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## Award for Best Oral Presentation by a First Timer

# Hunting zebra: retrieving rare disease guidelines

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**Abstract**
*The EAHIL 2014 conference provided the opportunity to present a piece of work carried out by a team of information professionals for RARE-Bestpractices (RBP), an international project to promote exchange of information and knowledge in rare disease. The authors work for Healthcare Improvement Scotland (HIS), a publicly funded organisation which uses evidence, scrutiny and improvement science to facilitate the delivery of safe, effective and patient-centred healthcare. HIS is one of fifteen European partners contributing to RBP with our team providing the core information professional support for the project. Work to develop a rare disease guideline search protocol was presented in order to raise awareness of RARE-Bestpractices, and to demonstrate the engagement of information professionals in multidisciplinary research projects.*

*Key words:* rare diseases; information storage and retrieval; library collection development; guidelines as topic.

**Zebra?** *'When you hear hoofbeats behind you, don't expect to see a zebra'*
The title of the presentation refers to the use of the word 'zebra' to describe a surprise diagnosis or a rare disease (RD). Use of the term is generally attributed to the above aphorism used by a Professor of Medicine at the University of Maryland (1) when reminding students that the most likely cause of presenting symptoms is a common condition; they should refrain from looking for rare or exotic diagnoses in the first instance.

**Rare diseases are not rare**
In Europe a condition is defined as a rare, or orphan, disease if it affects five or fewer people per 10,000 of the population. There are currently between six and eight thousand known rare conditions; individual diseases may only affect a handful of people but together this adds up to over 30 million people across Europe living with a rare disease. RDs are usually life threatening or chronically disabling and significantly impact on patient and carer quality of life. Individual conditions may affect different body systems in varying ways but, taken as a group, RDs tend to share common characteristics which can lead to healthcare inequality:

- *There is often a delay to correct diagnosis and a lack of knowledge on best clinical practice once a diagnosis is made.* Most clinicians will never observe the vast majority of rare conditions and so lack experience of recognising and managing RD patients.

- *There can be a lack of patient information and support, potentially isolating patients and carers.* It should be said, however, that where they exist, RD patient organisations tend to be highly motivated. The team at HIS have collaborated with patient groups during the work on the RBP project and the knowledge, organisation and enthusiasm of these groups is second to none.

- *There can be limited treatment options.* Due to the often very low number of cases, it can be difficult or unethical to carry out traditional clinical research (e.g. randomised controlled trials) in the RD populations, leading to a dearth of evidence to support treatment options. Pharmaceutical companies may be reluctant to invest in the production of orphan drugs as they are unlikely to recoup development costs due to the low uptake of medicines.

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- *There can be physical and financial barriers to accessing best care.* Clinical experts or specialist centres specific to individual rare conditions are few and far between; a patient may have to travel considerable distances in order to access the most appropriate services.

Addressing these inequalities is a priority for the European Union (2) and there are a number of RD initiatives currently in progress. This includes RARE-Bestpractices.

**RARE-Bestpractices**

RARE-Bestpractices is a four-year EU-funded project to develop an online platform to promote the sharing of knowledge and information on rare diseases. Co-ordinated by the Italian National Institute of Health, there are fifteen European project partners and multiple advisory board members from around the world, making this a truly global initiative. The project is centred on the use and development of RD clinical guidelines to promote information sharing and best practice in the rare disease community. There are eight work streams ranging from co-ordination and dissemination activities to comprehensive pieces of work on economic evaluations of medicines and clinical guideline methodology *(Figure 1)*.

The team at HIS have been leading on work package four (WP4), the collection of existing guidelines and research recommendations. As the project has progressed and partner organisations have recognised the skills and knowledge that information professionals have to offer, our team has also contributed to the majority of the other work packages. A key output of WP4 is the development of two new online databases for rare disease guidelines and research recommendations. Presenting at EAHIL 2014 proved an excellent opportunity to raise awareness of these new information sources.

**Hunting zebra (rare disease) guidelines**

The aim of the presentation was to share a piece of work carried out to identify which information resources provide the best access to published guidelines on rare conditions.

*Methods*

A review of the literature was carried out to establish if there was any current practice in the area of rare disease guideline retrieval. The search results provided some interesting articles on rare disease information seeking behaviour but no material specifically on locating rare disease guidelines.

HIS already searches for and makes use of existing guideline documents to inform the development of national guidelines and clinical standards and indicators for Scotland. As such, we have a comprehensive search protocol used to identify published guidelines. Figure 2 lists the sources included in the HIS guideline search protocol. However, nearly all HIS work focuses on health conditions or issues which affect a large proportion of the Scottish population. The existing HIS search protocol is effective in identifying guidelines for common diseases; our team examined the return and percentage yield of the same protocol for guidelines on RD.


**Fig. 1.** Presentation slide providing an overview of the RBP work packages.

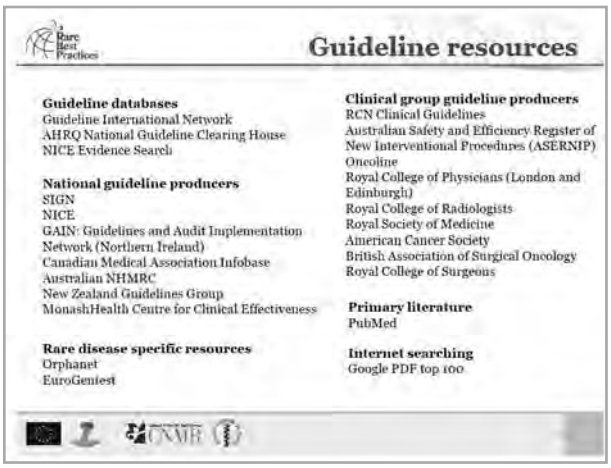


**Fig. 2.** Presentation slide listing the guideline resources used for testing.

We supplemented the standard HIS resource list with two known RD information sources. Orphanet is a comprehensive database of RD information providing a one page information summary for each individual rare condition. This summary sometimes includes links to clinical guidelines, but coverage is sporadic and appears to be at the discretion of the individual summary authors. EuroGentest is another EU-funded initiative aiming to streamline and standardise genetic testing methods. The outputs of this project are disease-specific *gene cards*: standardised best practice statements for laboratory testing.

We selected a purposive sample of three conditions, based on prevalence (3): Turner syndrome (prevalence of 20/100000), Huntington's disease (7/100000) and the ultra rare/ultra orphan Costello syndrome (300 cases reported). Terms for each of these conditions were used to search all of the resources listed in Figure 2. Search results were sifted to include any English language documents - we had no resource for translation - published in the last 10 years (2003-2013) which were described as a guideline or best practice document AND contained recommendations.

*Results*

The majority of resources in the HIS protocol did not return any results for our test conditions. Table 1 provides a summary of the results from resources which recalled at least one document.

**Table 1.** Guideline search results (taken from Hilton Boon *et al.* (4)).

| Source | Turner syndrome | | Huntington's | | Costello | |
|---|---|---|---|---|---|---|
| | Recall | Yield | Recall | Yield | Recall | Yield |
| G-I-N database | 2 | 0 (0) | 1 | 1 (100) | 1 | 0 (0) |
| National | 71 | 0 (0) | 12 | 1 (8.3) | 6 | 0 (0) |
| Orphanet | 1 | 0 (0) | 5 | 1 (20) | 2 | 0 (0) |
| Eurogentest | 2 | 0 (0) | 65 | 1 (1.5) | 1 | 0 (0) |
| PubMed | 27 | 3 (11.1) | 34 | 4 (11.8) | 1 | 0 (0) |
| Evidence Search | 393 | 2 (0.5) | 52 | 0 (0) | 53 | 0 (0) |
| Google pdf first | -- | 4 (4) | -- | 7 (7) | -- | 0 (0) |
| Pearl growing | -- | 0 | -- | 6 | -- | 0 |
| Total | 596 | 4 (0.7) | 269 | 11 (6.5) | 64 | 0 (0) |

*Discussion*

The key messages from our findings were presented as follows:

- The overarching picture is one of very low yield; of the 1029 documents retrieved, only 15 met our inclusion criteria. This points to the need for a new database to save time and effort for anyone attempting to access RD guidelines.
- The existing large guideline databases, well known to those working in the discipline of guideline development, performed poorly in our test searches. This is likely to be because of the differences in guideline development processes between common and rare conditions; e.g. Guidelines International Network (G-I-N) requires a subscription which may act as a barrier to the small groups of rare disease specialists who are likely to author RD guidelines.
- It is not unsurprising that national guideline developers and professional bodies are not key sources of RD information; limited resource usually means that these types of organisations tend to focus on common conditions.
- Citation database and internet searching appear to be the most effective way of identifying RD guidelines. This is likely to be due to journal and internet publishing offering a straightforward method of guideline dissemination for small and specialised guideline development groups.
- Limiting the search results to English language excluded potentially relevant documents and so any future search protocol should make an effort to include non-English publications.

*Conclusion*

Based on the results of our test searches, HIS has developed a list of resources specific to the task of RD guideline retrieval. This list will be implemented as a minimum resource set to locate guidelines to populate the RARE-Bestpractices database. We used only a very small sample to test these resources and so will continue to review the protocol as we progress through the project. A full report of the work presented here, plus additional information on the RBP project and databases, has been published in the project journal (4).

**Earn your stripes**

The presentation concluded with further information about the RARE-Bestpractices project, namely what the next steps are and how the conference audience, as information professionals, could get involved. Audience members were encouraged to access the project website (www.rarebestpractices.eu) or contact the HIS team for further details.

RBP next steps

- HIS has now completed a consultation with the project partners and patient groups to identify the sample of rare diseases which will be used to populate the guideline database in the first instance.
- Training in guideline retrieval and database record creation has begun for the project partners contributing to collection development.
- A prototype of the database infrastructure is about to undergo testing.
- Planning has begun for workshops on the use of the AGREE II critical appraisal tool for RD guidelines.

Opportunities to contribute

- *Create content for the database.*
  The sustainability and disease coverage of the online platform is reliant on contribution from the wider health community; the skills of health librarians and information professionals can contribute to the success of the resource beyond the duration and scope of the funded project.

- *Attend an AGREE workshop.*
  Places may be available for those who can contribute to the critical appraisal of rare disease guidelines.

- *Share practice and get published.*
  The RBP project has developed a new online, no fees journal *Rare Diseases and Orphan Drugs*(5) which welcomes articles on all aspects of RD practice, including information work.

- *Be aware.*
  Contributing to the project can be as easy as knowing and telling others that new information resources specifically for rare diseases are currently in development. The databases are due to go live in 2015 and should be an important resource for those contributing to best practice in rare disease.

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