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BMJ Open

Compliance with pathology testing guidelines in Australian general practice: protocol for a secondary analysis of electronic health record data

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024223
Article Type:	Protocol
Date Submitted by the Author:	15-May-2018
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Keywords:	<p>Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, PATHOLOGY, PRIMARY CARE</p>

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Manuscripts

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3 **Compliance with pathology testing guidelines in Australian general practice: protocol for a**
4 **secondary analysis of electronic health record data**

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3 **Pathology testing in Australian general practice and compliance with guideline**
4 **recommendations: A study protocol for a secondary analysis of electronic health record data**
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6
7 **ABSTRACT**
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10 **Introduction** In Australia, general practitioners usually provide the first point of contact for patients
11 with non-urgent medical conditions. Appropriate and efficient utilisation of pathology tests by general
12 practitioners forms a key part of diagnosis and monitoring. However over- and under- utilisation of
13 pathology tests have been reported across several tests and conditions, despite evidence-based
14 guidelines outlining best practice in pathology testing. There are a limited number of studies
15 evaluating the impact of these guidelines on pathology testing in general practice. The aim of our
16 quantitative observational study is to define how pathology tests are used in general practice and
17 investigate how test ordering practices align with evidence-based pathology guidelines.
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21 **Methods and analysis** Access to non-identifiable patient data will be obtained through electronic
22 health records from general practices across three primary health networks in Victoria, Australia.
23 Numbers and characteristics of patients, general practices, encounters, pathology tests, and problems
24 managed over time will be described. Overall rates of encounters and tests, alongside more detailed
25 investigation between subcategories (encounter year, patient's age, gender, and location, and general
26 practice size) will also be undertaken. To evaluate how general practitioner test ordering coincides
27 with evidence-based guidelines, five key candidate indicators will be investigated: full blood counts
28 for patients on clozapine medication; international normalised ratio (INR) measurements for patients
29 on warfarin medication; glycated haemoglobin (HbA1c) testing for monitoring diabetes; vitamin D
30 testing; and thyroid function testing.
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47 **Ethics and dissemination** Ethics clearance to collect data from general practice facilities has been
48 obtained by the data provider from the RACGP National Research and Evaluation Ethics Committee
49 (NREEC 17-008). Approval for the research group to use these data has been obtained from
50 Macquarie University (5201700872). This study is funded by the Australian Government Department
51 of Health Quality Use of Pathology Program (Agreement ID: 4-2QFVW4M). Findings will be
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3 reported to the Department of Health and disseminated in peer-reviewed academic journals and
4 presentations (national and international conferences, industry forums).
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7 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

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- 10 • The study population will be drawn from a large region in Victoria, Australia, and is expected
11 to contain a large sample population (data from approximately 350 general practices), along
12 with a large number of demographic variables (e.g., region, gender, age).
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- 15 • Electronic health records contain a vast amount of information on patients, allowing us to
16 control for potential interacting or predictive variables on patient outcomes using statistical
17 modelling.
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- 20 • Some electronic health record fields may not be completely standardised across practices and
21 could contain inconsistencies and missing information; which may limit the volume of data
22 that can be extracted and analysed.
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- 25 • Some medications being investigated in this study may be prescribed and/or monitored by
26 specialists, which may result in cases being missed.
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32 **INTRODUCTION**

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35 In Australia, general practitioners (GPs) are usually the first point of contact for patients with non-
36 emergency health problems. They play an important role in the early detection, prevention (including
37 shared-care arrangements) and treatment of disease (1). Pathology tests are a key part of general
38 practice assisting GPs in diagnosing, screening, treating, and monitoring diseases. The past decade has
39 seen an increase in both visits to and problems managed by GPs in Australia, resulting in an estimated
40 24.2 million additional pathology tests being ordered in 2015-2016 compared to 2006-2007 (2).
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49 Appropriate and timely utilisation of pathology tests can improve the quality and outcome of patient
50 care. However, both over- and under- utilisation of pathology tests have been frequently observed in a
51 range of clinical scenarios (3,4). Several guidelines have been established to encourage better
52 utilisation of pathology tests among GPs across Australia, the US, Canada, and the UK. These include
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3 initiatives such as *Choosing Wisely* (5), *National Institute for Health and Clinical Excellence (NICE)*
4 (6), and *Royal Australian College of General Practitioners (RACGP) Guidelines for preventative*
5 *activities in general practice* (7). Currently, there is little evidence on how test ordering practices by
6
7 GPs align with these recommendations and guidelines in Australia, and elsewhere. A survey of 600
8
9 US doctors revealed only 21% of doctors were familiar with the *Choosing Wisely* campaign.
10
11 However doctors aware of the campaign had a lower proportion of unnecessary pathology testing (8).
12
13 In Australia, increased awareness of best-practice in vitamin D test ordering is reported to have
14
15 contributed to a reduction in healthcare costs and potentially unnecessary tests (9). Considering the
16
17 importance of pathology testing for managing diseases, a better understanding of how pathology
18
19 testing by GPs coincides with evidence-based guidelines will be invaluable for the success of
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21 management and disease-prevention strategies.
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27 Until recently, the survey-based *Bettering the Evaluation and Care of Health (BEACH)* study
28
29 provided the most comprehensive data on Australian GP activity (2). However, its cross-sectional
30
31 design prevented it from reporting longitudinal patient level changes and outcomes. The BEACH
32
33 study was discontinued in 2016, and has since left a gap in our understanding of GP activity;
34
35 particularly in relation to pathology test ordering. The extensive use of computers by Australian GPs
36
37 has prompted interest in the use of electronic health record (EHR) data as a research source for
38
39 monitoring the quality of GP services, and has led to research and publications based on EHR data
40
41 (10). The Australian Department of Health funded NPS Medicinewise MedicinesInsight dataset
42
43 contains a national collection of electronic health records (EHRs) from 650 practices covering over
44
45 3,300 GPs and nearly 3.6 million active patients (11). This dataset has been used in several population
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47 health research projects, and has demonstrated the value of EHR data in research (12). This study will
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49 use EHR data from the POLAR Data Space, containing de-identified data from consenting general
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51 practices collected on behalf of Australian PHNs from approximately 350 practices. POLAR Data
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53 Space has added measures to ensure robust and accurate data, and implements standardised
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55 terminologies to make the data more approachable for research use. This study, undertaken in
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57 collaboration with POLAR Data Space Research Consortia and its associated Primary Health
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3 Networks (PHNs), will facilitate a comprehensive analyses of general practice activity and its
4 relationship to pathology testing in Australia through EHR data.
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8 **Objectives:**

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12 The objectives of this study are to:

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14 1. Describe general practice activity and characteristics of pathology test ordering based on
15 electronic health record data;
- 16
17 2. Investigate compliance with evidence-based guidelines to determine the appropriateness and
18 quality use of pathology in general practice.
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23 **METHODS AND ANALYSES**

24 **Study design**

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27 A retrospective observational study of Australian general practice health records and pathology
28 testing data.
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33 **Data source**

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36 Data to be used in this study will be provided by the POLAR Data Space (10). POLAR Data Space
37 collects de-identified data from consenting general practices on behalf of Australian PHNs: including
38 Gippsland, Eastern Melbourne, and South Eastern Melbourne PHNs. Data are extracted from
39 approximately 350 practices in urban and rural regions in Victoria, Australia. The primary purpose of
40 the data collection is to provide information to improve patient care at the practice level and
41 population health initiatives at the PHN level. POLAR Data Space has ethics approval for the
42 collection, storage and de-identification of the data which it makes available for approved research
43 governed by the involved PHNs.
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53 The data source will include pooled general practice patient data extracted from Best Practice,
54 Medical Director, and Zedmed EHRs. Data will include de-identified demographic information about
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3 patients and general practices, as well as visit records (diagnosis, past history, medications) and
4 pathology test records (test name and result). Both historical and current information about patients
5 will be acquired, providing a longitudinal record.
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8 9 **Study Population**

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11 The study population will consist of all patients who visited any of the general practices included in
12 the study, and had their visit recorded in the practices' EHR software.
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15 16 **Variables**

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18 The following criteria will be adopted to accurately describe general practice activity and ensure data
19 quality: (i) A patient will be distinguished by a unique (non-identifiable) patient code recorded within
20 a general practice and included if determined to be an active patient (i.e. has visited the GP three or
21 more times in the past two years, not deceased; (ii) An encounter (i.e. consultation, visit) will be
22 defined as a patient visit recorded by a doctor or nurse during which an action (e.g. consultation,
23 prescription) is performed, and will be identified through a variable indicating the visit type (e.g.
24 surgery, administrative, phone call); (iii) A pathology test will be defined as either a panel of
25 interrelated tests (e.g. full blood count) or an individual test (e.g. troponin test); (iv) Where possible,
26 standardised records such as Logical Observation Identifiers Names and Codes (LOINC) and
27 Systematized Nomenclature of Medicine (SNOMED) terminologies will be prioritised to identify
28 variables; otherwise, free-text data will be searched for terms of interest (e.g. "diabetes" or its
29 abbreviated forms in the diagnosis field, excluding "not diabetes").
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44 **Analyses**

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46 Data examination and analysis will be performed using Stata/MP 15.1 (StataCorp, College Station,
47 Texas, USA). The methods outlined in this protocol are structured according to the *Strengthening the*
48 *Reporting of Observational Studies in Epidemiology* (STROBE) checklist of items to be included in
49 observational studies (13).
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54 ***Characteristics of general practice activity and pathology testing***

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3 In line with Objective 1 of this study, we will analyse and describe Australian general practice
4 characteristics and activity. These characteristics can subsequently be compared to reports on national
5 demographics and healthcare statistics, such as *Australian Institute of Health and Welfare's* (AIHW)
6 annual reports.
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11 Sample population characteristics will be reported. This will include describing the characteristics of
12 patients, general practices, encounters, tests, and problems managed across time. Subsequent analyses
13 will describe overall median rates of encounters and tests, alongside more detailed investigation
14 between subcategories (encounter year, patient's age, gender, and postcode, and number of active
15 general practitioners in practice) using the following indicators: encounters per patient per year, and
16 tests per encounter.
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24 The differences between subcategories will be further described as incidence rate ratios by generalised
25 linear modelling (Poisson or negative binomial, whichever is appropriate).
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28 ***Best practice guidelines-based analyses***

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31 In line with Objective 2 of this study, we will describe the extent to which pathology ordering
32 practices among Australian GPs aligns with evidence-based pathology testing guidelines. Five initial
33 candidate indicators have been identified for analyses.
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37 **1) Monitoring patients on clozapine medication**

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40 Rationale:

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42 Clozapine is a highly effective antipsychotic drug that is used for managing chronic schizophrenia.

43
44 However, clozapine use can result in neutropenia in nearly two percent of patients, and
45 agranulocytosis in one percent (14); warranting close monitoring of patients taking clozapine.

46
47 Although clozapine is prescribed by specialists, monitoring is more frequently managed by GPs
48 through shared-care arrangements (15). After 18 weeks of initiation and monitoring under a specialist,
49 GPs can also prescribe clozapine. Australian guidelines recommend patients on clozapine medication
50 have blood tests for white blood cell and neutrophil counts weekly for the first 18 weeks of initiation,
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3 and monthly thereafter (16,17). Furthermore, a patient cannot obtain clozapine from the pharmacist
4 without a recent blood test. Currently, the state of monitoring for patients on clozapine medication is
5 not known.
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8 9 Analysis:

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11 The study population will be patients who are being prescribed clozapine by the GP (and therefore
12 also needing to be monitored). The timeframe will include records after the first entry of the
13 prescription into the EHR software, and before medication is discontinued (or patient is deceased or is
14 no longer an active patient). The demographic characteristics of patients on clozapine medication as
15 well as number of full blood counts for these patients will be described overall, by patient gender, age,
16 and location, general practice size, and year of test. The number of full blood counts per patient per
17 year will also be described, overall and by the demographic characteristics, by counting the number of
18 full blood count tests conducted for each patient on clozapine medication for each available year.
19 Subsequently, the median number of full blood count tests per patient per year will be calculated, with
20 the inter-quartile range. For patients with more than one test, the time between tests will be
21 determined. Subsequently, median time between tests will be calculated, with the inter-quartile range.
22 As clozapine may also be prescribed by specialists, it may not be possible to determine when the
23 medication was initiated through the EHR software. Consequently, it may not be possible to
24 differentiate patients who require weekly tests from patients who require monthly tests. Nonetheless,
25 it is expected patients on clozapine medication will have at least one full blood count test within
26 approximately four to six weeks of a prior test; which will indicate compliance with guidelines.
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44 **2) Measuring international normalised ratio (INR) levels for patients on warfarin medication**

45 46 Rationale:

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48 Warfarin is a highly effective and widely-used anticoagulant in Australia. However, it is also one of
49 the most common causes of prescribed medication-related mortality, due to its risk of causing
50 bleeding (18). Best practice guidelines recommend that the initiation of warfarin medication should be
51 accompanied by frequent International Normalised Ratio (INR) measurements until a stable
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3 therapeutic range is reached. After INR levels are stable, testing frequency should be once every four
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5 to six weeks: unless a change (e.g. initiation of another medication) which can affect INR levels
6
7 occurs (19,20). Failure to correct INR levels is associated with increased mortality (21).

8 9 Analysis:

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11 The sample population will be patients with a warfarin prescription. Only data entered after the first
12
13 instance the prescription is recorded in the GP's computer and before the patient permanently stops
14
15 the medication (or death) will be considered for analysis. As the pathology test frequency and repeat
16
17 interval requirements for patients treated with warfarin are similar to the requirements for clozapine,
18
19 similar reporting standards will be used. As with clozapine medication, it may not be possible to
20
21 differentiate patients who are initiating warfarin medication from those who have reached stable INR
22
23 levels. Despite this, based on best practice guidelines, it is expected that patients on warfarin
24
25 medication will have at least one INR measurement approximately within four weeks of a prior
26
27 measurement; which will be the criteria used to determine compliance with guidelines.

30 31 3) Glycated haemoglobin (HbA1c) testing for management of diabetic patients

32 33 Rationale:

34
35 It is estimated that over one million Australians are diagnosed with diabetes, 85% of whom have type
36
37 2 diabetes (22). Poor management of diabetes can lead to a range of complications, including
38
39 cardiovascular and renal diseases, and retinopathy (23). Best practice guidelines recommend recurrent
40
41 glycated haemoglobin (HbA1c) testing in at least half-yearly intervals for patients with diabetes (24).
42
43 HbA1c levels are a good indicator of long-term blood glucose control over the previous 8-12 weeks.
44
45 Uncontrolled glucose leading to high HbA1c levels may indicate increased risk of diabetes-related
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47 complications. As such, under-testing may be associated with failure to identify complications.

48 49 50 Analysis:

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52 The sample population will be patients diagnosed with type 2 diabetes. Only data after the diagnosis
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54 being recorded and before death will be included. The analyses will be conducted and reported in a
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3 similar structure as outlined previously for clozapine and warfarin medication pathology testing
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5 guidelines. Based on the best practice guidelines, it is expected that a minimum of two HbA1c tests
6
7 will be conducted in a year for patients diagnosed with diabetes.

8 9 **4) Frequency of vitamin D testing**

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11 Rationale:

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14 A study on vitamin D testing found a considerable number of potentially unnecessary vitamin D tests
15
16 ordered by Australian GPs (25). This has led to changes in funding programs and the establishment of
17
18 guidelines, suggesting only patients at risk of complications that may arise due to low vitamin D
19
20 levels (e.g. pregnant women, older patients at risk of falls, patients with osteoporosis) should be tested
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22 (26). Ultimately, an overall reduction of vitamin D tests was observed (9); however, studies on
23
24 whether the tests are being ordered according to the guidelines are limited (27).

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27 Analysis:

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30 To understand if vitamin D tests are being ordered according to guidelines, population and
31
32 demographic characteristics associated with higher vitamin D testing will be investigated. The sample
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34 population will be all patients; from which patients who had a vitamin D test will be identified and
35
36 flagged (as the outcome variable). Univariate and multivariate logistic regression models will be fitted
37
38 to identify any variation in vitamin D testing by the demographic characteristics of patients,
39
40 diagnoses, and general practices. Differences will be reported as odds ratios and their 95% confidence
41
42 intervals. Descriptive characteristics (patient's gender, age, and location, general practice's size, and
43
44 year of test) of the sample population will also be described.

45 46 **5) Thyroid Function Tests**

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48 Rationale:

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51 Thyroid dysfunction can occur due to over- or under-function of the thyroid gland, and can lead to
52
53 cardiovascular diseases or subclinical hypothyroidism (remains asymptomatic) (28). Guidelines
54
55 recommend assessing thyroid dysfunction by initial thyroid-stimulating hormone (TSH) tests, which
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3 may be followed up by free triiodothyronine (fT3) and free thyroxine (fT4) tests to assist with
4 diagnosis if an abnormal TSH result is observed (29). Otherwise, fT3 and fT4 tests are not
5 recommended without a prior TSH test. In Australia, there are currently no screening guidelines for
6 when and how frequently TSH tests should be conducted among adults. The benefit of screening for
7 thyroid disease, or even treating subclinical hypothyroidism, remains uncertain (30). It would be
8 valuable to understand the demographics for and frequency of TSH test ordering by Australian GPs.
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14 Analysis:

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17 To describe thyroid function test use by Australian GPs, patients with TSH, fT3, and fT4 tests will be
18 identified from the data. The associations with population characteristics and diagnoses in TSH, fT3,
19 and fT4 testing will be investigated and reported by univariate and multivariate logistic regression
20 models, similar to the reporting of vitamin D testing outlined previously. In addition to the population
21 and general practice demographics, the odds of fT3 and fT4 testing by prior TSH test result, and
22 normal/abnormal TSH test will also be analysed.
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30 The descriptive characteristics for TSH, fT3, and fT4 tests will be described overall, and by patient
31 gender, age, and location, general practice size, and year of test. The number of fT3 and fT4 tests will
32 be further described by TSH testing status: without a prior TSH test, simultaneously ordered with a
33 TSH test, and following a reported TSH test. Where TSH test results are available, fT3 and fT4 tests
34 following TSH testing will be further described by whether the initial TSH test was normal or
35 abnormal.
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43 **Sample size considerations**

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45 The study will be based on a dynamic cohort, with the number of practices, GPs, and patients
46 expected to rise. Current estimates suggest that the study will have data from 350 general practices.
47 Therefore, it is expected that there will be ample scope to detect significant variation in practices
48 across patient and general practice demographic domains.
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54 **DISCUSSION**

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3 Pathology tests play an important role in general practice. There are guidelines outlining best practice
4 for utilising tests, although the role of these guidelines in decision making is not well established.
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6
7 A limitation of using electronic health records is that recording of clinical data is not always well-
8 standardised, resulting in variation and inconsistencies in the information available (31). Issues may
9 arise due to free-text data with no standard formatting, absence of recorded comorbidities and
10 diagnoses or missing data (32), which are addressed by prioritising standardised terms and adopting
11 stringent criteria to define variables. The POLAR program already codes and organises significant
12 amounts of extracted data, and LOINC and SNOMED, both of which are available, provide
13 standardised pathology tests and diagnoses. Another limitation of this study is that the study
14 population will be drawn from only one region of Australia (Victoria), and the results may not be
15 nationally representative.
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18
19 This research will help define the extent to which evidence-based best practice guidelines influence
20 decision making in general practices. To date, difficulties in obtaining patient data from EHR
21 softwares have hindered studying pathology test ordering in general practice. This study will be one
22 of the first in Australia to extensively investigate the impact of best practice guidelines on GP testing
23 patterns. The study can ultimately lead to better efficiency in pathology testing and improvements in
24 patient outcomes by providing much needed information on the adherence of GPs to pathology testing
25 guidelines.
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28 29 30 31 32 33 34 35 36 37 38 39 40 **Ethics and Dissemination**

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43 Ethics clearance to collect data from general practice facilities has been obtained by the data provider
44 from the RACGP National Research and Evaluation Ethics Committee (NREEC 17-008). Approval
45 for the research group to use these data has been obtained from Macquarie University (5201700872).
46
47 The data will be de-identified and reported at an aggregate level, and the results will neither identify
48 GPs nor patients.
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53 The results of this study will be reported to the Australian Government's Department of Health,
54 disseminated in peer-reviewed academic journals, and presented in national and international
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3 conferences and industry forums. The involvement of the PHNs in the research process also allows
4 for the research findings to inform their activities at an early stage, reducing the usual 'research into
5 practice' delay.
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7

8 9 **Contributors**

10
11 This study is jointly undertaken through a collaboration between Centre for Health Systems and
12 Safety Research at Macquarie University, the Royal College of Pathologists of Australasia Quality
13 Assurance Programs, POLAR Data Space (Outcome Health, Eastern Melbourne PHN, Gippsland
14 PHN and South Eastern Melbourne PHN). AG initiated the project and led the development of the
15 Quality Use of Pathology Program (QUPP) grant proposal. AG, JIW, LL, LP, TB, CP, and NR are
16 chief investigators on the project and have contributed to the grant proposal and protocol in their area
17 of expertise. From the PHNs, MS, RW, and ED contributed their expertise in general practice to the
18 protocol. AM, from Outcome Health, has contributed his expertise in EHR data to the protocol. RAH,
19 GS, and GSF are members of the project team and contributed to the protocol in relation to describing
20 the procedures of data collection, validation, and analyses procedures. RAH and GS prepared the first
21 draft of this protocol based on the grant proposal. All authors have reviewed and approved the final
22 version of this protocol.
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36 **Funding**

37
38 This study is independently executed through funding by a grant from the Australian Government
39 Department of Health, Quality Use of Pathology Program (Agreement ID: 4-2QFVW4M). This
40 Australian national grants program aims to improve health and economic outcomes from pathology
41 tests.
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47 **Competing Interests**

48
49 None declared.
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52 **REFERENCES**

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BMJ Open

Compliance with pathology testing guidelines in Australian general practice: protocol for a secondary analysis of electronic health record data

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024223.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Jul-2018
Complete List of Authors:	Sezgin, Gorkem; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Georgiou, A; Macquarie University, Australian Institute of Health Innovation Hardie, Rae-Anne; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Li, Ling; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Pont, Lisa; University of Technology Sydney Faculty of Health; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Badrick, Tony; Royal College of Pathologists of Australasia, QAP Franco, Guilherme; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Westbrook, Johanna; Macquarie University Faculty of Medicine and Health Sciences, Centre for Health Systems and Safety Research, Australian Institute of Health Innovation Rinehart, Natalie; Outcome Health McLeod, Adam; Outcome Health Pearce, Christopher; Outcome Health Shearer, Marianne; Gippsland Primary Health Network Whyte, Robin; Eastern Melbourne Primary Health Network Deveny, Elizabeth; South Eastern Melbourne Primary Health Network
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Evidence based practice, Pathology
Keywords:	Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, PATHOLOGY, PRIMARY CARE, Australia

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3 **Compliance with pathology testing guidelines in Australian general practice: protocol for a**
4 **secondary analysis of electronic health record data**

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3 **Pathology testing in Australian general practice and compliance with guideline**
4 **recommendations: A study protocol for a secondary analysis of electronic health record data**
5

6 **ABSTRACT**

7 **Introduction** In Australia, general practitioners usually provide the first point of contact for patients
8 with non-urgent medical conditions. Appropriate and efficient utilisation of pathology tests by general
9 practitioners forms a key part of diagnosis and monitoring. However over- and under- utilisation of
10 pathology tests have been reported across several tests and conditions, despite evidence-based
11 guidelines outlining best practice in pathology testing. There are a limited number of studies
12 evaluating the impact of these guidelines on pathology testing in general practice. The aim of our
13 quantitative observational study is to define how pathology tests are used in general practice and
14 investigate how test ordering practices align with evidence-based pathology guidelines.
15
16

17 **Methods and analysis** Access to non-identifiable patient data will be obtained through electronic
18 health records from general practices across three primary health networks in Victoria, Australia.
19 Numbers and characteristics of patients, general practices, encounters, pathology tests, and problems
20 managed over time will be described. Overall rates of encounters and tests, alongside more detailed
21 investigation between subcategories (encounter year, patient's age, gender, and location, and general
22 practice size) will also be undertaken. To evaluate how general practitioner test ordering coincides
23 with evidence-based guidelines, five key candidate indicators will be investigated: full blood counts
24 for patients on clozapine medication; international normalised ratio (INR) measurements for patients
25 on warfarin medication; glycated haemoglobin (HbA1c) testing for monitoring diabetes; vitamin D
26 testing; and thyroid function testing.
27
28

29 **Ethics and dissemination** Ethics clearance to collect data from general practice facilities has been
30 obtained by the data provider from the RACGP National Research and Evaluation Ethics Committee
31 (NREEC 17-008). Approval for the research group to use these data has been obtained from
32 Macquarie University (5201700872). This study is funded by the Australian Government Department
33 of Health Quality Use of Pathology Program (Agreement ID: 4-2QFVW4M). Findings will be
34 reported to the Department of Health and disseminated in peer-reviewed academic journals and
35 presentations (national and international conferences, industry forums).
36
37

38 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 39
- 40 • The study population will be drawn from a large region in Victoria, Australia, and is expected
41 to contain a large sample population (data from approximately 350 general practices), along
42 with a large number of demographic variables (e.g., region, gender, age).
 - 43 • Electronic health records contain a vast amount of information on patients, allowing us to
44 control for potential interacting or predictive variables on patient outcomes using statistical
45 modelling.
 - 46 • Some electronic health record fields may not be completely standardised across practices and
47 could contain inconsistencies and missing information; which may limit the volume of data
48 that can be extracted and analysed.
 - 49 • Some medications being investigated in this study may be prescribed and/or monitored by
50 specialists, which may result in cases being missed.
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INTRODUCTION

In Australia, general practitioners (GPs) are usually the first point of contact for patients with non-emergency health problems. They play an important role in the early detection, prevention (including shared-care arrangements) and treatment of disease (1). Pathology tests are a key part of general practice assisting GPs in diagnosing, screening, treating, and monitoring diseases. The past decade has seen an increase in both visits to and problems managed by GPs in Australia, resulting in an estimated 24.2 million additional pathology tests being ordered in 2015-2016 compared to 2006-2007 (2).

Appropriate and timely utilisation of pathology tests can improve the quality and outcome of patient care. However, both over- and under- utilisation of pathology tests have been frequently observed in a range of clinical scenarios (3,4). Several guidelines have been established to encourage better utilisation of pathology tests among GPs across Australia, the US, Canada, and the UK. These include initiatives such as *Choosing Wisely* (5), *National Institute for Health and Clinical Excellence (NICE)* (6), and *Royal Australian College of General Practitioners (RACGP) Guidelines for preventative activities in general practice* (7). Currently, there is little evidence on how test ordering practices by GPs align with these recommendations and guidelines in Australia, and elsewhere. A survey of 600 US doctors revealed only 21% of doctors were familiar with the *Choosing Wisely* campaign. However doctors aware of the campaign had a lower proportion of unnecessary pathology testing (8). In Australia, increased awareness of best-practice in vitamin D test ordering is reported to have contributed to a reduction in healthcare costs and potentially unnecessary tests (9). Considering the importance of pathology testing for managing diseases, a better understanding of how pathology testing by GPs coincides with evidence-based guidelines will be invaluable for the success of management and disease-prevention strategies.

Until recently, the survey-based *Bettering the Evaluation and Care of Health (BEACH)* study provided the most comprehensive data on Australian GP activity (2). However, its cross-sectional design prevented it from reporting longitudinal patient level changes and outcomes. The BEACH study was discontinued in 2016, and has since left a gap in our understanding of GP activity; particularly in relation to pathology test ordering. The extensive use of computers by Australian GPs has prompted interest in the use of electronic health record (EHR) data as a research source for monitoring the quality of GP services, and has led to research and publications based on EHR data (10). The Australian Department of Health funded NPS Medicinewise MedicinesInsight dataset contains a national collection of electronic health records (EHRs) from 650 practices covering over 3,300 GPs and nearly 3.6 million active patients (11). This dataset has been used in several population health research projects, and has demonstrated the value of EHR data in research (12). This study will use EHR data from the POLAR Data Space, containing de-identified data from consenting general practices collected on behalf of Australian PHNs from approximately 350 practices. POLAR Data Space has added measures to ensure robust and accurate data, and implements standardised terminologies to make the data more approachable for research use. This study, undertaken in collaboration with POLAR Data Space Research Consortia and its associated Primary Health Networks (PHNs), will facilitate a comprehensive analyses of general practice activity and its relationship to pathology testing in Australia through EHR data.

Objectives:

The objectives of this study are to:

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- 2
- 3 1. Describe general practice activity and characteristics of pathology test ordering based on
- 4 electronic health record data;
- 5 2. Investigate compliance with evidence-based guidelines to determine the appropriateness and
- 6 quality use of pathology in general practice.
- 7

8 **METHODS AND ANALYSES**

9

10 **Study design**

11 A retrospective observational study of Australian general practice health records and pathology
12 testing data. The study will run for a period of approximately two years spanning from early 2018 to
13 late 2019.
14

15 **Data source**

16 Data to be used in this study will be provided by the POLAR Data Space (10). POLAR Data Space
17 collects de-identified data from consenting general practices on behalf of Australian PHNs: including
18 Gippsland, Eastern Melbourne, and South Eastern Melbourne PHNs. Data are extracted from
19 approximately 350 practices in urban and rural regions in Victoria, Australia. The primary purpose of
20 the data collection is to provide information to improve patient care at the practice level and
21 population health initiatives at the PHN level. POLAR Data Space has ethics approval for the
22 collection, storage and de-identification of the data which it makes available for approved research
23 governed by the involved PHNs.
24

25 The data source will include pooled general practice patient data extracted from Best Practice,
26 Medical Director, and Zedmed EHRs. Data will include de-identified demographic information about
27 patients and general practices, as well as visit records (diagnosis, past history, medications) and
28 pathology test records (test name and result). Both historical and current information about patients
29 will be acquired, providing a longitudinal record. It is expected that the data will span a period of over
30 a decade, from early 2000's to early 2018.
31

32 **Study Population**

33 The study population will consist of all patients who visited any of the general practices included in
34 the study, and had their visit recorded in the practices' EHR software.
35

36 **Variables**

37 The following criteria will be adopted to accurately describe general practice activity and ensure data
38 quality: (i) A patient will be distinguished by a unique (non-identifiable) patient code recorded within
39 a general practice and included if determined to be an active patient (i.e. has visited the GP three or
40 more times in the past two years, not deceased); (ii) An encounter (i.e. consultation, visit) will be
41 defined as a patient visit recorded by a doctor or nurse during which an action (e.g. consultation,
42 prescription) is performed, and will be identified through a variable indicating the visit type (e.g.
43 surgery, administrative, phone call); (iii) A pathology test will be defined as either a panel of
44 interrelated tests (e.g. full blood count) or an individual test (e.g. troponin test); (iv) Where possible,
45 standardised records such as Logical Observation Identifiers Names and Codes (LOINC) and
46 Systematized Nomenclature of Medicine (SNOMED) terminologies will be prioritised to identify
47 variables; otherwise, free-text data will be searched for terms of interest (e.g. "diabetes" or its
48 abbreviated forms in the diagnosis field, excluding "not diabetes").
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50 **Analyses**

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3 Data examination and analysis will be performed using Stata/MP 15.1 (StataCorp, College Station,
4 Texas, USA). The methods outlined in this protocol are structured according to the *Strengthening the*
5 *Reporting of Observational Studies in Epidemiology* (STROBE) checklist of items to be included in
6 observational studies (13).
7

8 ***Characteristics of general practice activity and pathology testing***

9
10 In line with Objective 1 of this study, we will analyse and describe Australian general practice
11 characteristics and activity. These characteristics can subsequently be compared to reports on national
12 demographics and healthcare statistics, such as *Australian Institute of Health and Welfare's* (AIHW)
13 annual reports.
14

15 Sample population characteristics will be reported. This will include describing the characteristics of
16 patients, general practices, encounters, tests, and problems managed across time. Subsequent analyses
17 will describe overall median rates of encounters and tests, alongside more detailed investigation
18 between subcategories (encounter year, patient's age, gender, and postcode, and number of active
19 general practitioners in practice) using the following indicators: encounters per patient per year, and
20 tests per encounter.
21

22 The differences between subcategories will be further described as incidence rate ratios by generalised
23 linear modelling (Poisson or negative binomial, whichever is appropriate).
24

25 ***Best practice guidelines-based analyses***

26
27 In line with Objective 2 of this study, we will describe the extent to which pathology ordering
28 practices among Australian GPs aligns with evidence-based pathology testing guidelines. Five initial
29 candidate indicators have been identified for analyses.
30

31 **1) Monitoring patients on clozapine medication**

32
33 Rationale:

34 Clozapine is a highly effective antipsychotic drug that is used for managing chronic schizophrenia.
35 However, clozapine use can result in neutropenia in nearly two percent of patients, and
36 agranulocytosis in one percent (14); warranting close monitoring of patients taking clozapine.
37 Although clozapine is prescribed by specialists, monitoring is more frequently managed by GPs
38 through shared-care arrangements (15). After 18 weeks of initiation and monitoring under a specialist,
39 GPs can also prescribe clozapine. Australian guidelines recommend patients on clozapine medication
40 have blood tests for white blood cell and neutrophil counts weekly for the first 18 weeks of initiation,
41 and monthly thereafter (16,17). Furthermore, a patient cannot obtain clozapine from the pharmacist
42 without a recent blood test. Currently, the state of monitoring for patients on clozapine medication is
43 not known.
44
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47 Analysis:

48 The study population will be patients who are being prescribed clozapine by the GP (and therefore
49 also needing to be monitored). The timeframe will include records after the first entry of the
50 prescription into the EHR software, and before medication is discontinued (or patient is deceased or is
51 no longer an active patient). The demographic characteristics of patients on clozapine medication as
52 well as number of full blood counts for these patients will be described overall, by patient gender, age,
53 and location, general practice size, and year of test. The number of full blood counts per patient per
54 year will also be described, overall and by the demographic characteristics, by counting the number of
55 full blood count tests conducted for each patient on clozapine medication for each available year.
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3 Subsequently, the median number of full blood count tests per patient per year will be calculated, with
4 the inter-quartile range. For patients with more than one test, the time between tests will be
5 determined. Subsequently, median time between tests will be calculated, with the inter-quartile range.
6 As clozapine may also be prescribed by specialists, it may not be possible to determine when the
7 medication was initiated through the EHR software. Consequently, it may not be possible to
8 differentiate patients who require weekly tests from patients who require monthly tests. Nonetheless,
9 it is expected patients on clozapine medication will have at least one full blood count test within
10 approximately four to six weeks of a prior test; which will indicate compliance with guidelines.
11

12 **2) Measuring international normalised ratio (INR) levels for patients on warfarin medication**

13
14 Rationale:

15
16 Warfarin is a highly effective and widely-used anticoagulant in Australia. However, it is also one of
17 the most common causes of prescribed medication-related mortality, due to its risk of causing
18 bleeding (18). Best practice guidelines recommend that the initiation of warfarin medication should be
19 accompanied by frequent International Normalised Ratio (INR) measurements until a stable
20 therapeutic range is reached. After INR levels are stable, testing frequency should be once every four
21 to six weeks: unless a change (e.g. initiation of another medication) which can affect INR levels
22 occurs (19,20). Failure to correct INR levels is associated with increased mortality (21).
23

24
25 Analysis:

26
27 The sample population will be patients with a warfarin prescription. Only data entered after the first
28 instance the prescription is recorded in the GP's computer and before the patient permanently stops
29 the medication (or death) will be considered for analysis. As the pathology test frequency and repeat
30 interval requirements for patients treated with warfarin are similar to the requirements for clozapine,
31 similar reporting standards will be used. As with clozapine medication, it may not be possible to
32 differentiate patients who are initiating warfarin medication from those who have reached stable INR
33 levels. Despite this, based on best practice guidelines, it is expected that patients on warfarin
34 medication will have at least one INR measurement approximately within four weeks of a prior
35 measurement; which will be the criteria used to determine compliance with guidelines.
36

37 **3) Glycated haemoglobin (HbA1c) testing for management of diabetic patients**

38
39 Rationale:

40
41 It is estimated that over one million Australians are diagnosed with diabetes, 85% of whom have type
42 2 diabetes (22). Poor management of diabetes can lead to a range of complications, including
43 cardiovascular and renal diseases, and retinopathy (23). Best practice guidelines recommend recurrent
44 glycated haemoglobin (HbA1c) testing in at least half-yearly intervals for patients with diabetes (24).
45 HbA1c levels are a good indicator of long-term blood glucose control over the previous 8-12 weeks.
46 Uncontrolled glucose leading to high HbA1c levels may indicate increased risk of diabetes-related
47 complications. As such, under-testing may be associated with failure to identify complications.
48

49
50 Analysis:

51
52 The sample population will be patients diagnosed with type 2 diabetes. Only data after the diagnosis
53 being recorded and before death will be included. The analyses will be conducted and reported in a
54 similar structure as outlined previously for clozapine and warfarin medication pathology testing
55 guidelines. Based on the best practice guidelines, it is expected that a minimum of two HbA1c tests
56 will be conducted in a year for patients diagnosed with diabetes.
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4) Frequency of vitamin D testing

Rationale:

A study on vitamin D testing found a considerable number of potentially unnecessary vitamin D tests ordered by Australian GPs (25). This has led to changes in funding programs and the establishment of guidelines, suggesting only patients at risk of complications that may arise due to low vitamin D levels (e.g. pregnant women, older patients at risk of falls, patients with osteoporosis) should be tested (26). Ultimately, an overall reduction of vitamin D tests was observed (9); however, studies on whether the tests are being ordered according to the guidelines are limited (27).

Analysis:

To understand if vitamin D tests are being ordered according to guidelines, population and demographic characteristics associated with higher vitamin D testing will be investigated. The sample population will be all patients; from which patients who had a vitamin D test will be identified and flagged (as the outcome variable). Univariate and multivariate logistic regression models will be fitted to identify any variation in vitamin D testing by the demographic characteristics of patients, diagnoses, and general practices. Differences will be reported as odds ratios and their 95% confidence intervals. Descriptive characteristics (patient's gender, age, and location, general practice's size, and year of test) of the sample population will also be described. To obtain an understanding of the reasons for vitamin D testing, other tests ordered simultaneously will be identified and examined, as well as preceding medication prescriptions and diagnoses.

5) Thyroid Function Tests

Rationale:

Thyroid dysfunction can occur due to over- or under-function of the thyroid gland, and can lead to cardiovascular diseases or subclinical hypothyroidism (remains asymptomatic) (28). Guidelines recommend assessing thyroid dysfunction by initial thyroid-stimulating hormone (TSH) tests, which may be followed up by free triiodothyronine (fT3) and free thyroxine (fT4) tests to assist with diagnosis if an abnormal TSH result is observed (29). Otherwise, fT3 and fT4 tests are not recommended without a prior TSH test. In Australia, there are currently no screening guidelines for when and how frequently TSH tests should be conducted among adults. The benefit of screening for thyroid disease, or even treating subclinical hypothyroidism, remains uncertain (30). It would be valuable to understand the demographics for and frequency of TSH test ordering by Australian GPs.

Analysis:

To describe thyroid function test use by Australian GPs, patients with TSH, fT3, and fT4 tests will be identified from the data. The associations with population characteristics and diagnoses in TSH, fT3, and fT4 testing will be investigated and reported by univariate and multivariate logistic regression models, similar to the reporting of vitamin D testing outlined previously. In addition to the population and general practice demographics, the odds of fT3 and fT4 testing by prior TSH test result, and normal/abnormal TSH test will also be analysed.

The descriptive characteristics for TSH, fT3, and fT4 tests will be described overall, and by patient gender, age, and location, general practice size, and year of test. The number of fT3 and fT4 tests will be further described by TSH testing status: without a prior TSH test, simultaneously ordered with a TSH test, and following a reported TSH test. Where TSH test results are available, fT3 and fT4 tests

1
2
3 following TSH testing will be further described by whether the initial TSH test was normal or
4 abnormal.

5 6 **Sample size considerations**

7 The study will be based on a dynamic cohort, with the number of practices, GPs, and patients
8 expected to rise. Current estimates suggest that the study will have data from 350 general practices.
9 Therefore, it is expected that there will be ample scope to detect significant variation in practices
10 across patient and general practice demographic domains.
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12 13 **Patient and Public Involvement**

14 There was no involvement of patients or the public in this study.
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18 **DISCUSSION**

19 Pathology tests play an important role in general practice. There are guidelines outlining best practice
20 for utilising tests, although the role of these guidelines in decision making is not well established.
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22 A limitation of using electronic health records is that recording of clinical data is not always well-
23 standardised, resulting in variation and inconsistencies in the information available (31). Issues may
24 arise due to free-text data with no standard formatting, absence of recorded comorbidities and
25 diagnoses or missing data (32), which are addressed by prioritising standardised terms and adopting
26 stringent criteria to define variables. The POLAR program already codes and organises significant
27 amounts of extracted data, and LOINC and SNOMED, both of which are available, provide
28 standardised pathology tests and diagnoses. Another limitation of this study is that the study
29 population will be drawn from only one region of Australia (Victoria), and the results may not be
30 nationally representative. One other limitation is related to the indicators being measured.
31 Medications, such as clozapine and warfarin are generally prescribed by specialists, whom might also
32 continually monitor the patient's status. In such cases, observed compliance with guidelines in general
33 practice may be low. Furthermore, a patient monitored by a general practitioner may have occasional
34 visits to their specialist, who may order the tests, rather than the GP.
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38 This research will help define the extent to which evidence-based best practice guidelines influence
39 decision making in general practices. To date, difficulties in obtaining patient data from EHR
40 softwares have hindered studying pathology test ordering in general practice. This study will be one
41 of the first in Australia to extensively investigate the impact of best practice guidelines on GP testing
42 patterns. The study can ultimately lead to better efficiency in pathology testing and improvements in
43 patient outcomes by providing much needed information on the adherence of GPs to pathology testing
44 guidelines.
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46 47 **Ethics and Dissemination**

48 Ethics clearance to collect data from general practice facilities has been obtained by the data provider
49 from the RACGP National Research and Evaluation Ethics Committee (NREEC 17-008). Approval
50 for the research group to use these data has been obtained from Macquarie University (5201700872).
51 The data will be de-identified and reported at an aggregate level, and the results will neither identify
52 GPs nor patients.
53

54 The results of this study will be reported to the Australian Government's Department of Health,
55 disseminated in peer-reviewed academic journals, and presented in national and international
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3 conferences and industry forums. The involvement of the PHNs in the research process also allows
4 for the research findings to inform their activities at an early stage, reducing the usual ‘research into
5 practice’ delay.
6

7 **Contributors**

8 This study is jointly undertaken through a collaboration between Centre for Health Systems and
9 Safety Research at Macquarie University, the Royal College of Pathologists of Australasia Quality
10 Assurance Programs, POLAR Data Space (Outcome Health, Eastern Melbourne PHN, Gippsland
11 PHN and South Eastern Melbourne PHN). AG initiated the project and led the development of the
12 Quality Use of Pathology Program (QUPP) grant proposal. AG, JIW, LL, LP, TB, CP, and NR are
13 chief investigators on the project and have contributed to the grant proposal and protocol in their area
14 of expertise. From the PHNs, MS, RW, and ED contributed their expertise in general practice to the
15 protocol. AM, from Outcome Health, has contributed his expertise in EHR data to the protocol. RAH,
16 GS, and GSF are members of the project team and contributed to the protocol in relation to describing
17 the procedures of data collection, validation, and analyses procedures. RAH and GS prepared the first
18 draft of this protocol based on the grant proposal. All authors have reviewed and approved the final
19 version of this protocol.
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23 **Funding**

24 This study is independently executed through funding by a grant from the Australian Government
25 Department of Health, Quality Use of Pathology Program (Agreement ID: 4-2QFVW4M). This
26 Australian national grants program aims to improve health and economic outcomes from pathology
27 tests.
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30 **Competing Interests**

31 None declared.
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