

2021

Kynurenic acid may underlie sex-specific immune responses to COVID-19

Yuping Cai

Daniel J. Kim

Takehiro Takahashi

David I. Broadhurst
Edith Cowan University

Hong Yan

See next page for additional authors

Follow this and additional works at: <https://ro.ecu.edu.au/ecuworkspost2013>



Part of the [Immunology and Infectious Disease Commons](#), and the [Physical Sciences and Mathematics Commons](#)

[10.1126/scisignal.abf8483](https://doi.org/10.1126/scisignal.abf8483)






Cai, Y., Kim, D. J., Takahashi, T., Broadhurst, D. I., Yan, H., Ma, S., ... Iwasaki, A. (2021). Kynurenic acid may underlie sex-specific immune responses to COVID-19. *Science Signaling*, *14*(690), article eabf8483. <https://doi.org/10.1126/scisignal.abf8483>

This Journal Article is posted at Research Online.
<https://ro.ecu.edu.au/ecuworkspost2013/10712>

Authors

Yuping Cai, Daniel J. Kim, Takehiro Takahashi, David I. Broadhurst, Hong Yan, Shuangge Ma, Nicholas J. W. Rattray, Arnau Casanovas-Massana, Benjamin Israelow, Jon Klein, Carolina Lucas, Tianyang Mao, Adam J. Moore, M. Catherine Muenker, Ji Eun Oh, Julio Silva, Patrick Wong, Albert I. Ko, Sajid A. Khan, Akiko Iwasaki, Caroline H. Johnson, and Yale IMPACT Research team

Estimating the economic cost of nurse sensitive adverse events amongst patients in medical and surgical settings

Aileen Murphy¹   | Peter Griffiths²  | Christine Duffield^{3,4}  | Noeleen M. Brady⁵  | Anne Philomena Scott⁶ | Jane Ball⁷ | Jonathan Drennan⁸  

¹Cork University Business School, University College Cork, Cork, Ireland

²Health Sciences, University of Southampton, Southampton, UK

³Nursing and Health Services Management, University of Technology, Sydney, NSW, Australia

⁴Nursing and Midwifery, Centre for Health Services Management and Edith Cowan University, Sydney, NSW, Australia

⁵School of Nursing and Midwifery, University College Cork, Cork, Ireland

⁶National University of Ireland Galway, Galway, Ireland

⁷School of Health Sciences, University of Southampton, Southampton, UK

⁸School of Nursing and Midwifery, University College Cork, Cork, Ireland

Correspondence

Aileen Murphy, Cork University Business School, University College Cork, College Road, Cork T12 AK54, Ireland.
Email: Aileen.Murphy@ucc.ie

Funding Information

The research is funded by the Department of Health and Health Research Board under research grant FSN-2017-001.

Abstract

Aims: To identify the costs associated with nurse sensitive adverse events and the impact of these events on patients' length of stay.

Design: Retrospective cohort study using administrative hospital data.

Methods: Data were sourced from patient discharge information ($N = 5544$) from six acute wards within three hospitals (July 2016–October 2017). A retrospective patient record review was undertaken by extracting data from the hospitals' administrative systems on inpatient discharges, length of stay and diagnoses; eleven adverse events sensitive to nurse staffing were identified within the administrative system. A negative binomial regression is employed to assess the impact of nurse sensitive adverse events on length of stay.

Results: Sixteen per cent of the sample ($n = 897$) had at least one nurse sensitive adverse event during their episode of care. The model revealed when age, gender, admission type and complexity are controlled for, each additional nurse sensitive adverse event experienced by a patient was associated with an increase in the length of stay beyond the national average by 0.48 days ($p = .001$). Applying this to the daily average cost of inpatient stay per patient (€1456), we estimate the average cost associated with each nurse sensitive adverse event to be €694. Extrapolating this nationally, the economic cost of nurse sensitive adverse events to the health service in Ireland is estimated to be €91.3 million annually.

Conclusion: These potentially avoidable events are associated with a significant economic burden to health systems. The estimates provided here can be used to inform and prepare the way for future economic evaluations of nurse staffing initiatives that aim to improve care and safety.

Impact: As many of these nurse sensitive adverse events are avoidable, in addition to patient benefits, there is a potential substantial financial return on investment from strategies such as improved nurse staffing that can reduce their occurrence.

KEYWORDS

adverse events, costs, economics, nurse staffing, nursing, nursing sensitive outcomes, patient outcomes

1 | INTRODUCTION

Internationally, there is an increased focus on ensuring patient safety and quality of care (Ehsani et al., 2006); this is driven, in part, by the substantial rate of adverse events in hospital settings (Rafter et al., 2017; Schwendimann et al., 2018; Thomas & Brennan, 2001; Vincent et al., 2001). These adverse events can result in serious health outcomes for patients and financial consequences for health systems (Ehsani et al., 2006; Kjellberg et al., 2017). The clinical implications and human burden associated with adverse events are well established (Needleman et al., 2006) with an economic analyses of the costs of these adverse events now emerging (Mittmann et al., 2012). These economic approaches include several retrospective cohort studies, employing regression analyses to estimate costs attributable to all adverse events. These studies have identified that average additional costs associated with adverse events range from €1396 to €5550 per event (Brown et al., 2002; Ehsani et al., 2006; Hoonhout et al., 2009; Kjellberg et al., 2017; Pappas, 2008; Rafter et al., 2017; Vincent et al., 2001) or from €5850–€9505 per person (Brown et al., 2002; Ehsani et al., 2006; Hoonhout et al., 2009; Kjellberg et al., 2017; Rafter et al., 2017; Vincent et al., 2001).

2 | BACKGROUND

While some adverse events are unavoidable, the key challenge is preventable adverse events; that is, those events that occur in health care as a result of errors of commission or omission (Schwendimann et al., 2018). Estimates from international studies reveal that adverse events can occur in anywhere between 3%–22% of admissions (Rafter et al., 2017; Schwendimann et al., 2018), of which anywhere between 50% (de Vries et al., 2008) and 73% (Rafter et al., 2017) are considered preventable. One approach to determining the economic costs of adverse events is through the measurement of nurse sensitive adverse events, which, following Needleman et al., (2002) seminal work, are defined as patient outcomes that are potentially sensitive to nursing care.

One factor that can contribute to the risk of certain adverse events is nurse staffing, with low levels of nurse staffing associated with a number of adverse outcomes including mortality (Aiken et al., 2014; Driscoll et al., 2018; Griffiths et al., 2019; Kane et al., 2007; Needleman et al., 2006, 2011), missed care (Ball et al., 2018; Kalisch, 2006; Recio-Saucedo et al., 2018), hospital-acquired pneumonia (Griffiths et al., 2018) and increased length of stay (LOS) (Duffield et al., 2011; Griffiths et al., 2018; Kalisch, 2006; Twigg et al., 2013). Without adequate staffing, nurses may not have the capacity to proactively minimize an adverse event that requires early

detection and prompt intervention. However, as health services internationally are operating in an environment where resources are scarce and efficiencies are widely sought (Mittmann et al., 2012), nurse staffing is frequently the area of the health workforce that is reduced when savings are required (Pappas, 2008; Williams et al., 2017), and as a consequence, nurse sensitive adverse events can increase, which have significant human and economic costs.

A number of studies have explored the costs associated with an adverse event in a hospital setting (Kjellberg et al., 2017); however, there are a limited number of studies that have explored the relationship between nurse staffing and the costs associated with nurse sensitive adverse events in both medical and surgical patients. Those studies that have identified nurse sensitive adverse events predominantly align costs to medication errors, falls, pneumonia, urinary tract infections and pressure ulcers (Pappas, 2008; Tchouaket et al., 2017). Nurse sensitive adverse events are generally costed as a combined variable or individually with valid sample sizes ranging from 2495 (Pappas, 2008) to 2699 patients (Tchouaket et al., 2017). Overall prevalence of nurse sensitive adverse events were shown to range from 14.4% (surgical patients) to 21.5% (medical patients) with costs per case increasing by \$1029 for medical patients and \$903 for surgical patients who experienced an adverse event (Pappas, 2008). Previous studies have analysed costs at patient level within an individual hospital system with few studies identified that examined costs in a national system. Therefore, as Pappas (2008) highlights, there is a need to identify the costs associated with these adverse events. This will allow nurse leaders and policy makers to identify how the nursing resource in the provision of quality health care can impact on the economic outcomes associated with patient care (Pappas, 2008).

One approach to determining the economic costs of adverse events is through the measurement of adverse events that are sensitive to changes in nursing input, referred to as nurse sensitive outcomes. Needleman et al., (2002) created a list of possible outcomes which can be considered sentinel events sensitive to nursing; these include hospital-acquired urinary tract infections, pressure ulcers, pneumonia, deep venous thrombosis, upper gastrointestinal bleeding, central nervous system complications, sepsis, shock/cardiac arrest, wound infection, pulmonary failure and physiological/metabolic derangement. Employing the aforementioned outcomes, this study estimates the economic burden associated with nurse sensitive adverse events in acute care settings.

In addition, in recent years, a number of health systems have introduced a more systematic approach to determining nurse staffing levels and skill mix in hospital settings; the introduction of these systematic approaches has been associated with a need to identify the economic benefits of their introduction. However, with a few exceptions, studies in this area are limited and a recent review found an

absence of economic evaluations of staffing methodologies or tools (Griffiths et al., 2020).

In 2018, the Department of Health in Ireland published a policy document titled a *Framework for Safe Nurse Staffing and Skill Mix in General and Specialist Medical and Surgical Care Settings in Adult Hospitals in Ireland* (henceforth referred to as the *Framework*) (Department of Health, 2018). This document set out a number of recommendations, including the introduction of nursing hours per patient day to determine staffing levels. The introduction of the *Framework* was aligned to a programme of research which is examining the relationship between intentional changes to nurse staffing and outcomes, including the extent to which economic costings of adverse events related to patient outcomes change according to variations in nurse staffing. This includes examining the extent to which the costs in increasing nurse staffing are offset by a reduction in costs associated with a reduction in adverse events (see Drennan et al., 2018 for further details of the research). The first stage in this process, and the aim of this paper, is to identify costs associated with nurse sensitive adverse events and the impact of these events on patients' LOS.

3 | THE STUDY

3.1 | Aims

The aims of this study were to identify the costs associated with nurse sensitive adverse events and the impact of these events on patients' LOS.

3.2 | Design

A retrospective patient record review was undertaken by extracting data from the hospitals' administrative systems.

3.3 | Participants

Data were collected from six acute adult wards within three Irish hospitals from July 2016 to October 2017 for 5544 admitted patients; these patients had a minimum stay of 24 h, and all were adult patients (aged 18 years and older). Hospitals in Ireland are classified into four generic types ranging from Model 1 (community hospital with sub-acute inpatient beds), Model 2 (inpatient care for low-risk medical patients), Model 3 (larger district hospital that admits acute medical and surgical patients) and Model 4 (large university teaching hospitals) (Acute Medicine Programme Working Group 2010). The hospitals in this study included a Model 2 hospital (109 beds), a Model 3 hospital (235 beds) and a Model 4 hospital (670 beds); in total, there are 38 hospitals in Ireland in Bands 2 to 4. The wards in each of the study hospitals were enrolled in a pilot study implementing a safe nurse staffing framework in medical, surgical and specialist settings in Ireland

(Drennan et al., 2018). One of the first phases of this research was to estimate the costs associated with nurse sensitive adverse events.

3.4 | Data collection

In line with previous studies that estimate cost of total adverse events (Ehsani et al., 2006; Hoonhout et al., 2009; Mittmann et al., 2012), a retrospective patient record review was undertaken by extracting data from the Hospital In-Patient Enquiry (HIPE) system. The HIPE system is the method used in Ireland for collecting data on inpatient discharges and includes data on LOS and diagnoses within the hospital setting (O'Loughlin et al., 2005). Diagnoses are captured by ICD-10 codes and assigned diagnostic-related group (DRG) codes; the latter codes group cases that are clinically similar and that consume similar amounts of health care resources. In this study, ICD-10 codes are employed to determine the presence of an adverse outcome sensitive to nursing, and DRG codes are employed to estimate prices as described below.

3.5 | Nurse sensitive adverse events assessment

Based on the work of Needleman et al., (2002), 11 outcomes sensitive to nurse staffing were identified within the HIPE system: hospital-acquired urinary tract infections, pressure ulcers, hospital-acquired pneumonia, deep venous thrombosis, upper gastrointestinal bleeding, CNS complications, hospital-acquired sepsis, shock/cardiac arrest, wound infection, pulmonary failure and physiological/metabolic derangement: herein referred to as nurse sensitive adverse events. These outcomes were identified from the hospital discharge database using the algorithm developed by Needleman et al., (2002) in the United States. The US algorithm used the US ICD-9 coding system whereas Ireland uses the ICD-10; this is the same system used in Australia and New Zealand where McCloskey and Diers (2005) mapped the original ICD-9 codes in Needleman's study to the ICD-10 codes and these were used in this study (see Drennan et al., 2018 for further details).

3.6 | Validity

The identification of costs associated with nurse sensitive adverse events at patient and unit level, as in this study, has been reported as having greater validity than measuring costs from large administrative data sets that do not distinguish from those events that are not nurse sensitive (Pappas, 2008). The analysis of the HIPE data allows costs to be estimated at patient level.

3.7 | Pricing methodology

Data from HIPE are not linked to a financial system that generates costs/prices per patient; however, the Health Pricing Office (HPO, 2019) has published a price list which provides the prospective

description of prices to be paid for providing services for admitted patients by DRG. These prices are based on retrospective cost and activity data, and adjustments are made for funding policies, reflecting expected expenditure and available budgets. The primary function of the HPO price list is to inform budget allocations for acute public hospitals in Ireland (where the payer is also the provider). We employed this list to estimate the price of episodes of care captured in the data set (using assigned DRGs) and to compare LOS to national averages for those DRGs.

The national price list (HPO, 2019) is generated through activity-based funding (ABF) methods using a relative measure of resource consumption called weighted units; these are set so that the average resource consumption across all cases is one. Cases that consume resources more or less than average resource consumption have a weighted unit greater or less than one. To estimate weighted units, the Health Pricing Office estimate relative values (RVs) associated with the diagnosis. There are separate RVs for day cases and inpatients and furthermore, there are separate RVs for inpatients that have a typical LOS, referred to as inliers, and for high and low outliers; that is, LOSs that are substantially above or below the inlier range. The monetary value of any case is the total weighted unit multiplied by the base price associated with one weighted unit (for further information on methodology employed see HPO (2019)). For example, for a patient assigned DRG IO3B (hip replacement, minor complexity), the price list reveals the national average LOS is 7.2 days (range 2–20 days); the RV associated with this DRG is 2.083 which applies to LOS ranging from 2–20 (referred to as inlier relative value) and price is set at €10,038 (weighted unit base price is approximately €4819). LOS above 20 is associated with 0.098 RV per additional day (there is no lower RV for this DRG). Therefore, if a patient who is assigned DRG IO3B has a LOS of 23 days, they have three high outlier days. Their total weighted unit then is the RV for the inlier period (2.083) plus the RV for the high outlier days (0.098×3 days), giving a price of €11,456 for the episode. This translates to €498 daily average (total price/LOS). This methodology is employed to estimate total and daily average prices for all patients enrolled in the study.

3.8 | Data analysis

In line with previous studies (Brown et al., 2002; Ehsani et al., 2006; Hoonhout et al., 2009; Kjellberg et al., 2017; Rafter et al., 2017; Vincent et al., 2001), to estimate the financial impact of nurse sensitive adverse events, we determined their impact on LOS, specifically on LOS beyond the national average for that DRG termed 'additional LOS'. We hypothesized that the presence of nurse sensitive adverse event(s) will increase LOS, to which we can assign a price to quantify the economic impact of nurse sensitive adverse events. LOS is treated as a count variable (nonnegative integer). As there was overdispersion in the count data (where the mean of the variable is smaller than the variance of the variable; Jones, 2007), we employ a negative binomial model (over the Poisson model) (Deb et al., 2017). This count model is a generalization of the Poisson regression

model because it has the same mean structure as a Poisson regression and it has an extra parameter (a gamma-distributed error term) to model the overdispersion (Cameron & Trivedi, 2005). Maximum likelihood estimates are used, wherein iterations are generated until the change in log likelihood is sufficiently small. Within the model, the outcome (y) depends on a set of explanatory variables (x), and it is assumed the probability of the event occurring (λ) = $\exp(x\beta)$. The exponential function is employed to ensure that the intensity of the process so that the mean number of events, given x , is positive (Jones, 2007). Within the model the coefficients can be tested using a conventional t test; the conditional mean is a function of the explanatory variables, and alpha estimates the degree of overdispersion in the data. The variance is a quadratic function of the mean, and the approach has been applied extensively in health studies (Jones, 2007). The function form can be presented as $\log(\lambda_i) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \dots + \beta_k x_{ik} + \sigma \epsilon_i$, where λ_i is the expected value of the outcome variable y_i for subject i , x_i are the independent variables with corresponding regression coefficients β_n and $\sigma \epsilon_i$ is the disturbance term (see Cameron and Trivedi (1998)). In this study, the additional LOS is the dependent variable (y); the explanatory variables (x) are the number of nurse sensitive adverse events, patients' age and gender, admission type and case complexity. Incidence rate ratios and the average marginal effects are estimated. Data were analysed using Stata Version 14 (StataCorp, 2015).

4 | ETHICAL CONSIDERATIONS

The research ethics committees of the three hospitals in which the research took place granted ethical approval.

5 | RESULTS

5.1 | Characteristics of the sample

In total, data were collected on 5544 inpatients; 50% of patients were male and the average age was 62.4 years (SD 19.56) (see Table 1). The majority of patients were admitted as emergency cases (vs. elective) (83%). With regard to complexity, over a third of patients in the sample were classified as having major complexity, 11% intermediate and 52% minor (this classification was determined from the DRG assigned). The mean LOS was 9.9 days (see Table 1); 10% of patients had LOS beyond the national average for their DRG.

Applying the HPO methodology, as discussed above, to the DRGs and LOS data extracted for the sample, we estimated the price per admission for patients in the study. The average price per admission was €8544 (SD €13,318). The average daily price per patient included in the study, based on their individual LOSs, was €1456 (SD €1515).

Sixteen per cent of the sample ($n = 897$) had at least one nurse sensitive adverse event during their episode of care. Of these, 76% had one event; 20% two events; and 4% had three or more nurse sensitive

TABLE 1 Summary statistics of sample.

Variable	Full sample (n = 5544)				Nurse sensitive AE (n = 897)			
	Mean	SD	Min	Max	Mean	SD	Min	Max
Age (years)	62.36	19.56	16	103	71.84	16.01	17	103
Male (1,0)	0.50	0.50	0	1	0.48	0.50	0	1
Emergency admission (1,0)	0.84	0.37	0	1	0.94	0.23	0	1
LOS (days)	9.91	13.79	1	219	18.32	22.11	1	219
Addition LOS ^a (1,0)	0.44	0.50	0	1	0.48	0.50	0	1
Additional LOS (days)	2.60	5.63	0	88.1	4.37	8.92	1	219
High outlier LOS ^b (1,0)	0.10	0.30	0	1	0.19	0.40	0	1
High outlier LOS (days)	1.33	7.68	0	191	3.44	13.94	0	191
Any nurse sensitive AE (1,0)	0.16	0.37	0	1	1.00	-	1	1
# of nurse sensitive AEs	0.21	0.53	0	4	1.29	0.56	1	4
Minor complexity (1,0)	0.52	0.50	0	1	0.18	0.38	0	1
Intermediate complexity(1,0)	0.36	0.48	0	1	0.71	0.45	0	1
Major complexity (1,0)	0.11	0.32	0	1	0.11	0.31	0	1
No complexity (1,0)	0.01	0.11	0	1	0.00	0.05	0	1
Total price pp (€)	8544	13,318	641	193,526	15,310	25,550	1513	193,526
Average daily price pp	1456	1515	63	23,833	1185	1413	63	13,532

Notes: n = sample size.

Abbreviations: AE, adverse event; DRG, diagnostic-related group; LOS, length of stay; pp, per patient; SD, standard deviation.

^aLOS greater than average LOS per DRG, as per national estimates (HPO, 2019).

^bLOS exceeds inlier range per DRG, as per national estimates (HPO, 2019).

adverse events. Amongst those who had nurse sensitive adverse events, the average number was 1.3 (SD 0.56). Metabolic derangement was the most frequently occurring event (36.7%, $n = 330$), followed by hospital-acquired pneumonia (24.9%, $n = 223$) and urinary tract infection (22.6%, $n = 203$). Those who had at least one nurse sensitive adverse event were predominately female (52%), had an average age of 71.8 years, 94% were classified as an emergency admission and 71% were assigned a DRG with an intermediate complexity classification level. In addition, amongst those patients who experienced at least one nurse sensitive adverse event, the mean LOS was 18.32 days (see Table 1); 19% of patients had LOS beyond the national average for their DRG, which was 4.37 days on average.

5.2 | Length of stay

Table 2 presents results from the negative binomial regression model that estimates the impact of nurse sensitive adverse events on LOS while controlling for patient characteristics. The base categories are female, non-emergency admission and no complexity.

The Wald chi-square statistic (7 degrees of freedom for the full model) tests that all of the estimated coefficients are equal to zero (a test of the model as a whole); here, the p value ($<.0001$) suggests that the model is statistically significant. The log-transformed over dispersion parameter ($1/\alpha$) is also estimated and the likelihood ratio test examines if α equals zero (comparing this model of a

Poisson model). Here, the associated chi-square value with 1 degree of freedom is $1.7e+04$, suggesting the alpha is non-zero and the negative binomial model is more appropriate than the Poisson model. The coefficients for number of nurse sensitive adverse events and major and intermediate complexity are all statistically significant.

For ease of interpretation, the results are presented as incident rate ratios (see Table 2): each nurse sensitive adverse event was associated with a 25% increase in additional LOS ($p = .001$), holding all else constant. To understand the model better in terms of LOS, the marginal effects (see Table 2, lower panel) were estimated. Holding all else constant, each nurse sensitive adverse event was associated with increasing the LOS beyond national average by 0.48 days ($p = .001$). Other factors influencing additional LOS were admission type and complexity. Those patients who were an emergency admission had a reduced LOS beyond national average (0.3 days [$p = .04$]), while those classified with an intermediate or major complexity have increased LOSs beyond national average, 3.53 and 3.70 days, respectively ($p = .001$).

5.3 | Economic impact

Using the results of the negative binomial regression, whereby each nurse sensitive adverse event increased the LOS beyond national average by 0.48 days and applying the estimated daily average price of inpatient stay per patient (€1456), we estimated the economic

TABLE 2 Negative binomial regression: impact of nurse sensitive adverse event on length of stay.

	Coef.	SE	z	$p > z^a$	95% confidence interval	
No. of nurse sensitive AEs	0.224	0.044	5.080	>.001	0.137	0.310
Age (standardized)	-0.018	0.024	-0.760	.447	-0.066	0.029
Male	0.040	0.047	0.850	.397	-0.052	0.131
Emergency admission	-0.148	0.064	-2.310	.021	-0.274	-0.022
Minor complexity	0.533	0.238	2.240	.025	0.067	0.999
Major complexity	1.735	0.239	7.250	>.001	1.266	2.204
Intermediate complexity	1.658	0.245	6.770	>.001	1.178	2.137
_cons	-0.266	0.239	-1.110	.265	-0.734	0.202
/lnalpha	0.904	0.028	5.080		0.849	0.959
alpha	2.469	0.069	-0.760		2.337	2.609

Likelihood ratio test of alpha =0: $\text{chibar2}(01) = 1.7e+04$; Prob \geq $\text{chibar2} = .000^{b,c}$

Number of observations: 5544; Wald chi-square statistic (7 degrees of freedom) = 684.85
Prob > chi-square >.0001; Pseudo- $R^2 = .0315$

Incidence rate ratios	IRR	SE	z	$p > z^a$	95% confidence interval	
No. of nurse sensitive AEs	1.251	0.055	5.080	>.001	1.147	1.363
Age (standardized)	0.982	0.024	-0.760	.447	0.936	1.030
Male	1.040	0.049	0.850	.397	0.949	1.140
Emergency admission	0.862	0.055	-2.310	.021	0.760	0.978
Minor complexity	1.704	0.405	2.240	.025	1.070	2.715
Major complexity	5.668	1.356	7.250	>.001	3.546	9.059
Intermediate complexity	5.246	1.284	6.770	>.001	3.247	8.477
_cons	0.766	0.183	-1.110	.265	0.480	1.224
/lnalpha	0.904	0.028			0.849	0.959
Alpha	2.469	0.069			2.337	2.609

Marginal Effects(Delta-method)	Margin	SE	z	$p > z^a$	95% confidence interval	
No. of nurse sensitive AEs	0.477	0.094	5.050	>.001	0.292	0.661
Age (standardized)	-0.039	0.052	-0.760	.447	-0.141	0.062
Male	0.084	0.100	0.850	.397	-0.111	0.280
Emergency admission	-0.316	0.137	-2.310	.021	-0.585	-0.048
Minor complexity	1.136	0.507	2.240	.025	0.143	2.129
Major complexity	3.698	0.514	7.190	>.001	2.690	4.705
Intermediate complexity	3.533	0.525	6.720	>.001	2.503	4.563

Note: Base categories: female, non-emergency admission and no complexity.

^aThe z value follows a standard normal distribution which is used to test against a two-sided alternative hypothesis that the Coef. is not equal to zero. The probability that a particular z test statistic is as extreme as, or more so, than what has been observed under the null hypothesis is defined by $p > z$.

^bLikelihood ratio test of alpha =0. This is the likelihood ratio chi-square test that the dispersion parameter alpha is equal to zero.

^cChibar2(01) indicates that the distribution on the likelihood ratio test statistics is a 50:50 mixture of a chi-square with no degrees of freedom and a chi-square with 1 degree of freedom (rather than the usual chi-square with 2 degree of freedom) (StataCorp, 2015).

impact associated with each nurse sensitive outcome to be €694; this accumulated to €0.8 million for the study population.

6 | DISCUSSION

This is the first study in Ireland to report the costs associated with nurse sensitive adverse events and builds on previous research in this

area through the use of routinely collected data and by considering a wider range of nurse sensitive adverse events than previously reported (Pappas, 2008; Tchouaket et al., 2017). The occurrence of a nurse sensitive adverse event was 16%; this is higher than adverse events previously reported by Tchouaket et al., (2017) in Canada (6.2%), similar to rates reported for surgical patients (14.4%) but lower than that reported for medical patients in the United States (21.5%) (Pappas, 2008). However, it is of note that this study measured a wider range

of nurse sensitive adverse events compared with previous research; in particular, when compared with Pappas (2008) and Tchouaket et al., (2017) whose research measured five nurse sensitive adverse events. As would be expected, and similar to other studies, patients who experienced a nurse sensitive adverse event while in hospital had a longer LOS when compared with patients without (Ehsani et al., 2006).

The descriptive statistics reveals higher additional LOS amongst those who had at least one nurse sensitive adverse event compared with the general sample (2.60 compared with 4.37). This is at the lower end of Tchouaket et al., (2017) estimates that adverse events added 4.0 to 12.3 days to LOS, depending on the adverse event experienced by the patient. Additionally, the regression reveals that each nurse sensitive adverse event increases average LOS beyond the national average by 0.48 days. In addition, we estimated the average cost associated with each nurse sensitive adverse event to be €694; this was lower than the costs identified in the United States, where the cost per adverse event per case increased by €1590 in medical patients and €1396 in surgical patients (2008 USD converted to 2019 EUR) (Pappas, 2008).

A previous study in Ireland identified a total of 247 adverse events in 211 admissions, and assigned an average cost for adverse events of €5550, accumulating to over €194 million annually (Rafter et al., 2017). The study presented here advances on this methodology. Rather than applying an average cost for events, we take into consideration the patients' diagnosis and compare their length of stay to what is typical for that diagnosis and assign values using the recently published Admitted Patient Price List (HPO, 2019). Therefore, applying more precise estimates, as advocated by Drummond et al., (2015). Furthermore, while Rafter et al., (2017) considered 247 adverse events, we have focused on only 11 events that are considered to be particularly sensitive to nursing care which we estimate to have an economic burden of €91.3 million annually. Considering these results in the context of the Irish health budget, these potentially avoidable adverse events represent 0.56% of the 2018 total government expenditure on health care of €16.2 billion (Connors, 2018).

Following the international financial crisis of 2008, there was pressure on national public health care services to make cost savings either through staff reductions or replacing qualified staff with unregistered roles. This resulted in the reduction of the nursing workforce in Ireland between 2008 and 2014 where there was a 10.7% decrease in nurses at staff nurse grade (Williams & Thomas, 2017). Simultaneously, health care costs are rising, inhibiting investments in new initiatives, even those aimed at improving patient safety (Kjellberg et al., 2017). This has direct consequences for front line personnel such as nurses, whose workload has increased due to increasing patient complexity and dependency (Duffield et al., 2011, 2018). Nursing staff play a central role in ensuring patient safety and patient surveillance. In light of cost reduction efforts, resulting shortages and ensuing pressures, these staff have to increase their workloads and provide efficiencies. While nursing costs represent at least 50% of most hospitals' expenses, this cohort of staff drive overall hospital quality and safety and are an important component of hospitals' infrastructure, as well as an effective intervention for achieving operational efficiency and success (Coster

et al., 2018; Pappas, 2008). Knowing the costs of preventable adverse events from an economic perspective is valuable, and estimates can be used to inform decisions regarding designing and investing in patient safety initiatives, health policy and priority setting (Hoonhout et al., 2009; Mittmann et al., 2012). However, the evidence that does exist in this area is both limited and mixed (Griffiths, Ball, Drennan, et al., 2016; Twigg et al., 2015). This study estimates the economic costs associated with potentially avoidable adverse events in Ireland, using outcomes that Needleman et al., (2002) demonstrated to be sensitive to nurse staffing and are readily available from hospital administrative systems.

The estimated average cost of nurse sensitive adverse events calculated here can be used in economic evaluations of initiatives that aim to improve patient care and safety, such as the introduction of the Framework for Safe Nurse Staffing and Skill Mix (Department of Health, 2018). Previous literature demonstrates that work related stressors, for example, could result in adverse events (Kjellberg et al., 2017; Nielsen et al., 2013; Rasmussen et al., 2014); therefore, initiatives that aim to prevent such events have the potential to generate significant cost savings to the health system. For example, increasing nurse staffing levels and improving nurse-to-patient ratios have been found to reduce patient mortality (Aiken et al., 2014; Driscoll et al., 2018; Griffiths et al., 2016, 2019; Rothberg et al., 2005) and generate financial savings (Needleman et al., 2006; Newbold, 2008; Rothberg et al., 2005; Twigg et al., 2013). Studies, such this one, provide information on health care costs which can be used alongside initiatives preventing adverse events thus providing insights into the mechanisms for improving safety, patient satisfaction and perhaps generating cost savings (Kjellberg et al., 2017). In particular, as this study estimates costs directly attributable to care provided, they can be employed in economic evaluations of initiatives that aim to improve care and safety. For instance, aggregating the results of our study to the Irish acute hospital population (approximately 633,155 inpatients discharged annually (excluding maternity and paediatric patients), a 16% likelihood of nurse sensitive adverse events and with 1.3 on average per patient suggests the annual economic impact of nurse sensitive adverse events is €91.3 million for the health service. Considering these potential costs avoided in the context of existing funding, €91.3 million is approximately 1.6% of annual funding to the acute health division (based on 2018 figure of €5589 million; Department of Health, 2019) or 42% of the additional funds annually required to clear the national acute sector's expenditure deficit (average €214 million annually; Duff, 2017).

6.1 | Limitations

Recent studies estimating costs of adverse event have employed a variety of methods, the choice of which is often dependent on data availability. Most recently, Kjellberg et al., (2017), employed patient level cost data, that is to say the actual cost per patient. Over the past number of years, efforts have been made to introduce ABF in Ireland (HSE, 2015; McElroy & Murphy, 2014; Murphy & McElroy, 2015). The result of this culminated in the publication of the ABF

2019 Admitted Patient Price List, which we employ here. However, the HIPE system is not yet linked to a financial reporting system. In the absence of this, we used the ABF price list to generate the expected price per episode for patients in the sample. While this may underestimate the true cost of patients' care, it is aligned with current reimbursement practices in the Irish hospital system where prices are estimated based on case complexity and LOS and therefore represents the best available estimates. Furthermore, associated readmissions or other related health care costs were excluded in the analysis. With regard to the approach taken, we are limited to the pricing list available which does not provide a per diem (daily) cost per DRG. We realise that an additional stay beyond the national average for that DRG may not result in an actual change in price assigned unless the additional stay falls in the high outlier category. While 16% of patients had at least one nurse sensitive adverse event, only 9% of those (68) had an outlier LOS, while 54% (415) had LOSs beyond the DRG's average. This suggests outlier LOS would lack sensitivity as a parameter for the type of events examined here. In addition, in estimating the cost, we had to assume costs are evenly distributed across an entire episode of care. Therefore, while we acknowledge the value assigned to nurse sensitive adverse events in this analysis is a proxy for the true cost, and may be an underestimation, it is the best estimate available.

7 | CONCLUSION

This study estimates the economic cost of nurse sensitive adverse events in the acute care setting throughout Ireland; however, the approach used will also be applicable to researchers and policy makers internationally. These estimates quantify, in monetary terms, the value of potentially avoidable adverse events, which are substantial at €91.3 million annually. The estimates provided here can be used to inform and prepare the way for future economic evaluations of nurse staffing initiatives that aim to improve patient care and safety. Such analyses could inform future budgetary and resource allocation decisions; thereby providing effective information to support financial, managerial and policy functions in the health service while maintaining and improving patient outcomes. While not all nurse sensitive adverse events are preventable, the identification of these events in secondary data and the impact that they have on patient outcomes and costs can facilitate the identification of those that can be avoided and used in the measurement of the association between nurse staffing levels and proportion of adverse events that occur in health care settings.

ACKNOWLEDGEMENTS

We would like to acknowledge the Department of Health and Health Research Board (Grant FSN-2017-001) for funding the study. We would also like to acknowledge the support of the Chief Nurse's Office, Department of Health and the Office of the Nursing and Midwifery Services Director, Health Services Executive as well as Group Directors of Nursing, Directors of Nursing and their teams

and HIPE Officers in each of the research sites. Responsibility for the information and views set out in this publication lies entirely with the authors and not with the funders.

CONFLICT OF INTEREST

Jonathan Drennan is a member of the Editorial Board of the *Journal of Advanced Nursing*.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/jan.14860>.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

ORCID

Aileen Murphy  <https://orcid.org/0000-0003-3062-0692>

Peter Griffiths  <https://orcid.org/0000-0003-2439-2857>

Christine Duffield  <https://orcid.org/0000-0001-6534-8743>

Jonathan Drennan  <https://orcid.org/0000-0001-7365-4345>

TWITTER

Aileen Murphy  @aileenmurphy

Noeleen M. Brady  @NoeleenMBrady

Jonathan Drennan  @JdaDrennan

REFERENCES

- Aiken, L. H., Sloane, D. M., Bruyneel, L., Van den Heede, K., Griffiths, P., Busse, R., Diomidous, M., Kinnunen, J., Kózka, M., Lesaffre, E., McHugh, M. D., Moreno-Casbas, M. T., Rafferty, A. M., Schwendimann, R., Scott, P. A., Tishelman, C., van Achterberg, T., & Sermeus, W. (2014). Nurse staffing and education and hospital mortality in nine European countries: A retrospective observational study. *The Lancet*, *383*(9931), 1824–1830. [https://doi.org/10.1016/S0140-6736\(13\)62631-8](https://doi.org/10.1016/S0140-6736(13)62631-8).
- Ball, J. E., Bruyneel, L., Aiken, L. H., Sermeus, W., Sloane, D. M., Rafferty, A. M., Lindqvist, R., Tishelman, C., Griffiths, P. & Consortium, R. C. (2018). Post-operative mortality, missed care and nurse staffing in nine countries: A cross-sectional study. *International Journal of Nursing Studies*, *78*, 10–15. <https://doi.org/10.1016/j.ijnurstu.2017.08.004>.
- Brown, P., McArthur, C., Newby, L., Lay-Yee, R., Davis, P., & Briant, R. (2002). Cost of medical injury in New Zealand: a retrospective cohort study. *Journal of Health Services Research & Policy*, *7*(1_suppl), 29–34. <https://doi.org/10.1258/135581902320176449>.
- Cameron, A., & Trivedi, P. (1998). *Regression analysis for count data*. Cambridge University Press.
- Cameron, A., & Trivedi, P. (2005). Chapter 20: Models of Count Data. In *Microeconometrics: Methods and Applications* (pp. 665–691). Cambridge University Press.
- Connors, J. (2018). Budget 2019: Health Budget Oversight & Managemet: Alignment of Health Budget and National Service Plan (Oct 2018 ed.). Ireland IGEES, Dept of Public Expenditure & Reform.
- Coster, S., Watkins, M., & Norman, I. J. (2018). What is the impact of professional nursing on patients' outcomes globally? An overview of research evidence. *International Journal of Nursing Studies*, *78*, 76–83.

- de Vries, E. N., Ramrattan, M. A., Smorenburg, S. M., Gouma, D. J., & Boermeester, M. A. (2008). The incidence and nature of in-hospital adverse events: A systematic review. *BMJ Quality & Safety*, 17(3), 216–223. <https://doi.org/10.1136/qshc.2007.023622>.
- Deb, P., Norton, E. C., & Manning, W. G. (2017). *Health econometrics using Stata*, Vol. (3): , Stata Press.
- Department of Health. (2018). *Framework for Safe Nurse Staffing and Skill Mix in General and Specialist Medical and Surgical Care Settings in Ireland*. Department of Health. Retrieved from <https://www.gov.ie/en/publication/2d1198-framework-for-safe-nurse-staffing-and-skill-mix-in-general-and-speci/>
- Department of Health. (2019). *Health In Ireland: Key Trends 2019*. Retrieved from Dublin, Ireland. <https://www.gov.ie/en/publication/f1bb64-health-in-ireland-key-trends-2019/>
- Drennan, J., Duffield, C., Scott, A. P., Ball, J., Brady, N. M., Murphy, A., Dahly, D., Savage, E., Corcoran, P., Hegarty, J., & Griffiths, P. (2018). A protocol to measure the impact of intentional changes to nurse staffing and skill-mix in medical and surgical wards. *Journal of Advanced Nursing*, 74(12), 2912–2921. <https://doi.org/10.1111/jan.13796>.
- Driscoll, A., Grant, M. J., Carroll, D., Dalton, S., Deaton, C., Jones, I., Lehwaldt, D., McKee, G., Munyombwe, T., & Astin, F. (2018). The effect of nurse-to-patient ratios on nurse-sensitive patient outcomes in acute specialist units: A systematic review and meta-analysis. *European Journal of Cardiovascular Nursing*, 17(1), 6–22. <https://doi.org/10.1177/1474515117721561>
- Drummond, M. F., Sculpher, M. J., Claxton, K., Stoddart, G. L., & Torrance, G. W. (2015). *Methods for the economic evaluation of health care programmes*. : Oxford University Press.
- Duff, N. (2017). Spending Review: Acute hospital expenditure review. Department of Public Expenditure and Reform. Retrieved from <https://igees.gov.ie/wp-content/uploads/2015/02/Acute-Hospital-Spending-Review.pdf>
- Duffield, C., Diers, D., O'Brien-Pallas, L., Aisbett, C., Roche, M., King, M., & Aisbett, K. (2011). Nursing staffing, nursing workload, the work environment and patient outcomes. *Applied Nursing Research*, 24(4), 244–255. <https://doi.org/10.1016/j.apnr.2009.12.004>.
- Duffield, C., Roche, M., Twigg, D., Williams, A., Rowbotham, S., & Clarke, S. (2018). Adding unregulated nursing support workers to ward staffing: Exploration of a natural experiment. *Journal of Clinical Nursing*, 27(19–20), 3768–3779. <https://doi.org/10.1111/jocn.14632>
- Ehsani, J. P., Jackson, T., & Duckett, S. J. (2006). The incidence and cost of adverse events in Victorian hospitals 2003–04. *Medical Journal of Australia*, 184(11), 551–555. <https://doi.org/10.5694/j.1326-5377.2006.tb00378.x>
- Griffiths, P., Ball, J., Bloor, K., Böhning, D., Briggs, J., Dall'Ora, C., Iongh, A. D., Jones, J., Kovacs, C., Maruotti, A., Meredith, P., Prytherch, D., Saucedo, A. R., Redfern, O., Schmidt, P., Sinden, N., & Smith, G. (2018). Nurse staffing levels, missed vital signs and mortality in hospitals: retrospective longitudinal observational study. *Health Services and Delivery Research*, 6(38), 1–120. <https://doi.org/10.3310/hsdr06380>.
- Griffiths, P., Ball, J., Drennan, J., Dall'Ora, C., Jones, J., Maruotti, A., Pope, C., Recio Saucedo, A., & Simon, M. (2016). Nurse staffing and patient outcomes: Strengths and limitations of the evidence to inform policy and practice. A review and discussion paper based on evidence reviewed for the National Institute for Health and Care Excellence Safe Staffing guideline development. *International Journal of Nursing Studies*, 63, 213–225. <https://doi.org/10.1016/j.ijnurstu.2016.03.012>.
- Griffiths, P., Ball, J., Murrells, T., Jones, S., & Rafferty, A. M. (2016). Registered nurse, healthcare support worker, medical staffing levels and mortality in English hospital trusts: A cross-sectional study. *British Medical Journal Open*, 6(2), e008751. <https://doi.org/10.1136/bmjopen-2015-008751>.
- Griffiths, P., Maruotti, A., Saucedo, A. R., Redfern, O. C., Ball, J. E., Briggs, J., Dall'Ora, C., Schmidt, P. E., & Smith, G. B. (2019). Nurse staffing, nursing assistants and hospital mortality: retrospective longitudinal cohort study. *BMJ Quality & Safety*, 28(8), 609–617. <https://doi.org/10.1136/bmjqs-2018-008043>.
- Griffiths, P., Saville, C., Ball, J., Jones, J., Pattison, N., & Monks, T., & Group, S. N. C. S. (2020). Nursing workload, nurse staffing methodologies and tools: A systematic scoping review and discussion. *International Journal of Nursing Studies*, 103, 103487. <https://doi.org/10.1016/j.ijnurstu.2019.103487>.
- Hoonhout, L. H. F., de Bruijne, M. C., Wagner, C., Zegers, M., Waaijman, R., Spreeuwenberg, P., Asscheman, H., van der Wal, G., & van Tulder, M. W. (2009). Direct medical costs of adverse events in Dutch hospitals. *BMC Health Services Research*, 9, 27. <https://doi.org/10.1186/1472-6963-9-27>.
- HPO. (2019). ABF 2019 Admitted Patient Price List. DRG Prices for Inpatients and Daycases 2019. Retrieved from Dublin, Ireland. <https://www.hpo.ie/abf/ABF2019AdmittedPatientPriceList.pdf>
- HSE. (2015). Activity-Based Funding Programme: Implementation Plan 2015–2017. Retrieved from https://health.gov.ie/wp-content/uploads/2015/07/ABF_Implementation_Plan_20_05_2015.pdf.
- Jones, A. (2007). *Applied econometrics for health economists: a practical guide*. CRC Press.
- Kalisch, B. J. (2006). Missed nursing care: A qualitative study. *Journal of Nursing Care Quality*, 21(4), 306–313. <https://doi.org/10.1097/00001786-200610000-00006>.
- Kane, R. L., Shamliyan, T. A., Mueller, C., Duval, S., & Wilt, T. J. (2007). The association of registered nurse staffing levels and patient outcomes: Systematic review and meta-analysis. *Medical Care*, 45(12), 1195–1204. <https://doi.org/10.1097/MLR.0b013e3181468ca3>.
- Kjellberg, J., Wolf, R. T., Kruse, M., Rasmussen, S. R., Vestergaard, J., Nielsen, K. J., & Rasmussen, K. (2017). Costs associated with adverse events among acute patients. *BMC Health Serv Res*, 17(1), 651. <https://doi.org/10.1186/s12913-017-2605-5>
- McCloskey, B. A., & Diers, D. K. (2005). Effects of New Zealand's health reengineering on nursing and patient outcomes. *Medical Care*, 43(11), 1140–1146. <https://doi.org/10.1097/01.mlr.0000182549.85761.cd>.
- McElroy, B., & Murphy, A. (2014). An economic analysis of money follows the patient. *Irish Journal of Medical Science*, 183(1), 15–22. <https://doi.org/10.1007/s11845-013-1050-7>.
- Mittmann, N., Koo, M., Daneman, N., McDonald, A., Baker, M., Matlow, A., Krahn, M., Shojania, K. G., & Etchells, E. (2012). The economic burden of patient safety targets in acute care: A systematic review. *Drug, Healthcare and Patient Safety*, 4, 141–165. <https://doi.org/10.2147/DHPS.S33288>.
- Murphy, A., & McElroy, B. (2015). Patient level costing in Ireland: Process, challenges and opportunities. *Irish Journal of Medical Science (1971-)*, 184(1), 47–51. <https://doi.org/10.1007/s11845-014-1114-3>
- Needleman, J., Buerhaus, P., Mattke, S., Stewart, M., & Zelevinsky, K. (2002). Nurse-staffing levels and the quality of care in hospitals. *New England Journal of Medicine*, 346(22), 1715–1722. <https://doi.org/10.1056/NEJMsa012247>.
- Needleman, J., Buerhaus, P., Pankratz, V. S., Leibson, C. L., Stevens, S. R., & Harris, M. (2011). Nurse staffing and inpatient hospital mortality. *New England Journal of Medicine*, 364(11), 1037–1045. <https://doi.org/10.1056/NEJMsa1001025>.
- Needleman, J., Buerhaus, P. I., Stewart, M., Zelevinsky, K., & Mattke, S. (2006). Nurse staffing in hospitals: Is there a business case for quality? *Health Affairs*, 25(1), 204–211. <https://doi.org/10.1377/hlthaff.25.1.204>.
- Newbold, D. (2008). The production economics of nursing: A discussion paper. *International Journal of Nursing Studies*, 45(1), 120–128. <https://doi.org/10.1016/j.ijnurstu.2007.01.007>.

- Nielsen, K. J., Pedersen, A. H., Rasmussen, K., Pape, L., & Mikkelsen, K. L. (2013). Work-related stressors and occurrence of adverse events in an ED. *The American Journal of Emergency Medicine*, 31(3), 504–508. <https://doi.org/10.1016/j.ajem.2012.10.002>
- O'Loughlin, R., Allwright, S., Barry, J., Kelly, A., & Teljeur, C. (2005). Using HIPE data as a research and planning tool. *Irish Journal of Medical Science*, 174(4), 66. <https://doi.org/10.1007/bf03168987>.
- Pappas, S. H. (2008). The cost of nurse-sensitive adverse events. *Journal of Nursing Administration*, 38(5), 230–236. <https://doi.org/10.1097/01.NNA.0000312770.19481.ce>.
- Rafter, N., Hickey, A., Conroy, R. M., Condell, S., O'Connor, P., Vaughan, D., Walsh, G., & Williams, D. J. (2017). The Irish National Adverse Events Study (INAES): The frequency and nature of adverse events in Irish hospitals—a retrospective record review study. *BMJ Quality & Safety*, 26(2), 111–119. <https://doi.org/10.1136/bmjqs-2015-004828>.
- Rasmussen, K., Pedersen, A. H. M., Pape, L., Mikkelsen, K. L., Madsen, M. D., & Nielsen, K. J. (2014). Work environment influences adverse events in an emergency department. *TRIAL*, 7, 10–0949.
- Recio-Saucedo, A., Dall'Ora, C., Maruotti, A., Ball, J., Briggs, J., Meredith, P., Redfern, O. C., Kovacs, C., Prytherch, D., Smith, G. B., & Griffiths, P. (2018). What impact does nursing care left undone have on patient outcomes? Review of the literature. *Journal of Clinical Nursing*, 27(11–12), 2248–2259. <https://doi.org/10.1111/jocn.14058>.
- Rothberg, M. B., Abraham, I., Lindenauer, P. K., & Rose, D. N. (2005). Improving nurse-to-patient staffing ratios as a cost-effective safety intervention. *Medical Care*, 43(8), 785–791. <https://doi.org/10.1097/01.mlr.0000170408.35854.fa>.
- Schwendimann, R., Blatter, C., Dhaini, S., Simon, M., & Ausserhofer, D. (2018). The occurrence, types, consequences and preventability of in-hospital adverse events – a scoping review. *BMC Health Services Research*, 18(1), 521. <https://doi.org/10.1186/s12913-018-3335-z>.
- StataCorp. (2015). Stata Statistical Software: Release 14. StataCorp., LP. Stata Statistical Software: Release 14. : StataCorp., LLC; 2014.: StataCorp., LLC.
- Tchouaket, E., Dubois, C. A., & D'Amour, D. (2017). The economic burden of nurse-sensitive adverse events in 22 medical-surgical units: Retrospective and matching analysis. *Journal of Advanced Nursing*, 73(7), 1696–1711. <https://doi.org/10.1111/jan.13260>
- Thomas, E. J., & Brennan, T. A. (2001). *Errors and adverse events in medicine: An overview. Clinical Risk Management: Enhancing Patient Safety* (pp. 31–43). : BMJ Publishing.
- Twigg, D. E., Geelhoed, E. A., Bremner, A. P., & Duffield, C. (2013). The economic benefits of increased levels of nursing care in the hospital setting. *Journal of Advanced Nursing*, 69(10), 2253–2261. <https://doi.org/10.1111/jan.12109>.
- Twigg, D. E., Myers, H., Duffield, C., Giles, M., & Evans, G. (2015). Is there an economic case for investing in nursing care—what does the literature tell us? *Journal of Advanced Nursing*, 71(5), 975–990. <https://doi.org/10.1111/jan.12577>.
- Vincent, C., Neale, G., & Woloshynowych, M. (2001). Adverse events in British hospitals: Preliminary retrospective record review. *BMJ*, 322(7285), 517–519. <https://doi.org/10.1136/bmj.322.7285.517>.
- Williams, D., & Thomas, S. (2017). The impact of austerity on the health workforce and the achievement of human resources for health policies in Ireland (2008–2014). *Human Resources for Health*, 15(1), 62. <https://doi.org/10.1186/s12960-017-0230-3>.

How to cite this article: Murphy A, Griffiths P, Duffield C, et al. Estimating the economic cost of nurse sensitive adverse events amongst patients in medical and surgical settings. *J Adv Nurs*. 2021;77:3379–3388. <https://doi.org/10.1111/jan.14860>

The *Journal of Advanced Nursing (JAN)* is an international, peer-reviewed, scientific journal. *JAN* contributes to the advancement of evidence-based nursing, midwifery and health care by disseminating high quality research and scholarship of contemporary relevance and with potential to advance knowledge for practice, education, management or policy. *JAN* publishes research reviews, original research reports and methodological and theoretical papers.

For further information, please visit *JAN* on the Wiley Online Library website: www.wileyonlinelibrary.com/journal/jan

Reasons to publish your work in *JAN*:

- High-impact forum: the world's most cited nursing journal, with an Impact Factor of 2.561 – ranked 6/123 in the 2019 ISI Journal Citation Reports © (Nursing; Social Science).
- Most read nursing journal in the world: over 3 million articles downloaded online per year and accessible in over 10,000 libraries worldwide (including over 6,000 in developing countries with free or low cost access).
- Fast and easy online submission: online submission at <http://mc.manuscriptcentral.com/jan>.
- Positive publishing experience: rapid double-blind peer review with constructive feedback.
- Rapid online publication in five weeks: average time from final manuscript arriving in production to online publication.
- Online Open: the option to pay to make your article freely and openly accessible to non-subscribers upon publication on Wiley Online Library, as well as the option to deposit the article in your own or your funding agency's preferred archive (e.g. PubMed).