TECHNISCHE UNIVERSITÄT DRESDEN

Brochure accompanying the final presentation of the project „BIDA-SE“

Implementation possibilities and clinical benefit of Big Data applications in the context of rare diseases

A co-operation between
the Professorship for Medical Informatics (MI) and the
Center for Evidence-Based Healthcare (ZEGV)
of the Technical University Dresden

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Content

BIDA-SE – The project

Background and project objective

Rare diseases occur with a frequency of <5/10,000 people, affect about 3-6% of the population and comprise an estimated 5,000-8,000 individual diseases [1-5]. Due to their rarity and manifold manifestations, there are increasing challenges for patient care (e.g. delayed diagnosis, lack of therapeutic options) [6], [7]. Big Data applications are one possibility for improving the care of people with rare diseases [8-9].

So far, however, there is no concrete, comprehensive concept for the use of Big Data for the care of people with rare diseases in Germany. The project „Implementation possibilities and clinical benefit of Big Data applications in the context of rare diseases - BIDA-SE" (funding reference number: ZMVI1-2519DAT702, duration: 03/2019-02/2020, extended until 05/2020) should therefore work on how to integrate Big Data applications with added value into the care practice for people with rare diseases.

The following questions should be answered:

- What is a multidisciplinary, practical scenario using Big Data applications for the care of people with rare diseases and what measures are recommended for medium-term implementation?
- What clinical benefits do physicians see for care and how would patients accept a Big Data-supported care process?
- What are the technical, systemic, organisational and legal barriers and how can they be overcome?
- What are the economic implications of the developed scenario?

The project directly addresses the objectives of the National Action Plan for Rare Diseases (1) to support the initial contact with the primary care provider and (2) to develop or explore technologies for di-

agnosis. The focus is on the interfaces between the established general practitioners and specialists and the centres for rare diseases in order to channel access to the centres.

The project was divided into three phases:

1. **Analysis of the current situation**: First, the interdisciplinary patient care pathway was modelled and possible big data applications and data / data sources were identified.
2. **Initial scenario development**: This was followed by the interdisciplinary development of a future scenario for the implementation of Big Data applications in the care process.
3. **Evaluation and adaption of the scenario**: Finally, the scenario was evaluated with regard to its acceptance, benefits for care, economic implications and limits / barriers for medium-term implementation. Based on the results of the evaluation, a catalogue of measures for medium-term implementation was developed.

Within the individual phases, the focus was on interdisciplinarity, which is why different stakeholders such as physicians, IT experts, patients, patient representatives, health care researchers, IT security officers and the data protection officer of the Technical University Dresden were involved. To ensure the relevance and feasibility of the scenario, a portfolio of methods consisting of literature analysis / reviews, workshops, online surveys and an economic analysis was used.

The project team

The professorship for Medical Informatics (MI) at the Institute for Medical Informatics and Biometry took over the overall project management. Together with the Centre for Evidence-Based Health Care (ZEGV), an interdisciplinary, practical scenario using Big Data technologies for the care of people with rare diseases and a plan of action for its medium-term implementation was developed.

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Big Data and rare diseases?

According to MARR [10] „Big Data“ can be described by 5 dimensions (the so-called "5Vs"):

- Volume: amount of the data
- Velocity: speed with which data sets can be generated and evaluated
- Variety: variety of data types and sources
- Veracity: truthfulness and credibility of data
- Value: value of the data

For the context of rare diseases, the "variety" dimension is particularly relevant, i.e. the diversity of data and sources. To deal with this complexity, a whole range of methods and technologies has been developed in recent years...

- ...for data storage, e.g. databases for the distributed storage of data
- ...for data access, e.g. methods for processing input data
- ...for analytical processing, e.g. analytical methods for finding patterns
- ...for visualizations, e.g. interactive visual representations, which help to communicate correlations
- ...for data integration, e.g. methods for importing data from different sources
- ...for data governance and security, e.g. technologies that regulate access to data or methods for data encryption

Our aim in the project was to investigate how these technologies and methods can be integrated with added value in a care process for people with rare diseases.

1 – Ist-Analyse

What is the current care situation and IT infrastructure for people with rare diseases?

Current care situation

With the help of a literature analysis and a workshop with experts (n=6) from the outpatient and inpatient medical profession and form centres for rare diseases, the current pathway for people with rare diseases was developed and mapped in a comprehensive process model

The process includes the following sub-processes (see Figure 1):

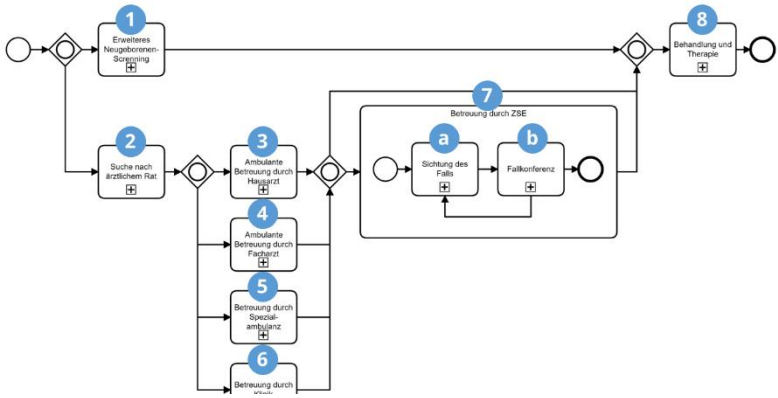

Figure 1: Overview of the pathway of people with rare diseases

1. Neonatal screening
2. Search for medical advice
3. Outpatient care by the family doctor
4. Outpatient care by the specialist
5. Care in a special outpatient clinic
6. Inpatient care in a clinic
7. Cae by a centre for rare diseases:
    a. Review of the case
    b. Case conference
8. Treatment and therapy.

Aktuelle IT-Landschaft

For an overview of already existing applications and their advantages and disadvantages, a literature analysis was made. In the following, the identified groups of Big Data based applications in the context of rare diseases and related examples are listed.

Big Data based applications for the documentation and naming of rare diseases

Register for naming of rare diseases

Rare disease registries can be understood as catalogues of names of rare diseases and relevant information. The presentation of the information bases on specific criteria, such as the allocation of content or dependence on diseases or the geographical distribution of care facilitates. Examples are

- *Orphanet*[1] collects and aggregates information on rare diseases and provides a nomenclature of rare diseases (Orpha codes) [11].
- *se-atlas*[2] is an information platform that aggregates and geographically visualises information on rare diseases care institutions (e.g. specialised centres for rare diseases, self-help groups) [12].

Coding and taxonomies

With the help of codes and taxonomies, diseases can be clearly named. Up to now, rare diseases have been underrepresented in coding systems: For example, ICD10 (International Classification of Diseases and Related Health Problems) lists only 355 of the approx. 6,000 – 8,000 rare diseases [11]. Alternative coding systems help to close this gap. Examples are:

- *Orpha codes*[3], which are used to sort and identify the several diseases hierarchically [11].

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[1] *https://www.orpha.net/consor/cgi-bin/index.php?lng=DE*
[2] *https://www.se-atlas.de/*
[3] *https://www.orpha.net/consor/cgi-bin/index.php?lng=DE*

- *HPO*[4] (Human Phenotype Ontology) provides a database of bioinformatics resources to facilitate the description and analysis of patient's phenotypes [13].
- *OMIM*[5] (Online Mendelian Inheritance in Man) provides a database of genetic information (human genes and genetic disorders) [14].

[4] *https://hpo.jax.org/app/*
[5] *https://www.omim.org/*

Big Data based applications for (differential) diagnostics

Support through comparable information

The (differential) diagnostics can be supported by comparable information. Thus, registries of biomaterials, clinical studies or patient information are useful, which are based on extensive database and are used primarily for research purposes [15-17]. Examples are:

- Registries for biomaterials: *RD-HUB*[6] is a web-based, centralized database of biomaterials with an explicit focus on rare tissue samples [15].
- Registries for clinical trials and pathways: *ClinicalTrials.gov*[7] is a registry of clinical trials, where both the trial information is structured and the data are presented in an accessible way [16].
- Registries for clinical trials and patient registries: *CEMARA* (Centres Maladies Rares) allows the registration of patients with rare diseases and the comprehensive description of their disease course [17].

Suggestion-based applications

Based on an input of symptoms or other free-text terms for a suspected disease, suggestion-based applications use algorithms to search for matches to listed diseases, so that a ranking of suggested diagnoses can be displayed [18, 19]. Examples are:

- *FindZebra*[8] is a search engine for rare diseases. Symptoms and phenotypes can be entered into a search field, whereupon diseases that match or are similar to each other as well as diseases-associated genes are listed [18].
- *PhenX*[9] is a project for the integration of epidemiological and genetic data, with focus on the extent to which environmental data or information (e.g. dietary habits) can be described so that comparison and aggregation across studies is possible [15].

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[6] *https://www.rarediseasesnetwork.org/spotlight/january2012/rd-hub*
[7] *https://clinicaltrials.gov/*
[8] *http://www.findzebra.com/*
[9] *https://www.phenx.org/*

- *FACE2GENE*[10] is an application that uses a picture of the face to calculate a similarity profile to genetic diseases. This results in a ranking of suggested diseases [20].

Structured anamnesis and medical findings
With the help of structure questionnaire, the information about the patient's condition, which is usually available in unstructured form (e.g. medical report, textual findings), is to be recorded in a clear manner so that a quick overview of the patient's history can be created and (differential) diagnosis accelerated [21]. An example is:

- *Marburger method of anamnesis*: The completed questionnaires are automatically read in and stored in a relational database, which allows to filter and search for different aspects of the patient's condition (e.g. medication, symptoms) in a short time [21].

[10] *https://www.face2gene.com/*

Big Data based application for therapy and treatment

Big Data based applications for the documentation of quality of life and treatment processes.

The management of patient data and information on the course of the disease as well as therapy and treatment progress can help to facilitate comprehensive disease management in the care of people with rare diseases. One example is:

- Using *Data Collection Tools* in conjunction with *PROMIS*[11] (Patient-Reported Outcomes Measurement Information System) , information about the patient's quality of life can be recorded by telemedicine, for example by documenting information about pain, emotional stress and physiological functions [15].

[11] *http://www.healthmeasures.net/explore-measurement-systems/promis*

Big Data based applications for generating and collection information

Social networks

Social networks are formed by complex relationships between different people and their interactions [22]. Social networks for doctors guarantee the exchange of experiences, problems and findings from medical practice and research; they are comparable to consultations or case conferences. Social networks for patients allow above all the personal exchange of questions, problems, findings and experiences within a particular disease groups; these are comparable with the self-help groups.

- Social networks for doctors: *DataGenno* is a platform for doctors to exchange information on primarily genetic questions and findings [22].
- Soziale networks for patients: *PatientsLikeMe*[12] is a platform for patients that enables [22].

Digital communication

Messenger applications, chat functions and / or other possibilities of digital communication enable all parties involved in the pathway to exchange information. One example is:

- With the help of *videoconferencing systems (e.g. Cisco*[13]*, Adobe Connect*[14]*, Skype4Business*[15]*)* different participants can communicate like for example within virtual tumour boards [23].

[12] *https://www.patientslikeme.com/*
[13] *https://www.cisco.com/c/de_de/products/conferencing/index.html*
[14] *https://www.adobe.com/de/products/adobeconnect.html*
[15] *https://www.skype.com/de/business/*

2 – Future Scenario and Evaluation

What would be a possible future scenario for the care of people with rare diseases and how is it evaluated?

The future scenario

How did we develop the future scenario?

An expert workshop (N=10) with physicians, patient representatives, IT experts, health care researchers and the data protection officer of the University Hospital Carl Gustav Carus Dresden was held to determine which of the identified Big Data technologies and applications could be used with added value in the healthcare process (improvement of the scope and/or quality of care for rare diseases). This has resulted in a model of future care for people with rare diseases (see Figure 2), which focuses on the use of Big Data applications to support diagnosis. In order to make the future scenario comprehensible for a wide range of target groups (including patients), the scenario was converted into a visual form at the end of the expert workshop (see Figure 3 and Figure 4).

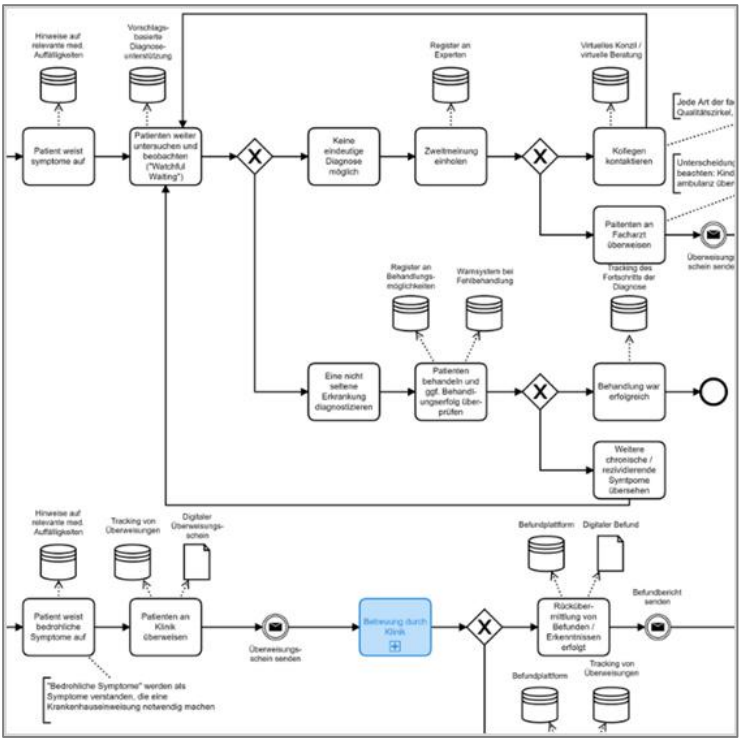

Figure 1: Section of the model illustration of the future supply path. In order to make the scenario easily understandable for different target groups, the model illustration was converted into a "tangible" scenario illustration

What would be a possible future scenario for the care of people with rare diseases?

The scenario was divided into two sections. First, a typical situation of current health care for people with rare diseases was described; then a possible future scenario for the use of Big Data applications to support the diagnosis of people with rare diseases was presented.

A possible scenario today

First, a possible situation today with our example patient Fred (see Figure 3):

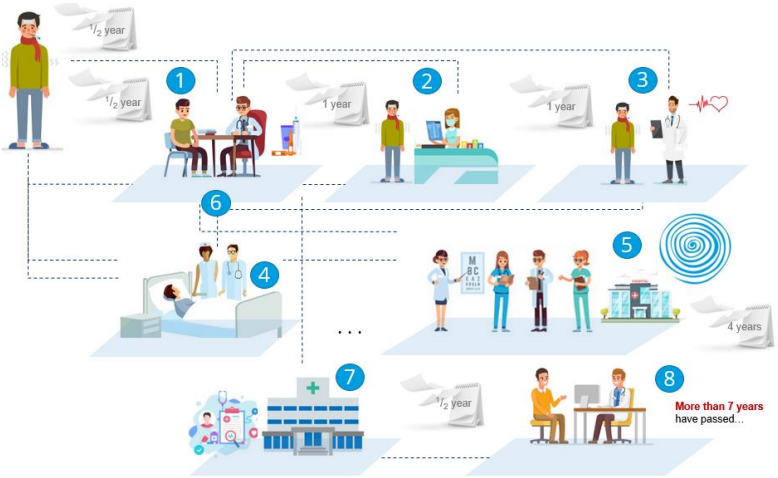

Figure 2: A possible scenario today

1	Fred has been suffering from severe fever for some time, feels increasingly weak and has joint pain. Fred decides to go to the **general practitioner**. The general practitioner suspects that the symptoms of a frequently occurring disease are behind the complaints and prescribes appropriate medication. However, Fred's health condition worsens. He suffers from increasingly severe pain. The general practitioner arranges for further examinations and tries other medicines, but these do not work either. He is at a loss and refers Fred to a specialist.
2	The **specialist** carries out further examinations and Fred is prescribed new medication. However, Fred is still in pain. The specialist does not know what to do and sends Fred back to the general practitioner. The general practitioner is still at a loss.

3	The general practitioner refers Fred to a **specialist with a different focus**. The specialist also conducts tests. However, the specialist cannot find any cause for Fred's complaints. Fred is getting worse and worse.
4	One day Fred is so exhausted and weakened that he has to be hospitalized. At the **hospital** further examinations are carried out. Fred receives medication and is discharged. The symptoms calm down a bit and Fred recovers first. But soon there are new attacks.
5	Fred consults even **more physicians** and **clinics** and **special outpatient clinics**, but nobody can help him.
6	During another stay in **hospital** a physician tells Fred about the rare fever syndrome. Fred goes to his general practitioner with this information. The general practitioner then registers Fred at a centre for rare diseases and sends Fred's patient records.
7	The **Rare Disease Centre**'s case manager receives the documents and sends questionnaires to the general practitioner and Fred for further information. The completed questionnaires and documents are then forwarded to the Centre's physician in charge. The latter checks the documents and prepares a case summary. The Centre physician examines the patient case and then selects experts for the case conference to discuss the respective patient case. This also applies to the case of Fred. Here the assumption is made that it is a rare fever syndrome. The centre summarises its findings in a short description and sends Fred to a specialist for further treatment.
8	The **specialist** gives Fred a suitable medicine. As a result, Fred's health improves; he can go back to work and actively participate in life. **It took more than 7 years until Fred received the right diagnosis and the right medical help...**

A possible scenario in the future

Technologically, it would be possible to accelerate the diagnosis process of rare diseases by linking information. Imagine in the not too distant future, the situation for Fred would look like this (see Figure 4).

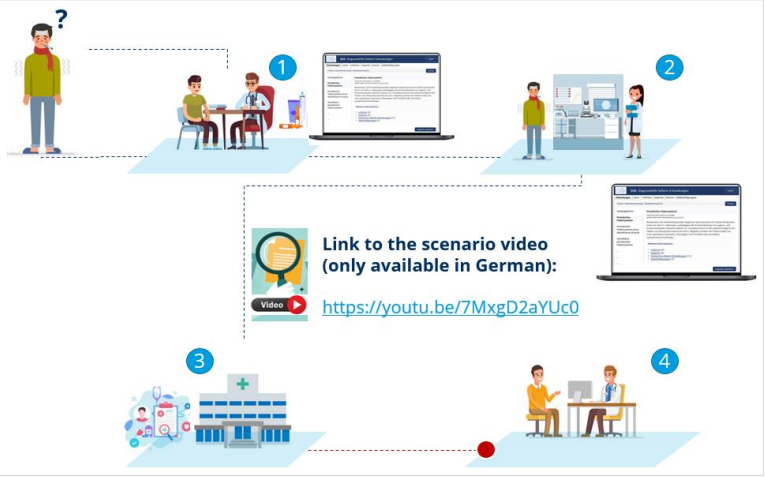

Figure 3: A possible scenario in the future

1

Our patient Fred is in the same health situation and the first contacts with his **general practitioner** could not alleviate his problems. The general practitioner has a patient case with Fred that he has never encountered before and has doubts that he falls into one of the known categories.

The general practitioner therefore accesses a **diagnosis support system** via the Internet.

This is based on various rare disease databases from which information can be retrieved and offers a search facility for difficult medical cases. The general practitioner enters Fred's symptoms and then receives - based on intelligent

	algorithms - a list of suggested diagnoses, weighted by the degree to which the search terms and diseases match. Furthermore, additional information is provided for each illness, such as guidelines, the contact details of experts for this illness and information on existing self-help groups. The general practitioner concludes that Fred's symptoms could be caused by a rare disease and refers Fred to a specialist. Fred's physician creates an electronic access code for the search entries and results, which is then sent electronically to the specialist together with Fred's findings.
2	The **specialist** also accesses the **diagnostic support system** via the Internet and reads Fred's electronic access code. She immediately sees all the entries and search results of the general practitioner and carries out further examinations. The specialist now enters the additional findings of her further diagnostics and sees that Fred could most likely suffer from a rare fever syndrome. She then registers Fred at a centre for rare diseases and digitally transmits the patient records to the centre and back to the general practitioner.
3	The case manager of the **Centre for Rare Diseases** checks all documents and consolidates the digital findings. The documents are then forwarded to the Center physician, reviewed and discussed in the case conference. This confirms the suspicion that Fred suffers from a rare fever syndrome.
4	Fred is then sent to a **specialist**, from whom he receives further treatment. Fred's health improves as a result.

The complete scenario is available as video via the following link: https://youtu.be/7MxgD2aYUc0 (only available in German).

Evaluation

How did the different target groups evaluate the scenario?

An online survey was conducted to evaluate the developed future scenario using Big Data technologies for the care of people with rare diseases. In the period from October 8, 2019 to November 10, 2019, a total of 113 physicians, patients, patient representatives, IT experts and health care researchers were interviewed with the online survey tool "SoSciSurvey" (www.soscisurvey.de) regarding their general acceptance, perceived benefits for patient care, economic implications of the scenario and potential challenges for the medium-term implementation of the scenario (see Figure 5).

	General acceptance	Benefits for patient care	Economic implications	Challenges for implementation
Physicians (N=9)	X	X	X	X
Patients / Patient representatives (N=69)	X	X		X
IT Experts (N=14)	X			X
Health care researchers (N=21)	X	X	X	X

Figure 4: Surveyed topic complexes per target group

With regard to these issues, the following tendency statements can be derived from the results of the online survey:

Complex of topics	Key messages
General acceptance of the scenario *the following were questioned: physicians, patients / patient representatives, IT experts, health care researchers*	• Usefulness of the application for medical work and patient care • Trust in the application • Implementation of the scenario is a good idea • Scenario has potential for long-term success • Divided opinion on the medium-term implementation of the scenario
Benefits for patient care *the following were questioned: physicians, patients / patient representatives, health care researchers*	Potential of the scenario is seen in: • Acceleration of diagnosis and therapy initiation • Increase of the diagnostic reliability • Avoidance of double services (especially diagnostic) • Improvement of cross-sectoral treatment
Economic implications *the following were questioned: physicians, health care researchers*	• Adjustment of the reimbursement situation desired / necessary • From the perspective of physicians and health care researchers: profitability of the scenario

Complex of topics	Key messages
Challenges for implementation *the following were questioned: physicians, patients / patient representatives, IT experts, health care researchers*	Seven thematic fields with need for action have been identified: • Financing and investment • Data protection and data security • Standards / Data sources / Data quality • Technology acceptance • Integration into the daily work routine • Knowledge about availability • Habits and preferences / role of physicians

The results of the survey were used to develop a catalogue of measures together with those involved in the health care process, which contains concrete recommendations for the medium-term implementation of the scenario, taking into account the technical, organisational and legal requirements.

3 – Measures for action and Conclusion

What action is needed for a successful implementation of the scenario?

Action plan

The action plan was developed in several rounds during the third workshop. The experts (N=10) from the previous workshops were involved. At the beginning of each workshop, the team of moderators presented a topic area with a need for action, which emerged from the results of the online survey. The experts then worked individually to develop a solution to the problem and presented it to the plenum. Together the experts evaluated the proposed solutions and determined the three most important proposals (if more than three proposals were developed). These top three were then evaluated according to their priority and the amount of work involved in their implementation. The final text of the formulated measures was prepared by members of the project team after the workshop. Similar measures were summarized. A total of 15 measures were derived from the 7 topics requiring action.

Topic 1: Financing and Investment

Challenges

- High costs for IT infrastructures
- Lack of financial resources for acquisition and operation
- Lack of compensation for the additional effort of use
- Missing fee schedule position

Measures for action

- To ensure continuous use of the system by physicians, the additional cost of using the application should be reibursed. For the outpatient sector in particular, this can be done by introducing a corresponding fee schedule position with a uniform evaluation standard. The prerequisite for this is a positive benefit assessment of the application. Responsible for this would be the top organs of self-administration in the health care system.

- Investments and support for financing are needed to ensure an appropriate IT infrastructure (e.g. suitable hardware, software and telecommunications facilities). This is where health policy measures (e.g. by the Federal Ministry of Health or the top self-governing bodies) can help by providing financial supplements for users (e.g. GP practices, centres for rare dieases, special outpatient clinics) on the basis of defines quality criteria on the basis of defined quality criteria.

Topic 2: Data protection and data security

Challenges

- Privacy and data security concerns (e.g. protection against hacking, cyber theft, phishing)
- Lack of infrastructure for the protection-worthy handling of sensitive patient and treatment data in electronic communication relationships
- Lack of trust of patients with regard to the misuse of data by e.g. insurers, health insurance companies
- Lack of patient understanding of what happens to their own data and the potential risks of misuse

Measures for action

- A data protection concept must be explicitly formulated on the basis of data protection and legal requirements. For this purpose, (1) data flows, process flows, access rights, storage locations and deletion periods etc. must be precisely defined and (2) transparency for medical staff and patients must be guaranteed with regard to the structure of data processing, data processing processes, the software used and data flows. Such a concept should be developed by developers, users and data protection officers.
- In order to promote patients' acceptance, understanding and confidence in the application, information should be provided on the opportunities and possible risks involved in collecting, processing and storing their personal and health data. This should be done directly by the medical institution (or by the treating physicians). In addition, appropriate publicity campaigns can be initiated with the involvement of self-help groups for rare diseases. In addition to the use of conventional media, such as talks, brochures and flyers, the use of other forms of information transfer, such as explanatory videos, is recommended.
- When developing the application, the principles of data economy and data minimization must be followed. This can

be achieved by cooperation between experts in software development and experts in data protection.

Topic 3: Standards / Data sources / Data quality

Challenges

- Lack of standards
- Lack of standardised forms for data input
- Lack of data quality / incompleteness and inaccuracy of patient data
- Problems in data collection due to the diversity of sources and the difficulty in selecting the "best sources”
- Limited adoption of common data models by e.g. general practitioners, specialists, rare disease centres
- Difficulties in identifying and classifying data, e.g. ICD10, SNOMED, HPO
- Difficulties in bringing together relevant data so that it can be used to model the problems

Measures for action

- In order to ensure high data quality and national and international comparability, it should be possible to use the existing terminology consistently. For this purpose, harmonisation can be achieved by means of metadata. For implementation, developers should work together with institutions for data standardization.
- To increase interoperability, the development of a core data set for the context of rare diseases should be based on existing standards. For this purpose, relevant data should be identified and modelled using metadata, with the involvement of medical and technological expertise and institutions for data standardisation (e.g. DIMDI).
- To improve data quality, standardised forms for data acquisition should be developed and used. This can be done by an iterative process similar to piloting, where the application is first implemented in individual organizational units and then in other organizational units. This should be done in cooperation between developers and users.

Topic 4: Technology acceptance

Challenges

- Physicians' fear of ...
    - new technologies
    - liability in case of misdiagnosis
    - demanding the use of the system by patients ("mass demand")
- Lack of experience and knowledge of physicians in relation to the use of the application
- Lack of confidence of physicians in the application (timeliness of data, correct functioning)
- Lack of patient confidence in the application (due to the long suffering)
- Patients' fear of incorrect functioning of the system by physicians (entering the wrong keywords leads to incorrect diagnosis)

Measures for action

- In order to ensure knowledge of the application and its handling, corresponding contents should be firmly anchored in the training of end users and further training and further education opportunities should be offered. This can be done through training institutions (e.g. universities, schools of health and nursing) and other educational institutions (e.g. medical association).
- In order to ensure trust and a high level of readiness for use, the added value of the application should be illustrated and the potential end users should be involved in the development process. The management level of the institution as well as key users / clinical champions can be responsible for this.

Topic 5: Integration into the daily work routine

Challenges

- Lack of time of the physicians
    - for using the system (entering search words)
    - for informing patients about the system (including aspects of data misuse)
- Lack of integration of the application into existing workflows

Measures for action

- The system should fit into the existing IT landscape as well as enable interoperable data exchange. Developers are responsible for creating the corresponding prerequisites (including interfaces and standards); company-specific prerequisites must be in place for provision and operation (e.g. implementation by IT experts on site).
- In terms of change management, the application should be integrated into processes by re-structuring existing workflows. This can be the responsibility of the management level of the institution as well as the key users / clinical champions and multipliers.

Topic 6: Knowledge about availability

Challenges

- Lack of patient knowledge that such applications exist and can be used for care
- Lack of knowledge of physicians that such applications exist and how to use them

Measures for action

- The existence of the system and its benefits should be advertised both to patients and users. This can be done by means of appropriate congresses, further training, specialist journals and posters in the practices. On the other hand, campaigns could also be initiated to disseminate success stories and training videos via the Internet.

Tolic 7: Habit and preferences

Challenges

- Lack of doubt on the part of physicians about their current strategy (there is no "rethinking" of another possible diagnosis)
- Lack of willingness on the part of doctors to "hand over" their patients (physicians prefer to try out for themselves)
- Rejection by the physicians that someone or "something" (=application/system) interferes with their diagnosis
- No "admitting" of own ignorance/ gaps in knowledge

Measures for action

- The application should be perceived as assistance to the physicians and not as competition. This point of view should already be conveyed during medical education by the training institutions and should also be communicated, for example, by professional societies and associations.
- A timely, technology-oriented and patient-centred self-image of physicians should be promoted by raising awareness in medical education by the training institutions (e.g. universities, health and nursing schools). In order to improve interdisciplinary cooperation between experts, additional networking opportunities (e.g. platforms, congresses) should be created for professional exchange through professional societies and associations.

BIDA-SE – Our conclusion

Even if the current health care situation still presents many challenges, we are optimistic because …

- … there is a great willingness on the part of all those involved in the care process to address these challenges,
- … there is a whole range of technological solutions that could be further developed for meaningful use and
- … concrete measures have been identified to help realise a future scenario to improve the care situation for people with rare diseases.

References

[1] M. Lelgemann and R. Francke, 'Seltene Erkrankungen in professionellen Versorgungssystemen', *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, vol. 51, no. 5, pp. 509–518, 2008, doi: 10.1007/s00103-008-0522-9.

[2] B. Wetterauer and R. Schuster, 'Seltene Krankheiten: Probleme, Stand und Entwicklung der nationalen und europäischen Forschungsförderung', *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, vol. 51, no. 5, pp. 519–528, 2008, doi: 10.1007/s00103-008-0524-7.

[3] M. Frank, D. Eidt-Koch, I. Aumann, A. Reimann, T. O. F. Wagner, and J.-M. Graf von der Schulenburg, 'Maßnahmen zur Verbesserung der gesundheitlichen Situation von Menschen mit seltenen Erkrankungen in Deutschland: Ein Vergleich mit dem Nationalen Aktionsplan', *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, vol. 57, no. 10, pp. 1216–1223, Oct. 2014, doi: 10.1007/s00103-014-2040-2.

[4] L. Schöls, T. Gasser, I. Krägeloh-Mann, H. Graessner, T. Klockgether, and A. Münchau, 'Zentren für seltene neurologische Erkrankungen', *Aktuelle Neurol.*, vol. 45, no. 03, pp. 178–186, 2018, doi: 10.1055/s-0043-114000.

[5] A. Schieppati, J.-I. Henter, E. Daina, and A. Aperia, 'Why rare diseases are an important medical and social issue', *The Lancet*, vol. 371, no. 9629, pp. 2039–2041, 2008, doi: 10.1016/S0140-6736(08)60872-7.

[6] T. Voigtländer, '„Orphan diseases": Warum seltene Erkrankungen viele Netzwerke brauchen', *Monatsschr. Kinderheilkd.*, vol. 160, no. 9, pp. 863–875, 2012, doi: 10.1007/s00112-012-2668-7.

[7] Bundesministerium für Gesundheit, 'Seltene Erkrankungen', *Bundesgesundheitsministerium*, 01-Apr-2019. [Online]. Available: https://www.bundesgesundheitsministerium.de/themen/praevention/gesundheitsgefahren/seltene-erkrankungen.html. [Accessed: 01-Apr-2019].

[8] T. Müller, A. Jerrentrup, and J. R. Schäfer, 'Computerunterstützte Diagnosefindung bei seltenen Erkrankungen', *Internist*, vol. 59, no. 4, pp. 391–400, 2018, doi: 10.1007/s00108-017-0218-z.

[9] S. C. Groft and M. Posada de la Paz, 'Preparing for the Future of Rare Diseases', in *Rare Diseases Epidemiology: Update and Overview*, M. Posada de la Paz, D. Taruscio, and S. C. Groft, Eds. Cham: Springer International Publishing, 2017, pp. 641–648.

[10] B. Marr, *Big Data: Using SMART big data, analytics and metrics to make better decisions and improve performance*. Wiley & Sons, 2015.

[11] S. Aymé, B. Bellet, and A. Rath, 'Rare diseases in ICD11: making rare diseases visible in health information systems through appropriate coding', *Orphanet J. Rare Dis.*, vol. 10, no. 1, 2015, doi: 10.1186/s13023-015-0251-8.
[12] J. Haase, T. O. F. Wagner, and H. Storf, 'se-atlas – Versorgungsatlas für Menschen mit seltenen Erkrankungen: Unterstützung bei der Recherche nach Versorgungseinrichtungen und Selbsthilfeorganisationen', *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, vol. 60, no. 5, pp. 503–509, May 2017, doi: 10.1007/s00103-017-2529-6.
[13] S. Köhler *et al.*, 'The Human Phenotype Ontology in 2017', *Nucleic Acids Res.*, vol. 45, no. 1, pp. 865–876, 2016, doi: 10.1093/nar/gkw1039.
[14] A. Hamosh, A. F. Scott, J. S. Amberger, C. A. Bocchini, and V. A. McKusick, 'Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders', *Nucleic Acids Res.*, vol. 33, no. 1, pp. 514–517, 2005, doi: 10.1093/nar/gki033.
[15] Y. R. Rubinstein *et al.*, 'Creating a global rare disease patient registry linked to a rare diseases biorepository database: Rare Disease-HUB (RD-HUB)', *Contemp. Clin. Trials*, vol. 31, no. 5, pp. 394–404, 2010, doi: 10.1016/j.cct.2010.06.007.
[16] S. A. Bell and C. Tudur Smith, 'A comparison of interventional clinical trials in rare versus non-rare diseases: an analysis of ClinicalTrials.gov', *Orphanet J. Rare Dis.*, vol. 9, no. 1, p. 170, 2014, doi: 10.1186/s13023-014-0170-0.
[17] P. Landais *et al.*, 'CEMARA an information system for rare diseases', *Stud. Health Technol. Inform.*, pp. 481–485, 2010, doi: 10.3233/978-1-60750-588-4-481.
[18] T. Müller, A. Jerrentrup, and J. R. Schäfer, 'Computerunterstützte Diagnosefindung bei seltenen Erkrankungen', *Internist*, vol. 59, no. 4, pp. 391–400, Apr. 2018, doi: 10.1007/s00108-017-0218-z.
[19] G. M. Sacco, 'e-RARE: Interactive Diagnostic Assistance for Rare Diseases through Dynamic Taxonomies', in *2008 19th International Conference on Database and Expert Systems Applications*, Turin, Italy, 2008, pp. 407–411, doi: 10.1109/DEXA.2008.61.
[20] T. Fujiwara, Y. Yamamoto, J.-D. Kim, O. Buske, and T. Takagi, 'PubCaseFinder: A Case-Report-Based, Phenotype-Driven Differential-Diagnosis System for Rare Diseases', *Am. J. Hum. Genet.*, vol. 103, no. 3, pp. 389–399, 2018, doi: 10.1016/j.ajhg.2018.08.003.
[21] J. König, L. Grigull, H.-W. Fritsch, and F. Klawonn, 'IT-Unterstützung zur Diagnosefindung seltener Erkrankungen – Umfassende Datenanalyse bei

komplexen Fällen', *Klin.*, vol. 44, no. 01, pp. 16–21, 2015, doi: 10.1055/s-0035-1544983.

[22] F. F. Costa, 'Social networks, web-based tools and diseases: implications for biomedical research', *Drug Discov. Today*, vol. 18, no. 5–6, pp. 272–281, 2013, doi: 10.1016/j.drudis.2012.10.006.

[23] M. Renovanz, N. Keric, C. Richter, A. Gutenberg, and A. Giese, 'Patienten-zentrierte Versorgung', *Nervenarzt*, vol. 86, no. 12, pp. 1555–1560, 2015, doi: 10.1007/s00115-015-4473-8.

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