

Enabling novel digital endpoints in clinical trials for regulatory purposes:

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Bringing efficiency to the industry by creating a service based ecosystem



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Title: Enabling novel digital endpoints in clinical trials for regulatory purposes: bringing efficiency to the industry by creating a service based ecosystem

Stream: Trends & Technology (TT)

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Ecosystem for digital:

- Diagnostics
- Endpoints
- Companion solutions

Problem Statement

Digital measure challenges across the industry

1. Development and Management Challenges

- Validation process
- Clinical relevance
- Evolution of algorithms and technology
- ...

2. Challenges of collaboration & asset sharing

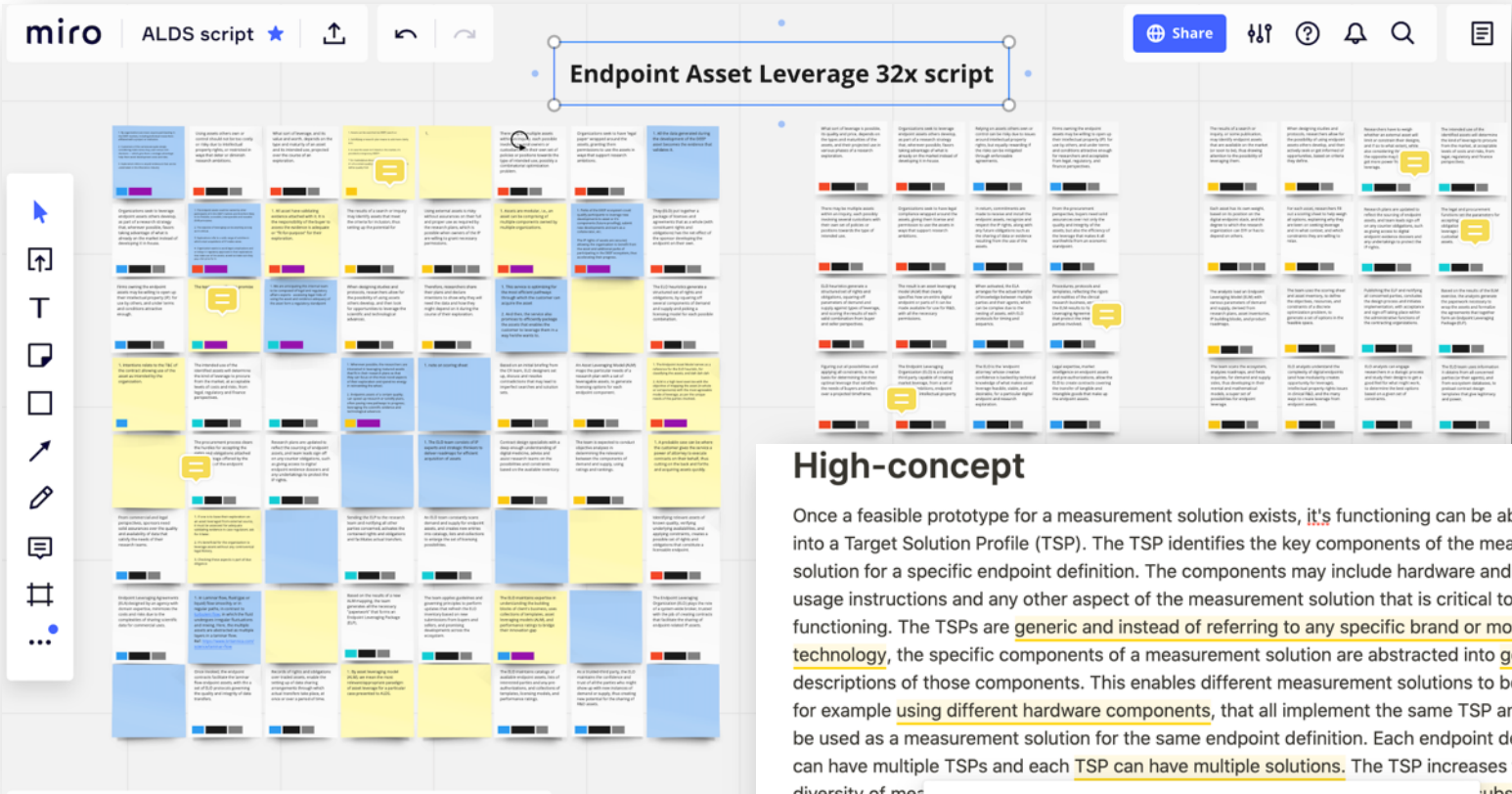
- Need for environment of trust
- Complexity of transactions

3. Immature ecosystem

- Lack of harmonisation by regulators
- Lack of industry-wide standard for methods & services
- Low / no availability of consistent services



Leveraging current environment



1) “Coding” of the current landscape into strategic service designs

2) Interactive workshop with 30+ organizations

High-concept

Once a feasible prototype for a measurement solution exists, its functioning can be abstracted into a Target Solution Profile (TSP). The TSP identifies the key components of the measurement solution for a specific endpoint definition. The components may include hardware and software, usage instructions and any other aspect of the measurement solution that is critical to its functioning. The TSPs are generic and instead of referring to any specific brand or model of technology, the specific components of a measurement solution are abstracted into generic descriptions of those components. This enables different measurement solutions to be created, for example using different hardware components, that all implement the same TSP and thus can be used as a measurement solution for the same endpoint definition. Each endpoint definition can have multiple TSPs and each TSP can have multiple solutions. The TSP increases the diversity of measurement solutions and enables the upgrading and subsequent validation of measurement solutions.

Full-Script

10y- Sponsors are reducing avoidance of high technological complexity solution can afford jeopardizes evidence gap in the evidence

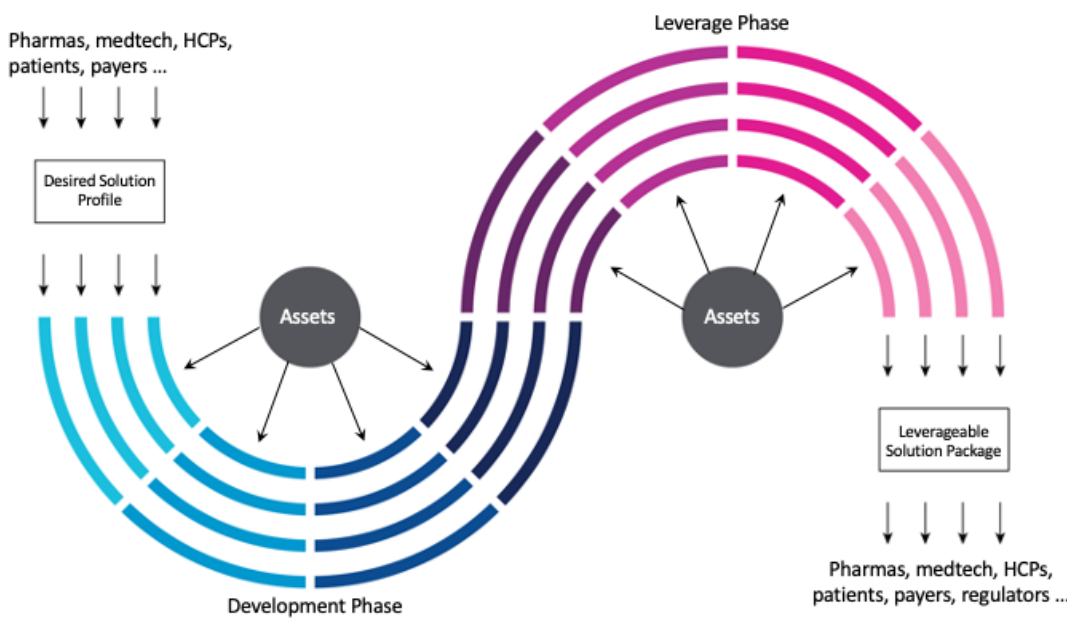
- Open (12) Resolved
- Earle Bain 06/10/2020
To make the overall easier to follow, I want to bring the concept up first. I.e., What problem is it? Future state vs. current uncertainty and how established it will be easier to understand.
- Stefan Nicolet 06/10/2020
what if a software or hardware contains too generic could lead to wrong interpretation.

Use of terms from the V3 framework, which can't be misconstrued	DC's notes	2B Publishing TSP	Sentence level	Reword statement(s)	Text, especially terminology with regulatory meaning prone to misinterpretation by stakeholders from different backgrounds (eg, regulatory, tech, clinical etc) * re-frame to reduce this * test for effectiveness
Advances on the "in-sensor MEMS level" should be included;	DC's notes	2B Publishing TSP	Script level	Re-coding 32x	Refine coding to capture this nuance in the profile well because changes on Transducer level, algorithm → effects the data; "need to be aware of all this to avoid GIGO"
TSP considers more things than what's included in the script	DC's notes	2B Publishing TSP	System level	Re-coding 32x Technical discussions	* follow up with Jeremy to expand the notion of T

3) Re-coding and refining

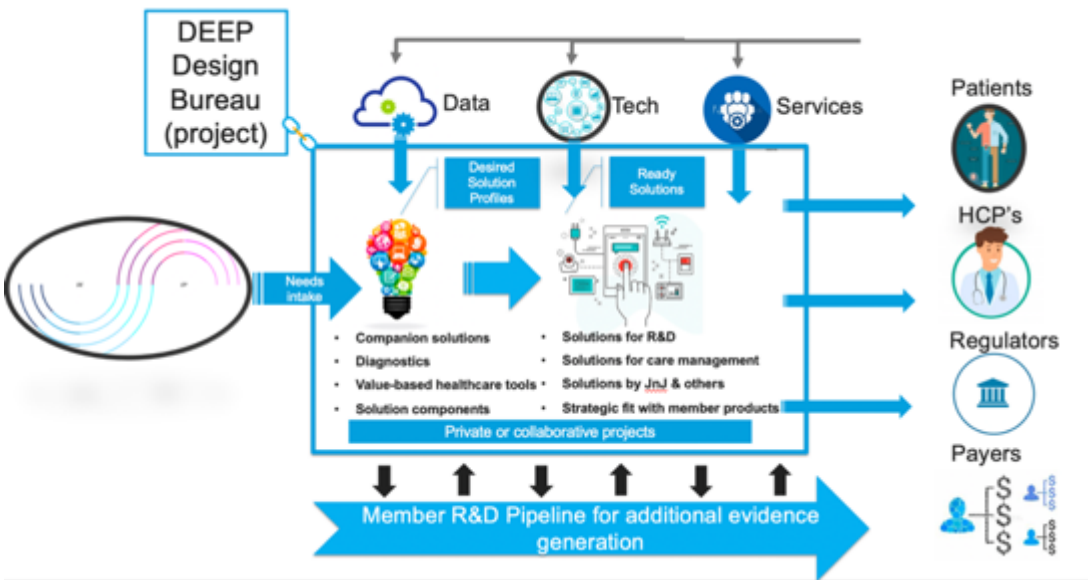
What is DEEP – Two Sides

Ecosystem of new services



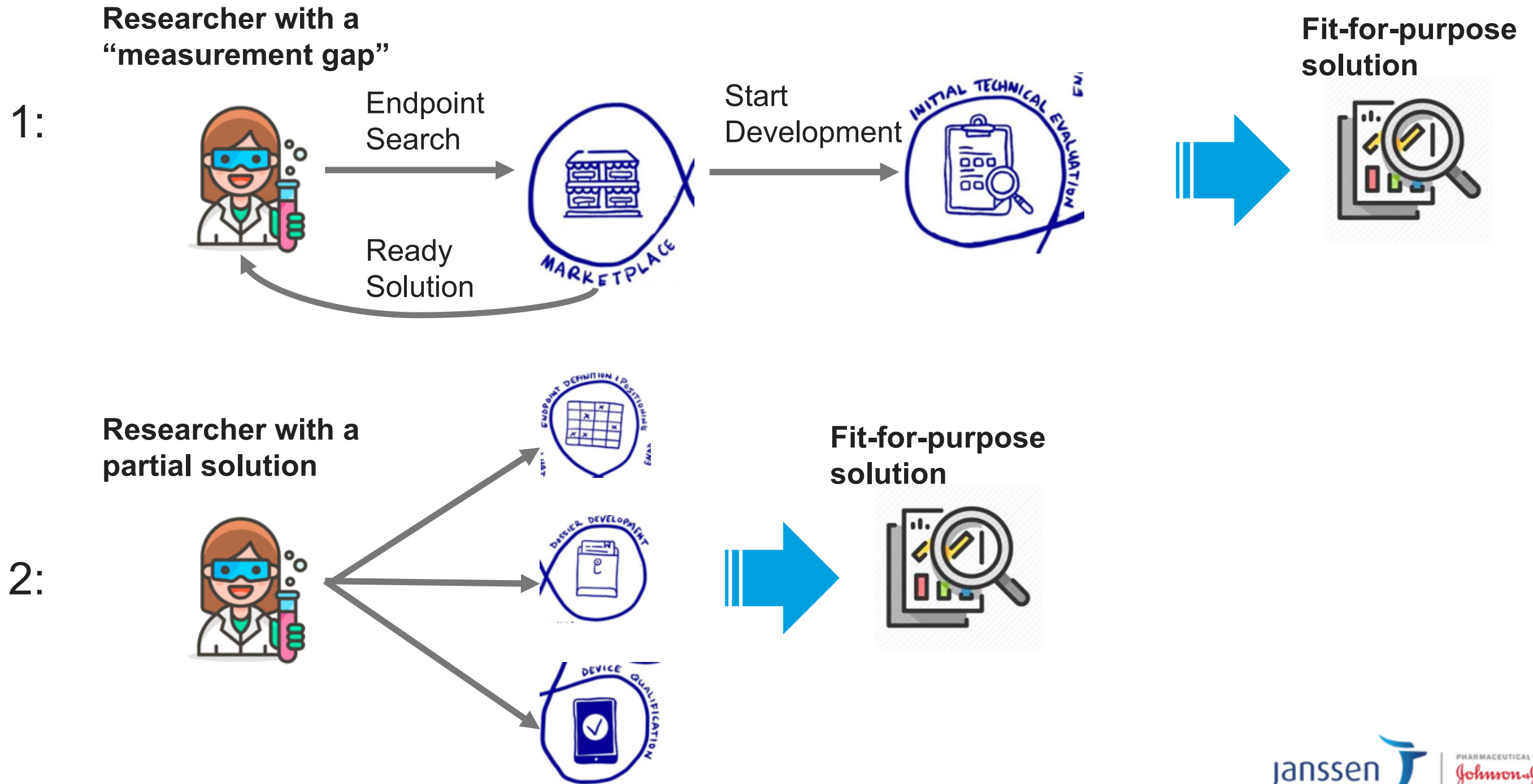
Harmonized and efficient services

Marketplace for collaboration & asset trading

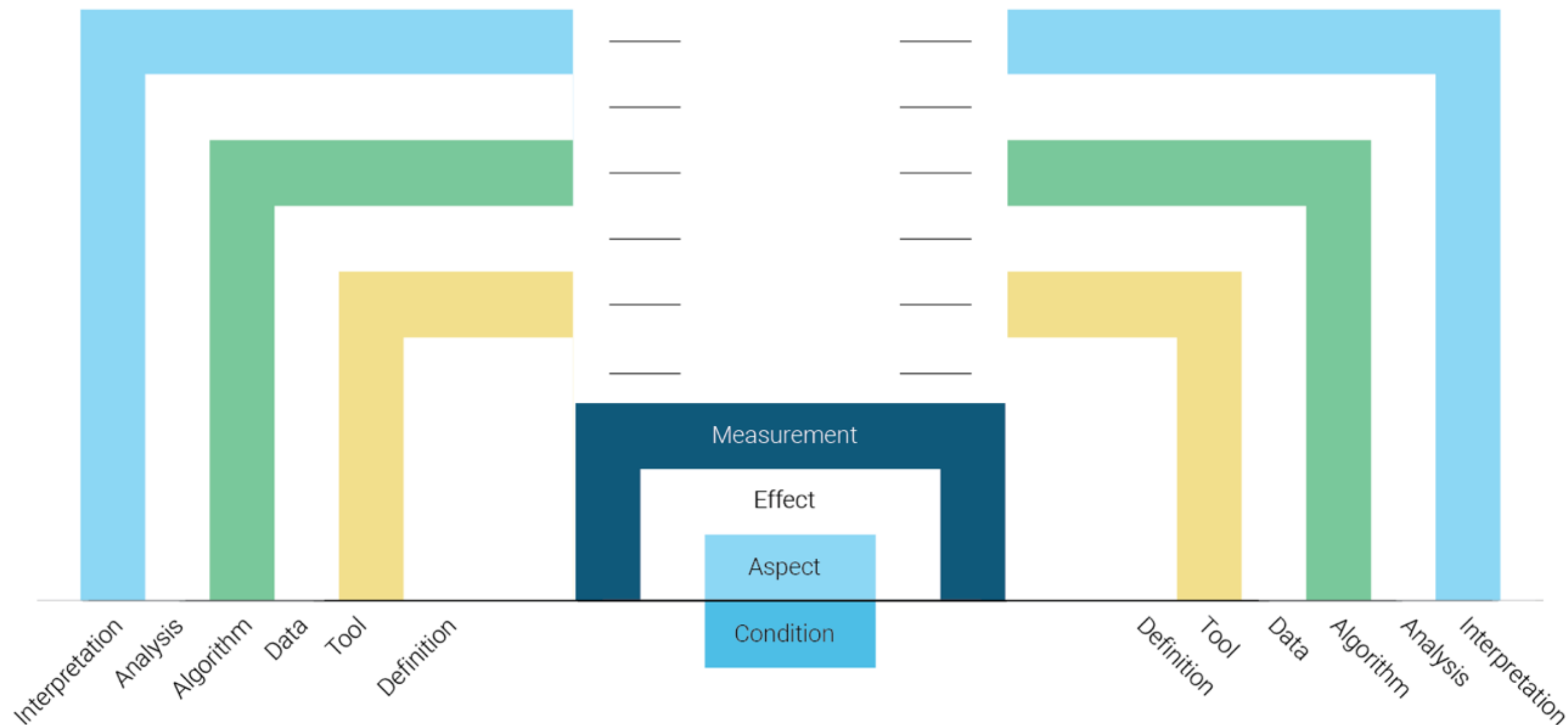


Standardized and efficient asset transactions

DEEP Offers Different Starting Points



Layered Endpoint Asset Model



Example Endpoint Definition

Meaningful Aspect of Health: ability to perform ambulatory services

Concepts Of Interest:

- walking capacity
- lower extremity balance
- lower extremity strength

Outcome to be measured:

- Steps per day
- Duration of walking bouts per day
- Frequency of walking bouts per week

Endpoint:

- Percentage of patients with >15% decrease in activity monitoring from baseline
- Percent change from baseline stepping compared to placebo at week 4 and 7
- Percentage of inactive patients with a mean of <6000 steps per day at week 8

Why?

Evidence for Endpoint Definition

“Strength is not the issue, it’s just that I get out of breath so easily”

“I can move around the house ok and like to keep myself busy...”

Concepts Of Interest:

walking capacity



~~lower extremity balance~~

~~lower extremity strength~~

Outcome to be measured:

- ~~• Steps per day~~
- Duration of walking bouts per day
- ~~• Frequency of walking bouts per week~~

Most relevant outcome

“... but just walking my dog, if I go more than 5 minutes I need to stop and catch my breath. ”

Example endpoint stack

Condition: Pulmonary hypertension

Aspect: Ability to perform ambulatory services

Effect: Improvement in continuous walking capacity

Measurement: Duration of walking bouts per day

Tool: actigraphy device to measure movement, steps and include time stamps

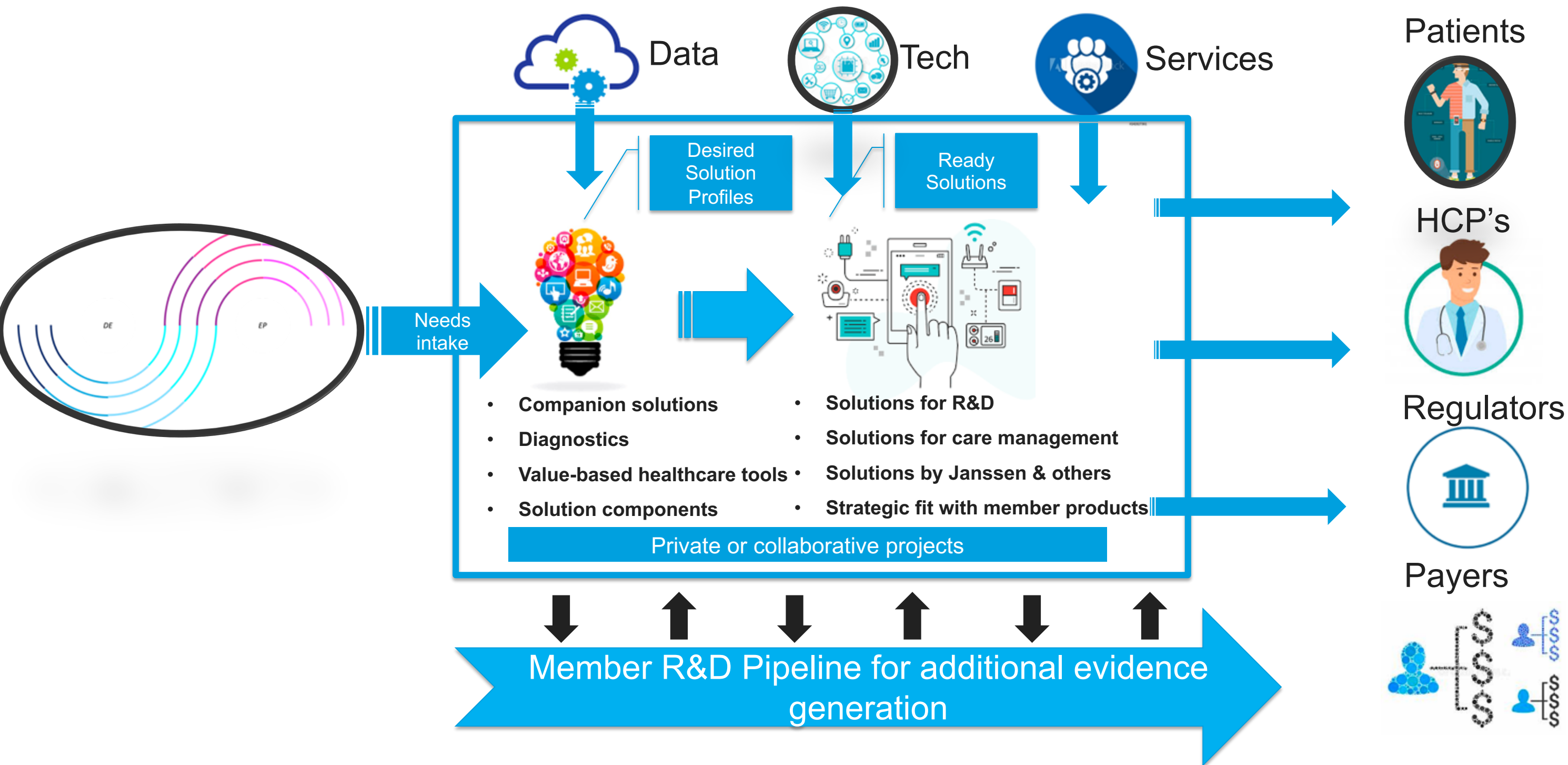
Data: actigraphy datasets w timestamps, location/position changes, to train or feed the algorithm

Algorithm: AI to crunch the data to turn signals into information

Analysis: turn information into insights, to get to duration (and number) of walking bouts per day

Interpretation: meaning of a change in duration and # of walking bouts per day for a patient

Definition digital endpoint:
change in continuous walking capacity measured by avg/median and max duration of walking bouts per day in patients with PH as a proxy for their ability to perform ambulatory services.



New Taxonomy Needed

Already
established

ICD-10 chapters

Chapter	Block	Title
I	A00–B99	Certain infectious and parasitic diseases
II	C00–D48	Neoplasms
III	D50–D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
IV	E00–E90	Endocrine, nutritional and metabolic diseases

J45	Asthma
Excl.:	acute severe asthma (J46) chronic asthmatic (obstructive) bronchitis (J44.-) chronic obstructive asthma (J44.-) eosinophilic asthma (J82) lung diseases due to external agents (J60-J70) status asthmaticus (J46)
J45.0	Predominantly allergic asthma

Disease domains

Physical
activity

Respiratory
symptoms

...

Meaningful
aspects

Walking capacity

Ability to perform
intense activities

Attacks caused by
physical activity

...

Concepts of
Interest

Step count

Time spent doing
intense activities

Continuous activity
count measurement

More work needed – can this be crowdsourced?

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Thank you



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Science Conference

Acknowledgements

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