BENEFITS OF CALCULATING AND COMMUNICATING TO GPs A DRUG BURDEN INDEX (DBI) IN ELDERLY PATIENTS DISCHARGED FROM THE EMERGENCY DEPARTMENT (ED) – A PILOT STUDY

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**STATEMENT OF COMPLIANCE**

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95)

**PROTOCOL SYNOPSIS**

|  |  |
| --- | --- |
| Title | Benefits of calculating and communicating to GPs a Drug Burden Index (DBI) in elderly patients discharged from the Emergency Department- a pilot study |
| Objectives | Primary: to demonstrate that inappropriate polypharmacy in elderly patients can be reduced by effectively communicating to primary care providers the burden of toxic and/or unnecessary medications being taken by their patients. Secondary: 1. What is the incidence of medium and High Drug Burden Index scores among the RNSH ED patient cohort?2. What changes, if any, are made to patients’ prescribed medications by their GPs after the receipt by the GP of Drug Burden Index scores for their patients?3. What changes, if any, are seen in patients’ DBI scores one month after their discharge from ED?4. Are any changes in patients’ DBI sustainable over a six month period? |
| Study Design | Evaluation study |
| Planned Sample Size | 250 |
| Selection Criteria | Elderly (>65 years old) patients with no significant cognitive impairments, who are taking one or more prescribed medications, who have presented to the ED and are discharged to home |
| Study Procedures | Data collection, Drug Burden Index calculation, Patient follow-up questionnaires |
| Statistical Procedures | Sample Size Calculation:Analysis Plan: |
| Duration of the study | 1 year |

# Study Management

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| --- | --- |
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* 1. **Funding and resources**

This study is wholly funded by a grant from the HCF Research Foundation

# INTRODUCTION AND BACKGROUND

* 1. **Background Information**

Polypharmacy is very common in elderly Australians and has been associated with increased presentations to EDs with conditions such as falls, fractures, confusion, faints and dizziness (Nishtala et al 2014).

Many medications have side effects and complex interactions, which can both cause and exacerbate negative effects on balance, co-ordination, vision and cognitive function. Of particular concern are psychoactive drugs (sedatives, antipsychotics, antidepressants), anticholinergic medications, antihypertensives and cardioactive drugs.

Medications with sedative or anticholinergic properties have been implicated in a higher rate of adverse drug reactions (ADR) in older people, in particular impaired physical function, cognitive deterioration and functional decline (Hilmer et al 2007, Han et al 2008, Gnjidic et al 2009, Gnjidic et al 2014).

Numerous studies have demonstrated strong associations between IP in older patients and presentations to Emergency Departments (EDs) with conditions such as falls, long bone fractures (neck of femur, wrist), confusion, delirium, faints and dizziness. Amongst elderly patients, 20-30% of hospital admissions are medication-related and 20% will have an adverse drug reaction during admission (Bennett et al 2014, Gnjidic et al 2014, Nishtala et al 2014).

* 1. **Research Question**

Does the calculation - and communication to GPs -of the drug burden index in elderly patients who are discharged from the Emergency Department lead to review, and where appropriate, revision of the patient’s prescribed medicines such that the patient’s drug burden is decreased?

* 1. **Rationale for Current Study**

An ED presentation is a potential opportunity to review patients’ medicines and initiate the process of prescription review: however, EDs are not currently resourced to calculate DBIs. In addition, the prescription of medications for chronic conditions is rightly viewed as the domain of General Practice. However, many elderly patients have not had their medications reviewed or rationalised for many years and their prescriptions may no longer be appropriate, helpful or still effective. Often patients are taking multiple drugs from the same therapeutic class. GP-supervised withdrawal of inappropriate medicines (‘deprescribing’) is safe and may improve quality of life in older people. Studies indicate that over 90% of older adults would like to have a medication withdrawn. In 2015, reducing IP in the elderly was acknowledged as a priority at a national stakeholders meeting of clinicians, consumers, academics and policy makers.

There are a number of tools described in the medical literature that can be used to assess the drug load, or burden, borne by an individual patient. Two validated examples include the Beer’s Criteria and the more recent Drug Burden Index (Hilmer et al. 2007).

The Drug Burden Index (DBI) measures the effect of cumulative exposure to both anticholinergic and sedative medications on physical and cognitive function. Higher DBI is associated with increased functional impairment, falls, long bone fractures, frailty, hospitalisation, GP visits, morbidity and mortality (Figure 1). The burden of each individual medication (B) is calculated by the following equation:

B = D/(δ + D)

where: D is the daily dose taken by the subject, and δ is the minimum efficacious daily dose. . For each medication, the drug burden can range from 0 to 1. A value of 0.5 indicates the dose to be the minimum recommended daily dose.

The Burden, B, may be due to effects associated with anticholinergic drugs (BAC)orsedative drugs (Bs), respectively. The Drug Burden Index is defined as the sum of the burdens of the anticholinergic and sedative properties of medications (Hilmer 2009). Assuming that the anticholinergic and sedative effects of different drugs are additive in a linear fashion, it is postulated that BAC and BS are proportional to a linear additive model of pharmacological effect. Therefore,

Total Drug Burden (DBI) = *B*AC + *B*S

where: *B*AC and *B*S each represent the linear additive sum *o*f *D*/(*δ* + *D*) for every anticholinergic or sedative drug to which the subject is exposed.

And: D is the daily dose taken by the subject:

and δ is the minimum efficacious daily dose.

DBI results can be categorised as low-, medium-, or high-range. The latter two categories are associated with the most adverse effects and indicate that the patient’s prescribed medications should be reviewed with the aim of removing unnecessary medications and making other adjustments as appropriate. For this study, a low (individual) drug burden is defined as <0.5, a ‘medium’ is defined as between 0.51 and 1.0 and high drug burden is defined as ≥ 1.01.

This project will apply the DBI to quantify the ‘load’ or burden of medications that have been associated with multiple ED presenting problems. The DBI is readily calculated in a clinical setting in approximately twenty minutes and will soon be accessible online State-wide in hospital patient tracking systems eg eMR, eMM.



Figure 1. Summary of aspects of the DBI (from Kouladjian et al 2014)

We will calculate a DBI for all elderly patients who present to the ED prior to their discharge home. All patients discharged from Australian EDs are required to be given a Discharge Referral Note (DRN) documenting their ED assessment and treatment. The DRN is also transmitted electronically to the patient’s nominated GP and it is feasible to e-attach the ED-calculated DBI to the patient DRN. We will follow-up consenting patients by telephone one month and six months after their discharge from ED to ascertain whether their GPs have acted upon the DBI information in their patients’ DRN. We will then attempt to re-calculate repeat DBIs to compare against the ED-calculated value, and thus gain insights into how effective and sustainable the DBI/DRN approach is in influencing GP prescribing behaviour.

# STUDY OBJECTIVES

* 1. **Primary Objective**

To demonstrate that inappropriate polypharmacy in elderly patients can be reduced by effectively communicating to GPs the burden of toxic and/or unnecessary medications being taken by their patients.

* 1. **Secondary Objectives**

1. What is the incidence of medium and High Drug Burden Index scores among the RNSH ED patient cohort?

2. What changes, if any, are made to patients’ prescribed medications by their GPs after the receipt by the GP of Drug Burden Index scores for their patients?

3. What changes, if any, are seen in patients’ DBI scores one month after their discharge from ED?

4. Are any changes in patients’ DBI sustainable over a six month period?

5. Is there any evidence that re-presentation rates are related to changes in DBI?

# STUDY DESIGN

* 1. **Type of Study**

This project is an Evaluation Study.

* 1. **Study Design**

This study will evaluate the benefits, if any, of communicating elderly patients’ Drug Burden Index scores to their GPs. We will use convenience sequential sampling to recruit our study population. The study will run for 12 months. Recruiting will be continuous throughout the first six months of the study or until the target sample size of 250 participants is achieved, whichever occurs first.

*Inclusion criteria:* Patients > 65 years of age without significant cognitive impairment (ie Six Item Screener score of >4) who are taking at least one prescribed medication and who have attended RNSH Emergency Department and were discharged to home.

*Exclusion criteria:* Patients below the age of 65 years, patients with significant cognitive impairments, or patients who are admitted to RNSH as in-patients or who are transferred as in -patients to another care facility (eg rehab, private hospital).

All consenting patients will have their DBI scores calculated at three points in time: admission to ED, one month after their discharge, and six months after their discharge. Post-discharge data collection will be via telephone follow-up interview. During the follow-up interviews participants will also be asked if they have been re-admitted to an ED.

 **Data collection:**

*Pre-trial audit*: prior to commencement of DBI calculations we will undertake a pre-trial audit of medications taken by patients over the age of 65 years who present to the ED and are discharged to home. The following data will be collected: MRN, Age, Gender, Presenting problem(s), any relationship of presenting problems to medications taken, the number of presentations during a) the previous month and b) the previous year; and the generic names and 24-hour dosage of medications with: Anticholinergic, Sedative, or Vasodilating properties, beta or calcium channel blockers, and analgesics. These data will be collated by a Research Pharmacist from First Net.

*Data collection point 1*: collate information collected as part of routine ED procedures regarding participants’ prescribed medications, record reason for ED presentation

*Data collection point 2*: collect information on participants’ prescribed medications during first (1 month post-discharge) telephone interview

*Data collection point 3*: collect information on participants’ prescribed medications during second (6 month post-discharge) telephone interview*,* and information regarding having been re-admitted to an ED.

**Data Analysis:**

Calculate DBIs at:

* time of initial ED presentation – DBI 0
* one month post-discharge – DBI 1
* six months post-discharge – DBI 6

Calculate the incidence of Medium and High Drug Burden Index scores among the RNSH ED patient cohort (Secondary Objective 1)

Compare

* DBI 0 and DBI 1
* DBI 0 and DBI 6
* DBI 1 and DBI 6

Assess changes in participants’ Drug Burden Index after GPs receive their patients’ DBIs after discharge from ED (Secondary Objective 3)

Assess sustainability of any GP-initiated changes (Secondary Objective 4)

Undertake qualitative/ semi-quantitative review of GPs changes, if any, in prescribing

Discern the relationship, if any, between re-presentations to ED and DBI risk range (Secondary Objective 5)

* 1. **Number of Participants**

250

* 1. **Study sites**

This study will be conducted wholly at Royal North shore Emergency Department with 250 participants.

* 1. **Expected Duration of Study**

This study will commence recruiting in March 2017 and the project will finish in March 2018. Recruitment will be ongoing until 250 participants are recruited, or until the end September 2017, whichever occurs first. Follow-ups will occur from the beginning of September 2017 until the completion of the project in March 2018.

* 1. **Primary and Secondary Outcome Measures**

*Primary outcomes*

Determine overall reductions (if any) in participants’ DBI scores: if significant reductions in DBIs are found, this will fulfil the Primary Objective of the study.

*Secondary Outcomes*

The data set will report the overall incidence of Medium and High-range Drug Burden Index scores among the RNSH ED patient cohort. This information is especially valuable in the context of other, allied projects aiming to reduce drug-related morbidity and mortality.

The data will allow insights into the sustainability of any GP-initiated moves to reduce patients’ DBIs. This information will be valuable with respect to planning further interventions with the aim of reducing DBIs.

Information linking DBIs to re-presentation rates is valuable in the context of other, allied projects aiming to reduce drug-related morbidity and mortality.

1. **PARTICIPANT ENROLLMENT**
	1. **Recruitment**

All elderly patients (>65 years of age) without significant cognitive impairments, who are currently taking at least one prescribed medication, who present to the ED and are later discharged from ED to their home are potential participants. Potential participants will have been screened for cognitive status as part of the routine ED process. Patients scoring above 4 on a six item screener (SIS), and who are to be discharged to home, will be invited to join this study.

Potential participants will be approached by the Research Pharmacist (RP) after the decision has been made to discharge them to home. The RP will introduce him/herself and ask the patient if they are interested in hearing about a research project which they could potentially participate in. The RP will give a short verbal explanation of the project, and if the person indicates that they are interested, will provide the potential participant with an information sheet and consent form. The RP will go through these documents with the person if required and will answer any questions about the project. If the person decides to participate they will be requested to sign the Consent form. It will be made clear to all potential participants that their participation is entirely voluntary, can be withdrawn with no consequences at any time, and that their care will be completely unaffected by their decisions in this matter.

* 1. **Eligibility Criteria**
		1. **Inclusion Criteria**

Inclusion criteria: Patients > 65 years of age who are currently taking at least one prescribed medication, without significant cognitive impairment (ie Six Item Screener score of >4), who have attended RNSH Emergency Department and were discharged to home.

* + 1. **Exclusion Criteria**

Exclusion criteria: Patients below the age of 65 years, patients who have significant cognitive impairments, patients who are not taking any prescribed medications or patients who are admitted to RNSH as in-patients or who are transferred as in -patients to another care facility (eg rehab, private hospital).

# Informed Consent Process

With respect to our pre-trial audit, we are seeking to waive consent for the collection of these data. It is impracticable to obtain consent from all participants not least because many patients will present at a time of day when the Research Pharmacist is not present. We have undertaken a risk assessment of this approach which indicates that the sole risk associated with the collection of these data is that confidentiality may be breached. We consider that we can safeguard against any harm occurring via this route by adhering to strict Privacy Protection principles and by de-identifying the data at the earliest possibility. After data cleaning, MRNs will be permanently removed. No person will have access to these data except the Research Pharmacist and the Study Investigators: the confidentiality and privacy conditions set out in elsewhere in this Protocol will also apply to the audit data. We submit that this proposal satisfies the conditions for a waiver set out in the National Statement section 2.3.10.

With respect to the trial process (ie DBI calculations), after having identified potential participants and gained the permission of the treating doctor, the RP will approach the patient, introduce him/herself, and briefly explain the study to the patient. If the patient shows interest in the study, the RP will explain the study in more detail and give the patient an information sheet. The RP will encourage potential participants to ask any questions they may have, and will ensure that it is understood that participation is voluntary, any information given will be treated in confidence, and that consent can be withdrawn at any point without affecting their treatment or their relationship with their treating team. The patient will then be asked to sign a consent form.

* 1. **Participant Withdrawal**
		1. **Reasons for withdrawal**

The study is extremely unlikely to be terminated early as it is a low risk, no-intervention study which is fully funded. In the event of early termination there would be no consequences except possibly the need for RNSH to negotiate the return of funds to the grant provider.

# STUDY VISITS AND PROCEDURES SCHEDULE

|  |  |  |  |
| --- | --- | --- | --- |
|  | Event | Information collected from participant | Information collected from ED records |
| *Data collection point 1* | Patient recruited to study whilst in ED |  | Prescribed medicationsReason for presentation to EDGP’s details |
| *Data collection point 2* | First telephone follow-up interview | Prescribed medicationsAny ED re-presentations |  |
| *Data collection point 3* | Second telephone follow-up interview | Prescribed medicationsAny ED re-presentations |  |

# ADVERSE EVENT REPORTING

There is a potential for participants to become anxious about their medications should they discover that they have a Medium or High-range DBI. There is also a potential for participants to decide to cease taking their prescribed medications. The Patient Information form will contain assurances that the calculation of a Medium of High-range DBI is not in itself a reason to become unduly concerned, but that it is a reminder to seek an appointment with their GP to discuss and/or review their prescribed medications sooner rather than later. The Patient Information form will also advise patients not to discontinue their medications until they have consulted with their GP.

# STATISTICAL METHODS

* 1. **Sample Size Estimation**

The sample size is limited by the period of available funding for the project (6 months) and the expected number of potential participants presenting to ED during this six month period. In the absence of any pilot data, if we look at a 50% change in DBI over the period of the study with alpha 0.05/beta 0.2 and 80% power, our target sample is 126 patients over the period of the trial.

* 1. **Statistical Analysis Plan**

DBI data collected at the initial ED visit and at subsequent phone interview by the research pharmacist will be analysed by GEE logistics regression analysis using the binary outcome measures of high DBI (> 1.0) vs low/medium DBI (0 – 1.0) and by linear regression analysis for % change/ mean in DBI over time and across groups.

Data analysis will be with IBM SPSS Statistics V22 (2016)

# DATA MANAGEMENT

* 1. **Data Collection**

Data for the first DBI calculation will be obtained with the patient’s consent from ED records. Data for the second and third DBI calculations will be obtained from consenting participants by telephone interview.

* 1. **Data Storage**

All data will be entered into the Project Tablet at the time of data collection in order to calculate DBIs. All data will then be entered into spreadsheets on a password protected computer located within a secure office area, which will be backed up weekly. The tablet and backup will be stored in a locked cabinet in the office of the PI (Dr Mark Gillett). All data analysis will be undertaken by the Research Pharmacist, on the project computer, within the secure office area in the ED. No person other than the Investigators and Research Pharmacist shall have access to the data.

* 1. **Data confidentiality**

In order to successfully conduct the follow-up interviews with participants, it will be necessary for the Research Pharmacist to have access to participants’ names and telephone numbers. After the completion of the second interviews, each participant’s identifying information will be removed from all records and their file will be coded with an alphanumeric identifier. The key to the codes linking participants’ identifying information with their allocated code number will be stored by the PI in a locked cabinet and no person other than the PI will have access to it. At the conclusion of all data collection activities the key will be destroyed and the data will thus be de-identified.

Publications arising from this research will focus on cohort-level analyses of factors influencing DBIs: no individual’s results will be reported.

* 1. **Study Record Retention**

All records relating to this project will be securely stored for 5 years after the completion of the project, at which time they will be securely destroyed.

# ADMINISTRATIVE ASPECTS

* 1. **Independent HREC approval**

This study has been approved by the Northern Sydney Local Health District HREC, reference number:

* 1. **Amendments to the protocol**

Any amendments will be submitted to the HREC for review prior to implementation as per HREC guidelines.

* 1. **Participant reimbursement**

No reimbursements will be made to participants.

* 1. **Financial disclosure and conflicts of interest**

This study is funded by a Grant from the HCF Research Foundation. There are no conflicts of interest.

# USE OF DATA AND PUBLICATIONS POLICY

It is envisaged that this project will yield two peer reviewed publications. One will report the extent of inappropriate polypharmacy among this sample of older patients. The second publication will report data regarding the sustainability of any GP-initiated moves to reduce patients’ DBIs. Both publications will bear all Investigators’ names and include appropriate acknowledgment of The Research Pharmacist’s contributions.

Due to the potential of this approach, if proven, to prevent polypharmacy-related ED presentations, it is anticipated that data generated during this trial will be disseminated more widely including to Policy makers (ACI) and to other potential stakeholders. A separate report will be made to the funding provider (HCF

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