With the development and rise of antibiotic resistance there is a strong public health need for new antibiotics. However, new antibiotics face significant scientific, regulatory, clinical and economic challenges. As discussed in a recent ISPOR panel, it is difficult to quantify their value with, for example, a lack of return on investment being problematic.

Acute bacterial skin and skin structure infections (ABSSSI) was recently described by the US Food and Drug Administration (FDA) as a bacterial infection of the skin with a lesion size area of ≤25 cm² (based on the area of redness, oedema or induration) including the following three types of infection: cellulitis/erysipelas, wound infection and major cutaneous abscess. In this context, surgical site infections (SSI) is reportedly the most common healthcare-associated infection with approximately 543,149 annually across the European Union and the European Economic Area (EU/EEA) and are associated with longer post-operative hospital stays and therefore costs.

This study aimed to understand the current and additional evidence required to help quantify the potential value of new antibiotics for ABSSSI and SSI. More specifically, it examined the epidemiology, economic and human burden of ABSSSI and SSI with a focus on the European region.

Methods

Targeted literature reviews

Four targeted literature reviews (TLR) were conducted in September 2017 in the Embase® and MEDLINE® databases to gather evidence in ABSSSI and SSI. Epidemiology (TLR1), utility and health-related quality of life (HRQL) (TLR2), economic modelling (TLR3) and cost and resource use (TLR4).

Table 1 summarises the methods used, the search date limits and the review eligibility criteria. In addition, bibliographic searches and manual searching of grey and published literature were performed to identify relevant literature of interest.

Abstracts of citations were screened methodically by a reviewer, and eligible studies were included. Following abstract review, full-text articles of the potentially relevant studies were reviewed by a single reviewer. Data extraction of the included studies was carried out by an independent reviewer.

Table 1: Method summary (PICO5)

<table>
<thead>
<tr>
<th>Category</th>
<th>Study type</th>
<th>Language</th>
<th>Date limits</th>
<th>Case number</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR1</td>
<td>Epidemiology</td>
<td>English only</td>
<td>2013-2016</td>
<td>12</td>
<td>Adult patients with ABSSSI (n=2904)</td>
<td>ABSSSI antibiotics</td>
<td>No restriction</td>
</tr>
<tr>
<td>TLR2</td>
<td>Utility/HRQL</td>
<td>English only</td>
<td>2012-2016</td>
<td>312</td>
<td>Adult patients with SSTI</td>
<td>ABSSSI antibiotics</td>
<td>No restriction</td>
</tr>
<tr>
<td>TLR3</td>
<td>Economic modelling</td>
<td>English only</td>
<td>2011-2016</td>
<td>28</td>
<td>SSTI (n=4)</td>
<td>ABSSSI antibiotics</td>
<td>No restriction</td>
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<tr>
<td>TLR4</td>
<td>Cost and resource use</td>
<td>English only</td>
<td>2011-2016</td>
<td>1,368</td>
<td>Adult patients with SSI</td>
<td>ABSSSI antibiotics</td>
<td>No restriction</td>
</tr>
</tbody>
</table>

Health economics and outcomes research expert interviews

To complement the targeted literature reviews, interviews with health economics and outcomes research experts from the European Union Five (EU5) were conducted. The aim was to gain further insights into the best approaches to data gaps and to understand what they considered important for patient management, patient access and combating resistance.

The themes included in Figure 2 were discussed during the interviews and the interviewees provided information that they considered key to their country.

Figure 1: HEOR expert interview themes

Results

Targeted literature reviews

Figure 2 shows the number of studies included. A total of 48 EU studies were included for qualitative synthesis. Figure 3 shows the distribution of studies by location. Limited European studies were studied.

Figure 2: PRISMA details

Discussion

There are several challenges associated with the introduction of new antibiotics including significant scientific, regulatory, clinical and economic challenges. For example, health technology assessment (HTA) bodies mustvery demonstrate of clinical superiority, whereas antibiotics are normally investigated in non-inferiority trials. In fact, clinical evidence does not address benefits beyond the individual patient, the public health threat.

Limited large, homogenous epidemiology studies were conducted for the EU. However, from the studies retrieved diabetes is reported as the most prevalent comorbidity, presence of mixed pathogens and rapidly increasing levels of resistance to many commonly used antibiotics.

Limited economic modelling and evidence of the use of new antibiotics is available and may be due to the lack of head-to-head comparison trials for ABSSSI. Given that ABSSSI is highly heterogeneous, and comedited conditions play an important role in its burden, future economic evaluations are warranted to better assess the burden of ABSSSI and SSI, and highlight a need for further studies to understand the true value in terms of efficacy, safety and ultimately in terms of associated healthcare costs.

Conclusions

Alternative and innovative HTA approaches are needed to assess the value of antibiotics, including consideration of broader public health benefits. This review highlights the evidence base for ABSSSI and SSI in the European Union and for HTA, economic modelling, and cost and resource use, principally in Europe. Further data generation in this area is needed. There is awareness of the requirement for more studies, however, there is a need to understand the evidence base in terms of efficacy, safety and ultimately in terms of associated healthcare costs.

References

1. ISPOR panel (IP20): How Can We Assess the Value of New Antibiotics, 2017
2. FDA, Guidance for Industry. Acute Bacterial Skin and Skin Structure Infections: Developing Drugs for Treatment. 2013
3. European Centre for Disease Prevention and Control: Clinical recommendations for the use of linezolid in ABSSSI. 2011

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