The Problem – Where’s that deterioration of the patient’s condition coming from?

If a new event is regarded to be caused by the medication, further information which drug is the most likely is needed.
We compare summary of product characteristics (SPC), the SIDER Side Effect Resource, OpenVigilIFDA and OpenVigil 2 as possible sources of information.
SPCs and SIDER – which relies on data from SPCs – cannot be entirely trusted, unfortunately (fig. 1).

Our solution: OpenVigilFDA at bedside

Case reports: Liver damage (gGT↑)
A patient at a radiotherapy ward developed increased gamma-glutamyltransferase (gGT) blood levels. Ultrasound did not reveal filiae in the liver.
OpenVigilFDA was used to rank the RRR of all drugs of the patient for this adverse event (fig. 2, cf. material and methods below). Pantoprazole was identified as the most likely agent and subsequently stopped. Omeprazole and ranitidine showed comparable associations with increased gGT (fig. 3, tab. 1). Therefore, a magaldrate was chosen for this patient. The condition improved.

Of note, we used this approach successfully for a similar patient who also developed an increased gGT while on pantoprazole and for yet another patient where dipyrone (INN: metamizol) was identified.

Comparison with other data:
OpenVigil 2 uses cleaned data obtained by other cleaning procedures than OpenVigilFDA. The lower-bound of the 95%-confidence interval of the ROR was calculated (fig. 4).
All data are summarized in tab. 1:

Tab. 1: Comparison of frequencies and risks for gGT increased

<table>
<thead>
<tr>
<th>Drug</th>
<th>SPC</th>
<th>SIDER</th>
<th>OpenVigilFDA (RRR)</th>
<th>OpenVigil 2 [lb ROR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pantoprazole</td>
<td>Uncommon (0.1-1%)</td>
<td>Yes (no frequency data)</td>
<td>1.9</td>
<td>1.97</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>No</td>
<td>No</td>
<td>1.48</td>
<td>1.22</td>
</tr>
<tr>
<td>MCP</td>
<td>No</td>
<td>No</td>
<td>0.96</td>
<td>0.25</td>
</tr>
<tr>
<td>L-Thyroxine</td>
<td>No</td>
<td>No</td>
<td>0.98</td>
<td>1.01</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Uncommon (0.1-1%)</td>
<td>No</td>
<td>1.78</td>
<td>1.63</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Rare (0.01-0.1%)</td>
<td>No</td>
<td>1.68</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Summarizing, all methods deliver comparable results. While it takes several minutes to operate OpenVigil 2 or SIDER or to download all relevant SPCs, OpenVigilFDA can provide this information within a few seconds.

Case reports: Thrombocytopenia
A patient at a neurosurgery ward developed spontaneous bleedings and thrombocytopenia during treatment with three anticonvulsants.
OpenVigilFDA was used to rank all drugs of the patient for the adverse event (fig. 5).
Levetiracetam was stopped. The condition improved.

Comparison with other data:

A case of isolated thrombocytopenia:
A female patient at a radiotherapy ward developed an isolated thrombocytopenia, i.e., no concomitant anaemia or neutropenia. Based on our previous experience with bone marrow damaging radiooncologic treatments, this could not be explained.
In this case, OpenVigil 2 was used to rank all drugs (fig. 6). Dexamethasone appears to confer the highest risk. Since dexamethasone is used generally at our ward in patients with failing bone marrow due to the radiooncologic therapy, we assumed this signal to be caused by confounding. Cefpodoxime could be stopped because antibiotic treatment was no longer necessary. The condition improved.

Material and Methods: Individual German SPCs, SIDER and OpenVigil 2 and OpenVigilFDA were used to extract information on the frequency and association of drugs and certain adverse events. These OpenVigil tools operate on D.S. American pharmacovigilance data. All data were extracted Dec 2015 to Feb 2016 using the latest datasets. We use a reverse disproportionality analysis (rDPA) to extract the Reporting Odds Ratio (ROR), an adaption of the Odds Ratio or the Relative Reporting Ratio (RRR), in magnitude and explanatory power similar to RORs for assessing the strength of the possible association. The lower bound of the ROR (lb ROR) is used for very conservative signal generation. Where applicable, multiple adverse event terms were concatenated with Boolean logic (AND, NOT, …) and confounders were eliminated.


http://openvigil.sf.net