ISPOR 2018: CHALLENGES AND LESSONS LEARNED FROM ELECTRONIC RECRUITMENT AND VALIDATION OF PATIENTS FOR OUTCOME RESEARCH STUDIES IN RARE DISEASES

CHALLENGES AND LESSONS LEARNED FROM ELECTRONIC RECRUITMENT AND VALIDATION OF PATIENTS FOR OUTCOME RESEARCH STUDIES IN RARE DISEASES

Monica Hadi, **Evidera**

Joe Waby, **Global Perspectives**

Paul Swinburn, **Evidera**

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Evidera | PPD

Speakers

Monica Hadi, PhD
Research Scientist
Patient-Centered Research
Evidera, UK
Monica.Hadi@Evidera.com

Joe Waby
Project Team Director
Market Research and Insights
Global Perspectives
Joe@Global-Perspectives.eu

Paul Swinburn, MRes
Senior Research Scientist
Patient-Centered Research
Evidera, UK
Paul.Swinburn@Evidera.com

Workshop Agenda

Content	Presenter
Background and aims • Aims of this workshop and key takeaway messages.	Monica Hadi 5 mins
Online recruitment of rare disease patients • Overview of the types of challenges that can be faced during online recruitment of rare disease patients. Recruitment through various available platforms, such as social medial and patient associations, will be discussed.	Monica Hadi 10 mins
Validation techniques in rare disease studies • Standard and also more novel validation techniques will be presented, along with their adaptation and application in rare disease studies.	Joe Waby 20 mins
Real-life case studies and outcomes • A couple of case studies will be presented, with challenges and resolution. The impact and implications of these challenges on study findings and interpretation in rare disease research will be discussed.	Paul Swinburn 15 mins
Discussion and questions	All 10 mins

WiFi Network: ISPOR | **Password: CERTARA2018**

This Workshop Will Use Live Polls

For attendees using the mobile app:

- Open the app, Select "More", Select "Live Polling/Q&A", Select your session from the list.

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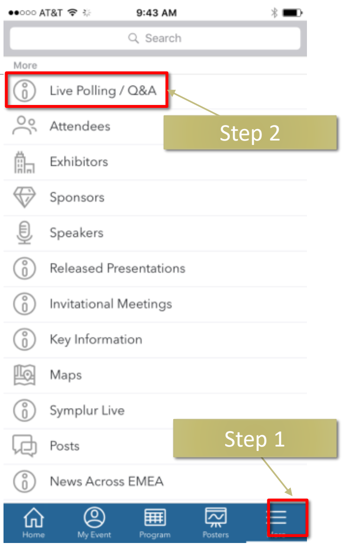
- Go to your web browser and type in: https://myispor.cnf.io/, Select your session



BACKGROUND AND AIMS

Monica

Why Is It Important To Recruit And Validate Rare Disease Patients For Outcome Research Studies?

Patients with rare diseases face debilitating conditions with limited treatment options.

Rare disease patients are often engaged with online communities in regards to their condition and treatments. Patients want to discuss and share their experiences, with the intention and hope that treatments and outcomes will improve as a result of their participation and contribution.

Electronic recruitment and survey completion is a popular and cost-effective way of accessing hard to reach patient groups, particularly in rare disease research. However, it is essential to be able to validate patients to ensure accuracy and to produce reliable data.

Several challenges remain with assessing the reliability and validity of electronic patient data.

❖How can we engage patients from the rare disease community in our research?

❖How can we trust that the patients are those we are looking to recruit?

❖How can we be ensured that patients understand and are engaged in the study?

Aims Of This Workshop

The aim of this workshop is to present challenges and lessons learned from electronic recruitment and validation of patients for outcome studies in rare diseases.

Key take away messages from this workshop:

- ➢Ways to improve study design for the rare disease population.
- ➢Achieve quick, accurate, and reliable recruitment of rare disease patients.
- ➢Acknowledging the limitations of online data capture.

ONLINE RECRUITMENT OF RARE DISEASE PATIENTS

Monica

Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: Have you ever used online recruitment for rare disease studies?

Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: What is the primary reason for which you have conducted online recruitment?

Recruitment Strategy Should Be Designed To Suit The Target Audience

1.The patient audience in question

1.The sample size required to draw meaningful conclusions

1.The level of electronic validation that is required to ensure the patients are those we are looking to recruit.

Recruitment Strategy Should Be Designed To Suit The Target Audience

- **The patient audience in question.**
  - How common is the disease? A different recruitment strategy needs to be applied depending on the rare disease incidence rate, e.g. 1 in 1,000 people or 1 in 1 million within the general population.
  - Where are the patients located? Some rare diseases might be more common in particular geographical locations.
  - How engaged are patients with the rare disease community? Some rare diseases can be more physically and psychologically burdening on patients and their caregivers.
- **The sample size required to draw meaningful conclusions.**
  - Often large sample sizes are desirable in order to provide more confidence in the conclusions drawn from the available data. In order to increase sample size, it might be advantageous to accept patients from sources with less documented evidence.
  - A combination of recruitment techniques and available recruitment sources is more likely to result in a larger sample size.
- **The level of electronic validation that is required to ensure the patients are those we are looking to recruit.**
  - An effective screener is needed that is tailored to the patient audience, with considerations for recruitment inclusion and exclusion criteria.

Rare Disease Patients Can Be Recruited Electronically From A Number Of Sources

Potential Recruitment source	Advantages	Challenges
Clinical sites	Direct contact with physicians and patients allows recruitment of rare patients and near 100% validation of eligibility.	High cost and longer timelines. Sometimes lack of willingness or engagement from sites, physicians, and patients to participate.
Physician referrals	Eligibility confirmed by a physician who can also engage the patient	Difficult to get high numbers of patients. Depends on the country and regulations.
Patient associations	Patient associations will post information about the project and patients can register their interest in the study.	A lot depends on the patient association secretary/gatekeeper and whether they want to spend time and effort on the study.
Social media/internet support groups	Rare disease patients often use social media to help find information and support for their disease or condition. This allow for a direct link to the patient.	Need to engage patients individually. Work intensive. Low response rate. Often social media groups are closed and need administrators permission to post.
Recruiter networks and databases	Databases of engaged patients who want to take part in studies.	The databases are not very big and can become out of date.
Patient panels	Can get high numbers of patients for rare diseases as a specialist panel has been built.	Panel owners may not reveal identity of panellists, and cannot verify on telephone. Engagement may be low.
Consumer panels	Can have hundreds of thousands of panel members and therefore many rare patients.	Low engagement and inability to verify other than via profiling.
Shared open survey links	Can get lots of respondents quickly.	Can't be certain that the respondents are who they say they are.

VALIDATION TECHNIQUES IN RARE DISEASE STUDIES

Joe

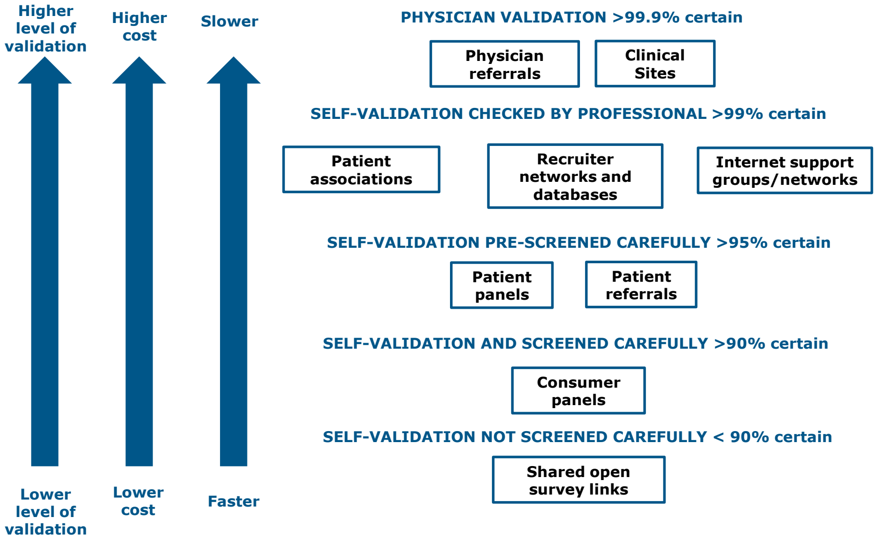
Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: How much do you trust patient data gathered from online surveys?

How much do you trust patient data gathered from online surveys?

Different Recruitment Sources Have Different Levels Of Validation Associated With Them



PHYSICIAN VALIDATION >99.9% certain

- Physician referrals
- Clinical Sites

SELF-VALIDATION CHECKED BY PROFESSIONAL >99% certain

- Patient associations
- Recruiter networks and databases
- Internet support groups/networks

SELF-VALIDATION PRE-SCREENED CAREFULLY >95% certain

- Patient panels
- Patient referrals

SELF-VALIDATION AND SCREENED CAREFULLY >90% certain

- Consumer panels

SELF-VALIDATION NOT SCREENED CAREFULLY < 90% certain

- Shared open survey links

Validation Of Patients Is Allied To The Following Three Factors

1.Patient knowledge

1.Patient engagement

1.Patient honesty

Patient Knowledge

If the eligibility criteria is too technical, patients may not have the required knowledge to self assess their fit with the validation criteria.

- Screeners should be designed and worded in a way that patients can understand and engage with the study.
- A physician will be able to confirm by checking medical records.
- An experienced recruiter can support with the interpretation of technical or complicated concepts, and also help motivate and engage patients to take part in the study.

There should be considerations for cultural differences amongst rare disease patients regarding disease awareness and knowledge.

- In English speaking countries, rare patients are often engaged and knowledgeable about their condition, specifically if there is opportunity to select health care provider and treatment. This is perhaps less apparent in countries where patients are traditionally more likely to depend on their health care provider for information.
- Knowledge is also allied to technology skills and access to information.

Patient Engagement

Some recruitment techniques can result in patients being less engaged in the study design and process.

- With consumer panels, respondents are used to receiving many surveys and as a result, they may not always pay full attention to the survey questions.
- This can lead to low quality data (speeders, flat liners), which are indicators of low engagement from patients.
- In these instances, an experienced recruiter can help engage patients by highlighting the importance and value of the study.

Interestingly, rare disease patients are often part of a highly engaged community and wish to contribute to the advancement of disease awareness and availability of treatments.

- Rare disease patients often want to discuss and share their experiences, with the intention and hope that treatments and outcomes will improve as a result of their participation and contribution.

Patient Honesty

The risk of wrongful recruitment or dishonesty from the respondents side is of particular issue when using open survey links.

- Usually this is caused via open links or open recruitment methods for online studies via the internet that do not involve human or profiling validation steps.
- In these instances, the study investigators and/or recruiters have less opportunity to screen and engage patients.
- This in turn increases the chance of a “fake” patient being involved, whom may not have a diagnosis of the rare disease in question, but whom may be interested in the offered patient incentive.
- It is important that survey access is limited to those who have already been validated at a basic level. The screener then should do the remaining validation.

This is particularly important for rare patients, as the incentive is often attractive in order to maximise the sample size.

- It is important that basic validation steps are carefully designed and implemented.

Methods To Increase Validation Of Patients

- **Careful selection of recruitment techniques.**
  - If possible, tend towards those techniques with higher validation levels.
- **Confirmation of diagnosis.**
  - By doctor’s notes or CRFs.
  - By photos of the medication.
  - By copies of patient healthcare records etc.

Experienced human recruiters to check validation of patients.
- Going through the screener carefully.
- Clarifying terminology with patients.
- Engaging patients.

A good screener.
- Hidden.
- Using patient language.
- Tested survey instrument (cognitively debriefed).

Check for and remove bad data.
- Use respected panel providers.
- Remove speeders and flatliners for online surveys.
- Do validation of engagement checks for DCEs.

CASE STUDIES AND OUTCOMES

Paul

Case Study 1; Patient Knowledge

Recruitment method	**Recruitment of N=150 End Stage Renal Disease Patients with Anaemia in the US on dialysis to take part in a 30min online survey.**
Validation method	It was essential to validate that the respondents actually had a diagnosis of anaemia. Patients were asked to get their HCP to sign a short note with their Haemoglobin count at their next dialysis session.
Challenges	• Patients lacked knowledge of their condition. *How do you validate the Haemoglobin count when patients might not know what it is?* • Recruitment took longer than expected (3-4 months) and it was challenging to engage patients to seek a HCPs note.
Lessons learned	• In these instances, a sufficient timeline must be allowed for recruitment and validation, and the study team must explore ways to motivate patients to take part in the study (e.g. explain the objective of the study clearly). • It was also helpful to allow some flexibility and accept notes signed by either a clinician or nurse. • An additional incentive was also provided to patients for their time to seek a HCP note.
Outcomes	Successful recruit the 150 ESRD patients who subsequently completed the online survey.

Case Study 2; Patient Honesty

Recruitment method	**Recruitment of N=100 Type 1 Gaucher Disease Patients with to take part in a 45min online survey.** **Patients were recruited through a patient association, and they shared the link to the online survey with their members.**
Validation method	Screener and inclusion criteria was kept to a minimal due to the nature of the condition (hard to recruit patients) and the research design (perhaps too data driven and less engaging).
Challenges	• Recruitment was slow and it was difficult to engage patients with the research. A significant sum incentive sum was offered to those participants. • There was sudden surge in patient engagement and n=26 patients completed the survey within a few days. Once the data was investigated in detail, it appeared that the information provided was identical (i.e. all 45 year old male with the same medication).
Lessons learned	• The study team and recruiters should investigate any sudden surge of patient engagement, reviewing the collected data in detail. • In these instances, even a sufficient recruitment timeline may not yield the aspired sample size due to availability of patients and interest in the study.
Outcomes	Data was collected from N=65 patients in total which appeared genuine in nature, which is still considered a “large” sample size for the study design and population.

DISCUSSION AND QUESTIONS

Conclusion And Take Away Points

Improving study design for rare disease patients requires careful planning of the recruitment and validation process ahead of study and in order to achieve realistic targets and to anticipate potential challenges.

It is important to allow or a feasibility assessment, rather than assuming one specific approach will definitely work.

When conducting electronic outcome research in rare diseases, it is helpful to tailor the recruitment and validation process to that specific study.

- Recruitment should consider factors such as patient audience, sample size, and level of validation required.
- Validation is allied to patient knowledge, patient honesty, and patient engagement.

The study team should work closely with experienced recruiters to draw up the most appropriate recruitment strategy and to monitor the recruitment and validation process in order to achieve accurate, and reliable recruitment of rare disease patients.

DISCUSSION AND QUESTIONS

Monica Hadi
Monica.Hadi@Evidera.com

Joe Waby
Joe@Global-Perspectives.eu

Paul Swinburn
Paul.Swinburn@Evidera.com