Stress ulceration describes injury of the gastrointestinal (GI) mucosa in response to stressors such as hypoperfusion, hypoxia, reperfusion, and imbalance between gastric acid production and mucosal defence mechanisms. Endoscopic evidence of stress ulceration is seen in most patients soon after admission to the intensive care unit, with clinical severity ranging from endoscopic findings only to life-threatening haemorrhage. Certain subgroups of critically ill patients have increased risk of clinically significant GI bleeding (Table 1), with rates of 3.7% in those with coagulopathy and those needing >48 hours of mechanical ventilation, compared with 0.1% in patients without these risk factors. Clinically significant GI bleeding should be prevented where possible as it is associated with a significant attributable morbidity, mortality and increased length of stay in the ICU.

Non-pharmacologic methods for preventing stress ulceration include rapid reversal of shock, providing enteral nutrition and avoiding gastrotoxic medications. Additionally, stress ulcer prophylaxis (SUP) medications are commonly prescribed to ICU patients, frequently as part of “bundles” of general care such as the FASTHUG (feeding, analgesia, sedation, thromboembolic prophylaxis, head-of-bed elevation, stress ulcer prevention, and glucose control) mnemonic. We are unaware of any Australian SUP prescribing guidelines for critically ill patients. Knowledge of Australian SUP prescribing practices has previously been limited to snapshot surveys showing that proton pump inhibitors (PPIs) are increasingly used as first-line SUP agents, histamine-2 receptor blockers (H2RBs) are sometimes used, while sucralfate and antacids are used infrequently — similar to studies in other regions. Apart from evidence showing superiority of H2RBs over sucralfate or antacids, there is insufficient evidence to make a definitive recommendation on a particular type of SUP at this time.

Studies in the United States have shown a high incidence of SUP prescribing to critically ill patients who do not have current evidence-based indications for SUP medication and that ICU-prescribed SUP medications are frequently continued when patients are discharged to the ward, and not ceased on hospital discharge. We are unaware of any published data showing an Australian perspective on this. We investigated the hypothesis that many Australian patients who were prescribed SUP medication while critically ill have this inappropriately continued beyond the ICU setting.

**ABSTRACT**

**Objective:** To determine how frequently stress ulcer prophylaxis (SUP) medications prescribed in the intensive care unit are inappropriately continued on the ward and on hospital discharge.

**Design:** Retrospective cohort study; chart review.

**Setting:** Two Australian ICUs: one tertiary centre and one metropolitan centre.

**Participants:** We included 387 adult, non-pregnant patients who were admitted to the ICU between 1 February 2011 and 31 March 2011 and who survived to hospital discharge.

**Main outcome measures:** Rate of unnecessary continuation of ICU-prescribed SUP medications on the ward and on discharge from hospital.

**Results:** While in the ICU, 329 of the 387 patients (85%) were prescribed SUP medications. Of the 233 patients who had not been taking acid-suppressive medications before admission to the ICU, 190 were prescribed SUP medications in the ICU. Of these 190 patients, most (63%) had their SUP continued in the ward without any obvious indication, and many (39%) had their SUP medications inappropriately continued on discharge from hospital.

**Conclusions:** SUP medications commenced in ICU are frequently continued unnecessarily, both in the wards and on hospital discharge.

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**Methods**

This was an Australian retrospective observational study, conducted at one tertiary and one metropolitan ICU. The Southern Health Human Research Ethics Committee approved the study as a quality assurance exercise; hence, the requirement for informed consent was waived.

The files of all non-pregnant patients aged over 18 years who were admitted to the ICU from 1 February 2011 to 31 March 2011 and who survived to hospital discharge were hand searched by two of us (KJF or KLB). Demographic data collected included age, sex, ICU length of stay, admission source (elective v emergency) and ICU campus (tertiary v metropolitan).
Data were collected for all acid-suppressive medications (ASMs) (PPIs, H2RBs, sucralfate and antacids), including dose, frequency and route of administration, location of commencement and cessation (pre-ICU, ICU, ward or hospital discharge), and indications (Table 2). Patients without one of these indications were considered to have continued receiving their SUP medication inappropriately. Patients who were taking ASMs before ICU admission were considered separately. Data were collected on the initial ASM used, and whether this was changed or ceased during hospital admission.

Pre-specified subgroups for analysis included:
- cardiac surgical v other surgical patients
- surgical v medical patients
- elective v emergency ICU admissions
- age ≤ 65 years v > 65 years
- metropolitan v tertiary centre
- male v female patients.

Statistical analysis was performed by a Southern Health biostatistician, using Excel 2010 (Microsoft). Proportions were compared with χ² analysis using Yates correction for 2 × 2 tables.

### Results

This study included 387 patients, of whom 85% received SUP medication in the ICU (Figure 1). Demographic data are summarised in Table 3.
There were 233 patients who had not been taking ASMs before ICU admission. Most (63%) of the 190 patients who had newly received SUP medications in the ICU continued receiving these medications in the ward without any obvious indication, and 75 patients (39%) had these medications continued at discharge from hospital, despite having no indication for SUP medication on record (Figure 2).

By the time they were discharged from hospital, 29 of the 146 patients who were known to be taking ASMs before ICU admission (20%) had their prescription changed to a different drug, and 11 (8%) had their ASM ceased. Only two patients had a documented indication for these changes.

Of the prespecified subgroups, the tertiary ICU prescribed significantly more SUP medications than the metropolitan centre (92% v 69% of patients, respectively). The high number of cardiac surgical patients at the tertiary centre may explain this, as cardiac surgical patients were prescribed significantly more SUP medications than other surgical patients. Significantly more elective than emergency patients (89% v 74%) inappropriately continued receiving SUP medications in the ward, although this difference became insignificant by the time of discharge from hospital. No other statistically significant differences were noted (Table 4).

Discussion

Our study showed that SUP medications commenced in the ICU are often unnecessarily continued beyond the ICU setting. Most (63%) of the patients who were prescribed new SUP medications while critically ill had these medications continued in the ward without any obvious indication, and 39% had SUP medications inappropriately continued at hospital discharge. This is particularly significant, as recent evidence suggests that SUP may not benefit critically ill patients as much as previously suggested.\(^2^1\)\(^-\)\(^2^3\) This may be due to changes in overall ICU care which have decreased the baseline risk of stress ulceration — particularly early enteral nutrition and improved resuscitation from shock, which decrease the baseline risk of stress ulceration in the ICU. Despite this emerging evidence, but consistent with a 2005 Australian survey,\(^9\) 85% of our study population received SUP medications while in the ICU.

Studies from the US show similar rates (24.4%\(^2^0\) to 31%\(^1^7\)) of inappropriate continuation of ICU-prescribed SUP medication on hospital discharge. Inadequate understanding of appropriate indications for SUP and perceived lack of harm from these medications may be contributing to these medication errors. Similar factors may have played a role for the 38 of our patients who had their pre-ICU ASM ceased or changed without an obvious reason during their hospital discharge.\(^2^4\)
admission. Additionally, almost all of our patients (95%) who received SUP medication were prescribed PPIs — compared with the 45% reported previously,9 despite no clear data to suggest superiority of PPIs over H2RBs in reducing mortality in ICU patients.10,23

The difference in SUP prescription between the two ICU campuses may reflect a different unit casemix, varying policies or guidelines, different medical staff or other factors such as pharmacist presence on ward rounds. Subgroup differences in ward-based inappropriate continuation of ICU-prescribed SUP became statistically insignificant at hospital discharge, suggesting that interventions to reduce unnecessary SUP prescription should be hospital-wide rather than targeted at particular groups.

The sequelae of unnecessary ASMs in this patient group are unknown; however, there are many documented adverse reactions to the short- and long-term use of H2RBs and PPIs, including increased incidence of community- and hospital-acquired pneumonia24,25 (including ventilator-associated pneumonia), *Clostridium difficile* disease,26-28 interstitial nephritis and allergic reactions,29 osteoporosis and fractures,30 vitamin B12 deficiency,31 and potential interactions with other medications such as those that require an acidic environment for absorption. The adverse effects of polypharmacy in elderly patients are well documented,32,33 and most of our patients were elderly. Evidence from interventions reducing polypharmacy in the elderly34,35 could perhaps be used to plan similar studies in post-ICU patients; however, interventional studies attempting to decrease unnecessary SUP prescription overseas have had varying degrees of success.18,36,37

This study has important limitations. It looked at a relatively small number of patients in only two ICUs; therefore, the findings may represent a local problem only, rather than overall Australian practice, although anecdotally this seems unlikely. The study’s retrospective nature may have led to missed indications for prescribed ASMs due to poor documentation in the clinical record or missing data. We have not adjusted for multiple comparisons; hence, some findings may be due to chance alone. We have not studied outpatient changes in medication, and may be unaware of cases where ASMs are appropriately ceased after hospital discharge.

This study raises several important questions that deserve further research. Although most of our ICU patients receive SUP medication, is this practice evidence-based? What are the sequelae of unnecessary SUP prescription for the post-ICU patient? Perhaps most importantly, how can the unnecessary prescription of SUP medication be decreased? Should intensivists be responsible for stopping SUP medications on ICU discharge, or perhaps, for providing a “stop date” for the ward, analogous to that for antibiotics commenced in the ICU? Quantifying the financial cost of inappropriate SUP prescribing to the health care system and to individuals would also be important for future studies.

**Conclusion**

This study showed a high rate of inappropriate continuation of SUP medication beyond the ICU setting. Clinicians should give more consideration to stopping SUP (and other) medications that are no longer required, to prevent possible patient harm, as well as unnecessary costs for individuals and the health care system. Further studies are needed to quantify these outcomes in more detail.

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**Table 4. Stress ulcer prophylaxis (SUP) treatment in 233 patients not taking acid-suppressive medications before admission to the intensive care unit**

<table>
<thead>
<tr>
<th>Patient subgroup</th>
<th>Received SUP in the ICU</th>
<th>SUP continued inappropriately in the ward (n = 150)</th>
<th>SUP continued inappropriately on discharge (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac surgical</td>
<td>55/58 (95%)*</td>
<td>46/49 (94%)</td>
<td>19/22 (86%)</td>
</tr>
<tr>
<td>Other surgical</td>
<td>47/64 (73%)*</td>
<td>33/41 (80%)</td>
<td>23/29 (79%)</td>
</tr>
<tr>
<td>&gt;65 years old</td>
<td>86/106 (81%)</td>
<td>61/72 (85%)</td>
<td>37/44 (84%)</td>
</tr>
<tr>
<td>&lt;65 years old</td>
<td>104/127 (82%)</td>
<td>59/78 (76%)</td>
<td>38/55 (69%)</td>
</tr>
<tr>
<td>Male</td>
<td>124/147 (84%)</td>
<td>81/97 (84%)</td>
<td>53/68 (78%)</td>
</tr>
<tr>
<td>Female</td>
<td>66/86 (77%)</td>
<td>39/53 (74%)</td>
<td>22/31 (71%)</td>
</tr>
<tr>
<td>Elective admission†</td>
<td>66/79 (84%)</td>
<td>50/56 (89%)*</td>
<td>26/31 (84%)</td>
</tr>
<tr>
<td>Emergency admission†</td>
<td>122/150 (81%)</td>
<td>68/92 (74%)*</td>
<td>48/67 (72%)</td>
</tr>
<tr>
<td>Metropolitan ICU</td>
<td>75/108 (69%)*</td>
<td>40/49 (82%)</td>
<td>28/36 (78%)</td>
</tr>
<tr>
<td>Tertiary ICU</td>
<td>115/125 (92%)*</td>
<td>80/101 (79%)</td>
<td>47/63 (75%)</td>
</tr>
<tr>
<td>Surgical</td>
<td>102/122 (84%)</td>
<td>79/90 (88%)*</td>
<td>42/51 (82%)</td>
</tr>
<tr>
<td>Medical</td>
<td>88/111 (79%)</td>
<td>41/60 (68%)*</td>
<td>33/48 (69%)</td>
</tr>
</tbody>
</table>

* Indicates a statistically significant result. † Eight patients did not have admission source data available.
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Competing interests
None declared.

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