BMJ Open Diagnosing Potentially Preventable Hospitalisations (DaPPHne): protocol for a mixed-methods data-linkage study

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To cite: Passey ME, Longman JM, Johnston JJ, *et al.* Diagnosing Potentially Preventable Hospitalisations (DaPPHne): protocol for a mixed-methods data-linkage study. *BMJ Open* 2015;**5**: e009879. doi:10.1136/bmjopen-2015-009879

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2015-009879>).

Received 1 September 2015

Revised 16 October 2015

Accepted 27 October 2015

CrossMark

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ABSTRACT

Introduction: Rates of potentially preventable hospitalisations (PPH) are used as a proxy measure of effectiveness of, or access to community-based health services. The validity of PPH as an indicator in Australia has not been confirmed. Available evidence suggests that patient-related, clinician-related and systems-related factors are associated with PPH, with differences between rural and metropolitan settings. Furthermore, the proportion of PPHs which are actually preventable is unknown. The Diagnosing Potentially Preventable Hospitalisations study will determine the proportion of PPHs for chronic conditions that are deemed preventable and identify potentially modifiable factors driving these, in order to develop effective interventions to reduce admissions and improve measures of health system performance.

Methods and analysis: This mixed methods data linkage study of approximately 1000 eligible patients with chronic PPH admissions to one metropolitan and two regional hospitals over 12 months will combine data from multiple sources to assess the: extent of preventability of chronic PPH admissions; validity of the Preventability Assessment Tool (PAT) in identifying preventable admissions; factors contributing to chronic PPH admissions. Data collected from patients (quantitative and qualitative methods), their general practitioners, hospital clinicians and hospital records, will be linked with routinely collected New South Wales (NSW) Admitted Patient Data Collection, the NSW Registry of Births, Death and Marriages death registration and Australian Bureau of Statistics mortality data. The validity of the PAT will be assessed by determining concordance between clinician assessment and that of a 'gold standard' panel. Multivariable logistic regression will identify the main predictor variables of admissions deemed preventable, using study-specific and linked data.

Ethics and dissemination: The NSW Population and Health Services Research Ethics Committee granted ethical approval. Dissemination mechanisms include engagement of policy stakeholders through a project Steering Committee, and the production of summary reports for policy and clinical audiences in addition to peer-review papers.

INTRODUCTION

Potentially preventable hospitalisations (PPH; also referred to as admissions for ambulatory

care sensitive conditions) are admissions considered to be potentially preventable with effective, timely outpatient care in the period immediately prior to admission.¹ The concept of PPH admissions originated in New York in the early 1990s¹ and since then has been widely used as an indicator of effectiveness of, or access to, primary healthcare in many countries. In Australia, the rate of PPH is a key performance indicator (KPI) in the National Healthcare Agreement (NHA)² and the National Health Performance and Accountability Framework³ and is therefore tied directly to hospital funding.

PPH conditions are categorised as vaccine-preventable, acute or chronic, with the specific conditions classified as PPH varying across countries. According to the NHA definition,² there were more than 772 000 PPH admissions in Australia in 2012–2013, accounting for 10.3% of all public hospital admissions, with higher rates in remote and very remote areas.⁴ Over half of Australian PPH admissions are attributable to chronic conditions, with congestive cardiac failure (CCF), chronic obstructive pulmonary disease (COPD), diabetes complications and angina accounting for over 97% of all chronic PPH admissions.⁴

Despite its use, however, the validity of PPH as an indicator of effectiveness or access to care has not been definitively confirmed in the Australian setting.⁵ Although one Australian study found that better self-rated access to care was associated with lower rates of PPH in urban areas, this was not the case in rural areas.⁶ Furthermore, a number of socioeconomic and behavioural factors were associated with PPH,⁶ leading the authors to suggest that the association between health-care effectiveness and access and PPH is complex, requiring further research.⁶ Preliminary work undertaken by the current research team confirmed this complexity.^{7–9} Indeed, a recent study found personal

sociodemographic and health characteristics, rather than general practitioner (GP) supply, are major drivers for PPH in Australia, particularly for chronic conditions.¹⁰

In an attempt to reduce unnecessary admissions to hospital, and achieve KPI targets related to PPH admissions, policymakers and health services have developed and implemented programmes specifically targeting patients with PPH admissions, such as the New South Wales (NSW) Chronic Disease Management Program, with the aim of improving the coordination of their care.¹¹ In doing this, a population-level indicator is now being used at the individual level to identify patients who may benefit from additional support. However, this response to PPH admissions is significantly limited by the fact that the proportion of PPH admissions that is *actually* preventable is unknown and there is no easy way for a health system or researchers to identify *which individual admissions* are actually preventable. PPH are identified on the basis of diagnostic codes in hospital administrative data.^{12–15} While this approach takes advantage of the availability of administrative data sets, it overestimates rates of preventable admissions because it also captures an *unknown number* of admissions that are necessary and could not feasibly have been prevented. Few studies have attempted to assess preventability of individual admissions, and almost all of these have focused on readmissions. A recent systematic review of the preventability of readmissions reported a median proportion of 27.1% as actually preventable, however estimates ranged from 5% to 79%.¹⁶ No such studies have been undertaken in Australia.

Very little is known about patients' perspectives of the underlying factors contributing to individual PPH admissions.¹⁷ Understanding patients' views on what influenced their decision to go to hospital, the support they received in the lead-up to their admission, and what may have helped to prevent the admission, may help identify leverage points and mechanisms for reducing PPH admissions.

In order to develop and target effective interventions to reduce PPHs, and to inform the appropriate use of PPH measures as indicators of health system performance, we need to identify the proportion of PPH admissions that are considered preventable and identify the drivers of these preventable admissions.

The DaPPHne project aims to do this. Its specific objectives are to:

1. Validate a tool for use by clinicians and researchers to assess the preventability of individual admissions;
2. Determine the proportion of chronic PPH admissions among community-dwelling patients ≥ 45 years that is deemed to be preventable;
3. Identify factors contributing to PPH admissions classified as preventable;
4. Recommend refinements to PPH measures that can be applied nationally and internationally to provide more robust health service performance measurement based on admissions deemed to be preventable

5. Identify interventions to reduce chronic PPH admissions.

Definition of preventability

In this study, we use the definition of a preventable admission provided in the box below. We were unable to identify any clear timeframes for preventability in the PPH literature, although the original work by Billings *et al.*¹ referred to the 'period immediately prior to admission'. Based on our understanding of the literature, and in consultation with clinicians and other researchers in the field, we determined that a 3-month time frame was reasonable and that the definition should include access to and utilisation of health and social services, as well as patient health behaviours.

A preventable admission is defined as an unplanned admission which could have been prevented if:

1. Appropriate, adequate, accessible and good quality support in the community* had been available and accessed in the preceding 3 months, and/or
2. Appropriate individual health behaviours, for example, disease self-management, had occurred in the 3 months prior to admission.

*Support in the community might include primary healthcare, family/neighbour/friend/social support, health or non-health community services.

METHODS AND ANALYSIS

This mixed methods data linkage study of approximately 1000 chronic PPH admissions will combine a wide range of study-specific and routinely collected data to enable exploration of the factors contributing to chronic PPH admissions. One metropolitan and two regional hospitals will participate.

The substudies to be undertaken are:

1. Comprehensive data collection for each admission to identify factors associated with preventable admissions including data collected from the patient, hospital records and the patients' GP (if available). Two senior hospital clinicians will complete an assessment of the preventability of each admission. Admissions deemed preventable will be compared with those deemed not preventable to identify patient, clinician and system factors associated with preventable admissions.
2. Validation of a Preventability Assessment Tool (PAT): For the first 150 admissions with complete data, the assessment by hospital clinicians using a PAT that we have previously developed and piloted¹⁸ will be compared against a 'gold standard'—an assessment by a panel of senior clinicians, using a modified version of the process developed by Oddone *et al.*¹⁹ This will be done separately for the metropolitan and the two regional hospitals (ie, 150 admissions for each) to allow assessment of validity in both settings due to

the different service characteristics and demographics of the catchment populations. The metropolitan hospital serves a younger and more ethnically diverse population, with a greater proportion of people who do not speak English at home.

3. Qualitative study: A subset of approximately 20 consenting patients will participate in semistructured interviews to elicit their perspectives of the circumstances leading up to their admission, and whether they can identify any measures that may have prevented their hospital admission. Interviews will be analysed thematically.
4. Predicting preventability using routinely collected data: Study-specific data will be linked to administrative data relating to hospital admissions and deaths. These linked data will be used to develop models to predict the preventability of individual admissions using routine administrative data and investigate how additional items (eg, measures of self-rated health) can improve the prediction of preventability.

The contribution of each substudy to the study objectives is shown in [table 1](#).

Recruitment

Research nurses will be employed at each hospital to facilitate participant recruitment and data collection. Through close liaison with emergency department (ED) staff, the research nurses will identify all patients presenting to the ED who potentially meet the eligibility criteria (see below). Once a decision has been made to admit a patient, the research nurse will confirm eligibility and invite them to participate. Patients will provide written consent to all aspects of the study, with the option of declining individual substudies. To minimise bias in selection of patients, while accommodating the extensive data collection requirements, patients will be recruited every second week, and *all* eligible patients will be invited during recruitment weeks, regardless of the time of day or day of week, or whether they have previously

participated in the study. During the alternate (non-recruitment) weeks, the research nurse will complete data collection for patients recruited the previous week (ie, hospital clinical data, GP data). As there is considerable seasonal variation in admission rates for these conditions, patients will be recruited over a 12-month period.

Sample eligibility criteria

Eligible patients are community-dwelling adults aged ≥ 45 years with an unplanned admission to any of the participating hospitals with a primary diagnosis of selected chronic PPH conditions (CCF, COPD, diabetes complications and angina as defined by the Australian Institute of Health and Welfare²⁰—see [table 2](#)). Exclusion criteria are cognitive impairment such that the patient is unable to give informed consent; patient living in residential aged care facility, prison or other facility; final discharge diagnosis not one of the specified inclusion diagnoses; and transfer from another hospital.

Data sources and collection

Data will be collected regarding each eligible and consenting admission via patient questionnaire, the PAT, GP interview and extraction of hospital clinical data, as described below.

Patient questionnaire

The research nurse will administer a study-specific questionnaire, taking approximately 30 min to complete. Information will be collected regarding sociodemographic characteristics, health status (SF-36v2²¹); psychological distress (Kessler 10²²); disease self-management (Partners in Health Scale²³); health literacy (REALM-R²⁴ and Chew²⁵); lifestyle risk factors; social support (abbreviated Duke Social Support Index²⁶ and subscales of the ENRICHED Social Support Inventory²⁷); medications adherence and complications (Morisky 8-item Medication Adherence questionnaire²⁸

Table 1 Relationship between project objectives and substudies

	Substudy 1: comprehensive data collection for each admission	Substudy 2: validation of the PAT	Substudy 3: qualitative study	Substudy 4: data linkage
Objective 1: validate PAT	X	X		
Objective 2: assess proportion of PPH admissions deemed preventable	X	X		
Objective 3: identify factors contributing to preventable hospitalisations	X		X	X
Objective 4: recommend refinements to PPH measures	X			X
Objective 5: identify interventions to reduce chronic PPH admissions	X		X	X

PAT, Preventability Assessment Tool; PPH, potentially preventable hospitalizations.

Table 2 Diagnoses for inclusion

	<i>Congestive cardiac failure</i>
	Any of the following as principal diagnosis only
I 50	Heart failure
I 50.0	Congestive heart failure
I 50.1	Left ventricular failure
I 50.9	Heart failure, unspecified
I 11.0	Hypertensive heart disease with (congestive) heart failure
J 81	Pulmonary oedema
	<i>Angina</i>
	Any of the following as principal diagnosis only
I 20	Angina pectoris
I 20.0	Unstable angina
I 20.1	Angina pectoris with documented spasm
I 20.8	Other forms of angina pectoris
I 20.9	Angina pectoris, unspecified
I 24.0	Coronary thrombosis not resulting in myocardial infarction
I 24.8	Other forms of acute ischaemic heart disease
I 24.9	Acute ischaemic heart disease, unspecified
	<i>Chronic obstructive pulmonary disease</i>
	Any of the following as principal diagnosis only
J 41	Simple and mucopurulent chronic bronchitis
J 42	Unspecified chronic bronchitis
J 43	Emphysema
J 44	Other chronic obstructive pulmonary disease
J 47	Bronchiectasis
	J20 as principal diagnosis ONLY if additional diagnoses of J41, J42, J43, J44, J47
J 20	Acute bronchitis
	<i>Diabetes and diabetes complications</i>
	Any of the following as principal diagnosis only
E 10	Type 1 diabetes mellitus with or without complications
E 11	Type 2 diabetes mellitus with or without complications
E 12	Malnutrition-related diabetes mellitus
E 13	Other specified diabetes mellitus
E 14	Unspecified diabetes mellitus
	E 10–E 14 as additional diagnoses where the principal diagnosis is one of
E 87.0	Hyperosmolarity
E 87.2	Acidosis
G 45	Transient ischaemic attack
G 50–G 64	Nerve disorders and neuropathies
H 25–H 28	Cataracts and lens disorders
H 30–H 36	Retinal disorders
H 40 & H 42	Glaucoma (all)
I 20	Angina pectoris
I 21–I 22	Myocardial infarction
I 23–I 25	Other acute and chronic ischaemic heart diseases
I 25	Chronic ischaemic heart disease
I 50	Heart failure
I 60–I 64, I 69	Stroke and sequelae
I 70–I 74	Peripheral vascular disease
K 05	Gingivitis and periodontal diseases
N 00–N 29	Kidney diseases including end-stage renal disease
Z 49	Renal dialysis

and items from the Pit Medication Risk Assessment Form²⁹), and access and barriers to healthcare including contact with GPs, specialists and allied health professionals in the previous 12 months.

Preventability Assessment Tool

Given the importance of having a method to assess the preventability of individual PPH admissions, the PAT was developed for use by senior hospital clinicians to assess

the preventability of individual chronic PPH admissions. The tool, based on an extensive literature review and consultation with clinicians, draws on the earlier work of Oddone *et al*¹⁹ and Arozullah *et al*³⁰ who assessed preventability of general medical readmissions and admissions using a retrospective audit process. Our tool can be used by clinicians during the admission, rather than retrospectively, and is designed specifically for PPH admissions. It also considers individual and social factors more extensively than the earlier work and defines the timeframe for preventability as the previous 3 months.

Clinicians are asked to indicate the reason for admission and to rate the extent to which they consider that a range of patient, clinician and system factors contributed to that admission (using a scale of 1–4). The tool concludes with a global assessment of the preventability of the admission (given currently available services and social support) on a scale of 1–10, action that could have been taken to prevent the admission, and asks for suggestions for improved/additional services/social support which could have helped prevent the admission. The PAT has had face and content validity confirmed and was assessed in a small pilot study in two hospitals.¹⁸ It takes about 5 min to complete.

For each admission, the research nurses will provide copies of the PAT to the medical registrar and a senior nurse caring for the patient and facilitate form completion.

Structured GP telephone interview

Patients' GPs will be interviewed regarding: care provided; practice factors; adherence to selected elements of the guidelines for management of patients' PPH diagnoses; other chronic conditions (including mental health) and/or social issues with the potential to impact on patients' self-management; and use of out-of-hospital clinical and non-clinical services. Finally, GPs will be asked to consider whether, assuming available services and social support, the admission was preventable (as defined above) and if so, what action could have been taken to prevent the admission. GPs will also be asked for suggestions for improved and/or additional services and/or social support which could have helped prevent the admission. The interview will take 15–20 min and GPs will be reimbursed for their time.

Hospital clinical data

The research nurses will extract clinical data from the hospital records for the participants' current admission and the most recent previous admission. Items extracted from the patients' notes will include reasons for presentation to hospital, principal diagnoses and comorbidities, medications on admission, and discharge information. For admissions included in the validation of the PAT, clinical notes for the first 24 h and the hospital discharge summary will also be obtained to assist the expert panel involved in the PAT validation (similar to the study by Oddone *et al*¹⁹).

Qualitative study

Participants who have consented to participate in the qualitative study will be contacted for an interview. Purposive sampling will be used to ensure a range of sex, age, condition, location and a majority of preventable admissions (as determined by the PAT), in order to ensure sufficient data regarding preventable admissions. Sampling will cease when saturation of themes is reached.

This substudy will use semistructured interviews to elicit patient perspectives. Interviews will explore the circumstances around the admission on the day of admission (including why and how they made the decision to seek help), their state of health and any changes to it in the 3 months leading up to the admission; their home/social and health services support (and any changes to this support) in the 3 months leading up to the admission, and whether they can identify anything that may have helped to prevent the admission. An interview guide will be used to focus the discussion. Interviews will be recorded and transcribed verbatim.

Data linkage

Data collected through the PAT, patient and GP questionnaires will be linked to the NSW Admitted Patient Data Collection (APDC), which includes records for all separations from all NSW public and private hospitals and NSW Registry of Births, Death and Marriages (RBDM) death registration (fact-of-death) and ABS mortality data for the period February 2009 to December 2016 (end of recruitment).

The Centre for Health Record Linkage (CHeReL) will perform the linkage, using probabilistic record linkage techniques and ChoiceMaker software.³¹ Quality assurance data show false-positive and false-negative rates of around 0.5%.³²

Analysis plan

Substudy 1: Identifying factors associated with preventable admissions

Analysis will be performed using STATA V.9.0. Univariate comparisons of patient characteristics, clinical problems, use of services and care provided will be undertaken using standard statistical tests (χ^2 test for categorical variables and t tests or non-parametric equivalents for continuous variables). The primary outcome for assessment of preventability will be the judgement of the hospital clinicians using the PAT. The choice of whether the assessments of the physicians or senior nurses, or a combination, is used will depend on the outcome of the validation of the tool (see Substudy 2 below).

Multivariable logistic regression will be performed to identify the main predictor variables for preventable admissions as determined by the PAT (outcome variable, coded as 0=not preventable, 1=preventable). Initially all variables with $p < 0.25$ in the univariate analyses will be included as predictor variables in the model. The influence of each variable will be assessed using Wald tests,

with stepwise removal of variables with $p \geq 0.05$. Age and gender will be retained in the model regardless of significance. The possible clustering by site will be addressed by including site as a fixed variable in the model, and assessing interaction effects. It is possible that some patients will have multiple admissions and this will be explored using generalised estimating equations to adjust for clustering. The analysis will identify factors amenable to interventions as well as patient characteristics associated with preventable admissions.

For those admissions deemed preventable, the gaps in services and other factors that the clinicians (ie, GPs and senior hospital clinicians) or patient identify as contributing to this admission will be coded and summarised using descriptive statistics and qualitative analysis. Variables for these analyses will be derived from the GP interview, the PAT and the patient questionnaire.

Substudy 2: Validation of the PAT

The judgement of an expert panel, consisting of a hospital physician, GP and community nurse with expertise in chronic disease management, will be used as the 'gold standard' for validation of the PAT. The data collected in the patient questionnaire, hospital clinical data (including a copy of all clinical data from the first 24 h of admission), the hospital discharge summary and structured GP interview will be consolidated into a non-identifiable 'case summary' for review by the expert panel. Following training, each member of the panel will review each summary, blinded to the assessments made by the hospital clinicians or each other, and provide an assessment of whether they were 'reasonably confident that this admission was preventable' (yes/no). For those classified as 'preventable', panel members will identify interventions they consider could have prevented the admission. When discrepancies in the assessment of preventability occur between the panel members, a meeting of the panel will be convened to discuss the case and come to consensus. The process is based on that developed by Oddone *et al.*¹⁹ but with the following modifications: more information is provided to the panel to make their assessment, including data from the GP and the patient; and the panel includes a wider range of clinicians, thereby bringing different perspectives to the assessment.

Concordance between the assessment of preventability made by each of the hospital clinicians using the PAT, and the assessment of the expert panel will be assessed separately (ie, physician and senior nurse separately) and in combination (ie, both assess as preventable, neither assess as preventable), using the κ statistic, sensitivity and specificity. The optimal cut-off score for the PAT scale will be determined post hoc.

Following validation of the PAT, this tool will be used to assess preventability of all study admissions in Substudy 1.

Substudy 3: Qualitative study

Interviews will be audio recorded, with the recordings professionally transcribed verbatim and analysed thematically following Braun and Clarke.³³ These transcripts will be initially coded into broad categories and subcategories and then synthesised into themes. The analysis will take place from the beginning of data collection and continue until saturation of themes is reached.

Substudy 4: Predicting preventability using routinely collected data

Logistic regression will be used to build predictive models for the preventability of specific admissions, as defined according to the PAT, using stepwise approaches. The predictive variables derived from the APDC will include patient age, sex, remoteness of residence and other demographics, the principal and other diagnoses recorded in the index admission, principal and other procedures, comorbidity indices, incident versus subsequent admissions, and source of referral. An automated approach to variable selection will be adopted, using the full range of APDC variables, because the purpose of predictive modelling is to create the best model to predict future events using the data available, rather than to test a priori hypotheses regarding the contribution of causal factors. Finally, we will explore whether adding additional items derived from questionnaire data (eg, self-rated health, social isolation and medication adherence) to administrative data results in improvements to the predictive power of the models, by comparing model fit metrics.

Statistical analysis will be performed with SAS V.9.3.³⁴ Analysis of linked data will be performed within a dedicated workspace in the Secure Unified Research Environment (SURE, <https://www.sure.org.au/>) remote access data laboratory.

Statistical power

Sample size

Based on admission data it is anticipated there will be approximately 3960 eligible admissions to the participating hospitals over the 12-month recruitment period. The following assumptions are applied to sample size and power calculations: Second weekly recruitment; 50% consent rates; 15% loss due to meeting exclusion criteria; 10% missing data on the PAT and 15% having missing GP data. Based on these assumptions, we anticipate recruiting 990 patients, with 644 with complete data. The conservative power calculations below assume 600 patients with complete data.

For a power of 80%, and $\alpha = 0.05$, table 3 shows the difference detectable for various rates of the factor of interest in the non-preventable group if 15%, 25% and 35% of admissions are classified as preventable. For example, if 25% of admissions are classified as preventable, and the factor of interest (eg, no contact with GP in month prior to admission) occurs in 10% of the non-preventable group, we will have power to detect a

Table 3 Difference detectable for various rates of the factor of interest and proportions of admissions classified as preventable

Rate of factor of interest in non-preventable groups	Proportion classified as preventable		
	15%	25%	35%
	Difference detectable		
10%	11.7%	9.5%	8.6%
20%	14.4%	11.7%	10.6%

difference in prevalence of 9.5% between the two groups. With a greater proportion classified as preventable, we are able to detect smaller differences between the groups. Previous studies of preventability of readmissions have estimated proportions of 25.8% to 53.0% preventable¹⁶ and Arozullah *et al*³⁰ in their study of general medical admissions deemed 43% were preventable. Thus, our power calculations based on assumptions of 15–35% deemed preventable are conservative estimates.

Validation of the PAT

For the validation of the PAT, if 20% are deemed preventable, a sample of 150 patients gives power to estimate a κ statistic $>0.6 \pm 0.08$; and a sensitivity or specificity of 0.9 with a precision of ± 0.1 , and $\alpha = 0.05$. If more admissions are classified as preventable, the precision is increased.

ETHICS AND DISSEMINATION

Ethical approval has been obtained from the NSW Population and Health Services Research Ethics Committee. All patients will provide written informed consent prior to any study-related data being collected.

This policy-relevant research has implications for addressing the growth in PPH admissions and the consequent pressure on the health system in Australia and internationally. The findings will help determine both the proportion of chronic PPH admissions that are deemed preventable, and the modifiable drivers contributing to preventable admissions, and will thus help generate an evidence base for the development and targeting of interventions to reduce chronic PPH admissions. Subsequent trials will be developed to test these interventions. More appropriately targeted interventions have the potential to improve the health and quality of life of people with chronic conditions and reduce PPH admissions.

The project aims to produce a validated tool for prospectively assessing the preventability of individual admissions, enabling identification of chronic PPH admissions which are considered preventable and the underlying modifiable factors contributing to them, at the time of admission. The validated PAT will be available to researchers and policymakers in other settings, enabling international comparative research and an

understanding of how factors that drive preventability are influenced by social and health systems.

With governments facing growing demands on health systems internationally, the research is also of immediate relevance to accountability for taxpayer-funded health-care, as PPH admissions are used as a performance indicator in many countries. In Australia, the rate of PPH is a KPI in the NHA² and the National Health Performance and Accountability Framework³ and is therefore tied directly to hospital funding. Our research will inform possible refinements to PPH measures using administrative data that can be applied nationally and internationally to provide more robust performance measurement and may influence policies regarding health service funding.

In order to facilitate dissemination and translation of the findings, we are working closely with a range of policymakers and service providers who provide input through the project Steering Committee. All the funding partners are actively engaged in the Steering Committee, enabling rapid dissemination and discussion of results as they are available. In addition to peer-reviewed academic papers, dissemination to a broader audience will include engagement of policy stakeholders through the production of summary reports and presentations for policy and clinical audiences, at state, national and international levels.

Acknowledgements The authors thank the study partners (Mid North Coast Local Health District, Western Sydney Local Health District, North Coast Primary Health Network and the NSW Agency for Clinical Innovation), research nurses, and the staff and management of participating hospitals and General Practices.

Collaborators The DaPPHne investigator team comprises MP, LJ, JL, GM, Lesley Barclay, DE, Vahid Saberi, Sabrina Pit, BC, Stewart Dowrick, JJ and MR.

Contributors MP, LJ, JL, GM and DE had overall responsibility for conceptualisation of this study. MP lead development of original grant application, supported by JL, LJ and MR. MP, JL, LJ, GM, MR, BC, DE and JJ contributed to the design of the study. JJ drafted this paper with the support of MP and JL, and all contributors approved the final draft.

Funding The DaPPHne study is funded by partner agencies, which at the time of writing, are: the Mid North Coast Local Health District, Western Sydney Local Health District, North Coast Primary Health Network and the NSW Agency for Clinical Innovation.

Competing interests None declared.

Ethics approval NSW Population and Health Services Research Ethics Committee.

Provenance and peer review Not commissioned; internally peer reviewed.

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