



Developing a core outcome set for Lyme disease

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Overview of the session

- Why are outcomes important?
- What are the problems with outcomes?
- What is a core outcome set?
- Why do we need a core outcome set for Lyme disease?
- What are the aims of the LYME-COS project?



Why are outcomes important?

- To help patients, doctors and other health professionals make decisions about treatments, we need evidence about what works best.
- Treatments are developed and tested by researchers to make sure they work and are safe.
- Researchers do this by measuring an 'outcome'.



What are the challenges of measuring outcomes?

Study A

- How fast you can blow air out of your lungs (peak flow)
- Night time wheeze
- Asthma related quality of life



Study B

- How fast you can blow air out of your lungs (peak flow)
- Hospitalisation
- Days off work



An example of an outcome

A study to find out how well a new asthma treatment works might measure:

- How fast you can blow air out of your lungs (peak flow)
- Night time wheeze
- Asthma related quality of life

These are all outcomes



Why is it a problem to measure different things?

- In this example we can only compare and combine the results from both studies for one outcome.
- We cannot compare or combine the other results because we would not be comparing like with like.



Another problem with outcomes – bias in reporting

- A research study decides to collect information on several outcomes.
- After looking at the results of the study they only publish results for some of the outcomes. For example, the ones that show a significant difference between groups.
- This means that when we look at the evidence we don't have all of the results and the information we do have might be biased.

(Dwan et al, PLoS ONE 2008)

Choice of outcomes and research waste

- Measuring different things
- Only reporting some of the results

Waste in research

It takes longer to find out if a new treatment works and, if it does work, it takes longer for it to be made available to patients.

The extent of the problem

We noted considerable heterogeneity between studies, and these differences precluded a formal meta-analysis. (*immunocompromised, critically ill people*)

"Many trials reported on CVD risk factors, particularly in primary prevention, but heterogeneity precluded meta-analyses for some outcomes". (*CVD risk and diet*)

"No study reported relevant data on diabetes and cardiovascular related **morbidity, mortality and quality of life**." (*Preventing Type 2 DM - 2008*)

"Most RCTs did not investigate patient-important outcomes" (*Preventing Type 2 DM - 2017*)

"Important priorities include development of an internationally agreed **core outcome set** for future trials in acute severe asthma exacerbations" (*acute paediatric asthma*)

What is the situation for outcomes in Lyme disease research?

"Antibiotic treatment is the mainstay of management for Lyme disease."

The studies published on the management of Lyme disease use differing outcomes, which are often poorly defined.

The development of a **core outcome set** has been identified as a high priority because it would allow comparison across trials and allow appropriate meta-analysis to strengthen results.

The methods used should be patient-focused and include patient input on priority outcomes and how they should be measured."

NICE guideline [NG95], recommendations for research 2018.

What is a core outcome set?

An agreed standardised set of outcomes that should be measured and reported, as a *minimum*, in all clinical trials in specific areas of health or health care.



COMET definition, 2010

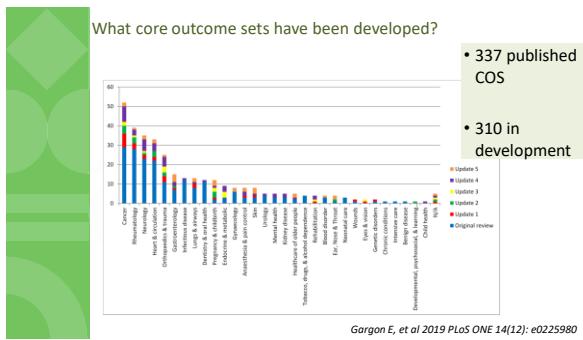
What are the benefits of a core outcome set?

- If all studies in a particular health condition used the same outcomes, they could all be compared and combined.
- This would reduce waste by making best use of all the research.
- When a set of main outcomes has been agreed for a health condition, it's called a '**core outcome set**'.



Increases consistency of outcomes
Helps to reduce reporting bias.





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A core outcome set for clinical trials of the management of Lyme disease

- Consistency
- ↓ selective reporting
- Systematic reviews
- Appropriate and relevant outcomes

<https://comet-initiative.org/Studies/Details/1902>

Step 1: Deciding the scope of the core outcome set

Step 1: Scope

International Steering Committee

- People with Lyme Disease
- Health Professionals
- Researchers in the field

Agreed protocol and scope

- Health condition and target population
- Interventions
- Setting

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Step 2: Generate a long list of outcomes

Step 2: Identify existing knowledge

Systematic review

- Published randomised trials
- Published research of people's experience of Lyme disease
- Review of active registered clinical trials

This will generate a long list of outcomes that will be taken forward to an online consensus process.

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Step 3: Seek consensus on the most important outcomes

Step 3: Consensus Process

Online Delphi survey

Two surveys delivered online

Survey 1

- Rate importance of each outcome on the list.
- Rate anonymously.
- Opportunity to add anything missing from the list.

Survey 2

- Results from survey 1 summarized.
- Opportunity to see how other groups of stakeholders have rated each outcome.
- Reflect on own ratings and ratings of each group.
- Re-rate importance.

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Step 3: Stakeholders

Step 3: Consensus Process

Delphi survey participants

- People with Lyme disease/ people who have had Lyme disease
- Healthcare professionals involved in the treatment of Lyme disease.
- Researchers in the field of Lyme disease

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Step 4: Discuss and finalise the core outcome set

Step 4: Consensus Meeting

Online consensus meeting

A smaller group of people who took part in the Delphi survey get together to discuss the results.

To be included in the core outcome set all groups of people taking part have to agree that the outcome is critically important and should always be measured.

Sometimes the importance of an outcome differs between groups and discussion can help understand the reasons for this.

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What happens after the core outcome set is agreed?

A core outcome set represents "what" to measure.

Future work will need to agree how each of the agreed outcomes should be measured.



Step 5: Report the final the core outcome set

Step 5: Reporting

Reporting the final core outcome set

The results of the work will be written up.

The write up will include an academic publication and also a plain language summary.

Sharing the core outcome set is important to help increase uptake.

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Useful links

An animated video describing core outcome sets

<https://www.youtube.com/watch?v=g1MzI2mzK1U>

A plain language summary of core outcome sets

<https://www.comet-initiative.org/assets/downloads/COMET%20Plain%20Language%20Summary%20v4.pdf>

A plain language summary of Delphi surveys

<https://www.comet-initiative.org/assets/downloads/Delphi%20plain%20language%20summary%20for%20COMET%20website.pdf>

Thank you



Q&A for Nicola Harman

Attendee	Question
Heather Dorricott-Tilley	Can a core outcome set include outcomes that you can't measure or that are difficult to measure?
	<p>The core outcome set aims to find out which outcomes are critically important to measure in all future research. Essentially "what" should be measured. Once the "what is agreed" the next important step is to agree how each of the outcomes is measured. This involves looking at all of the methods/measurement tools already available and how good they are. The how stage should also consider the overall patient and researcher burden of the methods chosen. Agreeing "how" outcomes should be measured will also identify if there isn't a reliable measure of an outcome or if there are challenges in its measurement so that these can be addressed in future work.</p>
Julia Knight	How will patients be invited to take part in the survey? Through charities, through social media etc?
	<p>Patients will be invited through social media and through patient organisations, including overseas patient organisations.</p>
Anne Cruikshank	same question in relation to contacting doctors
	<p>Health professionals will be invited through social media, professional organisations and personal contacts of the steering committee. We will aim for both national and international participation.</p>
ZH	Borreliosis is a multi-system disease, with multiple different symptoms, and different levels of severity dependant on multiple factors. How can this be considered in creating outcomes? Will there be different outcomes dependent on organs affected and level of severity?
	<p>We will consider all outcomes in the Delphi survey and will work to present these in a good way that takes into account the multi-system nature of Lyme disease and also the different stages of Lyme disease. Core outcome sets have successfully been developed in other health areas that affect multiple systems, for example, type 2 diabetes.</p>