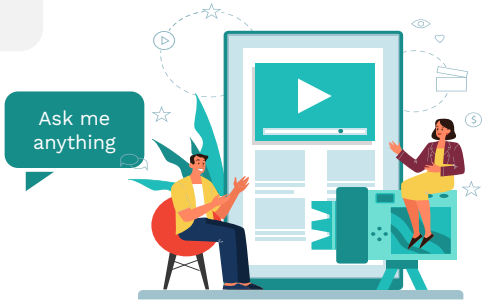
Virtual Journal club



Digital Biomarkers

Quantifying the Benefits of Digital Biomarkers and Technology-Based Study Endpoints in Clinical Trials: Project Moneyball

Aug 3, 2022 11am ET

Hiro Mori, MBA
CNS Solution Owner
Koneksa Health
Brussels, Belgium

Stig Johan Wiklund, PhD
Chief Scientific Officer
Captario
Gothenburg, Sweden

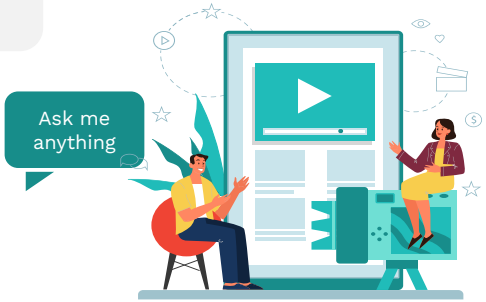
Paul Strijbos PhD
Product Development Neuroscience
F. Hoffmann-La Roche Ltd
Basel, Switzerland

Jen Goldack, MBA
CEO
DiMe Society
Moderator

But first, housekeeping

- Please note today's session is being recorded
- To ask a question for discussion during Q&A, please:
  - Either 'raise your hand' in the participant window and moderator will unmute you to ask your question live, or
  - Type your question into the chat box
- Slides and recording will be available after today's session

Virtual Journal club



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Moneyball – *our inspiration*

Your goal shouldn't be to buy technologies.

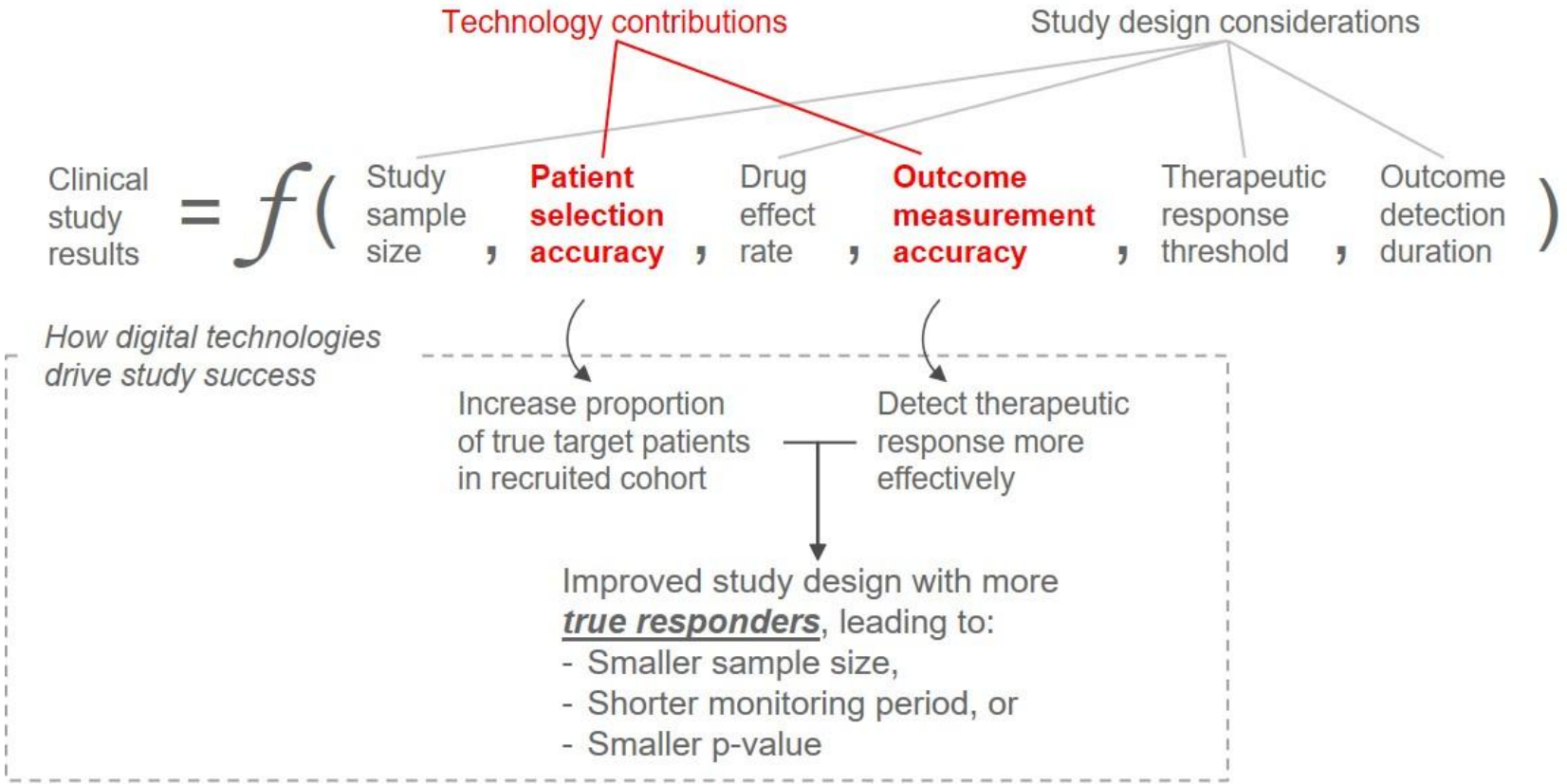
Your goal should be to buy clinical study successes.

In order to buy clinical study successes in terms of p-value **you need to buy true responders.**

There is an optimized study design we can afford.

Miller B. Moneyball (film). USA: Columbia Pictures; 2011.

Win with digital biomarkers



https://www.karger.com/Article/FullText/525255, Figure 1

Roche – SYSNAV – University of Oxford Partnership

Cocreating novel wearable technology and functional dEPs

Prof Laurent Servais
Neuromuscular Centre,
University of Oxford UK

UNIVERSITY OF OXFORD

ACTIMYO

syde

Roche

Paul Strijbos
Collaboration &
Strategy lead

sysnav
NAVIGATION TECHNOLOGIES

Damien Eggenspieler
Healthcare lead

ActiMyo® and Syde® wearable technology enables measurement of disease progression in the real world

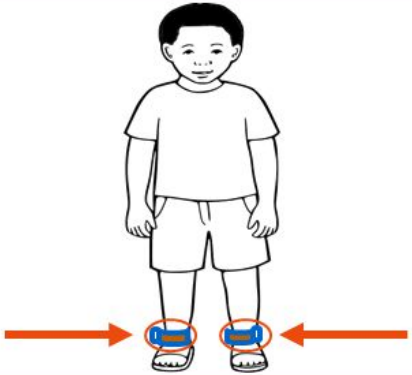
Commercialized by **SYSNAV Navigation Technologies**

ActiMyo®
(2011)

Syde®
(2021)

- Magneto-inertial technology
- Validated and sophisticated fusion algorithms
- Class I MD, GDPR Compliant, QMS
- Measures movement continuously during daily living with high accuracy and precision
- Pediatric and adult use
- Optimized for clinical trial use

ActiMyo ® /Syde ® can be worn in different configurations (usually worn on the ankles)



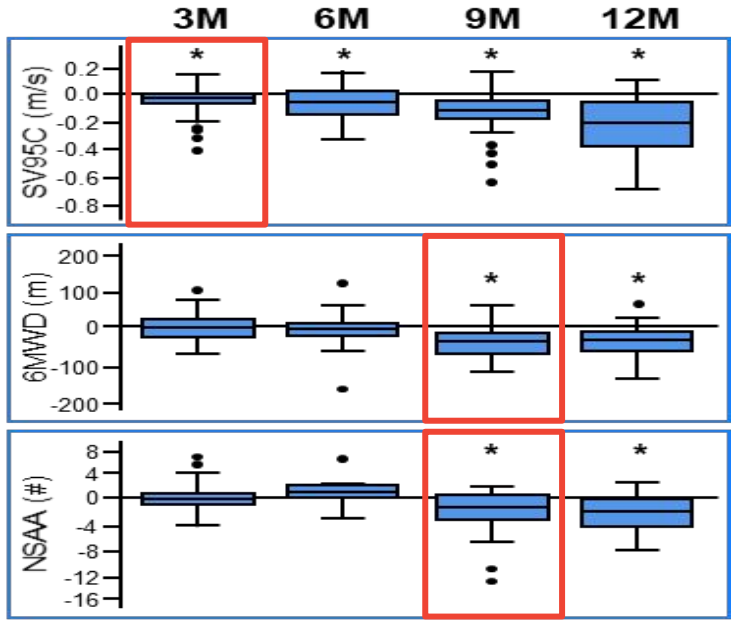
The participant wears the sensors during waking hours. Sensor data are uploaded to a secure cloud environment every night

Development of a new real-world endpoint: SV95C

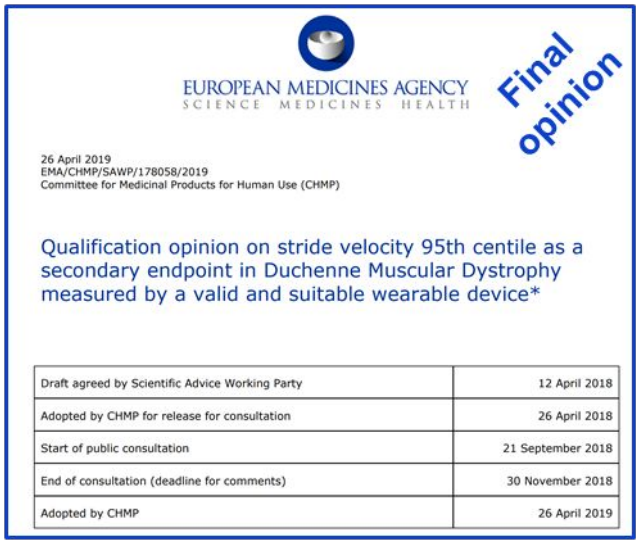
SV95C is a digital measure of peak ambulation performance during normal daily living.

It represents the minimum velocity of the 5% of the fastest strides taken by a wearer[1]

- **Differentiates** healthy boys from boys with DMD
- Is **sensitive to therapeutic intervention** (steroids)
- SV95C **MCID compares** to that seen with NSAA, 6MWT
- **Correlates** with 6MWT, NSAA and 4SC
- **In DMD, detects early** decline in natural history or improvement due to the initiation of corticoid treatment
- **SV95C precedes loss of performance** in DMD with 6MWT



Regulatory qualification of SV95C: An industry first


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Final opinion

26 April 2019
EMA/CHMP/SAWP/178058/2019
Committee for Medicinal Products for Human Use (CHMP)

Qualification opinion on stride velocity 95th centile as a secondary endpoint in Duchenne Muscular Dystrophy measured by a valid and suitable wearable device*

Draft agreed by Scientific Advice Working Party	12 April 2018
Adopted by CHMP for release for consultation	26 April 2018
Start of public consultation	21 September 2018
End of consultation (deadline for comments)	30 November 2018
Adopted by CHMP	26 April 2019


ScienceDirect

Short communication

European regulators' views on a wearable-derived performance measurement of ambulation for Duchenne muscular dystrophy regulatory trials ☆

Marion Haberkamp[a], Jane Moseley[b], Dimitrios Athanasiou[c], Fernando de Andres-Trelles[d], André Elferink[e], Mário Miguel Rosa[f], Armando Magrelli[g,*]


COMMENT · 29 SEPTEMBER 2020

Digital health technologies in clinical trials for central nervous system drugs: an EU regulatory perspective

Digital health technologies have the potential to help address some of the challenges in the clinical development of drugs for central nervous system disorders. This article discusses strategies for the development of such tools in the context of the European regulatory environment.

Valentina Mantua, Celso Arango, Pavel Balabanov & Florence Butlen-Ducuing

Office of Therapies for Neurological and Psychiatric disorders, Human Medicines Division, European Medicines Agency, Amsterdam, The Netherlands.

Contact

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2017 — 2018 — 2019 — 2020

FDA COA Qualification Program (#000103)

COA, clinical outcome assessment; SV95C, stride velocity 95th centile.

1. European Medicines Agency. Qualification opinion on stride velocity 95th centile as a secondary endpoint in Duchenne muscular dystrophy measured by a valid and suitable wearable device (2019). Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondaryendpoint-duchenne-muscular-dystrophy en.pdf. (Accessed February 2022); 2. Haberkamp M, et al. Neuromuscul Disord. 2019; 29:514–516; 3. Mantua V, et al. Nat Rev Drug Discov. 2021; 20:83–84.

Regulatory qualification of SV95C

Final EMA opinion[1]

"Stride velocity 95th centile (SV95C) measured **at the ankle…**

…is an **acceptable secondary endpoint in pivotal or exploratory drug therapeutic studies** for regulatory purposes…

…when measured by a **valid and suitable wearable** device…

… to **quantify a patient's ambulation ability** directly and reliably in a continuous manner in a home environment and as an **indicator of maximal performance"**

- Quantifies **baseline performance**[1]
- Monitors **disease progression** and **treatment benefits**[2]
- **Complementary** to traditional endpoints in collecting efficacy evidence and **potential to replace** traditional endpoints[3]


Digital Biomarkers

Review Article

First Regulatory Qualification of a Novel Digital Endpoint in Duchenne Muscular Dystrophy: A Multi-Stakeholder Perspective on the Impact for Patients and for Drug Development in Neuromuscular Diseases


Commentary

Stride Velocity 95th Centile: Insights into Gaining Regulatory Qualification of the First Wearable-Derived Digital Endpoint for use in Duchenne Muscular Dystrophy Trials

EMA, European Medicines Agency; SV95C, stride velocity 95th centile.

1. European Medicines Agency. Qualification opinion on stride velocity 95th centile as a secondary endpoint in Duchenne muscular dystrophy measured by a valid and suitable wearable device (2019). Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondaryendpoint-duchenne-muscular-dystrophy en.pdf. (Accessed February 2022); 2. Servais L, et al. Digit Biomark. 2021; 5:183–190; 3. Servais L, et al. J Neuromuscul Dis. 2021. doi: 10.3233/JND-210743. Online ahead of print.

Dramatic impact of SV95C on study design and patient burden

Robust assessment of MCID ensures clinical studies are adequately powered to demonstrate meaningful change

	6MWT	SV95C
MCID	30-meter difference	0.1 m/s (~6.24% decline, 36-meter difference on 6MWT) (*Studies ongoing to confirm validity*)
Sample size required	>100 patients per treatment arm	14 patients per treatment arm *(DMD >7 years of age; 6MWT baseline <450m)*

- **Improved sensitivity** and reliability of SV95C versus 6MWT
- The ability to conduct smaller, shorter clinical studies using SV95C confers **a significant advantage** in rare diseases (where there are fewer patients) over traditional endpoints

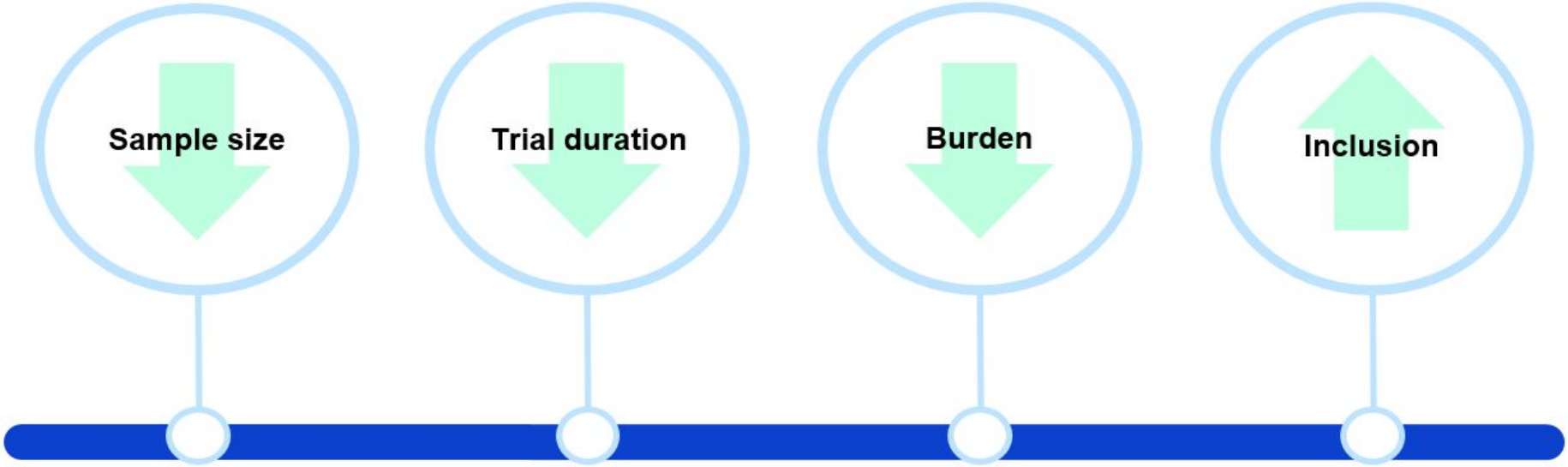
6MWT, 6-minute Walk Test; DMD, Duchenne muscular dystrophy; MCID, minimally clinically importance difference; SV95C, stride velocity 95th centile.

1. Servais L, et al. J Neuromuscul Dis. 2021. doi: 10.3233/JND-210743. Online ahead of print.

What does SV95C mean for DMD?[1]

Multi-stakeholder impact, benefiting the entire health ecosystem

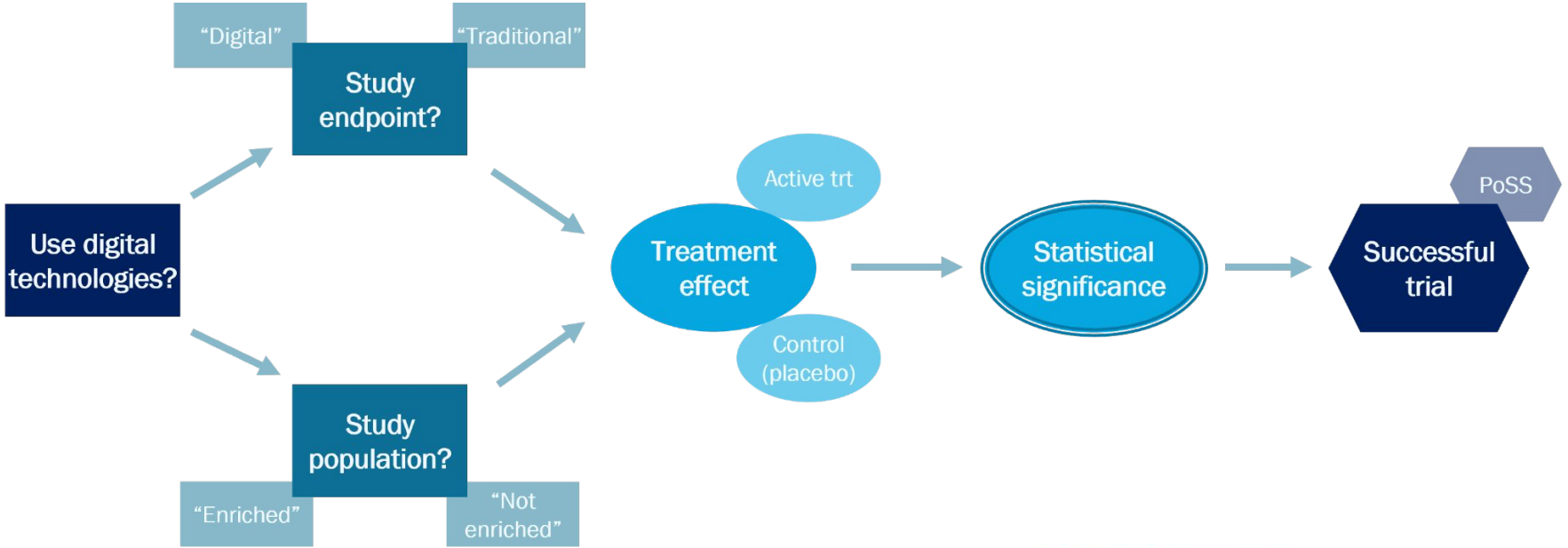
Benefits of using highly sensitive digital endpoints in drug development



DMD, Duchenne muscular dystrophy.

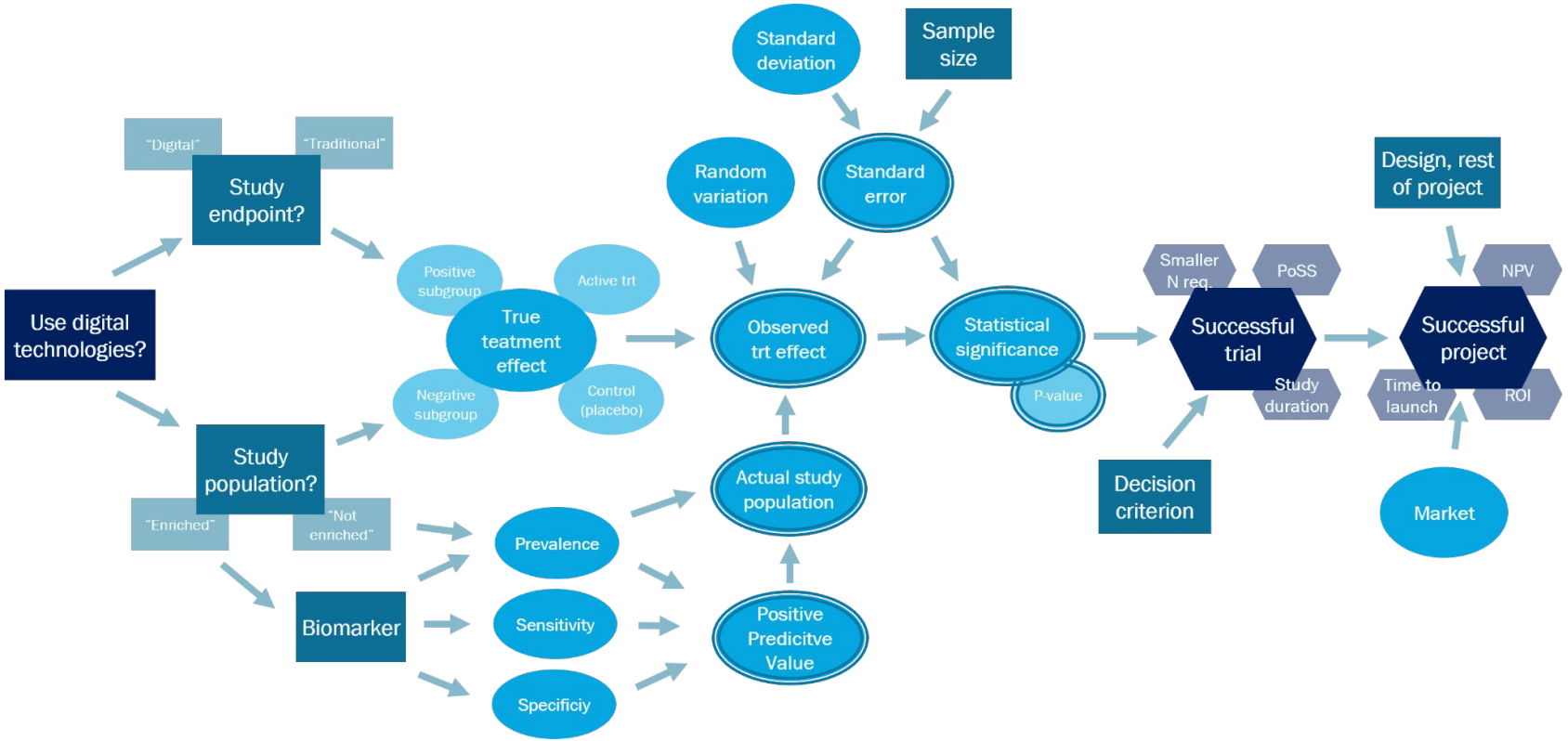
1. Servais L, et al. Digit Biomark. 2021; 5:183–190.

Core components of quantitative model



Modelling and Monte Carlo simulation performed using CAPTARIO SUM

Components of quantitative model
- some details and extension



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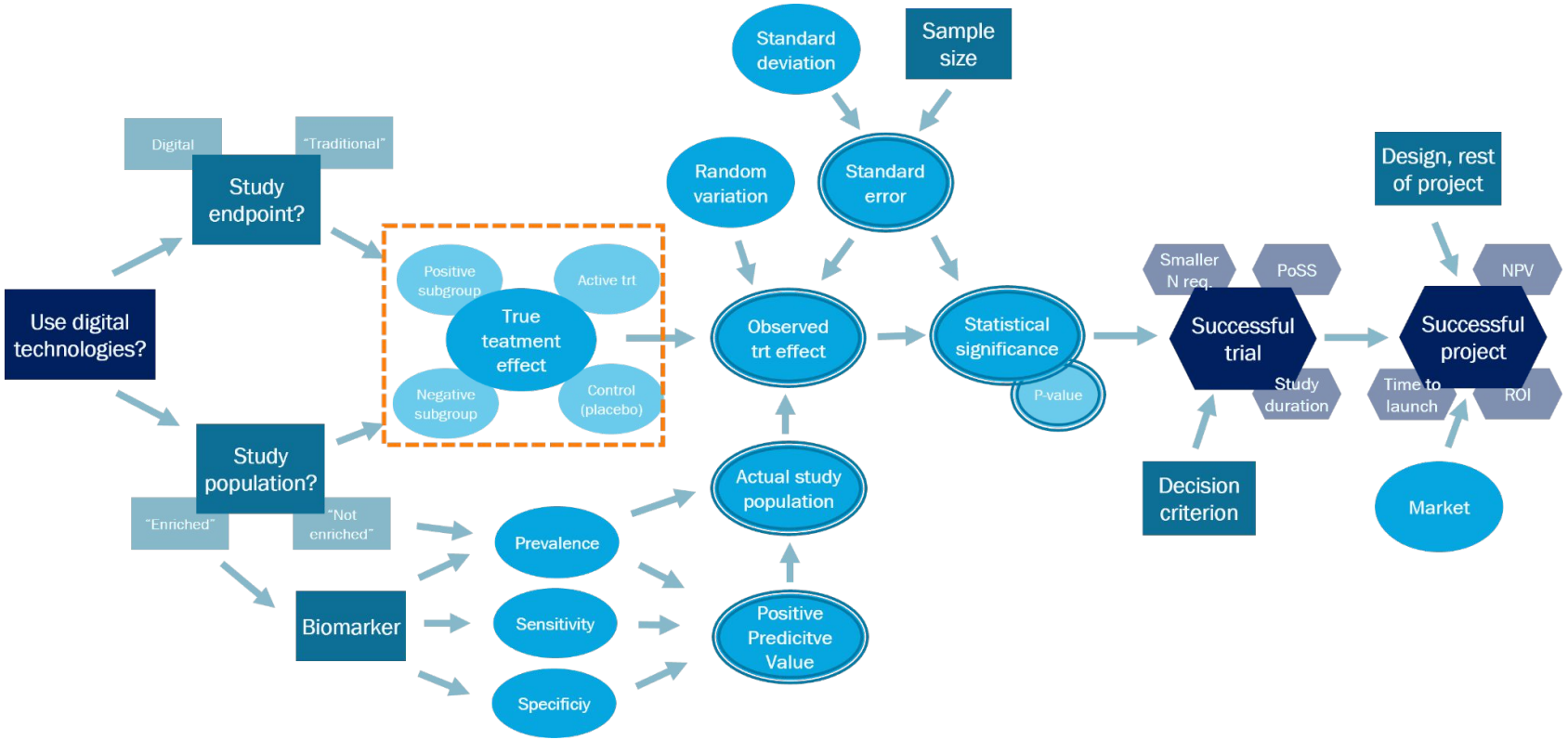

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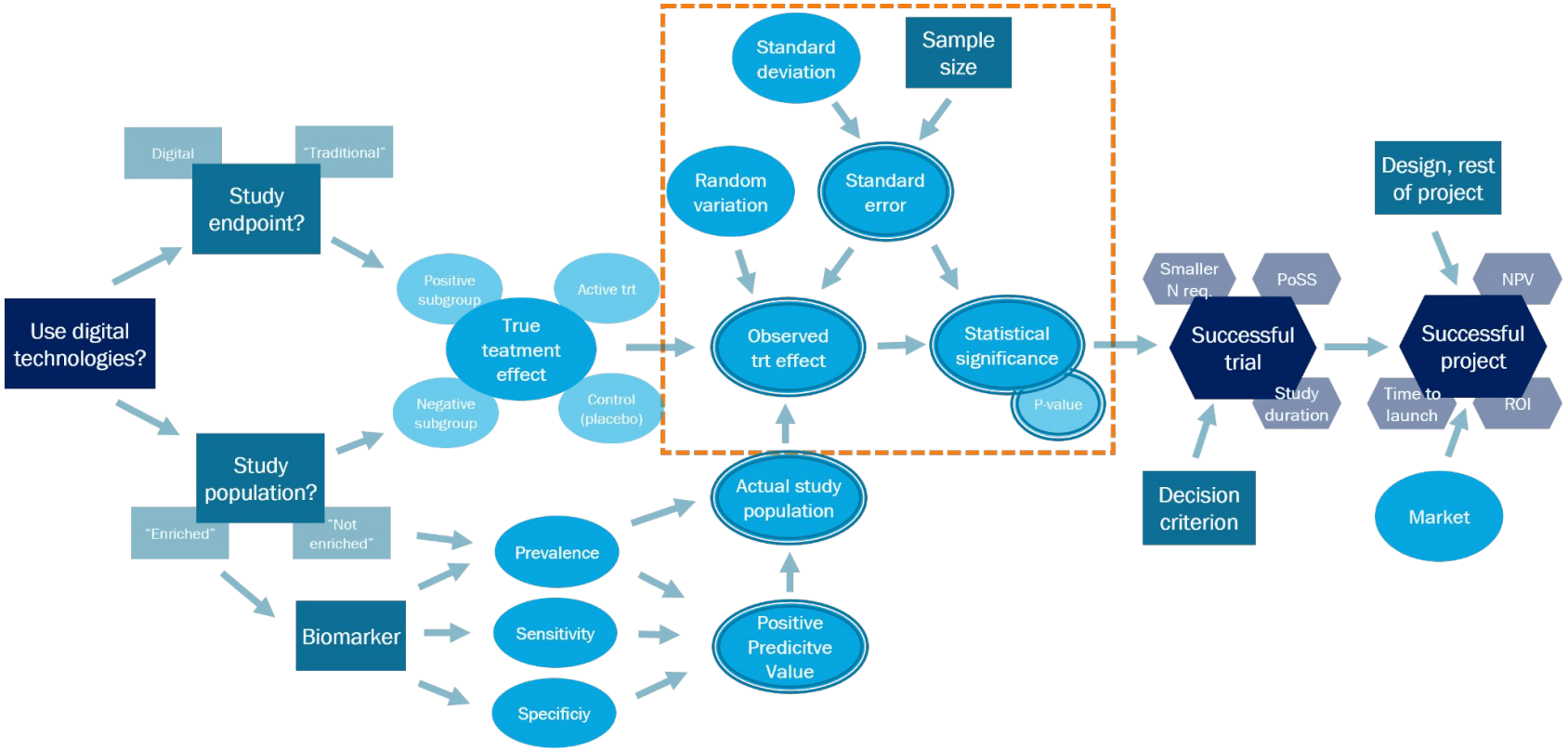

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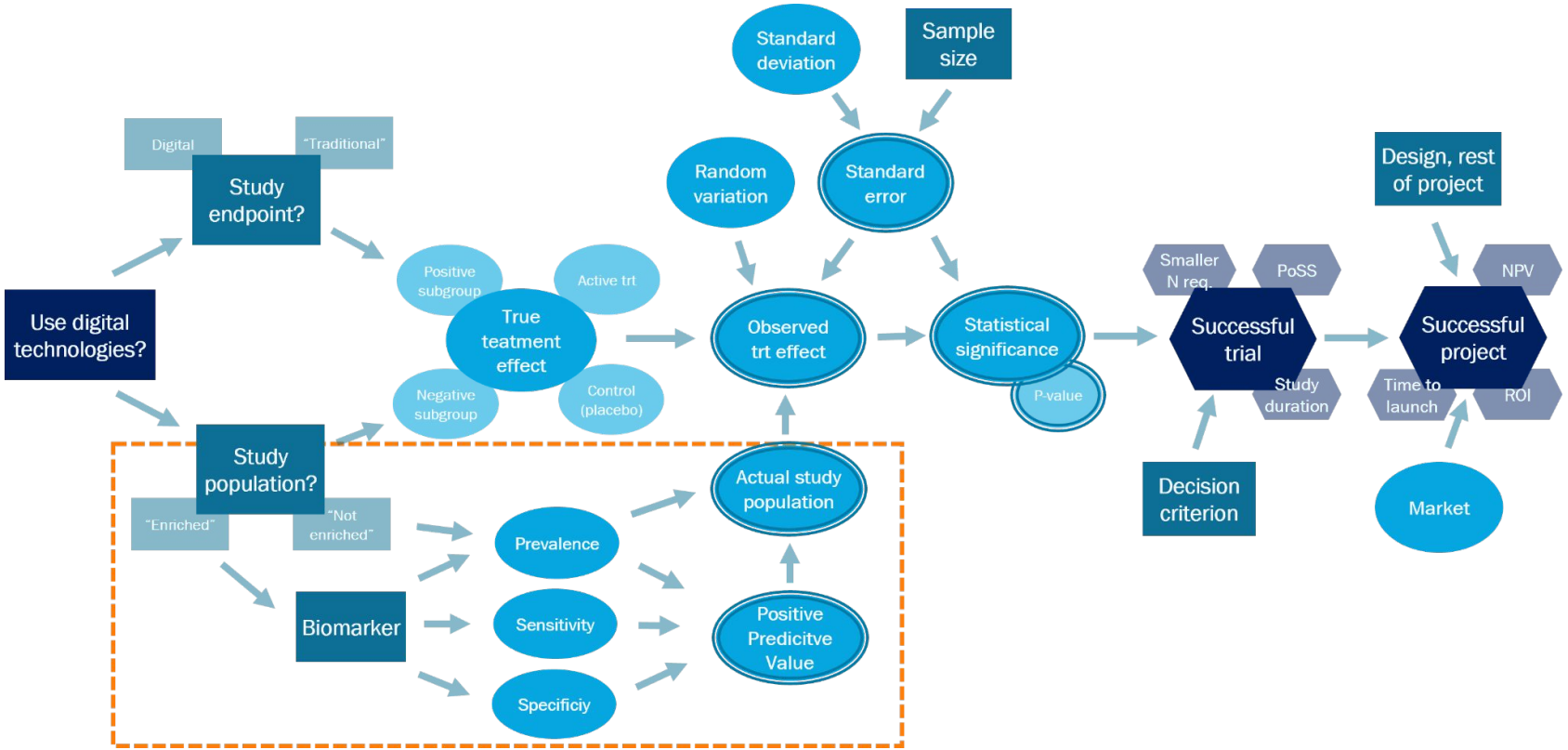

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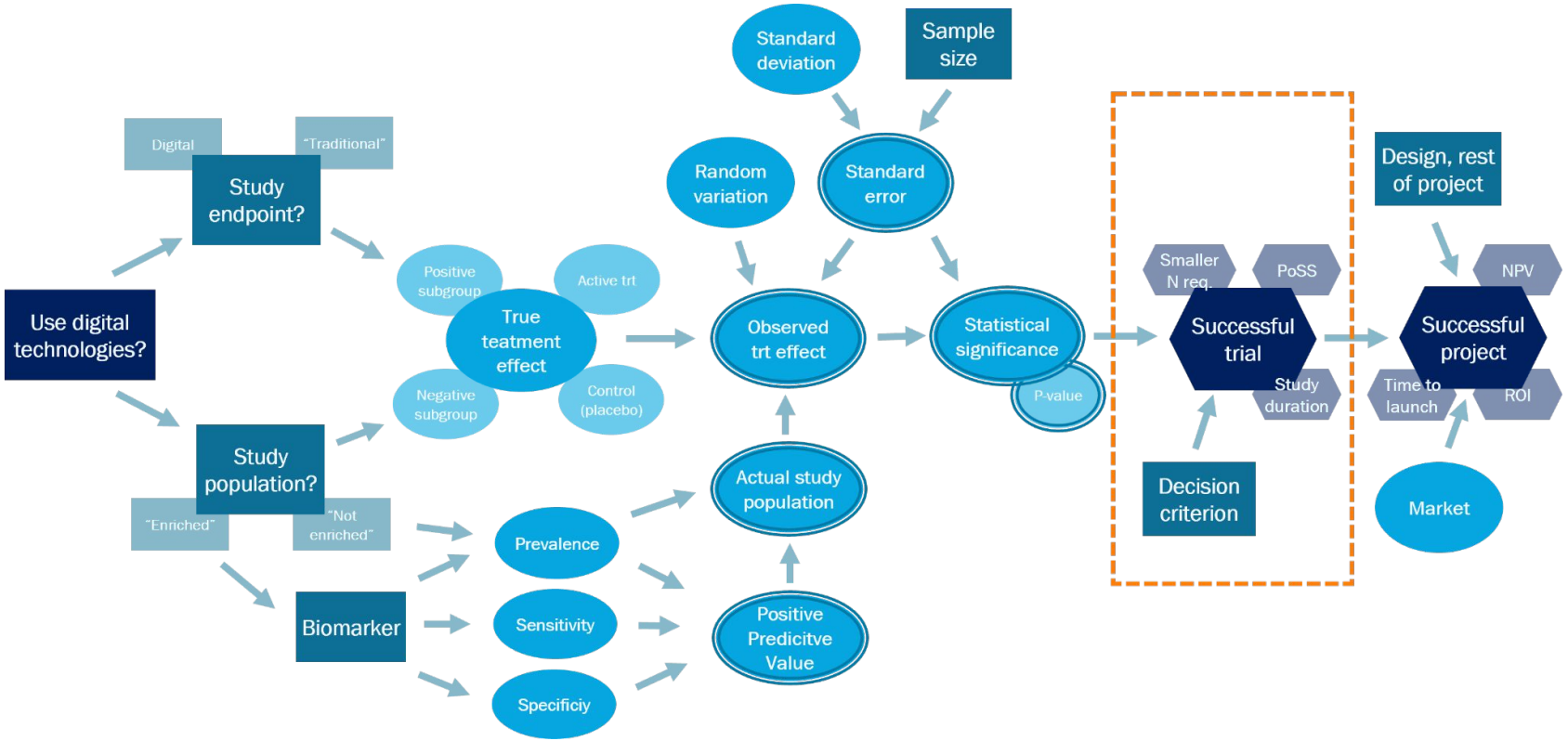

Components of quantitative model

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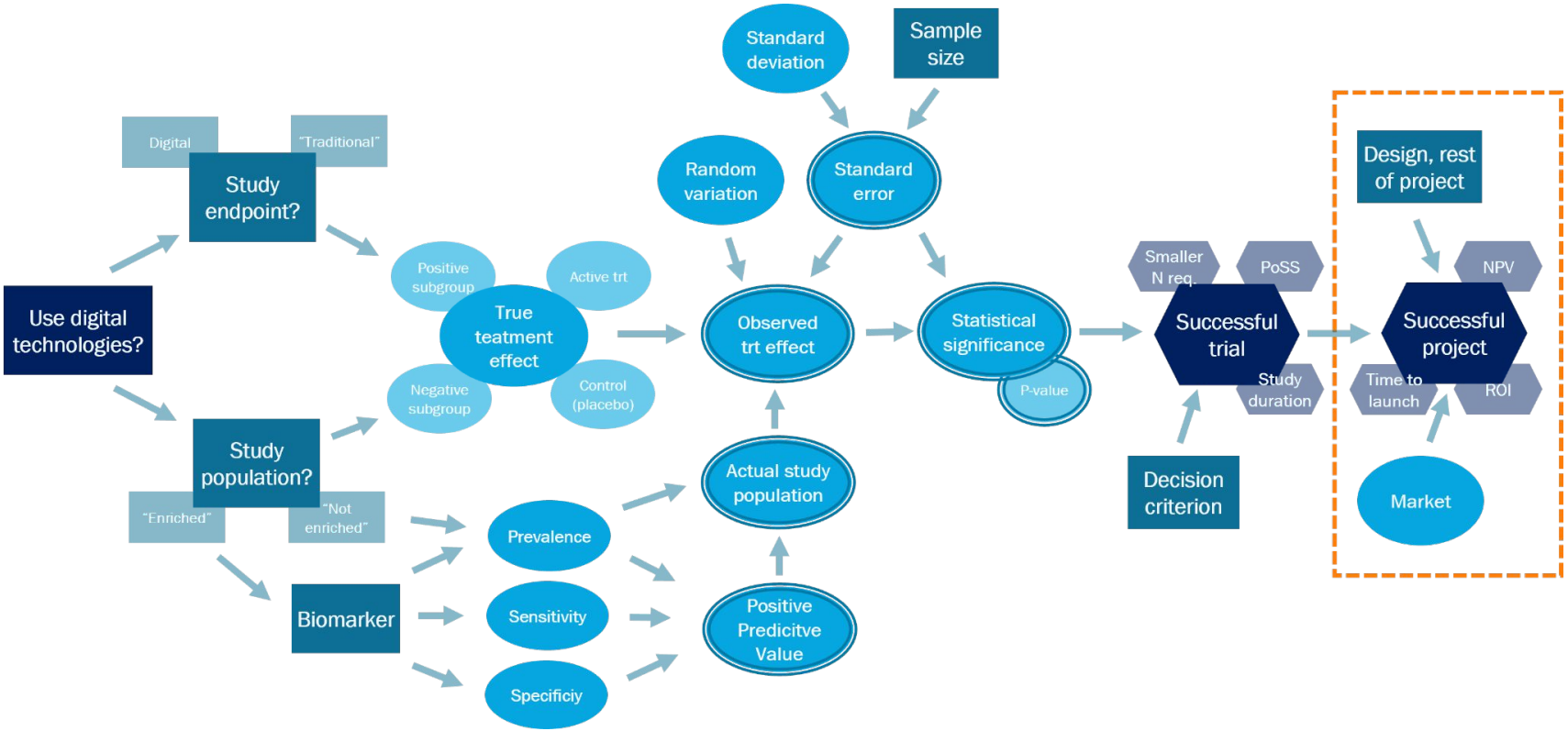
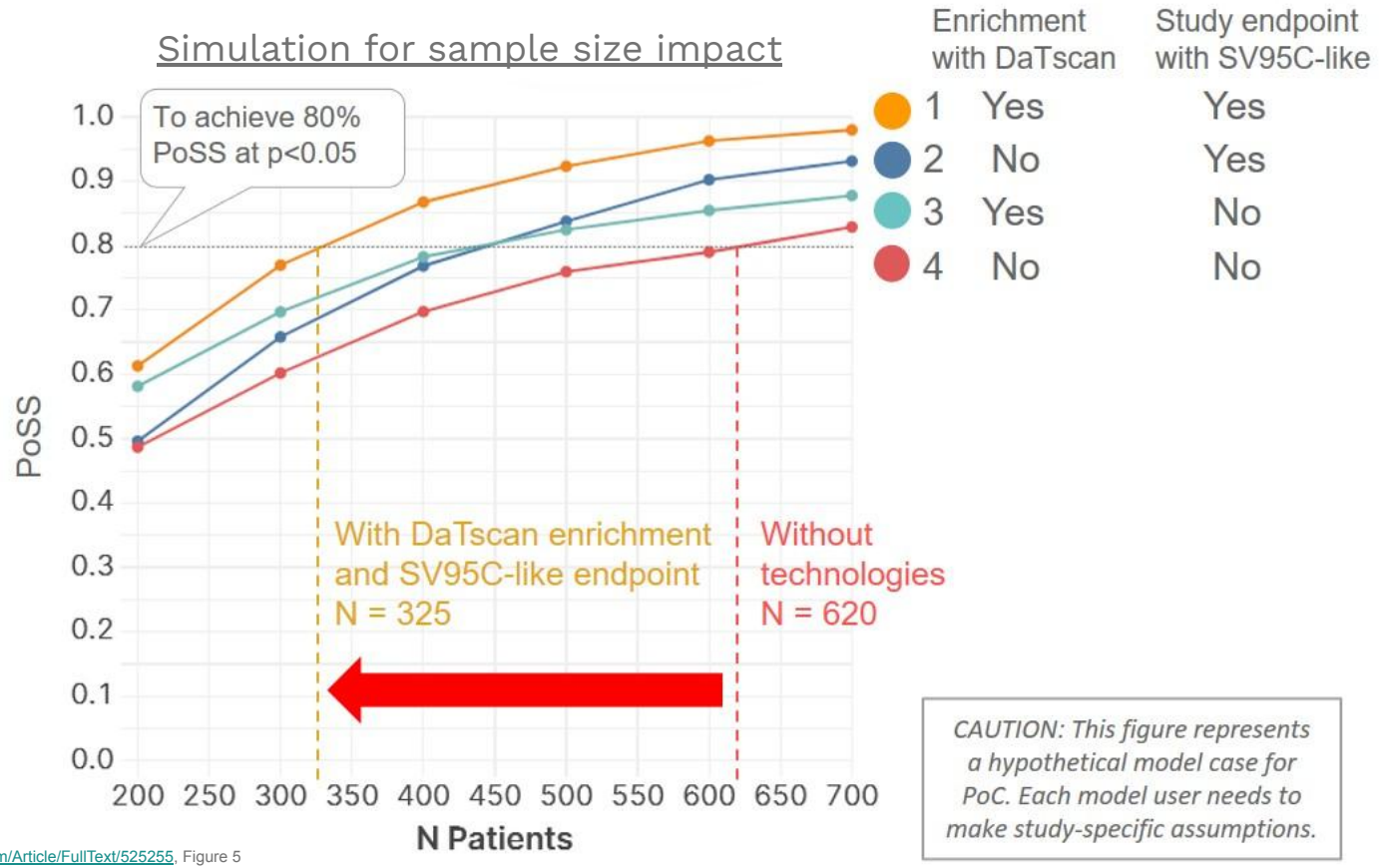
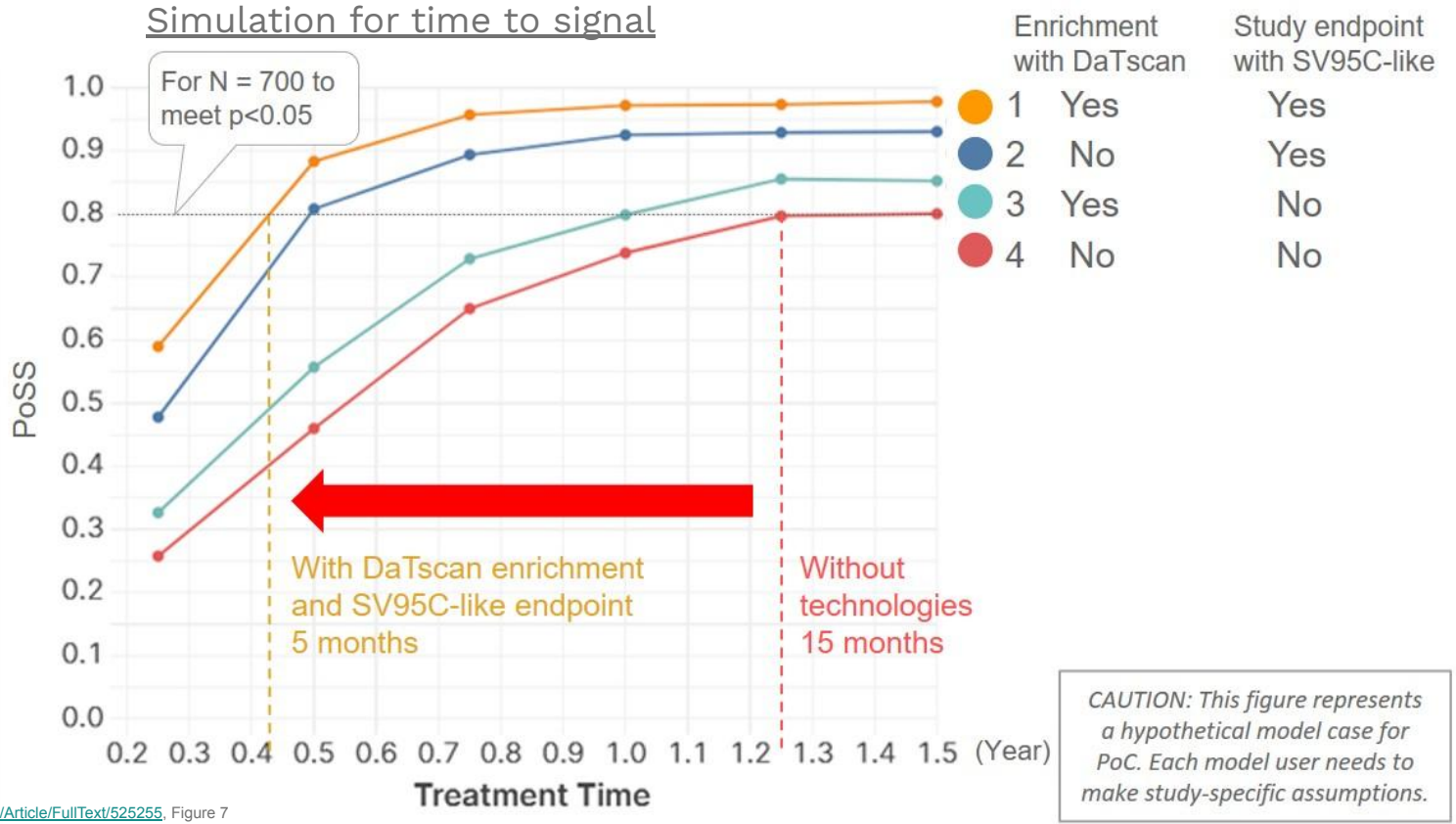


Biomarkers can reduce sample size



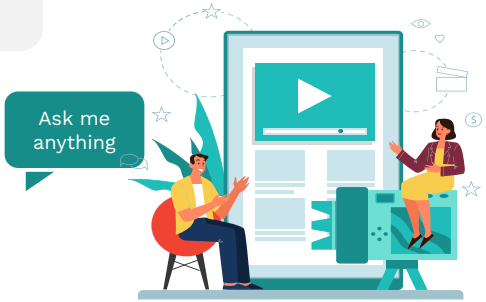
https://www.karger.com/Article/FullText/525255, Figure 5

Or time to market



https://www.karger.com/Article/FullText/525255, Figure 7

Virtual Journal club



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DIGITAL MEDICINE SOCIETY

NOCTURNAL SCRATCH

Digital Measures Development

Nocturnal Scratch as a Digital Endpoint for Atopic Dermatitis

Public launch event

Sept. 8, 2022 | 10 a.m. ET

Founding Project Partners

abbvie

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

NOVARTIS

Pfizer

ucb

Project Collaborators

Advancing Innovation in Dermatology

almirall

gsk GlaxoSmithKline

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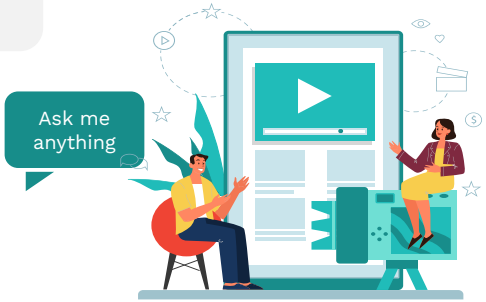

Digital Biomarkers

Considerations for Conducting Bring Your Own “Device” (BYOD) Clinical Studies

September 15, 2022 11am ET

Pirinka Georgiev
Associate Director
Pfizer
Minnesota, USA

Krishna Jhaveri
Clinical Lead
Motion BioSensors Group
New York, USA

Jen Goldack, MBA
CEO
DiMe Society
Moderator

THANK YOU

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