New Roles in Digitalization, Data Science and Health Care Research

Prof. Dr. Karl Broich, President BfArM
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Overview

Digitalization, Big Data, Real World Data,... - Chances and Challenges

Activities and projects at national & European level on data-driven decision-making: From “DiGA-Fast-Track” to Research Data Centre – BfArM at key interfaces

Reliable data collection, exchange and further use: Interoperability

Conclusion and Outlook
Digitalization in Healthcare – a variety of new chances, new approaches in daily care, for recruiting and conducting clinical trials ...
Example: RWD for Virtual Clinical Trial Arms

Emulating Control Arms for Cancer Clinical Trials Using External Cohorts Created From Electronic Health Record-Derived Real-World Data

Katherine Tan¹, Jonathan Bryan¹, Brian Segal¹, Lawrence Bellomo¹, Nate Nussbaum¹, Melisa Tucker¹, Araceli Z. Torres¹, Carrie Bennett¹, William Capra², Melissa Curtis¹ and Rebecca A. Miksad¹


Our summary

Real-world data (RWD) derived from electronic health records (EHR) can be used to create external comparator cohorts. This exploratory study assessed whether EHR-derived patient cohorts can emulate the control arms of published clinical trials that supported FDA approvals of anticancer therapies across multiple tumor types. Researchers evaluated the impact of specific real-world cohort construction analytic decisions on observed endpoints and found that results were variable depending on specific analytic decisions.
...Fields of Application of Big Data and Algorithms..

**Optimization...**
- Planning and Organization of Clinical Trials
- Regulatory Decision Making
- Optimization of health care processes / workflows

**Knowledge**
- Research on the complexity and mechanisms of diseases
- Increased knowledge about rare/orphan diseases
- (Faster / better) monitoring

**Personalisation**
- "Personalised" prevention
- Prediction and risk profiling
- Facilitation of specific diagnosis
- Novel, more "individualized" therapies (effect, interaction, AE)
- Individualized prognosis
Digitalization in Healthcare – a variety of new chances, new approaches, but also *new challenges*...
Central tasks of the BfArM...

- To license and to improve the safety of drugs
- To register and to evaluate the risks of medical devices
- To monitor the traffic with narcotics and precursors
- To establish classifications, terminologies, standards and data based information systems for health care...
... at key interfaces in growing e-health ecosystems
Digital Medical Devices - Initiatives of the BfArM

- BfArM im Dialog „Medical Apps“
  - Apps as Medical Devices;
  - Clinical trials,
  - Data safety,
  - Reimbursement

- BfArM im Dialog „Cyber Security“
  - Perspectives:
  - Hackers,
  - Manufacturers;
  - Sensitization
  - Support

- Innovation Office
  - Support & Advice – „Project Guidance“

- Public Health Journal
  - „E-Health and Medical Devices“

- Digital Healthcare Act
  - „DiGA-Fast-Track“
What is a „DiGA“?

Definition of Digital Health Applications (DiGA)

• CE-marked Medical Device of risk class I or IIa
• Supports the recognition, monitoring, treatment or alleviation of diseases, injuries or disabilities
• Main function is based on digital technology
• Used only by the patient or by the patient and the healthcare provider together – patient centricity

Requirements for being listed in the DiGA Directory

• Safety and performance (CE-marking according to MDD/MDR)
• Data protection, information security and further quality requirements (e.g. interoperability)
• Positive healthcare effects
Positive healthcare effects of DiGA

DiGA listed in the directory must have proven at least one of these positive healthcare effects:

**Medical Benefits**

- improving state of health
- shortening of the duration of the disease
- extension of survival
- improvement in the health-related quality of life

**Patient-relevant improvement of structure and processes in healthcare (pSVV).**

**supporting the health behaviour of patients or integrating the processes between patients and healthcare providers.**

Might be one of the following:

1. coordination of treatment procedures,
2. alignment of treatment with guidelines / recognized standards,
3. adherence,
4. facilitating access to care,
5. patient safety,
6. health literacy,
7. patient autonomy,
8. coping with illness-related difficulties in everyday life,
9. reduction of therapy-related efforts and strains for patients and their relatives
The DiGA-Directory: Transparency and Guidance for Users, Health Care Professionals, Statutory Health Insurances...

https://www.bfarm.de/EN/MedicalDevices/DiGA/_node.html

https://digabfarm.de/de

https://diga.bfarm.de/de/verzeichnis/316
Overview: DiGA in the Directory (n=20)

**Status**
- preliminary listing: 5
- permanent listing: 15

**DiGA with...**
**patient-relevant improvement of structure & processes in healthcare**
- DiGA with pSVV: 6
- DiGA without pSVV: 14

**DiGA with...**
**a medical benefit**
- without med benefit: 1
- med benefit: 19

**Evidence**
- RCT: 18
- RCT + retrospective analysis: 1
- meta analysis: 1

status: 30th August 2021
DiGA as Part of German e-Health Structure: Interoperability

Legend:
- Interoperability interfaces which must be implemented
- Future extensions which have already been set
- Optional interfaces
National Competence Centre for Medical Terminologies / Semantics Centre at the BfArM

SNOMED CT global clinical terminology is introduced in Germany
Licenses issued through Germany’s MII

**Standardisation & Semantics (inter-)national:**
- Publication of official classifications such as
  - ICD-10-GM (§§ 295 und 301 SGB V)
- Implementation ICD-11 in Germany
- Maintenance of classifications, medical terminologies, thesauri, nomenclatures and other conceptual systems as a service for the health care system

**SNOMED-CT**
- Routine licence for health care

**DVG / DiGA Ordinance:**
- Commitment to interoperable design of DiGA taking into account recognised standards (HL7/SNOMED CT, ...)

Interoperability - terminology / technically
Usability of Real World Data
(e.g. data from health insurance)

- As the **volume of data increases**, so does the scope and usability of secondary data
- **Strongly increasing** research with health insurance data
- **Increasing impact** of secondary data
- **Modern** methods allow data-driven insights
The Research Data Center is currently being extended to offer more data and to increase the throughput of analyses.

**Research platform**
- Enabling researchers by bringing complex analyses to the data
- Modern analysis tools available (e.g. R, Python)
- Data protection within the platform

**Availability**
- Accessible for authorized users and purposes
- Data are reusable for future projects

**Future-proof design**
- Scalability to adjust resources in a massively growing field
- Design with AI readiness in mind
Data at the Research Data Center

- All 72 Mio. with statutory health insurance in Germany
- Information from all health care sectors linked on the individual level
- Longitudinal data starting from 2009
- Ensured interoperability with established code systems (ICD10, ATC, SNOMED CT)
Real-World-Data (RWD) at the Research Data Centre of the BfArM

- Prescriptions
- Diagnoses
- GKV claims data
- Population
- Procedures
- Lab tests
- Medical imaging
- Medical Report
- ePA Electronic Health Records
- Digital interventions
- GKV claims data
- Population
- Procedures
- Lab tests
- Medical imaging
- Medical Report
- ePA Electronic Health Records
- Digital interventions
AI Infrastructure in the Research Division at the BfArM

Technical specifications of the AI/HPC network

- 2x IBM POWER SYSTEM AC922 server (8335-GTH)
- IBM FlashSystem 5100 NVMe Storage System
- IBM WATSON MACHINE LEARNING ACCELERATOR
- IBM Spectrum Virtualize Software
  (8 NVIDIA V100 GPUs, 512 GB DDR4, 50 TB ext. Storage)

- NVLink 2.0 for fast bidirectional bandwidth between CPUs and GPUs
- Network: 10 Gb Ethernet, I/O architectures: PCIe gen4
- OpenPOWER Linux scale-out server (Red Hat Enterprise Linux operating system)

➢ System is especially designed for Deep Learning and AI, high-performance analytics, and high-performance computing
Projects including machine-learning approaches

- **EMPAR**: Influence of metabolic profiles on drug therapy safety in routine care. Use of ANNs to predict pharmokogenetic, -epidemiologic and -economic associations. Status: near completion (sponsored by the Innovation Fund of the G-BA; support code 01VSF16047)


- **ANKA**: Combined analyses of adverse events and routine clinical data using machine learning methods. The project includes in part preliminary work for causality assessment of ADE-reports using sophisticated DL (deep learning) NPL- (natural language processing)- techniques. Status: in progress (sponsored by own funds of the BfArM and IMBIE)

- In addition, machine learning techniques are used in several bioinformatics routines and analyses, e.g. in the analysis of metabolic profiling, gene expression and sequencing data
Current Research - Example from Medical Device Area:
Propose Free-Text Classification by using Textmining and Similarity Scores

<table>
<thead>
<tr>
<th>2.5.2 Best Similars</th>
<th>New incident to be classified</th>
<th>Already classified Incidents</th>
<th>Dissimilarity score</th>
<th>FDA classification</th>
<th>Reference number of the incident already classified</th>
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<tbody>
<tr>
<td>high impedance of the pace/sense conductor (&gt;3000 ohms) and oversensing after 45 months of service life</td>
<td>Information indicated that the lead was replaced after 46 months of service life because of high impedance of the lead.</td>
<td>0.093</td>
<td>c(&quot;High Impedance&quot;, &quot;Oversensing&quot;)</td>
<td>0298</td>
<td></td>
</tr>
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Goal:
✓ First medical campus in Europe to implement and evaluate innovative medical 5G applications

BfArM:
✓ Development and evaluation of a novel medical device incident reporting app
✓ taking advantage of mobile technologies & 5G to support fast, easy and helpful reporting by healthcare professionals
✓ In cooperation with: University Hospital Düsseldorf; Vodafone GmbH, Düsseldorf; RWTH Aachen University; FH Dortmund University of Applied Sciences; Brainlab AG, Munich; Bergische Universität Wuppertal/ SIKoM+
3. Towards a European Health Data Space

EC supporting digital "EU-Health Data Space“ Pharmaceutical Strategy

EU network strategy 2025 + DARWIN EU
EMA Regulatory Science Strategy 2025
HMA-EMA Big Data Task Force Top-Ten-Recommendations for data
HMA & EMA Network Strategy – Pillar Innovation & Digitization

Big Data Steering Group; EU Telematics; EU Innovation Network, ...
BDSG workplan

Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21
DARWIN (Advisory Board)

- National and EU regulation of medicines:
  - Drug development – disease epidemiology, unmet need, historical controls, planning
  - Authorisation – contribution to BR, controls, extrapolation to general and/or special populations
  - Post-authorisation – benefit-risk monitoring, extension of indication, risk minimisation measures

DARWIN EU will significantly increase the capacity of the Network to undertake high-quality observational studies based on real-world data.

- Additional benefits as EU partners participate and access the platform:
  - European Commission – key use case for the European Health Data Space
  - National governments to support health policy and delivery of healthcare systems
  - HTA bodies and payers to support better quality decisions on cost-effectiveness
  - EU health agencies - use cases specific for EFSA, ECDC, ECHA, JRC
  - EU patients - faster access to innovative medicines and safe and effective use
Conclusion and outlook

Digitization, big data and AI:

- many opportunities, great potential for better health care and knowledge gain, also for regulatory questions on benefits and risks in everyday health care

DiGA Fast-Track:

- Important component of the digitalization of the health system
- Germany pioneer with regard to procedures for reimbursement, with a high degree of transparency for users, doctors, health insurers

- Continuous further development: From DiGA to DiPA to...? From checklists to certificates for more clarity and transparency – data protection

Making data usable and available for relevant research and/or regulatory questions requires harmonised (semantic and technical) standards

Working together: BfArM is involved at national & European level at important interfaces (classifications; research data centre, DARWIN, etc.) together with other actors and partners to support digital transformation for patients’ benefits
Thank you very much for your attention!

Contact

Federal Institute for Drugs and Medical Devices
Prof. Dr. Karl Broich
President
Kurt-Georg-Kiesinger-Allee 3
D-53175 Bonn

www.bfarm.de
Phone +49 (0)228 99 307-3219