CRITICAL CARE TRANSITION PROGRAMS ON READMISSION OR DEATH: A SYSTEMATIC REVIEW AND META-ANALYSIS

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1 | INTRODUCTION

Leaving the intensive care unit (ICU) may not be the end of critical illness for all patients. Despite recovery and no longer need of life-sustaining therapies, deterioration may occur after ICU discharge leading to unplanned readmission or even death. Readmission to the ICU is associated with unfavorable results, such as longer hospital stay, higher mortality,1 and increased healthcare costs. In Sweden, unplanned readmission within 72 hours after ICU discharge is considered an adverse event.2 On the contrary discharge at the earliest appropriate time reduces unnecessary use of expensive health care and improves availability of beds for other critically ill requiring ICU admission.3 The decision when to discharge is a demanding challenge for intensivists, influenced by individual and teamwork factors.
in addition to organizational issues. Different interventions, for example, ICU liaison nurse (ICU LN), handover forms, outreach services, has been developed in order to improve the clinical handover between ICU and general ward at discharge.

At the moment, the benefits of use of ICU transition programs are not clear. Two previous systematic reviews have not been able to find a reduced mortality using ICU transition programs. Niven and colleagues suggested in their meta-analysis a reduced risk of ICU readmission with transition programs including an outreach team or ICU LN. Van Sluisveld and colleagues found that interventions including ICU LN and handover forms resulted in improved continuity of care and in reduced adverse events but no evidence of a reduction in ICU readmission.

Therefore, we aimed to systematically review randomized and non-randomized studies with historical control groups to examine whether critical care transition programs reduce ICU readmission or in-hospital mortality in adult ICU discharged patients, in comparison with usual care.

2 METHODS

2.1 Protocol and guidance

This systematic review with meta-analysis and trial sequential analysis (TSA) was conducted using established methods recommended by the Cochrane Handbook for Systematic Review of Interventions and the Grading of recommendations, assessment, development and evaluation (GRADE) working group. The protocol was registered in the International prospective register of systematic reviews (PROSPERO, no CRD42019121746) prior the review and deviations from the planned methods are presented in Table S1 Deviations. We reported the findings according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA).

2.2 Ethical issues

There is no funding for this study. This review does not require ethical approval or informed consent since there will be no direct contact with individual patients.

2.3 Eligibility criteria

Eligible studies met the criteria: Population: Adult patients (age ≥18 years) discharged alive from an ICU. Intervention: Critical care transition programs aimed to improve the clinical handover between ICU and general ward at discharge. Comparison: Adult patients discharged from the ICU outside or before a critical care transition program (usual care). Outcome: (Primary) Readmission and in-hospital mortality after ICU discharge. Secondary outcomes were length of stay (LOS) in the ICU and hospital after readmission, mortality at different time points in readmitted patients, if limitations of medical treatment were imposed after first ICU discharge, duration of mechanical ventilation, and renal replacement therapy after readmission. Study design: Randomized clinical trial, non-randomized including before-and-after, interrupted time series, and cohort study with historical control. The population was considered adult if discharged from an adult ICU or as indicated by the mean or median age. Publications were restricted to the English language but not to the follow-up length, publication status, or publication year.

2.4 Search strategy and data sources

The search strategy was developed by investigator (J.Ö.), who then presented and discussed with the other authors (T.M., J.G.), and made modifications through a consultation process. PubMed/MEDLINE, CINAHL, AMED, PsycINFO, and the Cochrane Central Register for Controlled Trials (CENTRAL) were searched from inception until 18 January 2019 with update 7 February 2020. Database searches were supplemented by screening the reference lists of relevant trials and reviews. Results were restricted to the English language. Details of the search strategy are presented in Table S2 Search.

2.5 Data extraction and bias assessment

Two independent investigators (J.Ö. and J.G.) screened the titles and abstracts of reports and reviewed each potentially eligible study in full text. Eligible studies that met any of the following exclusion criteria were not included in the review: no control population, ICU readmission not reported, post-ICU mortality not reported. Data were extracted in duplicate using a standardized form and created tables for the characteristics and outcomes. If studies did not report important outcomes of interest for inclusion or present information required to calculate the statistics in extractable format, authors were e-mailed (two attempts) for additional data. All pre-planned ICU readmission timeframes could not be assessed due to lack of data. When more than one follow-up time was provided for the outcome data, the longest follow-up during the same hospitalization was used.
The same investigators independently used the ROBINS-I for methodological assessment of observational studies in domains: bias due to; confounding, in selection of participants into the study, in classification of interventions, due to deviations from intended intervention, due to missing data, in measurement of outcomes, and in selection of the reported result. The authors were not contacted to clarify unclear ratings. Disagreements between the two investigators were resolved by discussion with the third author (T.M.). Assessment was visualized using robvis.11

2.6 | Data synthesis

All pooling analyses were done using random-effect model because of clinical and methodological heterogeneity. For dichotomous outcomes, we calculated and reported relative effects as risk ratios (RR, the ratio of the risk of an unfavorable outcome among ICU discharged patients in a transition program vs usual care) with 95% CI. A value of \( P < .05 \) was considered statistically significant. We assessed heterogeneity using the chi-squared test (threshold \( P = .10 \)) and quantified using the I² statistic, which describes the proportion of total variance across trials that is attributed to heterogeneity. According to the methods described in the Cochrane Handbook for Systematic Reviews of Interventions,7 we interpreted the amount of heterogeneity from I² values as low 0%-40%, moderate 30%-60%, and substantial 50%-90%. We planned to analyze the following modifiers of effect: (a) Type of intervention, (b) case mix, and (c) if goals-of-care were determined before ICU discharge. We were able to conduct subgroup analysis (threshold \( P = .10 \)) concerning type of intervention, but not the other domains due to insufficient data. For detection of publication bias, we used visual evaluation of funnel plot symmetry. We planned sensitivity analyses by performing meta-analyses on primary outcome based on study design and risk of bias.

We applied TSA (\( \alpha = 0.05 \) and \( \beta = 0.20 \)) since it reduces the risk of type-I error in a cumulative meta-analysis and may provide information on how many more patients need to be included.12 Information size was calculated as diversity-adjusted information size, suggested by the relative risk reduction (RRR) of the intervention in the included studies. We calculated the event proportion in the control group as an unweighted mean of the proportion with the outcome in the control groups of all the included studies. Sensitivity analyses were performed assuming RRRs of 25% and 10%.

We used RevMan software (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and TSA Viewer software, version 0.9 beta (Copenhagen Trial Unit, Copenhagen)13 to conduct conventional meta-analyses and trial sequential analysis, respectively.

2.7 | Grading of recommendations, assessment, development, and evaluation (GRADE)

We summarized the quality of evidence for primary outcomes applying GRADE-levels (high, moderate, low, and very low) by evaluating

| TABLE 1 Summary of exposure by primary outcome |
|-----------------------------------------------|
| Study                                      |
| Readmitted/discharged (n) | Readmitted/discharged | Dead/discharged (n) | Dead/discharged (n) | Readmission definition |
| Intervention | Control | Intervention | Control |
| Williams (2010)25 | 80/1435 | 85/1566 | 77/1435 | 86/1566 | Same hospitalization. |
| Al-Qahtani (2013)24 | 338/2363 | 276/1485 | 312/2363 | 232/1485 | Same hospitalization. |
| Al-Rajhi (2016)16 | N/A | N/A | N/A | N/A |
| Ball (2003)22 | 16/269 | 25/201 | 34/269 | 39/201 | Same hospitalization. |
| So (2018)71 | 18/185 | 44/184 | 33/185 | 49/184 | Same hospitalization. |
| Baxter (2008)15 | N/A | N/A | N/A | N/A |
| Elliott (2008)26 | 55/807 | 49/709 | 71/807 | 62/709 | Same hospitalization. |
| Chaboyer (2006)27 | 2/85 | 4/101 | 2/85 | 8/101 | Same hospitalization. |
| Chaboyer (2012)23 | 16/786 | 20/1001 | 31/786 | 40/1001 | Within 72 h. |
| Harrison (2010)28 | 21/2625 | 48/2526 | 247/2573 | 336/2526 | Within 48 h. |
| Garcea (2004)29 | 79/833 | 49/547 | 40/833 | 94/547 | Same hospitalization. |
| Pirret (2008)17 | N/A | N/A | N/A | N/A |
| Stelfox (2016)18 | N/A | N/A | N/A | N/A |
| Choi (2016)20 | 20/510 | 13/516 | 68/510 | 59/516 | Same hospitalization. |
| Bergamasco (2017)19 | 91/1361 | 35/380 | 237/1361 | 32/380 | Same hospitalization |

¹Calculated from percentage.
²Number of discharges determined through subtracting number of ICU deaths from total number of ICU admissions.
³Restricted to patients discharged to the ward and receiving a scheduled CCOS (critical care outreach service) visit within 48 h. Historical control group.
possible risk of bias, inconsistency, indirectness, imprecision, and publication bias using GRADEpro GDT software.\textsuperscript{14}

3 | RESULTS

The final yield was 15 studies investigating interventions facilitating the transfer from the ICU to the general ward, including 14 before-after and one matched cohort study. Studies were excluded from the quantitative analysis as they did not report the number of patients discharged to the ward following their initial ICU admission and/or events (Table 1, summary of exposure by primary outcome), and the corresponding authors were either not responding or unable to provide the requisite data.\textsuperscript{15-18} Two corresponding authors supplied originally not reported data on in-hospital mortality.\textsuperscript{19,20} The PRISMA flow chart demonstrates the screening process for the eligible studies and the reasons for exclusion (Figure 1, PRISMA flow chart).

All studies investigated interventions with an aim or subsidiary aim of facilitating the transfer from intensive care to the general
ward (Table 2, characteristics of the included studies). Studies evaluated, as defined by authors, the critical care outreach service/team (CCOS, n = 6), ICU LN (n = 2), rapid response team (RRT, n = 2), medical emergency team (MET, n = 2), a redesigned discharge process (n = 1), a multidisciplinary ICU team (n = 1), and an ICU consult service (n = 1). The studies included adults of both sexes with the female proportion ranging from in mean 34% to 51% and the age ranging from in mean 50 to 70 years. The ICUs were situated in various types of hospitals (tertiary, metropolitan, teaching, university/academic) nearly all with a medical-surgical case mix. The ICU length of stay (LOS) before discharged varied widely from 1 (median) to 12 (mean) days and the Acute Physiology and Chronic

| Study                  | D1 | D2 | D3 | D4 | D5 | D6 | D7 | Overall |
|-----------------------|----|----|----|----|----|----|----|---------|
| Al–Qahtani 2013       | X  | X  |    |    |    |    |    | X       |
| Al–Rajhi 2016         | X  | X  |    |    |    |    |    | X       |
| Ball 2003             |    |    | +  |    |    |    |    | X       |
| Baxter 2008           | X  | X  |    |    |    |    |    | X       |
| Chaboyer 2006         | X  |    | +  |    |    |    |    | X       |
| Chaboyer 2012         | X  |    | +  |    |    |    |    | X       |
| Elliott 2008          | X  |    | +  |    |    |    |    | X       |
| Garcea 2004           | X  | X  |    |    |    |    |    | X       |
| So 2018               | X  |    | +  |    |    |    |    | X       |
| Harrison 2010         | X  | X  |    |    |    |    |    | X       |
| Pirret 2008           | X  | X  | X  |    |    |    |    | !       |
| Stelfox 2016          |    |    | +  |    |    |    |    | ?       |
| Williams 2010         | X  | +  | +  |    |    |    |    | X       |
| Choi 2016             | X  |    | +  |    |    |    |    | X       |
| Bergamasco 2017       |    | +  | +  |    |    |    |    | X       |

**Risk of bias domains**

**Domains:**
- D1: Bias due to confounding.
- D2: Bias due to selection of participants.
- D3: Bias in classification of interventions.
- D4: Bias due to deviations from intended interventions.
- D5: Bias due to missing data.
- D6: Bias in measurement of outcomes.
- D7: Bias in selection of the reported result.

**Judgement**
- Critical
- Serious
- Moderate
- Low
- No information

![FIGURE 2](Risk of bias domains) [Colour figure can be viewed at wileyonlinelibrary.com]
### Table 2: Characteristics of the included studies

| Study                           | Years     | Methods                                              | Participants recruited and analyzed | Intervention Duration follow-up | Primary outcomes Secondary/tertiary outcomes                                                                 | Country Setting                                                                 |
|---------------------------------|-----------|------------------------------------------------------|-------------------------------------|---------------------------------|---------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Williams (2010)                  | 2007-2008 | Before-and-after prospective + retrospective (control) | Total 3001 (IG 1435; CG 1566) IG 54, CG 55 IG 35, CG 35 | Critical care nursing outreach service Until clinically stable | Hospital LOS from ICU admission to hospital discharge. Number of ICU readmissions during the same hospital admission, <48 h (early), >48 h (late). Survival to hospital discharge. Day of week/time of day discharged from the ICU, activities of outreaching nurse, delay to discharge from the ICU. | Australia Adult medical-surgical ICU, multi-center, tertiary-referral hospitals. |
| Al-Qahtani (2013)                | 2006-2010 | Before-and-after prospective + retrospective (control) | Total 3848 (IG 2363; CG 1485) IG 59, CG 59 IG 46, CG 47 | Rapid response team (RRT), intensivist-led Mandatory 48 h | Cardiopulmonary arrests (CA) and mortality. RRT referrals to ICU service from wards. Non-ICU CA, initiation of DNR status, transfers to ICU including transfers following CA, ward mortality, total hospital mortality. Admission characteristics including demographics, APACHE II score, main reason for ICU admission, predicted mortality by MPM II. DNR orders after ICU admission, CA in the ICU, need for tracheostomy, mechanical ventilation duration, ICU and hospital length of stay (LOS), ICU and hospital mortality. ICU readmission rates and post-ICU mortality and LOS. | Saudi-Arabia Adult medical-surgical ICU. Tertiary care, academic center.        |
| Al-Rajhi (2016)                  | 2009-2011 | Before-and-after concurrent control retrospective    | Total 398 (IG 194; CG 204) IG 69, CG 71 IG 45, CG 43 | ICU consult service N/A         | Hospital-wide CA rates, hospital mortality rates, 30-day mortality and ICU LOS of patients admitted to the ICU. ICU readmission 72 h and 14 d ICU readmission 30 d. Non-ICU code blue rates, demographic data including APACHE II. DNR orders. Time to ICU consult. | Canada Adult medical-surgical ICU. Tertiary care university center.            |
| Ball (2003)                      | 2000-2002 | Before-and-after retrospective                        | Total 470 (IG 269; CG 201) IG 50, CG 52 IG 41, CG 42 | Critical care outreach team, nurse-led Until clinically stable | Survival to discharge from hospital and ICU readmission. APACHE II, male, aged over 65, probability of in-hospital mortality, LOS ICU, medical or surgical diagnosis. | United Kingdom Adult medical-surgical ICU. Tertiary care center, teaching.       |
| So (2018)                        | 2014-2016 | Before-and-after prospective + retrospective (control) | Total 369 (IG 185, CG 184) IG 64, CG 69 IG 36, CG 32 | Critical care outreach team, nurse-led At least 3 d, until clinically stable | ICU readmission within 72 h. All ICU readmissions, hospital mortality, and 90-day mortality rate. | China Adult, medical-surgical ICU. Acute care tertiary hospital.                |

(Continues)
| Study          | Years     | Methods                                      | Participants recruited and analyzed | Intervention Duration follow-up | Primary outcomes Secondary/tertiary outcomes | Country          | Setting                                      |
|---------------|-----------|----------------------------------------------|-------------------------------------|---------------------------------|---------------------------------------------|------------------|---------------------------------------------|
| Baxter        | 2003-2006 | Before-and-after prospective + retrospective (control) | N/A                                | Medical emergency team (MET) 48 h after ICU discharge | Cardiac arrests (“Code Blue” calls), in-patient ICU admissions and readmissions, hospital mortality. Major post-operative complications, mortality, unplanned post-operative ICU admissions, post-cardiac arrest ICU admissions and outcomes, hospital mortality of ICU survivors. | Canada           | Two centers. Adult medical-surgical ICU. Tertiary care. |
| Eliott        | 2003-2006 | Before-and-after prospective                | Total 1516 (IG 807; CG 709) IG 65, CG 67 N/A | ICU LN Until clinically stable | ICU and hospital LOS, ICU and hospital mortality, ICU step-down days. ICU patient throughput, ICU readmissions and outcomes for the readmitted. | Australia        | Adult medical-surgical ICU, metropolitan university teaching hospital. |
| Chaboyer      | 2002      | Before-and-after prospective                | 186 (IG 85; CG 101) IG 56, CG 57 IG 41, CG 42 | ICU LN N/A | ICU discharge delay. Clinical characteristics including ICU and hospital LOS, readmission and in-hospital mortality. | Australia        | Adult medical-surgical ICU, tertiary referral hospital. |
| Chaboyer      | 2007-2009 | Before-and-after time-series design         | Total 1787 (IG 786; CG 1001) IG 56, CG 56 IG 36, CG 40 | Redesigned discharge process including handover sheet N/A | ICU discharge delay. Readmission, mortality after ICU discharge. | Australia        | Adult medical-surgical ICU, tertiary referral hospital. |
| Harrison      | 2005-2006 | Matched-cohort Prospective + retrospective (historical cohort control) | Readmission, total 5151 (IG 2625; CG 2526) In-hospital mortality, total 5099 (2573; CG 2526) IG 61, CG 60 IG 44, CG 44a | Critical care outreach service (CCOS) N/A | In-hospital mortality. ICU readmission and hospital LOS. | United Kingdom  | Adult, general critical care. 52 acute hospitals. |
| Garcea       | 1999-2003 | Before-and-after retrospective              | Total 1513 (IG 833; CG 547) IG 63, CG 65 IG 52, CG 41 | Critical care outreach service (CCOS) covering surgical wards Until clinically stable | ICU readmission rate. Length of ward stay prior to readmission. Reasons for readmission. APACHE II score on readmission, time of transfer, duration of stay, ventilated days, renal support days, inotrope days. ICU and in-hospital mortality. | United Kingdom  | Adult ICU. Referral/teaching hospital. |
| Pirret        | 2005-2007 | Before-and-after prospective                | N/A                                | Critical care outreach service, nurse-led Until clinically stable | ICU readmission rate. APACHE II scores and LOS of ICU readmissions, total ICU readmission mortality, ward MET and cardiac arrest calls. | New Zealand      | General ICU. Metropolitan tertiary hospital. |
Health Evaluation (APACHE) II score ranged between 12–23 (median) and 29–24 (Pre-RRT, mean). When comparing the cohorts within studies, three studies demonstrated a significant better health condition in the intervention group before ICU discharge.19,21,24 In two of them the intervention group were older,19,20 and in one male to a greater extent.19 Patients discharged outside the hospital or dead in the ICU could not be subjected to a follow-up intervention. The studies were judged to have overall serious (n = 14) or critical (n = 1) risk of bias (Figure 2, risk of bias). Specific items within each domain are shown in Table S3 ROBINS-I.

3.1 | Primary outcomes

3.1.1 | Readmission

Eleven studies that involved 20,475 ICU discharged patients were included in the present meta-analysis.19–29 An intervention facilitating the transfer from the ICU to the general ward seems to reduce the risk of readmission to the ICU (Figure 3, forest plot readmission) (RR 0.78; 95% CI: 0.64–0.96; N = 20,475). There was a significant and substantial heterogeneity among studies. TSA indicated lack of firm evidence for a beneficial effect of a critical care transition program for readmission (TSA-adjusted 95% CI: 0.59–1.03), since the traditional boundary (P = .05) but not the trial sequential monitoring boundary were crossed, and the required information size not reached (Figure 4, TSA readmission). Sensitivity analyses of RRRs (25% and 10%) were consistent with primary analysis (Figure S1). Our application of GRADE methodology led us to conclude that the accumulated evidence for this outcome is of very low quality (downgraded four levels) due to bias in the included studies, inconsistency in effect, difference in interventions, wide confidence intervals, and a required information size not met (TSA) (Table 3, summary of findings and GRADE).

3.1.2 | In-hospital mortality

The pooled results showed no difference in in-hospital mortality among discharged patients in a critical care transition program as compared to usual care (Figure 5, forest plot mortality) (RR 0.82; 95% CI: 0.64–1.06; N = 20,423). There was a significant and substantial heterogeneity among studies. In the TSA, neither the traditional boundary (P = .05) nor the trial sequential monitoring boundary or futility boundary were crossed suggesting a lack of firm evidence and more studies needed (TSA-adjusted 95% CI: 0.49–1.37) (Figure 6, TSA mortality). Sensitivity analyses of RRRs (25% and 10%) were consistent with primary analysis (Figure S2). The accumulated evidence for this outcome is of very low quality (downgraded four levels) due to bias in the included studies, inconsistency in effect, difference in interventions, wide confidence intervals, and a required information size not met (TSA) (Table 3, summary of findings and GRADE).
3.1.3 | Subgroup analysis

In the subgroup analysis according to type of intervention, CCOS and RRT were associated with a reduced risk or readmission and in-hospital mortality (only CCOS) after ICU discharge (Figures 3 and 5). The test for subgroup differences according to type of intervention indicated that there was no statistically significant subgroup effect (readmission: \( P = .16 \), mortality: \( P = .12 \)).

3.2 | Secondary outcomes, sensitivity analysis, and publication bias

The reporting of secondary outcomes was sparse and varied, preventing conduct of a meta-analysis. However, there were no significant differences between groups. Three studies reported on LOS ICU after readmission and none of these results achieved statistical significance. The nurse-led CCOR reduced LOS ICU for readmitted patients with, in mean 5–3 days and in median 4–3 days, respectively. Conversely, Garcea et al reported increased LOS ICU, from in mean 6.2–8.3 days following outreach. Three studies reported LOS in hospital and none of these results achieved statistical significance. One study investigating the RRT reported no difference between groups with a new DNR order after ICU discharge. Duration of mechanical ventilation and renal replacement therapy after readmission were reported in one study. After the introduction of an outreach team patients readmitted to the ICU were ventilated non-significantly longer (5.5 days vs 3.8 days) and there was no difference in renal support days.
all studies were non-randomized and judged at least serious risk of bias, no sensitivity analysis was conducted. The funnel plots used to evaluate the publication bias did not demonstrate any obvious asymmetry (Figures S3 and S4).

4 | DISCUSSION

This systematic review of observational studies, examining the effects of an intervention facilitating the transfer from the ICU to the general ward, suggested a modest and very uncertain reduced risk of readmission and no impact on in-hospital mortality after ICU discharge. Furthermore, the TSA on the risk of readmission indicated that our finding could be false positive and a need of more studies. Using the GRADE methodology we are led to conclude that the quality of evidence is very low.

The modest reduced risk of ICU readmission in our review is consistent with that of Niven et al\(^6\) (RR 0.87, 95% CI: 0.76-0.99), in which 4 of our 11 included studies in the quantitative analysis were considered. Additionally, they reported no significant effect on post-ICU hospital mortality (RR 0.84, \(P = .05\)) but not the trial sequential monitoring boundary indicating lack of firm evidence for a beneficial effect of 22% relative risk reduction. There is insufficient information to reject or detect an intervention effect of 22% RRR of readmission as the required information size is not yet reached.
Moreover, one of the included studies in our review that could not be quantitatively analyzed—the study by Stelfox and colleagues, included over 30 000 patients (which is approximately 50% more the patients in our analysis), and no association to ICU readmission or mortality was found.\textsuperscript{18}

Possible explanations for findings in our review must be considered. First of all, the interventions may have been aimed at the wrong population—they were implemented as a transition program for the general ICU population, while they may be effective only for discharged patients with factors that reflect a greater severity and complexity of illness and are associated with increased risk of readmission or death.\textsuperscript{30} And secondly, even if the interventions were aimed at patients with increased risk, the studies retrieved and analyzed data from the overall ICU discharged population which may have obscured an actual effect in a “high-risk population”. Third, the outcome measured might be wrong. Although ICU readmission and mortality are common, practical and objective metrics they may not fully reflect an effectiveness of a critical care transition program in terms of facilitating the discharge. In this meta-analysis the ICU LN and a redesigned discharge process did not seem to affect the risk of readmission or death. They were, however, associated with more efficient discharges\textsuperscript{23,27} and improved survival for patients requiring readmission.\textsuperscript{26} And indeed, the ICU readmission rate as a quality marker of a follow-up intervention may be flawed as patients deteriorating in the wards and requiring readmission are expected to be noticed.

There was no statistically significant subgroup effect analyzing type of intervention as defined in the studies. While risk reduction in both readmission and death was mainly attributed to the studies investigating CCOS, it would be unwise to draw conclusions as an unexplained high heterogeneity within the subgroup remained and these interventions vary in tasks performed, staffing, and coverage.\textsuperscript{28} Within the RRT subgroup the risk of readmission was reduced, but not death. In one study the in-hospital mortality actually increased.\textsuperscript{19} These numbers were not originally reported but obtained after contact with the corresponding author. The mechanism by which the mortality increased is unclear.

Although we adopted the appropriate measures, such as a protocol registration prior to statistical analyses and following...
established methods recommended by the Cochrane Handbook for Systematic Reviews, meta-analyses are only as good as the data reported in each study. Our findings are limited by the before-after design and that not all studies could be quantitatively analyzed. In four studies we could not ascertain either the number of patients discharged, readmitted, or dead necessary for a quantitative analysis. An additional potential limitation is the great clinical variability or heterogeneity found among the studies identified, complicating both the synthesis and interpretation of results. This variability affects both the transition programs being evaluated in the intervention and most likely the usual care (eg, pre-existing usual ICU discharge process) in the control populations. Finally, the exclusion of studies only reporting one of the study outcomes introduces a potential study selection bias affecting the strength of the meta-analytic estimate. Nonetheless, the funnel plot of the outcomes showed no apparent publication bias and in the absence of randomized controlled studies, they provide the best available evidence.

This review, including over 20 000 ICU discharged patients around the world in the last 20 years, challenges the effectiveness of critical care transition programs. We found no clear benefit in terms of reducing risk of readmission or death after ICU discharge. This conclusion should be interpreted with caution, since the present review was underpowered (according to TSA) and the included observational studies were considered to be of at least serious risk of bias. Either further robust methodology trials are required to develop

| Study or subgroup | Transition program | Usual care | Risk ratio  |
|-------------------|-------------------|------------|------------|
|                   | Events | Total | Events | Total | Weight | M-H, random, 95% CI | M-H, random, 95% CI |
| 1.2.1 CCOS         |        |       |        |       |         |                       |                       |
| Garcea 2004       | 40     | 833   | 94     | 547   | 9.5%    | 0.28 [0.20, 0.40]     |                       |
| Ball 2003         | 34     | 269   | 39     | 201   | 8.9%    | 0.65 [0.43, 0.99]     |                       |
| So 2018           | 33     | 185   | 49     | 184   | 9.2%    | 0.67 [0.45, 0.99]     |                       |
| Harrison 2010     | 247    | 2573  | 336    | 2526  | 11.2%   | 0.72 [0.62, 0.84]     |                       |
| Williams 2010     | 77     | 1435  | 86     | 1566  | 10.1%   | 0.98 [0.72, 1.32]     |                       |
| Subtotal (95% CI) | 5295   | 5024  | 48.8%  |       |         | 0.62 [0.43, 0.90]     |                       |
| Total events      | 431    | 604   |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |
| 1.2.2 ICU LN      |        |       |        |       |         |                       |                       |
| Chaboyer 2006     | 2      | 85    | 8      | 101   | 2.3%    | 0.30 [0.06, 1.36]     |                       |
| Elliott 2008      | 71     | 807   | 62     | 709   | 9.8%    | 1.01 [0.73, 1.39]     |                       |
| Subtotal (95% CI) | 892    | 810   | 12.1%  |       |         | 0.69 [0.23, 2.09]     |                       |
| Total events      | 73     | 70    |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |
| 1.2.3 Redesigned discharge process | | | | | | |
| Chaboyer 2012     | 31     | 786   | 40     | 1001  | 8.5%    | 0.99 [0.62, 1.56]     |                       |
| Subtotal (95% CI) | 786    | 1001  | 8.5%   |       |         | 0.99 [0.62, 1.56]     |                       |
| Total events      | 31     | 40    |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |
| 1.2.4 RRT         |        |       |        |       |         |                       |                       |
| Al-Qahtani 2013   | 312    | 2363  | 232    | 1485  | 11.2%   | 0.85 [0.72, 0.99]     |                       |
| Bergamasco 2017   | 237    | 1361  | 32     | 380   | 9.6%    | 2.07 [1.46, 2.94]     |                       |
| Subtotal (95% CI) | 3724   | 1865  | 20.8%  |       |         | 1.30 [0.54, 3.16]     |                       |
| Total events      | 549    | 264   |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |
| 1.2.5 MET         |        |       |        |       |         |                       |                       |
| Choi 2016         | 68     | 510   | 59     | 516   | 9.8%    | 1.17 [0.84, 1.62]     |                       |
| Subtotal (95% CI) | 510    | 516   | 9.8%   |       |         | 1.17 [0.84, 1.62]     |                       |
| Total events      | 68     | 59    |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |
| Total (95% CI)    | 11207  | 9216  | 100.0% |       |         | 0.82 [0.64, 1.06]     |                       |
| Total events      | 1152   | 1037  |        |       |         |                       |                       |
|                    |        |       |        |       |         |                       |                       |

**FIGURE 5** Forest plot examining the risk of in-hospital mortality after ICU among patients within a Transition Program vs usual care. Horizontal lines represent 95% confidence intervals (CI), CCOS, critical care outreach service; I², heterogeneity; ICU LN, intensive care unit liaison nurse; MET, medical emergency team; RRT, rapid response team; TP, transition program.
effective interventions, or possibly, these outcomes as a measure of effectiveness of critical care transition programs have had their day.

CONFLICT OF INTEREST
None of the authors declare any conflict of interest.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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