

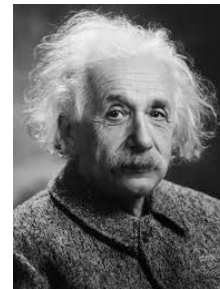
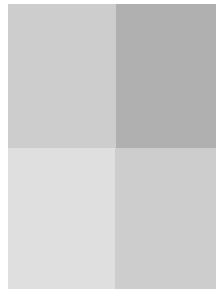
Does the concept of a “Sentient-Enterprise” apply to the clinical trial execution process?

Peter Grolimund, Senior Industry Consultant

10th of October 2016

The way we look at it

- It should be a short summary
- It should be max one page
- Dense the information it's too much
- Don't bother about the details they do not have time
- Isn't it not simpler than that? Short en it
- The message should be crisp
- It is a single sentence you need to provide§



- We need a dashboard
- We need to see in a simple overview what is happening
- We will measure KPI's
- We will increase our performance
- We will take corrective actions
- We might link the bonus to the KPI's

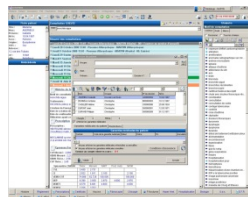
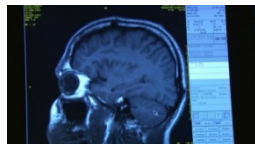
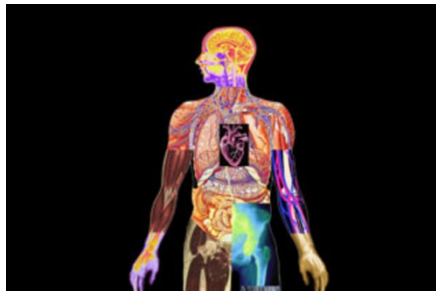


The complexity remains..



A single indicator for a complex system might not be sufficient

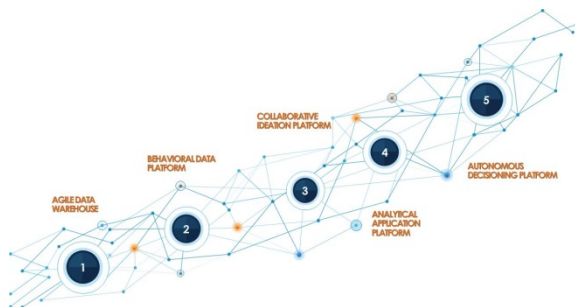
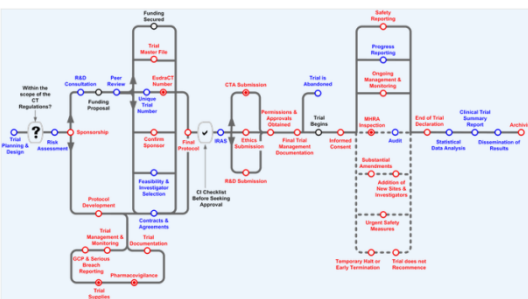
<http://www.health.com/health/gallery/0,,20513064,00.html#high-fever-0>



The complexity remains..

Priority	0,1 Low	0,3 Medium	0,6 High	
Medium	1.67%	10.00%	30.00%	Behind
Medium				
Low				
High				
Medium				
Low	1.67%	12.33%	7.50%	Work In Progress
High				
High				
Medium				
Medium				
Medium	3.33%	3.33%	0.00%	Closed
High				
Low				
Low				
Medium				
High	3.33%	3.33%	22.50%	Not Started
Medium				
Low				
High				
Low				

A single indicator for a complex system might not be sufficient

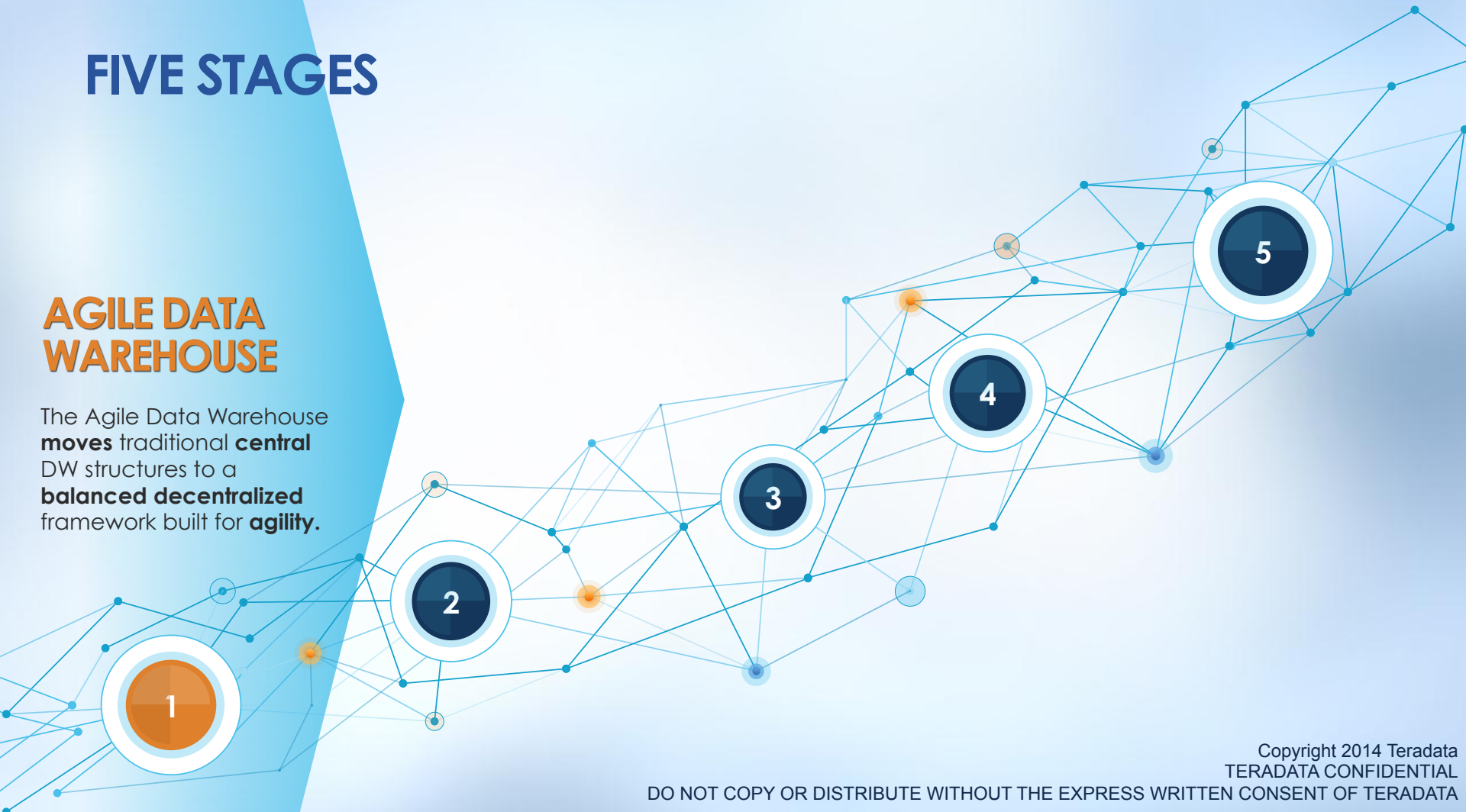


The sentient enterprise

FIVE STAGES

AGILE DATA WAREHOUSE

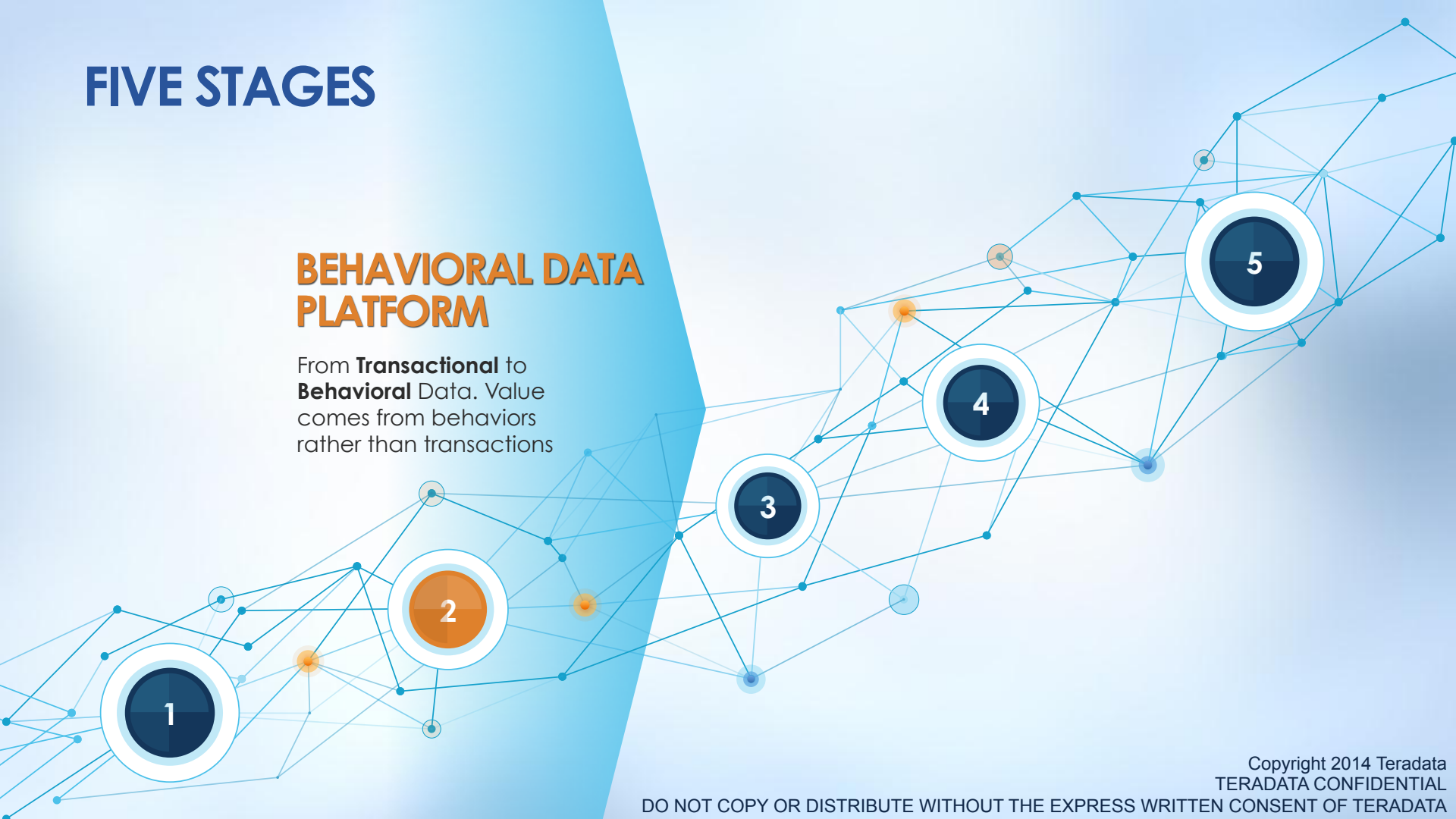
The Agile Data Warehouse **moves** traditional **central** DW structures to a **balanced decentralized** framework built for **agility**.



FIVE STAGES

BEHAVIORAL DATA PLATFORM

From **Transactional** to
Behavioral Data. Value
comes from behaviors
rather than transactions



FIVE STAGES

COLLABORATIVE IDEATION PLATFORM

LinkedIn for Analytics. From centralized Metadata to **Crowd Sourced Collaboration.** Social interactions connect the data within the enterprise



FIVE STAGES



ANALYTICAL APPLICATION PLATFORM

Analytical Apps. From static applications and ETL to agile **Self Service Apps.** From Extraction of Data to **Enterprise Listening.**

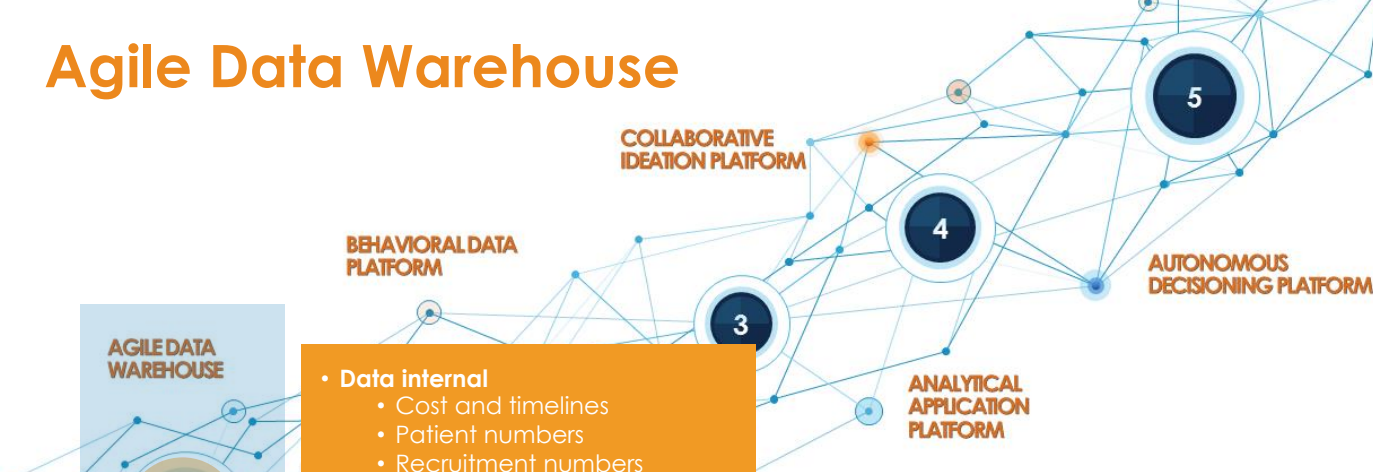
FIVE STAGES



AUTONOMOUS DECISIONING PLATFORM

Predictive Technologies
and **Algorithms**. From
focusing only 10% of time
on decision making and
90% of sifting through data
to **90% of decision making**
with the help of
automated algorithms.

Agile Data Warehouse

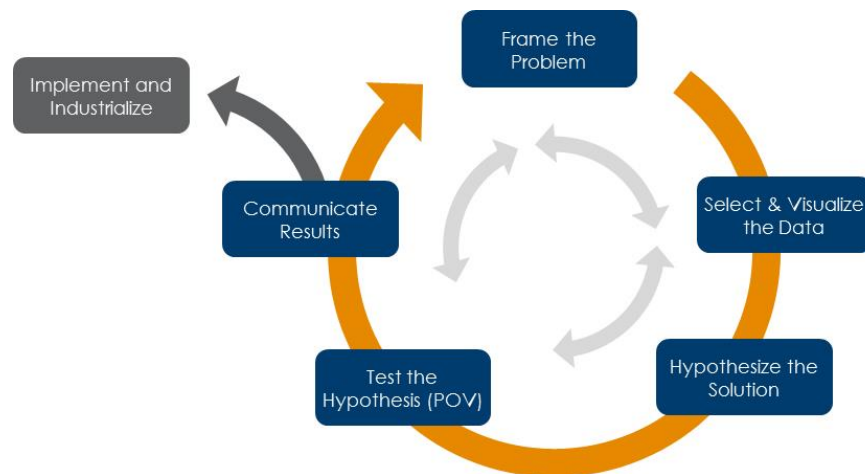


• Data internal

- Cost and timelines
- Patient numbers
- Recruitment numbers
- Investigators
- Drop out rate
- Safety data of all trials
- Clinical data pool
- Pre-clinical data
- Logs, web-logs
- Documents
- Device data / raw....

• Data external

- Recruitment numbers
- Dropout rates
- Recruitment countries
- Duration / Timelines
- Competitive trials
- Safety data
- RWE
- Publications (pubMED)
-



The Agile Datawarehouse

Case Study

*A Cancer Center Vision:
The development and state-wide adoption of a centralized scientific and
clinical Data Warehouse*

The Future of Personalized Medicine

Edward Martinez

(Former VP & CIO of Moffitt Cancer Center)

- What are the recruitment numbers from all similar trials (inclusion, exclusion criteria, indication, phase..)?
- What is the expected portion of patients fulfilling the criteria population against RWE data?
- Is there any competitive trial with the same population ongoing?
- Provide me the costs of the selected design and population based on former trials
- What are the common safety issues today in the existing treatments and compounds of the same family?
- What are the most frequent co-medications in today's treatment?

Find Caucasian females who have Breast Cancer, have received either chemotherapy or radiation and the number of tumor tissue samples we have

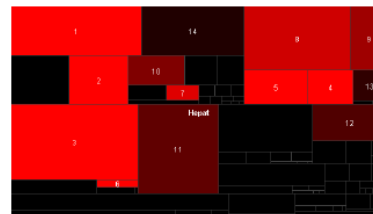
(Data Warehouse)

For patients with lung cancer, show top 10 administered drugs and gene expression profile associated with those tumors for patients with survival greater than 24 months

(Data Warehouse)

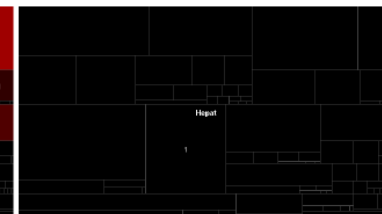
To qualify for a new clinical trial, show patients who have colon cancer, have smoked, have received a particular drug and have tissues samples available to study.

Drug=Propylthiouracil and (SOC='Hepat') Subset: <17 years



Rank	SOC	Term (PT)	EBGM
1	Hepat	Hepatitis	25.375
2	Hepat	Hepatic necrosis	23.838
3	Hepat	Hepatic failure	14.747
4	Hepat	Jaundice cholestatic	7.759
5	Hepat	Hyperbilirubinaemia	6.606
6	Hepat	Acute hepatic failure	4.402
7	Hepat	Autoimmune hepatitis	3.665
8	Hepat	Jaundice	3.397
9	Hepat	Cholestasis	2.969
10	Hepat	Hepatosclerosis	2.555
11	Hepat	Hepatic function abnormal	2.000
12	Hepat	Hepatomegaly	1.929
13	Hepat	Hepatitis cholestatic	1.956
14	Hepat	Hepatocellular injury	1.203

Drug=Methimazole and (SOC='Hepat') Subset: <17 years

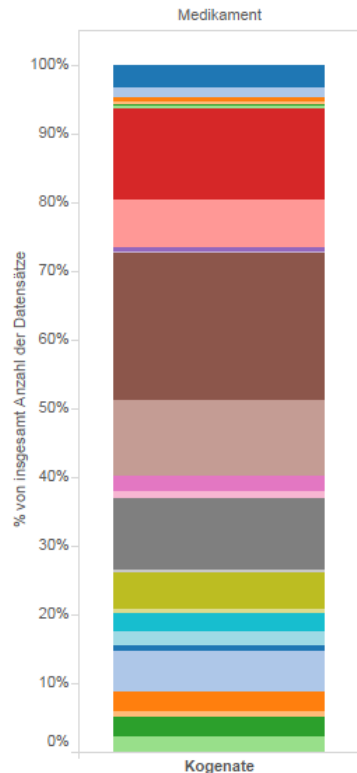


Rank	SOC	Term (PT)	EBGM
1	Hepat	Hepatic function abnormal	1.006

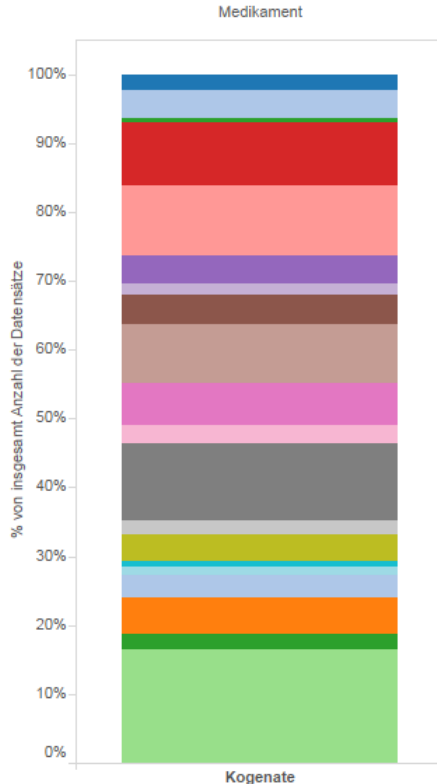
Figure 4 shows the MGPS values for these two drugs across age groups. The EBGM values for severe liver injury with propylthiouracil were higher in younger (≤ 17 yr) than older individuals (> 17 yr), regardless of whether the individual severe preferred terms or the severe liver injury custom term grouping these individual terms was used. The side-by-side comparison of overlapping/non-overlapping status of (EB05, EB95) intervals for severe liver injury adverse events for all age groups showed them to be higher with propylthiouracil than methimazole, and the propylthiouracil EBGM values were higher and did not overlap with the methimazole values.

The Agile Datawarehouse

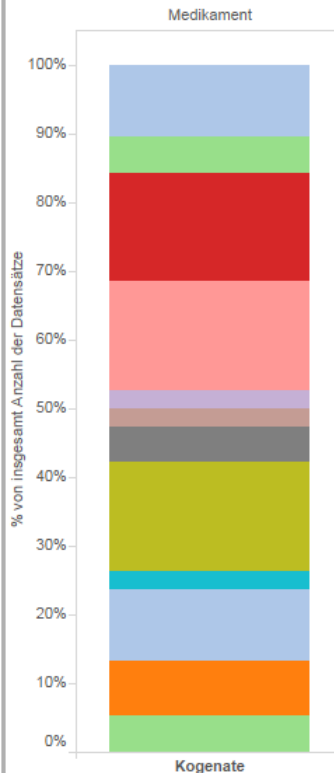
Side effects listed in the clinicaltrials.gov



Side effects in FDA AERS



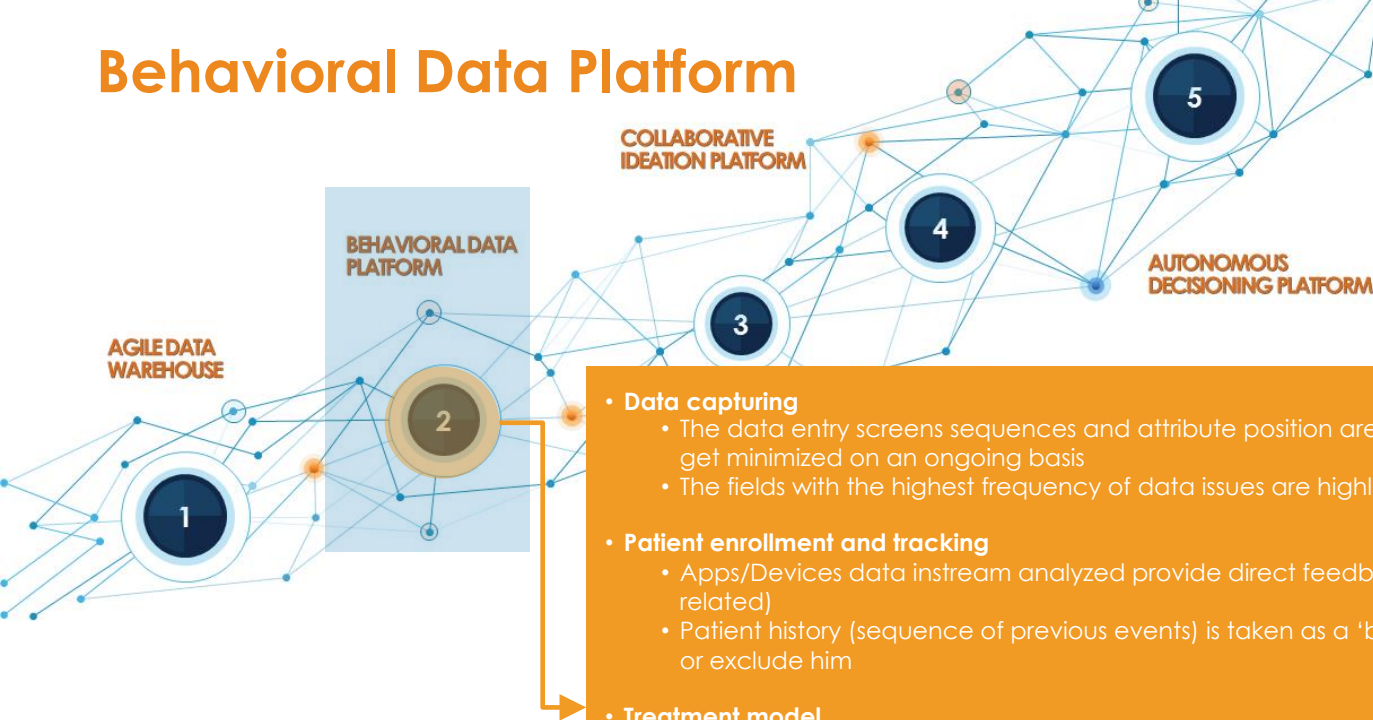
Side effects mentioned in drugs.com (prescription)



Soc Description

- Blood and lymphatic system disorders
- Cardiac disorders
- Endocrine disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl. metastatic)
- Nervous system disorders
- Psychiatric disorders
- Renal and urinary disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Surgical and medical procedures
- Vascular disorders

Behavioral Data Platform



- **Data capturing**

- The data entry screens sequences and attribute position are adjusted such that data quality issues get minimized on an ongoing basis
- The fields with the highest frequency of data issues are highlighted dynamically

- **Patient enrollment and tracking**

- Apps/Devices data instream analyzed provide direct feedback to the patient (e.g. compliance related)
- Patient history (sequence of previous events) is taken as a 'biomarker' to keep the patient on the trial or exclude him

- **Treatment model**

- Dosing gets automatically adjusted based on device values (e.g. Parkinson, dosing range)

- **Adaptive trial design to the extreme**

- Based on device data, sequence of events, the inclusion / exclusion criteria, the dosage, visit schedule are adjusted according to the incoming data

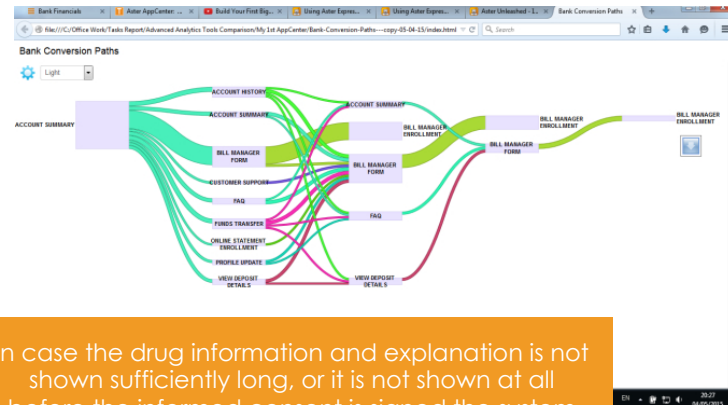
- **Analysis plan**

- Provision of common analytical plans for the set-up (end-points, population), and the related outputs
- Provision of a library of code frequently used for such outputs and tables generated out of all codes (e.g. using entiMICE metadata, analytics of analytics)

Behavioral Data Platform

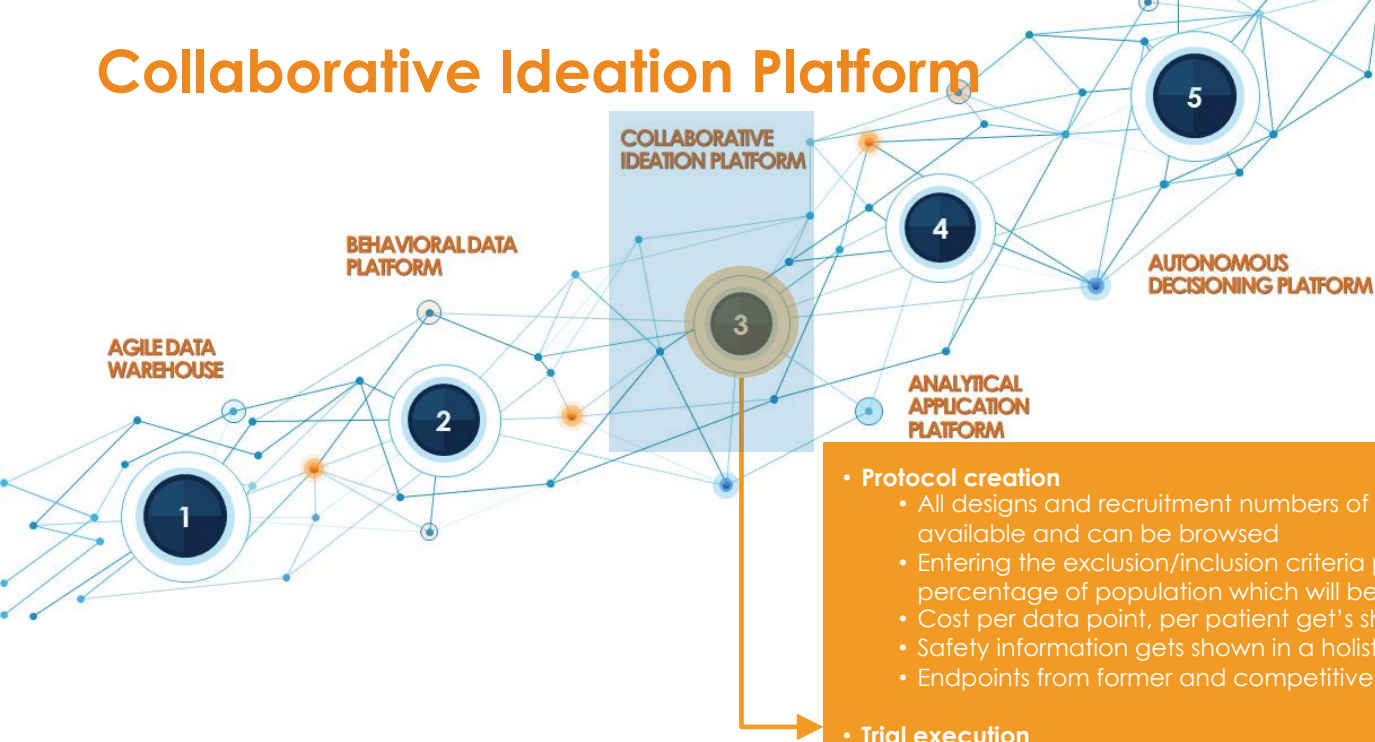


Life Click stream analysis



In case the drug information and explanation is not shown sufficiently long, or it is not shown at all before the informed consent is signed the system might alert the investigator, or inform the study manager

Collaborative Ideation Platform



• Protocol creation

- All designs and recruitment numbers of comparable internal / external trials are available and can be browsed
- Entering the exclusion/inclusion criteria provides visual information about percentage of population which will be covered (based on RWE)
- Cost per data point, per patient gets shown from the past trials
- Safety information gets shown in a holistic way
- Endpoints from former and competitive products are shown

• Trial execution

- Ongoing trials with comparable target population gets shown
- Investigator performance gets shown in a holistic way from former trials independent of the CRO

• Experience available inhouse / external

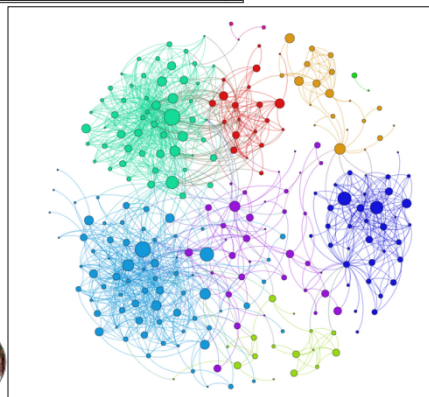
- Know-how gets identified by using CV's, LinkedIn and publication information
- Analytics of analytics identifying outputs and related codes and authors, frequency of used codes for certain outputs

Collaborative Ideation Platform

Analytics on Your Analytics



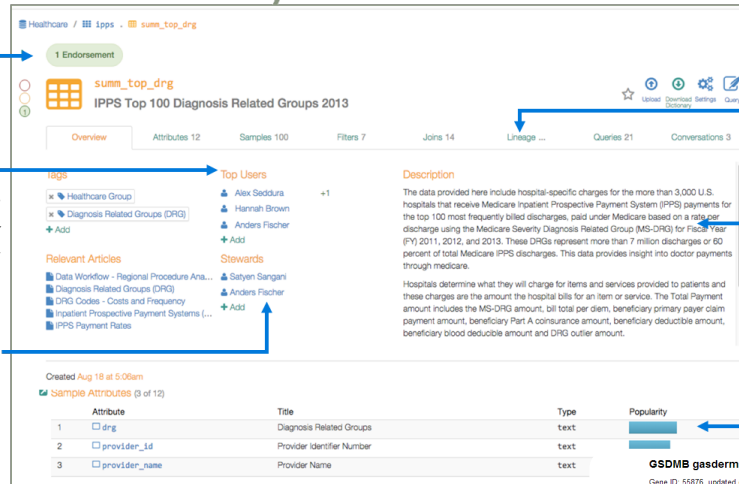
Role	Indication	Drug family	Rc
all	Infectious diseases		
		allergens	
		alternative medicines	
		herbal products	
		nutraceutical products	
		probiotics	
		anti-infectives	
		amebicides	
		aminoglycosides	



Endorsements,
deprecations
& warnings
propagate
best practices

Subject
matter
experts by
table usage

Data
stewards



Lineage tracks
deprecations
and changes

Like Wikipedia
for analytics

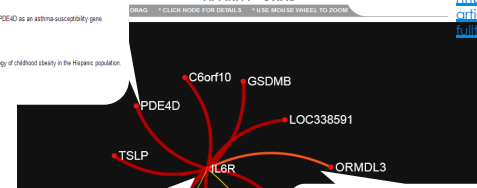
Popularity of
columns in
queries

PDE4D phosphodiesterase 4D, cAMP-specific
Gene ID: 5144, updated on 22-Sep-2013

Genome-wide association analysis identifies PDE4D as an asthma susceptibility gene.
HGRIQ GWAS Catalog
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3400000/>

New genetic loci identified for the pathophysiology of childhood obesity in the Hispanic population.
HGRIQ GWAS Catalog
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3400000/>

NAL BIOLOGY: GENE: "PDE4D"
AFFINITY - GWAS



IL6R Interleukin 6 receptor
Gene ID: 3570, updated on 14-Sep-2013

The IL6R variation Arg357Gln is a potential modifier of lung function in subjects with asthma.
Hagenaars GA, et al. J Allergy Clin Immunol. 2012 Aug; 130(2):255-261.

Interleukin-6 receptor gene (IL6R) polymorphism is associated with metabolic syndrome in female Taiwanese adolescents.

ORMDL3 ORM1-like 3 (S. cerevisiae)
Gene ID: 94103, updated on 10-Sep-2013

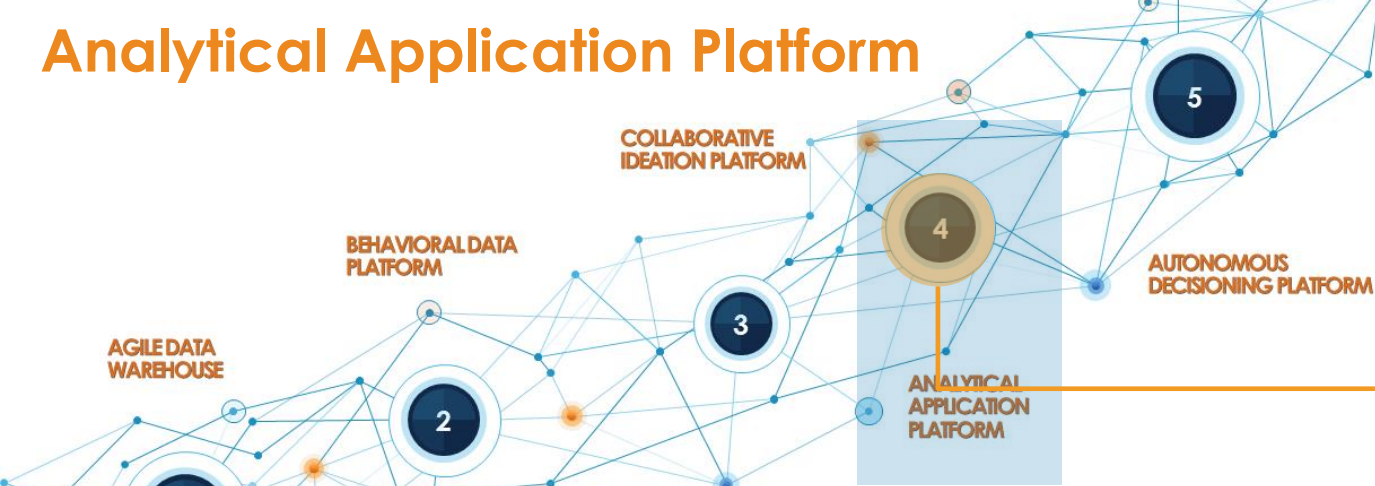
only the top SNPs

[http://www.igcnc.org/article/S0091-6749\(10\)01032-8/](http://www.igcnc.org/article/S0091-6749(10)01032-8/)

ORMDL3

3 (ORMDL3) were

Analytical Application Platform



- **Study planning**

- Affinity App to show comparable trials external and internal using special features (e.g. exclusion / inclusion criteria, endpoints, design, compounds, indications)
- Safety profile using all information (e.g. social media, FDA, internal Safety data, etc.)
- Patient journey from similar patients (RWE)

- **Study execution**

- Patient Journey on the trial with the real-world data
- Patient Journey from former Trials

- **Multidimensional cost evaluation**

- Different aspects for cost evaluation (e.g. cost per patient, cost per datapoint, cost for delayed execution – and patent time)

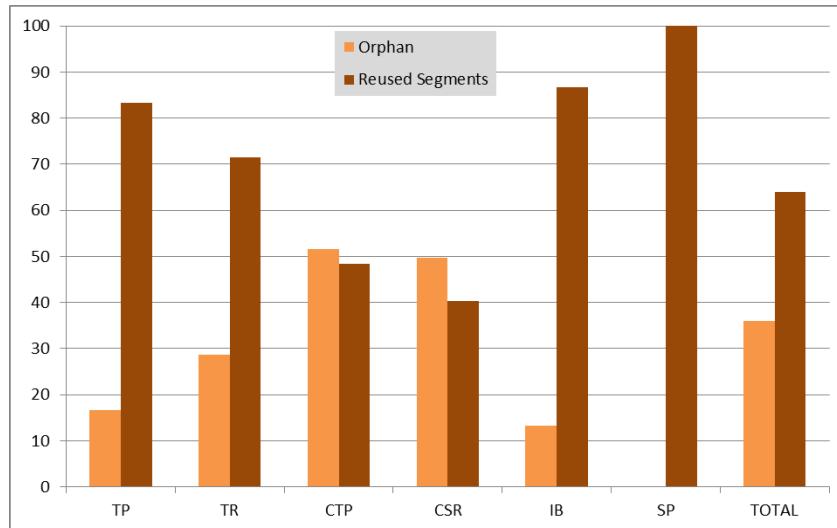
- **Skills and team**

- Graph of internal experience on such trials
- External experience in the organization and linkages (scientific, former roles)

By [Dr. Satish Tadikonda](#)
Applied Clinical Trials

The reused texts

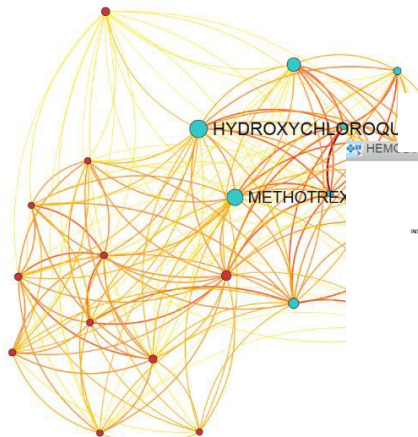
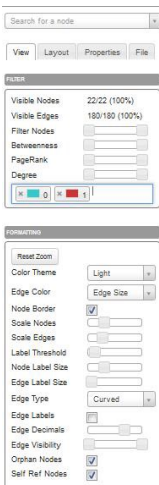
	Toxicology Protocol	Toxicology Report	Clinical Trial Protocol	Clinical Study Report	Investigators Brochure	Protocol Synopsis	TOTAL
Orphan	16.7	28.6	51.6	49.7	13.3	0	36
Reused Segments	83.3	71.4	48.4	40.3	86.7	100	64



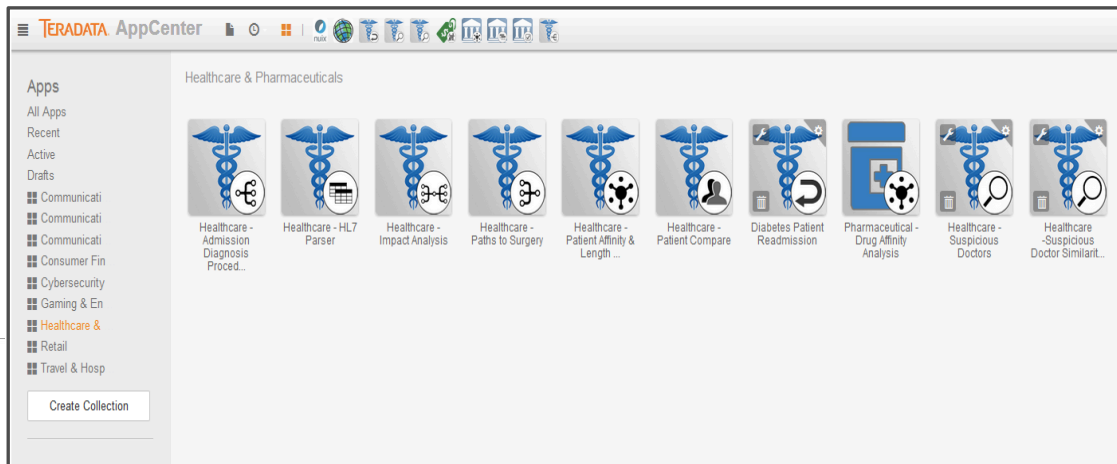
Toxicology Protocol (TP)
Toxicology Report (TR)
Clinical Trial Protocol (CTP)
Clinical Study Report (CSR)
Investigators Brochure (IB)
Protocol Synopsis (SP),

Apps some examples and the framework

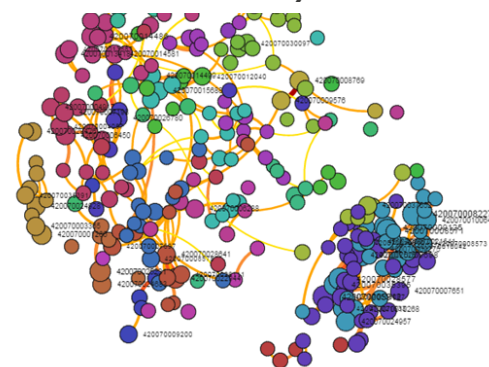
Drug Affinity Analysis



Paths that lead to surgery



Patient Cluster Analysis



Autonomous Decision Platform



- **Recruitment**
 - Analysis of ongoing recruitment pattern and avoiding the recruitment of patients when the distribution of the patients is not along the planned demographic distribution (dynamic exclusion criteria)
- **Dosing**
 - Personalized dosing as extreme adaptive design using 'biomarkers'
- **Visit schedule**
 - Visit schedule not along fixed time periods but based on agreed 'status' of the patients measured by devices and data
- **Exclusion of enrolled patients**
 - Agreed rules and status might exclude the patients from further progress on the trial

Autonomous decision Platform

DOSAGE INDIVIDUALIZATION

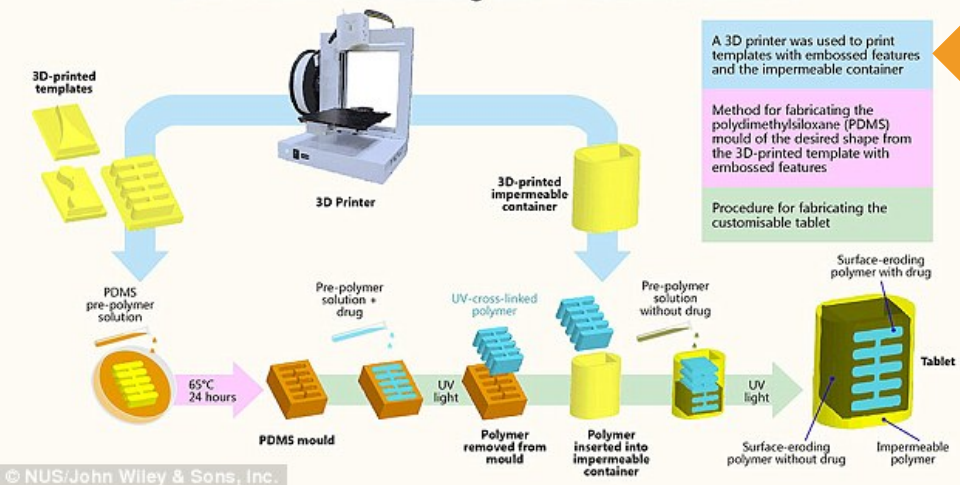
Definition : "Adaptation of the dosage regimen in function of the clinical characteristics of the individual, aiming to achieve the best possible therapeutic efficiency at the lowest risk of unwanted effects."

QUICK TAKE

Drug dosing goes digital with software
to personalize medication

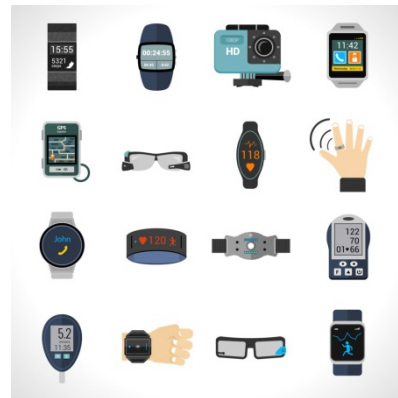
One pill to rule them all: 3D printed 'supertablet' can contain all your medications for the day

Procedure for Making Customisable Tablets



Outcome based adjustment
And reimbursement

single pill



TERADATA

SHIFTS OF THE FIVE STAGES

AGILE DATA WAREHOUSE

The Agile Data Warehouse **moves** traditional central DW structures **to a balanced decentralized framework** built for agility.

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From **Transactional** to **Behavioral Data**. Value comes from behaviors rather than transactions

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AUTONOMOUS DECISIONING PLATFORM

Predictive Technologies and Algorithms. From focusing only 10% of time on decision making and 90% of sifting through data to **90% of decision making** with the help of automated algorithms

Focus on the analytic approach before defining the tools ...

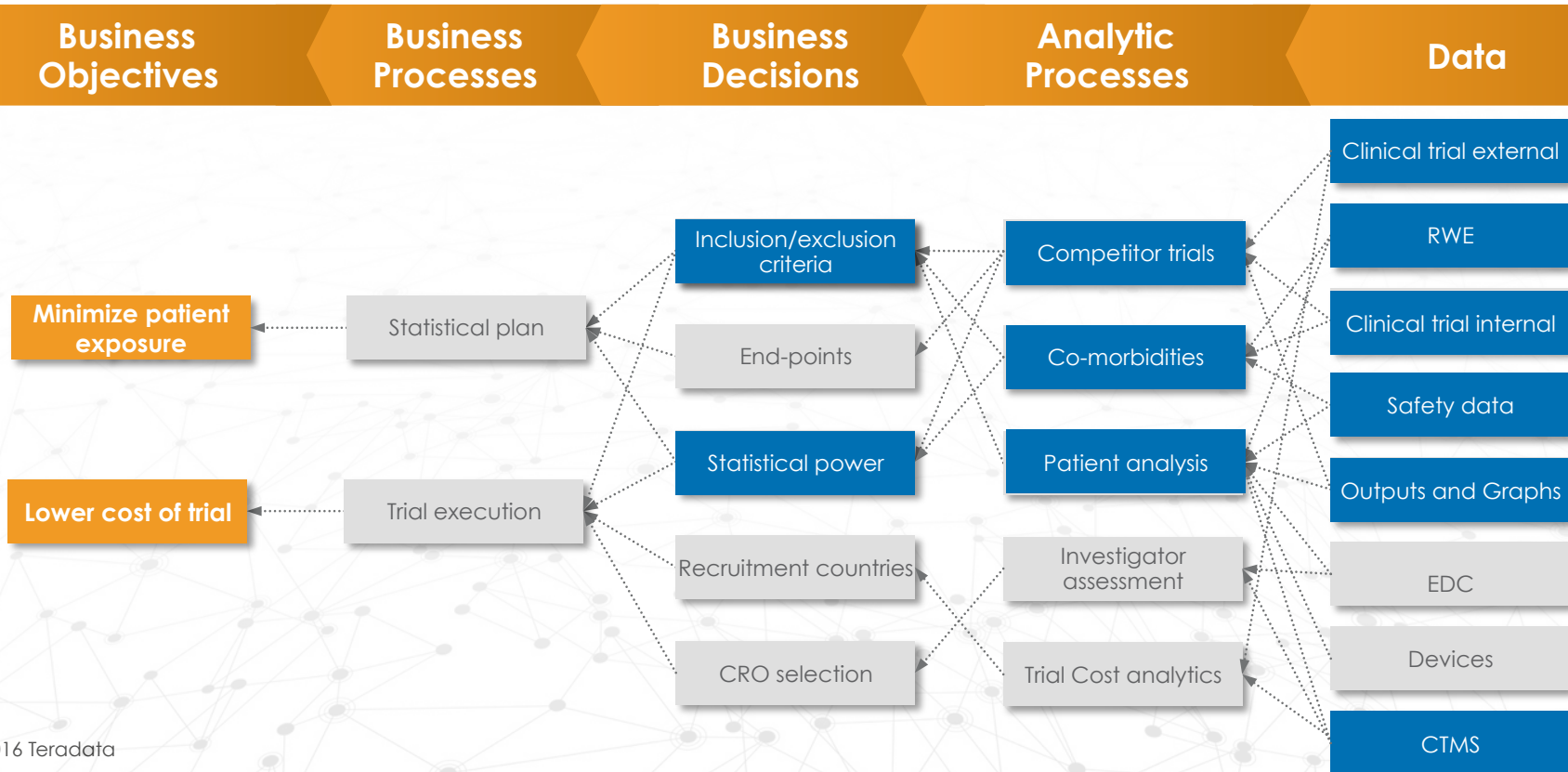
METHODOLOGY Before Technology!



Tools and technology will be an implementation decision
AFTER a project scope is agreed upon

Migrate From Projects To Frameworks

Shift focus from a single, tactical exercise to a comprehensive framework



TERADATA®