Communicating Benefit and Harm Information

SCOPE Workshop:
Risk Communication on Medicines
Madrid June 2016

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Professor of Pharmacy Practice, University of Leeds & Co-founder & Academic Advisor, Luto Research
Communicating with lay people

- Ernest Rutherford
  - New Zealand born
  - ‘Father of nuclear physics’

- Science “has no merit unless it can be explained to a barmaid”
1. Are we using the wrong language?
   - ‘Pharmacovigilance’?
   - ‘Benefit-risk’ or ‘benefit-harm’?

2. User testing – the how and why
   - User testing in a nutshell
   - Importance of using ‘real’ people

3. Ten tips for writing for lay people
   - Applying to PRAC wordings and others – fit for purpose?
   - SmPCs – fit for purpose?

4. Where is the benefit?
   - ‘Benefit’ information is still the poor relation
   - Impact of numerical benefit information

5. Summary
Background

Consumer medicines information research group

- Professor of Pharmacy Practice
- 25 year programme, funded by Department of Health, EU, DIA, TGA
- Expert advice to MHRA, EMA and FDA
- Leader of a World Universities Network collaboration

University Spin Out company

- Co-founder and academic advisor
- Develops, refines & tests health information
  - >20,000 participant interviews
- Patient information leaflets / package leaflets
- Educational materials for HCPs & patients
- RMP and Clinical Study Public Summaries
YOUR PRESCRIPTION FOR DISTALGESIC
(Dextropropoxyphene 32.5mg with Paracetamol 325mg)

Your doctor has prescribed Distalgesic tablets for the relief of your pain. Please read this leaflet carefully before you start to take the tablets.

1. Alcohol
   The consumption of alcohol whilst taking medicine may be dangerous therefore;
   
   **AVOID ALCOHOL WHilst TAKING DISTALGESIC**

2. Working
   Some people find that Distalgesic tablets make them drowsy or dizzy at first, especially if they are taking tranquillisers or sleeping pills as well. You should be careful when driving or operating machinery until you know your reaction to Distalgesic.

3. Dosage
   **TAKE NO MORE THAN TWO TABLETS AT A TIME**
   **TAKE NO MORE THAN EIGHT TABLETS A DAY**

4. Pregnancy
   You should not take Distalgesic or any other drugs during pregnancy unless your doctor knows you are pregnant and specifically prescribes them.

5. Overdosage
   **IF YOU SUSPECT THAT YOU, OR ANYONE ELSE, HAS TAKEN TOO MANY DISTALGESIC TABLETS DON’T DELAY, DIAL 999 FOR AN AMBULANCE IMMEDIATELY, THEN PHONE YOUR DOCTOR**

6. Remember
   These tablets have been prescribed for YOUR USE ONLY. Keep them in a safe place and do NOT allow anyone else to take them. Destroy unused tablets at the end of treatment. If you have any questions ask your doctor or pharmacist.
Patients value a balance of benefit & harm information
- Current balance in favour of harm information

Most patients want to know about any possible side-effects
- Which side effects to leave out?

Patients do not want written information as substitute for spoken information
- SCOPE Preference is face-to-face discussion with healthcare professional

Patients want information about all their medicines in context of information about the illness – not separate
- SCOPE Prefer one resource addressing disease and all medicines – not separate for each medicine

Patients don’t see improving compliance as role of information provision
- Some health professionals see improving compliance as prime function

Raynor DK et al Systematic review of research on written medicines information. HTA 2007
An informed patient is not necessarily an obedient patient.

- US RCAC ‘informed independent judgements’
- Patient empowerment’ means what it says
- An informed patient may decide to do see as right for them - and not professional advice - this is a good outcome

Use ‘Universal Precautions’

- Develop single easy to read & access pieces of information to benefit all patients - do not ‘target’ those with low literacy
- AHRQ: All people’s ability to make good decisions depends on easy to understand information
- Use plain language that anyone can understand
- Websites should be as easy & clear as possible for all
1. Are we still using the wrong language?

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Millions 'cannot read well enough for karaoke'
By Paul Bignell  Published: 17 December

Millions of adults have such poor reading skills that they struggle to keep up with karaoke lyrics, government research has found.

Research for the Department for Education found songs like Frank Sinatra's "New York, New York" require reading skills lacked by more than 5 million adults.
The wrong language

‘Pharmacovigilance’ or ‘Farmacovigilancia’

- How many members of public understand?
- How many health professionals understand?
- Should we be talking about: ‘Safety monitoring of medicines’?
The black triangle headline wording is:

- ‘This medicine is subject to additional monitoring’

But this is not the key message, which is:

- ‘We are closely watching this medicine for side effects’

Do lay people understand it?

- We don’t know because we have not user tested with real people

“Not sure what it means – maybe it’s that I will need more monitoring if I take these tablets”
The two words:
- risk and
- benefit
are not comparable

The appropriate phrasing is:
- The ‘chance of benefit’
- The ‘risk of harm’

So we should be talking about:
- harm / benefit
- benefit / harm
2. User Testing of Medicines Information – how and why?

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The ‘right language’ comes from User Testing

Making sure we are using the right language need the input of ‘real people’

PILs have to be used tested

• Can real people find and understand key pieces of information?
• How would describe in their own words
• What do they like and not like about the leaflet?

But EMA & NCA information is not tested

SCORE • Most MS do not pre-test safety communications
• 1 used peer reviewer – another has ‘in-house group’ for readability testing
What is User Testing?

Select key points of information

Recruit 10 people from target group

- Interviewed individually

(a) Quantitative aspect

Design & pilot a questionnaire which tests:

- Finding each piece of information
- Understanding (express in own words)

(b) Qualitative aspect

- Interview then moves to qualitative questions
- What did they like and not like about the document?
# Testing on ‘real people’

<table>
<thead>
<tr>
<th></th>
<th>Job Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fundraising Assistant</td>
</tr>
<tr>
<td>2</td>
<td>Administrator</td>
</tr>
<tr>
<td>3</td>
<td>Retired Primary School Teacher</td>
</tr>
<tr>
<td>4</td>
<td>Retired Air Traffic Controller</td>
</tr>
<tr>
<td>5</td>
<td>Christmas Grotto Manager</td>
</tr>
<tr>
<td>6</td>
<td>Unemployed Forklift Driver</td>
</tr>
<tr>
<td>7</td>
<td>Retired Bus Driver</td>
</tr>
<tr>
<td>8</td>
<td>Warehouseman</td>
</tr>
<tr>
<td>9</td>
<td>Cleaner</td>
</tr>
<tr>
<td>10</td>
<td>Stand-up comedian</td>
</tr>
</tbody>
</table>
Testing on ‘real people’

‘For patients you start as one of us and the membership makes you one of them’

Albert van der Zeijden

Patient who engage with these organisations likely to be more familiar with risk communication tools by virtue of being member – not representative of general population

SCOPE Consultation
User Testing is iterative process

- Test material
- Identify problems
  - the points people struggled with and their general comments
- Remedy problems
  - using research evidence & good practice in writing & design
- Test again

Raynor DK. User testing in developing medication information in Europe. Research in Social and Administrative Pharmacy 2013
A question

Which is the most likely cause of information failing a user test:

• People not finding?
• People not understanding?

A note: Do not confuse with ‘user testing’ of web sites
3. Ten tips for Writing for Lay People

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What are principles of good information writing & design?

1. **Short familiar words and short sentences**
2. **Short headings that stand out**
3. **Type as large as possible**
4. **Leave ‘white space’**
5. **Use bullets for lists**
6. **Be conversational**
7. **Use the ‘active voice’**
8. **Use non-justified text**
9. **Use bold lower case for emphasis**
10. **Pictures and graphs do not necessarily help**

Some preferred frequency text
Others preferred graphical presentation
Note – these are ‘expert patients’
<table>
<thead>
<tr>
<th>WITHOUT ALTEPLASE</th>
<th>WITH ALTEPLASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Smiley Faces Diagram" /></td>
<td></td>
</tr>
<tr>
<td><strong>The number of people who have recovered (completely or almost completely) or died 3 months after their stroke.</strong></td>
<td></td>
</tr>
<tr>
<td>☺ recovered ☹ not fully recovered ☹ died</td>
<td></td>
</tr>
</tbody>
</table>

Knapp, Wanklyn, Raynor et al. Developing and testing a patient information booklet for thrombolysis. *Int Journal of Pharmacy Practice* 2010
Out of 100 people:

With alteplase:
- 17 people died
- 33 survived, but did not fully recover
- 50 people completely or almost completely recovered

Without alteplase:
- 21 people died
- 41 survived, but did not fully recover
- 38 people completely or almost completely recovered
Tables and graphs?

A simple table

<table>
<thead>
<tr>
<th>Get mild headaches</th>
<th>10%</th>
<th>5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Get severe nausea</td>
<td>10%</td>
<td>5%</td>
</tr>
</tbody>
</table>


A colour-coded value tree

The value tree above shows the benefit and risk criteria that were used in the Rimonabant trial and the risk criteria were colour-coded as red. The benefit-risk balance was colour-coded using the definitions of each criterion in grey boxes. Although the colour-coding enhances the value of the presentation on the value tree already imply groupings. Intuitive terminologies chosen to be similar. The above value tree above was created in FreeMind.

An example of stacked bar graphs on transparency in risk communication


Stacked bar charts can be used to depict proportions (Lipsius and Hollands 1999). Stacked bar charts can also be used to display the benefit-risk trade-offs and to compare between options. The two bar graphs represent the same information on stroke and major bleeding events in patients with atrial fibrillation, in two different ways. The absolute effect of aspirin and warfarin becomes more transparent in the bar graph on the right when the reference population is included.

Mismatches can occur when the bar graph emphasises the foreground information by showing the bars without sufficient background information (e.g., bar chart on the left). This could lead to a misperception of the difference in probabilities between two events [Ander et al 2000; Kurz-Milcke et al 2008; Lipsius 2007]. The medical terminologies used e.g., stroke, major bleeding and atrial fibrillation should be defined and should accompany the visual display, especially when it is presented to an audience with little or no medical knowledge.
Writing for Lay People: Applying the top tips in practice

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Children born to women who take valproate in pregnancy can have serious problems.

- There is about a 1 in 10 chance of birth defects.
- There is a 3 to 4 in 10 chance of a wide range of early developmental problems – this can lead to significant learning difficulties.

B. Patient / Carer Checklist

I, the undersigned, understand

Why treatment with valproate rather than another medicine is considered necessary for me

The risks of an approximately 10% chance of birth defects and up to 30-40% chance of a wide range of early developmental problems that can lead to significant learning difficulties in children exposed to treatment with valproate during pregnancy.

Name of Patient/ Carer

Signature

Date
Be vigilant about signs of liver problems

If you observe any of the following, your liver may not be working properly:
- yellow skin/eyes
- darkening of the urine,
- light coloured stools,
- pain in the upper right belly,
- unusual fatigue (especially associated with other symptoms listed above)

- Seek urgent advice from a doctor who may advise you to stop taking Valdoxan.
Audit of first year

18 specific pieces of wording
11 did not follow good practice

- Renal failure chronic
- Mitochondrial disorder

September meeting

Patients with a certain human leukocyte antigen genotype (which is more frequent in Japanese and Korean patients, but is also found in Caucasians) are more prone to development of insulin autoimmune syndrome (disorder of the blood glucose regulating hormones with pronounced lowering of blood sugar levels) when treated with thioctic acid.
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Some people have a gene called ‘human leukocyte antigen’…….

which is more frequent in Japanese and Korean patients
Some people have a gene called ‘human leukocyte antigen’. This is more common in people from Japan and Korea .... but is also found in Caucasians
Some people have a gene called ‘human leukocyte antigen’. This is more common in people from Japan and Korea - **but is also found in other peoples ...**

are more prone to development of insulin autoimmune syndrome (disorder of the blood glucose regulating hormones with pronounced lowering of blood sugar levels) when treated with thiocytic acid.
Some people have a gene called ‘human leukocyte antigen’. This is more common in people from Japan and Korea, but is also found in other peoples. If you have the gene and take this medicine, you are more likely to have a problem with large drops in your blood sugar (called ‘insulin autoimmune syndrome’).
Some people have a gene called ‘human leukocyte antigen’.

- This is more common in people from Japan and Korea, but is also found in other peoples.
- If you have the gene and take this medicine, you are more likely to have a problem with large drops in your blood sugar (called ‘insulin autoimmune syndrome’).

Talk to your doctor if you think this affects you.
Writing for lay people is a skill: the last link in chain

You can apply the Ten Tips

- It will make a difference

However, to do it properly, you need to call on the experts

- So, when you ‘invite external experts’, don’t forget experts in writing for lay people

- Making information fit for lay people is the last link in the chain

Don’t let the bracelet fall
User Testing of SmPCs

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User Testing of SmPCs – with specialist doctors and GPs

Using an SPC

- What is an SPC?
- I can't remember looking at one

How easy to use?

- It seems a little bit muddled
- not terribly user friendly

- I don't really understand why it repeats itself

- It's very wordy, not very easy ..... because you are flicking ...... from one part to another

- I'm not sure what 'posology' means.
Treatment during rejection episodes: MPA (mycophenolic acid) is the active metabolite of mycophenolate mofetil. Renal transplant rejection does not lead to changes in MPA pharmacokinetics; dosage reduction or interruption of CellCept is not required. There is no basis for CellCept dose adjustment following cardiac transplant rejection. No pharmacokinetic data are available during hepatic transplant rejection.

- Renal transplant rejection does not lead to changes in MPA pharmacokinetics (MPA is mycophenolic acid; the active metabolite of mycophenolate mofetil). Therefore no dose reduction or interruption of CellCept treatment is required.
- There is no basis for CellCept dose adjustment following cardiac transplant rejection.
- No pharmacokinetic data are available during hepatic transplant rejection.
Summary Information

- Summary information is a key part of ‘Proposals for improvement’

Key information

- CellCept is used with ciclosporin and corticosteroids to prevent acute transplant rejection in patients with allogeneic renal, cardiac or hepatic transplants.
- Start CellCept within 72 hours of renal and 5 days of cardiac transplants. Give IV CellCept for the first 4 days after hepatic transplant, then start CellCept as soon as it can be tolerated. See Section 3 for the dose regimes.
- CellCept interacts with some other medicines, including some other anti-rejection drugs, anti-virals and antibiotics. Use with azathioprine is not recommended.
- Vaccines may be less effective during treatment - in particular, avoid live attenuated vaccines (see Section 4.2 – Special warnings: “Vaccinations”).
- CellCept should not normally be used during pregnancy - obtain a negative pregnancy test before treatment. Women should use effective contraception before, during and after treatment, and talk to their doctor straight away if they become pregnant. Breast-feeding is contra-indicated (see Section 4.4 – Pregnancy, Fertility and Lactation).
- The main side effects from co-administration of CellCept with ciclosporin and corticosteroids include diarrhoea, leucopenia, sepsis and vomiting.
- CellCept can cause bone marrow suppression. Tell patients to report immediately any sign of infection, unexpected bruising or bleeding. Take regular full blood counts (for frequency of blood counts and other information, see Section 4.2 – Special warnings: “Bone marrow suppression and neutropenia”).
- Patients having immuno-suppressive regimens including CellCept are at increased risk of lymphomas and other malignancies (particularly skin).
- If renal function deteriorates or the patient gets neurological symptoms, consider a differential diagnosis of opportunistic infection in immune-suppressed patients.

See over for the full information about CellCept
Important things that you need to know about Rebastatin

- **Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides.** This can help reduce your chance of getting heart problems or stroke. See Section 1: *What Rebastatin is and what it is used for.*

- **You need to keep to your cholesterol-lowering diet as well as taking this medicine.**

- **Some medicines affect how Rebastatin works.** This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. See *Taking other medicines* in Section 2.

- **Rebastatin can cause serious muscle problems in a very small number of patients.** If you get unexplained pain in your muscles, or they feel tender or weak - **stop taking** the medicine and talk to your doctor at once.

- **Do not drink grapefruit juice while taking this medicine.** This is because it could increase your risk of muscle damage.

- **If you are pregnant or trying to get pregnant or breast feeding, you must not take Rebastatin.** See *Pregnancy and Breast-feeding* in Section 2.

- **Now read all of the rest of this leaflet carefully.** It includes other important information on the safe and effective use of this medicine that might be especially important for you.

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*Dickinson, Raynor, Knapp, MacDonald. Therapeutic Innovation & Regulatory Science 2016*
Where is the benefit?

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Where is the benefit information?

- Research shows patients value information that contains a balance of benefit & harm information
- Current information focus mainly on the harm – notably patient leaflets:
  - “Common - may affect up to 1 in 10 people”
- Where is the numerical benefit information?
  - Without that, how can patients be truly informed?

Motivation for Rebecca Dickinson’s PhD
- co-funded by the MHRA & University of Leeds
If 20 people like you take Rebastatin over the next 5 years, 1 of them will be stopped from having a heart attack or stroke

Negative
- I found [numerical information] a bit depressing
  ‘Oh it only improves in 1 in 20 in 5 years’, well, I won’t bother!“
- 19 out of 20, I’d say it was a good pill.”

Positive
- I want to know] my chance and if the information was there ..... I would feel the information was treating me with respect”
- I quite like the facts being there because it will make me think”
If 17 people take rebastatin over the next 5 years, 1 of them will be prevented from having a heart attack or stroke

Lottery

“It's a bit like saying a lottery, we’ve got 17 people, one might be lucky and 16 won’t be lucky”

Surprise at low benefit

“The 1 in 17, I don't think would give me a lot of confidence”

“There’s too much emphasis on the bad side effects .... but I want to be drawn into what’s good ....I want the benefits to scream out at me”

Textual information preferred, but numerical can help with judgements

“I'd like to see that upfront [textual statement] but I'd perhaps be looking for something more ... quantified benefits to back that up”

“I think you do need some facts and figures, it’s interesting to know that if I take them I am less likely...and the percentage is worth knowing”
Key Points
Key points

- Use the right language – such as “harm” instead of “risk”
- ‘Expert’ patients & ‘real’ patients have equally important - but separate - roles in info development
- There is no substitute for involving ‘real’ patients in testing written information
- Use plain language that can be understood by all
- Use only simple pictures and graphs - and test them first
- More likely not to find or not understand?
- Design and layout equally important
- Without ‘benefit’ information – patients cannot be truly informed – and we are not treating them with respect
- Involve experts in writing for lay people
  – otherwise the bracelet may fall