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Title: The effect of nurse-to-patient ratios on nurse-sensitive patient outcomes in acute specialist units: a systematic review and meta-analysis

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ABSTRACT:

Background: Nurses are pivotal in the provision of high quality care in acute hospitals. The impact that nursing shortages have on the quality of care provided to patients in hospital can have disastrous consequences. In light of this, a review of the evidence on the effect of nurse staffing levels on patient outcomes is urgently required.

Aim: To undertake a systematic review examining the association between nurse staffing levels and nurse sensitive patient outcomes in acute specialist units.

Methods: Five electronic databases were searched for English published between 2006 and 2017. The primary outcomes were nurse sensitive patient outcomes.

Results: Of 3429 unique articles identified, 35 met the inclusion criteria. All were observational and the majority utilised large administrative databases. Higher staffing levels were associated with reduced mortality, mediation errors, ulcers, restraint use, infections, pneumonia, higher aspirin use and a greater number of patients receiving PCI within 90 minutes.   A meta-analysis involving 175 755 patients, from six studies, admitted to ICU and/or cardiac/cardiothoracic units showed that a low nurse-to-patient ratio decreased the risk of in-hospital mortality by 14% (0.86, 95%CI 0.79-0.94). However, the meta-analysis also showed high heterogeneity (I^2=86%).

Conclusion: Nurse-to-patient ratios influence many patient outcomes, most markedly mortality. More studies need to be conducted on the association of nurse-to-patient ratios with nurse sensitive patient outcomes to offset the paucity and weaknesses of

research in this area. This would provide further evidence for recommendations of optimal nurse-to-patient ratios in acute specialist units.

KEY WORDS:

Nursing, workforce, staffing, systematic review, nurse-to-patient ratio

Introduction

Over the last decade there has been a renewed focus upon what constitutes an adequate level of nurse staffing. This is in part due to some spectacular failures that have occurred in care provision for hospital in-patients leading to loss of life.[1,2] Organisations across countries have adopted different approaches to managing the nursing workforce. In Victoria, Australia and in the state of California, in America, standardised and mandatory nurse staffing levels have been in place for over a decade. In the UK there are national nurse staffing recommendations, but these are not mandated by law.[3,4] The notion of an optimal level of nurse staffing is somewhat controversial because there is no one size fits all approach to assessing staffing levels. This lack of clarity is further aggravated by a lack of consensus about the most appropriate way of estimating the size and mix of nursing teams because all measurement approaches have limitations.[4,5]

One of the challenges faced by managers responsible for staffing is finding a way to understand the influence of the multiple factors that make up each individual care environment which are likely to differ across organisations and countries. Donabedian grouped potential factors into three broad domains; structural factors (the people, paraphernalia and place that make up the healthcare delivery system), processes of care (how care is done through the interactions between health professionals and patients)

and subsequent outcomes (the end results of the care that takes place in the context of the organisation).[6]

To determine nurse-staffing levels, managers need to understand the underlying determinants which are patient factors (patient nursing need according to acuity and dependency levels), ward factors (patient throughput) and nursing staff factors (number and skill level).[7] Findings from a systematic review and meta-analysis, now a decade old, reported a significant association between increased nursing staffing in hospitals and improved nurse sensitive patients outcomes.[8] This review will examine recently published studies investigating associations between nurse staffing levels and nurse sensitive patient outcomes in acute specialist units.

Methods

To support the quality of the systematic review, a protocol was developed based on the PRISMA statement.[9] The review protocol was not registered.

Review objective

To identify studies, conducted in acute specialist units, which examine the association between nurse staffing levels (Nurse-to-Patient Ratio (NPR)) and nurse sensitive patient outcomes (as defined below).

Definitions

a) Nurse-to-Patient Ratio

NPRs are typically expressed in two ways; full time equivalents (FTE) of nurse to patient and the number of patients assigned to one nurse per shift. Another method is to calculate the number of nursing hours per patient bed days (NHPPD). There are other more complex approaches to measure nurse staffing requirements but there is no single recommended approach.[3] Many of the studies included in this review have determined NPRs. For example, a low NPR implies that one nurse is allocated to a smaller number of patients over a 24 hour period such as in ICU where the NPR is often 1:1 or 1:2 compared to general wards where the NPR is higher so one nurse is allocated more patients over a 24 hour period such as 1:4 (one nurse to four patients).

Moreover, little is known about how nurse staffing levels are managed across hospitals in Europe. NPRs are easily and cheaply measured but is a relatively blunt instrument that can function as one indicator, and can be triangulated with other measurement approaches, to establish safe nurse staffing levels.

b) Nurse sensitive patient outcome measures

The nurse sensitive patient outcomes measures included in this study were based on adverse events from previous studies that have been sensitive to changes in nurse staffing.[8,10] The nurse sensitive patient outcome measures we included were: mortality, failure to rescue, shock (including sepsis resuscitation), cardiac arrest, unplanned extubation, hospital acquired pneumonia, respiratory failure, surgical bleeding, heart failure/fluid overload, catheter associated urinary tract infection, pressure sores, patient falls, nosocomial bloodstream infection, medication error, length of stay, hospital-acquired sepsis, deep vein thrombosis, central nervous system complications, death, wound infection, pulmonary failure, and metabolic derangement.

Search strategy

The search strategy was developed by the research team with input from expert information technologists (Appendix 1). Electronic databases and grey literature was searched (Medline (OvidSP), Medline in Process (OvidSP), CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO), PsycInfo (OvidSP), Embase (OvidSP), HMIC (Health Management Information Consortium) (OvidSP), Cochrane Database of Systematic Reviews, Web of Science; Science Citation Index Expanded (ISI Web of Knowledge), Web of Science; Social Sciences Citation Index (ISI Web of Knowledge), Web of Science; Conference Proceedings Citation Index –Science (ISI Web of Knowledge), Web of Science; Conference Proceedings Citation Index- Social

Science & Humanities (ISI Web of Knowledge), Index to Theses, Proquest
Dissertations and Theses). A combination of keywords was used and controlled
vocabulary such as MeSH (Medical Subject Headings) when available. Search terms
included 18 terms on settings i.e., coronary care, high dependency, critical care,
intensive care, cardiac ward, intensive treatment unit and 17 terms relating to nursing or
manpower or skill mix i.e., nurse staffing, nurse ratio, nurse mix, nurse dose, nurse
workload and 78 nurse sensitive outcomes i.e., wound infection, pulmonary failure,
shock, pneumonia, length of stay, outcome, patient safety. The search was limited to
English language and conducted from January 2006 to February 2017. Conference
abstracts and reference lists of included studies were manually searched and additional
studies identified.

Inclusion criteria

Following the literature search, a team of reviewers worked in pairs to independently
screen titles and abstracts according to the inclusion criteria. Any disagreement between
reviewers was resolved by a third reviewer. Studies that met the following inclusion
criteria were included:

- Patients admitted to acute specialist units (e.g. Intensive Therapy Units/Critical
  Care/Intensive Care/Coronary Care, high dependency, step-down, cardiothoracic

surgery, and/or stroke units) with care provision for adults (over 18 years of age). Studies with mixed population ward and acute care were included.

- Investigating the effect of NPR using either FTE of nurse per patient day or the NHPPD

- published from January 2006 to February 2017 in English.

- Quantitative methodology

- Primary outcome measures:

    - at least one nurse sensitive outcome such as mortality, failure to rescue, shock, cardiac arrest, unplanned extubation, hospital acquired pneumonia, respiratory failure, surgical bleeding, heart failure/fluid overload/imbalance, urinary tract infection, pressure sores, patient falls, nosocomial bloodstream infection, medication error, pain control, unplanned readmission.

Data extraction

A tailor-made data extraction tool was developed a priori and piloted and refined. The tool included six screening questions to ensure papers fit with the review inclusion criteria (Appendix 2). Information was also extracted from each study to record under the following headings: bibliographic details; setting/country; study design; outcomes, findings/conclusions and quality assessment.

Quality Assessment

All included studies were assessed by the Newcastle-Ottawa Scale (NOS) to determine the quality of non-randomised studies.[11] This tool was designed to facilitate the incorporation of quality assessment into the systematic review. This tool has been used in previous Cochrane reviews for assessment of risk of bias in non-randomised studies. The content validity and inter-rater reliability of this scale was previously established. The NOS comprises of eight items: representativeness of cohort, selection of cohort, ascertainment of exposure, outcome of interest was not present at baseline, comparability of cohorts, assessment of outcome, length of follow-up and adequacy of follow-up.[11] Each item was awarded a '*' for meeting the criterion. A study was also awarded an additional '*' if the analysis was adjusted for potential confounding variables. The quality of each study was graded as low, medium or high according to the number of stars (*). The quality assessment was conducted independently by two reviewers. Disagreements were resolved by a third reviewer.

Statistical Analysis

As this systematic review involved cohort studies we used adjusted measures, as reported by authors, as the primary effect measures to control for confounding when it was available. Odds ratios were used as an appropriate effect measure if available. Other effect measures were: hazard ratios or risk ratios.

A meta-analysis was conducted on homogenous studies using a random-effect model with in-hospital mortality as the primary outcome. In studies where patient-to-nurse ratios were used, these were converted to NPRs by calculating the inverse ratio. The overall effect sizes will be presented in a forest plot. In studies where a pooled meta-analysis was unable to be performed, a narrative analysis will be undertaken.

Clinical homogeneity was assessed in terms of study cohort, hospital units, diagnosis and risk of bias. The I^2 was also used to determine statistical heterogeneity. If $I^2 > 40\%$ a random effects model will be used. A sensitivity analysis will also be conducted using a fixed-effects model was used to determine if the conclusions were different. Data analysis was conducted using review manager version 5.3.[12]

Results

We identified a total of 4472 studies from the literature search. After duplicates were removed 3429 records were screened using title and abstract. Of these, we identified 196 full-text articles for retrieval. We included 35 articles in the final analysis (see Figure 1). Reasons for exclusion included research relating to neonates, non-acute settings, no NPRs and no nurse sensitive patient outcomes were reported.

Insert Figure 1 - Study Flow Diagram

Description of studies

All of the 35 papers were cohort studies except for one point prevalence study. All of the studies had a large sample size derived from administrative datasets (Table 1). Fourteen studies were conducted in the USA/Canada/Mexico, 17 studies in Europe, three studies in China and one in Thailand. In terms of study setting, 11 studies included patients throughout the hospital including critical care, 19 studies restricted their cohort to intensive care units only (included cardiovascular patients), and five studies in specialist cardiac units.

Insert Table 1 – Characteristics of Included Studies

Quality appraisal

The NOS comprises of three principle domains: case selection, representativeness of cohorts, and measurement of outcome.[11] All 35 cohort studies met the criterion for representativeness of cohorts selection, five studies received one star and 24 studies received two stars for comparability of cohorts, 24 studies discussed outcome assessment and 35 studies defined their length of follow-up (Table 2).

Insert Table 2- Cohort Quality Appraisal

There were 24 studies that rated highly on the NOS for assessing the quality of non-randomised trials (Table 2). All of these studies controlled for several confounding factors in either their methodology or data analysis. The majority of these studies adjusted for age, co-morbidities and hospital characteristics as potential confounders. Seven studies were rated as low quality mainly due to the lack of comparability of cohorts.

Nurse-to-Patient Ratios

Various approaches were used to measure NPRs. Schwab et al calculated the NPR per shift (number of nurses per day/3 (per shift)/number of patients per day) using monthly census data.[39] Other studies used similar approaches.[17,24,25,32,34,38] Several authors provided less detail about how the NPR was calculated.[16,28,31,33] Valentin et al. calculated both the NPR by shift and the occupancy rate (maximum number of occupied beds divided by allocated beds), NPR for each shift in each unit and the relative turn over (number of admitted and discharged patients divided by the number of unit beds).[44] Cho et al. calculated the NPR based on the bed occupancy rate and then categorised it into grades.[19] Grade 1 indicated the number of beds per nurse was <0.5 up to Grade 9 when the ratio was >2.0. In Cho et al.[18], the ratio of bed occupancy rate to the number

of FTE nurses was used for calculation. This bed occupancy rate was extracted from the ICU survey data over a three-month period. Tourangeau et al. calculated the 'nursing staff dose' rather than a NPR.[43] This was calculated as the total nursing worked hours divided by the sum of weighted patient cases discharged from each hospital.

Stone et al. calculated the number of nursing hours per patient day (NHPPD) from payroll and ICU census data.[42] Diya et al.[20] calculated the NHPPD but did not stipulate how this was calculated. Van den Heede et al.[45,46] calculated the NHPPD daily for each ward. It was based on daily ward census data. A similar approach was adopted by Shuldham et al.[41] and Hart et al.[22] both of whom made the distinction between the numbers of hours worked by permanent staff versus temporary staff. Adjustment for staff sick leave and annual leave was not always accounted for suggesting that staffing ratios may have been overestimated.[14, 29] Sometimes day-to-day staffing levels were unobtainable in which case a proxy of highest NPR in a 24-hour period was used.[15]

4.4 Nurse Sensitive Outcomes

Mortality

There were 19 studies that examined mortality. Thirteen studies had a primary outcome of in-hospital mortality, one study examined 28-day mortality and five studies with 30-day mortality. Of the 19 studies, 10 were conducted in ICU, two studies in an acute

cardiac unit, two in the Emergency Department and seven studies recruited patients throughout the hospital regardless of unit including ICU/CCUs. Six studies reported odds ratios on all-cause in-hospital mortality of 175 755 patients admitted to ICU and/or cardiac/cardiothoracic units.[18,19,30,32,38,47] A meta-analysis was conducted on the six studies using a random effects model. The pooled analysis showed that a lower NPR decreased the risk of in-hospital mortality by 14%, (95%CI 0.79-0.94). However, the meta-analysis also showed high heterogeneity (I^2=86%) with one study showing a wide confidence interval. The pooled analysis was influenced by four of the six studies each ranging from 21-24%.[18,30,32,47]

Insert Figure 2 - MA

As the I^2 was>40% a sensitivity analysis was performed using a fixed effects model. The pooled analysis of the fixed effects model (OR 0.90, 95%CI 0.88-0.92) was similar to the random effects model (OR 0.86, 95%CI 0.79-0.94) despite the high heterogeneity.

Other Nurse Sensitive Outcomes

Fifteen studies examined the effect of NPRs on nurse sensitive outcomes other than mortality. Three studies examined mortality as a primary endpoint and nurse sensitive

outcomes as their secondary endpoint.[40,42,45] However, none of the studies combined all of the nurse sensitive patient outcomes, rather they typically selected three or four outcome measures. Three studies conducted in critical care units, reported an association between higher number of NHPPD[36,42] or a lower NPR[34] resulted in a reduction in events for nurse sensitive patient outcomes. Another study reported on medication errors and found that as the NPR increased so did the odds ratio for parenteral medication errors, some of which caused harm and death.[44] Lower NPR in critical care units were associated with a lower incidence of pressure ulcer development,[22,42] use of physical restraints[14] and incidence of nosocomial infection[24,39,42] including late onset ventilator assisted pneumonia.[25] In the Emergency Department, lower NPR increased the prescribing of aspirin on arrival to the Emergency Department and a percutaneous coronary intervention within 90 minutes of arrival.[26]

Evidence was less clear in studies where results were combined across setting such as high dependency and critical care units. One such study examined the association between NPRs and a range of nurse sensitive patient outcomes; there were few significant results.[41] However as the number of permanent staff compared to temporary staff increased, the rates of sepsis decreased.[41] Hart and Davis found that the use of agency staff was associated with a higher incidence of hospital acquired pressure ulcers but only in medical surgical units rather than critical care units and Coronary Care

settings.[22] A statistically significant association was also reported between lower NPRs on the ward and critical care unit settings and lower rates of failure to rescue.[36] Three studies reported no association between NPRs and nurse sensitive patient outcomes, after adjusting for confounding variables.[15,31,45] Merchant et al. reported no association between NPRs and in hospital cardiac arrests rates.[31] Similarly Blot et al. reported no association between NPRs and ventilator associated pneumonia, after adjusting for confounding variables.[15] Due to the heterogeneity in outcome measures no meta-analysis was performed.

Discussion

This analysis found that lower NPRs was associated with a decrease in risk of in-hospital mortality (OR 0.86, 95%CI 0.79-0.94) and nurse-sensitive outcomes. Due to the heterogeneity between studies particularly in NPRs, no recommendation can be made regarding the optimal ratio required to improve patient outcomes. However, studies do report the lower the NPR, the greater the reduction in in-hospital mortality. Unfortunately, all of these studies were observational so no causal relationship can be determined. This systematic review builds on work conducted previously by Kane et al.[8] who found a higher level of nurse staffing was associated with a lower mortality in ICU (OR 0.91, 95%CI 0.86 – 0.96), surgical wards (OR 0.84, 95%CI 0.8 – 0.89) and medical wards (OR 0.94, 95%CI 0.94 – 0.95) per additional 1.0 FTE nurse per patient

day.[8] Our meta-analysis found a decrease in risk of 14% in in-hospital mortality for every additional one decrease in patient load over 24 hours. All of the studies included in the meta-analysis rated high in the NOS quality assessment tool.

The meta-analysis was analysed with a random effect model as it is adjusted for heterogeneity. As the pooled effect had a high degree of heterogeneity (I^2=86%) a sensitivity analysis was conducted using a fixed effects model. The sensitivity analysis showed no difference between the two different models in the pooled analysis.

We also examined the effect of NPRs on nurse sensitive patient outcomes. There was a large degree of heterogeneity in the type of nurse sensitive patient outcomes that were measured as an end-point so no meta-analysis was conducted. Park et al. examined the effect of nurse staffing and failure-to-rescue (FTR) rates.[36] FTR rates were defined as mortality post an adverse event associated with post-surgical complications. Park et al. analysed data from an administrative dataset 159 non-ICUs and 158 ICUs from 42 hospitals.[36] In ICUs, they found a higher number of NHPPD was associated with a lower FTR rate (OR -0.022, 95%CI -0.39 - -0.005 (adjusted)).[36] Stone et al. also examined the effect of NPRs on nurse sensitive outcomes.[42] These outcomes included: central line bloodstream infections, ventilator assisted pneumonia, catheter associated urinary tract infection, 30-day mortality, and presence of decubitus pressure ulcers.

Their sample comprised of 15,846 patients from 51 ICUs in 31 hospitals. Stone et al. found that patients cared for with a higher number of NHPPD were 68% less likely to experience bloodstream infections (95%CI 0.15-0.17), 79% less likely to experience pneumonia (95%CI 0.08 – 0.53) and there was a 31% reduction in risk for a decubitus pressure ulcer (95%CI 0.49 – 0.98).[42] Cardiac outcomes were also improved with a lower NPR. Every 10% decrease in NPR was associated with a 7.1% increase in prescribing of aspirin on arrival and 6.3% decrease in time for a percutaneous coronary intervention within 90 minutes of arriving in hospital.[26]

O'Brien-Pallas et al. investigated the association of NPRs with nurse sensitive patient outcomes.[34] Their outcomes included: deep vein thrombosis, pressure ulcers, falls with injury, medical errors with consequences, pneumonia, catheter associated urinary tract infection and wound infections. O'Brien-Pallas et al. analysed an administrative dataset of 1,230 patients from 24 cardiac and cardiovascular units from six hospitals.[34] They calculated the NPR as the average number of patients cared for daily by a nurse on day shift during the data collection period. They found that for every additional patient per nurse, patients were 22% less likely to experience 'excellent or good quality care' and 35% more likely to experience a longer than expected length of stay.[34]

Limitations/Weakness of the Evidence Base

The results of this systematic review and meta-analysis should be interpreted with caution. There were several limitations associated with the review. Several studies combined patients from non-specialist units with special units which may have skewed the results. Stone et al. conducted a separate analysis for ICU and non-ICU units.[42] They found that in non-ICUs, NPrs was not statistically associated with rate of nurse sensitive patient outcomes. However, there was a reduction in rate of nurse sensitive patient outcomes in patients in an ICU with a lower NPR.

There was also a large degree of heterogeneity in how the NPRs were calculated. For example, Perez et al. did not stipulate how they calculated the NPR,[37] Van Den Heede et al. calculated the number of NHPPD[45,46] and Cho et al. calculated the number of patients/bed to total FTE.[18,19]

Conclusion

This systematic review found that there may be an association between lower NPRs and improved patient outcomes. The lower the NPR, patients were 14% less likely to experience in-hospital mortality.

More studies need to be conducted on the association of NPRs with nurse sensitive patient outcomes. However, there needs to be greater homogeneity in the nurse sensitive

endpoints measured and the calculation of the NPR. Such metrics should not be used in isolation but can contribute to a 'triangulated' approach to the decision making process about safe and sustainable nurse staffing levels.

Implications for Practice

- This review suggests that there may be an association between lower NPRs in adult acute specialist settings and a lower rate of adverse events in nurse sensitive patient outcomes. Data that should not be ignored.

- It provides an overview of the variations in NPRs across different countries and their impact on nurse sensitive patient outcomes.

- This review highlights the need for some agreement, at an international level, about the most appropriate way to measure nurse staffing levels. For many countries facing financial constraints in healthcare delivery complex and expensive techniques to address this challenge are unlikely to be adopted. Future studies should consider the human and financial cost of the rate of events in nurse sensitive patient outcomes in adult specialist care settings and model these against NPRs and skill mix to better understand where real cost savings are available.

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        cardiac surgery mortality and nurse numbers and educational level: Analysis of

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Table 1. Characteristics of Included Studies

Author, year of publication	Study Design	Sample & Setting (Population)	Measure of Nurse-to-Patient Ratio	Outcome Measures	Key Findings
Aitken et al. 2014[13]	Retrospective cohort study	422 730 patients who underwent surgery in 300 hospitals in nine European countries. Data was extracted from an administrative database for patient discharge data and prospective survey for nursing data	Number of patients divided by number of nurses for that shift. An average ratio across all respondents in the same hospital was then calculated.	30 day mortality	Mean NPR ranged from 5.2 – 12.7 As the NPR increased there was a 6% increase in risk of 30 day mortality (OR 1.068, 95%CI 1.031-1.106, p=0.0002)
Benbenbishty et al 2010[14]	Point prevalence study	669 patients in 34 general Intensive Care Units (ICU) in nine European countries	The nurse/patient ratio (NPR) was measured each shift over a 24hr period	Use of physical restraints	Nurse-to-patient ratio varied from 1:1 to 1:4 Number of restraints increased as the NPR increased (χ^2=17.17 p=0.001)
Blot et al 2011[15]	Prospective cohort study	27 ICUs in 9 European countries. Recruited 2585 patients who had mechanical ventilation after admission for treatment for pneumonia or who were ventilated for more than 24 hours irrespective of diagnosis on admission	NPR was measured as the standard ratio for each unit	Incidence of ventilator associated pneumonia (VAP)	NPR varied from 1: 1 to 1:3 VAP incidence was significantly lower in ICU units with 1:1 NPR compared to units with a ratio of >1:1 (9.3% vs 24.4%, p=0.002) (univariate analysis) However, after adjusting for confounders this association became not significant.
Checkley et al	Prospective	69 ICUs (medical and surgical), in	A definition of NPR was not	Annual mortality	Mean NPR was 1:1.8

1

2014[16]	cohort study	USA were surveyed about organisation structure. Patient outcomes were collected prospectively from US Critical Illness and Injury Trials Group Critical Illness Outcomes study Number of patients was not stated.	provided. However, each site provided nurse staffing numbers and number of beds.		(median 1:1.7) The annual mortality was 1.8% lower when the NPR decreased from 1:2 to 1:1.5 (95%CI 0.25%-3.4%) For every increase of one patient per nurse there was a 3.7% increase in annual ICU mortality (95%CI 0.5-6.8, p=0.02)
Chittawatanarat et al 2014[17]	Retrospective cohort study	104046 admissions to 155 ICUs in 87 hospitals, January-December 2011, Thailand using hospital databases from participating ICUs	NPR: number of nurses on each 8 hour rotation divided by the number of patient beds	Monthly mortality Ventilator days ICU length of stay	Mean NPR 1:0.50 Lower NPRs were associated with lower ventilator days (OR -2.08, 95%CI -5.377- -0.166, p = 0.037)
Cho et al 2008[18]	Retrospective cohort study	27,372 ICU patients with 26 primary diagnoses from ICUs in 236 hospitals (42 tertiary and 194 secondary) in Korea. Data was collected retrospectively from three national databases: ICU survey data, medical claims data & the National Health Insurance database	NPR calculated each shift	In hospital mortality	Secondary Care Intensive Care Unit Nurse patient ratio: 1:0.98 Every additional patient per nurse resulted in a 9% increase in the odds of death (OR = 1.09, 95%; CI 1.04-1.14) Each additional patient cared for by a nurse would result in an additional 15 deaths per 1000 patients Two & three additional patients were associated with an 18% and 29% increases in

					mortality, equivalent to 28 and 44 additional deaths per 1,000 patients, respectively. Tertiary Care Intensive Care Unit Nurse patient ratio 1:0.76 No significant findings related to mortality in these units
Cho et al 2009[19]	Retrospective cohort study	ICUs from 185 hospitals (40 tertiary and 145 secondary) in Korea Acute stroke patients admitted to ICU during hospitalisation aged < 18 years using retrospective data from an administrative dataset and prospective survey	NPR	In hospital mortality & 30 day mortality	Nurse patient ratio ranged from 1<0.50 to 1:2 Average NPR was 2.8pts/nurse In ICUs where the NPR was ≤1:1, patients were 73% less likely to experience in-hospital mortality compared to ICUs with a NPR≥1:1.5 (OR 0.26, 95%CI 0.09-0.8, p=0.019) Similar results were also found for 30-day mortality: ICUs where the NPR was ≤1:1, patients were 77% less likely to experience 30 day mortality compared to ICUs with a NPR≥1:1.5 (OR 0.23, 95%CI 0.07-0.78, p=0.018)
Diya et al	Retrospective	9054 elective surgery patients	Nursing hours per patient per	• Post-operative in-hospital	ICU

2012[20]	cohort study	(coronary artery bypass graft (CABG) or heart valve procedure) aged 20-85yrs from 28 Belgium hospitals in 2003. Retrospective review of clinical databases: • Belgian Nursing Minimum Dataset • Belgian Hospital Discharge Database	day (NHPPD)	mortality in ICU • Unplanned readmission to ICU or operating theatre • Unplanned readmission and/or in-hospital mortality in the general wards	11.12hrs:1 In hospitals with a large volume of cardiac procedures, higher NHPPD were associated with a lower rate of in-hospital mortality and a lower rate of a composite of unplanned readmissions and/or in-hospital mortality in ICU/operating theatre
Griffiths et al 2016[21]	Retrospective cohort study	Administrative data from 137 NHS acute hospital trusts of 9 669 555 medical admissions and 9 302 292 surgical admissions over 2 years (staffing was measured as beds per staff member). A cross sectional survey of 2917 registered nurses in a subsample of 31 trusts (measured patients per ward nurse).	NPR calculated as ratios of beds per nurse and averaging responses from all nurses in each specialty	In-hospital mortality	The average number of occupied beds per nurse was 1.53 and ranged from 0.69- 2.81. Higher mortality was associated with a higher NPR (RR 1.22, 95% CI 1.04 to 1.43, p=0.02) Trusts with an average NPR of 1:≤6 in medical wards had a 20% lower mortality rate compared to trusts with a NPR 1:>10 The relationship remained significant in the multivariable model (RR 0.89, 95% CI 0.83 to 0.95, p<0.01)
Hart & Davis 2011[22]	Retrospective cohort study	26 acute care units from 5 hospitals in USA. There were 15 medical/surgical units, 8 CCU, and 3 telemetry units. Data was extracted from the National Database of Nursing Quality Indicators (NDNQI) and the hospital's quality outcome data databases	Nursing hours per patient day (NHPPD)	• Cardio pulmonary resuscitation • Falls • Falls with injury • Hospital acquired pressure ulcers • Medication occurrences • Restraint use	Average total NHPPD ranged from 9.56 (SD+0.4) in medical/surgical wards to 18.27 (SD+3.9) in CCU Significant correlation between higher total NHPPD and lower incidence of

					hospital acquired pressure ulcers ($p<0.05$). Significant correlation between lower restraint use with higher NHPPD ($p<0.05$) No significant correlations between all other outcome measures and total NHPPD
He et al 2012[23]	Retrospective cohort study	1171 hospitals involving 1994 Critical Care units, 1328 stepdown units, 1663 medical wards, 1279 surgical wards, 2217 med-surgical wards and 434 rehabilitation units. Data was retrospectively extracted from National Database of Nursing Quality Indicators from 2004 to 2009	Nursing hours per patient day (NHPPD)	Falls	Average total nursing hours per patient day in ICU was 15.98 (SD 3.42). A higher number of NHPPD was associated with lower fall rates (OR 0.95, 95%CI 0.94-0.97, $p<0.001$)
Hugonnet et al 2007[24]	Prospective cohort study	Medical intensive care unit (ICU) of one university hospital in Geneva, Switzerland 1,883 patients from January 1999 to December 2002	NPR calculated as total number of nurses working during a 24-hr period divided by patients' census of that day	ICU acquired infections	Average total nursing hours per patient day was 15.98 (SD 3.42) An decrease of NPR by 1 patient was associated with a 30% infection risk reduction in univariate analysis. Association remained unchanged in multivariate model, indicating that none of the other variables examined were true confounding factors
Hugonnet et al 2007[25]	Prospective cohort study	Medical ICU in a university hospital in Geneva, Switzerland	NPR calculated as total number of nurses working during a 24-hr period divided	Early onset ventilator-associated pneumonia (VAP) Late onset VAP	Median daily NPRs were 1.9 nurse per patient; range 1.4 to 5.3 (IQR 1.8 to 2.2)

		2470 patients at risk for ICU-acquired infection admitted January 1999 - December 2002	by patients' census of that day All nurses' shifts equalled 8 hrs		A lower NPR ratio was associated with a decreased risk for late-onset VAP (HR 0.42, 95% CI 0.18 to 0.99) They estimated that 121 infections could be avoided if the NPR < 2.2
Johansen et al 2015[26]	Retrospective cohort study	1343 patients presenting to 73 EDs with acute coronary syndrome symptoms, 1 January 2008 to 31 January 2010, New Jersey, USA Data extracted from an administrative ED database	NPR calculated as average number of patients assigned per nurse	Aspirin on arrive PCI within 90 minutes	On average 15% of nurses cared for <10 patients/shift, 55% cared for 11-15 patients and 30% cared for 15-20 patients each shift. As NPR decreased there was a 7.1% increase in aspirin administration on arrival. Each additional patient was significantly associated with a 3.9% decrease in the likelihood of aspirin on arrival As NPR decreased there was a 6.3% decrease in number of patients achieving PCI in 90 minutes. Each additional patient significantly associated 1.4% decrease in PCI within 90 minutes
Kandler et al 2013[27]	Prospective survey design	194 adult & 78 child seizures in 27 UK video telemetry units	No definition of how NPR was calculated	The amount of time that health professionals took to attend seizures within 30 seconds	NPR in dedicated telemetry settings median 1:2 (range 1:4-1:1)

					NPR in non-dedicated telemetry settings median 1:5 (range 1:14-1:1.75) day time & 1:6 (range 1:16-1:1.75) night time As the NPR decreased, the number of nurses attending seizures within 30 seconds also increased: <1.5 NPR in 21% 1:5-1:2.5 in 29% >1:2.5 in 37%
Kim et al 2012[28]	Prospective cohort study	28 intensive care units (ICUs - 22 medical & 6 surgical) during July 2009 A sub sample of patients (n=251), diagnosed with severe sepsis	No definition of how NPR was calculated	28 day mortality Duration of ventilation Hospital length of stay ICU mortality	NPR was variable; 1:2 in (5 units), 1:3 in (10 units) and 1:4 or more (13 units) Lower NPR (1:2) was independently associated with a lower 28 day mortality (HR 0.459; 95% CI, 0.211-0.998)
Mark et al 2012[29]	Retrospective cohort study	600 hospitals involving 2380 hospital year observations, 2000-2006, USA. Data from the American Hospital Association Annual Survey of Hospitals, the California Office of Statewide Health Planning and Development, the Hospital Cost Report Information System, and the Agency for Healthcare Research and Quality's Health Care Cost and Utilization Project's State Inpatient Databases	NPR was based on Nursing Intensity Weights to develop measures of acuity-adjusted staffing	Failure to rescue Infections due to medical care Respiratory failure Postoperative sepsis	Nursing Intensity Weights ranged from 0.74-1.54. 3.03 FTEs of nurses per 1000 inpatient day Failure to rescue decreased significantly Infections due to medical care increased significantly

McHugh et al 2016[30]	Retrospective cohort study	11,160 adult patients between 2005 and 2007 in 75 hospitals in 4 USA states. Accessing data from Get-with-the-Guidelines Resuscitation database and American Hospital Association annual survey	NPR calculated as average number of patients reported by nurses on their unit on their last shift by the average number of nurses on the unit for that same shift	In-hospital mortality post in-hospital cardiac arrest	Average NPR not stated. As NPR decreased on medical-surgical units there was a 5% reduction in risk of in-hospital mortality post cardiac arrest in-hospital (OR 0.95; 95% CI, 0.91–0.99) ICU was not significant
Merchant et al 2012[31]	Retrospective cohort study	103,117 in-hospital cardiac arrests recorded in 433 hospitals in the US between 2003-2007. All hospitals were participating in the Get-with-the-Guidelines resuscitation registry	NPR calculated as Nurse:Bed ratios for each hospital taken from the American Hospital Association Ratios categorised: • Small 1: <0.5 • Medium 1:0.5-1 • High 1: >1	In-hospital cardiac arrest (IHCA) event rate = In-hospital cardiac arrest/each hospitals annual bed days	Nurse to bed ratio: Low (<0.5) 17 (4%) hospitals Medium (0.5-1) 161 (37%) hospitals High (>1) 255 (59%) hospitals Nurse:Bed ratio was not a significant predictor of IHCA despite the event rate being higher (1.13) in hospitals with a <0.5 nurse:bed ratio
Metnitz et al 2009[32]	Retrospective cohort study	85,259 admissions to 40 ICU units, 1998-2005 from the national Intensive Care Unit (ICU) database from the Austrian Centre for Documentation and Quality Assurance in Intensive Care Medicine	NPR calculated as number of patients assigned to each nurse	In-hospital mortality	NPR 1: 1.49±0.4 As NPR increased there was a significant chance of increasing death (OR 1.082, 95%CI 0.977-1.149) (unadjusted) As NPR increased there was a significant chance of increasing death when adjusted for age, sex, severity of illness & reasons for

					admission (OR 1.296, 95%CI 1.207-1.391)
Neuraz et al 2015[33]	Retrospective cohort study	5718 inpatients in 8 ICUs from 4 university hospitals, Lyon, France, Jan-Dec 2013. Data was extracted from three large databases: -Claims data used for inpatient stay - medical and nurse staff database -Human resources database.	No definition of how NPR was calculated	Mortality at time of ICU discharge by shift	NPRs ranged from 1:1 to 1: >2.5 As NPRs increased the risk of death increased by a factor of 3.5 (1.3-9.1) when the NPR was 1: >2.5
O'Brien-Pallas et al 2010[34]	Prospective cohort study	24 cardiac & cardiovascular units (11 critical care, 9 in-patient, remainder were step down or day surgery cases) in six hospitals in the Canadian provinces of Ontario and New Brunswick; four were teaching hospitals 1198 patients and 555 nurses	NPR calculated as average number of patients cared for by a nurse on day shift over the data collection period	Length of stay (LOS) Quality of care was assessed by manager as 'improved or deteriorated' More than one patient care interventions omitted More than one therapeutic intervention omitted	Mean NPR was 2.3±1.43 As NPR increased, 'good or excellent care' was 22% less likely and longer than expected LOS was 35% more likely
Ozdemir et al. 2016[35]	Retrospective cohort study	294 602 emergency admissions to 156 NHS Trusts from an administrative database from 1st April 2005 to 31st March 2010	No definition of how NPR was calculated	30-day mortality; 90-day mortality	NPR ranged from 1.88- 2.33 of nurses per patient Higher mortality rates were seen with higher NPRs [1.07 (1.01–1.13) P=0.024].
Park et al 2012[36]	Retrospective cohort study	512 adult non intensive care units (ICUs), 247 adult ICUs within 42 US teaching hospitals Data extracted from the 2005 University HealthSystem Consortium database	Nursing hours per patient day (NHPPD)	Failure to Rescue (mortality in surgical patients preceded by a hospital acquired complication such as pneumonia, DVT, pulmonary embolism, sepsis, acute renal failure, shock or cardiac arrest and gastrointestinal haemorrhage or acute ulcer)	15.52 NHPPD (2.03 SD) Statistically significant association between higher NHPPD and lower rates of failure to rescue in ICUs.

Perez et al 2006[37]	Prospective cohort study	A consecutive cohort of 2367 patients from 49 ICUs in Columbia	No definition of how NPR was calculated	Mortality ratios were calculated by dividing observed deaths by predicted deaths	NPRs • 1:3.0-7.0 in ICUs with highest mortality rates • 1:1.5-3.0 in ICUs with lowest mortality rates (p=.0237). ICU's with the lowest mortality rates had lower NPRs
Sakr et al 2015[38]	Point prevalence study	13796 adults in 1265 ICU in 75 countries on 7 May 2007	NPR recorded 10:00-11.00am and 10.00-11.00pm on a single day. Number of nurses working at the bedside during these time points and number of occupied beds	In-hospital mortality	Median NPR was 1.6 and interquartile range (IQR) from 1.05-2.2 NPR < 1:1.5 is independently associated with a lower risk of in-hospital death (OR 0.69, 95%CI 0.53-0.90, p<0.001) compared to NPR> 1:2
Schwab et al 2012[39]	Prospective cohort study	182 ITU's in Germany participated in 2007 involving 563,177 patient-days -45.5% interdisciplinary -21.4% medical -23.6% surgical -9.3% other specific ICU	NPR calculated as nurses per day (3 per shift)/patients per day Number of patients per day=number of patient-days in that month;	Nosocomial device associated infections: • number of ventilator infections • number of central venous catheter associated infections per 1000 device days	Median NPR (per shift): 1: 1.5 and IQR 1:1.3 -1:1.8 In univariate analysis lower NPRs were associated with fewer nosocomial infections (RR 0.42, 95% CI 0.32-0.55) In multivariate analysis, NPR was not associated with nocosomial infections
Sheetz et al. 2016[40]	Retrospective cohort study	Patients undergoing colectomy, pancreatectomy, esophagectomy, abdominal aortic aneurysm repair, lower-extremity revascularization, or lower extremity amputation. Data	NPR calculated as nursing full-time equivalents (FTE) X 1768/adjusted patient days	30-day mortality, major complications, and failure to rescue	No average NPR was provided Increasing NPR (range: OR 1.02 (1.01- 1.03) to OR 1.14

		extracted from the Medicare Provider Analysis and Review (MEDPAR) file claims data and American Hospital Association (AHA) Annual Survey Database from 2007 to 2010			(1.08–1.20), significantly influenced failure to rescue rates for all procedures
Shuldham et al 2009[41]	Retrospective cohort study	25,507 patients, including day cases, who were admitted to a tertiary cardio-respiratory NHS trust in England, April 2006-End of March 2007 Wards were grouped into lower dependency areas and the high dependency areas (ICU and HDU). Data was extracted from the corporate patient administration system	NHPPD: Overall number of nursing hours worked in a given day, divided this by the total number of patient hours on the ward or unit for that day and multiplied by 24 (h), i.e. nurse hours/patient hours x 24	• Deep vein thrombosis • Patient falls • Pneumonia • Pressure sores • Sepsis • Shock • Upper GI bleed	No average NHPPD was provided As the NHPPD decreased so did the risk of developing shock increase 3-fold (RR 3.48, 95%CI 1.368-6.865, p=0.009)
Stone et al 2007[42]	Retrospective cohort study	15,902 elderly Medicare patients from 51 intensive care units (ICUs) in 31 US hospitals in 2002. Data was extracted from the National Nosocomial Infection Surveillance system protocols, medicare files, American Hospital Association annual survey and prospective survey to nurses	NHPPD	• 30 day mortality • Catheter associated urinary tract infection (CAUTI) • Central line associated bloodstream infection (CLBSI) • Decubiti • Ventilator associated pneumonia (VAP)	Average NHPPD was 17 (SD ± 5.1) Higher NHPPD were significantly associated with a lower incidence rate of: • 30 day mortality (OR 0.81, 95%CI 0.69- 0.95, p≤0.001) • CLBSI (OR 0.32, 95%CI 0.15- 0.70, p≤0.05) • Decubiti (OR 0.69, 95%CI 0.49- 0.98, p≤0.01) • VAP (OR 0.21, 95%CI 0.08- 0.53, p≤0.05)
Tourangeau et al	Retrospective	46,993 patients aged <20,	Total inpatient clinical	30-day mortality	Average nursing hours to

2007[43]	cohort study	discharged between 1 April 2002 & 31 March 2003 in Canada Patients from one of four diagnostic groups: • Acute myocardial infarction • Pneumonia • Septicaemia • Stroke Data extracted from Ontario Discharge Abstract Database • Ontario Hospital Insurance Plan • Ontario Hospital Reporting System • Ontario Nurse Survey • Ontario Register Persons Database Statistics Canada 2001 Population Files	nursing worked hours (all nurse categories)/sum of weighted patient cases* discharged per hospital (for 2002-2003) * Weighted patient cases is an expression that reflects standardized patient volume based on their relative resource consumption		weighted patient cases was 36.2 (SD±9.3) Increase in number of nursing hours was associated with six fewer deaths for every 1000 discharged patients
Valentin et al 2009[44]	Prospective cohort study	1328 patients in 113 intensive care units from 27 countries 17 or 24 January 2007 Data extracted from staff who completed a bedside questionnaire	NPR calculated each shift	Parenteral Medication errors: wrong dose, wrong drug, wrong route, wrong time, missed medication	Median NPR: Day shift: 1.3 (IQR 1.0-1.8) Evening shift: 1.6 (IQR 1.2-2.0) Night shift: 2.0 (IQR 1.4-2.5) As the NPR increased, patients were 30% more likely to experience a parental medication error (OR 1.3, 95%CI 1.03-1.64, p=0.03) (multivariate regression)
Van den Heede et al 2009[45]	Retrospective cohort study	260,923 adults (20-85 years) acute in-patient hospitalisations in 115 Belgium acute hospitals in 2003	NHPPD: Hours of care provided by nurses divided by the number of patients	In-hospital mortality Deep venous thrombosis Failure to rescue	The mean acuity-adjusted nursing hours per patient day (NHPPD) was 2.62 (S.D. =

		Two administrative databases • Belgian Nursing Minimum Dataset (B-NMDS) • Belgium Hospital Discharge Dataset (B-HDDS)	being cared for over 24 hours and adjusted patient acuity	Shock or cardiac arrest Pressure ulcer Postoperative complications Postoperative respiratory failure Urinary tract infections Hospital acquired pneumonia Hospital acquired sepsis	0.29) No significant association was found between NHPPD and patient outcomes
Van den Heede et al 2009[46]	Retrospective cohort study	9054 adults (20-85 years) in 58 intensive care and 75 general nursing units representing 28 of the 29 Belgian cardiac centres in 2003 Data was extracted from two administrative databases • Belgian Nursing Minimum Dataset (B-NMDS) • Belgium Hospital Discharge Dataset (B-HDDS)	NHPPD: Total hours worked by a registered nurse during a 24hr period/ patient census for that day	In-hospital mortality	The median NHPPD was 11.9 (IQR 10.3-13.1) Greater NHPPD in postoperative general nursing units were associated with lower in-hospital mortality 44 patients (95% CI: 43-45) would not have died if all general postoperative cardiac nursing units had 3.5 NHPPD which corresponds to 4.9 fewer deaths per 1000 patients admitted for elective cardiac surgery
West et al 2014[47]	Retrospective cohort study	65 ICU representing 38168 patients in UK during 1998. Data extracted from Intensive Care National audit and Research Centre (ICNARC) casemix database	NPR calculated as nurses (full-time time equivalent) per bed on the census day	ICU mortality In-hospital mortality	Average NPR was not reported Lower NPRs were associated with lower ICU mortality and in-hospital mortality (OR 0.90, 95%CI 0.83-0.97)

CI- confidence interval
HR-hazard ratio
ICU- Intensive care unit

NHPPD- nursing hours per patient day
NPR- nurse-to-patient ratios
OR-odds ratio
RR-relative risk

Table 2: Summary of NOS Quality Assessment: Cohort Studies

Study	Selection				Comparability of cohorts#	Outcome			Evidence quality[1]
	Exposed cohort representative	**Non exposed cohort selection**	**Exposure ascertainment**	**Outcome not present at start**		**Assessment**	**Follow-up length**	**Follow up adequacy**	
Aitken et al 2014[13]	*	*	*	*	**	*	*	*	High
Benbenbishty et al 2010[14]	*	*	--	*	--	--	*	*	Low
Blot et al 2011[15]	*	*	*	*	**	*	*	*	High
Checkley et al 2014[16]	*	*	--	*	*	*	*	*	Moderate
Chittawatannarat et al 2014[17]	*	*	*	*	*	--	*	--	Moderate
Cho et al 2008[18]	*	*	*	*	**	--	*	*	High
Cho et al 2009[19]	*	*	*	*	**	--	*	*	High
Diya et al. 2012[20]	*	*	*	*	**	*	*	*	High
Griffiths et al 2016[21]	*	*	*	*	**	*	*	*	High
Hart & Davis 2011[22]	*	*	*	*	--	*	*	*	Low
He et al 2013[23]	*	*	*	*	**	*	*	*	High
Hugonnet et al 2007[24]	*	*	--	*	**	--	*	*	High
Hugonnet et al 2007[25]	*	*	*	*	--	--	*	*	Low
Johansen et al 2015[26]	*	*	*	*	**	*	*	*	High
Kandler et al 2013[27]	*	*	--	*	--	--	*	*	Low
Kim et al 2012[28]	*	*	*	*	**	*	*	*	High
Mark et al 2012[29]	*	*	*	*	*	*	*	*	Moderate
McHugh et al 2016[30]	*	*	*	*	**	*	*	*	High

Merchant et al 2012[31]	*	--	--	*	--	*	*	*	Low
Metnitz et al 2009[32]	*	*	*	*	**	*	*	*	High
Neuraz et al 2015[33]	*	*	--	*	**	--	*	*	High
O'Brien-Pallas et al 2010[34]	*	*	*	*	*	--	--	*	Moderate
Ozdemir et al 2016[35]	*	*	*	*	**	*	*	*	High
Park et al 2012[36]	*	*	*	*	**	*	*	*	High
Perez et al 2006[37]	*	--	--	*	--	*	*	*	Low
Sakr et al 2015[38]	*	*	--	*	**	--	*	*	High
Schwab et al 2012[39]	*	--	*	*	**	*	*	*	High
Seetz et al 2016[40]	*	*	*	*	**	*	*	*	High
Shuldham et al 2009[41]	*	*	*	*	--	--	*	--	Low
Stone et al 2007[42]	*	*	*	*	**	*	*	*	High
Tourangeau et al 2007[43]	*	*	*	*	*	*	*	*	Moderate
Valentin et al 2009[44]	*	*	*	*	**	--	*	*	High
Van den Heede et al 2009[45]	*	*	*	*	**	*	*	--	High
Van den Heede et al 2009[46]	*	*	*	*	**	*	*	*	High
West et al 2014[47]	*	*	--	*	**	*	*	*	High

Also includes controlling for potential confounders

1. Evidence quality:

    Low: downgrading from moderate to low based on design or lack of information in report

    Moderate: study met selection criteria (4 stars), comparability (1 star and upgraded a level for 2 stars), and outcome assessment.

    High: upgrading from moderate to high based on comparability of 2 stars

Figure

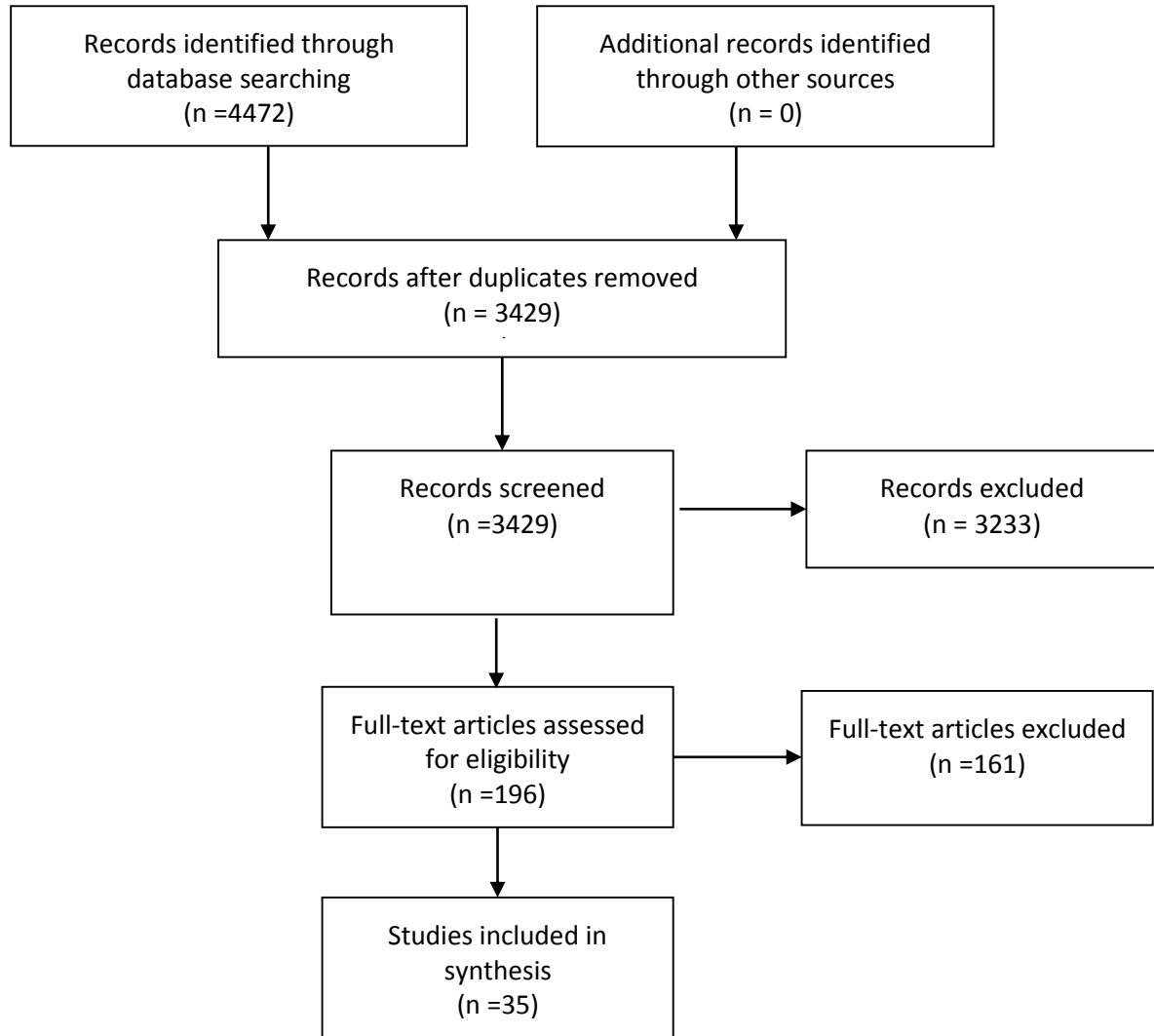**Figure 1. Flow Diagram of Study Selection**

Figure 2: The effect of nurse-to-patient ratios (NPRs) on in-hospital mortality

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Cho 2008	-0.0834	0.0227	23.9%	0.92 [0.88, 0.96]	
Cho 2009	-1.3471	0.5413	0.7%	0.26 [0.09, 0.75]	
McHugh 2016	-0.0513	0.0219	24.0%	0.95 [0.91, 0.99]	
Metnitz 2009	-0.2614	0.0343	22.3%	0.77 [0.72, 0.82]	
Sakr 2015	-0.3711	0.1346	8.0%	0.69 [0.53, 0.90]	
West 2014	-0.1054	0.0413	21.1%	0.90 [0.83, 0.98]	
Total (95% CI)			100.0%	0.86 [0.79, 0.94]	

Heterogeneity: Tau² = 0.01; Chi² = 36.88, df = 5 (P < 0.00001); I² = 86%
Test for overall effect: Z = 3.31 (P = 0.0009)

Favours Low NPR Favours High NPR