Hyperglycaemia frequently occurs in critically ill patients, with studies reporting that almost 70% of intensive care unit (ICU) patients, including diabetics, have blood glucose $\geq 110$ mg/dl. Hyperglycaemia is associated with complications, prolonged ICU and hospital stay, and increased mortality.

However, to date, no previous research has systematically reviewed the clinical burden of hyperglycaemia in ICUs in observational studies, which are in general more representative of real-world patients.

**Method**

We followed the Joanna Briggs methodology guideline to perform a systematic scoping review to identify relevant publications in Medline, Embase, and The Cochrane Library from January 2000 to December 2015. Two reviewers assessed studies for eligibility. Studies were included if they reported on mortality, infections, hospital/ICU length of stay, time on ventilation and ICU-acquired weakness in adult patients (≥18 years) with hyperglycaemia in ICUs. No definition for hyperglycaemia was set a priori. Data extraction was performed by one reviewer and checked by another.

**Results**

Overall, 4,388 records were retrieved. After deduplication, 3,063 titles were screened, 385 full-text articles were reviewed, and 77 studies (1,172,172 patients) were included in the review (Figure 1).

**Study design and methodology**

The majority of the included studies (74%) were conducted in either the USA (35 studies) or in Europe (22 studies). Most of the studies were retrospective (40) and 32 prospective. Most of the research available on the clinical burden of hyperglycaemia in ICU was conducted in trauma ICU patients (25 studies) and in mixed ICU patients (28 studies, including 10 conducted exclusively in cardiac ICU patients). Sample sizes varied widely from 28 patients to 779,785 patients. The most common blood glucose thresholds used to define hyperglycaemia were 200 mg/dl (18 studies), 110 mg/dl (15 studies) and 140 mg/dl (8 studies). The range of thresholds varied from 100 mg/dl to 300 mg/dl.

Regarding the method of blood glucose measurement, a high variability was observed across studies. Studies reported having measured either capillary (12 studies), arterial (11 studies), or venous blood glucose (8 studies), using either blood gas analysers, point-of-care glucometers, point-of-care finger sticks or laboratory interfaces. The timing/frequency of measurement was seldom reported in the included studies, with only ten studies reporting having measured blood glucose levels at ICU admission.

The majority of studies (68) reported on mortality. Other outcomes, such as ICU and hospital length of stay and infections were less frequently reported (38, 27 and 23 studies, respectively) (see Figure 2). Studies conducted in trauma and mixed ICU patients most frequently reported on hospital mortality and ICU and hospital length of stay. Infections were more commonly reported in trauma (43.5%) and cardiac ICU patients (17.4%). Mortality was reported together with ICU and hospital length of stay in 14 studies in trauma ICU patients, in four studies in mixed ICU patients and in one study in cardiac ICU patients.

**Studies reporting on infections**

Of the studies that reported on infections, only eight assessed whether hyperglycaemia was a risk factor for developing infections during ICU stay $^{14}$ and five of them $^{12,13,14,15,16}$ identified it as an independent risk factor for infections. Across these latter studies, hyperglycaemia, as an independent risk factor was assessed as hyperglycaemic index (ORan.8, 95% CI 1.3 - 2.5) $^{14}$, as blood glucose levels $\geq 200$ mg/dl (p=0.02; no ORs reported) $^{12}$, $^{14}$, $^{15}$, as infection rate in the ICU and hospital stay $^{13}$, (OR=6.04, 95% CI 1.8 - 20.0) $^{13}$, as infection rate in the ICU and hospital stay as a whole $^{14}$, (OR=1.82, 95% CI 1.0 - 3.1) $^{14}$, (OR=1.92, 95% CI 1.3 - 2.8) $^{16}$, as number of infections, septic shock, or death during ICU stay $^{14}$, (OR=0.67, 95% CI 0.46 - 1.0) $^{14}$, as number of infections, septic shock, or death during ICU stay as a whole $^{14}$, (OR=0.71, 95% CI 0.49 - 1.0) $^{14}$, (OR=0.6, 95% CI 0.3 - 0.9) $^{13}$, as severe infection $^{13}$, (OR=1.11, 95% CI 0.5 - 2.2) $^{13}$, as the number of infections and septic shock $^{14}$, (OR=1.77, 95% CI 0.45 - 5.2) $^{14}$.

**Studies reporting on ICU and hospital length of stay**

Of the studies that reported on ICU and hospital length of stay, only one assessed whether hyperglycaemic patients had an increased risk for longer ICU and hospital stay $^{14}$. This study showed that hyperglycaemia was an independent predictor of ICU and hospital length of stay, independent of Injury Severity Score (partial $r=0.01$) and age (partial $t$-test, $p=0.016$).

**Conclusions**

Hyperglycaemia at admission or acquired in ICU is significantly associated with increased disease severity and considerable burden on healthcare resources. The available literature on the burden of hyperglycaemia in ICU is highly heterogeneous in the blood glucose thresholds used, in how blood glucose is measured and monitored, and in how glucose levels are reported at the different points of time.

**Disclosures**

AD and MM are permanent employees of Nestlé Health Science. E.O, NP and JCP have received consulting fees from Nestle Health Science. Abstract prepared for the Clinical Nutrition Week 2017, conference of the American Society for Parenteral and enteral nutrition (ASPEN).

**Table 1—Hyperglycaemia as a risk factor for long-term mortality in ICU patients**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Sample size, n</th>
<th>Risk factor</th>
<th>Mortality type</th>
<th>Outcome (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deckers et al. 2013</td>
<td>All patients, n=11,324</td>
<td>Admission BG</td>
<td>20-year</td>
<td>Mld-OGI: ORan.1 (1.1 – 1.2) Severe-OGI: ORan.1 (1.1 – 1.1)</td>
</tr>
<tr>
<td>Dihlberg et al.</td>
<td>20-year among</td>
<td>Mld-OGI: ORan.1 (1.0 – 1.2) Severe-OGI: ORan.1 (1.1 – 1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olofsson et al.</td>
<td>15-day survivors</td>
<td>Mld-OGI: ORan.1 (0.8 – 0.8) Severe-OGI: ORan.1 (1.1 – 1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kadri et al. 2006</td>
<td>Non-diabetic patients, n=1,604</td>
<td>Admission BG</td>
<td>One-year mortality</td>
<td>Admission glucose (≥ 299 mg/dl) NHANES III (OR: 1.41, 95% CI 1.20 – 1.67) NHANES IV (OR: 1.35, 95% CI 1.19 – 1.51)</td>
</tr>
<tr>
<td>Manser et al. 2017</td>
<td>All patients, mixed medical-surgical units, n=1,694</td>
<td>BG, n=150 mg/dl</td>
<td>5-year mortality</td>
<td>NH-R2: 1.01 (1.01 – 3.36, p=0.0022)</td>
</tr>
</tbody>
</table>

**Studies reporting on infections**

Of the studies that reported on infections, only eight assessed whether hyperglycaemia was a risk factor for developing infections during ICU stay $^{14}$ and five of them $^{12,13,14,15,16}$ identified it as an independent risk factor for infections. Across these latter studies, hyperglycaemia, as an independent risk factor was assessed as hyperglycaemic index (ORan.8, 95% CI 1.3-2.5), as blood glucose levels $\geq 200$ mg/dl (p=0.02; no ORs reported) $^{12}$, $^{14}$, $^{15}$, as infection rate in the ICU and hospital stay $^{13}$, (OR=6.04, 95% CI 1.8 - 20.0) $^{13}$, as infection rate in the ICU and hospital stay as a whole $^{14}$, (OR=0.64, 95% CI 0.3 - 0.9) $^{13}$, as severe infection $^{13}$, (OR=1.11, 95% CI 0.5 - 2.2) $^{13}$, as the number of infections and septic shock $^{14}$, (OR=1.77, 95% CI 0.45 - 5.2) $^{14}$.