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Medication-related problems in critical care survivors: a systematic review

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ABSTRACT

Objectives There are numerous, often single centre discussions of assorted medication-related problems after hospital discharge in patients who survive critical illness. However, there has been little synthesis of the incidence of medication-related problems, the classes of medications most often studied, the factors that are associated with greater patient risk of such problems or interventions that can prevent them.

Methods We undertook a systematic review to understand medication management and medication problems in critical care survivors in the hospital discharge period. We searched OVID Medline, Embase, PsychINFO, CINAHL and the Cochrane database (2001–2022). Two reviewers independently screened publications to identify studies that examined medication management at hospital discharge or thereafter in critical care survivors. We included randomised and non-randomised studies. We extracted data independently and in duplicate. Data extracted included medication type, medication-related problems and frequency of medication issues, alongside demographics such as study setting. Cohort study quality was assessed using the Newcastle Ottowa Score checklist. Data were analysed across medication categories.

Results The database search initially retrieved 1180 studies; following the removal of duplicates and studies which did not fit the inclusion criteria, 47 papers were included. The quality of studies included varied. The outcomes measured and the timepoints at which data were captured also varied, which impacted the quality of data synthesis. Across the studies included, we found that as many as 80% of critically ill patients experienced medication-related problems in the posthospital discharge period. These issues included inappropriate continuation of newly prescribed drugs such as antipsychotics, gastrointestinal prophylaxis and analgesic medications, as well as inappropriate discontinuation of chronic disease medications, such as secondary prevention cardiac drugs.

Conclusions Following critical illness, a high proportion of patients experience problems with their medications. These changes were present across multiple health systems. Further research is required to understand optimal medicine management across the full recovery trajectory of critical illness.

PROSPERO registration number CRD42021255975.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

⇒ Survivors of critical illness experience multiple transitions of care following critical care discharge. As a result, there can be subsequent interruptions and disruptions with medication management.

WHAT THIS STUDY ADDS

⇒ As many as 80% of critical care survivors can experience problems with medication management during recovery. This includes unintentional discontinuation of chronic disease medications in up to a quarter of patients; conversely, many patients are continued, often inappropriately, on acutely prescribed drugs.

HOW MIGHT THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Further research is required to understand optimal medicine management across the full recovery trajectory of critical illness.

BACKGROUND

Patients admitted to critical care can often experience both rapidly changing organ dysfunctions and multiple transitions of care.[1] Both factors place patients at risk for disruptions of medications.[2 3] Medication regimens at hospital discharge can differ from preadmission medications, and when these changes are not appropriately managed across transitions of care, it can lead to subsequent patient harm.[4–6]

There are few standard guidelines as to how to prevent or detect-and-remediate afterwards, such disruptions in care. At present there are no published systematic reviews which attempt to synthesise key questions such as: how common are such medication-related problems after critical illness? Which medication classes are involved in these problems? Are some patients at greater risk? Moreover, there is no evidence summary examining what can be done to avoid patient harm from medication-related problems after a stay in the intensive care unit (ICU).

Therefore, we undertook a systematic review to understand medication management and medication problems in critical care survivors in the hospital discharge period. We hypothesised that there would be a broad spectrum of medication issues and challenges for survivors.

METHODS

Search strategy

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist was followed for reporting this systematic review.[7] The review protocol was registered with PROSPERO (CRD 42021255975).

Table 1 PICO model alongside design inclusion/exclusion criteria

Characteristics	Inclusion	Exclusion
Participants	Patients admitted to critical care	Patients without a critical care encounter
Interventions	Any as per definition	Studies that did not provide data on medicines at hospital discharge or in the posthospital discharge period
Comparisons	N/A	N/A
Outcomes	Medicine review at hospital discharge or in the posthospital discharge period	Medicine review in ICU or in hospital only
Study design	Randomised, quasi-experimental (parallel control group trials and pre/postintervention trials) observational	Case reports, reviews, editorials, quality improvement studies with interventions, theses or other commentaries

ICU, intensive care unit; N/A, not available; PICO, participant, intervention, comparison and outcomes .

PROSPERO and the Cochrane database were searched to ensure that no other systematic review was underway. One review was underway; this review aimed to examine the impact of a medication-related interventions during transitions of care between ICU settings and the general ward environment.[8] No review was examining the transition from hospital to home, or longer-term medication management in critical care survivors.

We electronically searched OVID Medline, EMBASE, PsychINFO, CINAHL and the Cochrane database. Our search took place on 20 July 2021, with an update undertaken on 31 August 2022. The search strategy, which was supported by an experienced librarian (SM), cross-referenced medicine management and critical illness with appropriate keywords and subject headings (see online supplemental file S1 for full details). The search was limited to research published between 2001 and 2022. This date restriction was applied as the importance of medicine safety and adverse event reporting was highlighted via the Institute of Medicine's seminal 'To Err is Human' white paper in 2000, with subsequent widespread implementation of changes to medicines reconciliation internationally.[9]

Study selection

The research question was generated via the participants, interventions, comparisons and outcomes (PICO) model (table 1).[10]

We included articles which met the following criteria: involving adults (admitted to an adult critical care environment) and including medicine management data at hospital discharge or following hospital discharge. Thus, we excluded studies which examined transitions of care in the hospital environment, or those which reported in-hospital medicine management in isolation. We also excluded studies which were not peer reviewed, were non-English language, included quality improvement interventions or were in abstract format only.

Each citation was independently reviewed for eligibility by two clinicians via a review of title and abstract, and then, where appropriate, full-text articles. All extracted papers also had their reference list hand-searched to ensure that all relevant papers had been included. AS, JM, SM, MA and PM undertook this process. Disagreement was resolved via regular meetings of this study team.

Quality assessment

Cohort study quality was assessed using the Newcastle Ottowa Score checklist.[11] This consists of the three main domains to assess the quality and risk of bias. These are: patient selection (cohort data source, representativeness and ascertainment of exposure to the outcome of interest), comparability of cohort and outcome assessment (including adequate follow-up time, acquisition of outcome and adequacy of follow-up). Data on risk of bias and the overall quality assessment can be found in online supplemental file S2.

Data extraction

Data were extracted by four clinicians (AS, JM, SM and PM) and entered into a standardised template. All data were cross-checked by a second reviewer. Any discrepancies were resolved by consensus. Data extracted included author, date, location, study design, population, number of patients studied, gender, age, time of follow-up, type of medicine reviewed and main study outcomes. Outcomes were chosen a priori, and the template was piloted before implementation.

Studies included in this review often examined different classes of medicines. For example, some examined analgesics and others cardiovascular drug management. We placed no restrictions on the type of drug examined as we were interested in obtaining a global view of medicine management.

RESULTS

Study selection

The database search initially retrieved 1180 studies; following the removal of duplicates, 1032 unique studies were identified for title and abstract review. A total of 938 studies were excluded as they did not meet the study inclusion criteria, leaving 94 full-text articles for review; 47 studies were then excluded during the full-text review, resulting in 45 papers meeting review inclusion (figure 1). Of note, two papers had the same population for analysis. However, both analyses examined different elements of care which were of interest, and so both were included.[12 13]

Summary of studies

Studies varied widely in their size, scope and methodology. Across the 47 included studies: 28 (60%) were from the USA, six (13%) from Canada, five (11%) from the UK, two (4%) from Australia and one (2%) each from Brazil, Belgium, Denmark, South Korea, Sweden and Switzerland. In total, 29 studies (62%) described medicine management at hospital discharge, and the remaining 18 studies (38%) examined medicine management in the posthospital discharge period. The full characteristics of included studies are presented in the online supplemental file S3. A summary of the main features of the research included is presented in table 2. Due to the heterogeneity of the study outcomes and the data captured, we were unable to undertake a meta-analysis.

Risk of bias

The quality assessment for the included studies is shown in online supplemental file S2. The overall quality of the studies varied. Across all 47 studies included, the median (IQR) Newcastle Ottawa score was 7 (5–8) for the studies included.

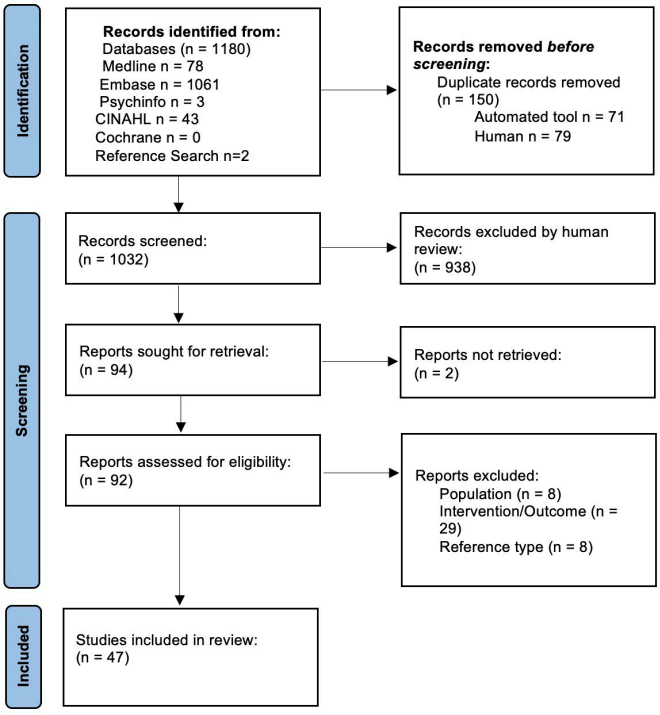

Figure 1 PRISMA flowchart.

Medication-related problems

Overview of included studies

Eleven studies described medication-related problems in critical care survivors[5 12–21] (online supplemental file S3, table 1). Two papers examined medication-related problems in the same population of older ICU survivors in the US.[12 13] Both studies were included as they focused on different elements of care. Across the studies there was a wide range of definitions and classifications used to define medication-related problems (table 3). Four studies examined medication-related problems at hospital discharge,[12 13 15 18] and the remaining seven studies examined medication-related problems within the ICU follow-up setting.[5 14 16 17 19–21] One study specifically examined the outcomes of patients admitted to critical care for COVID-19.[20]

Observations

There was variation in the number of patients impacted by medication-related problems. For example, a multicentre Canadian study of 834 patients reported that a third of patients were impacted by a medication-related problem at hospital discharge,[15] whereas in in a single centre study of older adults in the US, 85% of patients experienced a medication-related problem (defined as a potentially inappropriate medication).[13] In the ICU follow-up setting, 62.80–100% of patients who attended experienced a medication-related problem or required a pharmacy intervention.[5 14 19 21] These medication-related problems were classified as clinically significant in 86.40% of medication-related problems examined in one study, and 64% in a further single centre study.[5 19]

The studies varied in the types of drugs involved in medication-related problems. One study examined the proportion of patients unintentionally discharged from hospital with chronic medication omitted and found that approximately one-third of patients experienced problems with their chronic disease management medication.[15] A further study undertaken in the ICU follow-up setting found that 5.30% of patients did not have medications for chronic conditions restarted following discharge from hospital.[17] Two studies, one at hospital discharge and one based in the ICU follow-up setting, found that analgesics including opiates were the most likely medications to be involved in medication-related problems.[5 12]

Table 2 Overview of studies included in this review

Study characteristic (n=47)	N (%)
Geographical region	
Australia	2 (4)
Belgium	1 (2)
Brazil	1 (2)
Canada	6 (13)
Denmark	1 (2)
South Korea	1 (2)
Sweden	1 (2)
Switzerland	1 (2)
UK	5 (11)
USA	28 (60)
Study type	
Retrospective observational cohort	40 (85)
Prospective observational cohort	7 (15)
Study scope	
Multicentre	12 (26)
Single centre	35 (74)
Study population focus	
Mixed (general/mixed medical and surgical specialties)	29 (62)
Medical ICU (MICU)	6 (13)
Cardiac ICU (CICU)	1 (2)
Trauma/surgical/neurosurgical ICU	4 (9)
Elderly patient/chronic medications	5 (11)
Cancer centre general ICU	1 (2)
Acute kidney injury/renal replacement need	1 (2)
Medication type studied*	
Opiates/analgesics	12
Gastroprotection/acid suppressants	12
Psychotropic	14
Medication changes/PIMs/AIMs	11
Cardiovascular	4
Main timepoint examined	
Hospital discharge	29 (62)
Hospital discharge and post-discharge follow-up	5 (11)
Outpatient follow-up <6 months	8 (17)
Outpatient follow-up >6 to <9 months	2 (4)
Outpatient follow-up to >9 months to 1 year	2 (4)
Outpatient follow-up >1 year	1 (2)
Source of study data	
Clinical record including discharge prescription/summary	32 (68)
Face-to-face interview	7 (15)
National databases	8 (17)

*n=53 as some papers studied more than one medication class.
AIM, actually inappropriate medication; ICU, intensive care unit; PIM, potentially inappropriate medication.

Risk factors

Risk factors for medication-related problems at hospital discharge included the omission of medications at ICU discharge,[15] not being discharged home[12] and discharge from a surgical service.[12] Risk factors for medication-related problems in the ICU follow-up setting included hospital length of stay, and

Table 3 Terminology and definition of medication-related problems used across included studies

Terminology to define a medication-related problem	Definition	Study
Inappropriate medication Discontinuation	Unintentional discontinuation of chronic medications (eg, a statin or antiplatelet/anticoagulant)	Bell *et al* (2006)[22]
Discrepancy: the need for a pharmacy intervention	Interventions included dose adjustments, additional therapy, inappropriate therapy discontinued and patient/family counselling	Bottom-Tanzer *et al* (2020)[16]
PIMs AIMs	Beer criteria[63] For example, stress ulcer prophylaxis which should have been discontinued at ICU/hospital discharge	Morandi *et al* (2011)[12] Morandi *et al* (2013)[13] Galli *et al* 2016[18]
Medication-related problem	Included drug omissions, drug adjustments, duration of treatment advice; patient education and counselling (eg, re-titration of preadmission gabapentin for neuropathic pain)	MacTavish *et al* (2019)[5] MacTavish *et al* (2020)[19]
Pharmacist intervention	Included drug omissions, drug adjustments, adverse drug event identified or prevented, duration of treatment advice; patient education and counselling (eg, identification of adverse drug events such as hypoglycaemia)	Stollings *et al* (2018)[21]
Pharmacist intervention	Included GDMT optimisation, refill assistance, medication cost assistance, pill box provision, lab monitoring, medication cessation, medication addition and medication dose adjustment (eg, GDMT optimisation of heart failure drug treatment)	Adie *et al* (2021)[14]
Medication changes	Classified as appropriate or inappropriate based on discussion with clinical team, patient and ongoing clinical indication (eg, inappropriate continuation of anticoagulants)	MacTavish *et al* (2021)[20]
Potential medication errors and medicine-related problem	Included Inappropriate discontinuation of chronic medications, difficulties obtaining supplies, administration, information and understanding of the suitability of prescriptions (eg, inappropriate continuation of sedatives at hospital discharge)	Eijsbroek *et al* (2013)[17]

AIM, actually inappropriate medication; GDMT, guideline-directed medical therapy; ICU, intensive care unit; PIM, potentially inappropriate medication.

the number of ICU discharge medications and analgesic requirements at ICU discharge and at the clinic attendance.[5 19]

Gastrointestinal protection medications

Overview of included studies

There were 12 studies which examined the use of gastrointestinal protection agents in the hospital discharge period (online supplemental file S3, table 2).[17 22–32] This drug group includes proton pump inhibitors (PPI), H2 receptor antagonists and Sucralfate. Ten studies examined gastrointestinal protection use at hospital discharge,[23–32] one examined dispensing of gastric acid suppressors up to 90 days following discharge[22] and three studies examined gastrointestinal protection in the outpatient follow-up setting.[17 29 30]

Observations

The number of inappropriate gastrointestinal protection agent prescriptions reported at hospital discharge ranged considerably across the studies included. For example, in three studies, all gastrointestinal protection agents prescribed at hospital discharge were deemed to be prescribed inappropriately.[23 30 32] In contrast, a single centre study from the US found that only 15.7% of prescriptions at hospital discharge were inappropriate.[27] Three studies examined inappropriate continuation of these drugs beyond hospital discharge.[23 29 30] In the first, 58.20% of patients prescribed gastrointestinal protection at 3 months were prescribed them inappropriately.[30] The second study, which examined gastrointestinal protection at a 4-week telephone follow-up call, found that only 5% of patients prescribed gastrointestinal protection had a compelling reason for continuation.[29] In the most recent study, 64% of patients remained on proton pump inhibitors with no indication following hospital discharge.[23] Conversely, three studies highlighted that up to 15.40% of patients were not restarted on previously prescribed (prehospital) gastrointestinal protection at hospital discharge.[22 24 30]

Risk factors

Several risk factors for continued use of gastrointestinal protection medications were identified across three studies. Risk factors included discharge to a long-term care facility, an ICU admission a surgical (as opposed to medical) admission and mechanical ventilation.[22 23 25]

Psychotropic medications

Overview of included studies

Fourteen studies examined the use of psychotropic medications in survivors of critical care (online supplemental file S3, table 3).[33–46] Drugs included were antipsychotic and anxiolytic agents alongside antidepressants. Twelve studies examined psychotropic medications use in critical care survivors at hospital discharge;[34–45] one study examined their use up to 180 days following hospital discharge[33] and the final study examined the use of these medications up to 1 year posthospital discharge.[46]

Observations

Across the studies, in those patients prescribed psychotropic medications during admission, there was wide variation in the continued use of these drugs at hospital discharge (range 10.30–61%), although the appropriateness of this continued use was difficult to assess across the studies.[34–45] Four studies gave details on the prescription appropriateness at hospital discharge; one single centre US study found 54 of their cohort of 161 patients (34%) had been continued on antipsychotics or anxiolytics at hospital discharge, with no patient having a documented reason for their use.[37] In another single site study, 68.40% of patients prescribed atypical antipsychotics at hospital discharge had no ongoing indication for their use,[39] while a further study found that 24.40% of survivors treated with antipsychotics during critical illness, remined on these medicine at hospital discharge, despite two-thirds of these survivors having normal mental status documented.[45] Finally, a single centre cohort study based in a trauma and

neurosurgical unit found that 67.10% of prescriptions, the majority of which were for quetiapine, were inappropriate at hospital discharge.[44]

Risk factors

One large Danish registry study examined the use of antipsychotics in mechanically ventilated patients, in comparison with a hospitalised and a general population cohort, up to 1 year post-hospital discharge. In this study, they found that in those who had received mechanical ventilation, the risk of new psychoactive medication prescriptions increased in the first 3 months following hospital discharge in comparison with the hospital and general control population, although these differences had largely resolved by 12 months.[46] Another VA registry study in the US also found that patients with a diagnosis of sepsis were more likely to be continued on antipsychotics in the posthospital discharge phase (up to 180 days).[45] Seven studies found critical illness specific variables, such as ICU length of stay, severity of illness and the type of admission were risk factors for the continuation of psychotropic medications.[34 35 38 40–42 44]

Analgesia

Overview of included studies

In total, 12 studies examined the use of analgesics in the post-hospital discharge period (online supplemental file S3, table 4).[5 17 20 47–55] Analgesics examined included simple analgesics such as paracetamol alongside weak and strong opioids. Five studies examined the use of analgesia at hospital discharge,[47 48 50 52 55] three studies were based in the ICU follow-up setting[5 17 20] and six studies examined analgesics longitudinally across the critical care recovery period (up to 24 months following discharge.[48 49 51 53–55] Studies varied in their inclusion definition, with some studies examining chronic opioid use, some examining the outcomes of opioid naïve patients and others examining analgesics in all ICU survivors.

Observations

New analgesic prescribing was reported in 10 studies.[5 17 20 47 48 50–52 54 55] Five studies reported new analgesia prescriptions at hospital discharge (number of patients receiving new analgesics at hospital discharge (range 31.80–47.10%).[47 48 50 52 55] Three studies were set in the ICU follow-up setting, and two of the studies took place with the general ICU population and reported new analgesia requirements in 27% and 76% of patients included.[5 17] In one of these studies, 16% of the total patient cohort (183 patients) were receiving new opiate prescriptions in the post-ICU recovery phase.[5] A further study, also in the ICU follow-up setting, specifically examined new analgesic requirements in critically ill COVID-19 survivors and found a significant increase in the number of patients taking regular analgesia following severe COVID-19 infection.[20] The final study which reported increased analgesic use, demonstrated that 20% of patients filled new opiate prescriptions within 7 days of hospital discharge; however, persistent opiate use at 1 year fell to between 2.60–4.90%.

Conversely, a large population-based cohort study of elderly ICU survivors with chronic opioid use found relatively static opioid use in the posthospital discharge period (up to 180 days posthospital discharge), with 22% of patients on a higher dose of opiate compared with prehospitalisation, 19.80% receiving the same dose, and 21.50% of patients receiving a lower dose.[49]

Risk factors

Nine studies reported risk factors for continuation of analgesics.[47–52 54 55] Risk factors included a cardiac critical care and surgical admissions, a history of illicit drug use (including alcohol and substance use disorders), intubation, younger age, a diagnosis of sepsis, previous benzodiazepine use, chronic opiate use preadmission, a higher cumulative dose of opiate in the ICU and an ICU admission diagnosis of malignancy.

Cardiac medications

Overview of included studies

In total, four studies examined cardiac medication management in survivors of critical care (online supplemental file S3, table 5).[22 33 56 57] Two studies examined cardiac medication use at hospital discharge[56 57] and two studies examined their use following hospital discharge.[22 33]

Observations

One study found that 34% of patients were continued on midodrine at hospital discharge, with an estimated 50% of these prescriptions deemed inappropriate.[57] In the two studies which examined cardiac medications in the posthospital discharge period, between 15.10–22.80% of critical care and sepsis survivors did not have chronic cardiac medications such as statins and antiplatelets restarted or refilled.[22 33]

Risk factors

An ICU admission and a diagnosis of sepsis were risk factors for unintentional discontinuation of chronic cardiac medications.[22 33]

DISCUSSION

This systematic review aimed to understand changes to medication management and medication problems in critical care survivors during the hospital discharge period. It has found that as many as 80% of critical care survivors can experience problems with medication management during recovery.[13 19] This included unintentional discontinuation of chronic disease medications in up to a quarter of patients; conversely, we also found that many patients were continued, often inappropriately, on acutely prescribed drugs. Problems occurred across multiple classes of drugs, including gastrointestinal protection, psychotropic, analgesic and cardiac medications. Several risk factors for medication-related problems emerged including the need for mechanical ventilation, a sepsis diagnosis and a critical care admission (vs hospital admission only).

It is well recognised that pharmacists play a key role within the ICU setting. However, at present their role in recovery programmes is sporadic, and has not been integrated into national recommendations. For example, the UK Faculty of Intensive Care Medicine's Guidelines for the provision of intensive care services makes no mention of the pharmacist in the delivery of ICU after care.[58] The findings of this review would suggest that the role of the pharmacist within recovery programmes and across the recovery timeline more broadly may improve outcomes for patients, and potentially provide benefits to the healthcare system. More work in this area is required.

This review found inconsistent results in relation to pain management and opiate use in the posthospital discharge period. Studies demonstrated both relatively static use, as well as significant increases in opiate prescribing,[20 51] although synthesis of these data was hindered by the heterogeneity of the inclusion criteria across studies. It is important to recognise that no study

matched medication management and medication-related problems with patient reported outcomes, such as global quality of life or pain scores. We do not know if patients were discontinued opiates with the addition of subsequent substitutes, or if these drugs were inappropriately prescribed. Recent evidence has demonstrated chronic pain occurs in up to two-thirds of ICU survivors; as such, future research should link patient-reported outcomes (eg, pain scores with medicine management), thus ensuring a holistic picture of the challenges which patients face following hospital discharge.[59 60]

We were unable to undertake a meta-analysis with these data owing to the heterogenous nature of the research available. Studies varied in the definition of medication-related problems and examined these issues across various timeframes. Given this, future work should examine which outcomes are important to gather and the timeframe which is most appropriate. This step would allow data to be fully synthesised and relevant recommendations for practice to be established.

There are limitations to this review. First, we were unable to examine patient-level factors which could have contributed to the medication-related problems described across transitions of care. Socioeconomic factors such as educational attainment and access to adequate financial support are known to influence recovery from critical illness.[61 62] These social factors may have influenced issues such as medication-related problems and access to drugs within specific healthcare systems. Future work should examine patient demographics, alongside healthcare access following discharge, to understand any individual risk factors. Second, many of the studies included used large-scale national databases to examine outcomes. These databases have inherent problems; most notably in this review, the inability to understand why medicines may have been stopped or started. Third, there was a wide range of cohort sizes included in this review. There was also significant variation in the timepoint of measure, the type of measure and the setting in which the measure was undertaken. The event rate of medication errors was also inconsistently reported; having this event rate would have allowed an enhanced understanding of the interaction between the sample size and the outcomes described. This variation makes it challenging to compare studies and synthesise them accurately. Future work should endeavour to create a standardised approach to outcome measurement in this field.

CONCLUSIONS

Following critical illness, patients can experience problems and changes to medicines. These changes are present across multiple health systems and classes of medications. Further research is required to understand optimal medicine management across the full recovery trajectory of critical illness.

Contributors JM conceptualisation of the study AS and SM conducted the formal searches JM, AS, MA and PM conducted the analysis (formal analysis) JM, AS, PM and SM contributed to the interpretation of the findings (validation). All authors critically revised the paper for intellectual content and approved the final version of the manuscript.

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Date stamp – 31st May 2022

OVID databases: Medline, EMBASE, PsycInfo,

Search criteria:

1. (medication adj2 error*).mp.
2. (medication adj2 problem*).mp.
3. exp Medication Errors/
4. exp "Drug-Related Side Effects and Adverse Reactions"/ or exp Medication Errors/
5. exp Drug Prescri*/
6. (medication* adj2 intervention*).mp.
7. (prescri* adj2 error*).mp.
8. (prescri* adj2 intervention*).mp.
9. 7 or 8
10. 1 or 2 or 3 or 4 or 5 or 6
11. exp Medication Errors/ or medicine reconciliation.mp. or exp Drug Prescri*/ or exp Medication Reconciliation/
12. (inappropriate adj2 medication*).mp.
13. 9 or 10 or 11 or 12
14. exp Critical Care/
15. intensive care.mp.
16. critical care.mp.
17. 14 or 15 or 16
18. (hospital adj2 discharge).mp.
19. exp Patient Discharge/
20. (post adj2 discharge).mp.
21. (intensive adj2 care adj2 survivor*).mp.
22. exp Survivors/
23. 18 or 19 or 20 or 21 or 22
24. 13 and 17
25. 23 and 24
26. 17 and 23
27. exp Antipsychotic Agents/ or antipsych*.mp.
28. opi*.mp.
29. gastroprotect*.mp.
30. Histamine H2 Antagonists/ or Proton Pump Inhibitors/ or stress ulcer prophylaxis.mp. or Anti-Ulcer Agents/
31. acid suppress* therapy.mp.
32. 29 or 30 or 31
33. 26 and 27
34. 26 and 28
35. 26 and 32

EBSCO – CINAHL

S22	S12 AND S15 AND S21
S21	S16 OR S17 OR S18 OR S19 OR S20
S20	survivor*
S19	TX intensive n2 care n2 surviv*
S18	TX post n2 discharge*
S17	patient discharge
S16	TX hosp* n2 discharge
S15	S13 OR S14
S14	TX intensive care
S13	critical care

S12	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S11	TX inappropriate* n2 medic*
S10	medication reconciliation
S9	medic* reconciliation
S8	TX unintention* n2 medic*
S7	TX prescri* n2 intervention*
S6	TX prescri* n2 error*
S5	TX medic* n2 intervention*
S4	drug prescription*
S3	medication error
S2	TX medic* n2 problem*
S1	TX medic* n2 error*

Table S2: Quality Assessment

Author/Year	Design	Selection	Comparability	Outcome	Total
Academia et al (2020)	Observational cohort	3	1	3	**7**
Adie et al (2021)	Observational cohort	2	0	2	**4**
Bell et al (2006)	Observational cohort	4	2	3	**9**
Bell et al (2011)	Observational cohort	4	2	3	**9**
Blackett et al (2021)	Observational cohort	3	2	3	**8**
Bottom-Tanzer et al (2021)	Observational cohort	2	0	3	**5**
Choon et al (2021)	Observational cohort	3	1	3	**7**
Coe et al (2020)	Observational cohort	3	2	3	**8**
Dixit et al (2021)	Observational cohort	3	2	3	**8**
Eijsbroek et al (2013)	Observational cohort	2	0	1	**3**
Farley et al (2013)	Observational cohort	3	0	3	**6**
Farrell et al (2010)	Observational cohort	4	2	3	**9**
Farrokh et al (2017)	Observational cohort	3	0	2	**5**
Flurie et al (2015)	Observational cohort	2	0	3	**5**
Franchitti et al (2020)	Observational cohort	3	0	3	**6**
Galli et al (2016)	Observational cohort	2	2	2	**6**
Gilbert et al (2017)	Observational cohort	3	1	3	**7**
Hatch et al (2010)	Observational cohort	1	0	2	**3**
Jasiak et al (2013)	Observational cohort	2	0	3	**5**
Karamchandani, Schoaps et al (2019)	Observational cohort	3	0	3	**6**
Karamchandani, Pyati et al (2019)	Observational cohort	3	0	2	**5**
Kram et al (2015)	Observational cohort	3	0	3	**6**
Krancevich et al (2022)	Observational cohort	3	2	3	**8**
Lambert et al (2021)	Observational cohort	3	1	2	**6**
Levine et al (2019)	Observational cohort	3	0	3	**6**
MacTavish et al (2019)	Observational cohort	3	2	3	**8**
MacTavish et al (2020)	Observational cohort	4	2	3	**9**
MacTavish et al (2021)	Observational cohort	3	1	3	**7**
Marshall et al (2016)	Observational cohort	4	2	3	**9**

Mehta et al (2020)	Observational cohort	3	0	2	**5**
Morandi et al (2013)	Observational cohort	3	2	3	**8**
Morandi et al (2011)	Observational cohort	3	0	3	**6**
Murphy et al (2008)	Observational cohort	2	1	2	**5**
Rizvi et al (2019)	Observational cohort	4	2	3	**9**
Rowe et al (2015)	Observational cohort	2	2	3	**7**
Shin (2015)	Observational cohort	4	0	3	**7**
Stollings et al (2018)	Observational cohort	2	0	3	**5**
Tan et al (2016)	Observational cohort	3	0	3	**6**
Tollinche et al (2022)	Observational cohort	4	2	3	**9**
Tomichek et al (2016)	Observational cohort	3	2	3	**8**
Von Oelreich et al (2021)	Observational cohort	4	2	3	**9**
Wang et al (2018)	Observational cohort	3	1	3	**7**
Witcraft et al (2021)	Observational cohort	2	0	3	**5**
Wolht et al (2007)	Observational cohort	3	0	2	**5**
Wunsch et al (2014)	Observational cohort	4	2	3	**9**
Wunsch et al (2020)	Observational cohort	4	2	3	**9**
Yaffe et al (2017)	Observational cohort	3	2	3	**8**

S3: Table 1 POTENTIAL INAPPROPRIATE MEDICATION AND ACTUAL INAPPROPRIATE MEDICATION DATE EXTRACTION TABLE

Author	Yr	Country	ICU Population	Nature	Timeline	n	Gender	Age	Medication type	Results
Adie et al.	2021	USA	Cardiac	Single centre Retrospective, observational cohort study	Post-discharge CICU clinic: 2-week post discharge	106 (70)	M-71%	Median 65 (54 – 72)	Any	**Issues encountered:** Results described as n=number of interventions. Median number of pharmacist interventions = 4 (3-5), each patient had at least 1 intervention. Number of drugs requiring a dose adjustment (n=46), optimisation (n=42), change (n=18), addition (n=23), cessation (n=21). Median number of medication changes = 2 (1-3). Pillbox provision (n=8) and refill assistance (n=16). **Risk factors for problems:** Nil described **Protective factors against problems:** Nil described
Bell et al	2006	Canada	General	Multicentre Retrospective observational cohort study	Hospital discharge	834	M-57%	Median 65 (IQR 50-76)	Statins Antiplatelet and anticoagulant L-thyroxine Regular inhalers AST Allopurinol	**Issues encountered:** Medication discontinuation at discharge – n = 251/834 (33%) with 1 or more medications affected **Risk factors for problems**: Medications omitted at ICU discharge higher OR for omission at hospital discharge. **Protective factors against problems:** Admission to academic ICU, admission with medical diagnosis
Bottom-Tanzer et al	2020	USA	Trauma Medical	Single Centre Prospective observational cohort study	ICU-clinic: 2-, 12-, and 24-weeks post hospital discharge	70	M-59%	Mean 54.7 (SD 15.7)	Any	**Issues encountered:** n = 106/118 (94.6%) pharmacy reviews had one or more discrepancy. 116 interventions – dose adjustments (n = 19), additional therapy (n = 23), inappropriate therapy discontinued (n=27), patient/family counselling (n=47). **Risk factors for problems:** Nil described **Protective factors against problems:** Time from hospital admission: reduced average number of medication interventions at 24-week visit (0.8/pt) vs 2-week visit (1.2/pt)
Eijsbroek et al	2013	UK	General	Single Centre Retrospective observational cohort study	ICU-clinic: 3-, to 9-months post hospital discharge	21	M-53%	Mean 64.4 (SD 13)	Any	**Issues encountered:** Discontinuation of chronic medications and not restarted – 5.3%. Physical issues with medication management and comprehension issues with medications amongst patients and carers **Risk factors for problems:** Nil described **Protective factors against problems:** Nil described
Galli et al	2016	Brazil	Medical Cardiac Patients >60yrs old	Single centre Retrospective observational cross-sectional	Hospital discharge	486	M-55%	Median 71 (IQR 65-77)	Any	**Issues encountered:** n = 74/1864 (3.9%) PIMs identified in population during hospitalisation continued at hospital discharge. 41.1% of PIMs at discharge were medications initiated in ICU. **Risk factors for problems:** Unclear which specific to

				study						medications at discharge. **Protective factors against problems:** Nil described
MacTavish et al.	2019	UK	General	Single Centre. Retrospective observational cohort study	ICU-clinic: 6- weeks to 3-years post hospital discharge	47	M-66%	Median 52 (IQR 44-57)	Any	**Issues encountered:** n = 38/47 medication-related problem: Drug omissions – 20/47 (29%) Dose adjustment 13/47 (19%) Duration of treatment advice 12/47 (17%) Patient unaware of medication change – 26/47 (55%) Patient expressed concerns re medications – 28/47 (60%) 69 (18.6%) medications had problems at review, 44/69 (64%) classified with severity score >/= 3. **Risk factors for problems:** Number of pain medications at ICU discharge. Nil other variables significant. **Protective factors against problems:** Nil described
MacTavish et al.	2020	UK	Medical Surgical	Multicentre Prospective observational cohort study	ICU-clinic: 4- to 12- weeks post hospital discharge	183	M-56%	Median 58 (IQR 50-65)	Any	**Issues encountered:** Medication related problems = 198, Medication omissions – n = 27/198. Severity of MRP: Minor 27/198, Moderate 141/198, Severe 30/198. Medications most affected: Analgesia > CVS > GI > Neuroleptic **Risk factors for problems:** Hospital LOS, number of ICU discharge medications, and prescription of analgesia on WHO Step 2 classification. **Protective factors against problems:** Nil described
MacTavish et al.	2021	UK	General (COVID-19 survivors)	Single centre Prospective observational cohort study	3-7 months post hospital discharge. Setting: ICU recovery service	78	M-64%	Median 59 (IQR 54-67)	Medication changes	**Issues encountered:** Of the drugs prescribed, 135 (30%) were either new drugs or increased doses of previously prescribed drugs. Over 70% of patients were taking an increased dose of medicine or a new medicine. These new medications ranges in BNF classification. 94% of medication changes deemed appropriate by clinical team. There was a significant increase in number of patients taking regular analgesia following severe COVID-19 infection (23 (29.5%) vs 39 (50%), p< 0.001). **Risk factors for problems:** Unclear **Protective factors against problems:** Nil described
Morandi et al	2013	USA	General Patients >60 years old	Single centre Prospective observational cohort study	Hospital discharge	120	M-53%	Median 68 (IQR 64-74)	Any	**Issues encountered:** 250 PIMs and 80 AIMs identified at discharge. Opiates > anticholinergics > antidepressants > Non-benzodiazepine anxiolytic > AAP > other **Risk factors for problems:** Only significant for PIMS multivariable analysis: number of pre-hospital PIMs, discharge anywhere not to home, discharge from surgical service. Nil significant for AIMs.

										Protective factors against problems: Nil described
Morandi et al	2011	USA	General Patients >60yrs old	Single centre Prospective observational cohort study	Hospital discharge	120	NA	Median 68 (IQR 64-74)	Any	**Issues encountered:** 85% patients had PIM at discharge, 37% of patients had 3 or more PIMs at discharge. 50% of these PIMs initiated in ICU. Among 103 patients with at least 1 PIM, 59% had at least 1 AIM, 59% of these initiated in ICU. **Risk factors for problems:** Nil described **Protective factors against problems:** Nil described
Stollings et al	2018	USA	General	Single-centre Prospective observational cohort study	ICU-clinic: median 29 days post hospital discharge	56	M-57%	Median 48 (Range-35-57)	Any	**Issues encountered:** 22 (39%) patients had medication stopped, 18 (32%) had new medication initiated. ADEs identified in 9/56 (16%) patients, ADE preventative measures in 18 (32%) patients. **Risk factors for problems:** Nil described **Protective factors against problems:** Nil described

Key: NA – not addressed by the paper, PIM – potentially inappropriate medication, AIM – actually inappropriate medication, ADE – adverse drug event, AAP – atypical antipsychotic, AST – acid-suppressant therapy

S3: Table 2 GASTROPROTECTION MEDICATION

Author	Yr	Country	ICU Population	Nature	Timeline	n	Gender	Age	Results
Bell et al	2011	Canada	General Patients ≥ 66 years, with pre-ICU medication use.	Multicentre Retrospective observational cohort study.	Up-to 90 days post hospital discharge	16474	M-57%	Mean 75.4 (SD 5.61)	**Prescription changes at hospital discharge:** Discontinuation of medication n = 670/16474 (15.4%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** ICU stay vs hospitalisation not including ICU admission
Blackett et al.	2021	USA	Medical Cardiac Cardiothoracic Surgical Neurological	Single centre Retrospective, observational cohort study	Hospital discharge and first primary care visit	2467	M-59%	Highest age tertile: 18-56yrs	**Prescription changes at hospital discharge:** n=668 (27%) continued PPI at hospital discharge. 18/24 (64%) with available primary care records were continued PPI at this follow-up point. I**nappropriate discharge Rx:** All identified as having no indication for long-term PPI. **Factors associated with continuation:** Multivariable logistic regression model for those continued inappropriate PPI vs discontinued PPI found surgical vs medical admission, discharge to longer term care facility vs home, undergoing UGIE vs not and increased number of medications (>10 vs <8) in favour of inappropriate continuation. **Factors associated with discontinuation:** Nil at multivariable modelling
Eijsbroek et al	2013	UK	General	Single Centre Retrospective observational cohort study	ICU-clinic 3-9months post discharge	21	M-53%	Mean 64.4 (SD 13)	**Prescription changes at hospital discharge:** 2 additional patients prescribed PPI at discharge and follow-up. **Inappropriate discharge Rx?** 2 patients queried continuation at follow up **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Farley et al.	2013	Australia	Medical Surgical Cardiac	Multicentre Retrospective observational cohort study.	Hospital discharge	387	M–58%	Mean 67.7	**Prescription changes at hospital discharge:** n = 75/190 (36%) new SUPs continued n = 29/146 (20%) had pre-hospital SUP prescription changed n = 11/146 (8%) pre-hospital SUP discontinued **Inappropriate discharge Rx?** n = 75/190 (39%) deemed inappropriate. n = 9/11 pre-hospital SUP potentially discontinued inappropriately. **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Farrell et al.	2010	USA	General	Single centre Retrospective observational cohort study	Hospital discharge	210	M=52%	Median 61	**Prescription changes at hospital discharge:** n=36/185 (19.4%) survivors discharged home on new acid-suppressing medication. 85.9% of survivors who were admitted with ASM were discharged on one of these medications. 31.3% discharged on different ASM to admission. I**nappropriate discharge Rx:** n=35/114 (31%) survivors, not admitted on ASM, were discharged home on ASM with no indicated risk factors.

									Factors associated with continuation: On multivariable modelling ventilator dependent respiratory failure only significant risk for SUP use. **Factors associated with discontinuation:** Nil described
Franchitti et al	2020	Switzerland	General	Single centre Retrospective observational cohort study	Hospital discharge	140	M-69%	Median 65 (Range 17 – 92)	**Prescription changes at hospital discharge:** n = 30/130 (23.1%) new SUP continued. **Inappropriate discharge Rx?** Potentially inappropriate **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Hatch et al.	2010	USA	Medical Surgical	Single centre Retrospective observational cohort study.	Hospital discharge	356	M-59%	Mean 55 (SD 19)	**Prescription changes at hospital discharge:** n = 31/356 (8.7%) new SUP continued. **Inappropriate discharge Rx?** n = 31/197 (15.7%) deemed inappropriate of those discharged on SUP. **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Mehta et al.	2020	Canada	General Patient age ≥ 65	Single centre Retrospective observational cohort study.	Hospital discharge	66	M-67%	Mean 75.5 (SD 7.1)	**Prescription changes at hospital discharge:** non-naïve cohort: n = 27/31 (87%) survivors continued pre-hospital SUP. Naïve cohort: n = 9/11 (82%) survivors continued new PPI **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Murphy et al.	2008	USA	Surgical Level 1 trauma	Single centre Prospective, observational, cohort study	Hospital discharge and ICU-clinic: 4/52 post hospital discharge	248	M-63%	Median 58.0 (IQR 43 – 69.8)	**Prescription changes at hospital discharge:** n = 60/248 (24.2%) continued **Inappropriate discharge Rx?** n = 3/60 (5.0%) had compelling reason for continuation, unclear n = 57/60. **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Shin	2015	South Korea	General	Single centre Retrospective observational cohort study	Hospital discharge	622	UK	UK	**Prescription changes at hospital discharge:** n=359 (57.7%) continued newly initiated PPI at hospital discharge. Percentage of continued PPI use at hospital discharge increased over the 4-year study period – 48% (2010) to 71% (2013). I**nappropriate discharge Rx:** All deemed inappropriate continuation by author **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Tan et al	2016	Australia	General	Multicentre Retrospective observational cohort study	Hospital discharge	314	M-57%	60 (IQR 42-71)	**Prescription changes at hospital discharge:** n = 90/184 (48.9%) new SUP continued. **Inappropriate discharge Rx?** n = 81/90 (90%) deemed inappropriate **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Wohlt et al.	2007	USA	Medical Surgical	Single Centre.	Hospital discharge	394	M–58%	Mean 54 (SD 19.0)	**Prescription changes at hospital discharge:** n = 96/394 (24.4%) new GAS continued.

				Retrospective observational cohort.	and ICU-clinic: 3-months post hospital discharge				n = 3/394 (0.76%) discontinued GAS. n = 32/55 (58.2%) follow-up patients ongoing GAS prescription. **Inappropriate discharge Rx?** Yes, all continuations/discontinuations deemed inappropriate. **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described

Key: AST – acid-suppressant therapy, GAS – gastric-acid suppressant, PPI – proton-pump inhibitor, SUP – stress ulcer prophylaxis

S3: Table 3 Psychotropic medication data extraction table

Author	Yr	Country	ICU Population	Nature	Timeline	n	Gender	Age	Medication type	Results
Coe et al	2020	USA	General	Multi-centre. Retrospective observational cohort study.	Post hospital discharge: up to 180 days post discharge	134,999	M–96%	Mean 66.5 (SD 11)	**Antipsychotics**	**Prescription changes at hospital discharge:** Antipsychotic continued: total population n = 3278 (2.43%), ICU plus sepsis cohort = 361 (3.6%), ICU minus sepsis cohort = 2917 (2.3%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Diagnosis of sepsis at ICU admission **Factors associated with discontinuation:** Nil described
Dixit et al.	2021	USA	General	Multicentre Retrospective observational cohort study	Hospital discharge	300	M-65%	Median 69 (IQR 55-78)	**Antipsychotics**	**Prescription changes at hospital discharge:** 61% of patients continued antipsychotic at hospital discharge. **Inappropriate discharge Rx:** Unclear, some medications restarted post-ICU discharge. **Factors associated with continuation:** Discharge from 'mixed ICU' compared to medical and surgical ICU. **Factors associated with discontinuation:** Prolonged duration of antipsychotic prescription, longer ICU and hospital LoS reduced likelihood of continuation at hospital discharge. Antipsychotic discontinued in ICU had significantly lower OR for continuation of antipsychotic at hospital discharge.
Farrokh et al.	2017	USA	Medical Surgical Cardiac Neurosurgical	Single centre Retrospective observational, pseudo-randomised study.	Hospital discharge	100	M-76%	Median 65 (range 21-95)	**Atypical antipsychotics**	**Prescription changes at hospital discharge:** Medication continued: n = 23 (23%) **Inappropriate discharge Rx?** Unclear. CAM-ICU rarely documented **Factors associated with continuation:** Admission to SICU (30%) > CICU > CTICU > MICU (19%) **Factors associated with discontinuation:** Nil described
Flurie et al.	2015	USA	Medical	Single centre. Retrospective observational cohort study.	Hospital discharge	87	M-52%	-	**Antipsychotics**	**Prescription changes at hospital discharge:** Medication continued: n = 9/87 (10.3%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Higher proportion discharged on medication if continued from ICU to ward, n = 9/23 (39%). **Factors associated with discontinuation:** Nil described

Gilbert at al.	2017	USA	Medical Surgical Cardiac Neurosurgical	Single centre Retrospective observational cohort study.	Hospital discharge	161	M–35%	50	**Neuroleptics**	**Prescription changes at hospital discharge:** Medication continued: n = 54 (34%) **Inappropriate discharge Rx?** Study deemed all inappropriate because no documented physician notes for medication use in chronic management **Factors associated with continuation:** Multiple neuroleptics or trazadone during ICU stay **Factors associated with discontinuation:** Prescription of haloperidol in ICU
Jasiak et al	2012	USA	Medical	Single centre Retrospective observational cohort study	Hospital discharge	80	-	Mean 59 (SD 17.2)	**Antipsychotic**	**Prescription changes at hospital discharge:** Medication continued: n = 20/59 survivors (33.9%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** "Increased" ICU LOS, "increased" hospital LOS, final CAM-ICU positive. **Factors associated with discontinuation:** Nil described
Karamchandani et al.	2018	USA	Surgical Medical Cardiovascular Neurosurgical	Single centre Retrospective observational cohort study.	Hospital discharge	346	M–66%	Median 59.9 (Range 18 – 99)	**Atypical antipsychotic**	**Prescription changes at hospital discharge:** Medication continued: n = 174/314 survivors (55%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Continued care facility at DC, male, short hospital LOS, longer ICU LOS **Factors associated with discontinuation:** Nil described
Kram et al.	2015	USA	Medical Surgical Cardiac Neurosurgical Cardiothoracic surgical	Single centre Retrospective observational cohort study.	Hospital discharge	133	M–68%	Median 61.5 (IQR 45 - 71)	**Atypical antipsychotic**	**Prescription changes at hospital discharge:** Medication continued: n = 38/133 (28.6%) survivors **Inappropriate discharge Rx?** Potentially inappropriate, 26/38 had no ongoing reason for continuation **Factors associated with continuation:** Discharge to long term care facility, diagnosis TBI **Factors associated with discontinuation:** Nil described
Lambert et al.	2021	Belgium	General	Single centre Retrospective observational cohort study	Hospital discharge	196	M-78%	Median 67 (IQR 53-76)	**Antipsychotic**	**Prescription changes at hospital discharge:** following ICU initiation of medication, n=38 (19.4%) continued antipsychotic at hospital discharge. 25/41 (61%) patients discharged on antipsychotic had indication for continued antipsychotic discussed on discharge letter. **Inappropriate discharge Rx:** Unclear **Factors associated with continuation:** On multivariable logistic regression modelling – admission to medical ICU or receiving quetiapine increased risk of continued antipsychotic. **Factors associated with discontinuation:** Nil described

Levine et al.	2019	USA	Medical Surgical	Single centre Retrospective observational cohort study	Hospital discharge	124	Medical M-68% Surgical M-61%	Age >60yrs: Medical -62% Surgical -46%	**Antipsychotics**	**Prescription changes at hospital discharge:** n=29/78 (37.2%) medical ICU patients and n=25/46 (54.3%) surgical ICU patients continued antipsychotics at hospital discharge. **Inappropriate discharge Rx:** Unclear. **Factors associated with continuation:** Medical ICU patients – higher risk on multivariable analysis if history of pre-existing dementia (OR = 10, 95% CI 1.11 – 90.5), longer hospital stay and discharge to skilled nursing facility. Surgical ICU patients – severe TBI and initiation on quetiapine > olanzapine. **Factors associated with discontinuation:** Discharge to home in both medical and surgical populations.
Marshall et al.	2016	USA	Medical	Single centre Retrospective observational cohort study	Hospital discharge	3119	F-40%	Mean 66	**Antipsychotic**	**Prescription changes at hospital discharge:** n=642/3119 (21%) continued on newly initiated antipsychotics at hospital discharge. **Inappropriate discharge Rx:** Unclear **Factors associated with continuation:** Multivariable analysis higher risk if discharged to facility other than home (OR = 2.4, 95% CI 1.9 – 3.1), admission from ED (OR = 1.4, 95% CI 1.2 – 1.7). Prescription of quetiapine>olanzapine>haloperidol. **Factors associated with discontinuation:** Nil described.
Rowe et al.	2015	USA	Trauma-surgical Neurosurgical	Single centre Retrospective observational cohort study	Hospital discharge	341	F-30%	Median 50-55	**Antipsychotic**	**Prescription changes at hospital discharge:** n=82/341 (24%) prescribed new antipsychotic medication. Majority (81.8%) for quetiapine. **Inappropriate discharge Rx?** N=52/82 (67.1%) deemed inappropriate continuation as described in notes – no standardised measure of delirium used. **Factors associated with continuation:** Higher APACHE score at admission to ICU, longer ICU LoS (14 days +/-14 vs 4 days +/- 11), longer hospital LoS, received higher morphine equivalents during admission (1254mg +/- 4410.5 vs 198.5mg +/- 1094) and more benzodiazepine usage days during admission (14days +/- 12 vs 3 +/- 11) **Factors associated with discontinuation:** Nil described
Tomichek et al	2016	USA	Medical Surgical	Single centre Prospective observational cohort study	Hospital discharge	500	F-45%	Median 59 (IQR 49-69)	**Antipsychotic**	**Prescription changes at hospital discharge:** Medication continued: n= 42/172 (24.4%) of survivors treated with AP during ICU **Inappropriate discharge Rx?** Potentially inappropriate in 28/42 with documented normal mental status, potentially appropriate in 7/42 with ongoing delirium.

										Factors associated with continuation: Received AAP and not haloperidol during hospital stay **Factors associated with discontinuation:** Nil described
Wunsch et al.	2014.	Denmark	Medical	Multi-centre. Retrospective observational cohort study.	Post hospital discharge: filled prescription up to 1-year post discharge	24179	M-62%	Median age range: 65-79 = 10020	**Psychiatric medications**	**Prescription changes at hospital discharge:** Medication continued: At 3-month: n = 1261/9912 (12.7%) of survivors At 12-month: n = 101/6485 (1.6%) of survivors. 12-month risk of continuation similar to non-ICU population. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** ICU admission compared to general hospital admission. **Factors associated with discontinuation:** Nil described

S3_Table 4 ANALGESIA MEDICATION

Author	Yr	Country	ICU Population	Nature	Timeline	n	Gender	Age	Analgesia type	Results
Academia et al	2020	USA	Medical Cardiac	Single Centre Retrospective observational cohort study.	Hospital discharge	71	M-62%	Mean 56.7 (SD 13.5)	**OPIATE**	**Prescription changes at hospital discharge:** n= 32/71 (45%) new opiate prescribed. Oxycodone most frequent oral opiate prescribed. **Inappropriate discharge Rx?** 36.7% of new opioid prescription inappropriate based on pre-discharge analgesia requirements. **Factors associated with continuation:** CICU admission. **Factors associated with discontinuation:** Shorter duration (median 4 vs 9.8 days) inpatient opiate use.
Eijsbroek et al	2013	UK	General	Single centre Retrospective observational cohort study.	ICU-clinic: 3- to 9-months post discharge	21	M-52%	Mean 64.4 (SD 13)	**ALL**	**Prescription changes at hospital discharge:** n = 16/21 (76%) new analgesia. n = 13/17 new analgesic drugs non-opioid **Inappropriate discharge Rx?** Patients and carers raised concerns about unnecessary prescribing of analgesics and ineffective pain control. **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Karamchandani et al.	2019	USA	Surgical Veteran Hospital	Single centre Retrospective observational cohort study	3-months post hospital discharge and annually for 3-years	193328	M-97%	Mean 62.5 (9.0) and 66.8 (10.0)	**OPIATE**	**Prescription changes at hospital discharge:** n=7729 developed new, persistent opioid use (defined as use at 3-months). Annual decline of 6% per year in persistent opioid use. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Younger age (mean 62.5 vs 66.8 years) and greater prevalence of alcohol and substance use disorder. **Factors associated with discontinuation:** Nil described
Kranchevich et al.	2021	USA	Medical, surgical, cardiac.	Multicentre Retrospective observational cohort study.	Hospital discharge and post-hospital prescriptions at 3-, 6- and 12-months	342	M-64%	Mean 55.8	**OPIATE**	**Prescription changes at hospital discharge:** n = 164 (47.1%) new opiates prescribed at discharge. 5% of entire cohort had ≥ opiate fills in 12-months post discharge, significantly higher incident if discharged from hospital with opiate. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** history of illicit drug use, longer non-ICU LOS, ICU admission diagnosis of respiratory, surgical, trauma or malignancy. **Factors associated with discontinuation:** older age

MacTavish et al.	2020	UK	Medical, surgical	Multicentre Prospective observational cohort study	ICU-clinic: 4- to 12-weeks post hospital discharge	183	M-56%	Median 58 (IQR 50-65)	**ALL**	**Prescription changes at hospital discharge:** n = 50/183 (27%) new analgesia. New regular opioid use 30/183 (16%) **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
MacTavish et al	2021	UK	General (COVID-19 survivors)	Multicentre Prospective observational cohort study	3-7 months post hospital discharge (ICU clinic)	78	m-64$	Median 59 (IQR 54-67)	**Medication changes**	**Prescription changes at hospital discharge:** There was a significant increase in the number of patients taking regular analgesia following severe COVID-19 infection (23 (29.5%) vs 39 (50%), p<0.001). Of those patients who were receiving either no pain medication or non-opioid pain relief (WHO ladder step 1) before critical care, 8 (10%) were receiving weak or strong opioids (WHO ladder step 2 or 3). **Inappropriate: discharge RX**: not clear **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Tollinche et al	2022	USA	General ICU within Cancer Centre	Single centre Retrospective observational cohort study	Hospital discharge	848	M=56%	Median 64(IQR 52-72)	**OPIATE**	**Prescription changes at hospital discharge:** n=346 (40.8%) discharged with new opiate prescription. I**nappropriate discharge Rx:** Unclear **Factors associated with continuation:** Multivariable modelling found pre-admission benzodiazepine use (OR 3.01, 95% CI 1.41 – 6.45), diagnosis of sepsis at ICU admission (OR 12.99, 95% CI 8.58 – 19.67), and continuous opioid infusion >4h (OR 3.06, 95% CI 1.98 – 4.73) the highest factors linked to continued opioid prescription. **Factors associated with discontinuation:** Univariable analysis – use of propofol infusion, opioids and benzodiazepines during ICU stay associated with decreased odds of new opioid at discharge.
Wang et al	2018	Canada	General Patients >65 and chronic opioid pre-ICU admission	Multicentre Retrospective observational cohort study.	Post-hospital discharge: filled prescription at 80-days	28570	F-60%	Mean 76.7 (SD 7.1)	**OPIATE**	**Prescription changes at hospital discharge:** n = 12403/19584 (63.3%) survivors had filled an opiate prescription in 180-days post hospital discharge. n = 1841/19584 (9.4%) had not filled any opiate prescription in 180-days post hospital discharge. 22.0% of patients had higher MEQ dose cf. pre-hospitalization dose, 19.8% were receiving the same dose, and 21.5% a lower dose. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** COPD, medical patient, fentanyl as primary opioid at admission, concurrent benzodiazepine use at admission.

										Factors associated with discontinuation: Increased age, dementia, MV, tracheostomy, dialysis and codeine or oxycodone as primary opioid at admission.
Witcraft et al.	2021	USA	Medical	Single centre. Retrospective observational cohort study	Hospital discharge	66	M-53%	Mean 58.7 (SD 15.5)	**OPIATE**	**Prescription changes at hospital discharge:** n = 21 (31.8%) new analgesia **Inappropriate discharge Rx?** Possibly - median pain score at hospital DC 0 (IQR 0-5) **Factors associated with continuation:** Higher rate intubation and cumulative dose (opioid fentanyl equivalent dose) **Factors associated with discontinuation:** Nil described
Wunsch et al.	2020	Canada	General	Multicentre. Retrospective observational cohort study.	Post hospital discharge: filled prescription at day-7 and 1-year	25085	M-58%	Mean 61.7 (SD 17.9)	**OPIATE**	**Prescription changes at hospital discharge:** n = 5007 (20%) new opioid prescription filled at day 7. 'Persistent' opioid use at 1-year ranges from 2.6 - 4.9% depending on definition of 'persistent' used. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Surgical patient higher rate of opiate continuation compared to medical patient for both 7-day and 1-year prescription filling. **Factors associated with discontinuation:** Older patient, greater number comorbidities, longer ICU LOS.
von Oelreich et al	2021	Sweden	General	Multicentre Retrospective observational cohort	Up to 24 months post hospital discharge	204402	M=59%	Median 63 (IQR 46-73)	**OPIATE**	**Prescription changes at hospital discharge:** Both populations of opioid naïve and non-opioid naïve patients had initial peak of mean opioid consumption in first quarter following ICU admission. This declined over subsequent 24 months but not returning to baseline. 22,138 developed chronic opioid use following critical care (defined as at least one prescription days 1-90 and days 91-180 post discharge) I**nappropriate discharge Rx:** Unclear **Factors associated with continuation:** Multivariable analysis – higher risk of chronic opioid use: Pre-ICU opioid use (OR 10.31, 95% CI 9.96 – 10.67), acute care surgery (OR 1.40, 95% CI 1.24 – 1.37). **Factors associated with discontinuation:** Nil described.
Yaffe et al	2021	Canada	General	Single centre Retrospective observational cohort	Hospital discharge and annually up to 4-years post discharge	2595	M=60%	Median 46 (IQR 21)	**OPIATE**	**Prescription changes at hospital discharge:** Majority of patients (77%) were non-users of opiates at baseline. The number of non-opiate users in the whole population increased at hospital discharge (88%) and further at 12- and 36-month timepoints (91% and 94% respectively). This correlated to a reduction in intermittent (17% pre-admission – 2.6% at 48-months) and chronic opiate use (6.2% pre-admission – 1.8% at 48-months)

										l**nappropriate discharge Rx:** Unclear **Factors associated with continuation:** Chronic opiate use pre-admission and longer ICU LOS. **Factors associated with discontinuation:** Non-opiate user at pre-admission timepoint.

S3: Table 5 CARDIAC MEDICATIONS

Author	Yr	Country	ICU Population	Nature	Timeline	n	Gender	Age	Medication type	Cardiac
Bell et al	2011	Canada	General Patients ≥ 66 years, with pre-ICU medication use.	Multicentre Retrospective observational cohort study.	Up-to 90 days post hospital discharge	16474	M-57%	Mean 75.4 (SD 5.61)	Statin Antiplatelet Anticoagulant	**Prescription changes at hospital discharge:** n = 1484/10138 (14.6%) of patients on pre- ICU statins were discontinued. n = 552/2423 (22.8%) patients on pre-ICU antiplatelet/anticoagulant were discontinued. Higher OR of discontinuation in ICU population compared to non-ICU hospitalized cohort **Inappropriate discharge Rx?** Yes, results analysed as unintentional discontinuation **Factors associated with continuation: Nil** described **Factors associated with discontinuation:** Nil described
Choon et al	2021	UK	General Patients with AKI for KRT	Single centre Retrospective observational cohort study	Hospital discharge	91	M-55%	Median 61 (IQR 47-71)	Antihypertensive Statin Diuretics Anti-diabetic	**Prescription changes at hospital discharge:** Higher frequency of changes in not restarting pre-hospital medication**:** n=15/35 patients not restarted RAASi at discharge, n=7/20 patients not restarted antidiabetic drugs, n=8/25 patients not restarted a diuretic and n=23/39 not restarted a statin. I**nappropriate discharge Rx:** Unclear **Factors associated with continuation:** Nil described **Factors associated with discontinuation:** Nil described
Coe et al	2020	USA	General/VA Hospitals Statin prescription fill within 180days pre-hospital	Multicentre Retrospective observational cohort study.	Post hospital discharge (up to 180 days post discharge	82242	M–97%	Mean 67.9 (SD 9.5)	Statin	**Prescription changes at hospital discharge:** n = 899/5939 (15.1%) with sepsis diagnosis did not fill a statin prescription following discharge. n = 7611/76303 (10.0%) without sepsis diagnosis did not fill a statin prescription following discharge. **Inappropriate discharge Rx?** Unclear **Factors associated with continuation:** Adjusted to hospital performance, worse performing hospitals had 11% higher odds of discontinuation. **Factors associated with discontinuation:** Admission without sepsis had OR 0.83 (0.77, 0.90) of statin discontinuation
Rizvi et al	2019	USA	General	Single centre Retrospective observational cohort study	Hospital discharge	1010	M-57%	Mean 63.6 (SD 14.8)	Midodrine	**Prescription changes at hospital discharge:** n = 311/909 (34%) survivors continued medication. Discharge from hospital on midodrine had 1.6-fold higher risk of death in following year **Inappropriate discharge Rx?** Potentially inappropriate, 50% of survivors also prescribed antihypertensives.

										Factors associated with continuation: Congestive heart failure **Factors associated with discontinuation:** hypertension, use of IMV, surgical ICU admission, pharmacy intervention (small 10% sub-population reviewed)