# Statistical analysis plan for the Effectiveness of an Ambient Intelligent Geriatric Management system (AmbIGeM) to prevent falls in older people in hospitals: A stepped wedge pragmatic trial

The Ambient Intelligent Geriatric Management (AmbIGeM) system is a 3-cluster stepped wedge pragmatic trial, with an embedded qualitative process, designed to evaluate a wearable sensor device to alert staff of patients undertaking at-risk activities, for preventing falls in older patients compared to standard care. The trial occurred on three acute/subacute wards in two hospitals in Adelaide and Perth, Australia.

The AmbIGeM trial is registered on the Australian and New Zealand Clinical Trial Registry (ANZCTR 372816) and is funded by the National Health and Medical Research Council of Australia (project grant num 1082197). Ethical approval was granted by the Human Research Ethics Committees of The Queen Elizabeth Hospital (HREC/15/TQEH/17) and the Sir Charles Gairdner Hospital (HREC No: 2015-110).

This document describes the pre-specified statistical analysis plan developed by the chief investigators and trial statistician before completion of patient recruitment and data collection. The statistical analysis plan outlines the principles and methods of analysing and reporting the trial results. The use of a pre-specified plan aims to reduce the risk of analysis bias arising from knowledge of the trial results emerging during the conduct of the analysis.

Current version approved by the study chief investigators: 8 August 2019

## AIMS AND HYPOTHESES

The primary aim of the AmbIGeM trial is to determine whether the wearable sensor technology system safely reduces the falls rate when compared to usual care. The null hypothesis is that the response rate ratio of falls per occupied bed days during the intervention periods compared to the control periods is one ($H_0$: RRR=1), versus an alternative hypothesis that the RRR is not equal to one ($H_1$: RRR≠1).

Secondary aims will be assessed including a health economic analysis.

## DESIGN

### Population

The AmbIGeM study will be delivered across three wards in two hospitals in two states of Australia (South Australia (SA) and Western Australia (WA)). The wards include two geriatric evaluation and management units (GEMU) (one in each of SA and WA) and one general medicine ward (WA).
All patients aged 65 years and older admitted to the participating wards, excluding those receiving palliative treatment, will be recruited to the study. Waiver of consent was approved for WA and opt-out consent was approved for SA.

### Design, blinding and study setting

Full details of the trial design have been published previously (Visvanathan R, Ranasinghe DC, Wilson A et al. Inj Prev 2019;25:157-165). The trial will take 103 weeks to complete, with one ward crossing over from control to intervention every 25 weeks until all wards have experienced one or more time blocks exposed to the intervention. A 3-week period after the first 25-week control block is included concomitantly across all three sites to test the technology prior to the commencement of the first intervention period in SA. All wards will spend 25 weeks in the control period initially with successive wards crossing over every 25 weeks into intervention in the following pragmatic order to support implementation of the technology which was deployed from SA: SA GEMU, WA GEMU, WA General Medicine. There will be no blinding to the intervention of staff or patients.

## Intervention

The AmbIGeM intervention includes a wearable Bluetooth low energy (BLE) device with integrated sensors worn by patients in a singlet. The wearable device is positioned in a pocket in the singlet over the sternum for the purpose of transmitting movement signals, where these signals are collected by base stations and interpreted by software that identifies risk circumstances and responds 'intelligently' (tailored response) to those activities of a patient leading to situations of increased falls risk. When a risk circumstance is identified by the system, clinical staff will be alerted via a hand-held mobile device that they will wear or carry. A selected combination of vibrations and/or an alarm sound from the mobile device will alert staff. The alert will describe the patient, location and risk movement. Staff may then intervene and provide supervision to the patient where required.

## Outcome Measures

The primary outcome measure in this study will be the falls rate, calculated as the number of falls divided by the number of participant bed days (PBDs) in the participating wards during the control and intervention blocks. The fall definition already in use at the participating hospitals will be used for the study. A fall in this study is defined as 'an event which results in a person coming to rest inadvertently on the ground or floor or other lower level'. Research personnel will collect falls data (location, injury, time) from three sources: health systems computerised incident reports, daily enquiry of falls from ward team leader, and hand searching of patient medical notes or electronic health records.

The secondary outcome measures in this study are: i) proportion of participants falling; and ii) rate of injurious inpatient falls per 1000 PBDs. Injurious falls are those that cause bruising, laceration, fracture, loss of consciousness or if the patient reports persistent pain. Fractures will be confirmed by radiological confirmation.

## Data collection and follow-up

An online data management system was developed for use in this study. In addition to trial eligibility criteria, the following data is collected: demographic details (date of birth, gender, living arrangements pre-hospitalisation) within 72 hours of admission; primary reason for admission, if the patient was admitted with a fall in the last 7 days, the Charlson Co-morbidity Index, diagnoses of dementia or

delirium, number of medications (from medical discharge summary); falls (including location, injuries, date and time); adverse events; protocol deviations; post hospital discharge destination, and dates of admission to hospital and ward and discharge from ward and hospital. Additionally, for the economic evaluation the following is collected: use of hospital services including rehabilitation, emergency department presentations and readmissions and mortality (to 3 months post discharge from the study ward).

### Sample size and statistical power

Assuming a baseline falls rate of 7.7 per 1000 participant bed days (PBD) and an average length of stay of 12.3 days (based on earlier data from participating wards), then 924 patients were needed in a patient-level randomized trial to achieve 80% power at 5% significance level to detect a relative reduction in falls to 0.53 (i.e. a 47% reduction in the falls rate). Accounting for the clustered nature of the stepped wedge design required increasing the sample size by a factor of the expected intra-cluster correlation coefficient (ICC). Assuming an ICC of 0.002 [33] and an average cluster size of 800 patients over the 100 weeks of the study (excluding the three weeks technology testing period prior to the first intervention block), gives a design effect of 2.6 and so a total of 2400 patients was required.

## STATISTICAL ANALYSIS

### Principles

All analyses will be conducted on patient-level data. If consent for participation and data collection is withdrawn, the data will not be used. Analyses will be performed by intention to treat according to the control or intervention status of the ward at the time of the patient enrolment in the trial, regardless of compliance with the intervention. Patients recruited to the study during a control period will be censored when the ward transitions to the intervention, with falls and length of stay data only collected up until the time of transition. Missing data will not be imputed. Two-sided hypothesis testing at a significance level of 0.05 will be used. No adjustment for multiple tests will be made. Analyses will be conducted using SPSS Statistics version 24 or later (IBM) and R version 3.5.3 or later (R Core Team).

## Trial profile

Patient flow through the trial will be presented in a Consolidated Standards of Reporting Trials (CONSORT) diagram, including the number of patients who meet the trial eligibility criteria, the number of patients enrolled in the trial, and the number of patients included in the intention-to-treat dataset for analysis of the primary outcome.

## Participant characteristics

Patient characteristics at baseline will be tabulated by intervention group. Categorical variables will be presented as frequency counts (n) and a proportion of the number of patients with available data (%). Continuous variables will be presented as summary statistics for location (mean or median) and variability (standard deviation or interquartile range). The total counts for variables with missing data will be indicated as footnotes to individual tables.

## Analyses

The primary outcome of falls rate will be analysed using a Poisson generalized linear regression model including fixed effects for intervention, ward, and study period (1-4 wedges, consisting of 25 weeks each), to account for the clustered, stepped-wedge design of the study, and adjusted for the pre-specified covariate of the Charlson's Comorbidity Index. Due to the small number of wedges and study periods, the usual mixed effect model for stepped-wedge designs will not be used. The effect of intervention will be presented as rate ratio and 95% confidence interval (CI).

The secondary outcome of the rates of injurious falls will be analysed using the same adjusted Poisson generalized linear regression model as used for the primary outcome. Poisson models will be examined for overdispersion and underdispersion. The proportion of participants falling will be analysed by binary logistic regression, accounting for ward, study period, and Charlson's Comorbidity Index, with results reported as odds ratio and 95% CI.

Two sub-group analyses to assess the differential effect of intervention on outcomes will be performed on the pre-specified sub-groups of patients with and without dementia or delirium, and by day (0700-1959) or night (2000-0659), by including the presence of the sub-group factor as an interaction effect with intervention.

## Protocol compliance

Protocol non-compliance is captured in pre-specified protocol deviations which will be tabulated by intervention group and reported as frequency counts (n) and percentages (%).

## Adverse events

Adverse events and serious adverse events will be tabulated by intervention group and reported as frequency counts (n) and percentages (%).

## TABLES AND FIGURES

### Table 1: Patient characteristics

| | Control (N=) | Intervention (N=) | Total (N=) |
|---|---|---|---|
| Age, years (mean [SD]) | | | |
| Women (n [%]) | | | |
| Living in the community pre hospitalization (n [%]) | | | |
| Charlson's Co-Morbidity Index Score (mean [SD])* | | | |
| Proportion admitted with falls with or without fractures (n [%])* | | | |
| Proportion admitted with dementia (n [%])* | | | |
| Proportion admitted with delirium (n [%])* | | | |
| Top 5 Reasons for primary admission (n [%])*<br>Reason 1<br>Reason 2<br>Reason 3<br>Reason 4<br>Reason 5 | | | |
| Polypharmacy on discharge ≥5 medications (n [%])* | | | |
| Length of stay, days (median [IQR]) *<br>Total<br>SA GEM<br>WA GEM<br>WA Gen Med | | | |
| Death during admission (n [%])* | | | |
| Discharge destination (n [%])*<br>Community<br>Residential aged care (permanent)<br>Rehabilitation<br>Transitional care program<br>Died in hospital<br>Others | | | |

*obtained from patient discharge summary

**Table 2: Falls outcomes**

| | Intervention (N=) | Control (N=) | Total (N=) | Adjusted rate ratio (95% CI), P Value | Intracluster coefficient correlation |
|---|---|---|---|---|---|
| Falls, rate per 1000 participant bed days<br>N patients | | | | | |
| Injurious falls, rate per 1000 participant bed days<br>N patients<br>N falls with fractures<br>N patients with fractures | | | | | |
| Fallers, having one or more falls (n [%]) | | | | | |

**Table 3: Falls outcomes by dementia/delirium subgroup**

| | | Intervention (N=) | Control (N=) | Total (N=) | Adjusted rate ratio (95% CI) |
|---|---|---|---|---|---|
| Falls, rate per 1000 participant bed days | With dementia or delirium | | | | |
| | No dementia or delirium | | | | |
| Injurious falls, rate per 1000 participant bed days | With dementia or delirium | | | | |
| | No dementia or delirium | | | | |
| Fallers, having one or more falls (n [%]) | With dementia or delirium | | | | |
| | No dementia or delirium | | | | |

P-value for intervention by dementia/delirium interaction: p=

**Table 4: Falls outcomes by day/night subgroup**

| | | Intervention (N=) | Control (N=) | Total (N=) | Adjusted rate ratio (95% CI) |
|---|---|---|---|---|---|
| Falls, rate per 1000 participant bed days | Day | | | | |
| | Night | | | | |
| Injurious falls, rate per 1000 participant bed days | Day | | | | |
| | Night | | | | |
| Fallers, having one or more falls (n [%]) | Day | | | | |
| | Night | | | | |

P-value for intervention by day/night interaction: p=

**Table 5: Protocol deviations**

| N [%] | Control (N=) | Intervention (N=) | Total (N=) |
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**Table 6: Adverse events**

| N [%] | Control (N=) | Intervention (N=) | Total (N=) |
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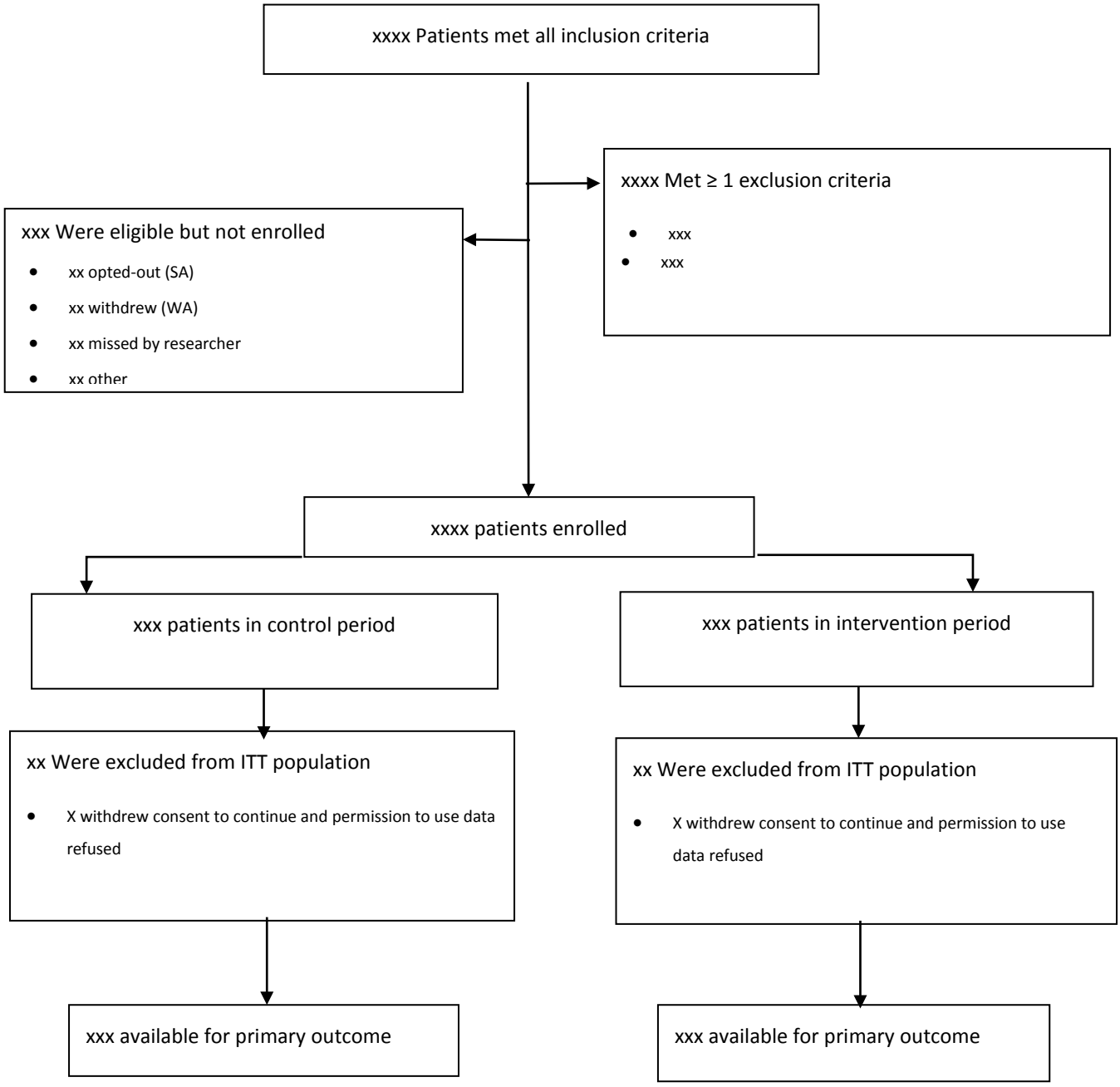
**Table 7: Withdrawals during study**

| N [%] | Control (N=) | Intervention (N=) | Total (N=) |
|---|---|---|---|
| Participant reasons | | | |
| Verbally indicating do not want or like the sensor | | | |
| Verbally indicating do not want or like the vest | | | |
| Believes too unwell | | | |
| Does not want to participate | | | |
| Other | | | |
| Family reasons | | | |
| Does not want to participate in research | | | |
| Does not believe patients wants or likes the sensor | | | |
| Does not believe patient wants or likes the vest | | | |
| Believes patient is too unwell | | | |
| Other | | | |
| Staff decision | | | |
| Too unwell | | | |
| Physically aggressive | | | |
| Other | | | |
| Palliative care | | | |
| Other reason | | | |

**Figure 1: CONSORT diagram**



**Version history:**

28 June 2019: Original version.

8 August 2019: Addendum: The following sentence was removed from the 'Principles' section: *Analysis will be blinded regarding the trial phase of each wedge (intervention or control).* It was decided that the trial statistician would be unblinded after final data entry was completed, due to the feasibility of remaining blinded given the small number of randomisation points in the design. All other Investigators will remain blinded until data analysis is complete.