



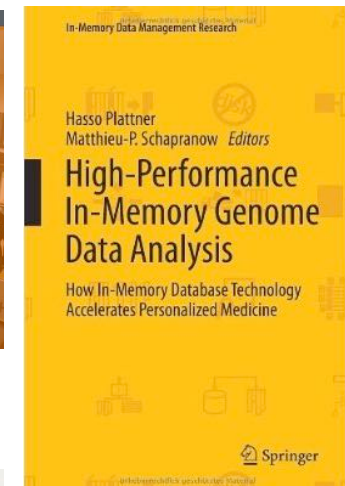
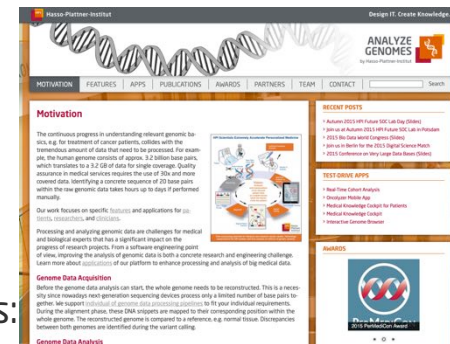
Use Case Oncology: Application Examples

Dr. Matthieu-P. Schapranow
Data Management for Digital Health
Summer 2017

Where to find additional information?



- **Online:** Visit we.analyzegenomes.com for latest research results, slides, videos, tools, and publications
- **Offline:** Read about it:
High-Performance In-Memory Genome Data Analysis:
In-Memory Data Management Research, Springer,
ISBN: 978-3-319-03034-0, 2014



- **In Person:** Register for 3rd Int'l Symposium on Big Data in Medicine Nov 20-21 in Potsdam in cooperation with HIMSS Europe



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2

Agenda

- Hasso Plattner Institute
- Mix and Match Your Presentation
- Discussion and Q&A



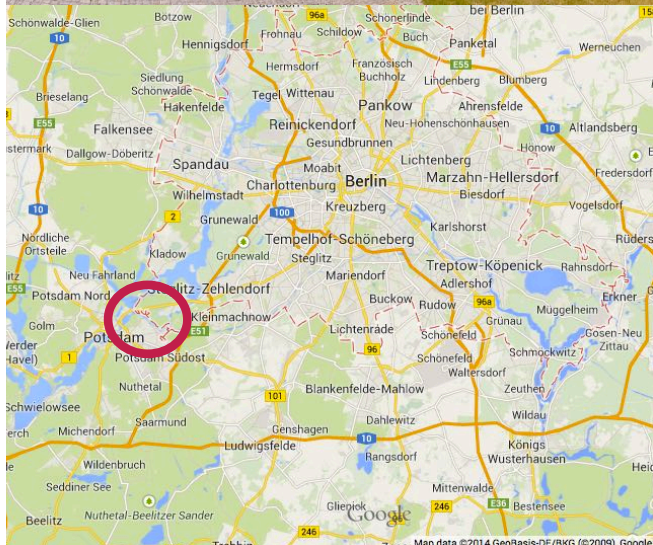
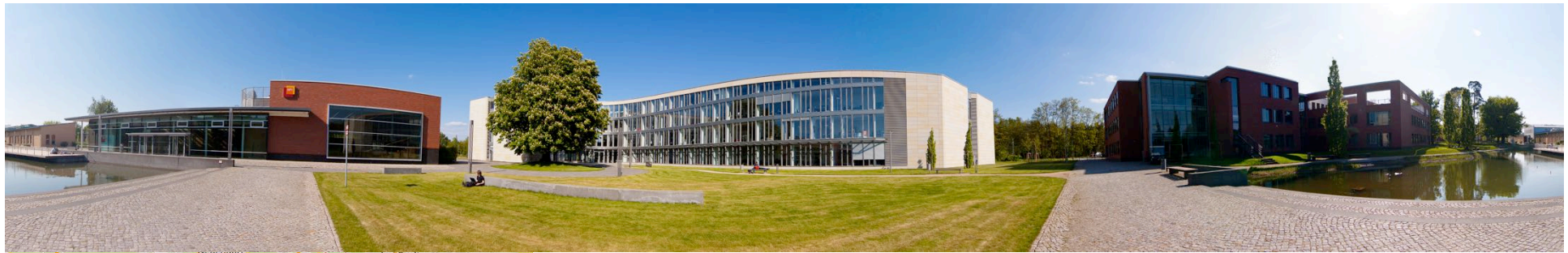
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3

<http://www.gahollywoodkiss.com/In-N-Out-Burger-Secret-Menu-.html>

What is the Hasso Plattner Institute, Potsdam, Germany?



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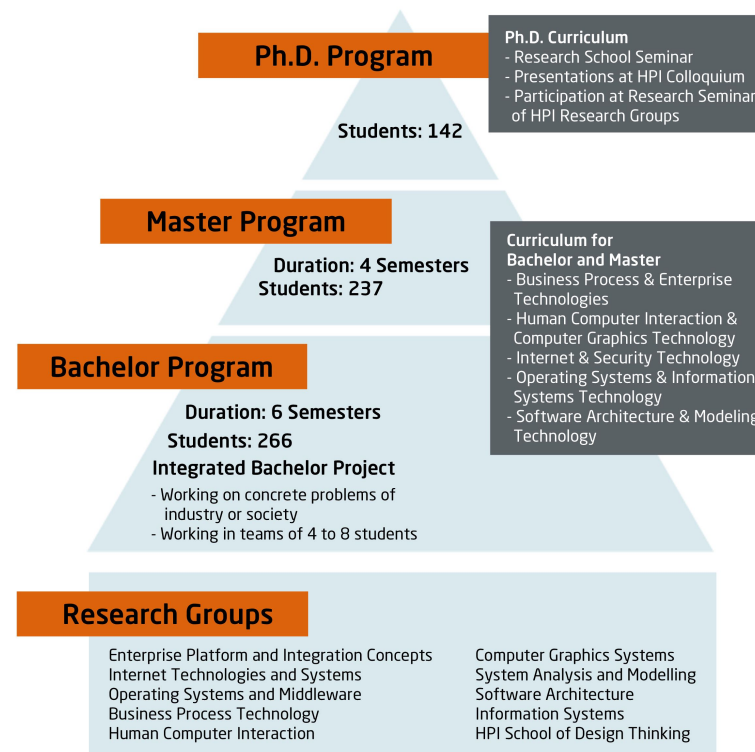
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4

Hasso Plattner Institute Programs



- Full university curriculum
- Bachelor (6 semesters)
- Master (4 semesters)
- Orthogonal Activities:
 - E-Health Consortium
 - School of Design Thinking
 - Research School



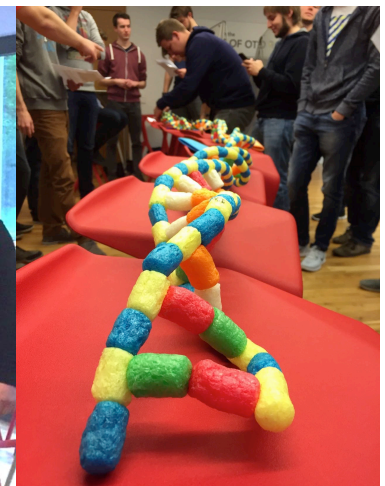
Status: February 2013

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5

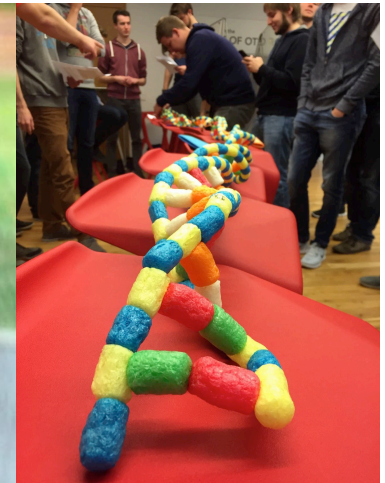
About the Lecture: Data Management for Digital Health 2017



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7

About the Lecture: Data Management for Digital Health 2017



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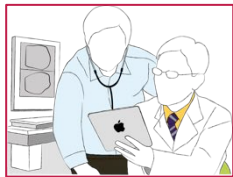
The Setting Actors in Oncology

■ Patients



- Individual anamnesis, family history, and background
- Require fast access to individualized therapy

■ Clinicians



- Identify root and extent of disease using laboratory tests
- Evaluate therapy alternatives, adapt existing therapy

■ Researchers



- Conduct laboratory work, e.g. analyze patient samples
- Create new research findings and come-up with treatment alternatives

Choose Your Perspective!

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9

The Setting

Actors in Oncology

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10

Gamification vs. Health App?



Anadolu Agency | Getty Images

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11

<http://www.startribune.com/how-pokemon-go-went-from-prank-to-phenomenon/387900342/>

What do citizens ask for?

- Myth: People are not interested in Digital Healthcare Services

Patient channel preferences,¹
frequency per year, %

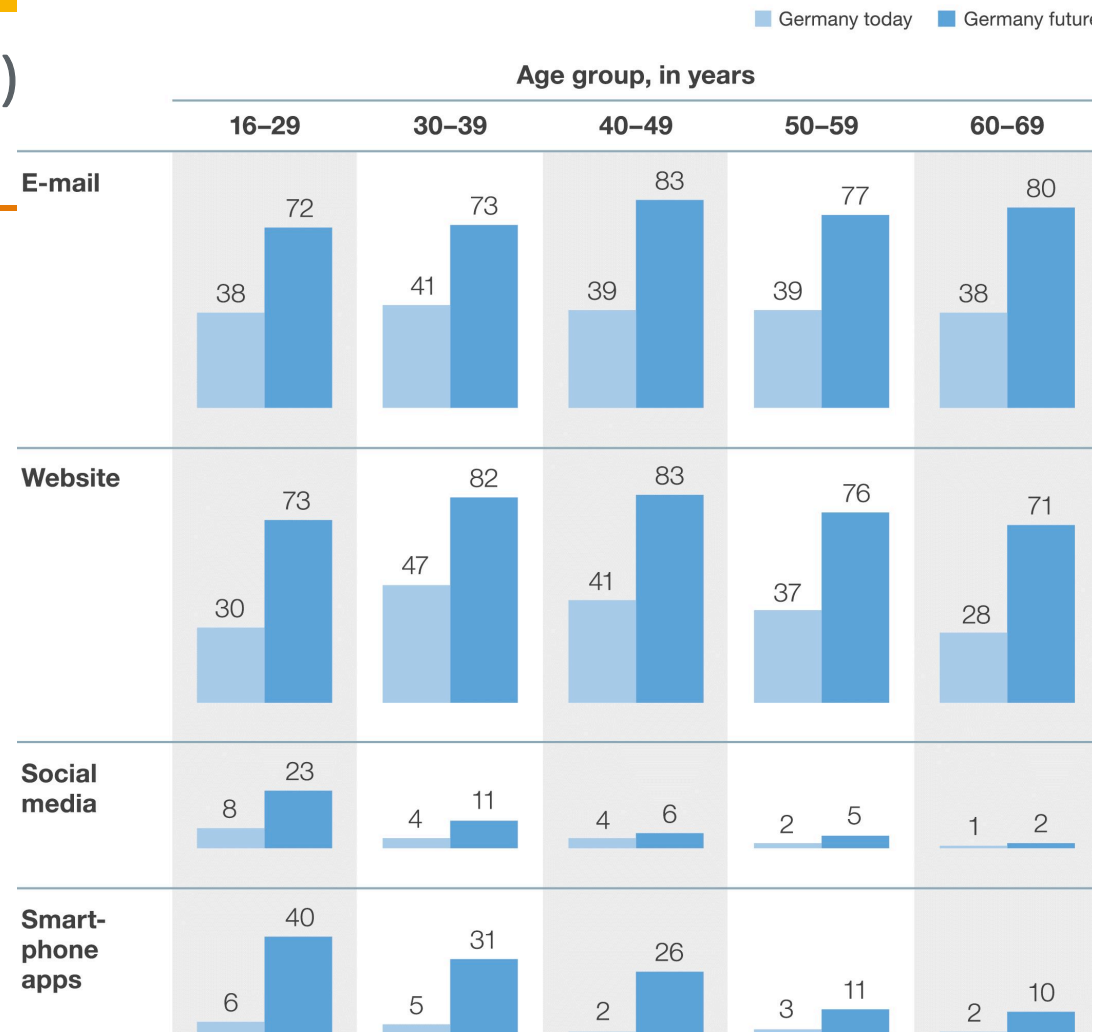
■ Not at all ■ 1 time ■ 2 times ■ 3–4 times ■ >4 times



¹Figures may not sum to 100%, because of rounding. Respondents were asked the following: *Thinking of all your interactions with your health system (doctors, hospitals, pharmacies, healthy-living websites, etc.) and social care in the last 12 months, please indicate the approximate number of times your interaction related to one of the following types.*

What do citizens ask for? (cont'd)

- Myth: The younger generation wants to use digital services only



Source: McKinsey Digital Patient Survey 2014

What do citizens ask for? (cont'd)



■ Myth: Patients require innovative features and apps in healthcare

Ranking of criteria for success of online proposition,¹ top 3 criteria, %

Germany

Ability to execute processes/receive services directly in the online platform 55

Fast availability of a personal contact person 48

Usability/accessibility of service offerings 39

United Kingdom

Increased awareness of online services 51

Ability to execute processes/receive services directly in the online platform 45

Fast availability of a personal contact person 43

Singapore

Increased awareness of online services 40

Wider range of value-added services 36

Width/clarity of information available 34

¹ Respondents were asked the following: *From your perspective, what needs to happen for you to use certain services online/on your mobile phone more frequently than in the past? Please select the three most important criteria for you.*

What do citizens ask for? (cont'd)

■ Myth: Personal healthcare data should never be donated for research purposes

Highest rate of comfort-ability or share of Yes

| Country | Age | Educat. |
|---------|-------|--------------|
| ES | 30-49 | Medium /High |
| CZ | 30-49 | High |
| ES | 30-49 | Medium |
| ES | 18-29 | Medium |
| UK | 30-49 | Medium |
| IE | 18-29 | Medium |

Large amounts of people's health data should be collected and analysed on an anonymous basis by health institutions, [...], to **enable improvements in the detection and treatment of diseases**.



You would give these institutions access to your health data as long as it is **amalgamated, anonymised and only used for statistical/research purposes**.



You would give these institutions access to your health data and **trust that they would store and use it appropriately**.



You would give these institutions permission to **store and analyse your data as personal and identifiable data** as this could help to **cure a disease** you or others might have.



■ very comfortable ■ comfortable ■ neutral ■ uncomfortable ■ it should not be allowed

Would you give permission for your insurance to **access your health and fitness data so they can adapt your insurance rate** according to your health behaviour and fitness level, i.e. you pay more or less depending on your lifestyle?



Would you be happy for your health and fitness data to be analysed by a **special health programme** or smartphone app, and to **receive recommendations** on how to live a healthier life and prevent the onset of certain diseases?



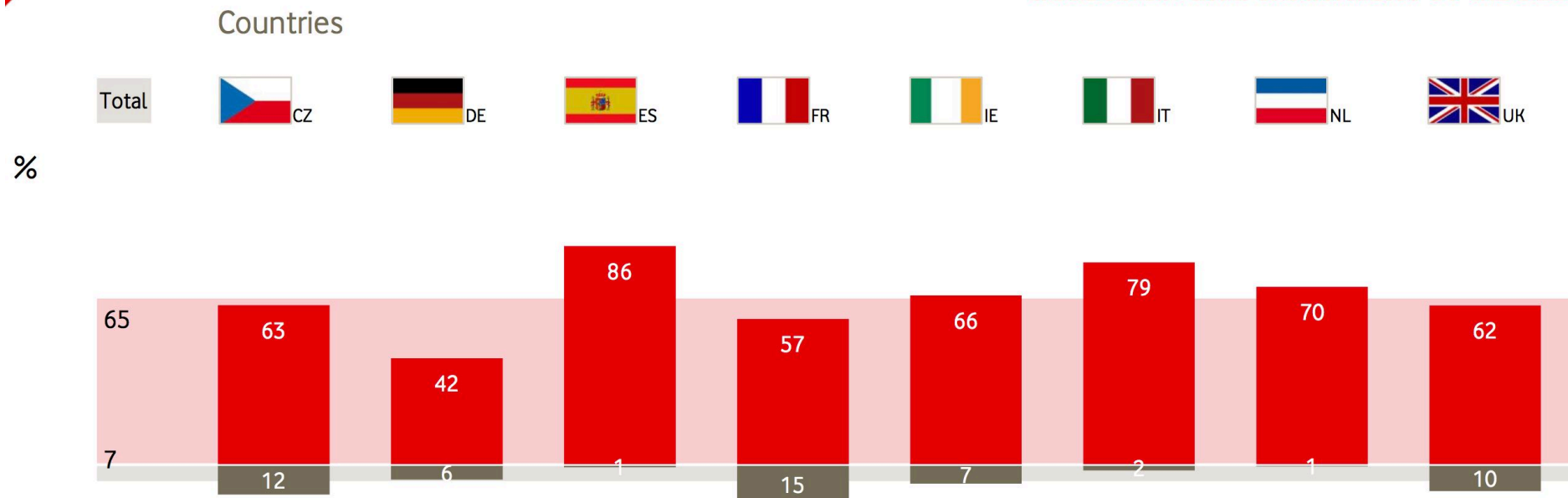
Source: Vodafone Inst. for Society and Commun., Big Data Survey, 2016 ■ Yes

■ No

What do citizens ask for? (cont'd)



Large amounts of people's health data should be collected and analysed on an anonymous basis by health institutions, [...], to enable improvements in the detection and treatment of diseases



Source: Vodafone Inst. for Society and Commun., Big Data Survey, 2016

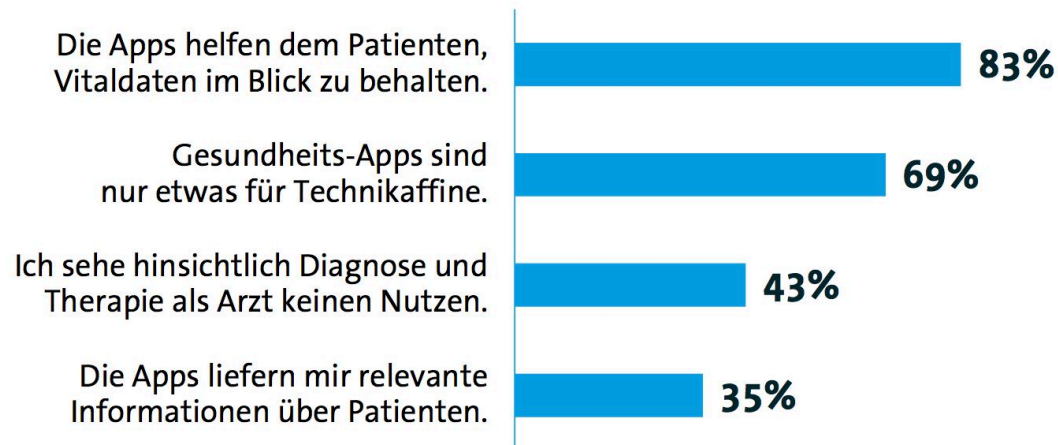
Mobile Apps in Healthcare

- CHARISMHA study of the BMG 2016
- >100k health apps available
- Major focus: Well-being and fitness
- Results
 - Prevention: Adequate use of apps can support prevention
 - Medical use: Quality issues if not licensed as medicine product
 - Research: Uses mobile apps for acquisition of data
- Missing solution to bridge the gap b/w low quality and high adaption rate of users



Medical Doctor's about Health Apps

Inwiefern stimmen Sie den Aussagen zu?*



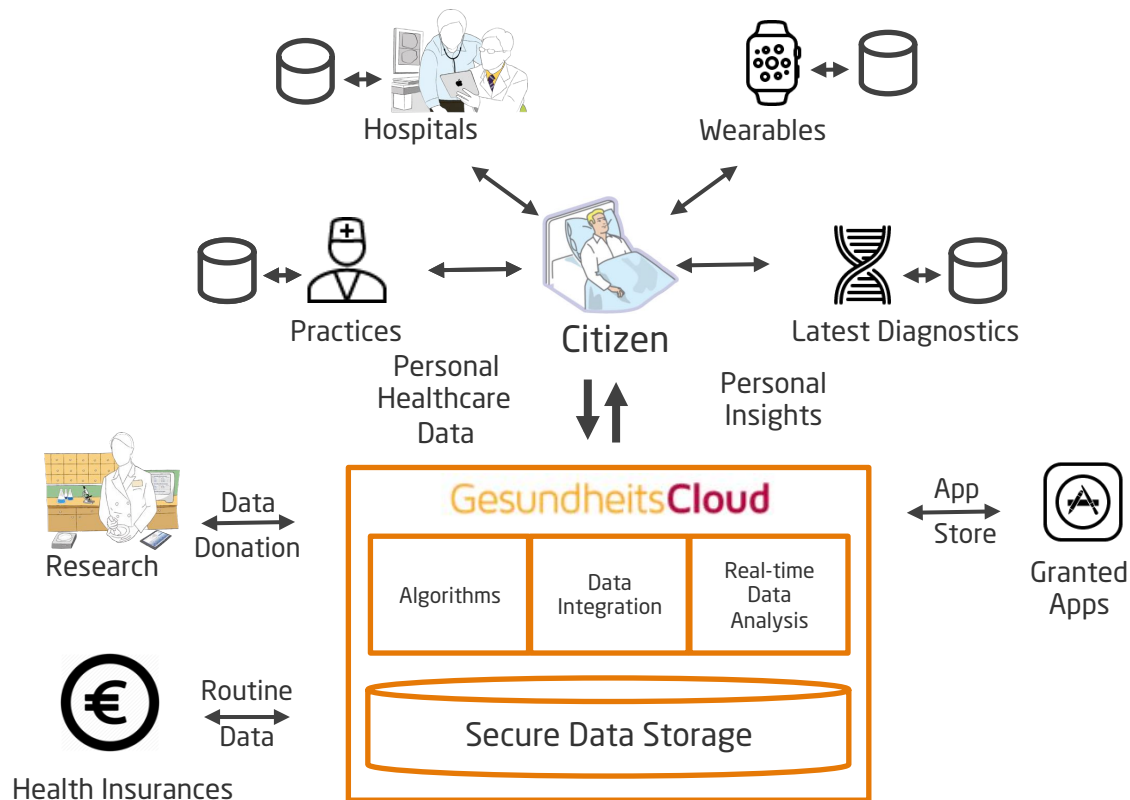
sitiv« in Prozent | Quelle: Bitkom Research

App Example: Data Donation Pass Control Your Personal Health Data

- Holistic access to your personal health record
- Subscribe to personalized notifications, e.g. about latest healthcare programs and clinical trials
- Donate your de-identified healthcare data to support registered research projects all over the globe



Control your Personal Health Data: GesundheitsCloud



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20

The Setting

Actors in Oncology

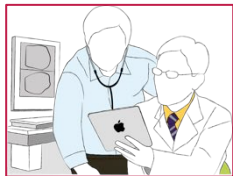
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The End...

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Application Examples**

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2017
21

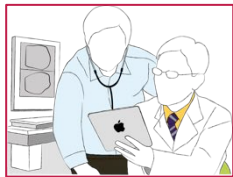
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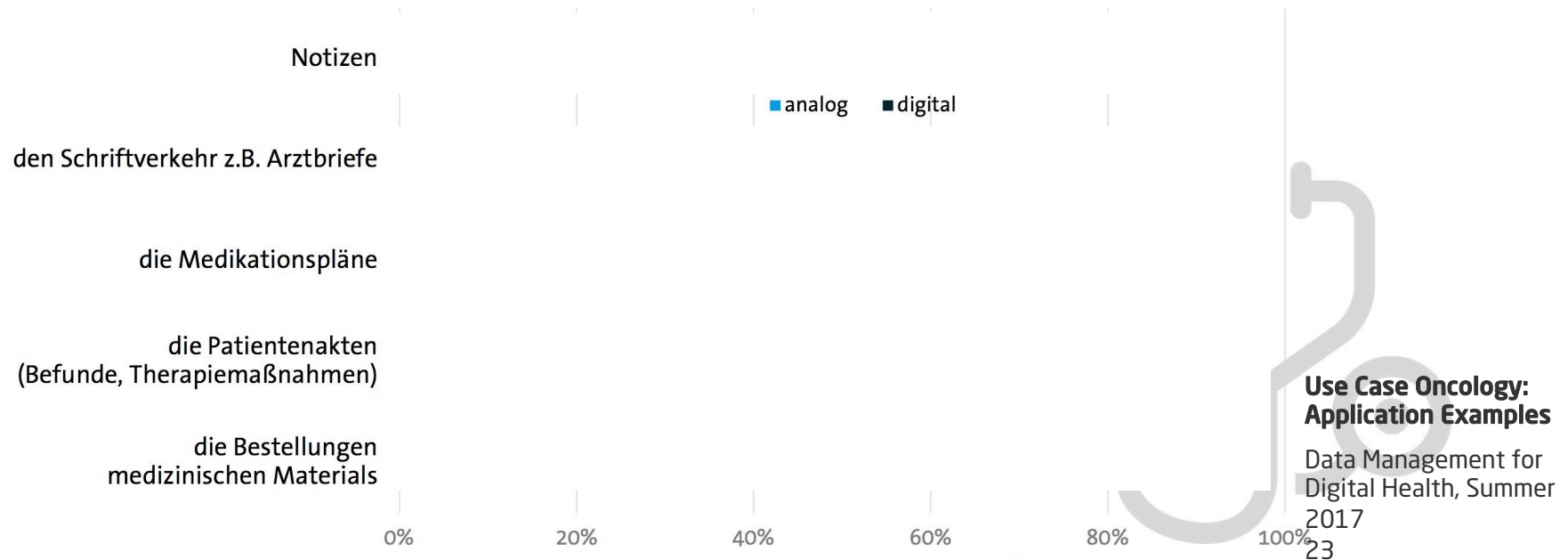
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Papier und Stift haben bei Ärzten noch nicht ausgedient

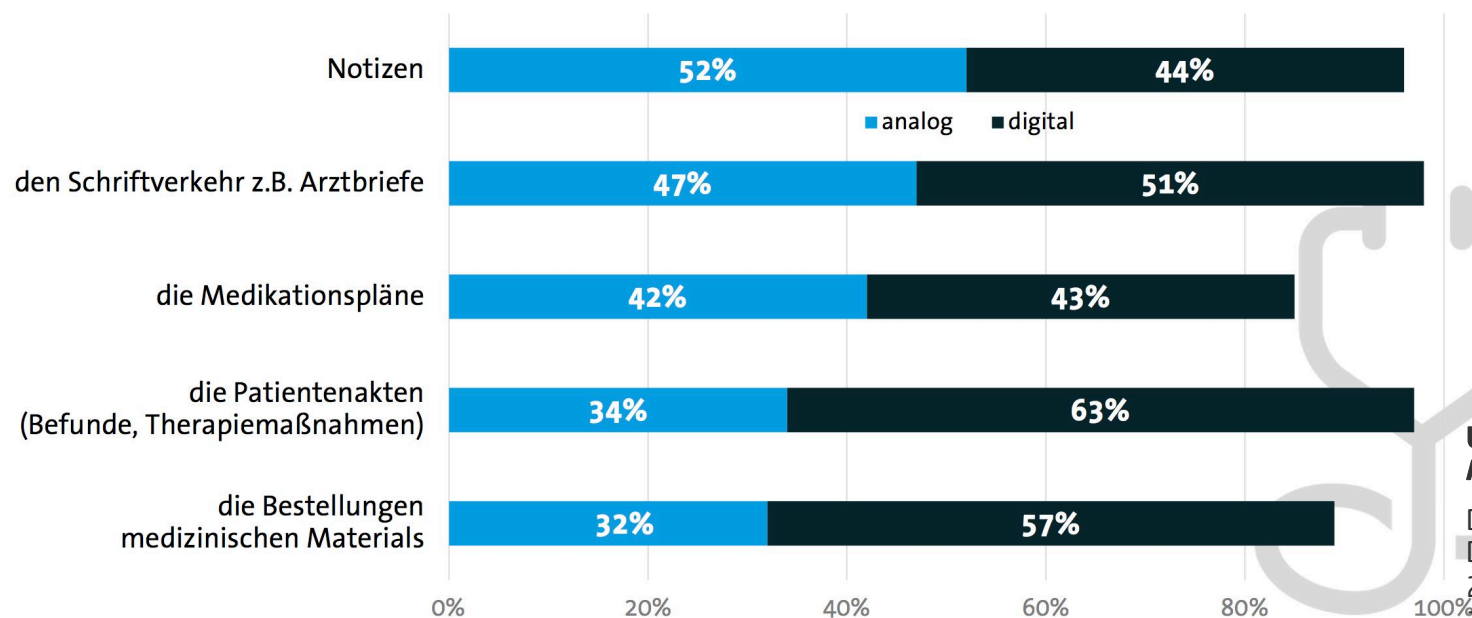
Wie verwalten Sie überwiegend...?



2 Basis: Alle befragten Ärzte (n=477), an 100 fehlende Prozent: »Gar nicht« und »Weiß nicht/k.A.«, | Quelle: Bitkom Research

Papier und Stift haben bei Ärzten noch nicht ausgedient

Wie verwalten Sie überwiegend...?



**Use Case Oncology:
Application Examples**

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Digital Health, Summer
2017
24

2 Basis: Alle befragten Ärzte (n=477), an 100 fehlende Prozent: »Gar nicht« und »Weiß nicht/k.A.«, | Quelle: Bitkom Research

Neue Herausforderung: Der „informierte“ Patient

Inwieweit treffen Ihrer Meinung nach die folgenden Aussagen zu?



64%

Ich empfinde den Umgang mit Patienten, die meinen, durch das Internet alles besser zu wissen, als anstrengend.

51%

Ich habe durch den Austausch mit gut informierten Patienten schon mal dazu gelernt.



48%



Patienten werden durch Informationen aus dem Internet mündiger.

**Use Case Oncology:
Application Examples**

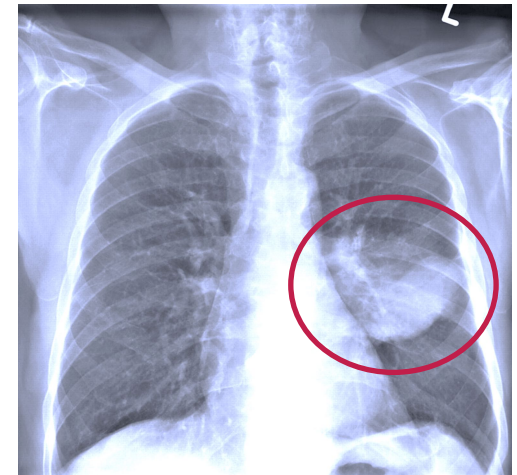
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25

Use Case: Precision Oncology

Identification of Best Treatment Option for Cancer Patient

- Patient: 48 years, female, non-smoker, smoke-free environment
 - Diagnosis: Non-Small Cell Lung Cancer (NSCLC), stage IV
 - Markers: KRAS, EGFR, BRAF, NRAS, (ERBB2)
1. Remove tumor through surgery
 2. Send tumor sample to laboratory for DNA extraction
 3. Sequence complete DNA of sample results in 750 GB of raw genome data
 4. Process raw genome data, e.g. alignment, variant calling, and annotate
 5. Identify relevant variants using international medical knowledge
 6. Support decision making, e.g. link to de-identified historic cases

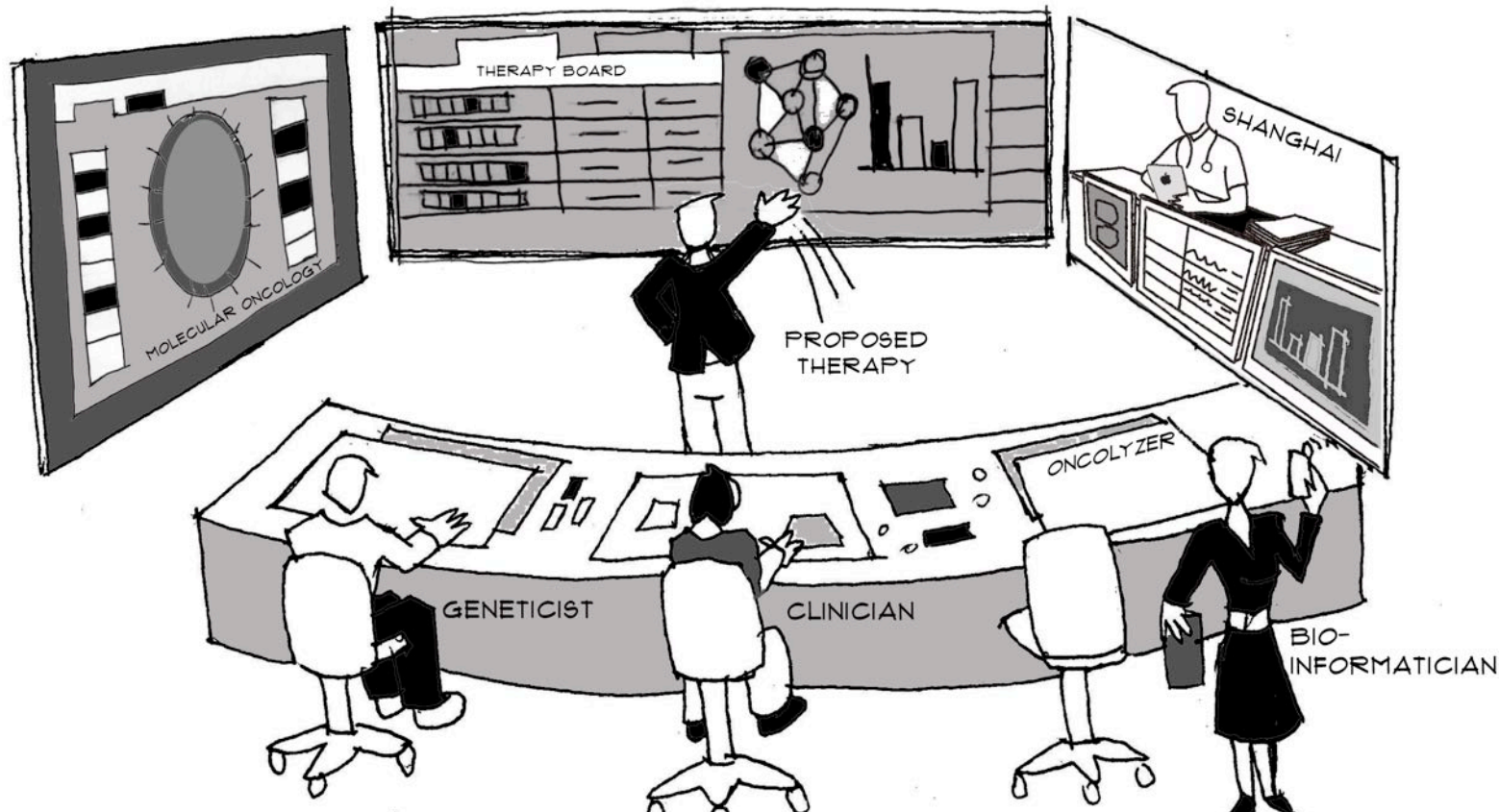


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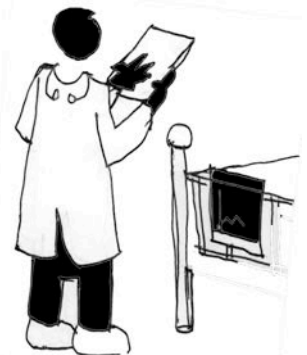
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26



Our Vision Medical Board Incorporating Latest Medical Knowledge



DOCTOR



Our Approach: AnalyzeGenomes.com In-Memory Computing Platform for Big Medical Data

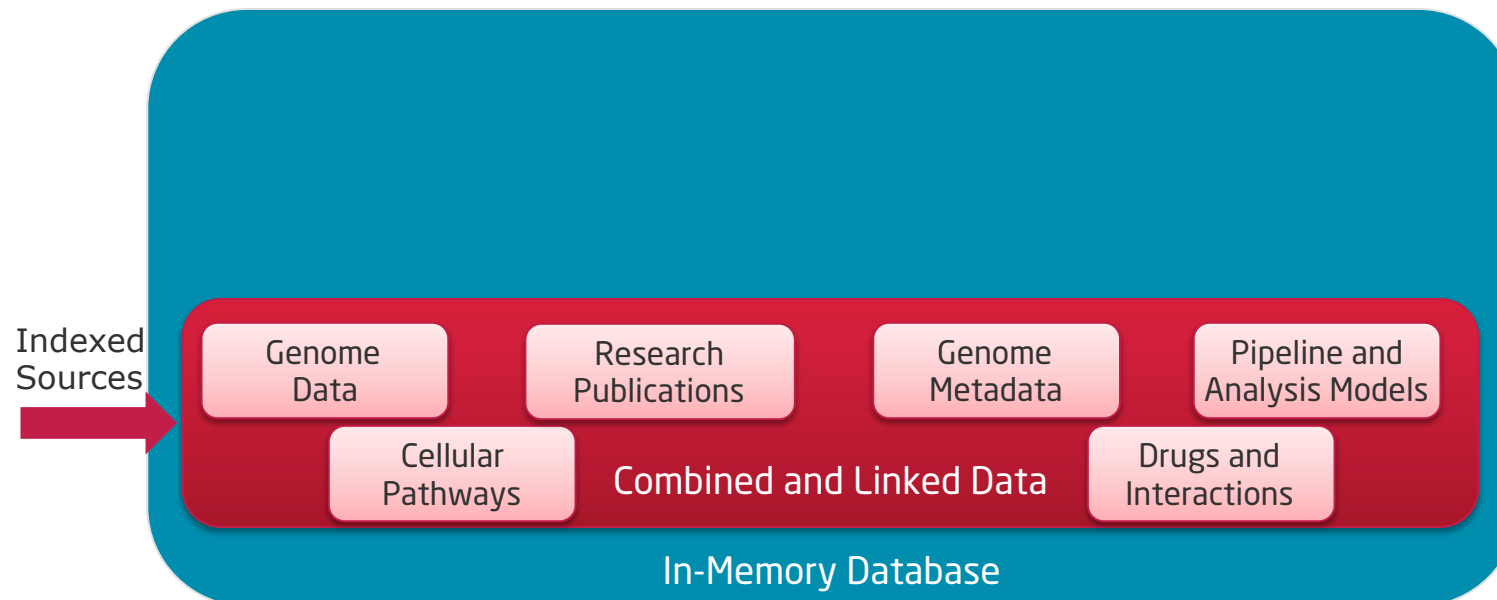


In-Memory Database

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29

Our Approach: AnalyzeGenomes.com In-Memory Computing Platform for Big Medical Data

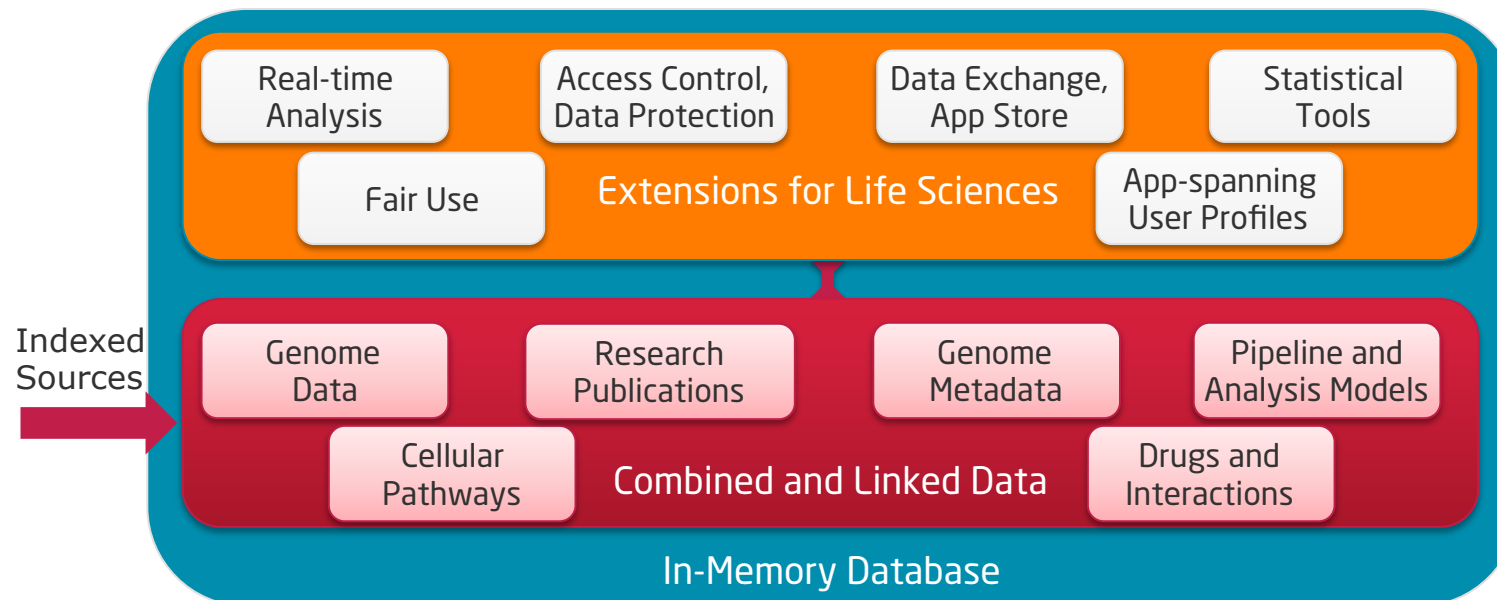


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30

Our Approach: AnalyzeGenomes.com

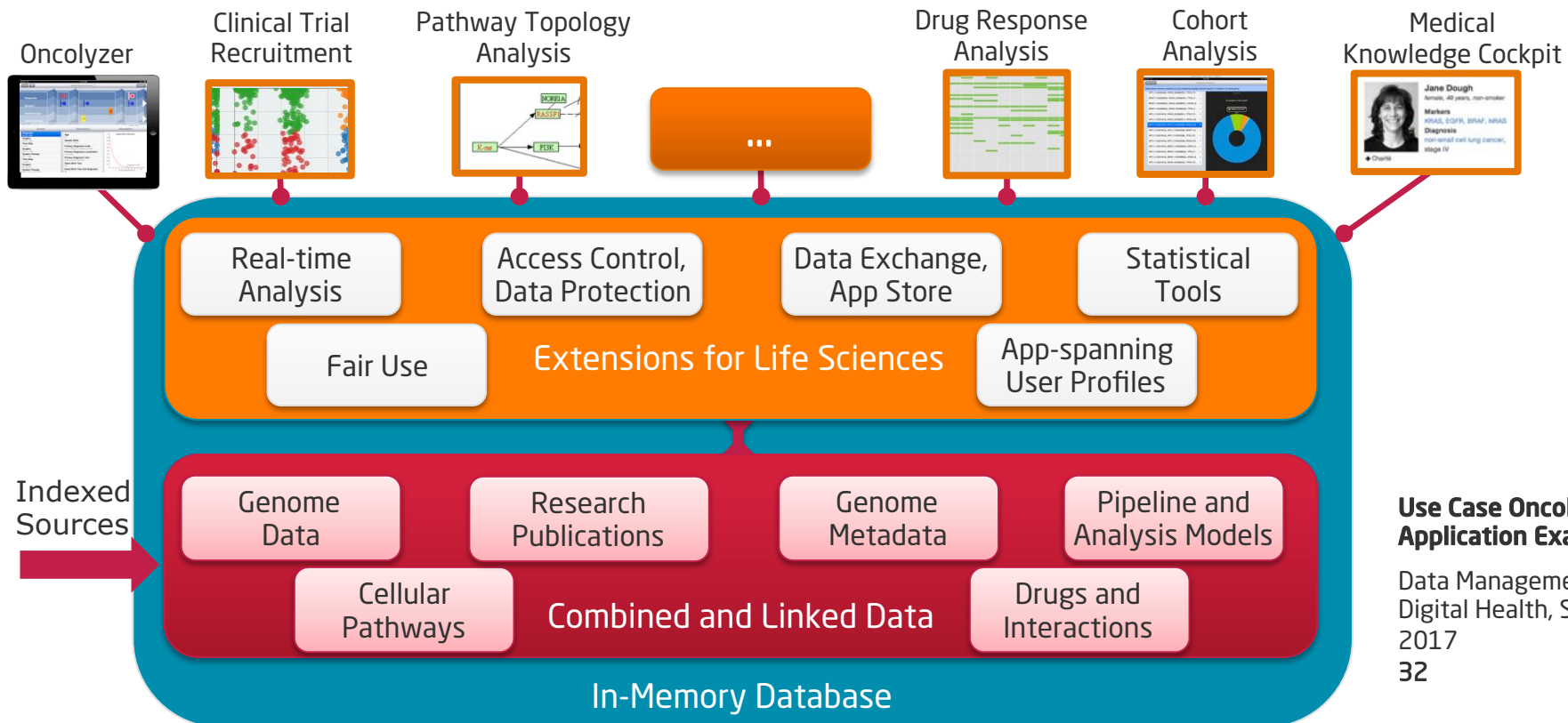
In-Memory Computing Platform for Big Medical Data



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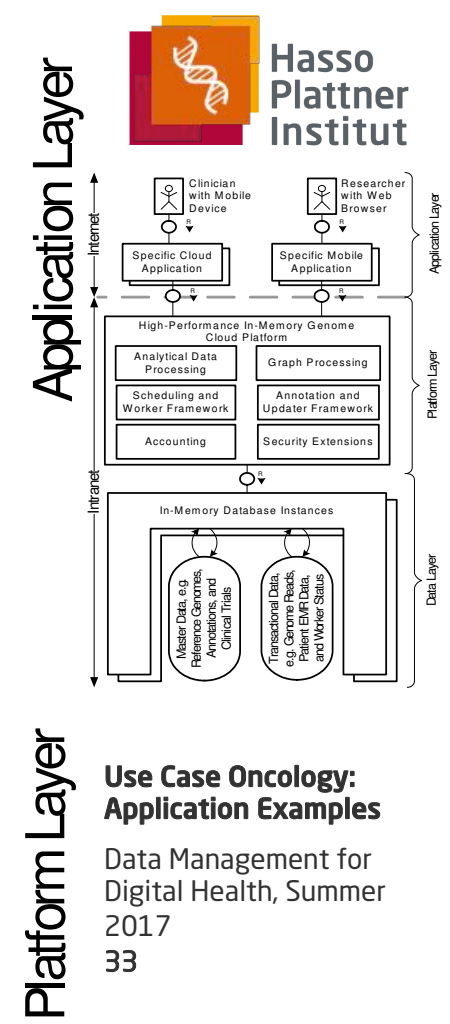
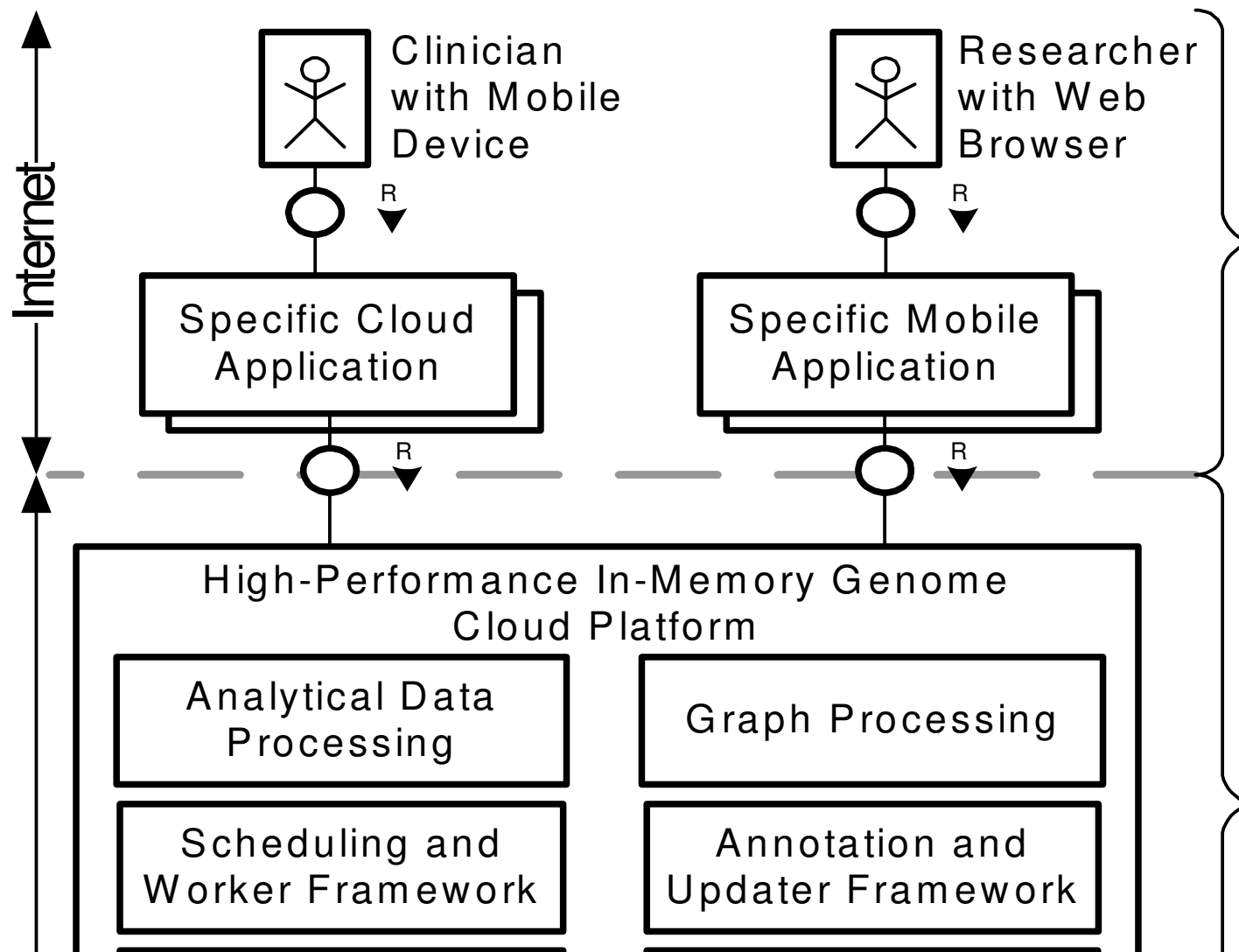
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2017
31

Our Approach: AnalyzeGenomes.com In-Memory Computing Platform for Big Medical Data



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2017
32



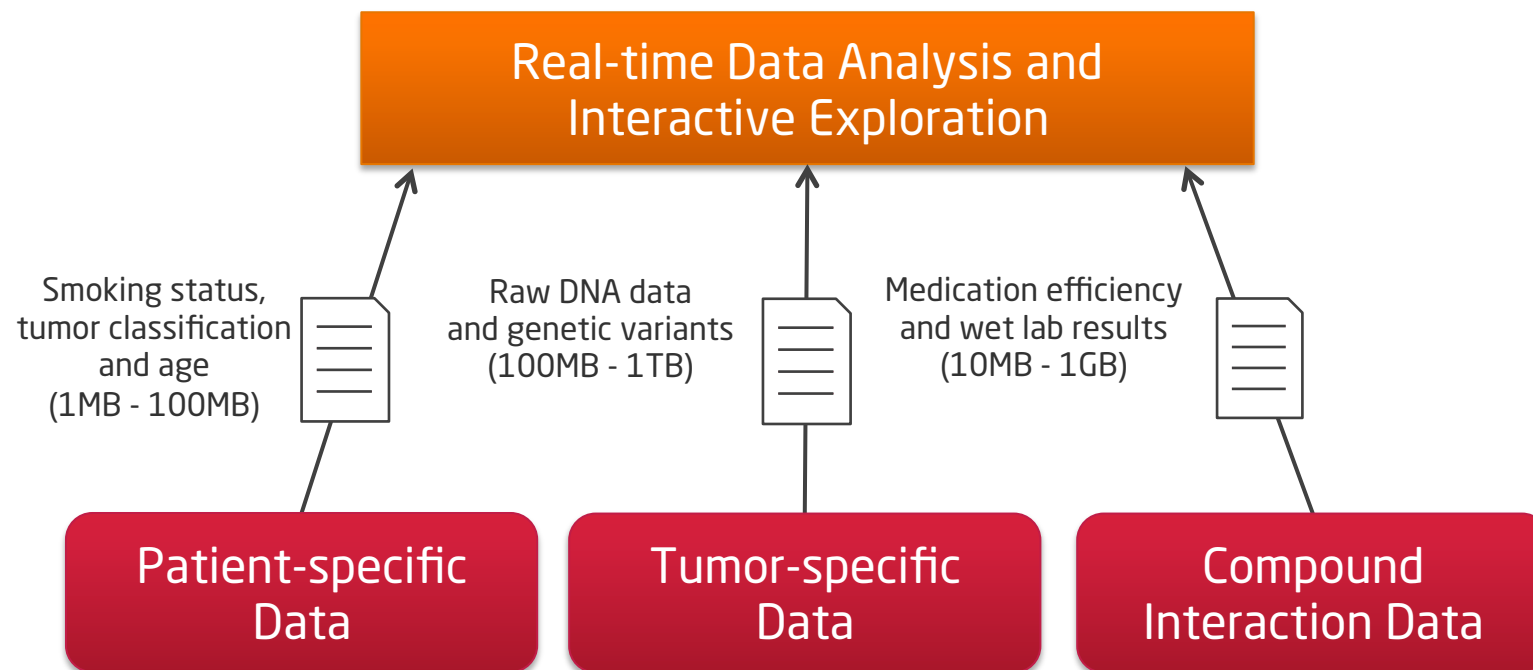
App Example: Identification of Optimal Chemotherapy



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34



■ Honored by the 2015 PerMediCon Award

Configuration

Results

1

First step: Choose which drugs' values should be predicted

- ☐ 5-FU
- ☐ Methotrexat
- ☒ Carboplatin
- ☐ Docetaxel
- ☒ Cetuximab
- ☐ Everolimus

carboplatin or cetuximab:
which to choose?

2

Second step: Choose which data should be factored into the prediction. You can choose a preset (click on the row) or create an own set.

Available Presets

| Preset Name | Drug T/C | Drug Recist | Non-functional Changes | Functional Changes via RS | Functional Changes via Genes | Age | Gender | T | N | M | Grading |
|----------------------------|----------|-------------|------------------------|---------------------------|------------------------------|-----|--------|---|---|---|---------|
| T/C Basic | ✓ | | ✓ | | | | | | | | |
| Recist Basic | | ✓ | ✓ | | | | | | | | |
| T/C Functional RS | ✓ | | | ✓ | | | | | | | |
| Recist Functional RS | | ✓ | | ✓ | | | | | | | |
| T/C Basic Complete | ✓ | | ✓ | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Recist Basic Complete | | ✓ | ✓ | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T/C Functional RS Complete | ✓ | | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Recist Functional RS | | ✓ | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

☐ Predict Drug Responses

OR

☒ Classify Drug Responses

You need to define the class borders, which distinguishes effectivity classes of drugs.
You can choose to use a predefined set, or define your own classes and save them for later use.

Available Classification Presets Choose one by clicking on a table row

| Preset Name | Definition |
|--------------|---------------------------------------|
| Recist Basic | 0.7 (good) 1.2 (stable) 2.0 (bad) |
| T/C Basic | 25.0 (good) 60.0 (stable) 100.0 (bad) |
| test2 | 1.0 (good) 10.0 (ok) 50.0 (bad) |

Custom Set Give a class a name and a class border

Keep in mind whether you want T/C or recist values to be classified, since they differ greatly in value ranges.

The lowest class border will go from 0 to the defined border.. Subsequent classes set the end of the defined class (so the class ranges from the predecessor class border to the defined border for this class). The largest class border (= the last class) will include all values, which do not fit into any other class, so the last border value is actually not that important.

Example: 25 (good), 75 (stable) and 100 (bad) - good ranges from 0-25, stable from >25 to 75, bad from >75 upwards.

Add Class:

+

Current Classes:

Save Class:

Predict Drug Response

Configuration

Results

Result SVM run for Carboplatin

| | Drug Class Probabilities <small>Recist</small> | | | |
|-------|--|--------|-------|--------------|
| Tumor | good | stable | bad | Actual Class |
| 10927 | 0.067 | 0.205 | 0.728 | bad |

Result SVM run for Cetuximab

| | Drug Class Probabilities <small>Recist</small> | | | |
|-------|--|--------|-------|--------------|
| Tumor | good | stable | bad | Actual Class |
| 10927 | 0.469 | 0.200 | 0.331 | good |

**cetuximab might be more
beneficial for the current case**

The Setting

Actors in Oncology

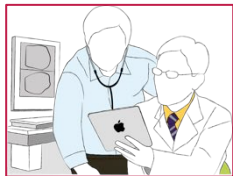
■ Patients



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Application Examples**

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2017
38

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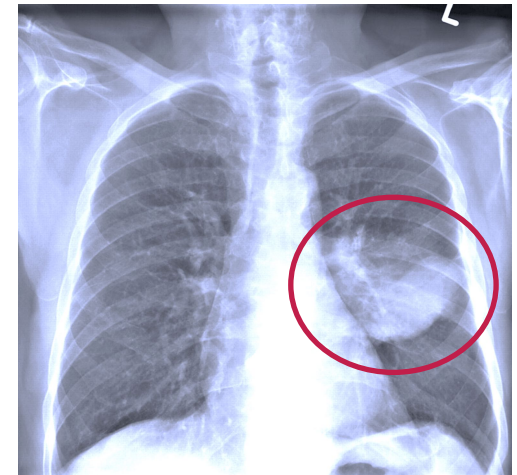
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2017
39

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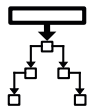
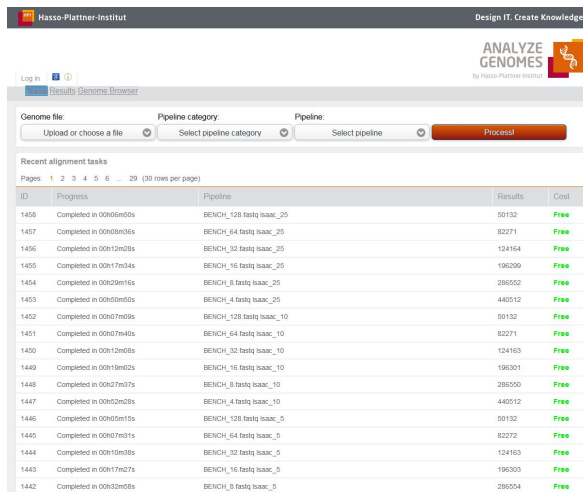


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40



App Example: Cloud-based Services for Processing of DNA Data



Standardized Modeling and runtime environment for analysis pipelines

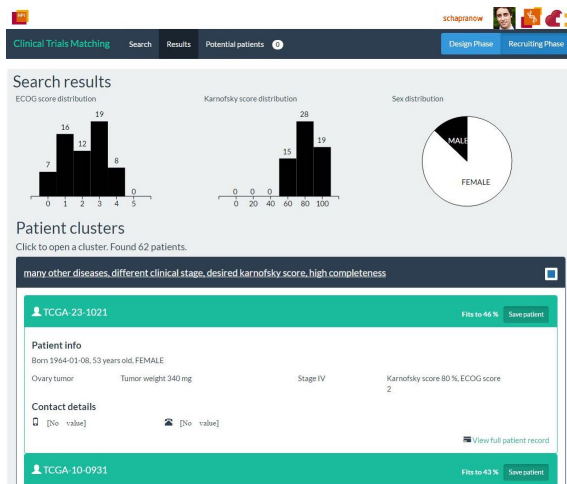
- Control center for processing of raw DNA data, such as FASTQ, SAM, and VCF
- Personal user profile guarantees privacy of uploaded and processed data
- Supports reproducible research process by storing all relevant process parameters
- Implements prioritized data processing and fair use, e.g. per department or per institute
- Supports additional service, such as data annotations, billing, and sharing for all Analyze Genomes services
- Honored by the 2014 European Life Science Award



**Use Case Oncology:
Application Examples**

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42

App Example: Real-time Assessment of Clinical Trial Candidates



- Supports trial design and recruitment process through statistical data analysis
- Real-time matching and clustering of patients and clinical trial inclusion/exclusion criteria
- Reassessment of already screened or participating citizens to reduce recruitment costs
- Integrates smoothly with the



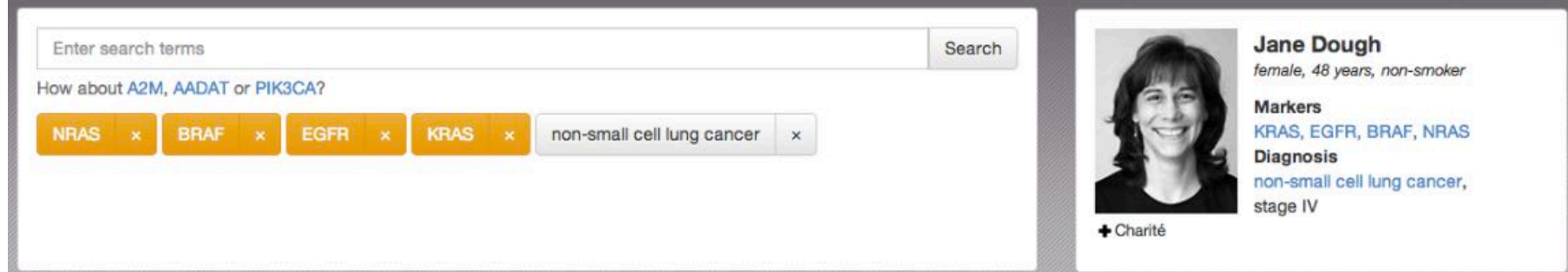
Real-time assessment of
clinical trial candidates

**Use Case Oncology:
Application Examples**

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2017
43

App Example: Medical Knowledge Cockpit for Patients and Clinicians

Medical Knowledge Cockpit



The screenshot shows the 'Medical Knowledge Cockpit' interface. On the left, there is a search bar with the placeholder text 'Enter search terms' and a 'Search' button. Below the search bar, a suggestion text reads 'How about A2M, AADAT or PIK3CA?'. Below this, there are four orange buttons labeled 'NRAS', 'BRAF', 'EGFR', and 'KRAS', each with a small 'x' icon to its right. To the right of these buttons is a grey button labeled 'non-small cell lung cancer' with an 'x' icon. On the right side of the interface, there is a profile card for 'Jane Dough'. It includes a black and white portrait photo of a woman, her name 'Jane Dough', and her details 'female, 48 years, non-smoker'. Below this, it lists 'Markers' as 'KRAS, EGFR, BRAF, NRAS' and 'Diagnosis' as 'non-small cell lung cancer, stage IV'. At the bottom of the profile card, there is a small icon and the text '+ Charité'.

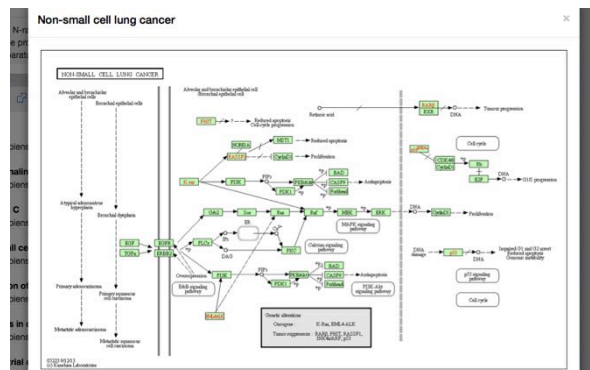
- Query-oriented search interface
- Seamless integration of patient specifics, e.g. from EMR
- Parallel search in international knowledge bases, e.g. for biomarkers, literature, cellular pathway, and clinical trials

Use Case Oncology: Application Examples

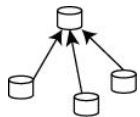
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Medical Knowledge Cockpit for Patients and Clinicians

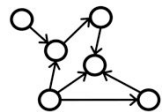
Pathway Topology Analysis



- Search in pathways is limited to “is a certain element contained” today
- Integrated >1,5k pathways from international sources, e.g. KEGG, HumanCyc, and WikiPathways, into HANA
- Implemented graph-based topology exploration and ranking based on patient specifics
- Enables interactive identification of possible dysfunctions affecting the course of a therapy before its start



Unified access to multiple formerly disjoint data sources



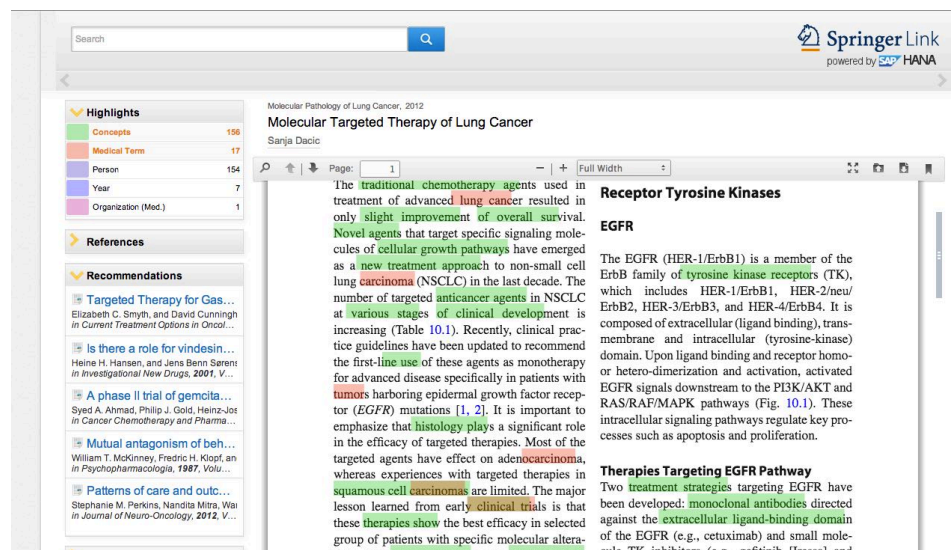
Pathway analysis of genetic variants with graph engine

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Medical Knowledge Cockpit for Patients and Clinicians

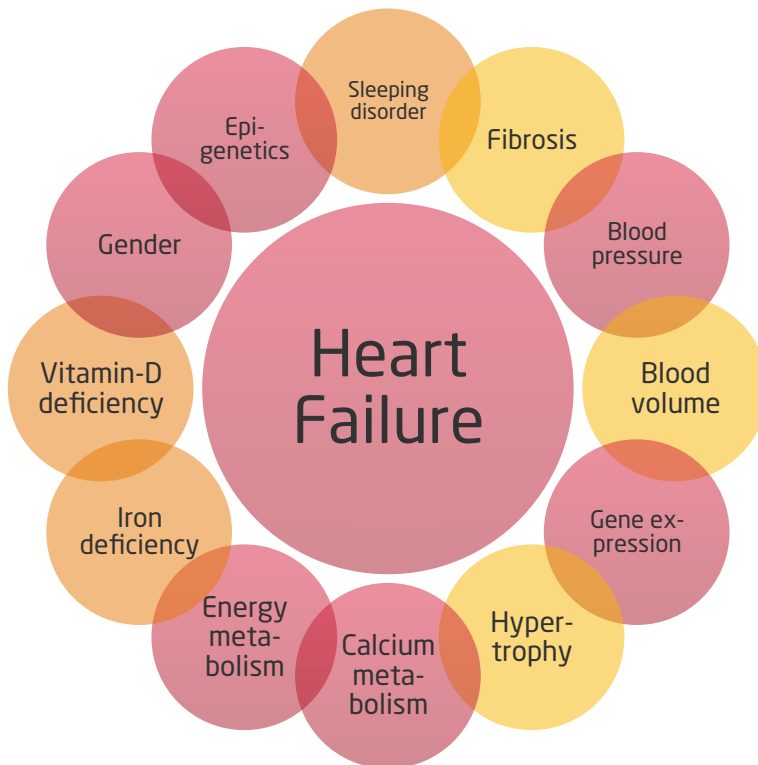
Publications



- Interactively explore relevant publications, e.g. PDFs
- Improved ease of exploration, e.g. by highlighted medical terms and relevant concepts

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46



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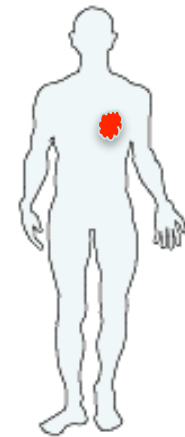
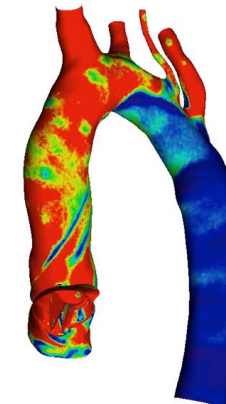


Use Case Oncology: Application Examples

47

Use Case: Establish Systems Medicine Model for Improved Treatment of Heart Failure

- Patient: 63 years, male, smoker
 - Diagnosis: Chronic heart insufficiency, stage III-IV
1. Appointment I (pre-surgery): Acquire systemic patient details, e.g. physiological and blood markers
 2. Predict outcome using clinical model with patient specifics
 3. Select adequate option and conduct valve replacement
 4. Equip patient with sensors to allow regular monitoring
 5. Appointment II 6 wks after surgery to validate outcome



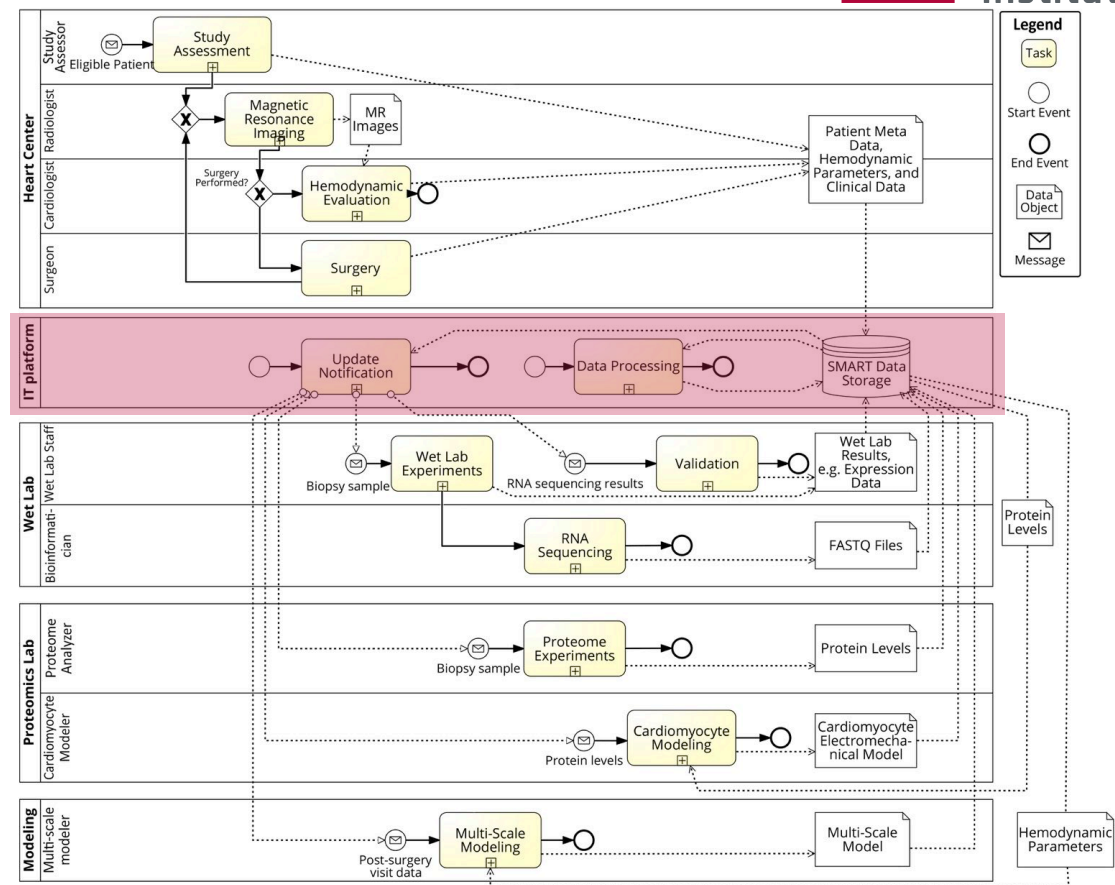
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48

Requirements Engineering for System Medicine

Computer-aided Systems Medicine Process

- Process definition through user interviews
- Identification of time-consuming and manual process steps
- Requirements for a computer-aided research process:
 1. Sharing of data
 2. Improved communication
 3. Reproducible data processing



Smart Analysis Health Research Access (SAHRA)



- Interdisciplinary partners collaborate on enabling interactive health research
- Current funding period: Aug 2015 – July 2018

■ Funded consortium partners:



- AOK
German healthcare insurance company



- data experts group
Technology operations



- Hasso Plattner Institute
Real-time data analysis, in-memory database technology



- Technology, Methods, and Infrastructure for Networked Medical Research
Legal and data protection

Supported by:



Federal Ministry
for Economic Affairs
and Energy

on the basis of a decision
by the German Bundestag



Smart Data

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50

App Example: Stratification of Hypertension Patients and Longitudinal Data Analysis

- Stratification of patient cohorts using patient specifics
- Automatic matching of similar patients and patient anamnesis
- Interactive graphical exploration of longitudinal patient data

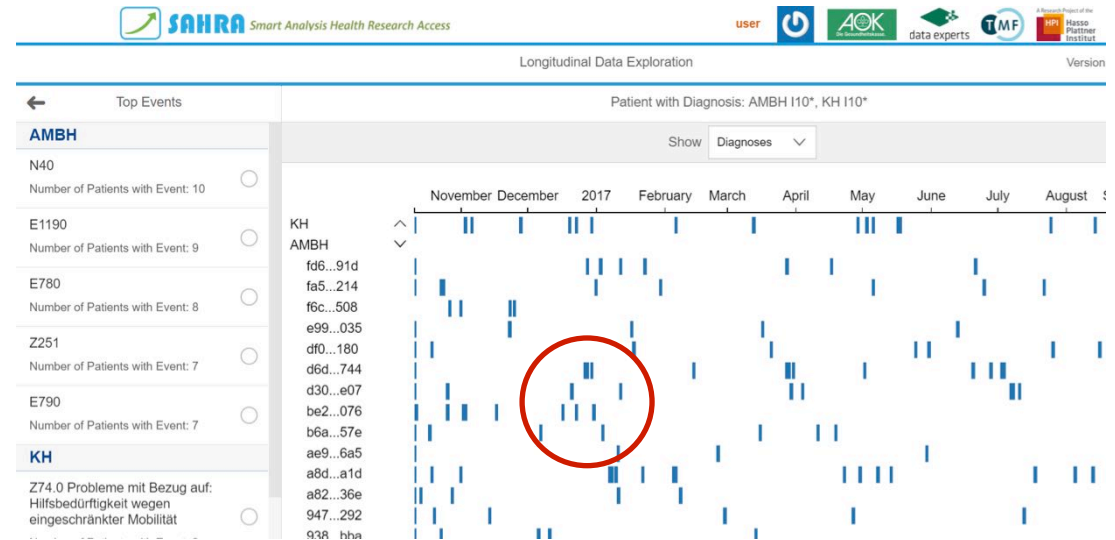


There are 1025 patients in 17 categories.

Show cluster within range

between 0 and 1025 patients

| Cluster | Patients | Average Demographic Similarity | |
|-----------------|----------|--------------------------------|---|
| ▶ Timeline (16) | 3 | 0 | ✓ |
| ▶ Timeline (15) | 4 | 0 | + |
| ▶ Timeline (14) | 11 | 0 | ✓ |
| ▶ Timeline (13) | 17 | 0 | + |
| ▶ Timeline (12) | 9 | 0 | + |
| ▶ Timeline (11) | 4 | 0 | + |



The Setting

Actors in Oncology

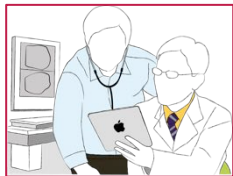
■ Patients



- Individual anamnesis, family history, and background
- Require fast access to individualized therapy

The End...

■ Clinicians



- Identify root and extent of disease using laboratory tests
- Evaluate therapy alternatives, adapt existing therapy

■ Researchers

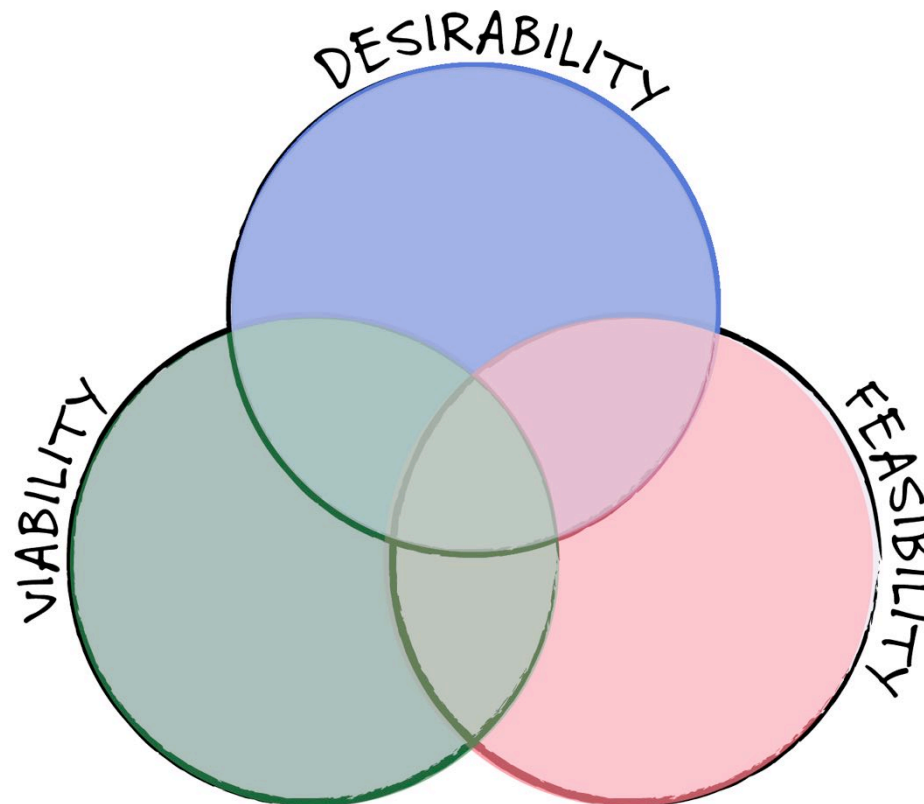


- Conduct laboratory work, e.g. analyze patient samples
- Create new research findings and come-up with treatment alternatives

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52

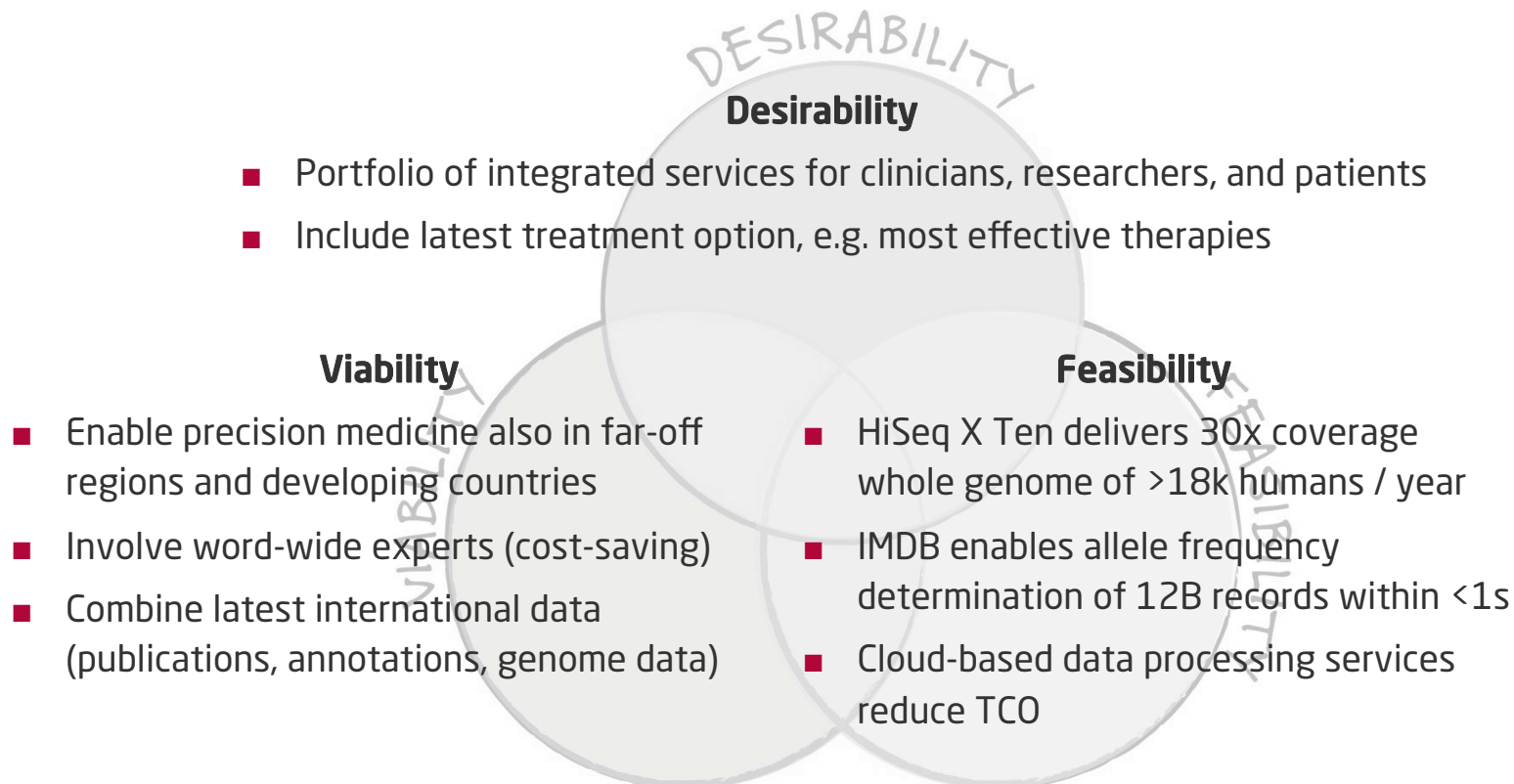
Our Methodology Design Thinking



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Our Methodology Design Thinking



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Join us for upcoming projects!

- Markers for cardiovascular diseases to assess treatment options (DHZB)
- Combine health data to improve health care research (AOK)
- Generously supported by



Federal Ministry
of Education
and Research



Federal Ministry
for Economic Affairs
and Energy



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What to Take Home?

Test it Yourself: AnalyzeGenomes.com

■ For patients



- Identify relevant clinical trials and medical experts
- Become an informed patient

■ For clinicians



- Identify pharmacokinetic correlations
- Scan for similar patient cases, e.g. to evaluate therapy efficiency

■ For researchers



- Enable real-time analysis of medical data, e.g. assess pathways to identify impact of detected variants
- Combined mining in structured and unstructured data, e.g. publications, diagnosis, and EMR data

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56

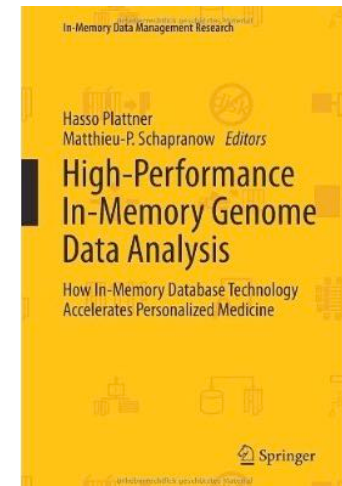
Keep in contact with us!



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57