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Full Title:

Cost-Effectiveness and Value of Information Analysis of an Ambient Intelligent Geriatric Management (AmbIGeM) System Compared to Usual Care to Prevent Falls in Older People in Hospitals

Short Title:

CEA and VoI of an Ambient Intelligent Geriatric Management System to Prevent Falls in Hospitals

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Abstract

Background

The Ambient Intelligent Geriatric Management (AmbIGeM) system combines wearable sensors with artificial intelligence to trigger alerts to hospital staff before a fall. A clinical trial found no effect across a heterogenous population, but reported a reduction in the injurious falls rate in a post hoc analysis of patients on Geriatric Evaluation Management Unit (GEMU) wards. Cost-effectiveness and Value of Information (VoI) analyses of the AmbIGeM system in GEMU wards was undertaken.

Methods

An Australian health care system perspective and 5-year time horizon were used for the cost-effectiveness analysis. Implementation costs, inpatient costs and falls data were collected. Injurious falls were defined as causing bruising, laceration, fracture, loss of consciousness, or if the patient reported persistent pain. To compare costs and outcomes, generalised linear regression models were used to adjust for baseline differences between the intervention and usual care groups. Bootstrapping was used to represent uncertainty. For the VoI analysis, 10,000 different sample sizes with randomly sampled values ranging from 1 to 50,000 were tested to estimate the optimal sample size of a new trial that maximised the Expected Net Benefits of Sampling.

Results

There were an adjusted 0.036 fewer injurious falls (adjusted rate ratio of 0.56) and AUD$4,554 lower costs in the intervention group. However, uncertainty that the intervention is cost-effective for the prevention of an injurious fall was present at all monetary values of this effectiveness outcome. A new trial with a sample of 4,376 patients was estimated to maximise the Expected Net Benefit of Sampling, generating a net benefit of AUD$186,632 at a benefits to cost ratio of 1.1.

Conclusions

The benefits to cost ratio suggest a new trial of the AmbIGeM system in GEMU wards may not be high-value compared to other potential trials, and that the system should be implemented. However, a broader analysis of options for preventing falls in GEMU is required to fully inform decision-making.

Trial Registration

Australian and New Zealand Clinical Trial Registry (ACTRN 12617000981325).

Keywords

Health Care Economics and Organizations; Preventive Health Services; Geriatric Assessment; Accidental Falls

Key Points for Decision Makers

- The benefits to cost ratio suggests a new trial of the Ambient Intelligent Geriatric Management system in geriatric wards may not be a high-value investment compared to funding other potential trials, and that the system should be implemented.
- The developed methods described provide a framework for Value of Information analyses of future clinical trials in which adjustment for imbalances in baseline characteristics are required.

1 Introduction

Falls among patients in Australian hospitals occurred at a rate of 4.0 falls per 1,000 hospital admissions in 2020-21 [1]. Falls can lead to a loss in independence [2], premature institutionalisation [3] and increased length of stay and hospital costs [4].

In the USA, the ceasing of reimbursements for costs relating to inpatient falls by the Centers for Medicare and Medicaid Services (CMS) [5], led to the increased use of object-based alarms (e.g. beds) despite the lack of evidence of benefit [6]. With wearable sensor technological advances, it has become possible to monitor multiple patients in multiple locations simultaneously. When coupled with artificial intelligence, alerts can be automatically triggered to staff, allowing them to offer supervision before a fall [7]. The novel Ambient Intelligent Geriatric Management (AmbIGeM) system was designed and then evaluated using a stepped wedge controlled clinical trial that included patients with dementia and delirium [8]. The trial was adequately powered, but found no statistically significant differences in the rate of falls and injurious falls and the proportion of fallers in the intervention periods compared to the control periods [8]. Patients perceived the intervention to be acceptable and a good idea and expressed no privacy concerns [9]. A post-hoc analysis found a statistically significant reduction in the falls (adjusted rate ratio 0.64, 95% CI 0.27, 1.68) and injurious falls (adjusted rate ratio 0.34, 95% CI 0.11, 1.15) rates in the intervention period compared to the control period for patients receiving care in Geriatric Evaluation Management Unit (GEMU) wards [8]. The GEMU wards are specialised sub-acute units providing for comprehensive geriatric assessment including multi-disciplinary management to older patients for age related conditions (e.g. cognitive impairment, reduced mobility, complex psychosocial problems) following a brief period of acute hospitalisation (e.g. acute general medicine or acute care of the elderly units) with the goal of helping older people live at home and in the community longer [10]. Therefore, when compared to the overall trial population, the GEMU population were significantly older, and more likely to be female, living in the community, present with dementia and/or delirium, have a history of falls and be admitted to hospital due to a fall with or without fracture. The GEM units are different to rehabilitation units where the primary clinical intent is to improve the functioning of a patient with an impairment, activity limitation or participation restriction due to a health condition with the patient medically stable and able to actively participate in therapy [10].

The trial results were interpreted as providing evidence to preclude further consideration of the general use of the AmbIGeM system for patients aged 65 years and older, but that consideration of the technology in GEMU wards may be warranted [8]. A cost-effectiveness analysis of the AmbIGeM system in GEMU wards

would inform the potential value of the system in the GEMU setting, but a Value of Information (VoI) analysis to estimate the expected value of further research may be particularly relevant in this case due to the post hoc basis for the cost-effectiveness analysis. VoI analyses compare the costs of undertaking further research with the expected value of further research to reduce the probability of making an implementation decision that does not maximise expected benefits (i.e., to reduce the probability of making the "wrong" decision) [11].

This paper presents a cost-effectiveness analysis and VoI analysis of the AmbIGeM system in GEMU wards to inform decisions of whether to fund the implementation of the AmbIGeM system in GEMU wards and to undertake further research to reduce uncertainty around such funding decisions, respectively.

2 Methods

2.1 Patients and Intervention

A stepped wedge pragmatic trial comparing the AmbIGeM system and usual care in three wards, the GEMU ward at The Queen Elizabeth Hospital (TQEH) in South Australia (SA) and the GEMU and general medicine wards at the Sir Charles Gairdner Hospital (SCGH) in Western Australia (WA), was conducted. Details of the trial protocol and effectiveness findings have been published elsewhere [8, 12]. Briefly, patients aged 65 years and over and admitted to participating wards were eligible for inclusion. All wards started with a 25-week control period and successively switched to intervention every 25 weeks in the following order SA GEMU, WA GEMU and WA general medicine. The GEMU wards spent less time in control (3 x 25-week periods) and more time in the intervention (5 x 25-week periods) period. Usual care at both hospitals comprised of routine best practice falls prevention activities, including falls risk screening and assessment, environment assessment, and implementing interventions for identified risk factors, such as appropriate positioning of call bells and mobility aids, adequate lighting, bed/chair sensor alarms, reduced clutter and compliance with restraint policies [13].

For the intervention, patients wore a singlet with a Bluetooth Low Energy (BLE) device with integrated sensors (triaxial accelerometer and gyroscope) positioned over the sternum in a customised pocket. When sensors detected high risk movements, staff were alerted by alarms via an application on mobile phones which clinical staff carried. The alarm could be set to detect a range of high-risk movements depending on individual patient risk as identified by clinical staff.

Ethics and governance approval was granted by the TQEH/Lyell McEwin Hospital /Modbury Hospital (HREC/15/TQEH/17), Curtin University (HRE2017-0449) and SCGH (PRN 2015-110). The trial was registered with the Australian and New Zealand Clinical Trial Registry (ACTRN 12617000981325).

2.2 Data

Trial outcomes included the experience of any fall, and injurious falls, the latter being defined as causing bruising, laceration, fracture, loss of consciousness, or if the patient reported persistent pain [14, 15]. Outcome events were collected by research personnel from computerized incident reports, daily enquiries with ward team leaders and hand searching of patient medical notes or electronic health records. As part of hospital policy, falls were recorded by clinical staff in the incident reporting system and medical records. Where research staff were uncertain regarding the recording of falls, the senior investigators (RV and KH) adjudicated.

Intervention costs included significant upfront costs (e.g., ceiling mounted devices, servers and connections to Wi-Fi systems) as well as BLE devices and training (annuitised over the expected 5-year lifetime of the devices), singlets and ongoing technology support. Other costs included inpatient admissions for patients who received care on a study ward during the study period. These costs were obtained from the finance departments of the study hospitals and reflect national costing guidelines for inpatient care [16].

Analyses were undertaken from the perspective of the Australian health care system as the intervention was implemented in public hospital settings. All cost data were in Australian dollars, and reflected costs in the year 2020. All inpatient admissions were less than one year in duration and so costs and outcomes were not discounted.

2.3 Cost-Effectiveness Analysis

A cost-effectiveness analysis of the AmbIGeM system was undertaken in the subgroup of trial participants who were managed in the GEMU wards (1,660 of the total 3,114). The primary outcome for the cost-effectiveness analysis was defined as the experience of one or more injurious falls during study patients' stay on a study GEMU ward, noting injurious falls provide a more homogenous and meaningful measure of patient outcomes than any fall [17].

A generalised linear regression model using log-transformed costs and including fixed effects for intervention, ward and time period was used to estimate the mean costs in the intervention and control groups. For the injurious falls outcome, a binary logistic regression model including fixed effects for intervention, ward and time period was used. The Charlson Comorbidity Index was also included in all of the models as a pre-specified covariate.

The mean costs and injurious falls probabilities for each treatment group were then compared. The incremental cost-effectiveness ratio (ICER) was defined as the incremental cost per admission without an injurious fall and was calculated by dividing the difference in expected total costs by the difference in the expected probabilities of an injurious fall between the two groups.

Bootstrapping was used to generate 95% confidence intervals (CI) and a cost-effectiveness plane to graphically represent the joint differences in mean costs and outcomes between the intervention and control groups. The resampling of data 1,000 times for the bootstrapping was considered adequate as re-running the bootstrap with a different random number seed did not significantly change the bootstrap estimates. Cost-effectiveness acceptability curves were generated to indicate the probability that the intervention is cost-effective compared with usual care at different monetary values for additional admissions without an injurious fall. Missing data were not imputed as there were no missing outcomes data and cost data were missing for only 7 (0.42%) patients.

2.4 Value of Information Analysis

There are three key measurements in a VoI analysis [11, 18], the:

- Expected Value of Perfect Information (EVPI), which describes the expected loss associated with the likelihood that the wrong decision is made, i.e., the AmbIGeM system is funded if it is not cost-effective, or it is not funded if it is cost-effective. This is equivalent to the expected value of eliminating all uncertainty from a single patient's perspective. Population EVPI is the EVPI per patient multiplied by the number of the future population who could benefit from the intervention (beneficial population). The beneficial population is estimated as the annual number of patients who would be eligible to receive the intervention being evaluated multiplied by the discounted number of years until the intervention of interest is likely to be superseded.
- Expected Value of Sample Information (EVSI), which describes the expected reduction in the EVPI from undertaking a specific new data collection exercise (usually a further research study, an increase in the number of study participants, or an extension to follow-up of an existing study). This is equivalent to the expected value of the reduction in uncertainty that would result from further research for an individual patient. Population EVSI is the EVSI per patient multiplied by the beneficial population.
- Expected Net Benefit of Sampling (ENBS), which subtracts the cost of collecting the new data from the population EVSI to give the net cost of undertaking further research.

Net monetary costs were estimated for each patient as their incurred health care costs plus a monetary value of $7,000 if a patient experienced an injurious fall. The assigned monetary value of an injurious fall represents the expected costs of generating health gains equivalent to the prevention of an injurious fall by the

Australian public health system. It was based on an assumption that the health effects of an injurious fall were equivalent to losing 0.25 of a Quality Adjusted Life Year (QALY) and a reported cost to generate a QALY in Australia of AUD$28,000 [19]. The assumption of a loss of 0.25 QALYs for an injurious fall is based on the NICE Clinical Guidelines for Falls assessment and prevention in older people and the following example: "a man aged 65.5 who is admitted to hospital and suffers a minor fall whilst an inpatient is calculated to have a utility of 0.434 following the fall. The patient leaves hospital on the 5th day and the fall utility decrement is changed to the minor fall utility decrement associated with being at home, so his utility becomes 0.782 for another 360 days (the rest of the year following his fall)" [20].

The analytic method to estimating the EVPI, EVSI and ENBS described by Wilson [11] was applied, incorporating the use of regression analysis to adjust analyses of net monetary costs for imbalances between the comparator and intervention groups with respect to potential confounders. A Q-Q plot of the log of the estimated net monetary costs justified an assumption that this parameter was normally distributed (see Supplementary Figure S1), which informed the selection of a generalised linear regression model to model log-transformed net monetary costs. The model was fitted as described in the *Cost-Effectiveness Analysis* section for the analysis of costs.

2.4.1 Expected Value of Perfect Information (EVPI)

To estimate the EVPI for the original clinical trial, 10,000 bootstrapped samples of the trial dataset were generated. For each sampled dataset of net monetary costs, the generalised linear regression model was fitted and the least-squares mean estimates of net monetary costs were derived from the model for the intervention and control groups. The mean incremental net monetary costs were then estimated for each bootstrap sample (i.e., intervention group mean net monetary costs minus control group mean net monetary costs). Drawing on the central limit theorem, the 10,000 estimates of the mean incremental net monetary costs were assumed to be normally distributed.

Each of the 10,000 bootstrap samples generate equally likely estimates of the incremental net monetary costs of the AmbIGeM system. A proportion of the estimates will indicate that the intervention has negative incremental net monetary costs and so should be funded, the remaining proportion will estimate positive incremental net monetary costs, indicating that the system should not be funded. With perfect information, the correct funding decision would be made in all of the 10,000 possible scenarios, such that incremental net monetary costs $\leq$ \$0 are estimated across all 10,000 bootstrap samples. With current information, a single decision to fund or not to fund the intervention is made across all 10,000 possible scenarios, which means that

incremental net monetary costs ≥ $0 are estimated for scenarios in which the 'wrong' funding decision is made. The EVPI is the difference between the mean of the incremental net monetary costs with perfect information and with current information.

2.4.2 Expected Value of Sample Information (EVSI)

The EVSI is estimated as the difference between a predicted posterior ('preposterior') EVPI that reflects the expected effects of additional data and the prior EVPI using the existing AmbIGeM trial data. The preposterior EVPI was estimated for 10,000 alternative sample sizes for a new clinical trial of the AmbIGeM system (of the same design as the original AmbIGeM trial). The new sample sizes were randomly sampled from a uniform distribution with minimum and maximum values of 1 and 50,000. The expected outputs for each participant in each of the 10,000 'new clinical trials' were sampled with replacement from the original AmbIGeM dataset. The sampled values were added to the original AmbIGeM dataset and the regression model for the log of the net monetary costs was re-fitted and the preposterior EVPI estimated, as described for the prior EVPI. A smooth monotonic curve was fitted to the 10,000 estimates of the preposterior EVPI values as a function of sample size, using the scam package [21] in R version 4.0.5 [22].

To estimate the Population EVSI, the annual number of bed days in GEMU wards in South Australia (201 beds) [23] was extrapolated to estimate bed days across Australia based on the proportion of the Australian population residing in South Australia (7%) [24]. This was divided by the mean length of stay (13.94 days) observed in the AmbIGeM trial to give the estimate of 70,000 inpatient episodes per year in GEMU wards across all Australian hospitals. In the base case:

- a 20% uptake rate by GEMU wards in hospitals across Australia was assumed (based on reports in the existing literature that few health service interventions are successfully implemented [25]), i.e., 14,000 inpatient episodes per year for which the AmbIGeM system would be used if implemented,
- a five-year time horizon was defined as the period over which the AmbIGeM system would be expected to remain a relevant intervention, reflecting a high rate of advancement in digital medical technologies, and the expected lifetime of the intervention device.

Thus, a total beneficial population of 70,000 inpatient episodes (14,000 per year multiplied by five years) was estimated. Discounting at a rate of 5% [26] was applied to the future population who could benefit.

2.4.3 Expected Net Benefit of Sampling (ENBS)

The ENBS is the expected benefit from undertaking further research (the Population EVSI) minus the total cost of undertaking further research. Expected research costs were informed by the costs of running the original

AmbIGeM trial, incorporating fixed costs of $500,000 and variable costs of $300 per patient. The ENBS is estimated as a function of the sample size of a new clinical trial to identify the sample size that maximises the ENBS. Scenario analyses were undertaken to illustrate the effects of varying assumptions regarding uptake of the AmbIGeM system, the time horizon and expected research costs.

3 Results

Of the 3,114 patients in the AmbIGeM trial, 1,667 (53.5%) were in GEMU wards. With cost data missing for 7 patients, the analyses were performed on 1,660 GEMU patients. A larger proportion of GEMU patients were in the intervention than in the control periods. Patient characteristics are presented in Table 1, showing almost all patients were living in the community prior to admission. Patients in the intervention periods were more likely to have a history of falls with or without fracture and to present with delirium or dementia. Unadjusted outcomes showed intervention patients were less likely to die during the admission or be discharged directly home.

Table 1 GEMU Participant Characteristics

	Intervention (n=997)		Control (n=663)		P-value	SMD
Age, years (mean [SD])	85.3	[7.68]	85.8	[7.73]	0.163	0.070
Female (%)	600	(60.2)	398	(60.0)	0.992	0.003
Living in the community pre-hospitalisation	975	(97.8)	646	(97.4)	0.760	0.023
Charlson's Co-Morbidity Index Score					0.741	0.056
None	168	(16.9)	103	(15.6)		
Mild	418	(41.9)	293	(44.2)		
Moderate	263	(26.4)	176	(26.5)		
Severe	148	(14.8)	91	(13.7)		
With delirium or dementia	371	(37.2)	214	(32.3)	0.045	0.104
Previous admission with fall +/- fractures	444	(44.5)	241	(36.3)	0.001	0.167
Reasons for primary admission (top 5 only)						
Infection	147	(14.8)	116	(17.4)	<0.001	0.319
Cardiovascular	87	(8.7)	82	(12.4)		
Falls with no fractures	189	(19.0)	85	(12.8)		
	91	(9.1)	66	(10.0)		

Other musculoskeletal, rheumatological	86	(8.6)	67	(10.1)		
Fracture +/- falls						
Polypharmacy on discharge ≥5 medications						
	874	(87.7)	572	(86.3)	0.452	0.041
Death during admission	14	(1.4)	23	(3.5)	0.009	0.134
Discharge destination					0.001	0.284
Community	541	(54.3)	391	(59.0)		
Residential aged care (permanent)	42	(4.2)	20	(3.0)		
Rehabilitation	89	(9.0)	57	(8.6)		
Transitional care program	79	(7.9)	47	(7.1)		
Other[a]	246	(24.6)	148	(22.3)		

Data presented as number (percentage), unless otherwise specified

SD standard deviation, *SMD* standardised mean difference

[a]Other includes palliative care, care awaiting placement program, hospital in the home, transfer to another hospital, residential aged care (respite)

3.1 Cost-Effectiveness Analysis

The adjusted rate of injurious falls per admitted patient was lower in the intervention group (0.035 for intervention and 0.071 for control), with a mean difference of -0.036 injurious falls per patient (95% CI -0.097, 0.025) and an adjusted rate ratio of 0.56 (95% CI 0.17, 1.79). Adjusted mean costs per patient were also lower in the intervention group (AUD$23,933) than the control group (AUD$28,487), with a mean cost difference of -AUD$4,554 (95% CI -$9,998, $890). The mean results indicate that the AmbIGeM system improves patient outcomes and reduces costs when used in GEMU wards.

Figure 1 presents the results of the bootstrapped analysis of uncertainty around the mean results, plotting the 1,000 joint estimates of the differences in injurious falls and costs. The majority of the estimates (79%) indicate that the intervention is more effective and less costly than usual care (the southeast quadrant). The southwest quadrant is the second most common quadrant, which represents estimates that indicate that the intervention is less costly, but also less effective. Translating these data into the cost-effectiveness acceptability curves presented in Figure 2 shows that the intervention had a high probability of being cost-effective at all monetary values for the prevention of injurious falls, but that some uncertainty remained.

[Figure 1 here]

[Figure 2 here]

3.2 Value of Information Analysis

The EVPI after the original trial was estimated to be AUD$58.27, representing the benefits of eliminating the uncertainty associated with the decision to fund the AmbIGeM system for a single patient. Applying this value to the estimated beneficial population of 70,000 patients generates a Population EVPI of AUD$3,708,478 over 5 years.

Table 2 presents the outputs from the VoI analysis for 10 potential new trials that could be undertaken to reduce the uncertainty around the cost-effectiveness of the AmbIGeM system. For a new trial with a sample size of 1,000, the EVPI is reduced by AUD$8.81, which is the EVSI per patient. The EVSI for the estimated beneficial population of 70,000 patients is AUD$560,694 over 5 years. However, the estimated cost to run a trial with 1,000 participants is AUD$800,000 so the ENBS is negative: - AUD$239,305.

Table 2 Value of Information Outputs by Sample Size of New Trial

Sample size of new trial	EVSI	Pop. EVSI (AUD$)	New trial costs (AUD$)	ENBS (AUD$)
1,000	$9	$560,694	$800,000	-$239,305
2,000	$17	$1,085,113	$1,100,000	-$14,887
3,000	$24	$1,521,704	$1,400,000	$121,704
4,000	$30	$1,881,924	$1,700,000	$181,924
5,000	$34	$2,174,681	$2,000,000	$174,681
6,000	$38	$2,409,524	$2,300,000	$109,524
7,000	$41	$2,594,725	$2,600,000	-$5,275
8,000	$43	$2,740,468	$2,900,000	-$159,532
9,000	$45	$2,852,479	$3,200,000	-$347,521
10,000	$46	$2,935,215	$3,500,000	-$564,785

AUD Australian dollars, *ENBS* Expected Net Benefit of Sampling, *EVSI* Expected Value of Sample Information, *Pop.* population

For a new trial of 3,000 participants the population EVSI is greater than the new trial costs, resulting in a positive ENBS of AUD$121,704 over 5 years. In Table 2, the ENBS continues to increase to a new trial population of 4,000 after which it declines, becoming negative again at a new trial size of 7,000 participants.

Figure 3 presents the plots for the EVSI, total cost of a new trial (Trial Costs) and ENBS as continuous functions of the total sample size. From the data presented in Figure 3, the maximum ENBS is AUD$186,632 corresponding to an optimal sample size of 4,376 participants.

[Figure 3 here]

Table 3 presents scenario analyses around the parameters used to estimate the beneficial population. The uptake scenario assumes increased uptake of the AmbIGeM system across GEMU wards in Australia, which increases the maximum ENBS to over AUD$4 million for a new trial of 8,341 participants. Reducing the time period over which the decision to use the AmbIGeM system remains relevant to 3 years or increasing the variable cost of a new trial to AUD$500 results in negative maximum ENBS, indicating further research is not warranted.

Table 3 Scenario Analyses around Population Size Parameters

	Base case	**Uptake scenario**	**Decision relevance scenario**	**New trial costs scenario**
Uptake	20%	50%	20%	20%
Time horizon	5 years	5 years	3 years	5 years
Beneficial population	70,000	179,000	43,000	70,000
Fixed cost (AUD$)	$500,000	$500,000	$500,000	$500,000
Variable cost (AUD$)	$300	$300	$300	$500
Optimal sample	4,376	8,341	2,023	1,758
Max ENBS (AUD$)	$186,632	$4,150,446	-$417,851	-$412,984

AUD Australian dollars, *ENBS* Expected Net Benefit of Sampling

4 Discussion

The key finding from the economic evaluation is that there is an almost 80% probability that the AmbIGeM system reduces falls and is cost saving from a health system perspective. Despite the small probability that the intervention is not cost-effective in GEMU wards, regardless of the value placed on the prevention of injurious falls, the base case VoI analysis estimated that further research that eliminated the estimated uncertainty would have an equivalent monetary value of AUD$3,708,478. Accounting for the costs of undertaking additional research, a new trial with a sample of 4,376 patients was estimated to maximise the ENBS, generating a net benefit of AUD$186,632. However, the ENBS was found to be highly sensitive to key input parameters, including the expected uptake of the intervention, the time horizon for the relevance of the intervention and the expected costs of new research. The interpretation of the base case VoI analyses is that further research would generate positive net benefits, but that does not necessarily mean that such research should be funded.

There are limited research funds and the opportunity costs (forgone benefits) of alternative research may be higher than the expected benefits of a new trial of the AmbIGeM system. The Collaborative Network for Value of Information (https://www.convoi-group.org/) lists VoI analyses published by the Network's 20 members, which shows that most published VoI analyses report the EVPI, but not the EVSI and ENBS. Searches of ConVOI and PubMed identified only four full VoI analyses published in the six years since 2017 [27-30]. ENBS do not reflect the magnitude of the investment required to generate the ENBS, so comparisons of benefits to investment ratios across VoI analyses provide the most informative basis for comparing the relative value of alternative new trials (noting variation in methods and context affect comparability).

The benefits to investment ratio of the new trial of the AmbIGeM system is 1.1 ($1,999,432/$1,812,800), for which crude comparisons can be made with three [27-29] of the four full VoI analyses published since 2017 (one of the studies [30] was recently published assessing a needle-free adrenaline autoinjector with an ENBS reported in the abstract but access to the full text was not yet available). In a VoI analysis of drug therapies for the management of gout [27], the base case results (assuming a value of a QALY of $60,000) imply new trial costs of around $21 million and benefits of around $550 million – a benefits to investment ratio of 26. Another full VoI analysis of a gene assay to inform treatment decisions for women with early-stage breast cancer presented results assuming a value of a QALY of $150,000 [29], for which a new randomised controlled trial that maximised ENBS was estimated to cost around $40 million and generate benefits of around $105 million, at a benefits to cost ratio of 2.6. In the third full VoI analysis, reducing unhealthy alcohol use in HIV-infected patients in East Africa [28] had a benefits to cost ratio of 1.2 (new trial

costs of $220,000 and benefits of $260,000) and was only considered worthwhile if policymakers intended to implement the intervention for a longer duration (i.e. over 10 years), otherwise conducting a new trial was not recommended. The limited comparisons indicate that a new trial of the AmbIGeM system may not be a high-value investment, a conclusion that is further supported by the presented scenario analyses in which plausible values for key VoI parameters – duration of decision relevance and costs of conducting a new trial – resulted in negative ENBS for any new trial of the AmbIGeM system.

An additional consideration is the finding from the process evaluation of the original trial that prespecified targets for adherence to the AmbIGeM system were not met and options for increasing adherence were proposed [8]. The VoI analyses reported in this paper do not reflect the potential effects of adaptations to the use of the evaluated technology that would be expected to increase the reductions in injurious falls and costs observed in the original trial. This introduces an interesting issue around the appropriate incorporation of such expectations into the VoI analysis. Should the observed intervention effects be adjusted upwards, which would increase the certainty that the intervention is cost-effective and reduce the expected value of additional research, or should only the expected effect estimates generated by future research be adjusted upwards, which would increase the value of additional research.

There are several limitations of the analyses reported in this paper. Firstly, the analyses are based on post-hoc analyses of the clinical trial, which are subject to claims of cherry-picking sub-groups for which positive results were observed and reduced the comparability of the intervention and control cohorts. However, the adherence evaluation undertaken alongside the clinical trial identified clear differences in the application of the AmbIGeM system between the general medicine and GEMU wards [8], which provides a rationale for the post-hoc analyses.

Imbalances in relevant baseline characteristics between the intervention and control groups required adjustment to published guidelines for VoI analyses [11]. The adjusted methodology involved the random sampling from the original trial dataset of expected costs and outcomes for individual patients in future clinical trials, regression-based adjustment of the sampled data representing the outputs from future clinical trials and the estimation of EVPI as a function of the sample size of future clinical trials. These developed methods provide a framework for VoI analyses of future clinical trials in which adjustment for imbalances in baseline characteristics are required.

As part of the estimation of the aggregate population for which research on the AmbIGeM system is expected to be relevant in Australia, it was assumed that usual care in the two GEMU wards included in the

original trial is representative of usual care in GEMU wards across Australia. The collection of injurious falls rates across a representative range of non-trial GEMU wards would inform the validity of the assumed representativeness of the trial GEMU wards.

Perhaps most importantly, the presented analyses should be replicated for alternative intervention options for preventing falls on GEMU wards; however, published evidence of such alternatives appears to be lacking. A recently published systematic review and meta-analysis of interventions to reduce falls in hospitals [31] identified two education interventions [15, 32] but both were conducted in populations that were not comparable to this study population and did not focus on injurious falls. The first education intervention [15] was an Australian study in which patients were admitted to one of five acute and subacute wards. One of the wards was for geriatric assessment and rehabilitation but no sub-analyses were reported. The other education intervention [32] was also an Australian study and involved a geriatric rehabilitation unit but specifically excluded patients with cognitive impairment (mini-mental examination scores <24). In the AmbIGeM study, 35% of the GEMU population had cognitive impairment. The implied interpretation of the cost-effectiveness and VoI analyses presented in this paper is that the expected benefits of further research on the AmbIGeM system in GEMU wards compared to usual care do not justify the expected research costs. Further, given the current lack of evidence on alternative intervention options for preventing falls on GEMU wards and until new relevant primary research is published, our recommendation is that the AmbIGeM intervention be implemented on GEMU wards. The analyses presented in this paper provide a framework for broader analyses, but we also suggest that an expert stakeholder group of clinicians, epidemiologists and health economists is assembled to interpret the results in light of the variation in the validity and relevance of the data available to inform the proposed analyses.

5 Acknowledgements

We would like to thank SA Health (Tomi Adejoro) and WA Health (Ian Massingham) for support and provision of data. We would also like to acknowledge the clinical, administrative and information technology staff from both hospitals, the research staff and students that supported the conduct of the trial.

6 Declarations

6.1 Funding

This study was funded by a project grant (1082197) from the National Health and Medical Research Council of Australia.

6.2 Conflicts of Interest

Previously, there was a patent filed (mid-2013) by Drs Ranasinghe and Visvanathan titled, "System, method, software application and data signal for determining movement" but this has since lapsed. Professor Visvanathan is the Head of Unit of the Aged & Extended Care Services at The Queen Elizabeth Hospital in South Australia within which the GEMU ward is a service. Professor Visvanathan is providing advice to Live 24/7, a start up based in San Jose, USA. Dr Dollard was awarded The Hospital Research Foundation Research Travel Award and Faculty of Health and Medical Sciences (University of Adelaide) Research Travel Award in 2017 to attend AmbIGeM related meetings. The remaining authors declare no other conflicts of interest.

6.3 Author Contributions

CP and JK designed and conducted the economic evaluation and value of information analysis, and contributed to the cost data collection, data interpretation and drafting of the manuscript. MS and EW contributed to the design and interpretation of the value of information analysis and drafting of the manuscript. RV and KH equally contributed to the study design, selecting participating sites, conducting the research, data collection, data interpretation and drafting of the manuscript. DR contributed to the technology design and implementation, conducting the research, data collection, data interpretation and drafting of the manuscript. KL designed and conducted the statistical analysis and contributed to interpretation and drafting of the manuscript. JD and AW were involved in the conduct of the study, data collection, data interpretation and drafting the manuscript.

6.4 Data Availability

Requests for health economics data should be directed to the senior author (jonathan.karnon@flinders.edu.au) and will require collaboration with the chief investigator team. Any requests will be assessed for scientific rigor (by a panel consisting of JK, RV, KH and DR) and given the involvement of hospital patient data, the request

must first meet ethics request guidelines and be approved by the ethics committees of TQEH/Lyell McEwin Hospital (LMH)/Modbury Hospital (MH), Curtin University, and SCGH. The requestor will be responsible for preparing documentation to the standard required to meet the conditions of the various ethics committees. A data sharing agreement will be necessary and funding requested for facilitation of this process and provision of data. Given the multiple analyses planned as well as underway currently, data sharing is at this stage embargoed for a further 2 years.

6.5 Ethics Approval

Ethics and governance approval was granted by the TQEH/Lyell McEwin Hospital /Modbury Hospital (HREC/15/TQEH/17), Curtin University (HRE2017-0449) and SCGH (PRN 2015-110).

6.6 Consent to Participate

A waiver of consent was approved in Western Australia and opt-out consent was approved in South Australia.

6.7 Consent for Publication

A waiver of consent was approved in Western Australia and opt-out consent was approved in South Australia.

6.8 Code Availability

The authors can provide more details upon request.

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