ-specific medicines per 100 patients newly diagnosed with HZ (Table 11).

TABLE 11: ANNUAL PRESCRIBING RATES FOR HZ MEDICINES FOR PATIENTS NEWLY DIAGNOSED WITH HZ, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

Time period	Incident HZ patients with ≥1 prescription (n)	New HZ diagnoses (n)	Prescribing rate per 100 patients	
			Rate	95% confidence limits
1 March 2012 – 28 February 2013	4,853	7,692	63.09	(61.40, 64.79
1 March 2013 – 28 February 2014	5,188	7,943	65.32	(63.82, 66.81)
1 March 2014 – 28 February 2015	5,511	8,299	66.41	(64.97, 67.84)
1 March 2015 – 29 February 2016	5,749	8,649	66.47	(65.06, 67.88)

1 March 2016 – 28 February 2017	5,643	8,843	63.81	(62.27, 65.36)

Annual prescribing rates over 5 years *for patients without a recorded diagnosis of HZ*

We defined the annual rate of prescribing for patients without a recorded diagnosis of HZ as:

$$\frac{\text{\# patients without a diagnosis of HZ with 1+ clinical encounters that year and prescribed HZ-specific medicines}}{\text{\# patients without a diagnosis of HZ with 1+ clinical encounters that year}} \times 100$$

The annual prescribing rates for patients without a recorded diagnosis of HZ were similar across the five years at 0.2 per 100 patients prescribed HZ-specific medicines per 100 patients without a diagnosis of HZ who visited the practice that year (Table 12).

TABLE 12: ANNUAL PRESCRIBING RATE PER 100 PATIENTS WITHOUT A RECORDED DIAGNOSIS OF HZ, MEDICINEINSIGHT, BETWEEN 1 MARCH 2012 AND 28 FEBRUARY 2017

			Prescribing rate per 100 patients without HZ	
Time period	Non HZ patients with ≥1 prescription (n)	Number of patients without a recorded diagnosis of HZ†	Rate	95% confidence limits
1 March 2012 – 28 February 2013	2,810	1,268,045	0.22	(0.20, 0.24)
1 March 2013 – 28 February 2014	2,548	1,344,938	0.19	(0.16, 0.20)
1 March 2014 – 28 February 2015	2,639	1,372,290	0.19	(0.18, 0.21)
1 March 2015 – 29 February 2016	2,856	1,384,518	0.21	(0.19, 0.22)
1 March 2016 – 28 February 2017	2,761	1,340,056	0.21	(0.19, 0.22)

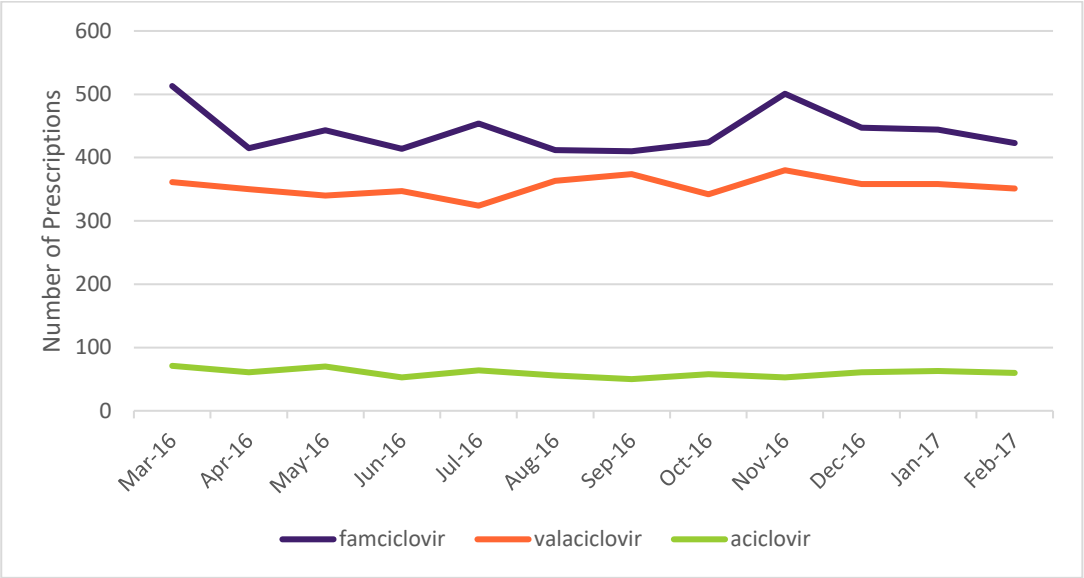
† *Patients were also required to have at least one clinical encounter at the practice during that year to be included in the denominator*

Question 4

Total number of prescriptions ordered per month over the last 12 months

Monthly prescription counts between 1 March 2016 and 28 February 2017 fluctuated slightly per medicine of interest, with famciclovir being the most frequently prescribed at approximately 450 scripts per month, followed by valaciclovir with approximately 370 scripts per month. Aciclovir was the least prescribed with fewer than 100 scripts per month. (Figure 3)

FIGURE 3: TRENDS IN MONTHLY PRESCRIPTION COUNTS BY MEDICINE OF INTEREST OVER 12 MONTHS, MEDICINEINSIGHT, 1 MARCH 2016 – 28 FEBRUARY 2017.



4.5. Adverse events for medicines of interest

Questions 1 and 2

The 10 most common adverse events for medicines of interest recorded in MedicineInsight

This was a cross-sectional analysis of recorded adverse events related to acyclovir, famciclovir, and valaciclovir, regardless of the indication for therapy and across the entire MedicineInsight database. We extracted all allergy and drug reaction records where the 'substance name' contained one of the generic or trade names as described in Appendix D, from the start of recording up to and including 28 February 2017. We compiled a merged list of adverse reactions to these medicines, categorising the reactions manually to MedDRA[11] categories. When multiple reactions were recorded, we noted each separately.

For comparison we searched the TGA database of adverse event notifications (DAEN) for all adverse event reports with the medicines of interest to 18 January 2017 (last available date).

A total of 909 adverse events were recorded for the medicines of interest, with the earliest recorded on 15 January 2005. Of these, 360 were missing details on the specific adverse event experienced.

The most common adverse events in the MedicineInsight program as compared to the TGA DAEN are presented in Table 13: The most common adverse events recorded in MedicineInsight were rash (n=151), nausea (n=69) and vomiting (n=57).

TABLE 13: 10 MOST COMMON ADVERSE EVENTS FROM MEDICINEINSIGHT COMPARED TO THOSE FROM THE TGA-DAEN

MedDRA system organ class	MedDRA reaction term	MedicineInsight count	TGA DAEN count
Skin and subcutaneous tissue disorders	Rash	151	54
Gastrointestinal disorders	Nausea	69	88
Gastrointestinal disorders	Vomiting	57	58
Nervous system disorders	Headache	35	66
Skin and subcutaneous tissue disorders	Urticaria	28	32
Gastrointestinal disorders	Diarrhoea	26	24

MedDRA system organ class	MedDRA reaction term	MedicineInsight count	TGA DAEN count
General disorders and administration site conditions	Oedema	18	1
Cardiac disorders	Palpitations	18	19
Skin and subcutaneous tissue disorders	Pruritus	13	37
Nervous system disorders	Dizziness	12	42

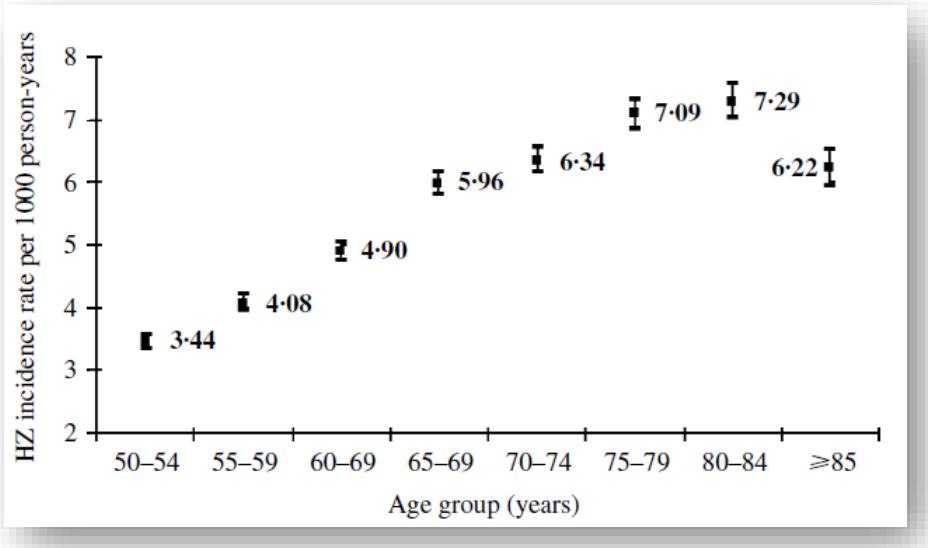
5. DISCUSSION

This is the first report to provide insights into herpes zoster in the primary care setting using MedicineInsight data, including the incidence of new cases, complications, laboratory testing, medicine utilisation and adverse events.

5.1. Patient profile with HZ

The average annual incidence in MedicineInsight was 6.2 new HZ cases per 1000 patients among individuals aged 35+ years, aligning with other Australian studies that report from 5.6 to 7 new cases per 1000 people across all ages.[2,4] As expected the incidence of HZ in MedicineInsight increased with age, peaking in patients aged 80 to 84 years, before decreasing after 85 years. These results align with other incidence rate patterns observed, including a study on the epidemiology of herpes zoster in the UK, based on a data source that is similar to MedicineInsight, the CPRD primary care database[12] (see Figure 2 and Figure 4).

FIGURE 4: HZ INCIDENCE RATE BY AGE GROUP – STUDY ON THE BURDEN OF HZ IN THE UK USING CPRD DATA[12]



The average annual incidence of HZ in patients aged 50+ years was 7.8 per 1000 patients in MedicineInsight and 5.2 per 1000 person-years in the UK study using CPRD data,[12] potentially higher in MedicineInsight due to differences between the Australian and UK populations and because the UK study was limited to immunocompetent patients who are at lower risk of HZ. An Australian study using the BEACH database of cross-sectional GP survey responses from 2006–13, estimated an annual incidence of 11.7 new HZ problems (including recurrences) per 1000 patients aged 50+ years.[4] The lower incidence estimate seen in this MedicineInsight report compared with the BEACH study might be explained in part because:

- MedicineInsight and BEACH are different types of data sources, and the studies used different patient samples, methodology and time periods
- the BEACH study included “recurrent problems” in their definition of new HZ cases, whereas the MedicineInsight report did not include recurrences of HZ in the definition
- some diagnoses may be recorded in the progress notes, which are not collected by MedicineInsight.

There was a proportion of patients in MedicineInsight who, despite not having a recorded diagnosis of HZ, were prescribed a pack size for one of the antiviral medicines that is only reimbursed on the PBS

for treating HZ. While these medicines are used to treat other herpes infections, because of the specific pack size prescribed, it is likely the majority of these prescriptions were for people who had HZ but their diagnosis was either not recorded by the GP or was entered in the progress notes which are not collected by MedicineInsight. Recording habits of GPs vary widely: it would be prudent to investigate this finding further and in future analyses consider widening the definition of HZ to include patients with a recorded diagnosis or a prescription for a HZ-specific pack size of an antiviral. While this finding needs further investigation, based on prescribing information, the total number of patients with HZ could be up to a third higher than the number of patients with a recorded diagnosis of HZ in MedicineInsight.

The incidence of HZ in MedicineInsight practices was highest in (and not significantly different between) New South Wales, Victoria, Queensland, South Australia, Tasmania and the Australian Capital Territory (ranging from 1.8 to 2.5 per 100 patients). There was some evidence to suggest that HZ incidence was lower in MedicineInsight practices in Western Australia (1.6 per 100 patients). Patients in MedicineInsight practices in the Northern Territory were significantly less likely to be diagnosed with HZ, with an incidence of 0.9 per 100 patients. The difference in incidence in the NT practices could be due to both the small sample size and sociodemographic differences in the practice population compared with MedicineInsight practices in the other states and territories.

In non-indigenous Australians the incidence of HZ was 2.2 per 100 non-indigenous patients compared with 1.4 per 100 indigenous patients (although the 95% confidence interval was comparatively wide, at 0.9 to 1.7 per 100 indigenous patients, indicating lower precision with this estimate). The difference in incidence between indigenous and non-indigenous patients could be explained by differences in the age distribution between the two groups, as HZ incidence sharply increases with age and the indigenous population have a younger age distribution.

Around 11% of patients with HZ were considered potentially immunocompromised in the year prior to their diagnosis, the majority of whom had record(s) of potentially immunosuppressive therapies which could increase the risk of herpes zoster, particularly in older patients.[2] This report provides an estimate of the proportion of patients who were ‘potentially immunocompromised’, rather than ‘definitely immunocompromised’, the latter being more difficult to ascertain using routinely collected health data. The detailed reasons for this are described in section 3.2.4.4.

5.2. Laboratory testing for HZ

The low number of total PCR tests ordered for suspected HZ events (n=931) was not surprising, given that HZ is routinely diagnosed clinically through the observation of the distinctive rash and symptoms. Only 13.1% of tests ordered were positive for the varicella zoster virus. Of the PCR tests in MedicineInsight, a fifth (n=196) were among patients with a recorded diagnosis of HZ. Interestingly, nearly all HZ PCR tests were ordered for patients in WA, the reasons for which need further exploration.

5.3. HZ-related complications

In this study one in four patients had a potentially HZ-related complication recorded within 12 months of their HZ diagnosis; as expected post-herpetic neuralgia was the most common complication affecting 18% of the population, and 2.5% of patients developed herpes ophthalmicus. The rate of herpes ophthalmicus was lower than the 10%–20% reported in other survey based studies,[10] possibly because patients access care for this condition outside of primary care (eg, opticians, hospitals). As explained in section 3.2.4.3, some conditions included in the definition of complications, such as pneumonia or stroke, occur commonly in the general population and may not be related to HZ; we recognise there will be some misclassification of conditions as HZ-related.

5.4. Prescribing patterns

Among the incident HZ population (35+ years), 65% had at least one prescription for an antiviral, compared to an Australian study using the BEACH database which found that antivirals were prescribed for 73.5% of new HZ problems managed in patients aged 50+ years.[4] The lower prescribing rate in MedicineInsight could be explained in part by the following factors.

- The different age groups studied. For example, if younger patients were less likely to be prescribed antivirals versus older patients (perhaps due to more uncertainty in the diagnosis in this age group), or if younger patients were to present less frequently within 72 hours of the rash versus older patients 50+ years.
- The BEACH study based the prescribing rate on the total number of prescriptions whereas the MedicineInsight study based the rate on the total number of patients with prescriptions (MedicineInsight patients with more than one prescription were only counted once).
- A proportion of patients in MedicineInsight were, despite not having a recorded diagnosis of HZ, prescribed a pack size for one of the antiviral medicines that is only reimbursed on the PBS for treating HZ. If the majority of these patients did indeed have HZ, despite the diagnosis not being recorded in MedicineInsight, the prescribing rate could be underestimated.

The proportions of medicines prescribed were similar between MedicineInsight (8% acyclovir, 53% famciclovir, and 38% valaciclovir) and the BEACH study (9% Aciclovir, 51% famciclovir and 40% valaciclovir). As expected, famciclovir and valaciclovir were the preferred medicines, given their greater bioavailability and less frequent dosing in comparison to aciclovir.[10]

5.5. Adverse events

In the entire MedicineInsight database, a total of 909 adverse events were recorded for the antiviral medicines of interest (famciclovir, valaciclovir, aciclovir), regardless of the indication for therapy. The most common adverse events were rash (n=151), nausea (n=69) and vomiting (n=57).

5.6. Conclusion

This report provides an introduction to the use of MedicineInsight data for HZ disease surveillance and will be expanded upon in Phase 2 to include information on vaccine surveillance.

The MedicineInsight resource provides the opportunity to better understand HZ within the Australian primary care setting. Based on these initial findings, some recommendations for further analyses include:

- Refining definitions, eg,
  - reviewing the definition of an HZ diagnosis, in consultation with experts, to understand the impact of including patients without a recorded diagnosis of HZ but with a relevant prescription and/or a positive test result for herpes zoster
  - conducting a validation study with contributing practices on HZ case ascertainment.
- Enhancing the statistical analyses, eg,
  - with age-standardisation
- Exploring the findings in more detail, eg,
  - further analysis of prescribing rates by age-group
  - understanding the relationship between age, being immunocompromised, and the risk of HZ
  - understanding recurrences of HZ
  - qualitative research on the HZ PCR testing rates.

With further detailed exploration of the findings in this report, the MedicineInsight resource is a valuable source of routinely collected data for surveillance.

6. GUIDE TO INTERPRETING DATA

When interpreting the information presented in this report, readers should note some of the limitations or caveats related to the MedicineInsight data:

- MedicineInsight data are dependent on the accuracy and completeness of data recorded in, and available for extraction from, the general practice clinical systems.
- Identification of conditions is dependent on the GPs recording these items in their clinical software systems. Conditions may be underreported in MedicineInsight data depending on GPs' recording practices.
- Our classification of HZ, HZ complications and immunocompromised conditions is based on commonly accepted definitions and has been reviewed by two GPs. However, there is likely to be variability in GPs' actual diagnostic labelling practices.
- Calculation of the relative proportion of different indications assumes that non-recording of conditions occurs at random.
- Medicine-use information from MedicineInsight relates to records of GP prescribing, and therefore differs in several important ways from national PBS dispensing data. Not all prescriptions and repeats will be dispensed, ie, prescription counts are an overestimate of dispensed prescription counts, specialist and hospital prescriptions are not included and there may be a delay of up to 12 months between prescribing and dispensing.
- Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Comparisons between regions should be interpreted with caution.
- A proportion of adverse reactions known to the GP may go unrecorded, eg, when the reaction is unremarkable or symptoms are managed elsewhere, eg, hospital.
- Coding of adverse reactions may differ between MedicineInsight and TGA for some reactions.
- Due to confidentiality issues we do not have access to progress notes, which may contain further information on reasons for prescriptions, reasons for encounters and diagnoses.
- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices.

7. APPENDICES

Appendix A: Glossary and abbreviations

Term	Definition	Description
95% CI	95% confidence interval	A 95% confidence interval provides information about a range of values that should contain the actual rate 95% of the time (95 times out of 100), as well as information on the direction and strength of the demonstrated effect. Wider confidence intervals reflect less certainty in the estimate of the rate. Confidence intervals enable conclusions to be drawn about the statistical plausibility and clinical relevance of findings.
ABS	Australian Bureau of Statistics	
ASGC	Australian Standard Geographical Classification	Used from 1984 to 2011 by the Australian Bureau of Statistics (ABS) to calculate geographical statistics. We use ASGC in this report to calculate rurality based on postcode (categorised as in major cities, inner regional, outer regional, remote and very remote areas).
ATC	Anatomical Therapeutic Chemical	System used to classify medicines into groups according to certain characteristics.
Average		Measurement of the 'central' value of a set of values.
BEACH	Bettering the Evaluation and Care of Health program	Cross-sectional program collecting information on GP activities in Australia.
Best Practice		Clinical management software for the GP.
CIS	Clinical information system	A generic term to describe one of several Australian national general practice software programs used by GPs to store patient/consultation/ prescription data (of which BP and MD are two examples).
Clinical Encounter	Any professional interchange between a patient and a healthcare professional	A clinical encounter was defined as all those encounters at the general practice that were: a) not identified as administrator entries nor encounters that had been transferred/imported from another practice (i.e. the "Provider ID" was valid and ≠ 0) and b) were not identified by predefined 'administration-type' terms found in the 'reason for encounter' field such as "administrative reasons"; "forms" recall", etc.
Clinically representative practice	A general practice that meets MedicineInsight data quality criteria and caters to 'typical' general practice patients rather than specialises, eg, in youth mental health	A clinically representative practice meets the following inclusion criteria applied by the MedicineInsight team: • established for at least 2 years before the end of the analysis period • has no interruptions to practice data of longer than 2 months in the 2 years to the end of the analysis period • records a history item, reason for encounter or reason for prescription in at least 10% of encounters • issues an average of at least 30 prescriptions per week • caters to usual general practice patients rather than specialises, eg, in youth mental health.

Condition		An illness or abnormality that interferes with a person's usual activities or wellbeing.
CRM	Customer Relationship Management	A database used for storing details of customers, etc. (eg, participating practices).
DoH	Commonwealth Department of Health	Federal department overseeing Australia's health system.
DUSC	Drug Utilisation Sub-Committee (PBAC)	Collects and analyses data on actual drug use and provides advice to PBAC.
DVA	Department of Veterans' Affairs (Australia)	Federal department responsible for delivering government programs for war veterans, defence force and federal police members and their dependents.
GP	General practitioner	
HZ	Herpes zoster	
Incidence		The number of new cases of a disease or condition in a population over a defined period of time. Can also be used to describe the number of new prescriptions or tests ordered over a period of time.
Incident		A new or 'first ever record' of a diagnosis of disease or condition in a patient previously unaffected
Longitudinal database		A set of statistical data that observes the same analysis units over a substantial period of time.
Median		The number separating the upper and lower half of a sample of values.
Medical Director 3		Clinical management software for the GP.
MedDRA		Standardised medical terminology for regulatory information about medical products used by humans. Allows the consistent coding of adverse drugs reactions to medicines.
PBAC	Pharmaceutical Benefits Advisory Committee	Committee making recommendations to the federal Minister of Health on which medicines should be available as pharmaceutical benefits.
PBS	Pharmaceutical Benefits Schedule	Program providing subsidised prescription medicines to Australians.
Practice		An organisation operating at one or more locations where GPs and other staff provide general practice consultations to the community, and which contributes data to MedicineInsight from a single clinical information system database.
Prevalence		Proportion of the population with a particular condition at a given time.
Rate		Measure or ratio of how two factors are associated with one another, eg, a proportion of patients with a condition or the incidence of prescriptions per consultation.
RPBS	Repatriation Pharmaceutical Benefits Scheme	
SAS	Statistical Analysis System (SAS Institute)	Statistical software program.
SEIFA	Socioeconomic indices for areas	Calculated by ABS index of relative socioeconomic advantage and disadvantage.

Site		The unit of data collection corresponding to either one practice or to several practices that share the same clinical system database. Practices combined into one site are typically under common administration or operating in the same geographical area.
TGA	Therapeutic Goods Administration	Australia's regulatory agency for medical medicines and devices.
TGA DAEN	TGA Database of Adverse Event Notification	

Appendix B: About MedicineInsight

The Australian Government funded NPS MedicineWise* in 2011 to establish and manage a longitudinal general practice data platform to improve the post-marketing surveillance of medicine use in Australia and support quality improvement activities in general practices. It is the first large-scale, national general practice data program in Australia that extracts longitudinal de-identified patient records from the software that general practices already use to manage patient records and write prescriptions.

MedicineInsight aims to:

- support quality improvement in participating general practices
- inform future policy and primary care research
- achieve better healthcare for Australians
- support sustainable Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Scheme (MBS).

By December 2016 the MedicineInsight program had recruited more than 550 general practices from around Australia to participate in the program. It currently includes administrative, clinical and prescribing records for more than 3.5 million active patients and more than 2000 GPs.

How MedicineInsight collects data

MedicineInsight extracts anonymised clinical data from general practices that use one of two CISs: *Best Practice* or *Medical Director 3.* The data available in these systems includes data entered directly by GPs or practice staff as well as system-generated data such as the time and date that records are accessed.

An all-of-practice data collection is conducted when a practice joins MedicineInsight. The extraction tool then collects incremental data weekly, enabling development of a longitudinal database in which patients within practices can be tracked over time.

The data MedicineInsight collects from general practices includes:

- patient demographic and clinical data entered directly by GPs and practice staff into the system
- system-generated data (eg, time and date the electronic medical records of a patient are accessed)
- practice and GP information for the administration of quality improvement activities by NPS MedicineWise
- prescriptions and pathology data. The pathology data is transferred directly into the CIS from pathology providers.

Patient level data are de-identified ‘at source’, meaning the patients’ personal identifiers such as name, exact date of birth and street address are not extracted by the tool. The data held in the MedicineInsight database are anonymous; however, each patient, practice and provider has a unique identifying number which enables patient data to be matched across multiple data tables within each practice.

Figure B1 provides an overview of how the MedicineInsight data flows, including how general practice reports and patients lists are provided back to a general practice, where any re-identification of patients occurs, and how data extracts and aggregated reports are provided.

* NPS MedicineWise is an independent, evidence-based, not-for-profit organisation established in 1998, which receives funding from the Australian Government Department of Health. Our mission is to enable the best decisions about medicines, health technologies and other health choices for better health and economic outcomes. Our vision is to lead innovation and improvement in health care by building trust, implementing change and demonstrating impact.

FIGURE B1 HOW MEDICINEINSIGHT DATAFLOW WORKS

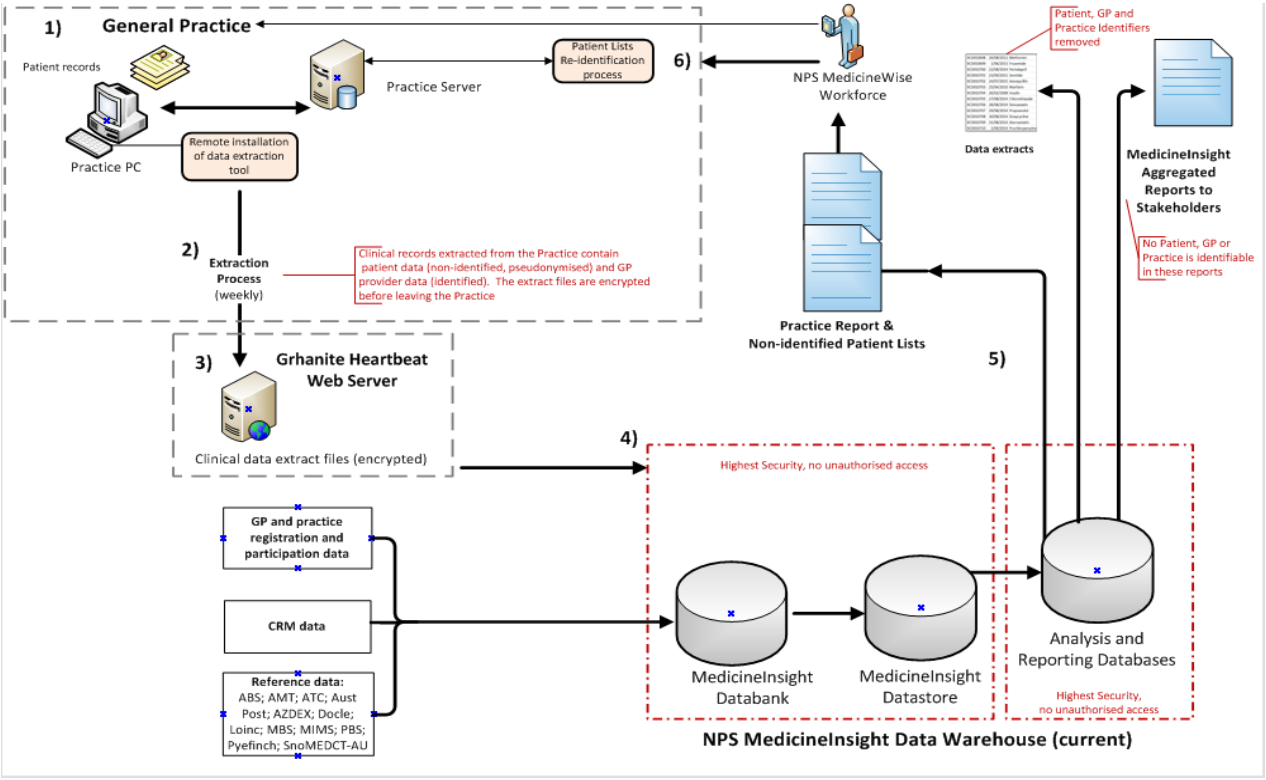
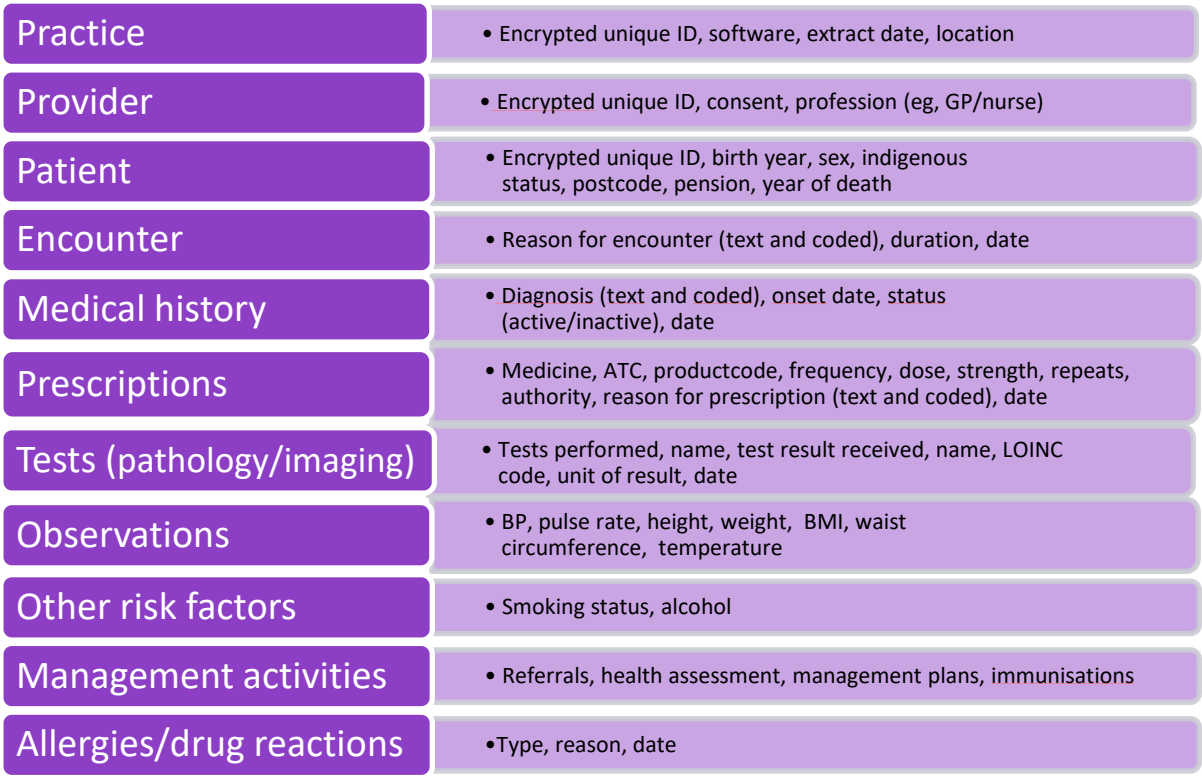


Figure B2 provides an overview of the data and the fields that are available from the MedicineInsight data extracted from the CISs. The data includes both coded and free-text fields. Not all the data fields contained in Figure B2 are currently available for inclusion in this report. For example, imaging results are saved in a general practice record in a 'report' PDF format rather than with the detailed results that are available on pathology tests. At this point MedicineInsight is unable to extract the imaging data from the PDF. Also progress notes, that could potentially identify individuals, are not collected by MedicineInsight.

Depending on the CIS at their practice, clinicians use coding systems such as 'Docle', 'Pyefinch' or 'ICPC' to enter medical terms into their system. However, it is not mandatory to use a code and clinicians can enter medical terms as free text. Some data used in this report, such as medical conditions, are derived from using a combination of different fields and analysis of the free text.

FIGURE B2 OVERVIEW OF MEDICINEINSIGHT DATA FIELDS



Recruitment of practices

Practices are recruited into MedicineInsight via a number of methods:

- The NPS MedicineWise Clinical Service Specialists (CSSs) who visit more than 15,000 GPs across Australia each year discuss the benefits of being involved in MedicineInsight with the GPs.
- The MedicineInsight recruitment team, and in the past other organisations that have been commissioned to assist with recruitment, make an initial phone call or email to practices in areas where recruitment is lower.
- GPs and practices may make expression of interest submissions after visiting the MedicineInsight website or hearing about MedicineInsight at conferences and other meetings and through other stakeholder groups such as Primary Health Networks (PHNs).
- Practices are recruited through specific targeted initiatives in which the PHNs are using MedicineInsight to support specific additional quality improvement initiatives (eg, Tasmania and Hunter New England and Central Coast).

After a practice agrees to participate in MedicineInsight and completes the paperwork, they are contacted by the extraction tool vendor from the University of Melbourne, who organise the remote installation of the extraction tool (GRHANITE), and by their local CSS, who organises their first MedicineInsight visit using the data extracted from the practice.

Figure B3 shows the geographical distribution of MedicineInsight practices and Table B1 describes the size and regional characteristics of MedicineInsight practices.

FIGURE B3 APPROXIMATE DISTRIBUTION OF MEDICINEINSIGHT PRACTICES.

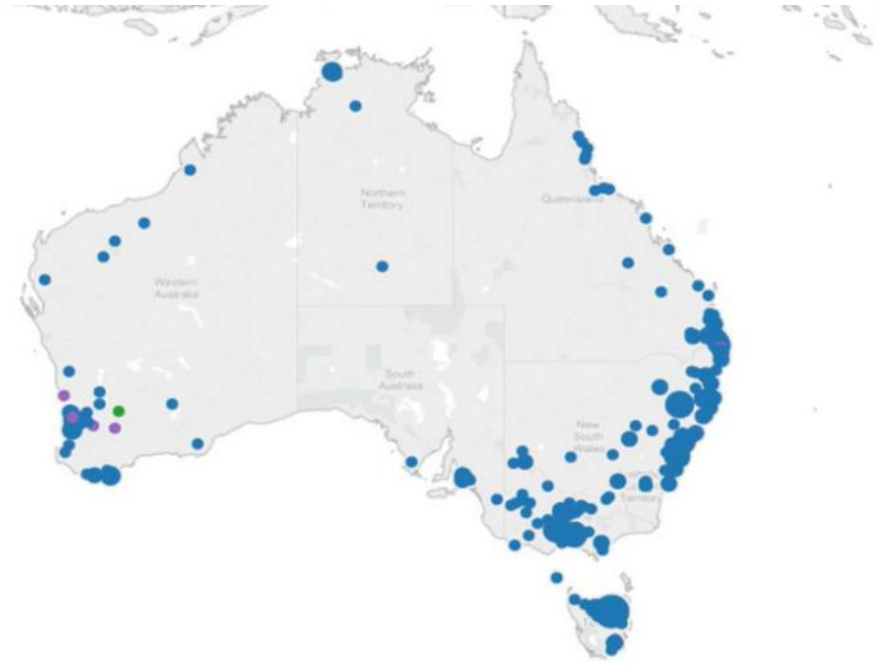


TABLE B1 CHARACTERISTICS OF MEDICINEINSIGHT PRACTICES (JUNE 2016)

Characteristic	MedicineInsight (June 2016) n=557
	%
Size	
1 GP	7
2–5 GPs	50
6 or more GPs (Note: 29% missing info for eMI)	44
Location (rurality)	
Major city	59
Inner/outer regional	37
Remote/very remote	3
State/Territory	
NSW	29
Vic	23
SA	4
Qld	20
Tas	8
WA	12
NT	2
ACT	2

How are the data used?

Increasingly there is recognition of the expanding uses for MedicineInsight data. At the end of December 2016 the data have been used for a range of activities, including:

- Post-marketing surveillance, including for drugs prescribed for chronic obstructive pulmonary disease (COPD), diabetes and asthma, antidepressants anticoagulants, testosterone, ezetimibe, quetiapine and antibiotics
- informing medicines policy, including a review of biological medicines used in general practice, monitoring the impact of changes to PBS restrictions for testosterone, and reviewing the use of antibiotics commonly used for respiratory tract infections
- supporting quality improvement activities in general practice by preparing monthly reports for each practice in areas including improving care for patients with diabetes, stroke, COPD, depression and antibiotic use. The reports compare practice activity with best practice guideline and comparable practice groups and can be accessed by practice staff and/or discussed at clinical meetings facilitated by an NPS MedicineWise Clinical Services Specialist (CSS). These meetings provide practice staff with an opportunity as a group to reflect on current practice, decide on areas for improvement and on how these may be implemented.
- primary care research, including evaluation of vaccination coverage, cardiovascular disease, chronic kidney disease, diabetes, pain, obesity and lung cancer. For more details see the NPS MedicineWise *MedicineInsight data* web page (www.nps.org.au/health-professionals/medicineinsight/interested-in-medicineinsight-data).

Quality improvement activities

Since 2013, NPS MedicineWise has been delivering routine practice reports from MedicineInsight for GPs, showing trends in clinical practice and prescribing to support effective educational interventions and quality improvement programs to assist GPs in delivering the best care to their patients.

In the 2015–16 financial year, more than 2000 health professionals from 318 general practices participated in MedicineInsight visits, which included a tailored practice report and facilitated meeting. Topics have included type 2 diabetes, stroke prevention, antibiotics and managing depression.

Additionally, all practices have access to an online report repository, allowing them to download their tailored updated practice reports as required. Since December 2016 more than 500 confidential practice reports are provided monthly to participating practices via an online portal and through clinical meetings facilitated by the NPS MedicineWise team of 61 CSSs. Reports are tailored for each practice and compare procedures and prescriptions between 'Your Practice 12 months ago', 'Your Practice now', and in comparison to all other MedicineInsight practices as well as information on data quality and completeness.

Data governance

NPS MedicineWise is the data custodian for the MedicineInsight program. Ownership of the original data remains with participating general practices, and MedicineInsight only contains anonymised patient data. The pilot MedicineInsight program was approved by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee in January 2013.

NPS MedicineWise has a data governance framework and policy to ensure rigour and transparency, and that information is collected ethically, legally, securely and confidentially. The framework complies with national and State legislation, including, but not limited to, Australian privacy laws and the Australian Privacy Principles.

NPS MedicineWise has an independent, external Data Governance Committee that was established in 2015 to provide advice to NPS MedicineWise on all aspects of the MedicineInsight data access model. The committee consists of external academics, practising GPs, an expert on data security, the Australian Bureau of Statistics (ABS), and legal and consumer advocates.

This group provides guidance and expertise to ensure appropriate governance is in place and provides advice to NPS MedicineWise on general data governance issues, the data access framework and decisions on data access for specific projects applying for MedicineInsight data.

A further separate independent development committee has been established to advise NPS MedicineWise on transition to a 'big data' environment on topics including data storage, security, coding standards, analysis, data accessibility and record linkage.

Further information and the MedicineInsight data book are available on the NPS MedicineWise website at www.nps.org.au/health-professionals/medicineinsight/interested-in-medicineinsight-data.

Representativeness of MedicineInsight data

To investigate the representativeness of MedicineInsight data, we compared:

- available demographic data for MedicineInsight GPs who had consented to participate in quality improvement activities to the most recent national data from General Practice Workforce Statistics 2014.[13]
- the demographics of MedicineInsight patients to the most recent national data from MBS statistics and a range of national data.[14,15,16,17,18,19]

Participating GPs

At June 2016, 1,511 GPs in MedicineInsight practices had consented to participate in quality improvement activities. These GPs are a younger-aged cohort and more likely to be female than those in national data. GPs located in NSW, Qld, WA and NT are currently under-represented in our data. Table B2 provides a detailed comparison of characteristics of these GPs (when data were available) to the available national data.

TABLE B2 CHARACTERISTICS OF MEDICINEINSIGHT GPS (WHO ARE INVOLVED IN QI ACTIVITIES) COMPARED WITH NATIONAL GP DATA[13]

Characteristic	MedicineInsight (August 2016) n=1483 %	DoH[13] (2014) n=33,275 %
Sex (eMI missing: n=569)		
Male	52	56
Female	48	44
Age group (eMI missing: n=597)		
Under 35	16	13
35–44	25	24
45–54	30	26
55–64	22	23
65+	7	13
Location (eMI missing: n=3)		
Major city	60	67
Inner regional	27	19
Outer regional	11	9
Remote/very remote	2	4
State/Territory		
SA	6	8
Vic	38	24
NSW	22	31

Characteristic	MedicineInsight (August 2016) n=1483 %	DoH[13] (2014) n=33,275 %
Qld	17	21
Tas	8	3
WA	8	10
NT	0	2
ACT	1	1

MedicineInsight patient cohort

MedicineInsight active patient cohort includes all patients who have visited a practice at least once in the previous 3 years. There are currently 4,354,413 patients in the patient cohort. This was based on data extracted from 506 MedicineInsight practices.

Patients presenting at MedicineInsight GP encounters in 2016 had a similar age profile to that of recipients of general practice-related MBS items[14] (Figure B4). The sex profile is also similar, with most MedicineInsight patients and MBS item recipients being female (54% vs 50%) (Table B3).

MedicineInsight has a similar proportion of Aboriginal and Torres Strait Islander patients to that in the BEACH data[16] (1.7%) but a smaller proportion compared with ABS census data[17] (2.5%). MedicineInsight has a similar representation of MedicineInsight patients across State/Territory and geographical areas, with a few exceptions: a higher proportion of patients in Tasmania and Western Australia, and fewer patients in South Australia (Table B3).

FIGURE B4 PATIENTS AT MEDICINEINSIGHT ENCOUNTERS (JUNE 2016) COMPARED WITH PATIENTS RECEIVING MBS GP SERVICES[14]

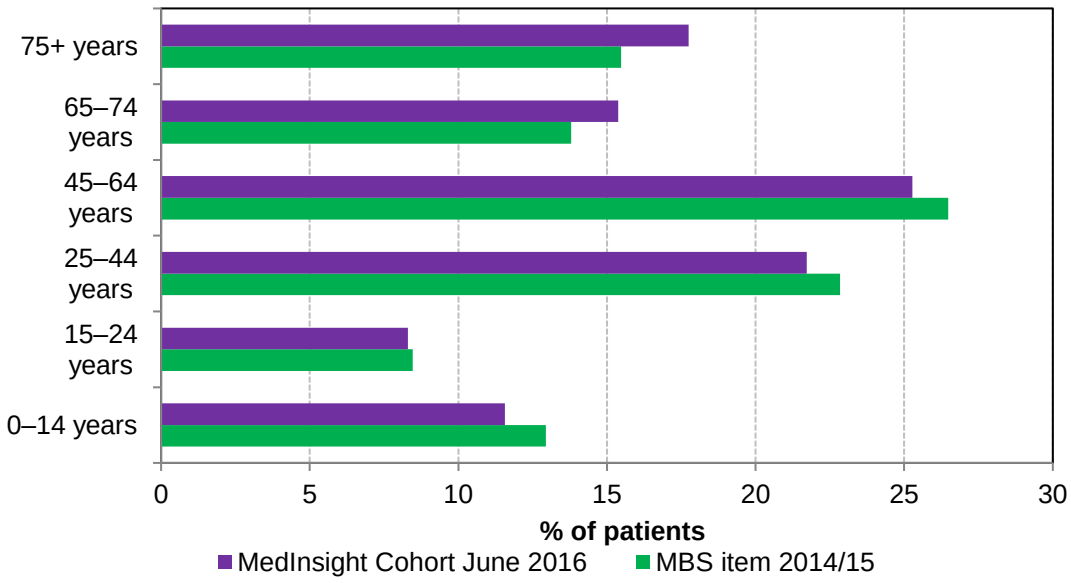


TABLE B3 CHARACTERISTICS OF MEDICINEINSIGHT PATIENT COHORT COMPARED WITH OTHER NATIONAL DATA

Sociodemographic characteristic	MedicineInsight cohort June 2016 n=4,354,413 %	National data (various sources) %
Gender		
Male	45.9	49.7[14]
Female	53.8	50.3

Sociodemographic characteristic	MedicineInsight cohort June 2016 n=4,354,413 %	National data (various sources) %
Missing/Other	0.4	
Aboriginal or Torres Strait Islander	1.9	1.7[16] 2.5[17]
Pension	24.5	23.1[18]
DVA	0.8	0.7[19]
Region		
Major city	66.8	70.9[15]
Inner regional	21.1	18.1
Outer regional	9.5	8.8
Remote	1.3	1.4
Very remote	0.3	0.9
State/Territory		
NSW	29.6	32.0[15]
Vic	24.3	24.8
SA	3.0	7.2
Qld	19.2	20.1
Tas	6.1	2.2
WA	13.8	11.0
NT	1.6	1.0
ACT	1.8	1.6

Weighting

Currently no weighting of the data has been undertaken to account for potential differences in the characteristics of the MedicineInsight patients and practices compared with those of national patients and practices. There are many technical considerations to be made about when and how to apply weightings to the dataset. Work is underway to determine the best approach to be undertaken in future analyses.

Completeness of MedicineInsight data

Analysis and interpretation of MedicineInsight data were limited by the accuracy and completeness of data entered, as well as the representativeness of the cohort compared with the population that usually attends Australian general practices.

To explore the completeness of the data we examined the completeness of a series of key indicators related to patient demographics, patient risk factors and condition recording in data extracted from 450 practices. Table B4 shows that most demographic variables are complete, and the recording of risk factors such as smoking status and blood pressure was moderately high and improving. Usually at least one diagnosis or reason for visit was recorded per visit; but there remains significant variation across the individual fields. We are working with practitioners to improve data completeness.

Progress notes within clinical records can provide richer information; however, due to privacy concerns and the inability to fully de-identify this information to date, we are not currently able to extract from this field.

TABLE B4 COMPLETENESS OF KEY MEDICINEINSIGHT INDICATORS IN 450 MEDICINEINSIGHT PRACTICES

Completeness indicator	Completeness assessment
Patient demographics practices	**Median (interquartile range)**
Year of birth field completeness	100% (100%–100%)
Sex field completeness	100% (100%–100%)
Indigenous status completeness	72% (47%–88%)

Completeness indicator	Completeness assessment
Patient risk factors recording practices	
Smoking status completeness	69% (58%–80%)
Patients 40+ years with a BP recording in last 12 months	42% (35%–49%)
Patients 16+ years with a BMI recording in last 12 months	15% (10%–22%)
Condition recording (last 12 months)	
History recorded at encounter (any)	77% (54%–90%)
History recorded at encounter (coded)	72% (60%–85%)
Reason for prescription (any)	33% (16%–51%)
Reason for prescription (coded)	17% (7%–29%)
Reason for visit (any)	71% (40%–88%)
Reason for visit (coded)	56% (27%–73%)

Appendix C: Pathology testing LOINC codes and text terms

TABLE C1 HZ PCR PATHOLOGY TEST DEFINITION

LOINC CODE	Atomic Test Name
11483–5	Varicella zoster DNA

Appendix D: Medicine and condition definitions

Medicine definitions for the treatment of HZ

TABLE D1 MEDICINES OF INTEREST FOR THE TREATMENT OF HZ

Medicine name
Aciclovir
Aciclovir 800 [Pharmacor] Tablet
Aciclovir Disp'tablet
Aciclovir Tablet
Aciclovir [Pharmacor]
Acihexal
Acihexal 800 mg Tablet
Acihexal Tablet
Acyclo-V
Acyclo-V 800 800 mg Tablet
Acyclo-V 800 Tablet
Apo-Famciclovir
Apo-Famciclovir Tablet
Apo-Famciclovir Tablets 250 mg, 20, 1
Apo-Famciclovir Tablets 250 mg, 21, 1
Apo-Famciclovir Tablets 500 mg, 30, 1
Apo-Valaciclovir
Apo-Valaciclovir Tablets 500 mg, 10, 2
Apo-Valaciclovir Tablets 500 mg, 30, 1
Apo-Valaciclovir Tablets 500 mg, 42, 1
Auro-Famciclovir
Chemmart Famciclovir
Chemmart Valaciclovir
Ezovir
Ezovir Tablet
Ezovir Tablets 250 mg, 21, 1
Famciclovir
Famciclovir AN

Medicine name
Famciclovir Generichealth
Famciclovir Sandoz
Famciclovir Sandoz Tablet
Famciclovir Sandoz Tablets 250 mg, 21, 1
Famciclovir SCP
Famciclovir Tablet
Famciclovir-GA
Famlo
Famvir
Famvir 250 mg Tablet
Famvir 500 mg Tablet
Famvir Tablet
Favic
Favic 250 Tablet
Genrx
Genrx Aciclovir
Genrx Aciclovir 800 mg Tablet
Shilova
Shilova Tablets 500 mg, 30, 1
Vaclovir
Vaclovir Tablet
Vaclovir Tablets 500 mg, 10, 2
Vaclovir Tablets 500 mg, 30, 1
Vaclovir Tablets 500 mg, 42, 1
Valaciclovir
Valaciclovir (as hydrochloride) Tablet
Valaciclovir Actavis
Valaciclovir Actavis Tablets 500 mg, 30, 1, 8134d
Valaciclovir AN
Valaciclovir GA
Valaciclovir GA Tablet
Valaciclovir Generichealth
Valaciclovir Pfizer
Valaciclovir RBX
Valaciclovir RBX Tablet
Valaciclovir Sandoz
Valaciclovir Sandoz Tablet

Medicine name
Valaciclovir Sandoz Tablet 500 mg, 10, 2
Valaciclovir SZ
Valaciclovir Tablet
Valacor
Valacor 500 Tablet
Valacor Tablets 500 mg, 30, 1
Valnir
Valnir Tablets 500 mg, 30, 1
Valtrex
Valtrex 500 mg Tablet
Valtrex Tablet
Valtrex Tablets 500 mg, 30, 1
Valvala
Valvala Tablet
Zelitrex
Zelitrex Tablet
Zovirax
Zovirax 800 mg Tablet
Zovirax 800 mg Disp'tablet
Zovirax 800 mg Tablet
Zovirax Disp'tablet

TABLE D2 MEDICINES AND THERAPIES THAT CAUSE IMMUNOSUPRESSION

Medicine name	Therapy - relevant search terms	Therapy - exclusions
Sulfasalazine	Chemo$	Chemosis$
Prednisolone		
Prednisone	Chemoprophyl$	
Cyclophosphamide	Radiotherapy	
Mercaptopurine	Radiation therapy	
Rituximab	Chemo-radiation	
Mycophenolate	Radiation treatment	
Abatacept	Radioactive iodine	
Etanercept	Radioiodine	
Adalimumab	Brachytherapy	
Ciclosporin	Therapy - exclusions	
Tacrolimus		
Azathioprine		
Methotrexate		

Condition definitions

A patient was defined as having a history of a condition of interest if they had ever had a recorded relevant term for that diagnosis in any designated text or code field in relevant diagnosis tables (history [currently active or inactive], reason for prescription and reason for visit).

Table D3 provides a summary of the terms included for HZ.

Terms used to identify immunocompromising comorbidities can be found in Table D4.

TABLE D3 DEFINITION FOR HZ; INCLUDED TERMS

Condition	Source	Included search terms	Excluded search terms
HZ	Text	herp$ and zost$	prevent$
HZ	Text	varicel$ and zost$	prophyl$
HZ	Text	shingle$	Imm$
HZ	Text	herpes zoster neuralg$	vac$
HZ	Text	neuralgia post herp$	Test$
HZ	Text	herpetic neuralg$	
HZ	Text	ramsay hunt	

TABLE D4 DEFINITION FOR IMMUNOCOMPROMISING CONDITIONS; INCLUDED/EXCLUDED TERMS

Condition	Source	Included search terms	Excluded search terms
HIV	Text	HIV	HIV serology / test
HIV	Text	AIDS	HIV exposure / contact
HIV	Text	Acquired Immunodeficiency Disease	HIV negative / -ve
HIV	Text	Human Immunodeficiency Virus	HIV counselling
Leukaemia	Text	Leukaemi$	
Leukaemia	Text	Leukemi$	
Leukaemia	Text	CLL	
Leukaemia	Text	CML	
Leukaemia	Text	AML	
Lymphoma	Text	Lymphoma	Lymphomatoid
Lymphoma	Text	Lymphosarc$	Pseudolymphoma
Lymphoma	Text	Hodgkins	

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3 Yawn BP, Saddier P, Wollan PC, et al. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. Mayo Clin Proc 2007;82:1341-9

4 Stein AN, Britt H, Harrison C, et al. Herpes zoster burden of illness and health care resource utilisation in the Australian population aged 50 years and older. Vaccine 2009;27:520-9.

5 Dworkin RH, Portenoy RK. Proposed classification of herpes zoster pain. Lancet 1994;343:1648.

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