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27 - 28 September 2021

ONLINE WORKSHOP

Digital Tools and Artificial Intelligence in Oncology Drug Development

Digital Experimental Cancer Medicine Team

Endpoints for digital tools

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Endpoints

- Endpoints for clinical trials
- Considerations for digital tools
- Technology clinical trial
- Determination of clinical benefit
- Guidance documentation - framework
- Resources

Clinical trial endpoints

- Outcome usually refers to the **measured variable**
- Endpoint refers to the **analysed parameter** (eg change in variable)
- Clinically meaningful endpoints reflect how a patient feels, functions or survives
- Endpoints may directly or indirectly (surrogate) represent or characterise the clinical outcome of interest
- A surrogate endpoint should correlate with changes in a clinically meaningful endpoint – may be easier to measure but relevance required

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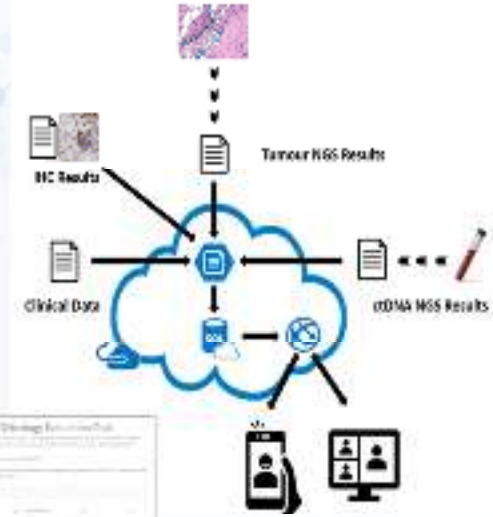
Digital tools



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Digital endpoint

- A precisely defined variable intended to reflect an outcome of interest that is statistically analysed to address a particular research question
- Derived from or includes digital measurement
- Can be clinical outcome assessments (clinical relevance established *de novo*) or biomarkers (reliable relationship with existing clinical outcome can be established).

Qualification of digital technology-based methodologies to support approval of medicinal products. EMA, 2020

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‘Technology’ clinical trial: assessing digital tools

4 important components

The Driver – augmenting clinical decision making to benefit the patient by

- Changing the role of the patient
- Changing the design, delivery and interpretation in early clinical trials
- Hypothesis testing, proof of concept and prototyping new technology
- Developing new care pathways

Formally assesses…

- Patient/clinical acceptability and feasibility
- Clinical Benefit
- Ethical and medicolegal implications
- Patient engagement and education tools

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Technology assessment | **Clinical Benefit**

‘Technology’ Clinical Trial

Right Hypothesis
Right way

Regulatory
& Ethical Navigation

Trial Delivery

Proven approach

Decision Science and Analytics

Technology assessment

- Demonstrating
  - Fitness-For-Purpose
  - Reliability, accuracy and precision
  - Convergent validity
  - Ability to detect change
  - Safety and user acceptance

Where relevant

  - Diagnostic and prognostic performance (sensitivity and specificity)
  - Sensitivity to change in clinical status

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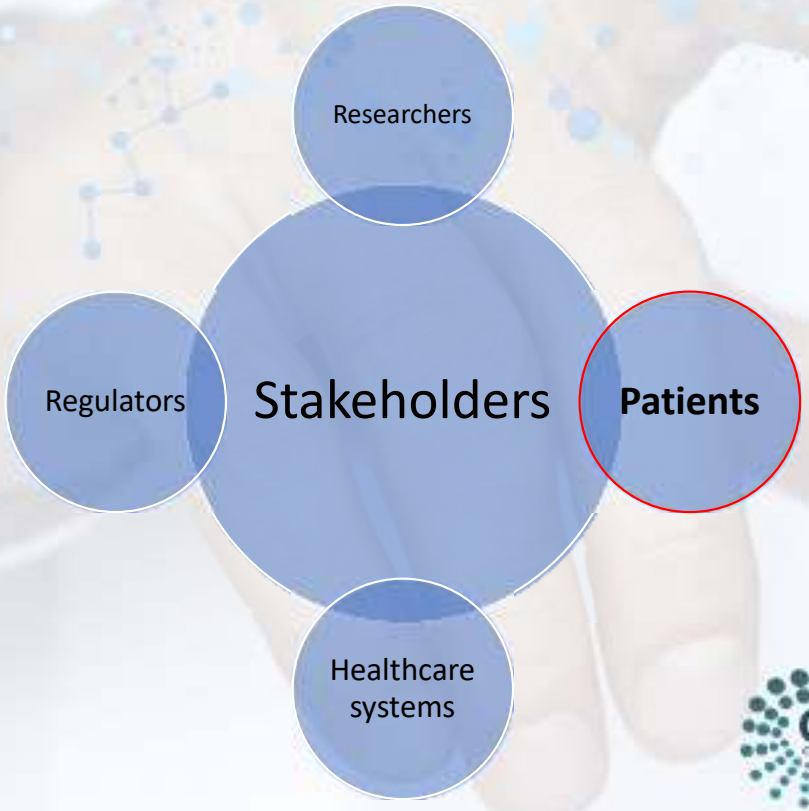
Determining clinical benefit



Endpoints must be:
Well-defined
Clinically meaningful
Reliable and reproducible

Benefits have greater weight if the impact on multiple stakeholders is clear

Patient benefit is critical

Potential benefits of digital tools

Patients

- Ease of communications or reporting of symptoms
- Less frequent hospital visits and reduced travel (off-site and remote data capture)
- Potential to reduce severe side effects/admissions with earlier detection & management
- Location-independent access to treatment
- Patient functioning in real-world setting
- Potential to streamline clinical investigations (time saved)

Healthcare providers

- Decrease missing data (continuous monitoring)
- Support Adherence
- Potential for rapid response
- Efficient use of resources (health economic benefits)
- Potential to reduce risk with better patient engagement

Potential benefits of digital tools

Clinicians/Researchers/Sponsors

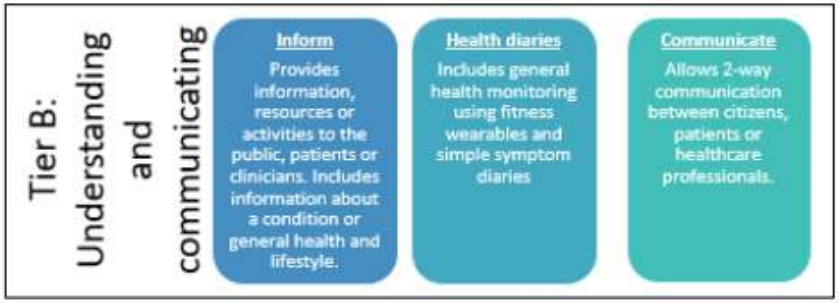
- Better understanding of patient experience in real time (not retrospective)
- Circadian variations
- Timing of side effects relative to dosing (oral medications)
- Subtle/short lived changes may be captured
- Opportunity to improve patient communication

Key considerations

- Beware of noise with continuous monitoring/wealth of data
- Know what is the important measurement
  - Magnitude of change
  - Change over a specific time
  - Earlier detection of change (toxicity)
  - Overall variability
- Clearly defined endpoints are critical

NICE guidance on level of evidence

- Functional classifications
- Broadly grouped by risk
- Risk may very within categories
- Higher level of evidence of benefit required where higher risk identified



Evidence standards framework for digital health technologies, NICE, 2018

NICE National Institute for Health and Care Excellence

NICE Framework

- Risk adjustment for
  - Vulnerable populations
  - More serious consequences of the tool not being effective
  - Level of support for use
  - Involvement of AI
  - Higher financial or organisational risk

Best practice standard
High risk

Minimum evidence standard
Low risk

NICE National Institute for Health and Care Excellence

Evidence standards framework for digital health technologies, NICE, 2018

Key considerations for evidence (where relevant)

- Plausible mode of action, deemed useful and relevant to the field by clinical experts
- Health information is valid, accurate, up to date and comprehensive
- High quality intervention
- User acceptability
- Relevance to current care pathways and ability to scale up
- Transparency of data
- Data: accurate, reproducible, relevant – tool detects clinically relevant changes/responses
- Technical data: not changed/modified in transmission, not biased
- Addresses disparity/does not create inequality
- Safeguarding considerations

NICE National Institute for Health and Care Excellence

Evidence standards framework for digital health technologies, NICE, 2018

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DIGITAL MEDICINE SOCIETY

Library of digital endpoints

69 Sponsors have collected digital endpoints

Primary, Secondary or Label Claim

Exploratory Only

Sponsors start digital endpoint development early

Digital Endpoints

Phase 0 1%

Phase 1 8%

Phase 2 38%

Phase 3 20%

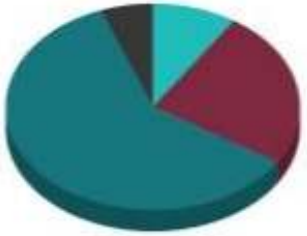
Phase 4 33%

>58% of examples

*Only drug trials with reported phases are included

Digital endpoints are being used across drug, device, and biologic development

Investigational Product



Drug	60.2%
Device	24.7%
Biologic	9.8%
Other	5.3%

Pharma trusts digital products, primary/ secondary endpoints

Endpoint Positioning

63 Primary endpoints

148 Secondary endpoints

14 Exploratory

225 UNIQUE ENDPOINTS

SOURCE: Digital Medicine Society (DiMe) Library of Digital Endpoints https://www.dimesociety.org/communication-education/library-of-digital-endpoints/

Summary

- Endpoints for digital tools should follow the same broad principles as standard clinical trial endpoints
- There are opportunities to adapt traditional endpoints or create new endpoints using digital tools incorporating simplified or improved data collection
- Clinically meaningful benefit is key
- Regulatory authorities have embraced the concept of technology clinical trials with broad support. NICE have created clear guidance with a framework
- Digital Medicine Society have created a library of endpoints currently in use with digital tools across registered trials

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Thank you