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Mortality Risk Following Delirium in Older Inpatients: A Systematic Review and Meta-Analysis

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Keywords: delirium | hospital | incidence | length of stay | mortality | older people | risk

ABSTRACT

Background: The onset of delirium in older inpatients is associated with worse outcomes, including longer length of hospital stay, loss of functionality, loss of cognitive function, sleep disorders, increased polypharmacy, higher rates of adverse effects, and mortality. Previous studies have analyzed mortality after delirium, but without discriminating between settings, time, or critical conditions.

Aims: To assess the pooled incidence of delirium and risk of mortality at different times after hospital admission in older people and its association with mortality and length of stay in hospitalized people aged 65 years or older.

Methods: This systematic review and meta-analysis included studies analyzing the incidence of delirium and mortality. MEDLINE, Scopus, and the Web of Science were searched from inception to December 2023. PRISMA guidelines were followed. Inclusion criteria were original peer-reviewed studies in medical hospital areas using validated screening or diagnostic methods and quantifying mortality at admission or after excluding surgical patients. Exclusion criteria were studies that included only participants with a single condition at baseline, such as cancer, pneumonia, or frailty, or who were admitted to a specific unit such as the intensive care unit, as well as studies that assessed delirium in surgical areas. Study quality was assessed with Joanna Briggs Institute Critical Appraisal tools. The statistical analysis was performed in RevMan v5.4.0 (Cochrane Collaboration, Oxford, UK), using a random-effects model to calculate incidence, mortality, and length of hospital stay along with their 95% confidence intervals (CIs). The PROSPERO registration number for the review was CRD42023491604.

Results: In the 32 included studies, the pooled cumulative incidence of delirium was 28.79% (95% confidence interval [CI] 24.06%, 33.51%). The mortality risk was higher in patients who had delirium during admission (odds ratio [OR] 5.23, 95% CI [3.45, 7.93]). This varied by time point: 1 month, OR 3.80 (95% CI 2.40, 6.00); 6 months, OR 3.48 (95% CI [2.01, 6.01]); 12 months, OR 2.73 (95% CI [2.07, 3.60]); 2 years, OR 2.09 (95% CI [1.57, 2.78]); and 5 years, OR 3.34 (95% CI [2.40, 4.64]). In the pooled analysis, mean length of hospital stay was 2.26 days (95% CI [0.54, 3.99]) longer in patients with delirium.

Linking Evidence to Action: This study shows the markedly increased risk of mortality in older people with delirium during hospital admission and over the first month, in addition to an increased length of stay. The onset of delirium leads to increased use of healthcare resources. These data help to quantify the impact that delirium has on the health of older people, with implications for health system management. The evidence highlights the need to implement preventive pharmacological treatment or multicomponent strategies that minimize the onset of delirium in the older population.

Trial Registration: The PROSPERO registration number for the review was: CRD42023491604, available at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=491604

1 | Introduction

Geriatric syndromes such as pressure ulcers, functional decline, incontinence, falls, and delirium are highly prevalent, multifactorial conditions in older adults. A straightforward definition is still elusive, but these syndromes are clinical conditions in older people that do not fit into discrete disease categories or accurately reflect the disease that is responsible for the shift in health status. There may be an occasional gap between the location of the underlying physiological damage and the ensuing clinical symptom (Magnuson et al. 2019).

Delirium is among these multifactorial geriatric syndromes. It is defined as a disturbance of attention and awareness, with acute and fluctuating development, and an additional cognitive disturbance that is associated with a direct physiological disturbance and cannot be explained in any other way (European Delirium Association and American Delirium Society 2014). The concurrence of predisposing and precipitating factors in older people increases the risk of developing delirium (Oh et al. 2017). Predisposing factors can include advanced age, history of stroke, diabetes, and dementia, while precipitating factors may be infection, hospitalization, certain drugs such as anticholinergic and antipsychotic drugs, or a surgical procedure (Oh et al. 2017).

The incidence of delirium in the older population ranges from 1% in those dwelling in the community to as much as 15%–60% in the hospital setting (Ritter et al. 2018). Rates also vary according to the exact hospital setting (e.g., intensive care unit [ICU], emergency department [ED]) (Chen et al. 2022; Han et al. 2022), or according to concomitant diseases such as dementia (Bauernfreund et al. 2022), cancer, stroke, COVID-19, or pneumonia (Abate et al. 2021). These rates can even ascend to 70% in long-term care due to the greater comorbidity and presence of predisposing factors in the older person (Komici et al. 2022).

The coexistence of multiple etiological factors in delirium suggests the involvement of several neurobiological processes in its pathophysiology, which still remain largely unclear (van Montfort et al. 2019). Delirium results from the interaction between a previous vulnerable neurobiological state and one or more predisposing or precipitating factors. These agents act through poorly understood neuropathogenic mechanisms, such as decreased oxidative metabolism of the brain, neuroendocrine stress response, and cytokine release. This situation leads to impaired behavior and attention (van Montfort et al. 2019). Several processes could contribute to this vulnerability, including impaired brain network connectivity in cholinergic and noradrenergic neurons, neuroinflammatory changes, and vascularization dysfunction leading to endothelial injury, blood–brain barrier (BBB) damage, and impaired cerebral perfusion (Maldonado 2017). A reversal has been observed in the relationship between the prefrontal cortex (executive network) and the posterior cingulate (mode network) (Choi et al. 2012; Raichle 2015).

1.1 | The Review

The onset of delirium in older people is associated with worse health outcomes, longer length of hospital stay (LOS), loss of functionality, loss of cognitive function, altered arousal, inattention, disorientation, memory deficits, disorganized thoughts, sleep disorders, increased polypharmacy, higher rates of adverse effects, and mortality (Rosgen et al. 2020; Tieges et al. 2021; Zhang et al. 2022). Mortality in older people with delirium has attracted research interest, and there are meta-analyses focusing on the critically ill population (Salluh et al. 2015), post-surgical delirium (Yan et al. 2023), and delirium associated with COVID-19 (Pranata et al. 2021; Shao et al. 2021). Aung Thein et al. (2020) performed a meta-analysis of mortality in the hospital setting, estimating a 3.18-fold higher risk following delirium and a 7.09-fold higher risk when delirium occurred in the ICU setting. Yan et al. (2023) analyzed mortality in older people with delirium at different time points in the following months, observing an increased risk in the month following the delirium episode and a decreased risk in subsequent months. To date, no meta-analysis has been performed analyzing the risk of mortality according to time point in older people admitted to regular hospital wards.

This study aims to assess the pooled cumulative incidence of delirium in people aged 65 years or older and admitted to regular hospital wards, its association with mortality across different time points, and its relation to LOS.

2 | Methods

2.1 | Design

This systematic review and meta-analysis included studies analyzing the association between delirium and risk of mortality in hospitalized older people, the incidence of delirium, and the associated LOS. The study protocol is registered in PROSPERO (CRD42023491604). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and flow chart were used to guide the research process and the study reporting (Figure 1).

2.2 | Search Strategy

The literature search was conducted in MEDLINE, Scopus, and the Web of Science, from database inception to 20 December 2023. Each database was searched using individual and combined terms, along with Medical Subject Headings (MeSH) and the Boolean operators AND/OR. Two reviewers (XX, YY) independently screened titles and abstracts.

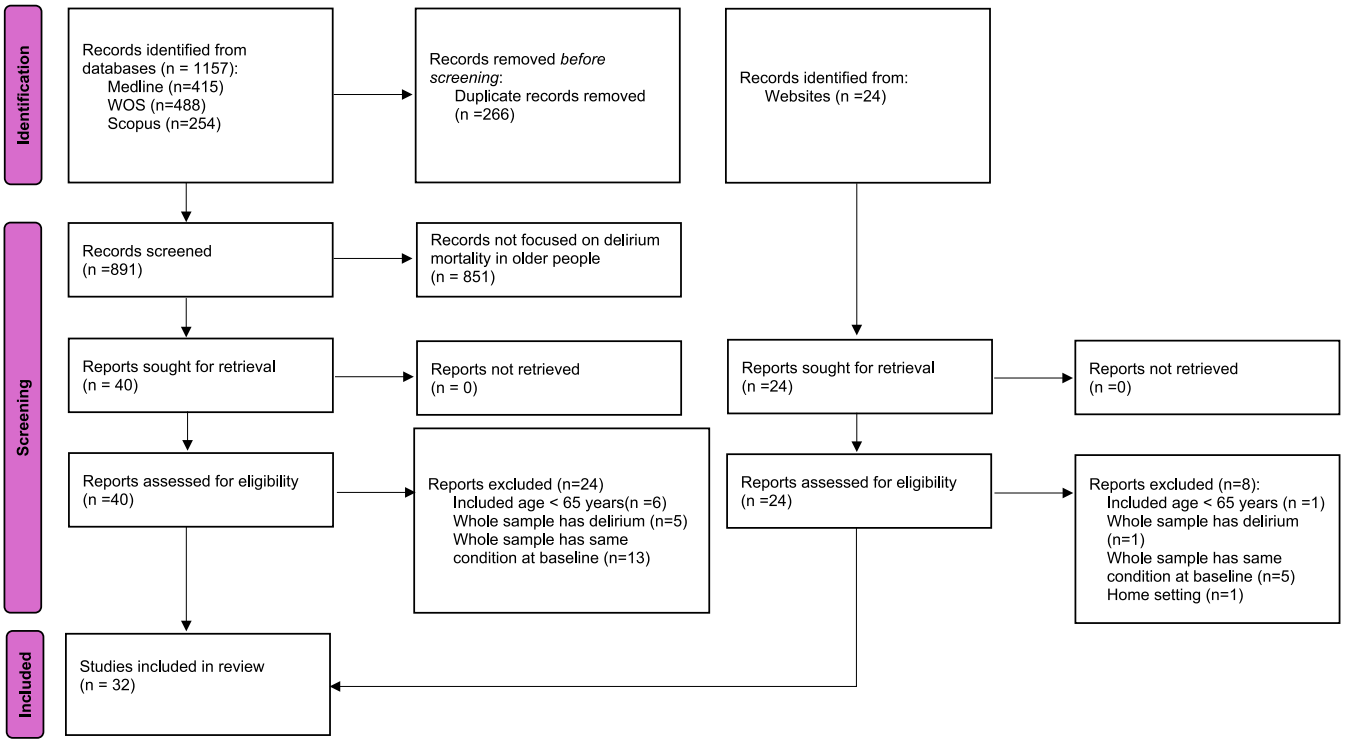


FIGURE 1 | PRISMA flow chart.

The research question was defined in the PICO format: (1) Patients: older adults (mean age 65 years or older); (2) Intervention: positive delirium assessment; (3) Control: negative delirium assessment; (4) Outcome: mortality rates in patients with and without delirium as a primary outcome, and length of stay as a secondary outcome.

The following search strategy was used: ((Older OR Aged OR Geriatric* OR Elder*) AND (Chronic* OR Morbidi*) AND (Delirium) AND (Death OR Death Sudden OR Mortality OR Survival) NOT (Covid-19) NOT (POD OR Surgic*) NOT protocol NOT review).

2.3 | Inclusion and Exclusion Criteria

Inclusion criteria were being 65 years or older and admitted to hospital medical wards. Included studies had to use validated tools to detect delirium and have a prospective observational or case–control design, reporting mortality rates in patients with and without delirium. We excluded studies that included only participants with a single condition at baseline, such as cancer, pneumonia, or frailty, or who were admitted to a specific unit such as the ICU, as well as studies that assessed delirium in surgical areas. Conflicts between reviewers were resolved by a third reviewer (ZZ).

2.4 | Search Outcome

For screening, every pertinent reference was uploaded to Zotero, and its automatic deduplication feature was used to remove duplicates. Nevertheless, more duplicates were found and eliminated throughout the manual screening procedure. XX and YY performed the preliminary screening of the title and abstract for every submission. These were screened against inclusion and exclusion criteria to determine their eligibility. Conflicts were discussed and resolved with YY. Three review authors (XX, YY, and ZZ) independently carried out full-text screening to guarantee uniformity in the utilization of inclusion and exclusion criteria. The screening procedure was reported using the PRISMA checklist (Appendix S1).

2.5 | Quality Appraisal

Three review authors (XX, YY, and ZZ) independently assessed the methodological quality of the included studies, using the 11-item checklist for critical appraisal published by the Joanna Briggs Institute (Munn et al. 2020). One point was assigned for every "yes" response on the checklist, while checklist items described as "no" or "unclear" scored 0 points. A total score of 8 points or more denoted "high quality;" 4–7 points, "moderate quality;" and 3 points or fewer, "low quality" (Shao et al. 2021; Shenkin et al. 2017). Disagreements were resolved by consensus on a case-by-case basis to help reach a conclusion.

2.6 | Data Abstraction

Three reviewers (XX, YY, ZZ) independently extracted data from the included studies. The data extracted included age, sex, number of patients, incidence/prevalence, delirium assessment tool, professional responsible for the assessment, delirium subtype, and comorbidity. Mortality rates at different time points were extracted, along with LOS and other data of interest such as survival or the distribution of delirium

subtypes. The first author, year of publication, and country were recorded.

2.7 | Data Synthesis

Qualitative and descriptive analyses were performed. The qualitative component consisted of a detailed description of the study characteristics; patient demographics; comorbidities; incidence, prevalence, or cumulative incidence of delirium; assessment method; attending professional, and mortality outcome by time point. Data were compared and presented as forest plots.

The quantitative analysis was performed using Cochrane Review Manager, version 5.4.0 (Cochrane Collaboration, Oxford, UK). The incidence proportion and its 95% confidence interval (CI) were determined using the online exact binomial ratio and CI calculator available at statpages.info/confint.html. Subgroup analyses were conducted on groupings created through the assessment tool (medical diagnostic criteria, Confusion Assessment Method [CAM, because it is the most widely used], and the CAM plus another instrument). Each outcome was analyzed using the odds ratio (OR) and 95% CI for dichotomous outcomes (mortality) and the mean difference (MD) for continuous outcomes (LOS). All results are presented in a forest plot. Analyses were performed using the random-effects meta-analysis model with the assumption that the true effect sizes may differ within the included studies, as they were conducted using different assessment methods and in different hospital conditions (Hedges and Vevea 1998). Heterogeneity was quantified using the I^2 statistic. Survival was assessed using the Kaplan–Meier method, and groups were compared using the log-rank test. Univariate Cox proportional regression analyses were performed according to the time points reported by the studies. These data were analyzed with SPSS Statistics version 26.0 (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

3 | Results

3.1 | Study Selection

The search of the electronic databases yielded 1157 records; after removing duplicates, 891 records remained. An additional 24 records were identified through other sources. Of these, 851 records were excluded, as they did not report mortality in delirium, leaving a total of 64 for full-text review. Some eligible studies were more than 30 years old, but since they had never been included in a meta-analysis, they were deemed relevant for inclusion. Following full-text review, 32 records were removed, leaving a total of 32 included studies (Figure 1). Reasons for exclusion were inclusion of younger adults ($n = 7$) (Andrews et al. 2020; Jayaswal et al. 2019; Lima et al. 2021; Pal et al. 2021; Pendlebury et al. 2015; van der Kuur et al. 2019; Wolters et al. 2014); analysis of the data as a whole cohort ($n = 6$) (Arinzon et al. 2011; Gual, Inzitari, et al. 2018; Koponen et al. 1989; Mehrabani et al. 2020; Soler-Sanchis et al. 2023; Wu et al. 2021); home-based setting ($n = 1$) (Isaia et al. 2009); and same medical condition on inclusion ($n = 18$) (Boustani et al. 2010; Chan et al. 2017; Cole et al. 2008; Fick et al. 2003; Jorge-Ripper et al. 2017; Li et al. 2023; Lisk et al. 2020; Miró et al. 2024; Mossello et al. 2020; Pieralli et al. 2014; Pisani et al. 2005; Pitkala et al. 2005; Pompei et al. 1994; Seiler et al. 2021; Sharma et al. 2012; Thomason et al. 2005; Tiwari et al. 2023; Uthamalingam et al. 2011).

3.2 | Methodological Quality of Included Studies

The JBI Critical Appraisal Systematic Reviews checklist was used to evaluate the methodological quality of the included studies, which showed moderate to high quality overall. Some studies did not analyze confounders or strategies to address these, and most did not report loss to follow-up or the strategies implemented to consider this in the analysis. Table 1 provides a thorough analysis.

Regarding the funnel plot analysis, some studies had small sample sizes, and most of the palliative care research showed effect sizes outside the funnel. However, the analysis of incidence and LOS shows studies on both sides, albeit at the top of the funnel. The analysis of mortality according to the time point shows estimates within the funnel area, suggesting that they would not affect the results of the meta-analysis (Figures 2–4).

3.3 | Study Characteristics

Thirty-two studies were included in the meta-analysis (Figure 1). Most took place in Europe ($n = 14$) (Adamis et al. 2006, 2007, 2017; Ardern et al. 1993; Cano-Escalera et al. 2022; Dani et al. 2018; Edlund et al. 2006; Eeles et al. 2010; Garcia-Pérez et al. 2023; González et al. 2005; Gual, Morandi, et al. 2018; Muresan et al. 2016; O'Keeffe and Lavan 1997; Ramsay et al. 1991) and North America ($n = 9$) (Alagiakrishnan et al. 2009; Dasgupta and Brymer 2015; Francis and Kapoor 1992; Hsieh et al. 2015; Leslie et al. 2005; McAvay et al. 2006; McCusker et al. 2002; Rockwood 1989; Wakefield 2002), while the rest were from Asia ($n = 5$) (Feldman et al. 1999; Lim et al. 2023; Painkra et al. 2023; Praditsuwan et al. 2013; Tosun Tasar et al. 2018), South America ($n = 3$) (González et al. 2009; Vázquez et al. 2010), and Oceania ($n = 1$) (Holden et al. 2008) (Table 2).

A total of 11,394 participants contributed data to the meta-analysis. The mean age was 80 years and over in 56.3% of the studies ($n = 18$) (Adamis et al. 2006, 2007, 2017; Dani et al. 2018; Dasgupta and Brymer 2015; Edlund et al. 2006; Eeles et al. 2010; Feldman et al. 1999; Garcia-Pérez et al. 2023; Gual, Morandi, et al. 2018; Leslie et al. 2005; Lim et al. 2023; McAvay et al. 2006; Muresan et al. 2016; O'Keeffe and Lavan 1997; Ramsay et al. 1991; Rockwood 1989; Vázquez et al. 2010), with male predominance in 21.9% ($n = 7$) (Adamis et al. 2006, 2017; Ardern et al. 1993; Edlund et al. 2006; Feldman et al. 1999; Ramsay et al. 1991; Wakefield 2002). Comorbidity was reported in 53% ($n = 17$) of the studies. The most prevalent conditions were cardiovascular, endocrine, and respiratory diseases. The most common tool used for assessment of comorbidity was the Charlson Comorbidity Index (CCI), generally with mean scores of 3 points or less (Eeles et al. 2010; González et al. 2009; Gual, Morandi, et al. 2018; Hsieh et al. 2015; McCusker et al. 2002; O'Keeffe and Lavan 1997; Vázquez et al. 2010) except (Lim et al. 2023), with a score of 6. The APACHE Acute Physiology and Chronic Health

TABLE 1 | Methodological quality of included studies.

Study ID	Population sample	Exposures	Exposure measured in a valid and reliable	Confounders	Strategies to address confounding	Participants free of the outcome	Outcomes measured in a valid and reliable way	Follow-up time reported	Reasons to loss to follow	Strategies to address incomplete	Appropriate statistical analysis used	Overall
(Adamis et al., 2006)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Adamis et al., 2007)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Adamis et al., 2017)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Alagiakrishnan et al., 2009)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Ardern et al., 1993)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Cano-Escalera et al., 2022)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Carrasco et al., 2005)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Dani et al., 2018)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Dasgupta & Brymer, 2015)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Edlund et al., 2006)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Eeles et al., 2010)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Feldman et al., 1999)	☺	☺	☺	☹	☹	☺	☺	☺	☺	?	☺	High
(Francis & Kapoor, 1992)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Garcia-Pérez et al., 2023)	☺	☺	☺	☹	☹	☺	☺	☺	☹	?	?	Moderate
(González et al., 2005)	☺	☺	☺	☺	?	☺	☺	☺	☹	?	☺	High
(González et al., 2009)	☺	☺	☺	☺	?	☺	☺	☺	☹	?	☺	High
(Gual et al., 2018)	☺	☺	☺	?	?	☺	☺	☺	?	?	☺	Moderate
(Holden et al., 2008)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Hsieh et al., 2015)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Leslie et al., 2005)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(Lim et al., 2023)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(McAvay et al., 2006)	☺	☺	☺	☺	?	☺	☺	☺	?	?	☺	High
(McCusker et al., 2002)	☺	☺	☺	☺	?	☺	☺	☺	☹	☹	☺	High
(Muresan et al., 2016)	☺	☺	☺	?	?	☺	☺	☺	?	?	☺	Moderate
(O'Keeffe & Lavan, 1997)	☺	☺	☺	☺	☺	☺	☺	☺	?	?	☺	HIgh
(Painkra et al., 2023)	☺	☺	☺	?	?	☺	☺	☺	?	?	☺	Moderate
(Praditsuwan et al., 2013)	☺	☺	☺	☺	☺	☺	☺	☺	?	?	☺	High
(Ramsay et al., 1991)	☺	☺	☺	☺	?	☺	☺	☺	?	?	?	Moderate
(Rockwood, 1989)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	?	Moderate
(Tosun Tasar et al., 2018)	☺	☺	☺	☺	?	☺	☺	☺	?	?	?	Moderate
(Vázquez et al., 2010)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	☺	Moderate
(Wakefield, 2002)	☺	☺	☺	☹	☹	☺	☺	☺	?	?	?	Moderate

Note: ☺ = yes; ☹ = no; ? = unclear. Checklist for cohort studies. Critical appraisal tools for use in Joanna Briggs Institute systematic reviews.

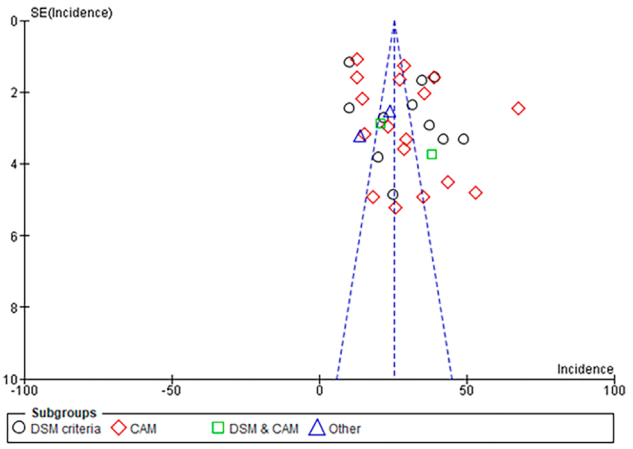


FIGURE 2 | Funnel plot of subgroup pooled incidence of delirium according to assessment tool.

Evaluation II Scale (APS) and Cumulative Illness Rating Scale (CIRS) were used in two studies (Carrasco et al. 2005; Dasgupta and Brymer 2015). The remaining studies ($n = 4$) reported comorbidity without using validated tools such as a number of diseases (Feldman et al. 1999; Praditsuwan et al. 2013) or the severity of illness (Francis and Kapoor 1992; Ramsay et al. 1991). Group differences according to comorbidity were found in only two studies, with higher comorbidity in patients with delirium (Carrasco et al. 2005; McCusker et al. 2002).

The tools for the detection of delirium were the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and revisions ($n = 10$) (Ardern et al. 1993; Dani et al. 2018; Edlund et al. 2006; Eeles et al. 2010; Francis and Kapoor 1992; O'Keeffe and Lavan 1997; Praditsuwan et al. 2013; Ramsay et al. 1991; Rockwood 1989; Tosun Tasar et al. 2018), CAM scale and versions ($n = 17$) (Adamis et al. 2006, 2007; Alagiakrishnan et al. 2009; Cano-Escalera et al. 2022; Carrasco et al. 2005; Dasgupta and Brymer 2015; Feldman et al. 1999; González et al. 2009; Gual, Morandi, et al. 2018; Holden et al. 2008; Hsieh et al. 2015; Leslie et al. 2005; McAvay et al. 2006; McCusker et al. 2002; Muresan et al. 2016; Painkra et al. 2023; Vázquez et al. 2010) or both ($n = 2$) (Adamis et al. 2017; González et al. 2005). In addition, the NEECHAM scale (Wakefield 2002), International Classification of Diseases, 10th revision (ICD-10) (Lim et al. 2023), and 3D+ tool (Garcia-Pérez et al. 2023) were used.

The professionals responsible for diagnosis were mainly physicians ($n = 13$) (Alagiakrishnan et al. 2009; Ardern et al. 1993; Carrasco et al. 2005; Dani et al. 2018; Edlund et al. 2006; Feldman et al. 1999; González et al. 2005, 2009; Lim et al. 2023; Praditsuwan et al. 2013; Ramsay et al. 1991; Rockwood 1989; Tosun Tasar et al. 2018), nurses ($n = 3$) (McAvay et al. 2006; McCusker et al. 2002; Wakefield 2002), an assistant team ($n = 1$) (Holden et al. 2008) and research staff ($n = 2$) (Francis and Kapoor 1992; Hsieh et al. 2015). In the rest of the studies, the person responsible for the assessment was not reported.

3.4 | Incidence

The pooled cumulative incidence of delirium was 28.79% (95% CI [24.06, 33.51]; test for overall effect: $Z = 11.95$, $p < 0.001$;

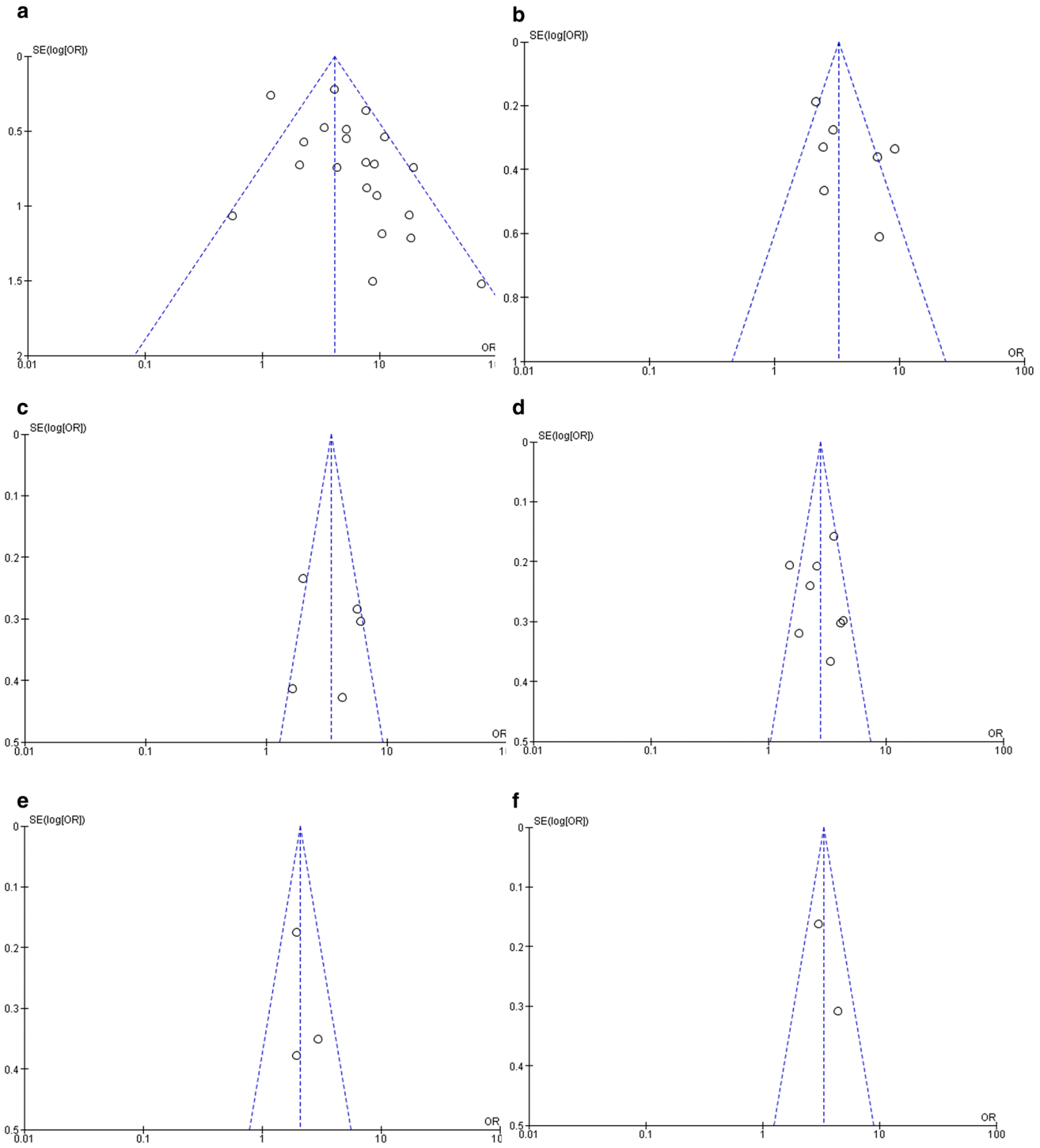


FIGURE 3 | Funnel plot of mortality in delirium older patients (a) in-hospital; (b) at 1 month; (c) at 3–6 months; (d) at 12 months; (e) at 18–24 months; (f) at 3–5 years.

heterogeneity: $\tau^2 = 176.15$; $\chi^2 = 1137.19$, degrees of freedom [df] = 31, $p < 0.001$; $I^2 = 97\%$; Figure 5). The tools for detecting delirium were the CAM scale (Adamis et al. 2006, 2007; Alagiakrishnan et al. 2009; Cano-Escalera et al. 2022; Carrasco et al. 2005; Dasgupta and Brymer 2015; Feldman et al. 1999; González et al. 2009; Gual, Morandi, et al. 2018; Holden et al. 2008; Hsieh et al. 2015; Leslie et al. 2005; McAvay et al. 2006; McCusker et al. 2002; Muresan et al. 2016; Painkra et al. 2023; Vázquez et al. 2010); the DSM criteria in its versions III, III-R, IV, and V (Ardern et al. 1993; Dani et al. 2018; Edlund et al. 2006; Eeles et al. 2010; Francis and Kapoor 1992; O'Keeffe and Lavan 1997; Praditsuwan et al. 2013; Ramsay et al. 1991; Rockwood 1989; Tosun Tasar et al. 2018); the ICD-10 (Lim et al. 2023); more than one of these methods (Adamis et al. 2017; González et al. 2005); and others (Garcia-Pérez et al. 2023; Wakefield 2002). Very similar pooled incidence rates

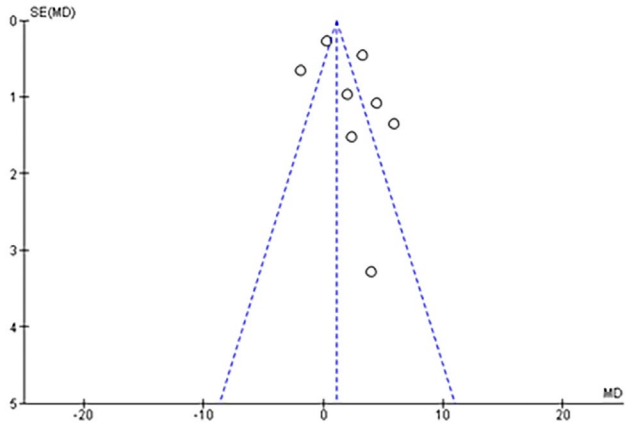


FIGURE 4 | Funnel plot for length of stay in older patients.

were found with the diagnosis of delirium via CAM (29.09%, 95% CI [20.5%, 38.98%]), DSM, and ICD criteria (30.87%, 95% CI [23.71%, 38.03%]), and both of these (29.09%, 95% CI [11.94%, 46.23%]). Lower rates were obtained in the studies using other instruments such as the NEECHAM scale and the assessment with the 3D+ system (18.89%, 95% CI [9.10%, 28.68%]) (Garcia-Pérez et al. 2023; Wakefield 2002).

3.5 | Mortality

Mortality was analyzed at different times. The magnitude of the increased risk in participants with delirium was highest during hospital admission ($n = 5633$, 21 studies, OR 5.23, 95% CI [3.45, 7.93]; $p < 0.001$; $\tau^2 = 0.45$; $\chi^2 = 49.95$, df = 20, $p < 0.001$; $I^2 = 60\%$; Figure 6).

Seven studies assessed mortality during the first month following the episode of delirium, finding nearly a four-fold increased risk ($n = 3350$, OR = 3.80, 95% CI [2.40, 6.00]; $p < 0.001$; $\tau^2 = 0.25$; $\chi^2 = 20.54$, df = 6, $p = 0.002$; $I^2 = 71\%$; Figure 6).

For other times, the estimated risk was as follows: 3–6 months, OR 3.48 (95% CI [2.01, 6.01]); 12 months, OR 2.73 (95% CI [2.07–3.60]); 18–24 months, OR 2.09 (95% CI [1.57, 2.78]); and 3–5 years, OR 3.34 (95% CI [2.40, 4.64]). Median 5-year survival was 569.6 days (standard error [SE] 12.73) in patients with delirium vs. 334.5 days (SE 11.9) in those without.

The risk of in-hospital mortality was analyzed in patients with comorbidity, as evaluated with the CCI ≤ 2 points, OR 5.88 (95% CI [3.64, 9.51]); and CCI = 6 points, OR 1.18 (95% CI [0.70, 1.40]); patients with less comorbidity showed a higher risk (Figure 7). Only one study reported mortality in patients with 6 points on the CCI; in addition, in the analysis of publication bias, two studies were observed outside the funnel, suggesting some bias in these results (Figure 8).

3.6 | Length of Stay

Of the 32 studies, 18 analyzed LOS, but only 8 ($n = 2920$) of these were amenable to meta-analysis. The remaining 10 could not be included due to the lack of a standard deviation. Mean LOS was 2.26 days (95% CI [0.54, 3.99]; $p = 0.01$) longer in the delirium group ($\tau^2 = 4.80$; $\chi^2 = 76.10$, df = 7, $p < 0.001$; $I^2 = 91\%$). The reported LOS between groups was consistently longer in patients with delirium, ranging from an MD of 0.30 days (95% CI [−0.24, 0.84]) in the study by Gual, Morandi, et al. (2018) to 5.90 days (95% CI [3.25, 8.55]) in the one by (González et al. 2005). The one exception was the study by (Ramsay et al. 1991), where mean LOS was 1.90 days (95% CI [−3.20, −0.60]) longer in patients without delirium (Figure 9).

Only three studies reported both CCI and LOS. In a sample with a mean CCI of 2, Vázquez et al. (2010) reported that LOS was on average 2.00 days longer (95% CI [0.09, 3.91], $p = 0.026$) in the delirium group. In another study in patients with a comorbidity index between 2 and 3 (Gual, Morandi, et al. 2018), there was no significant difference between groups in LOS (MD 0.30 days, 95% CI [−0.24, 0.84], $p = 0.268$). In the study by Lim et al. (2023) with a CCI of 6 points, mean LOS was 3.30 days longer (95% CI [2.40, 4.20] $p < 0.001$) in the delirium group.

4 | Discussion

This systematic review and meta-analysis show a pooled cumulative incidence of delirium of 28.79% in older people admitted to hospital wards. The risk of mortality associated with delirium was 5.23 times higher during hospital admission, 3.80 times higher at 30 days, 3.48 times higher at 6 months, 2.72 times higher at 12 months, 2.16 times higher at 24 months, and 3.34 times higher at 5 years.

The meta-analysis indicates that delirium incidence is within the range of estimates reported in previous reviews, of 5%–38% (Ahmed et al. 2014; Kalimisetty et al. 2017). Our incidence is higher than that observed in older people in the ED (15.2%) (Chen et al. 2022), in the postoperative setting (24%) (Igwe et al. 2023), and in admissions with cancer (22.6%–26.4% in medical wards and 17.04% in post-op) (Martínez-Arnau, Buigues, et al. 2023). These differences may be due to the heterogeneous inclusion criteria. Our study included patients admitted to a hospital unit for any cause, which means that not all had the same condition or disease. Patients with post-surgical delirium have all undergone medical treatment, while cancer patients are also receiving basic medical treatment, and this may act as a preventive factor in some cases (Han et al. 2022; Oh et al. 2017; Shao et al. 2021).

On the other hand, delirium incidence is lower than the estimates for subsyndromal delirium (36.4%) in older people (Gao et al. 2022), in older people with dementia (48.9%) (Han et al. 2022), and in older people with COVID-19 (44.5%) (Shao et al. 2021). Incidence of delirium is higher in people with more predisposing or precipitating factors and with certain specific risk factors, such as dementia or COVID-19 (Han et al. 2022; Oh et al. 2017; Shao et al. 2021).

The meta-analysis excluded studies in older patients with a single disease such as COVID-19, pneumonia, sepsis, or acute heart failure. The baseline existence of a common disease in all included participants could bias the analysis of pooled incidence and mortality (Han et al. 2022; Oh et al. 2017; Shao et al. 2021). All studies included people aged 65 years or older admitted to a

TABLE 2 | Characteristics of included studies.

Authors (year)	Country	Delirium / Age mean (SD or range)/% male	No delirium / Age mean (SD or range)/% male	Overall, the incidence and prevalence of delirium	Diagnostic tool/ professional	Morbidity index Mean (SD or range)/*n* (%) (DG vs. NDG)	Delirium Mortality % (*n*) Survival (days)	No delirium Mortality % (*n*) Survival (days)	Time point Mortality	Length of stay, days (DG vs. NDG) Mean (SD or range) Subtypes
Adamis et al. (2006)	UK	*N* = 33 82.8 (6.5)/59.6[a]	*N* = 61	O = 35.1 (*n* = 33) I = 28.7 (*n* = 27) *p* = 6.4 (*n* = 6)	CAM/NA	NA	*N* = 6 (18.2)	*N* = 3 (4.9)	In-hospital	DG 28.6 (23.5) 21.1 (18.2)[a] except exitus
Adamis et al. (2007)	Ireland	*N* = 47 84.6 (86.57)/32.9[a]	*N* = 117	O = 28.7 (*n* = 47) I = 25.6 (*n* = 42) *p* = 3.1 (*n* = 5)	CAM/NA	NA	*N* = 6 (14.3) *N* = 12 (28.6)	*N* = 8 (6.8) *N* = 23 (19.7)	In-hospital 6 months	NA
Adamis et al. (2017)	Ireland	*N* = 41 81.1 (6.5)/50[a]	*N* = 159	I = 20.5 (*n* = 41)	CAM, DSM-III, DSM-IIIR, DMS-IV, and DSM-V/NA	NA	*N* = 20 (48.8)	*N* = 35 (22)	12 months	9.76 (9.10) vs. 7.38 (6.94)
Alagiakrishnan et al. (2009)	Canada	*N* = 20 81 (74–87)/50	*N* = 112 79 (73–86)/NA	I = 15.2 (*n* = 20)	CAM/trained study personnel and confirmed by geriatrician	NA	*N* = 5 (25)	*N* = 4 (3.6)	In-hospital	18 (4–36) vs. 5 (3–10)
Ardern et al. (1993)	UK	*N* = 15 77.7 (NA)/53.3	*N* = 133 75.1 (NA)/49.6	I = 10.1 (*n* = 15)	DSM-III/ physician	NA	*N* = 1 (6.7)	*N* = 15 (11.3)	In-hospital	13.8 vs. 10.4
Cano-Escalera et al. (2022)	Spain	*n* = 200 84.37 (6.76)/45	*n* = 541 83.43 (6.67)/53.9	O = 27 (*n* = 200) I = 4 (*n* = 30) *p* = 22.9 (*n* = 170)	CAM/NA	NA	*N* = 9 (4.5) *N* = 36 (18) *N* = 45 (22.5) *N* = 79 (39.5)	*N* = 10 (1.8) *N* = 52 (9.6) *N* = 87 (16.1) *N* = 136 (25.1)	1 month 6 months 12 months 2 years	NA
Carrasco et al. (2005)	Chile	*N* = 57 80.5 (65–94)[a]/42.1	*N* = 51 75.3 (NA)/55	O = 52.8 (*n* = 57)	CAM/ geriatrician residents	APS: 13.2 vs. 9.6*	*N* = 4 (7)	*N* = 0 (0)	In-hospital	10.21 (7.74) vs. 5.78 (2.58) Type %: Hyperactive 22.6 Hyperactive 71.7 Mixed 5.7

(Continues)

TABLE 2 | (Continued)

Authors (year)	Country	Delirium / Age mean (SD or range)/% male	No delirium / Age mean (SD or range)/% male	Overall, the incidence and prevalence of delirium	Diagnostic tool/ professional	Morbidity index Mean (SD or range)/*n* (%) (DG vs. NDG)	Delirium / Survival (days)	No delirium / Survival (days)	Time point / Mortality	Length of stay, days (DG vs. NDG) Mean (SD or range) / Subtypes
							Mortality % (*n*)			
Dani et al. (2018)	UK	*N* = 73 83.1 (7.41)/41[a]	*N* = 637	O = 10.3 (*n* = 73)	DSM-IV/ Trained Psychiatrist	NA	*N* = 59 (81)	*N* = 311 (49)	3 years	NA
Dasgupta and Brymer (2015)	Canada	*N* = 355 84.4 (NA)/42	*N* = 880 81.8 (NA)/43.3	O = 28.74 (*n* = 355)	CAM/NA	APS: 7.71 vs. 6.37 CIRS: 9.74 vs. 9.69	*N* = 54 (15.2)	*N* = 37 (4.2)	In-hospital	15 vs. 6*
Edlund et al. (2006)	Sweden	*N* = 125 81.8 (6.3)/52.8	*N* = 275 79.4 (5.7)/59.6	O = 31.3 (*n* = 125)	DSM-IV/ physician	NA	*N* = 11 (8.8) *N* = 45 (36)	*N* = 5 (1.8) *N* = 55 (20)	In-hospital 12 months	15.4 (14.2) vs. 9.5 (7.8)* Type %: hypoactive 24; hyperactive 21.6; mixed 15.2; no classified 39.2
Eeles et al. (2010)	UK	*N* = 103 83.7 (5.8)/41	*N* = 175 81.8 (5.3)/42	O = 37.1 (*n* = 103) I = 8.3 (*n* = 23) *p* = 28.8 (*n* = 80)	DSM-IV/NA	CCI 2 (1.4) vs. 1.7 (1.4)	*N* = 37 (35.9)[b]	*N* = 12 (6.9)	In-hospital	30.3 vs. 17*
Feldman et al. (1999)	Israel	*N* = 11 83.2 (6.8)/72.7	*N* = 50 80.5 (6.9)/50	O = 18 (*n* = 11)	CAM/ experienced geriatrician	N chronic diseases 4 (1.2) vs. 2.5 (1.3)	*N* = 3 (27.3)	*N* = 1 (2)	In-hospital	18.2 (6.2) vs. 7.3 (5.3)*
Francis and Kapoor (1992)	USA	*N* = 50 (baseline) *N* = 45 (sample completed) 78.9 (6.1)/47	*N* = 179 (baseline) *N* = 160 (sample completed) 77.7 (5.6)/36	O = 21.8 (*n* = 50) I = 6.1 (*n* = 14) *p* = 15.7 (*n* = 36)	DSM-III-R/ investigator	Severity of illness: Mild (24 vs. 60) Moderate (67 vs. 37) Severe (9 vs. 3)	*N* = 4 (8) *N* = 22 (44)	*N* = 2 (1.1) *N* = 39 (21.7)	In-hospital 2 years	NA

(Continues)

TABLE 2 | (Continued)

Authors (year)	Country	Delirium / No delirium: Age mean (SD or range)/% male	Overall, the incidence and prevalence of delirium	Diagnostic tool/ professional	Morbidity index: Mean (SD or range)/*n* (%) (DG vs. NDG)	Delirium / No delirium: Mortality % (*n*) / Survival (days)	Time point: Mortality	Length of stay, days (DG vs. NDG): Mean (SD or range) / Subtypes
Garcia-Pérez et al. (2023)	Spain	*N* = 66 86.0 (83.0–90.0)[a]/66.6 *N* = 212 NA/33.3	O = 23.7 (*n* = 66)	3D+/NA	NA	*N* = 33 (50) *N* = 41 (62.1) *N* = 43 (65.2) *N* = 21 (9.9) *N* = 45 (21.2) *N* = 64 (30.2)	1 month 6 months 12 months	NA
González et al. (2005)	Spain	*N* = 65 78.47 (6.68)[c]/41.5 *N* = 106 76.36 (7.40)[d]/41.5	O = 38 (*n* = 65)	DSM-IV and CAM/ Psychiatrist	NA	*N* = 20 (34.5)[d] Survival 31.05 (23.16) *N* = 10 (11)[e] Survival 21.8 (11)	3 months	22.62 (21.37) vs. 18.67 (19.96)
González et al. (2009)	Chile	*N* = 192 81.5 (7.2)/38.6 *N* = 350 75.8 (7.0)/38	O = 35.4 (*n* = 192)	CAM/ geriatrician	CCI 1.8 (1.6) vs. 1.6 (1.6)	*N* = 16 (8.5) *N* = 33 (17.5) *N* = 49 (25.9) *N* = 6 (1.7) *N* = 14 (4.0) *N* = 20 (5.8)	In-hospital Post-discharge 3 months	NA
Gual, Inzitari, et al. (2018) and Gual, Morandi, et al. (2018)	Spain	*N* = 352 87.4 (86)/41.2 *N* = 557 84.8 (6.9–9/39.1)	O = 38.7 (*N* = 352)	CAM/NA	CCI 2.79 (1.6) vs. 2.76 (1.8)	*N* = 38 (10.8) *N* = 22 (3.9)	1 month	9 (4.1) vs. 8.7 (3.9)
Holden et al. (2008)	New Zealand	*N* = 56 80.9 (NA)/42.6 *N* = 136 75.8 (NA)/39.8	O = 29.2 (*n* = 56) I = 23.4 (*n* = 45) *p* = 5.7 (*n* = 11)	CAM and MMSE/Team[f]	NA	*N* = 4 (7) *N* = 4 (3.7)	In-hospital	NA
Hsieh et al. (2015)	USA	*N* = 38 83 (8)/47 *N* = 222 76 (8)/39	I = 14.6 (*n* = 38)	CAM-ICU/ Research Assistant	CCI 3 (1–5) vs. 2 (1–4)	*N* = 3 (8) *N* = 2 (1)	In-hospital	6 (4–10) vs. 5 (3–7)
Leslie et al. (2005)	USA	*N* = 115 80 (6.5)/39.7[a] *N* = 804	I = 12.5 (*n* = 115)	CAM/NA	NA	*N* = 48 (41.7) Survival 274 *N* = 174 (21.6) Survival 321	12 months	NA
Lim et al. (2023)	Singapore	*N* = 353 84.1 (6.0)/42.5 *N* = 549 86.1 (6.3)/41.5	O = 39.1 (*n* = 353)	ICD-10/ Physician	CCI[c] 6 (3) vs. 6 (3)	*N* = 27 (7.6) *N* = 74 (21) *N* = 36 (6.6) *N* = 60 (10.9)	In-hospital 1 month	8.7 (7.8) vs. 5.4 (4.6)*
McAvay et al. (2006)	USA	*N* = 55 79.8 (6.3)/39.7[a] *N* = 378 81.8 (8.1)/39.7	O = 12.7 (*n* = 55)	CAM/nurse	CCI 90 (20.8) > 1[a] 293 (67.7) ≥ 2[a]	*N* = 17 (30.1) *N* = 75 (19.8)	12 months	NA

(Continues)

TABLE 2 | (Continued)

Authors (year)	Country	Delirium / Age mean (SD or range)/% male	No delirium / Age mean (SD or range)/% male	Overall, the incidence and prevalence of delirium	Diagnostic tool/ professional	Morbidity index / Mean (SD or range)/*n* (%) (DG vs. NDG)	Delirium / Survival (days)	No delirium / Survival (days)	Time point / Mortality	Length of stay, days (DG vs. NDG) / Mean (SD or range) / Subtypes
							Mortality % (*n*)			
McCusker et al. (2002)	Canada	*N* = 243 65–74: 29 (11.9) 75–84: 99 (40.7) ≥85: 115 (47.3)/39.5	*N* = 118 65–74: 11 (9.3) 75–84: 53 (44.9) ≥85: 54 (45.8)/27.1	O = 67.3 (*n* = 243)	CAM/nurse	CCI 2.7 (2.0) vs. 2.1 (1.8)*	*N* = 96 (41.6) of 231	*N* = 16 (14.1) of 109	12 months	NA
Muresan et al. (2016)	Ireland	*N* = 46 81.13 (6.45)[a]	*N* = 154 NA	O 23 (*n* = 46) I = 6 (*n* = 12) *p* = 17 (*n* = 34)	CAM/NA	NA	*N* = 21 (45.65)	*N* = 34 (22.1)	15 months	NA
O'Keeffe and Lavan (1997)	Ireland	*N* = 94 82 (4)/39	*N* = 131 82 (6)/32	O = 41.8 (*n* = 94) I = 29 (*n* = 53) *p* = 18 (*n* = 41)	DAS and DSM-III/NA	CCI 2.1 (1.8) vs. 1.8 (1.8)	*N* = 15 (16) *N* = 29 (31)	*N* = 7 (5) *N* = 20 (15)	In-hospital 6 months	Geometric mean 21 vs. 11 days*
Painkra et al. (2023)	India	*N* = 18 NA	*N* = 52 NA	O 25.7 (*n* = 18)	CAM/NA	NA	*N* = 7 (38.8) *N* = 10 (55.5)	*N* = 4 (7.7) *N* = 8 (15.4)	In-hospital 1 month	NA
Praditsuwan et al. (2013)	Thailand	*N* = 110 78.8 (6.0)/41.8	*N* = 115 77.3 (5.8)/59.1	O 48.8 (*n* = 110) I = 40.4 (*n* = 91) *p* = 8.4 (*n* = 19)	DSM-IV/ Physician	N chronic diseases 3.7 (1.7) vs. 3.2 (1.7)	*N* = 28 (25.5) *N* = 48 (43.6)	*N* = 2 (1.7) *N* = 12 (10.4)	In-hospital 1 month	10 (3–61) vs. 8 (2–38)*
Ramsay et al. (1991)	UK	*N* = 22 83 (72–99)/52[a]	*N* = 88 NA	I = 20 (*n* = 22)	DSM-III-R/ Physician	Severity of illness: Severe 12% Moderate 60% Mild 28%	*N* = 14 (64)	*N* = 12 (14)	In-hospital	18 (3) vs. 19.9 (1.7)
Rockwood (1989)	Canada	*N* = 20 76.8 (65–91)/43.8[a]	*N* = 60	O = 25 (*n* = 20) I = 8.75 (*n* = 7) *p* = 16.25 (*n* = 13)	DSM-III/ Physician	NA	*N* = 3 (15)	*N* = 1 (1.7)	In-hospital	20 vs. 14

(Continues)

TABLE 2 | (Continued)

Authors (year)	Country	Delirium / Age mean (SD or range)/% male	No delirium / Age mean (SD or range)/% male	Overall, the incidence and prevalence of delirium	Diagnostic tool/ professional	Morbidity index / Mean (SD or range)/*n* (%) (DG vs. NDG)	Delirium / Survival (days)	No delirium / Survival (days)	Time point / Mortality	Length of stay, days (DG vs. NDG) / Mean (SD or range) / Subtypes
							Mortality % (*n*)			
Tosun Tasar et al. (2018)	Turkey	*N* = 273 75.81 (6.54)/57.5	*N* = 509 73.57 (6.02)/44	O = 34.9 (*n* = 273)	DSM-IV/ physician	NA	*N* = 164 (60) *N* = 197 (72.3)	*N* = 150 (29.3) *N* = 235 (46.1)	12 months 5 years	16 vs. 15
Vázquez et al. (2010)	Argentina	*N* = 52 82.60 (7.3)/44.2	*N* = 68 80.40 (5.6)/47.1	O = 43.3 (*n* = 52) I = 4.1 (*n* = 5) *p* = 39.2 (*n* = 47)	CAM/NA	CCI 2 (3) vs. 2 (7)	*N* = 11 (21.2) *N* = 33 (63.5) Survival 569 days (33.5%)	*N* = 1 (1.5) *N* = 32 (47) Survival 644 days (49%)	In-hospital 18 months	7 (6.75) vs. 5 (3)*
Wakefield (2002)	USA	*N* = 16 73 (4.6)/100[a]	*N* = 101 NA	I = 14 (*n* = 16)	NEECHAM/ Nurse	NA	*N* = 4 (25)	*N* = 0	In-hospital	13 vs. 8; Type %: hypoactive 69; mixed 25; hyperactive 6

Abbreviations: 3D/3D+, triage tool; APS, APACHE Acute Physiology and Chronic Health Evaluation II Scale; CAM, confusion assessment method; CCI, Charlson Comorbidity Index; CIRS, Cumulative Illness Rating Scale; DAS, Delirium Assessment Scale; DG, delirium group; DSM, Diagnostic and Statistical Manual of Mental Disorders and revisions (III: 3rd; III-R: 3rd rev.; IV: 4th; V: 5th); I, incidence; ICD-10, International Classification of Disease, 10th revision; IncD, incident delirium; LOS, length of stay; MMSE, Mini Mental State Examination; NDG, no delirium group; NEECHAM scale, Neelon and Champagne Confusion scale; NuDesc, Nursing Delirium Screening Scale; O, overall incidence; P, prevalence; SD, standard deviation.

[a]Entire sample data.

[b]Survival 162 days vs. 1444 days (25% mortality 435 days, 75% mortality > 5 years)*.

[c]Adjusted age.

[d]From 58 who completed follow-up.

[e]From 91 completed follow-up.

[f]Physician, psychogeriatricians, nurses, psychologist, and occupational therapist.

*Significant at < 0.05.

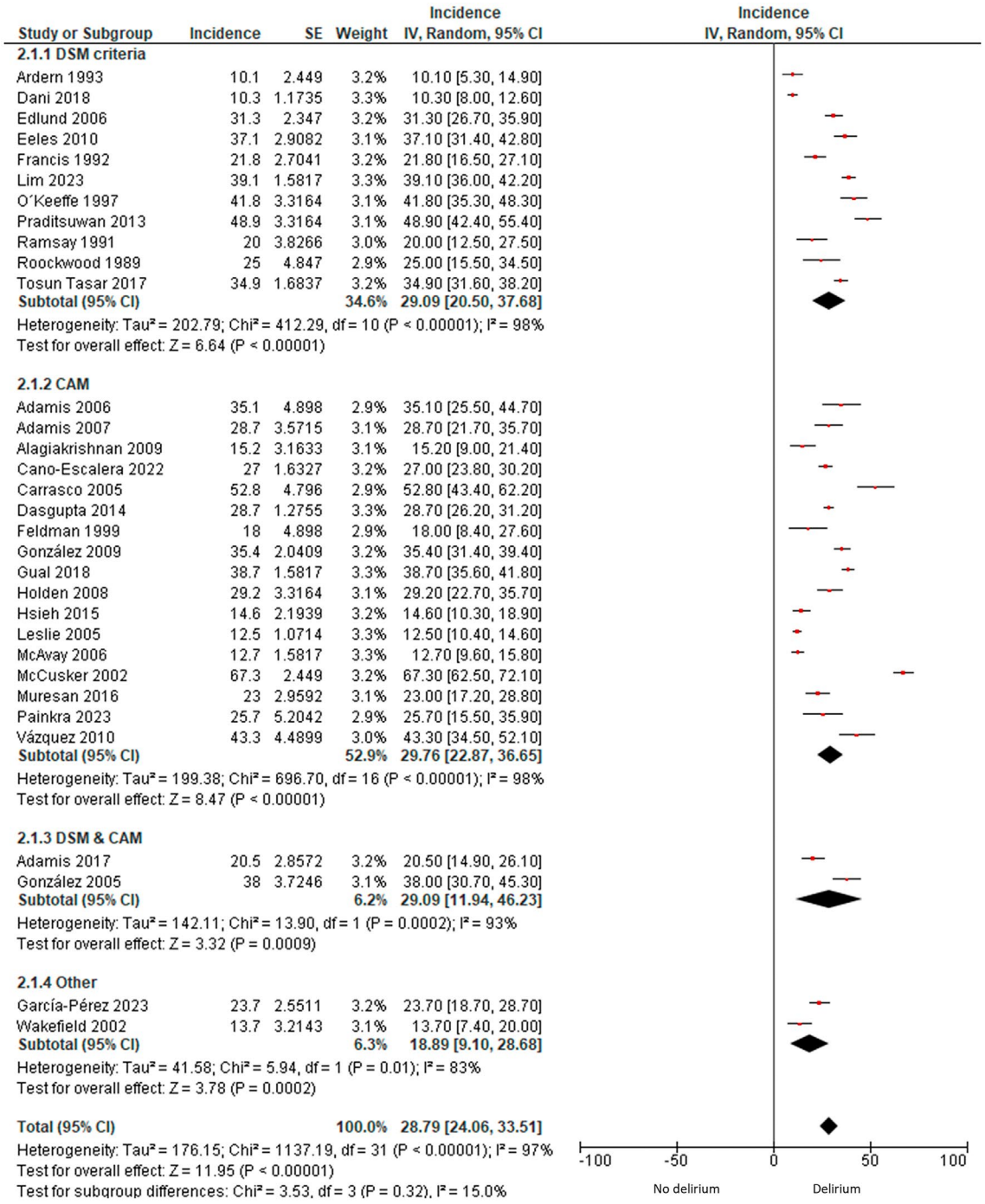
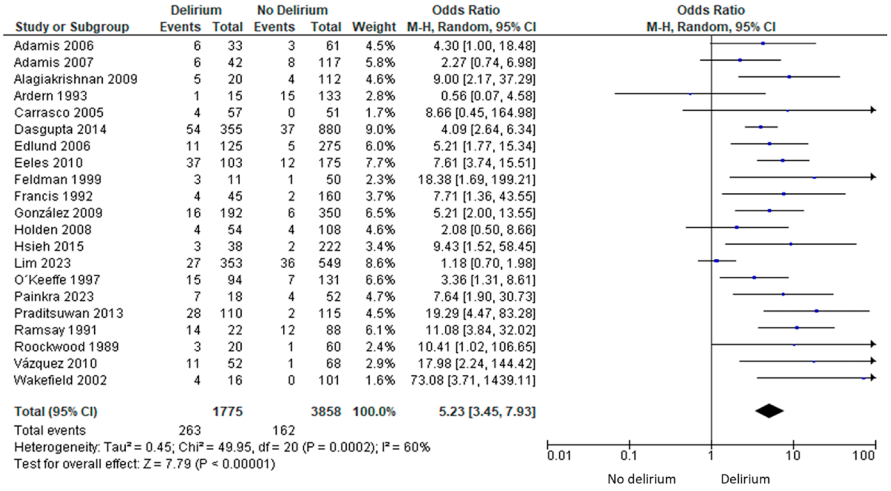


FIGURE 5 | Pooled incidence and subgroup pooled incidence of delirium in older patients, according to assessment tool. CI, confidence interval; I-V, inverse variance.

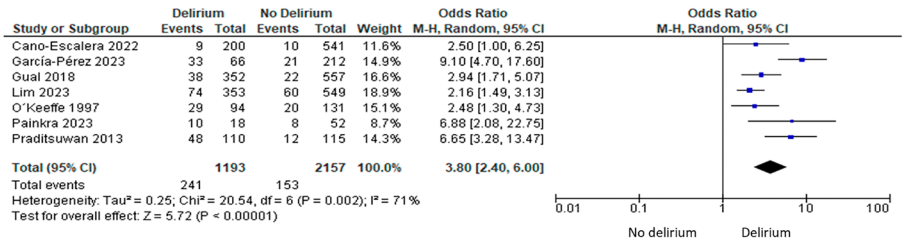
hospital medical unit, without prior knowledge of the etiology of delirium or the delirium-causing disease, and without a common baseline disease. These selection criteria favor the comparison of results.

Incidence also varied according to the assessment tool, with a higher incidence according to medical diagnostic criteria and the CAM scale (based on DSM criteria). The DSM and ICD medical criteria (European Delirium Association and American Delirium Society 2014), together with the CAM scale, are considered the gold standard for analyzing the diagnostic accuracy of most screening instruments. The CAM scale (Inouye et al. 1990) is validated for use by the whole care team (not exclusively physicians) and shows high sensitivity and specificity, making it among the most widely chosen instruments for detecting delirium worldwide. The use of different instruments could decrease sensitivity, especially in the presence of dementia (Shrestha and Fick 2023). Sensitivity could also differ in an exclusively older population, since the diagnostic accuracy of some instruments has been analyzed in the population aged 18 years or older, not only in older

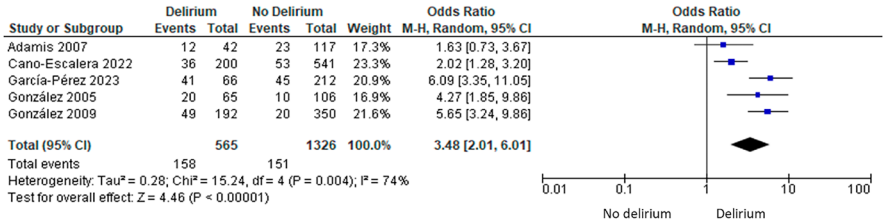
a. In-hospital mortality



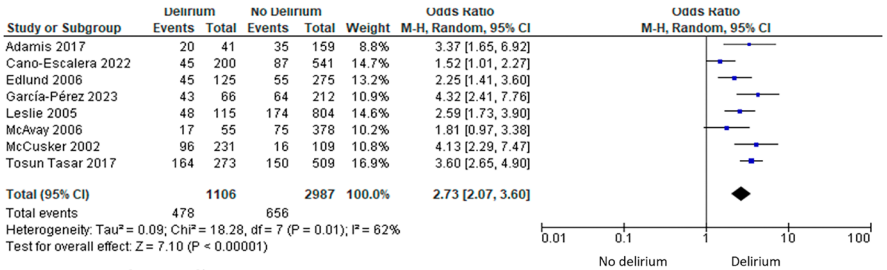
b. 1-month mortality



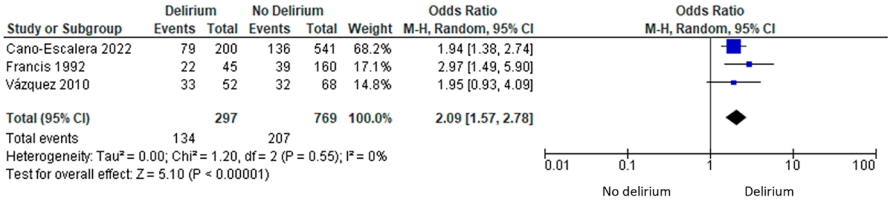
c. 3-6 months mortality



d. 12 month mortality



e. 18-24 month mortality



f. 3-5 year mortality

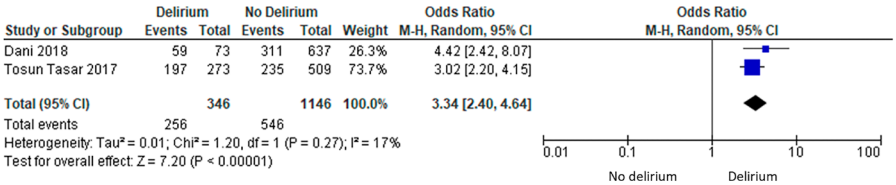


FIGURE 6 | Legend on next page.

FIGURE 6 | Mortality in older patients with delirium (a) in-hospital; (b) at 1 month; (c) at 3–6 months; (d) at 12 months; (e) at 18–24 months; (f) at 3–5 years. CI, confidence interval; M-H, Mantel–Haenszel.

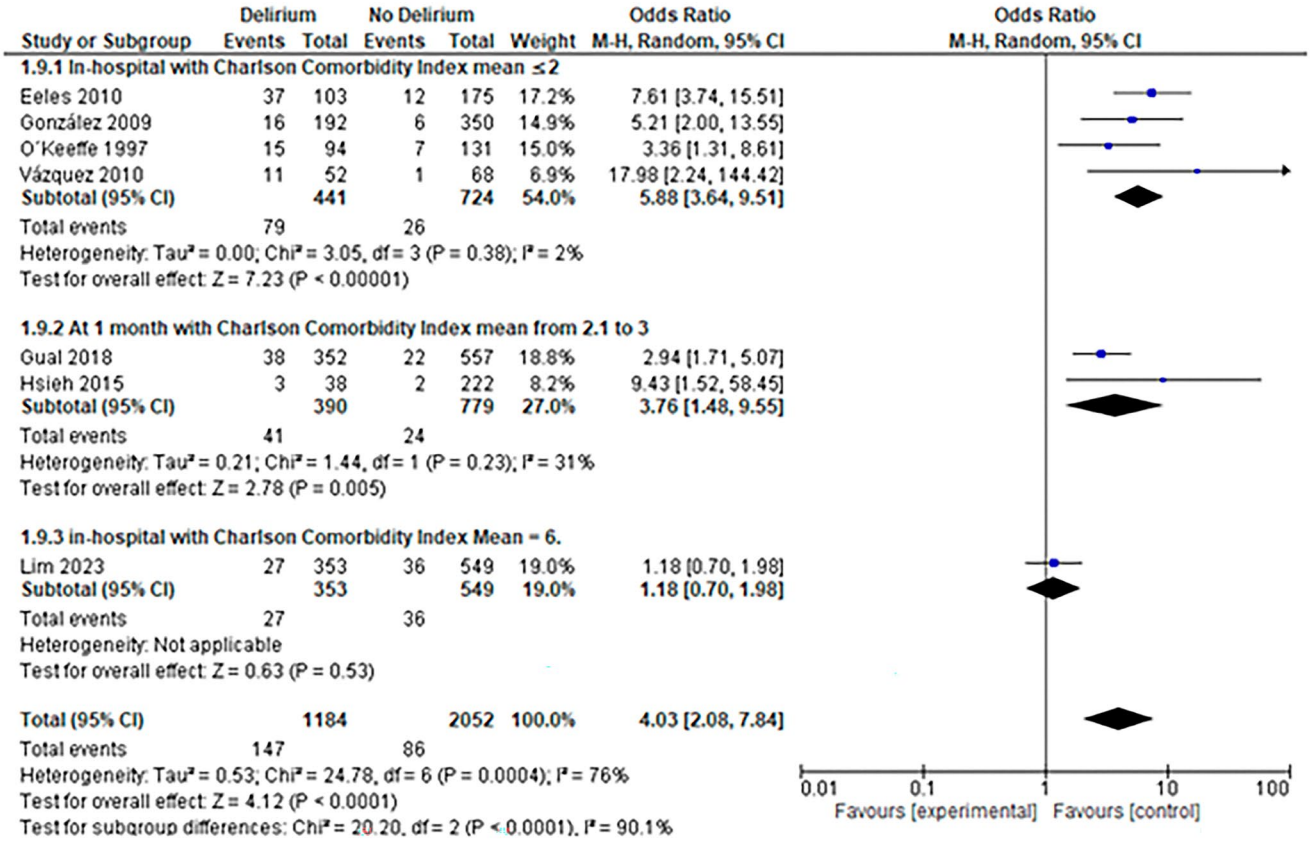


FIGURE 7 | Mortality in older patients with delirium according to morbidity: (a) in-hospital with Charlson Comorbidity Index mean ≤2; (b) at 1 month with Charlson Comorbidity Index mean from 2.1 to 3; (c) in-hospital with Charlson Comorbidity Index mean = 6. CI, confidence interval; I-V, inverse variance.

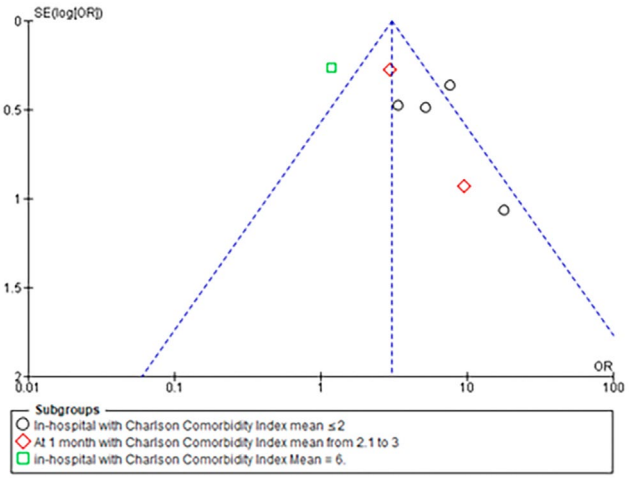


FIGURE 8 | Funnel plot for mortality according to morbidity.

people (Martínez-Arnau, Puchades-García, et al. 2023), whereas other scales have been specifically validated in the pediatric population (Delirium Measurement Info Cards 2024). Thus, it would be worthwhile to analyze the accuracy of the different assessment instruments in exclusively older populations. The detection of delirium by the family or unqualified professionals could also introduce bias (Zhou et al. 2023); however, this aspect was not an issue in our results, as it was physicians, nurses, the wider care team, or the researchers themselves who detected delirium in all our included studies.

The risk of mortality in older people admitted to the hospital is higher in the presence of delirium (Aung Thein et al. 2020). Ours is the first study to analyze the risk in this population at different time points. Previous reviews estimated an overall increased risk of 3.18-fold in older people with dementia, but these analyses did not consider temporality and included studies in different hospital areas and with different baseline conditions (Aung Thein et al. 2020). Our results corroborate the higher risk, quantified at more than five-fold during hospital admission and close to four-fold within the first month, as compared to other older people with the same medical conditions. Certainly, comorbidity directly affects the risk of mortality and other outcomes and could bias the results, but one strength of our findings is that only two (Carrasco et al. 2005; McCusker et al. 2002) out of the 32 included studies reported statistically significant differences in the comorbidity index between groups. In addition, our results

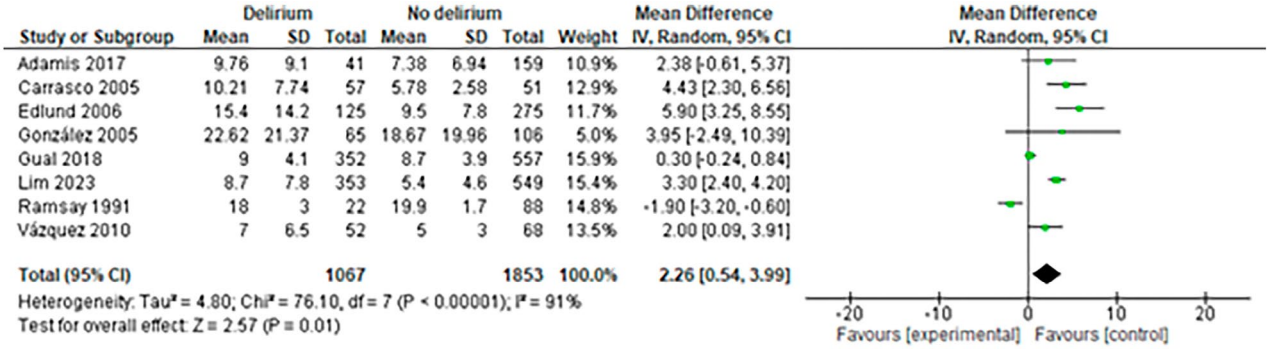


FIGURE 9 | Pooled mean difference in length of stay in older patients with versus without delirium. CI, confidence interval; I-V, inverse variance.

show moderate heterogeneity (60% to 71%) at both time points, in contrast to other meta-analyses with higher heterogeneity values, which included studies in critically ill patients, surgical patients, or patients with underlying pathology such as pneumonia or sepsis (Aung Thein et al. 2020; Goldberg et al. 2020). Taken together, these results underline the urgent need for strategies to prevent delirium in older people in the hospital setting; a 5-fold higher risk of death cannot pass unnoticed (Janssen et al. 2020; León-Salas, Trujillo-Martín, Martinez Del Castillo, et al. 2020; León-Salas, Trujillo-Martín, Martínez Del Castillo, et al. 2020; Sosnowski et al. 2023).

The estimated mortality risk decreases over time, from 3.48-fold at 6 months to 2.16-fold at 2 years, but it increases again at 5 years to 3.34-fold. These results are in line with meta-analyses performed in postoperative delirium, COVID-19, or dementia (Han et al. 2022; Munawar et al. 2023; Yan et al. 2023), which also show a higher risk during the hospital process and the following month, which is attenuated over time. In our study, the increased risk at 3–5 years after the episode could also be related to the advancing age of the participants. Survival was higher in older people without delirium, as also observed in other long-term studies (McAvay et al. 2006), as well as if delirium was reversed at hospital discharge.

LOS was also longer in patients with delirium. In the meta-analysis, the pooled mean difference in LOS between participants with and without delirium was 2.26 days. This finding is consistent with the literature (Elder et al. 2023; Yan et al. 2023), and researchers have been exploring which interventions to prevent delirium are more cost-effective, since longer hospitalizations have economic implications both in the hospital setting and for subsequent care in the community setting (León-Salas, Trujillo-Martín, Del Castillo, et al. 2020; León-Salas, Trujillo-Martín, Martínez Del Castillo, et al. 2020). Therefore, in addition to increasing the risk of mortality, delirium during admission increases LOS, adding more weight to the need to implement prevention strategies. LOS is related to increased dependency and decreased quality of life, along with both direct and indirect economic costs (Jackson et al. 2016).

4.1 | Strengths and Limitations

This is the first study to analyze the risk of mortality associated with delirium in hospitalized older persons according to the time point. Previous studies have analyzed mortality in older adults but in different hospital settings and with specific associated diseases. The analysis of mortality shows a pronounced increase in risk during hospital admission and over the first month. In addition, the pooled cumulative incidence of delirium was analyzed, along with the pooled mean LOS in these patients. The results help to quantify the impact that delirium has on the health of older people, including the wider biopsychosocial consequences in patients and their families, and on the management of the health system. In addition, the systematic quality assessment identified specific domains with the lowest methodological quality in the included studies, signaling areas to improve in future research.

On the other hand, our results are from inpatient medical wards, so they may not be generalizable to different hospital settings such as the ICU or ED, to specific diseases, or to long-term or home care. Included studies were heterogeneous, and most did not report a comorbidity index, rendering it impossible to perform a sub-analysis according to this indicator. Moreover, the presence of comorbidities is frequently omitted in medical records, and often the only information available is the reason for admission (e.g., cancer, heart disease, a fall, a hip fracture, etc.). Mortality outcomes at 1 year or longer should be interpreted in light of these considerations given the many life-limiting conditions in older people.

Additionally, because few included studies examined delirium subtype, we were unable to analyze data according to this feature. Furthermore, our results are limited to studies published in English or Spanish and indexed in the included databases, so there may be relevant studies that were not included in the meta-analysis.

4.2 | Implications

The risk of mortality associated with delirium should be analyzed in more depth. Knowing the actual risk attributable to delirium and in the presence of comorbidity would help in both understanding the syndrome and in analyzing outcomes. To better understand the impact on mortality and LOS following delirium in hospitalized older people, future research should (1) assess chronicity with a validated index and analyze the results according to comorbidity or in the presence of conditions such as frailty, pneumonia, cancer, or dementia; (2) analyze patients

in different settings separately, distinguishing between delirium in medical wards, critical areas such as the ICU or ED, and in post-surgical settings; (3) describe the time point of mortality in order to understand longitudinal risks; and (4) report mean LOS with its standard deviation to make it possible to perform meta-analyses.

5 | Conclusions

Older people admitted to medical hospital wards are vulnerable to the onset of delirium. This meta-analysis assessed the incidence of delirium and the risk of mortality in this population. Our results show an incidence of 28.79% and a mortality risk associated with delirium during hospital admission and over the following months. Further research following the same criteria is needed to analyze and compare results and to implement strategies to reduce the risk of delirium onset in older adults and, by extension, mortality.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data will be made available on request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.