Overestimation of the risk for adr’s due to the presentation in the package leaflets

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Background

Assessing the risk of drug treatment is important in the decision making by patients and is linked to compliance.
Background

Patients’ interpretation and estimation of risk depend on how the information is presented and may play a large role for how the receiver understands and interprets the information as well as the acceptance or denial of risk.
Background

EU Directive
- inclusion in the packaging of PIL is obligatory,
  - must be written and designed to be clear and understandable
  - the frequency of adverse drug reactions (ADRs) can be denoted by the use of five verbal descriptors
(e) a description of the adverse reactions which may occur under normal use of the medicinal product and, if necessary, the action to be taken in such a case; the patient should be expressly asked to communicate any adverse reaction which is not mentioned in the package leaflet to his doctor or pharmacist;
2. The package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals. The package leaflet must be clearly legible in the official language or languages of the Member State in which the medicinal product is placed on the market.
## Background

<table>
<thead>
<tr>
<th>Classification</th>
<th>Frequency Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>10%+</td>
<td>More than 1 per 10</td>
</tr>
<tr>
<td>Common</td>
<td>&gt; 1% and &lt; 10%</td>
<td>Less than 1 per 10 but more than 1 per 100</td>
</tr>
<tr>
<td>Uncommon</td>
<td>0.1% to 1%</td>
<td>Less than 1 per 100 but more than 1 per 1000</td>
</tr>
<tr>
<td>Rare</td>
<td>0.01% to 0.1%</td>
<td>Less than 1 per 1000</td>
</tr>
<tr>
<td>Very rare</td>
<td>up to 0.01%</td>
<td>(Less than 1 per 10,000)</td>
</tr>
</tbody>
</table>
The mean likelihood estimate given for the side effect was >4 times higher in the verbal group compared to the numerical group (34.2% vs 8.1%)

Generic substitution since 2002-10-01

A new product may be dispensed at each fill of the prescription
We tend to overestimate the risk for unusual and underestimate the risk for common events.

Presentation of the risk for adverse drug reactions in verbal form is associated with large individual differences and overestimation of the risk, increase in negative perceptions of the medicine that may increase non-compliant behaviour.
Objective

To study how the risk for adverse drug reactions is presented in patient information leaflets (PIL)
Main Outcome Measures

Which adverse drug reactions are mentioned, how the risk is expressed - verbally, numerically or both
162 patient information leaflets (PIL) for 40 substances were examined. For 34 of the 40 substances there were 2-13 different brands (generics).
## Material

<table>
<thead>
<tr>
<th>ATC-code</th>
<th>substances</th>
<th>No of substances</th>
<th>No of products</th>
</tr>
</thead>
<tbody>
<tr>
<td>C07</td>
<td>Beta blockers</td>
<td>8</td>
<td>42</td>
</tr>
<tr>
<td>C10</td>
<td>Lipid lowering agents</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>D05</td>
<td>Psoriasis, topical</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>D07AC</td>
<td>Corticosteroids topical</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>H02</td>
<td>Corticosteroids systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M01 AE</td>
<td>NSAID’s</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>M02</td>
<td>NSAIDs topical</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>N02</td>
<td>opioids</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>N05B</td>
<td>Anxiolytics</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>N06AB</td>
<td>Antidepressants (SSRIs)</td>
<td>6</td>
<td>34</td>
</tr>
<tr>
<td>R06A</td>
<td>Antihistamines</td>
<td>2</td>
<td>9</td>
</tr>
</tbody>
</table>
Results

The risk for adverse drug reactions expressed
both verbally and numerically - 63%
verbal expressions only - 16%
sometimes numerically, sometimes verbally only
and sometimes in a mix
Results

substances - several brands on the market

the ADR’s mentioned in PIL

23% (3/13) - 93% (37/40)

of those found in the Summary of Product Characteristics
Results

ADR’s presented in PIL for brands of the same substance varied from <50 – 100% correspondence.

Both the expression for the risk as well as frequencies varied to the same extent.
Conclusions

There is a large variation for the adverse drug reactions mentioned and how risk for ADRs' is expressed
Conclusions

When assessing the benefit-risk ratio of a drug treatment, the expression for the risk of an ADR in patient information leaflets may lead to that patients’ overestimate the risk and may contribute to non-compliant behaviour.
Conclusions

The differences between patient information leaflets for drugs with generic substitution may cause confusion and impaired trust for the dispensed drug, an impaired trust that may contribute to decreased compliance.
Thanks to the students

Lilly Eriksson & Eva Marklund
Gun Hillbur
Karolina Häggbom & Karin Sandström
Lotta Ljungström
Karoline Maricak
Liselott Mattsson & Maria Waaranperä
Linda Nyberg
Anna Sjöberg
Marie Thelaus
Thank you for your attention
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