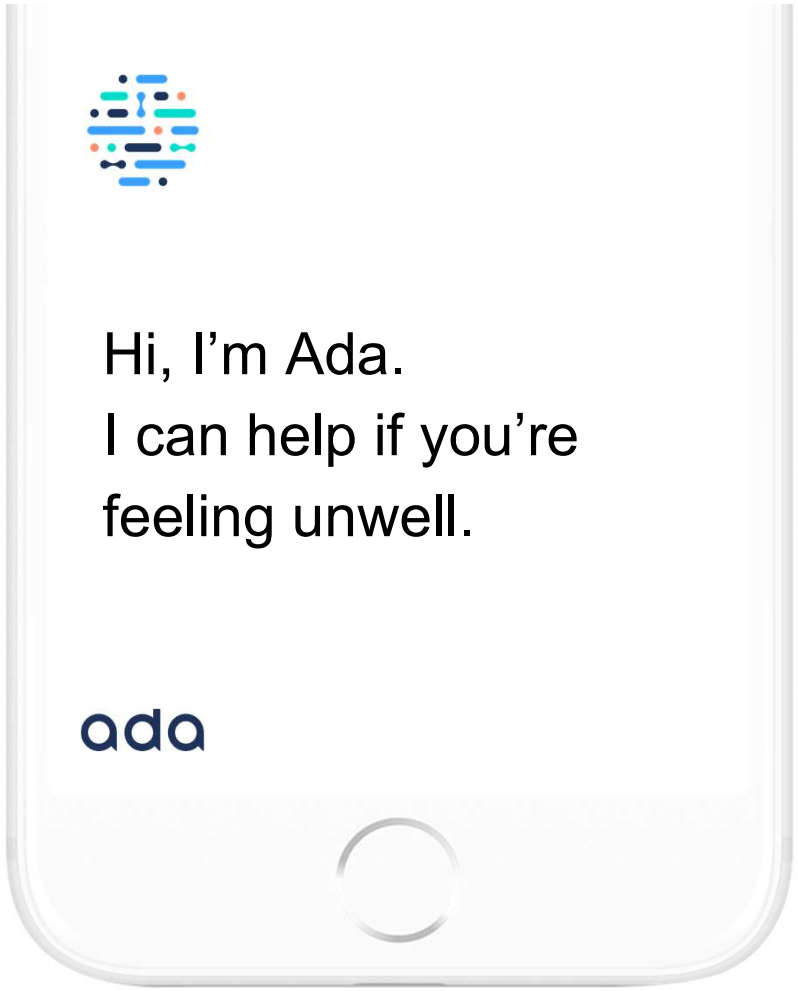


Philips-Universität Marburg
Institut für KI in der Medizin
Prof. Dr. Martin C. Hirsch

Diagnostik seltener Erkrankungen mit KI-Unterstützung

IQWIG-HERBST-SYMPOSIUM 2023

Herausforderung
Seltene Erkrankungen
24./25.11.2023

Kein Interessenskonflikt, aber zwei Hüte …

Gründer & Chief Science Advisor
Ada Health
Berlin

Professor & Direktor
Institut für KI in der Medizin
Philipps Universität Marburg


2015


Herr K

Herr K wird bei Frau Prof. Wagner in der MHH vorstellig

Prof. Dr. Annette Wagner

MHH Medizinische Hochschule Hannover

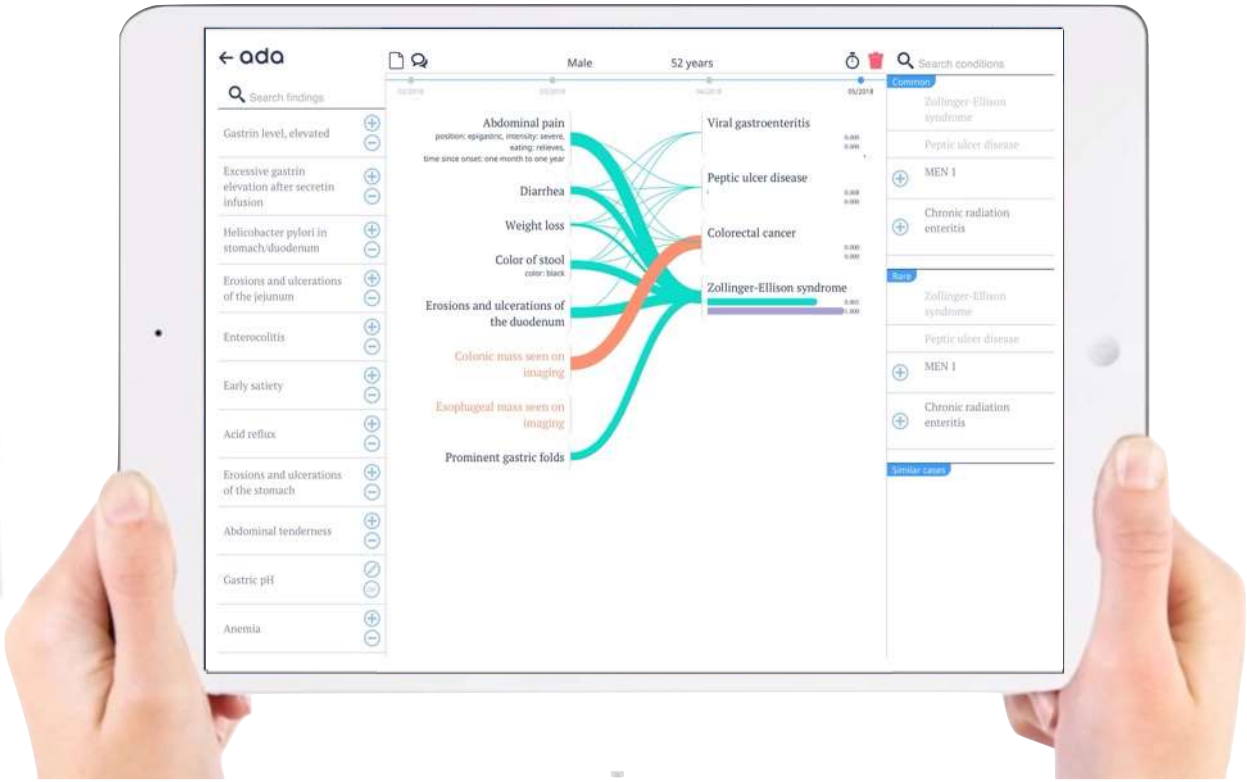
Einige Monate später hat Herr K eine Diagnose

IgG4-related disease

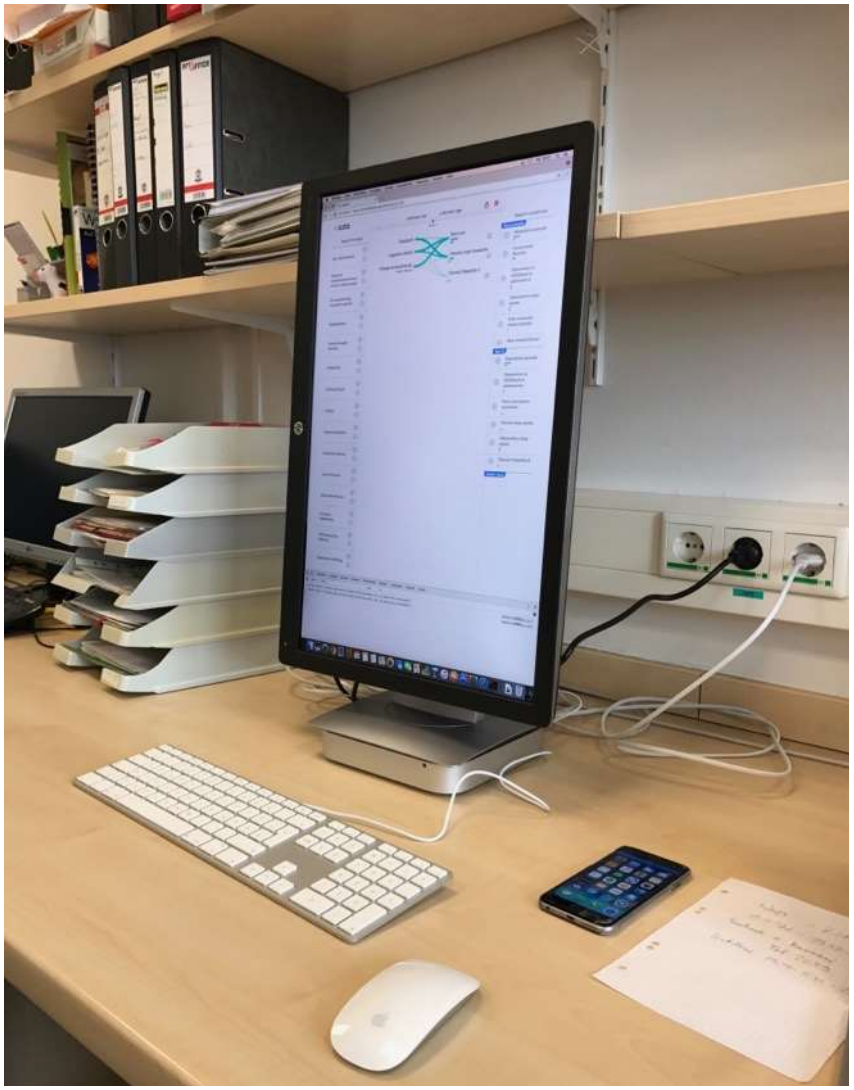
Prof. Dr. Annette Wagner

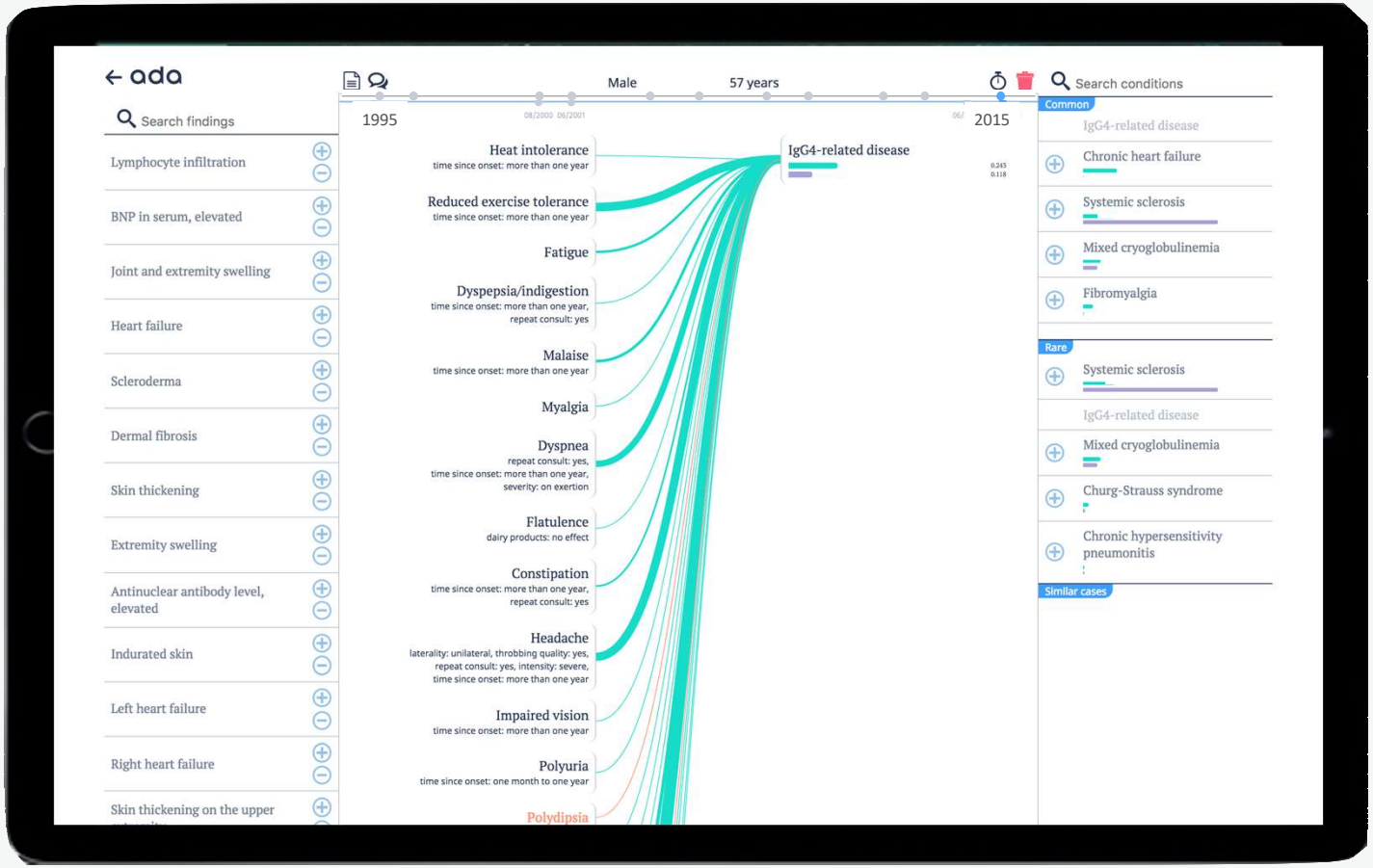
MHH Medizinische Hochschule Hannover

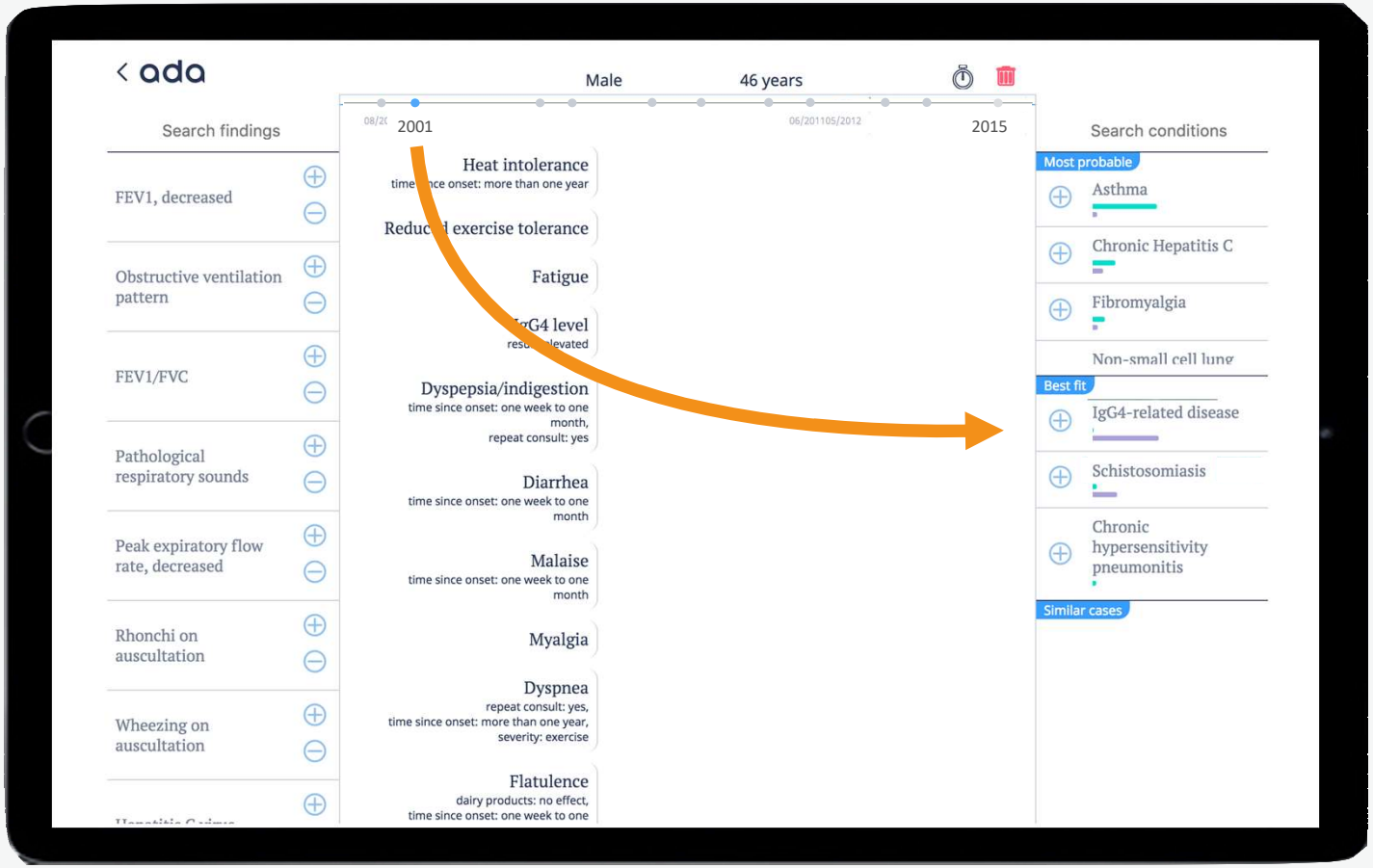
2016: Prototyp des KI-basierten Diagnose-Unterstützungssystems Ada DX



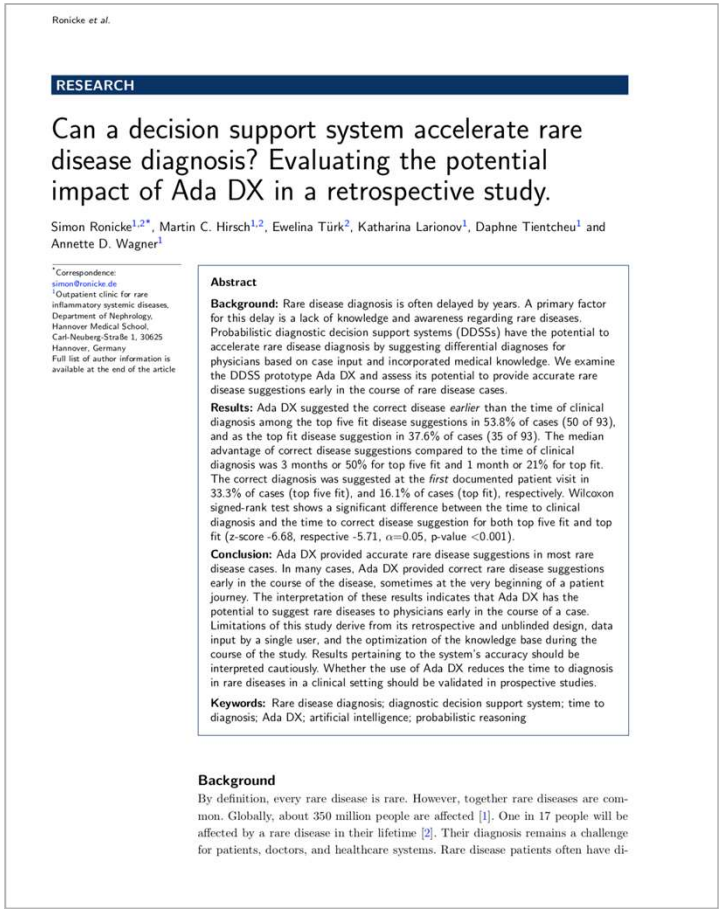
Daten von Herr K werden eingegeben




ada
Search findings
Lymphocyte infiltration
BNP in serum, elevated
Joint and extremity swelling
Heart failure
Scleroderma
Dermal fibrosis
Skin thickening
Extremity swelling
Antinuclear antibody level, elevated
Indurated skin
Left heart failure
Right heart failure
Skin thickening on the upper
Male
57 years
1995
2015
Heat intolerance
time since onset: more than one year
Reduced exercise tolerance
time since onset: more than one year
Fatigue
Dyspepsia/indigestion
time since onset: more than one year, repeat consult: yes
Malaise
time since onset: more than one year
Myalgia
Dyspnea
repeat consult: yes, time since onset: more than one year, severity: on exertion
Flatulence
dairy products: no effect
Constipation
time since onset: more than one year, repeat consult: yes
Headache
laterality: unilateral, throbbing quality: yes, repeat consult: yes, intensity: severe, time since onset: more than one year
Impaired vision
time since onset: more than one year
Polyuria
time since onset: one month to one year
Polydipsia
IgG4-related disease
Search conditions
Common
IgG4-related disease
Chronic heart failure
Systemic sclerosis
Mixed cryoglobulinemia
Fibromyalgia
Rare
Systemic sclerosis
IgG4-related disease
Mixed cryoglobulinemia
Churg-Strauss syndrome
Chronic hypersensitivity pneumonitis
Similar cases


ada
Male
46 years
Search findings
2001
2015
Search conditions
FEV1, decreased
Obstructive ventilation pattern
FEV1/FVC
Pathological respiratory sounds
Peak expiratory flow rate, decreased
Rhonchi on auscultation
Wheezing on auscultation
Heat intolerance
Reduced exercise tolerance
Fatigue
Dyspepsia/indigestion
time since onset: one week to one month, repeat consult: yes
Diarrhea
time since onset: one week to one month
Malaise
time since onset: one week to one month
Myalgia
Dyspnea
repeat consult: yes, time since onset: more than one year, severity: exercise
Flatulence
dairy products: no effect, time since onset: one week to one
Most probable
Asthma
Chronic Hepatitis C
Fibromyalgia
Best fit
IgG4-related disease
Schistosomiasis
Chronic hypersensitivity pneumonitis
Similar cases

orphanet Journal



Ronicke *et al.*

RESEARCH

Can a decision support system accelerate rare disease diagnosis? Evaluating the potential impact of Ada DX in a retrospective study.

Simon Ronicke[1,2*], Martin C. Hirsch[1,2], Ewelina Türk[2], Katharina Larionov[1], Daphne Tientcheu[1] and Annette D. Wagner[1]

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simon@ronicke.de
[1]Outpatient clinic for rare inflammatory systemic diseases, Department of Nephrology, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hannover, Germany
Full list of author information is available at the end of the article

Abstract

Background: Rare disease diagnosis is often delayed by years. A primary factor for this delay is a lack of knowledge and awareness regarding rare diseases. Probabilistic diagnostic decision support systems (DDSSs) have the potential to accelerate rare disease diagnosis by suggesting differential diagnoses for physicians based on case input and incorporated medical knowledge. We examine the DDSS prototype Ada DX and assess its potential to provide accurate rare disease suggestions early in the course of rare disease cases.

Results: Ada DX suggested the correct disease *earlier* than the time of clinical diagnosis among the top five fit disease suggestions in 53.8% of cases (50 of 93), and as the top fit disease suggestion in 37.6% of cases (35 of 93). The median advantage of correct disease suggestions compared to the time of clinical diagnosis was 3 months or 50% for top five fit and 1 month or 21% for top fit. The correct diagnosis was suggested at the *first* documented patient visit in 33.3% of cases (top five fit), and 16.1% of cases (top fit), respectively. Wilcoxon signed-rank test shows a significant difference between the time to clinical diagnosis and the time to correct disease suggestion for both top five fit and top fit (z-score -6.68, respective -5.71, α=0.05, p-value <0.001).

Conclusion: Ada DX provided accurate rare disease suggestions in most rare disease cases. In many cases, Ada DX provided correct rare disease suggestions early in the course of the disease, sometimes at the very beginning of a patient journey. The interpretation of these results indicates that Ada DX has the potential to suggest rare diseases to physicians early in the course of a case. Limitations of this study derive from its retrospective and unblinded design, data input by a single user, and the optimization of the knowledge base during the course of the study. Results pertaining to the system's accuracy should be interpreted cautiously. Whether the use of Ada DX reduces the time to diagnosis in rare diseases in a clinical setting should be validated in prospective studies.

Keywords: Rare disease diagnosis; diagnostic decision support system; time to diagnosis; Ada DX; artificial intelligence; probabilistic reasoning

Background

By definition, every rare disease is rare. However, together rare diseases are common. Globally, about 350 million people are affected [1]. One in 17 people will be affected by a rare disease in their lifetime [2]. Their diagnosis remains a challenge for patients, doctors, and healthcare systems. Rare disease patients often have di-

Retrospective study:
in 63.8% (51/94) of cases, correct rare disease suggestion given within Ada's top 5 conditions at a time *earlier* than the confirmed clinical diagnosis.

BMC

2021

Willmen et al. BMC Health Services Research (2021) 21:947
https://doi.org/10.1186/s12913-021-06926-y

BMC Health Services Research

RESEARCH Open Access

Health economic benefits through the use of diagnostic support systems and expert knowledge

Tina Willmen[1], Lukas Völkel[2], Simon Ronicke[3], Martin C. Hirsch[4,5], Jessica Kaufeld[1], Reinhard P. Rychlik[2] and Annette D. Wagner[1*]

Abstract

Background: Rare diseases are difficult to diagnose. Due to their rarity, heterogeneity, and variability, rare diseases often result not only in extensive diagnostic tests and imaging studies, but also in unnecessary repetitions of examinations, which places a greater overall burden on the healthcare system.
Diagnostic decision support systems (DDSS) optimized by rare disease experts and used early by primary care physicians and specialists are able to significantly shorten diagnostic processes. The objective of this study was to evaluate reductions in diagnostic costs incurred in rare disease cases brought about by rapid referral to an expert and diagnostic decision support systems.

Methods: Retrospectively, diagnostic costs from disease onset to diagnosis were analyzed in 78 patient cases from the outpatient clinic for rare inflammatory systemic diseases at Hannover Medical School. From the onset of the first symptoms, all diagnostic measures related to the disease were taken from the patient files and documented for each day.
The basis for the health economic calculations was the Einheitlicher Bewertungsmaßstab (EBM) used in Germany for statutory health insurance, which assigns a fixed flat rate to the various medical services.
For 76 cases we also calculated the cost savings that would have been achieved by the diagnosis support system Ada DX applied by an expert.

Results: The expert was able to achieve significant savings for patients with long courses of disease. On average, the expert needed only 27 % of the total costs incurred in the individual treatment odysseys to make the correct diagnosis. The expert also needed significantly less time and avoided unnecessary examination repetitions.
If a DDSS had been applied early in the 76 cases studied, only 51–68 % of the total costs would have incurred and the diagnosis would have been made earlier. Earlier diagnosis would have significantly reduced costs.

Conclusion: The study showed that significant savings in the diagnostic process of rare diseases can be achieved through rapid referral to an expert and the use of DDSS. Faster diagnosis not only achieves savings, but also enables the right therapy and thus an increase in the quality of life for patients.

Keywords: rare diseases, health economic costs, diagnosis support systems, artificial intelligence

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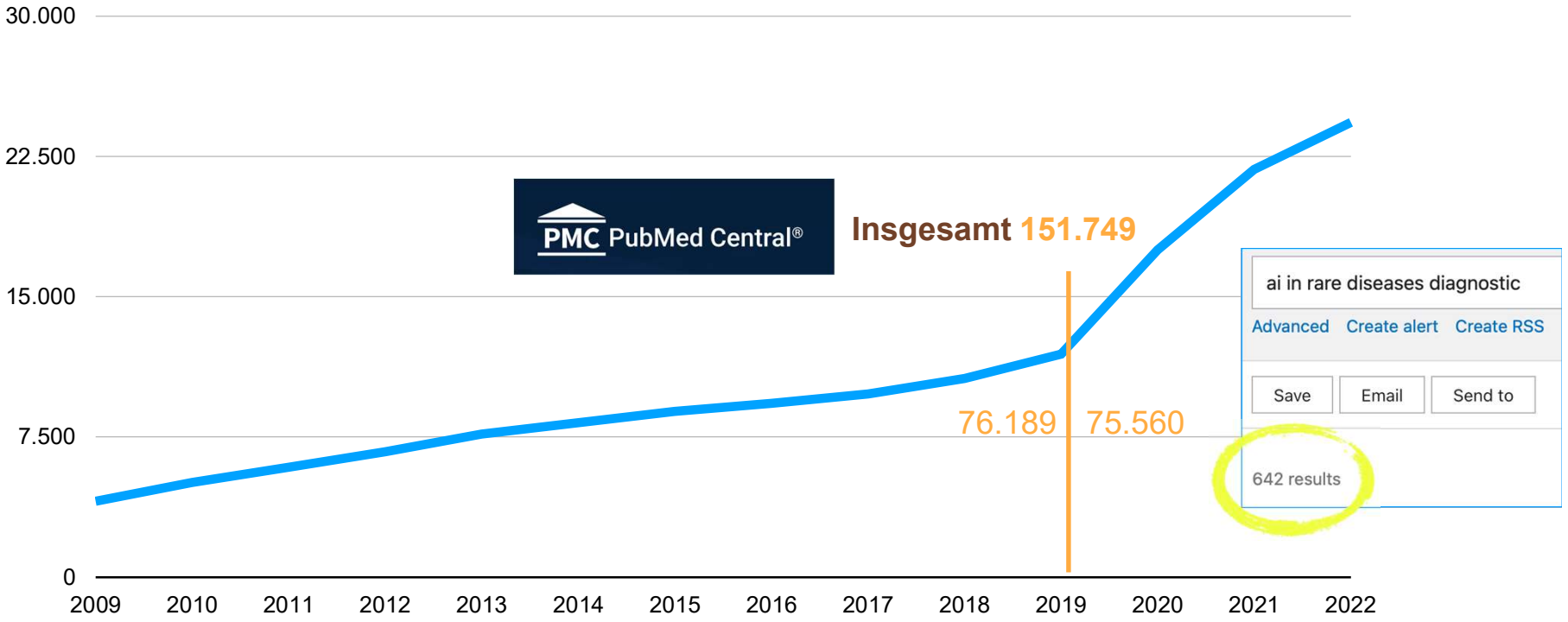
[1]Department of Nephrology, Hannover Medical School, Hanover, Germany
Full list of author information is available at the end of the article

MH Medizinische Hochschule Hannover

"If a DDSS had been used early, **only 51-68% of the total diagnostic costs would have been incurred**!"

Publikationen zu AI in Healthcare in den letzten 13 Jahren



Methodische Schwierigkeiten bei hoher Datenfülle und geringen Fallzahlen

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MINI REVIEW article

Front. Med., 05 October 2021
Sec. Pathology
Volume 8 - 2021 |
https://doi.org/10.3389/fmed.2021.747612

This article is part of the Research Topic
Insights in Pathology: 2021 - Digital Pathology and Artificial Intelligence
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Opportunities and Challenges for Machine Learning in Rare Diseases

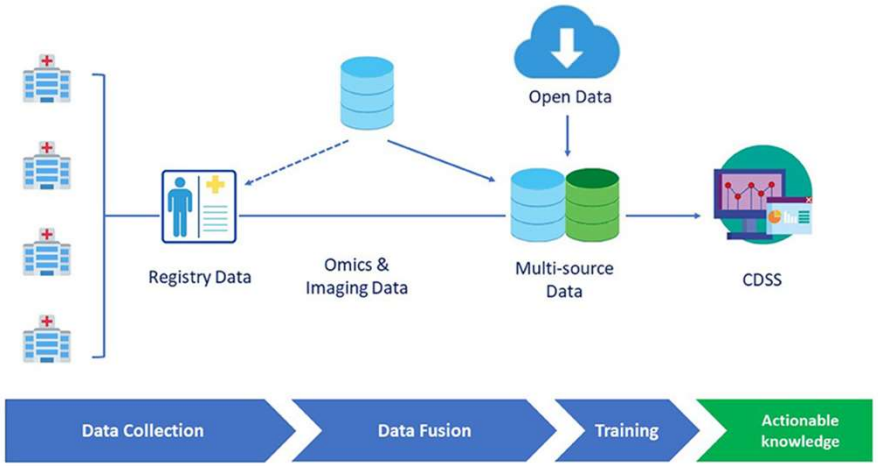
Sergio Decherchi[1†] Elena Pedrini[2†] Marina Mordenti[2*†] Andrea Cavalli[1,3]
Luca Sangiorgi[2]

[1] Computational and Chemical Biology, Fondazione Istituto Italiano di Tecnologia, Genoa, Italy
[2] Department of Rare Skeletal Disorders, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy
[3] Department of Pharmacy and Biotechnology (FaBiT), Alma Mater Studiorum – University of Bologna, Bologna, Italy

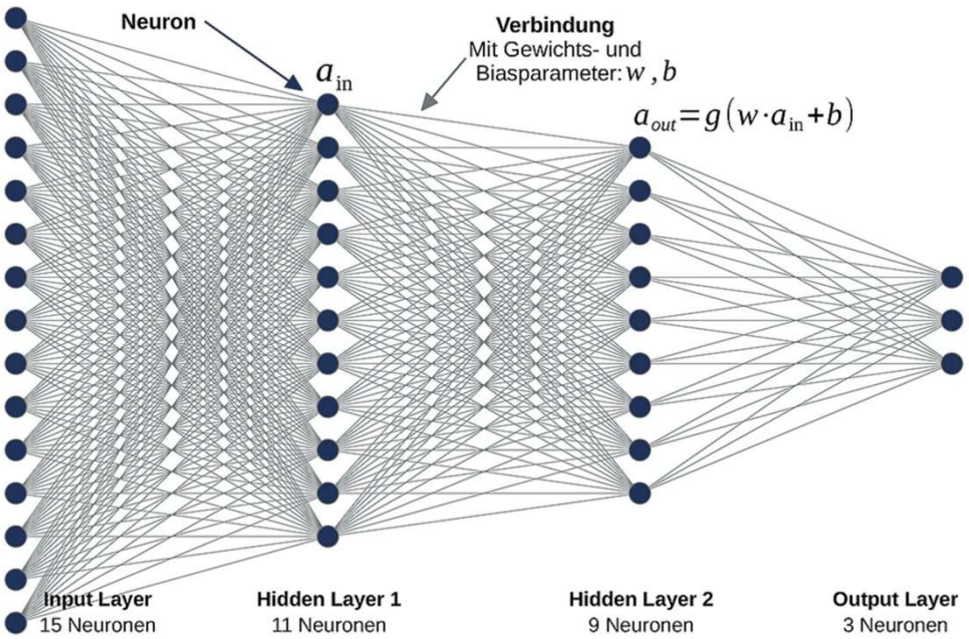
Rare diseases (RDs) are complicated health conditions that are difficult to be managed at several levels. The scarcity of available data chiefly determines an intricate scenario even for experts and specialized clinicians, which in turn leads to the so called "diagnostic odyssey" for the patient. This situation calls for innovative solutions to support the decision process *via* quantitative and automated tools. Machine learning brings to the stage a wealth of powerful inference methods; however, matching the health conditions with advanced statistical techniques raises methodological, technological, and even ethical issues. In this contribution, we critically point to the specificities of the dialog of rare diseases with machine learning techniques concentrating on the key steps and challenges that may hamper or create actionable knowledge and value for the patient together with some on-field methodological suggestions and considerations.

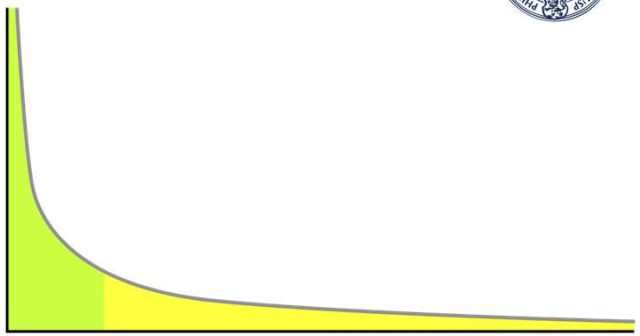
Introduction

A rare disease (RD) is defined as a low-prevalence condition that affects fewer than one in 2,000 people. Due to the frequent lack of knowledge and treatment (which makes them also known as "orphan diseases"), they represent a real emerging global public health priority. So

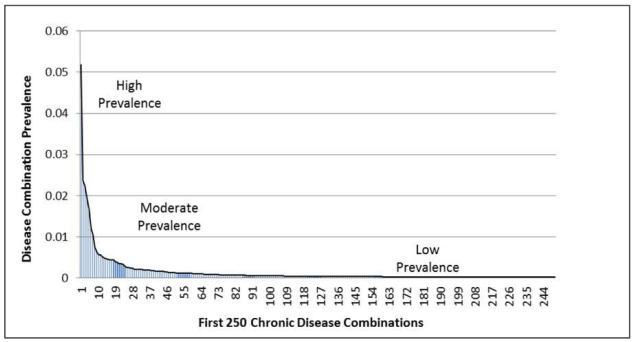


Das inhärente Problem heutiger ANN-Ansätze





Herausforderung: Long-Tails



Methodische Lösungsansätze für hohe Datenfülle und geringe Fallzahlen

GENETICS IN MEDICINE
An open access paper
www.nature.com

PMCID: PMC6752318
PMID: 30675030

Genet Med. 2019; 21(9): 2126–2134.
Published online 2019 Jan 24. doi: 10.1038/s41436-019-0439-8

Xrare: a machine learning method jointly modeling phenotypes and genetic evidence for rare disease diagnosis

Qigang Li, MSc,[#1] Keyan Zhao, PhD,[#1] Carlos D. Bustamante, PhD,[2,3] Xin Ma, PhD,[1,4] and Wing H. Wong, PhD[1,3,4]

Associated Data

Supplementary Materials

Go to: ▸

Abstract

Purpose

Despite the successful progress next-generation sequencing technologies has achieved in diagnosing the genetic cause of rare Mendelian diseases, the current diagnostic rate is still far from satisfactory because of heterogeneity, imprecision, and noise in disease phenotype descriptions and insufficient utilization of expert knowledge in clinical genetics. To overcome these difficulties, we present a novel method called Xrare for the prioritization of causative gene variants in rare disease diagnosis.

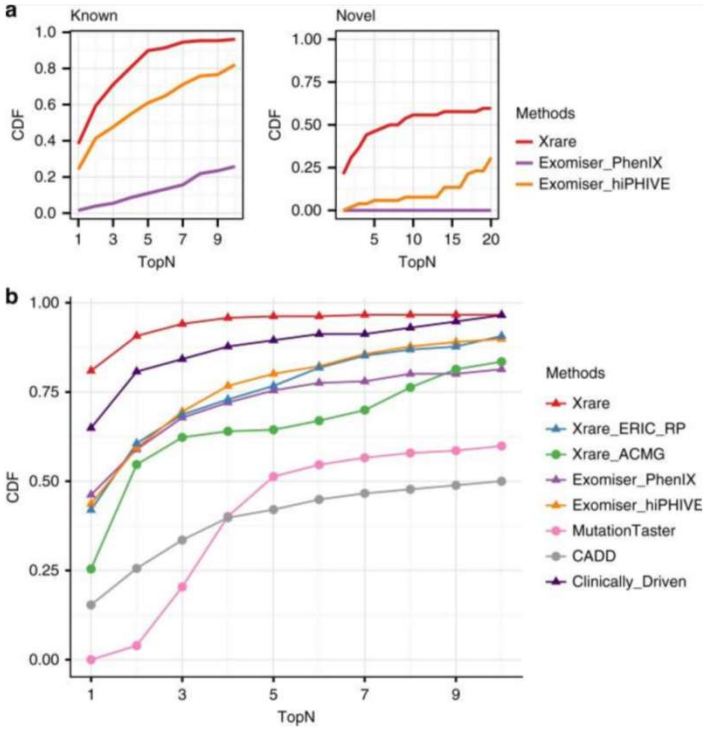
Methods

We propose a new phenotype similarity scoring method called Emission-Reception Information Content (ERIC), which is highly tolerant of noise and imprecision in clinical phenotypes. We utilize medical genetic domain knowledge by designing genetic features implementing American College of Medical Genetics and Genomics (ACMG) guidelines.

Results

ERIC score ranked consistently higher for disease genes than other phenotypic similarity scores in the presence of imprecise and noisy phenotypes. Extensive simulations and real clinical data demonstrated that Xrare outperforms existing alternative methods by 10–40% at various genetic diagnosis scenarios.

Xrare



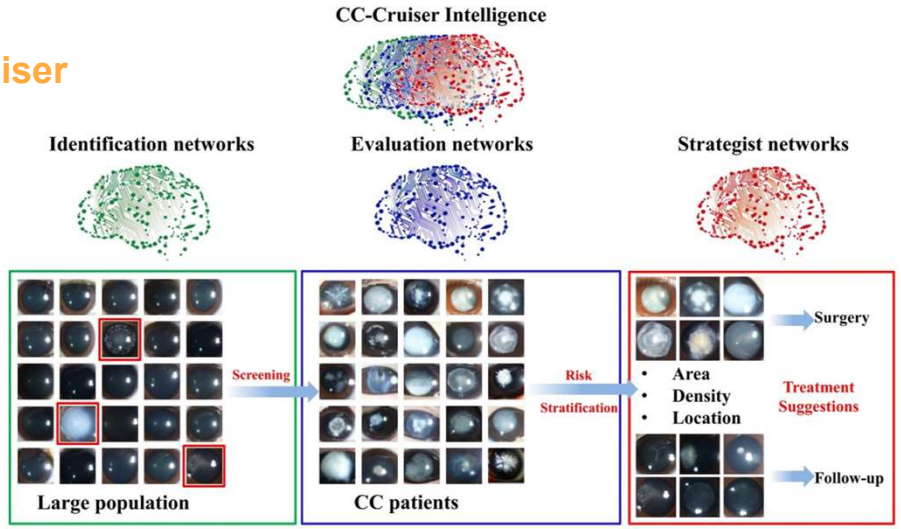
KI in der Erkennung seltener, angeborener Augenkatarakte bei Kindern

Abstract

Background

CC-Cruiser is an artificial intelligence (AI) platform developed for diagnosing childhood

CC-Cruiser



KI in der Erkennung SE-bedingter Gesichtsanomalien

nature genetics

TECHNICAL REPORT

https://doi.org/10.1038/s41588-021-01010-x

Check for updates

GestaltMatcher facilitates rare disease matching using facial phenotype descriptors

Tzung-Chien Hsieh[1,25], Aviram Bar-Haim[2,25], Shahida Moosa[3], Nadja Ehmke[4], Karen W. Gripp[5], Jean Tori Pantel[1,4], Magdalena Danyel[4,6], Martin Atta Mensah[4,7], Denise Horn[4], Stanislav Rosnev[4], Nicole Fleischer[2], Guilherme Bonini[2], Alexander Hustinx[1], Alexander Schmid[1], Alexej Knaus[1], Behnam Javanmardi[1], Hannah Klinkhammer[1,8], Hellen Lesmann[1], Sugirthan Sivalingam[1,8,9], Tom Kamphans[10], Wolfgang Meiswinkel[10], Frédéric Ebstein[11], Elke Krüger[11], Sébastien Küry[12,13], Stéphane Bézieau[12,13], Axel Schmidt[14], Sophia Peters[14], Hartmut Engels[14], Elisabeth Mangold[14], Martina Kreiß[14], Kirsten Cremer[14], Claudia Perne[14], Regina C. Betz[14], Tim Bender[14,15], Kathrin Grundmann-Hauser[16], Tobias B. Haack[16], Matias Wagner[17,18], Theresa Brunet[17,18], Heidi Beate Bentzen[19], Luisa Averdunk[20], Kimberly Christine Coetzer[3], Gholson J. Lyon[21,22], Malte Spielmann[23], Christian P. Schaaf[24], Stefan Mundlos[4], Markus M. Nöthen[14] and Peter M. Krawitz[1]✉

Many monogenic disorders cause a characteristic facial morphology. Artificial intelligence can support physicians in recognizing these patterns by associating facial phenotypes with the underlying syndrome through training on thousands of patient photographs. However, this 'supervised' approach means that diagnoses are only possible if the disorder was part of the training set. To improve recognition of ultra-rare disorders, we developed GestaltMatcher, an encoder for portraits that is based on a deep convolutional neural network. Photographs of 17,560 patients with 1,115 rare disorders were used to define a Clinical Face Phenotype Space, in which distances between cases define syndromic similarity. Here we show that patients can be matched to others with the same molecular diagnosis even when the disorder was not included in the training set. Together with mutation data, GestaltMatcher could not only accelerate the clinical diagnosis of patients with ultra-rare disorders and facial dysmorphism but also enable the delineation of new phenotypes.

Rare genetic disorders affect more than 6.2% of the global population[1]. Because genetic disorders are rare and diverse, accurate clinical diagnosis is a time-consuming and challenging process, often referred to as the 'diagnostic odyssey'[2], and all informative clinical features have to be taken into consideration. A large fraction of patients, particularly those with neurodevelopmental disorders, exhibit craniofacial abnormalities[3]. If the facial phenotype ('gestalt') is highly recognizable, such as in Down syndrome, it may also play an important role in establishing the diagnosis. Sometimes the gestalt is so characteristic or distinct that it reduces the search space of candidate genes or can be used to delineate new phenotype–gene associations[4]. However, the ability to recognize these syndromic disorders relies heavily on the clinician's experience. Reaching a diagnosis is very challenging if the clinician has not

[1]Institute for Genomic Statistics and Bioinformatics, University Hospital Bonn, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany. [2]FDNA Inc., Boston, MA, USA. [3]Division of Molecular Biology and Human Genetics, Stellenbosch University and Medical Genetics, Tygerberg Hospital, Tygerberg, South Africa. [4]Institute of Medical Genetics and Human Genetics, Charité-Universitätsmedizin Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany. [5]A.I. DuPont Hospital for Children/Nemours, Wilmington, DE, USA. [6]BIH Biomedical Innovation Academy, Charité-Universitätsmedizin Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany. [7]Institute for Medical Biometry, Digital Clinician Scientist Program, Berlin Institute of Health at Charité-Universitätsmedizin Berlin, Berlin, Germany. [8]Institute for Medical Informatics and Epidemiology, Medical Faculty, University of Bonn, Bonn, Germany. [9]Core Unit for Bioinformatics Data Analysis, Medical Faculty, University of Bonn, Bonn, Germany. [10]GeneTalk, Bonn, Germany. [11]Institut für Medizinische Biochemie und Molekularbiologie (IMBM), Universitätsmedizin Greifswald, Greifswald, Germany. [12]CHU Nantes, Service de Génétique Médicale, Nantes, France. [13]Institut du Thorax, INSERM, CNRS, Université de Nantes, Nantes, France. [14]Institute of Human Genetics, University of Bonn, Medical Faculty & University Hospital Bonn, Bonn, Germany. [15]Center for Rare Diseases Bonn, University Hospital Bonn, Bonn, Germany. [16]Institute of Medical Genetics and Applied Genomics, University of Tübingen, Tübingen, Germany. [17]Institute of Human Genetics, School of Medicine, Technical University Munich, Munich, Germany. [18]Institute of Neurogenomics, Helmholtz Zentrum München GmbH, German Research Center for Environmental Health, Neuherberg, Germany. [19]Norwegian Research Center for Computers and Law, Faculty of Law, University of Oslo, Oslo, Norway. [20]Department of General Pediatrics, Neonatology and Pediatric Cardiology, Medical Faculty, University Hospital, Heinrich-Heine-University, Düsseldorf, Germany. [21]Department of Human Genetics and George A. Jervis Clinic, NYS Institute for Basic Research in Developmental Disabilities, Staten Island, NY, USA. [22]Biology PhD Program, The Graduate Center, The City University of New York, New York, NY, USA. [23]Institute of Human Genetics, University of Lübeck, Lübeck, Germany. [24]Institute of Human Genetics, Heidelberg University, Heidelberg, Germany. [25]These authors contributed equally: Tzung-Chien Hsieh, Aviram Bar-Haim. ✉e-mail: pkrawitz@uni-bonn.de

GestaltMatcher

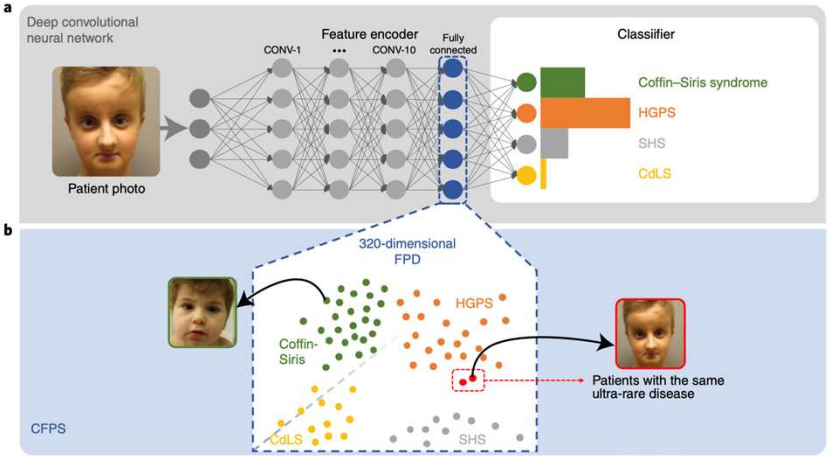


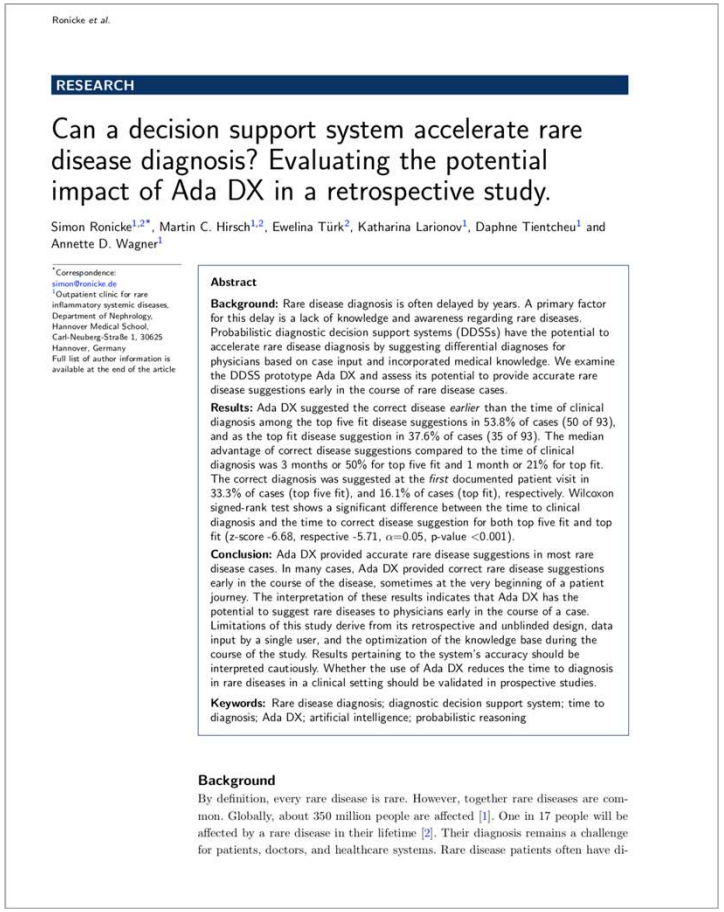
Fig. 2 | Concept of GestaltMatcher. a, Architecture of a DCNN consisting of an encoder and a classifier. Facial dysmorphic features of 299 frequent syndromes were used for supervised learning. The last fully connected layer in the feature encoder was taken as an FPD, which forms a point in the CFPS. **b**, In the CFPS, the distance between each patient's FPD can be considered as a measure of similarity of their facial phenotypic features. The distances can be further used for classifying ultra-rare disorders or matching patients with new phenotypes. Take the input image shown in the figure as an example: the patient's ultra-rare disease, which is caused by mutations in *LEMD2*, was not in the classifier, but was matched with another patient with the same ultra-rare disorder in the CFPS[4]. CONV-1, convolutional layer-1; CONV-10, convolutional layer-10; HGPS, Hutchinson–Gilford progeria syndrome; SHS, Schuurs-Hoeijmakers syndrome.

Übersicht SE-Diagnoseunterstützungssysteme

Tool name	Date	Data sources	Performances: Top 10 ranking	Related articles	URL
Phenomizer	2009	Phenotype concepts	NA	[63]	http://compbio.charite.de/phenomizer
BOQA	2012	Phenotype concepts	NA	[64]	http://compbio.charite.de/boqa/
Phenotips	2013	Phenotype concepts	NA	[65]	http://phenotips.org
FindZebra	2013	Phenotype concepts	63 %	[66]	http://www.findzebra.com/
PhenIX	2014	Phenotype concepts/genes	~ 99%	[67]	http://compbio.charite.de/PhenIX/
Phenolyzer	2015	Phenotype concepts/genes	~ 85%	[69]	http://phenolyzer.usc.edu
RDD	2016, 2017	Phenotype concepts	38 %	[2, 70]	http://diseasediscovery.udl.cat/
IEMbase	2018	Phenotype concepts	90 %	[54]	http://www.iembase.org/app
PubCaseFinder	2018	Phenotype concepts	57 %	[71]	https://pubcasefinder.dbcls.jp/
RDAD	2018	Phenotype concepts/genes	95 %	[73]	http://www.unimd.org/RDAD/
GDDP	2019	Phenotype concepts	~ 32%	[77]	https://gddp.research.cchmc.org/
Xrare	2019	Phenotype concepts/genes	~ 95%	[78]	https://web.stanford.edu/~xm24/Xrare/
CC-Cruiser	2017	Images	NA	[44]	https://www.cc-cruiser.com/
DeepGestalt	2019	Images	NA	[62]	https://www.face2gene.com/

KI basiert

orphanet Journal



Ronicke *et al.*

RESEARCH

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*Correspondence:
simon@ronicke.de
[1]Outpatient clinic for rare inflammatory systemic diseases, Department of Nephrology, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hannover, Germany
Full list of author information is available at the end of the article

Abstract

Background: Rare disease diagnosis is often delayed by years. A primary factor for this delay is a lack of knowledge and awareness regarding rare diseases. Probabilistic diagnostic decision support systems (DDSSs) have the potential to accelerate rare disease diagnosis by suggesting differential diagnoses for physicians based on case input and incorporated medical knowledge. We examine the DDSS prototype Ada DX and assess its potential to provide accurate rare disease suggestions early in the course of rare disease cases.

Results: Ada DX suggested the correct disease *earlier* than the time of clinical diagnosis among the top five fit disease suggestions in 53.8% of cases (50 of 93), and as the top fit disease suggestion in 37.6% of cases (35 of 93). The median advantage of correct disease suggestions compared to the time of clinical diagnosis was 3 months or 50% for top five fit and 1 month or 21% for top fit. The correct diagnosis was suggested at the *first* documented patient visit in 33.3% of cases (top five fit), and 16.1% of cases (top fit), respectively. Wilcoxon signed-rank test shows a significant difference between the time to clinical diagnosis and the time to correct disease suggestion for both top five fit and top fit (z-score -6.68, respective -5.71, α=0.05, p-value <0.001).

Conclusion: Ada DX provided accurate rare disease suggestions in most rare disease cases. In many cases, Ada DX provided correct rare disease suggestions early in the course of the disease, sometimes at the very beginning of a patient journey. The interpretation of these results indicates that Ada DX has the potential to suggest rare diseases to physicians early in the course of a case. Limitations of this study derive from its retrospective and unblinded design, data input by a single user, and the optimization of the knowledge base during the course of the study. Results pertaining to the system's accuracy should be interpreted cautiously. Whether the use of Ada DX reduces the time to diagnosis in rare diseases in a clinical setting should be validated in prospective studies.

Keywords: Rare disease diagnosis; diagnostic decision support system; time to diagnosis; Ada DX; artificial intelligence; probabilistic reasoning

Background

By definition, every rare disease is rare. However, together rare diseases are common. Globally, about 350 million people are affected [1]. One in 17 people will be affected by a rare disease in their lifetime [2]. Their diagnosis remains a challenge for patients, doctors, and healthcare systems. Rare disease patients often have di-

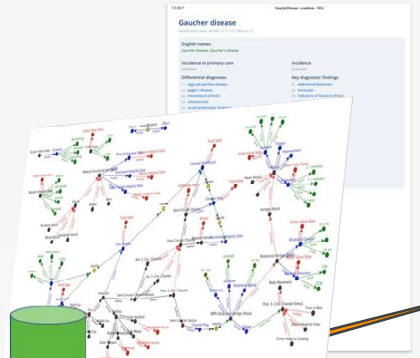
MHH Medizinische Hochschule Hannover

Retrospective study:
in 63.8% (51/94) of cases, correct rare disease suggestion given within Ada's top 5 conditions at a time *earlier* than the confirmed clinical diagnosis.

Der Ada-Ansatz einer Hybriden-KI

Ontologiebasierte Wahrscheinlichkeitsmodelle von Krankheitsbildern mit deep-learning Selbstoptimierung und probabilistischen Suchmechanismen kombinieren.

Machine Learning II
Labeled cases (SILVER Standard)



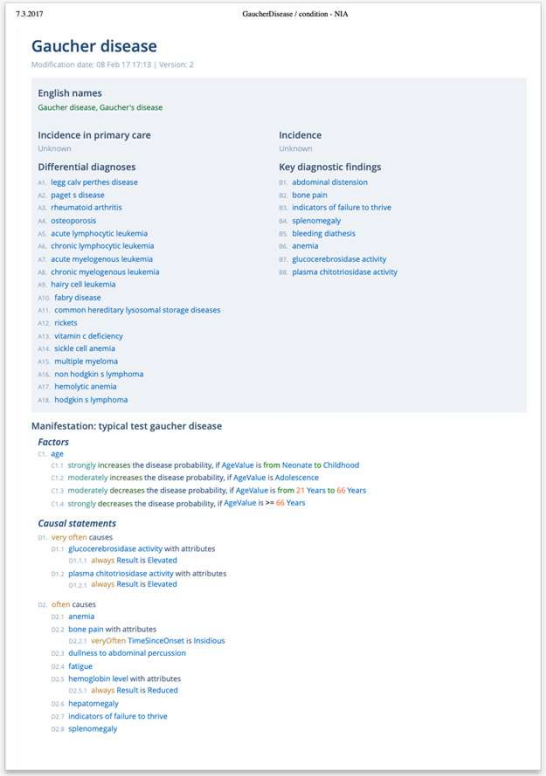
Modeling
MDL Diseases Profiles

Augmented QMR Bayesian Network

Machine Learning I
> 4.000 clinical cases, modelled in MDL (GOLD Standard)

Reasoning
> 4.000 clinical cases, modelled in MDL (GOLD Standard)

Wahrscheinlichkeitsmodell einer Erkrankung



7.3.2017 GaucherDisease / condition - NIA

Gaucher disease

Modification date: 08 Feb 17 17:13 | Version: 2

English names
Gaucher disease, Gaucher's disease

Incidence in primary care
Unknown

Incidence
Unknown

Differential diagnoses
A1. legg calv perthes disease
A2. paget s disease
A3. rheumatoid arthritis
A4. osteoporosis
A5. acute lymphocytic leukemia
A6. chronic lymphocytic leukemia
A7. acute myelogenous leukemia
A8. chronic myelogenous leukemia
A9. hairy cell leukemia
A10. fabry disease
A11. common hereditary lysosomal storage diseases
A12. rickets
A13. vitamin c deficiency
A14. sickle cell anemia
A15. multiple myeloma
A16. non hodgkin s lymphoma
A17. hemolytic anemia
A18. hodgkin s lymphoma

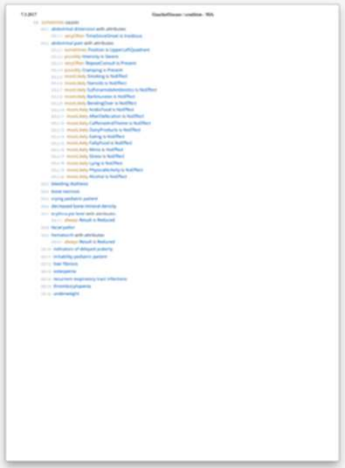
Key diagnostic findings
B1. abdominal distension
B2. bone pain
B3. indicators of failure to thrive
B4. splenomegaly
B5. bleeding diathesis
B6. anemia
B7. glucocerebrosidase activity
B8. plasma chitotriosidase activity

Manifestation: typical test gaucher disease

Factors
C1. age
C1.1 strongly increases the disease probability, if AgeValue is from Neonate to Childhood
C1.2 moderately increases the disease probability, if AgeValue is Adolescence
C1.3 moderately decreases the disease probability, if AgeValue is from 21 Years to 66 Years
C1.4 strongly decreases the disease probability, if AgeValue is >= 66 Years

Causal statements
D1. very often causes
D1.1 glucocerebrosidase activity with attributes
D1.1.1 always Result is Elevated
D1.2 plasma chitotriosidase activity with attributes
D1.2.1 always Result is Elevated

D2. often causes
D2.1 anemia
D2.2 bone pain with attributes
D2.2.1 veryOften TimeSinceOnset is Insidious
D2.3 dullness to abdominal percussion
D2.4 fatigue
D2.5 hemoglobin level with attributes
D2.5.1 always Result is Reduced
D2.6 hepatomegaly
D2.7 indicators of failure to thrive
D2.8 splenomegaly



Vorteil-1: Au

Differential diagnoses

A1. legg calv perthes disease
A2. paget s disease
A3. rheumatoid arthritis
A4. osteoporosis
A5. acute lymphocytic leukemia
A6. chronic lymphocytic leukemia
A7. acute myelogenous leukemia
A8. chronic myelogenous leukemia
A9. hairy cell leukemia
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Key diagnostic findings

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Manifestation: typical test gaucher disease

Factors

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- C1.2 moderately increases the disease probability, if AgeValue is Adolescence
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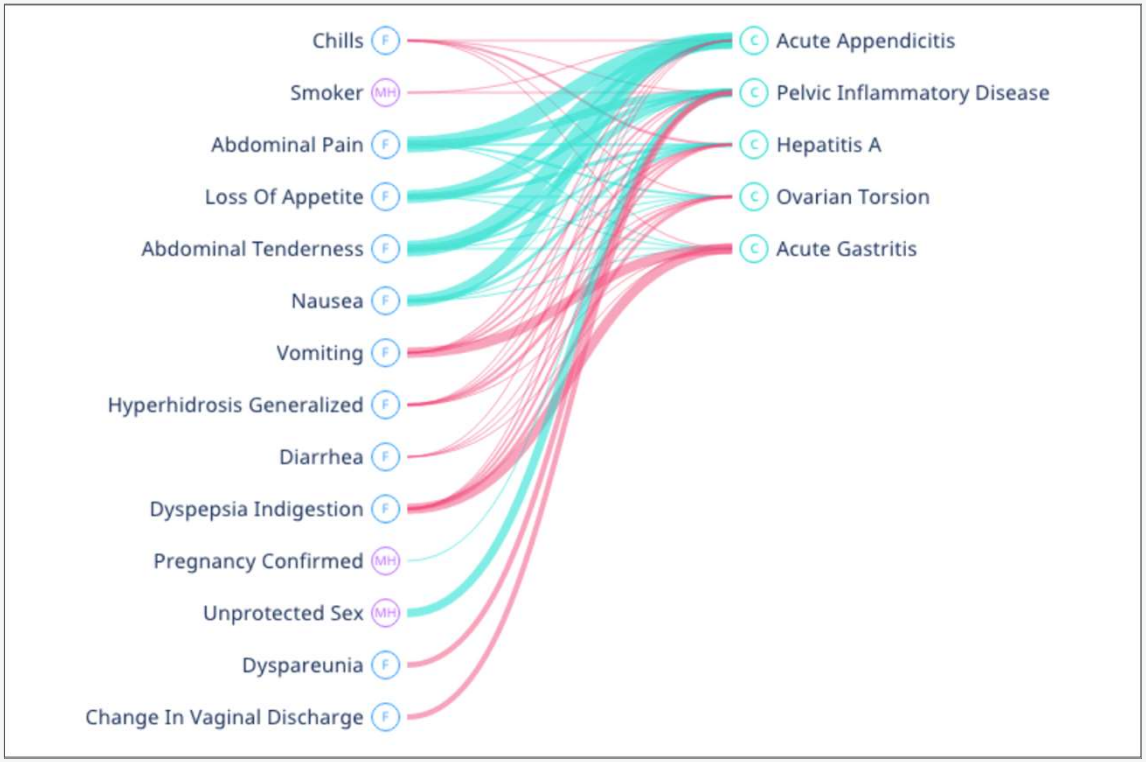
- C1.4 strongly decreases the disease probability, if AgeValue is >= 66 Years

Causal statements

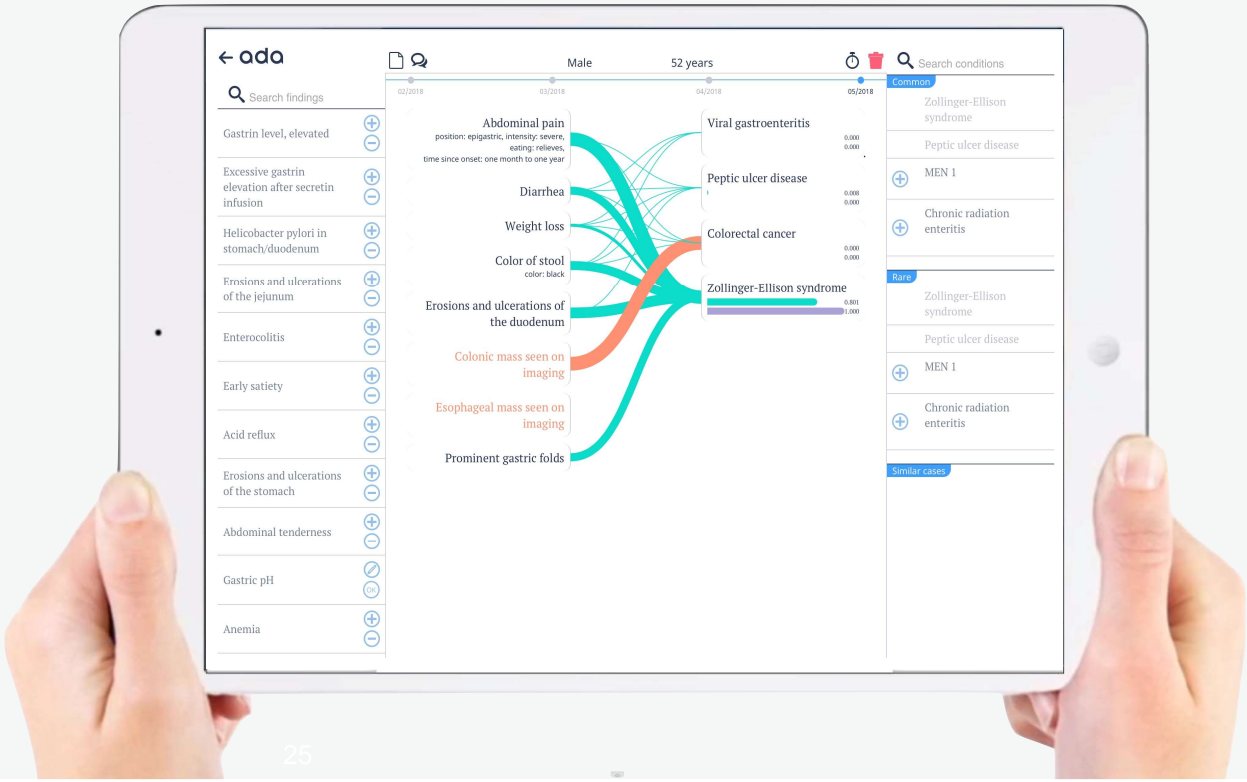
D1. very often causes
- D1.1 glucocerebrosidase activity with attributes
  - D1.1.1 always Result is Elevated
- D1.2 plasma chitotriosidase activity with attributes
  - D1.2.1 always Result is Elevated

D2. often causes
- D2.1 anemia
- D2.2 bone pain with attributes
  - D2.2.1 veryOften TimeSinceOnset is Insidious
- D2.3 dullness to abdominal percussion
- D2.4 fatigue

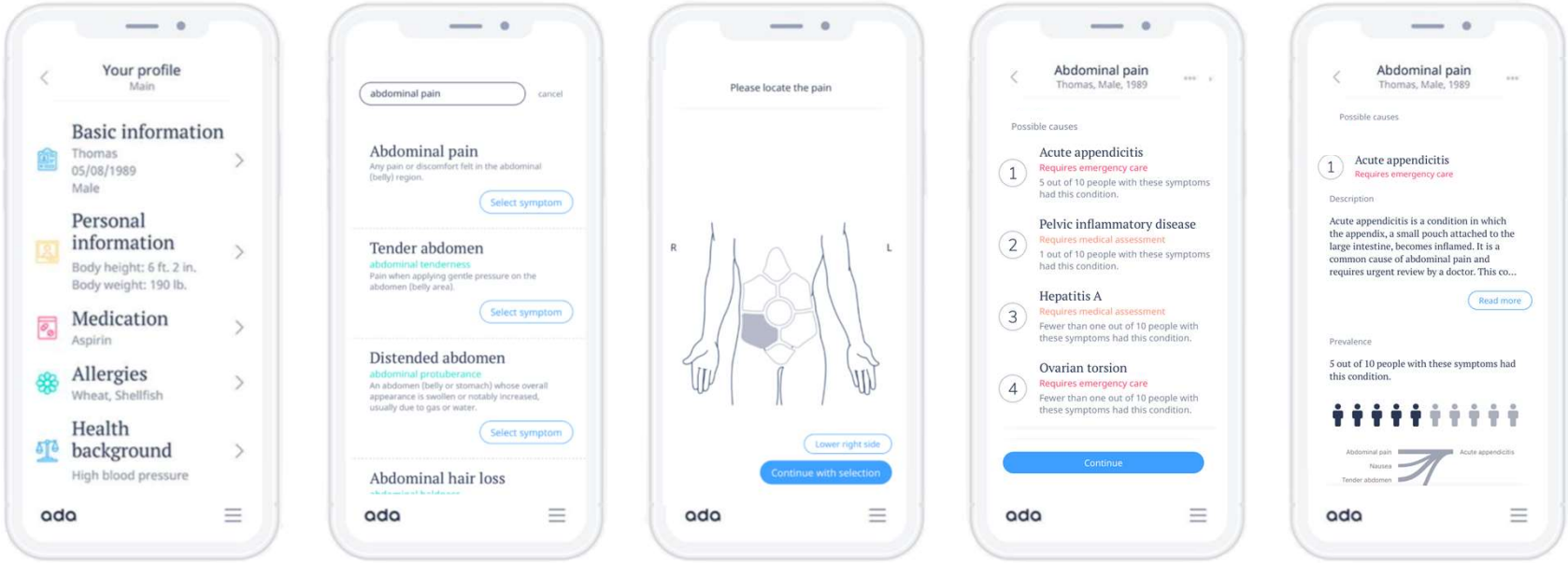
Vorteil-2: Transparenz der KI-Einschätzung



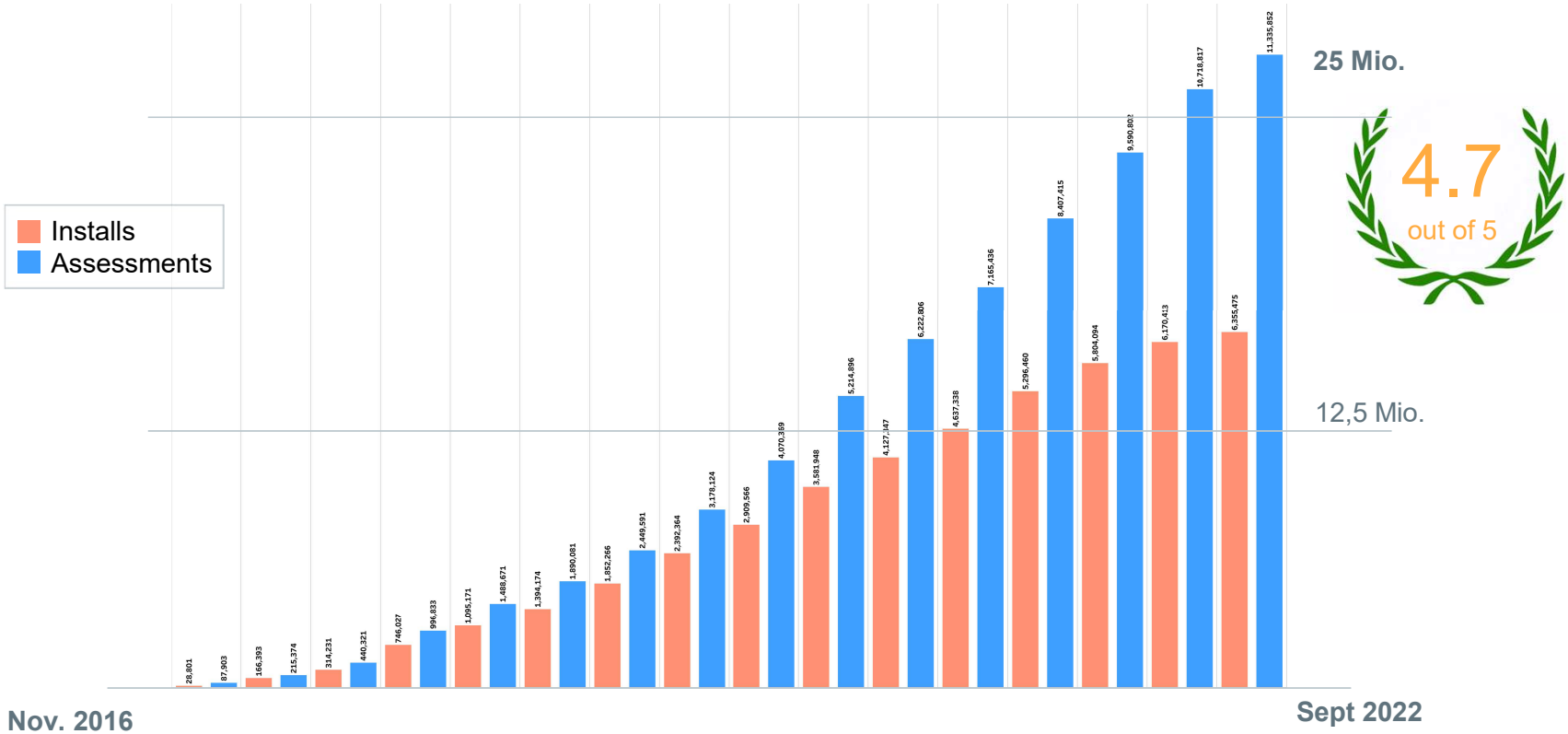
Hilfe auch für Bürgerinnen und Bürger – Der Ada Chatbot



Ada Chatbot – Diagnoseunterstützung auf dem Smartphone



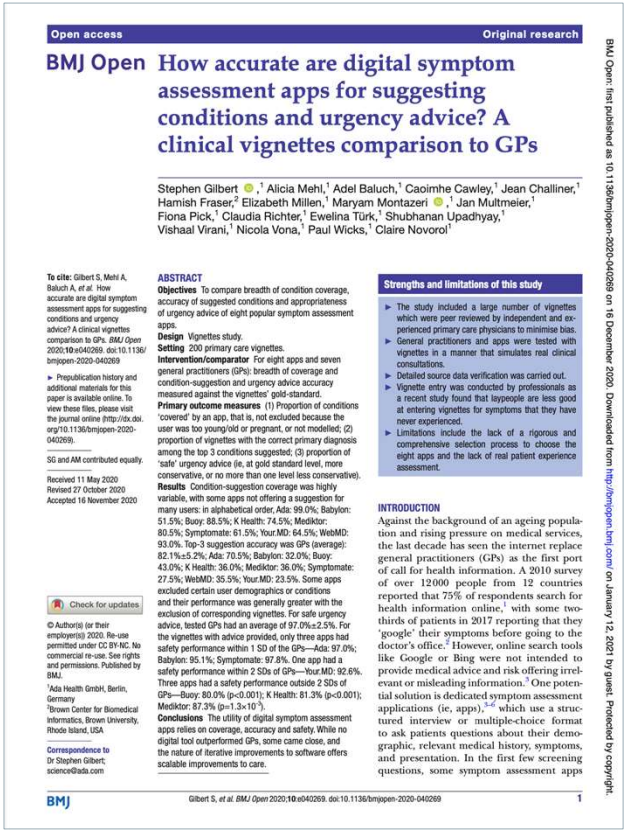
KI auf dem Smartphone hat eine niedrige Einstiegsschwelle



KI kann sich die Zeit nehmen, die der Arzt nicht mehr hat

Ada ist schon ziemlich akkurat

Nov. 2020; BMJ Open 2020;**10**:e040269. doi:10.1136/bmjopen-2020-040269



Open access Original research

BMJ Open

How accurate are digital symptom assessment apps for suggesting conditions and urgency advice? A clinical vignettes comparison to GPs

Stephen Gilbert ,[1] Alicia Mehl,[1] Adel Baluch,[1] Caoimhe Cawley,[1] Jean Challiner,[1] Hamish Fraser,[2] Elizabeth Millen,[1] Maryam Montazeri ,[1] Jan Multmeier,[1] Fiona Pick,[1] Claudia Richter,[1] Ewelina Türk,[1] Shubhanan Upadhyay,[1] Vishaal Virani,[1] Nicola Vona,[1] Paul Wicks,[1] Claire Novorol[1]

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SG and AM contributed equally.

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ABSTRACT

Objectives To compare breadth of condition coverage, accuracy of suggested conditions and appropriateness of urgency advice of eight popular symptom assessment apps.

Design Vignettes study.

Setting 200 primary care vignettes.

Intervention/comparator For eight apps and seven general practitioners (GPs): breadth of coverage and condition-suggestion and urgency advice accuracy measured against the vignettes' gold-standard.

Primary outcome measures (1) Proportion of conditions 'covered' by an app, that is, not excluded because the user was too young/old or pregnant, or not modelled; (2) proportion of vignettes with the correct primary diagnosis among the top 3 conditions suggested; (3) proportion of 'safe' urgency advice (ie, at gold standard level, more conservative, or no more than one level less conservative).

Results Condition-suggestion coverage was highly variable, with some apps not offering a suggestion for many users: in alphabetical order, Ada: 99.0%; Babylon: 51.5%; Buoy: 88.5%; K Health: 74.5%; Mediktor: 80.5%; Symptomate: 61.5%; Your.MD: 64.5%; WebMD: 93.0%. Top-3 suggestion accuracy was GPs (average): 82.1%±5.2%; Ada: 70.5%; Babylon: 32.0%; Buoy: 43.0%; K Health: 36.0%; Mediktor: 36.0%; Symptomate: 27.5%; WebMD: 35.5%; Your.MD: 23.5%. Some apps excluded certain user demographics or conditions and their performance was generally greater with the exclusion of corresponding vignettes. For safe urgency advice, tested GPs had an average of 97.0%±2.5%. For the vignettes with advice provided, only three apps had safety performance within 1 SD of the GPs—Ada: 97.0%; Babylon: 95.1%; Symptomate: 97.8%. One app had a safety performance within 2 SDs of GPs—Your.MD: 92.6%. Three apps had a safety performance outside 2 SDs of GPs—Buoy: 80.0% ($p<0.001$); K Health: 81.3% ($p<0.001$); Mediktor: 87.3% ($p=1.3\times10^{-3}$).

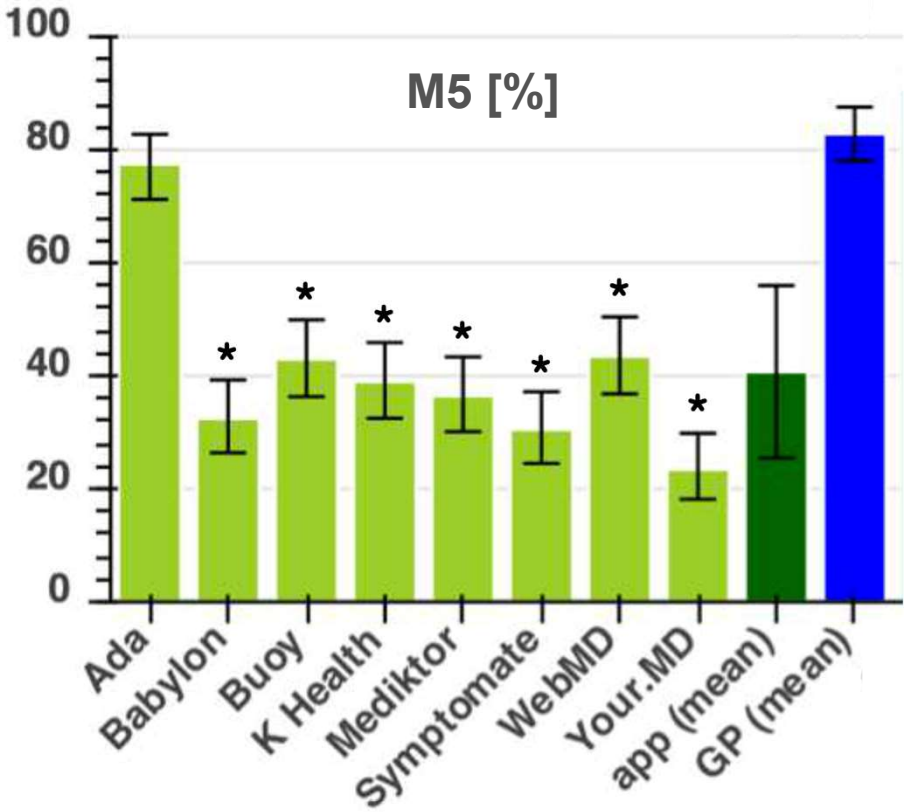
Conclusions The utility of digital symptom assessment apps relies on coverage, accuracy and safety. While no digital tool outperformed GPs, some came close, and the nature of iterative improvements to software offers scalable improvements to care.

Strengths and limitations of this study

- ► The study included a large number of vignettes which were peer reviewed by independent and experienced primary care physicians to minimise bias.
- ► General practitioners and apps were tested with vignettes in a manner that simulates real clinical consultations.
- ► Detailed source data verification was carried out.
- ► Vignette entry was conducted by professionals as a recent study found that laypeople are less good at entering vignettes for symptoms that they have never experienced.
- ► Limitations include the lack of a rigorous and comprehensive selection process to choose the eight apps and the lack of real patient experience assessment.

INTRODUCTION

Against the background of an ageing population and rising pressure on medical services, the last decade has seen the internet replace general practitioners (GPs) as the first port of call for health information. A 2010 survey of over 12 000 people from 12 countries reported that 75% of respondents search for health information online,[1] with some two-thirds of patients in 2017 reporting that they 'google' their symptoms before going to the doctor's office.[2] However, online search tools like Google or Bing were not intended to provide medical advice and risk offering irrelevant or misleading information.[3] One potential solution is dedicated symptom assessment applications (ie, apps),[3–6] which use a structured interview or multiple-choice format to ask patients questions about their demographic, relevant medical history, symptoms, and presentation. In the first few screening questions, some symptom assessment apps



KI kann sogar komplexe Erkrankungen erkennen

☆☆☆☆☆

‘Hi my name is Alyssa & for years I was having this sharp lower abdominal pain. I saw so many doctors & had so many tests & surgeries to try & figure out what was wrong, it started to take over my life. I couldn’t work, I couldn’t go to school & it was putting a lot of stress on my home life. Eventually I just gave up & tried to learn to live with this constant pain, then one day while on facebook I saw an ad for Ada & decided to give it try, I went through the whole process & finally she gave me the result of functional abdominal pain or **CAPS*** & while I read the sypmtoms & treatments I started to cry because finally, finally something was able to tell me what was wrong! I know she isn’t a real doctor but I went to a real doctor with this info & now I’m getting help that I’ve needing for years & I just want to thank you so much! ♡

***Cryopyrin-Associated Autoinflammatory Syndrome**

Very good app!!! They were spot on... they said I might have Sjogren's Syndrome which I had already gotten a diagnosis for... 22.2.2017

Quite a well designed app. Use it whenever I'm presenting signs and symptoms outside of the general sickness spectrum. Even helped me identify quite a serious thing (Crohn's Disease), which got me into the hospital and getting the treatment I will need. 19.3.2017

I tested this app to see if it could diagnose me with SLE (Lupus). I put in all my symptoms (around 20) that I deal with on a daily basis dealing with Lupus and sure enough the first option was SLE. It blew my mind! Always consult your doctor and seek medical attention when applicable, this is just an app. 1.4.2017

I have been diagnosed with a few things. before jumping into this app i decided to give it all of my symptoms and see what it thought i had. the top three answers were all three that i had. i was completely shocked bc the third one was a diagnosis that took my doctors years to find and was very rare! (multiple autoimmune diseases, fibromyalgia, etc) without a doubt completely thrilled. 3.5.2017

Seriously I have a fairly rare condition and I put in my symptoms and such it actually came up with my condition. this is truly amazing I defiantly will refer people to use it and I will absolutely continue to use it. ☺ 26.5.2017

This app is right on the money. It diagnosed a pretty rare medical condition my sister has. Bravo. 11.01.2018

Just out of curiosity i put in my symptoms of a rather rare disease that i have and it got it right based on my symptoms. I had several doctors who didn't even get it figured out for years. 4.3.2018

Seltene und sehr seltene, direkte und indirekte Autoimmunerkrankungen

		out of 4 Mio		
Rare disease in assessment result list		**total**	**on position #1**	**#2 or #3**
Antiphospholipid syndrome	rare	1.161	268	893
IgA nephropathy	rare	666	176	490
Rapidly Progressive Glomerulonephritis	rare	529	102	427
Antisynthetase syndrome*	very rare	720	115	605
Cryopyrin-associated periodic syndrome (CAPS)	very rare	175	18	157
Microscopic polyangiitis*	very rare	455	49	406

***Mittleres Assessment-Ergebnis anbei**

Seltene und sehr seltene, direkte und indirekte Autoimmunerkrankungen

		out of 4 Mio		
Rare disease in assessment result list		**total**	**on position #1**	**#2 or #3**
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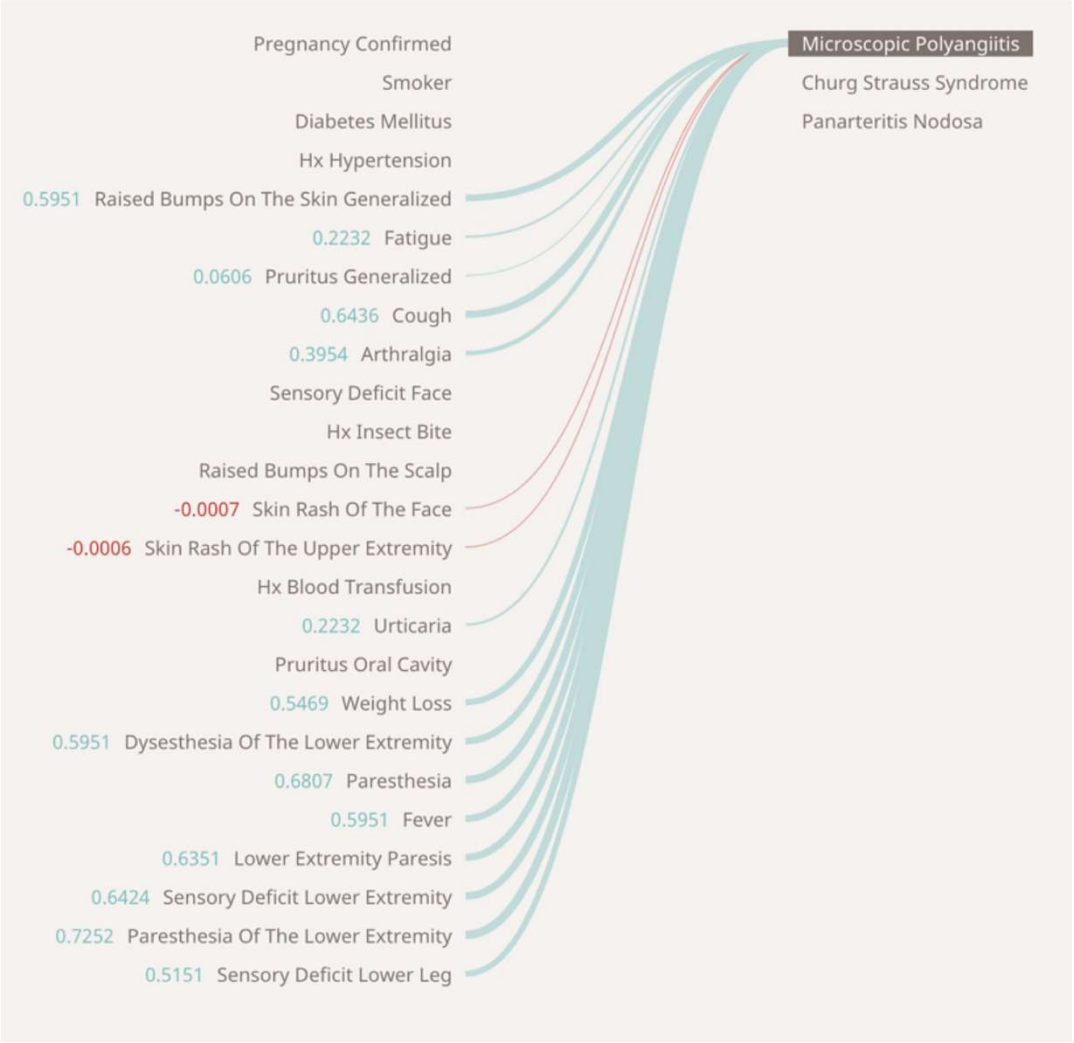
Cryopyrin-associated periodic syndrome (CAPS)	very rare	175	18	
Microscopic polyangiitis*	v			

„CAPS is found in about one in 360,000 to 1,000,000 people." => 4-11 in 4 Mio.

*Mittleres Assessment-Ergebnis anbei

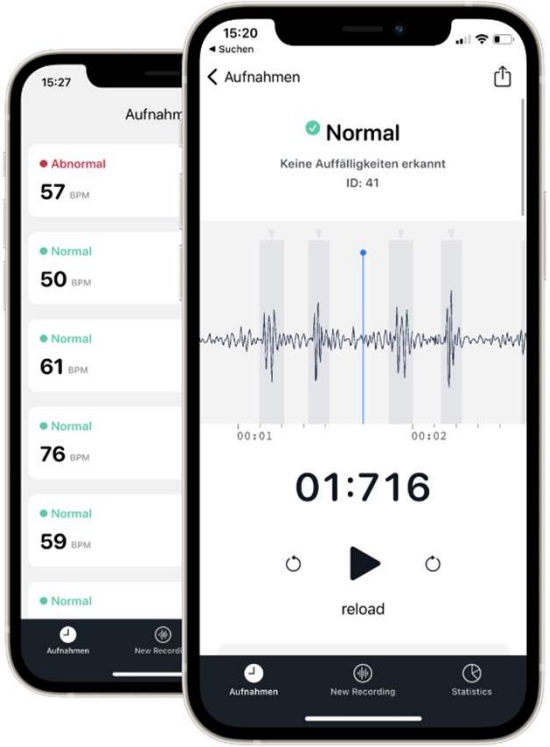

Pregnancy Confirmed
Smoker
Diabetes Mellitus
Hx Hypertension
0.5951 Raised Bumps On The Skin Generalized
0.2232 Fatigue
0.0606 Pruritus Generalized
0.6436 Cough
0.3954 Arthralgia
Sensory Deficit Face
Hx Insect Bite
Raised Bumps On The Scalp
-0.0007 Skin Rash Of The Face
-0.0006 Skin Rash Of The Upper Extremity
Hx Blood Transfusion
0.2232 Urticaria
Pruritus Oral Cavity
0.5469 Weight Loss
0.5951 Dysesthesia Of The Lower Extremity
0.6807 Paresthesia
0.5951 Fever
0.6351 Lower Extremity Paresis
0.6424 Sensory Deficit Lower Extremity
0.7252 Paresthesia Of The Lower Extremity
0.5151 Sensory Deficit Lower Leg
Microscopic Polyangiitis
Churg Strauss Syndrome
Panarteritis Nodosa

KI hat keinen Zeitdruck

Fazit KI-basierte Symptom Checker

KI-gestützte Symptom-Checker können schon heute **SEs ins Blickfeld Erkrankter (und Heilender) rücken**.

Smartphone-Mikrophon mit KI auskultiert Herz und Lunge



PhysioNet

Search

Database Open Access

The CirCor DigiScope Phonocardiogram Dataset

Jorge Oliveira, Francesco Renna, Paulo Costa, Marcelo Nogueira, Ana Cristina Oliveira, Andoni Elola, Carlos Ferreira, Alipio Jorge, Ali Bahrami Rad, Matthew Reyna, Reza Sameni, Gari Clifford, Miguel Coimbra

Published: Jan. 28, 2022. Version: 1.0.1

96 %

Gesamtgenauigkeit

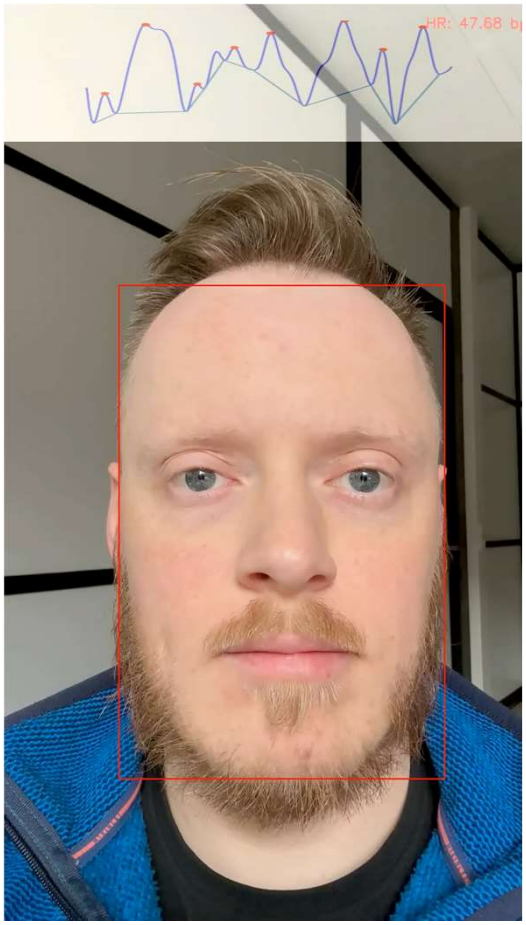
95 %

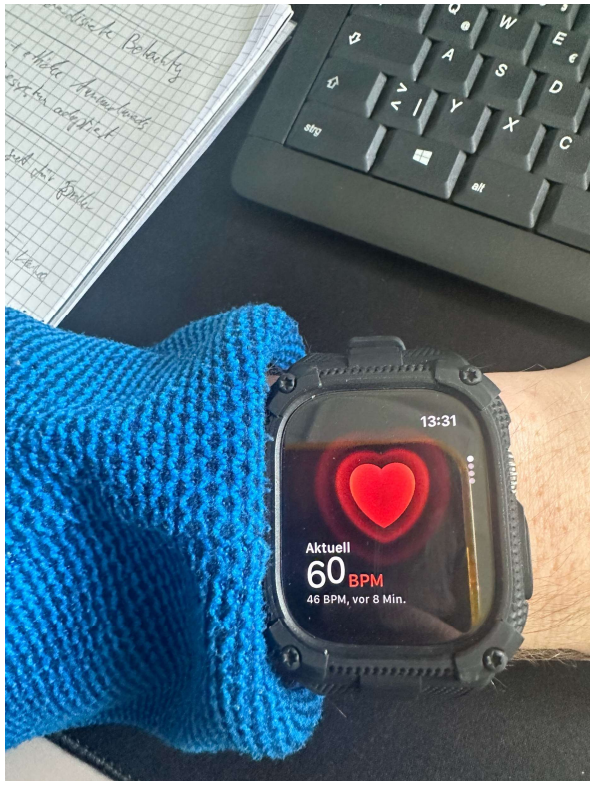
Sensitivität über alle Klassen

92 %

Spezifität über alle Klassen

Smartphone-Kamera mit KI misst kontaktlos Blut- und Atemfrequenz





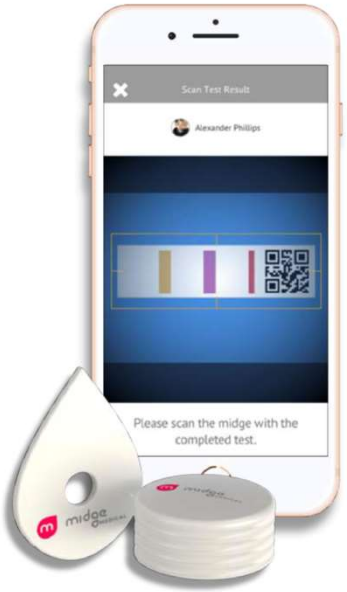

67 BPM
10:09
2 sec
It helps to rest your arms on a table or your legs.


Results
Blood Oxygen
10:09
95%
Done
You can view Blood Oxygen measurements in the Health app on iPhone


Current
16:05
Heart Rate
68 BPM
72 BPM, 3m ago


32
AQI
UVI
3.6
68 BPM • 2 MINUTES AGO
4 MINUTES
52
68°

Messung von Blutwerten zuhause



1 Peel & Disinfect

Midge holds a cleaning pad cover to disinfect skin surface.

2 Test

Patient applies the device:

- A lancet penetrates the skin and extracts up to 15 µl of blood;
- Blood sample flows into a microfluidic reactor and through the Lateral Flow Assay.

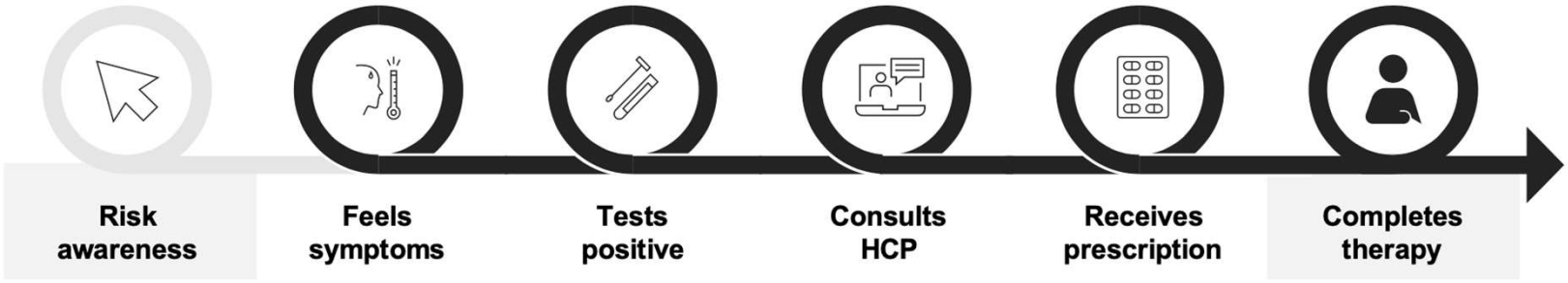
3 Results in 5 min

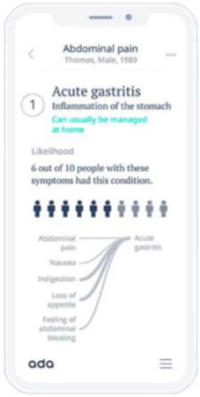
The results are processed and evaluated using a smart phone.

Fazit

In Kombination mit Sensoren, einfachen Blutwerten und Zeitreihen werden Symptom-Checker eine immer wichtigere Vordiagnostik liefern.

Patient targeting





KI-Symptom Checker eigenen sich schon heute zum Patient-Targeting.

Und was ist mit Large Language Models (LLM) wie GPT4 oder Med-Palm 2?

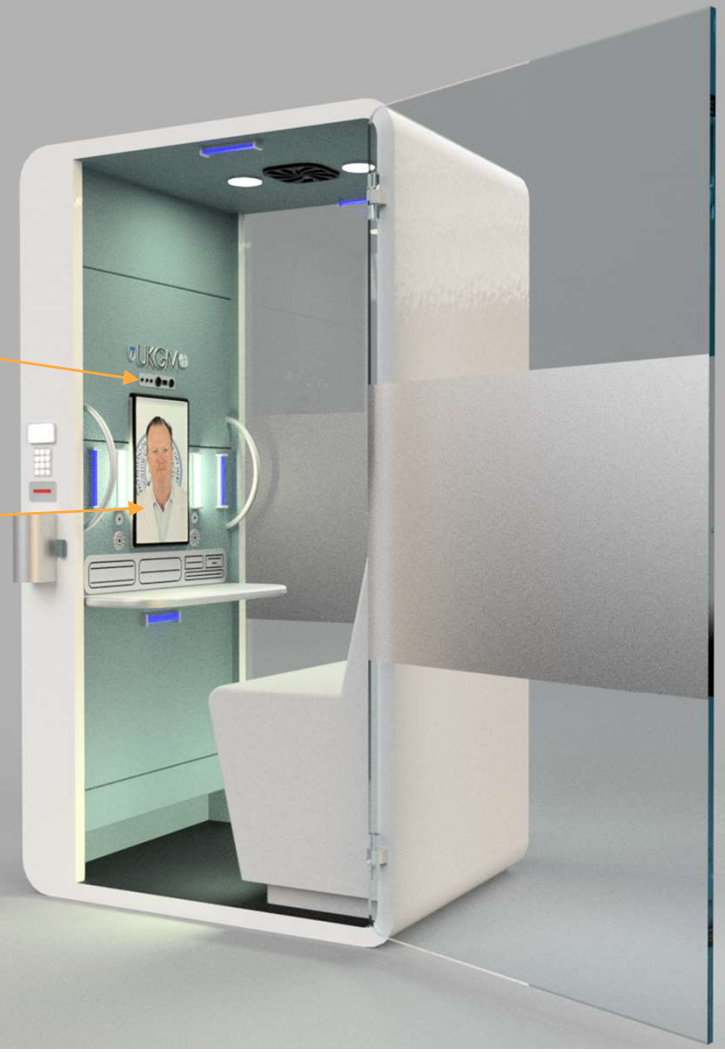

Philipps
Universität
Marburg

LLMs werden natürliche Sprach-Interfaces ermöglichen

Vitalwerte
kontaktlos messen

Informationen
kontaktlos erheben
(Verwaltungsdaten,
Anamneseinfos, Sonstiges)

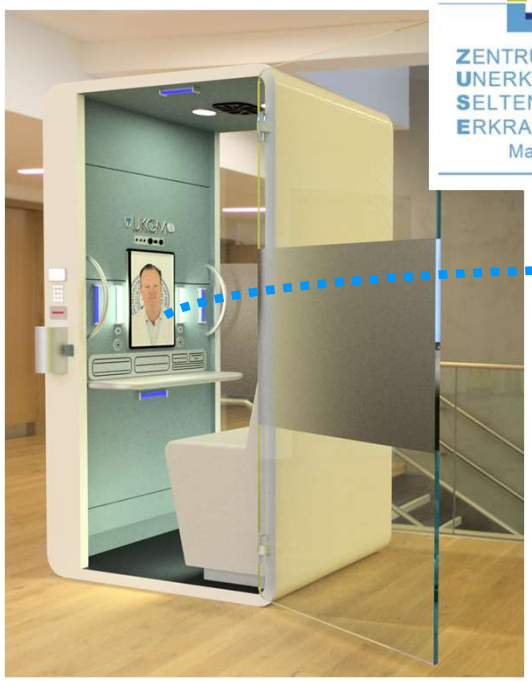
Ersteinschätzung vornehmen



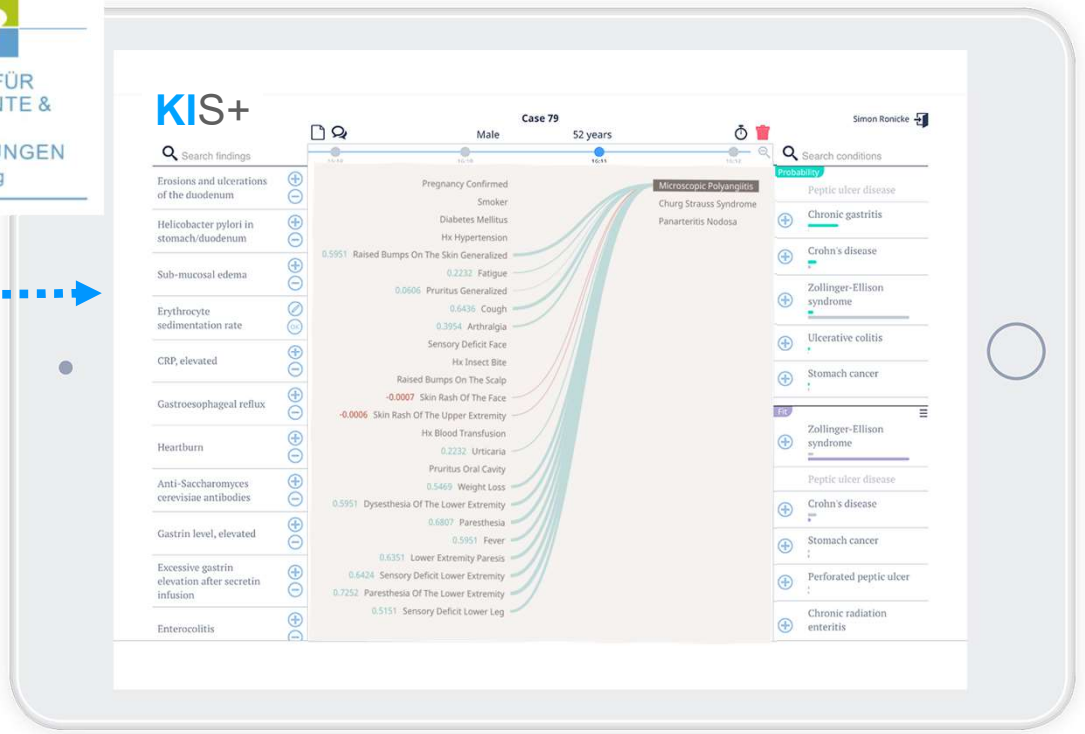

Notaufnahme
Eingang
Kinderärztlicher
Bereitschaftsdienst
ÄBD
Zentrale
Notaufnahme
Notaufnahme
Kinder-Notaufnahme
FAT
1


UKGM

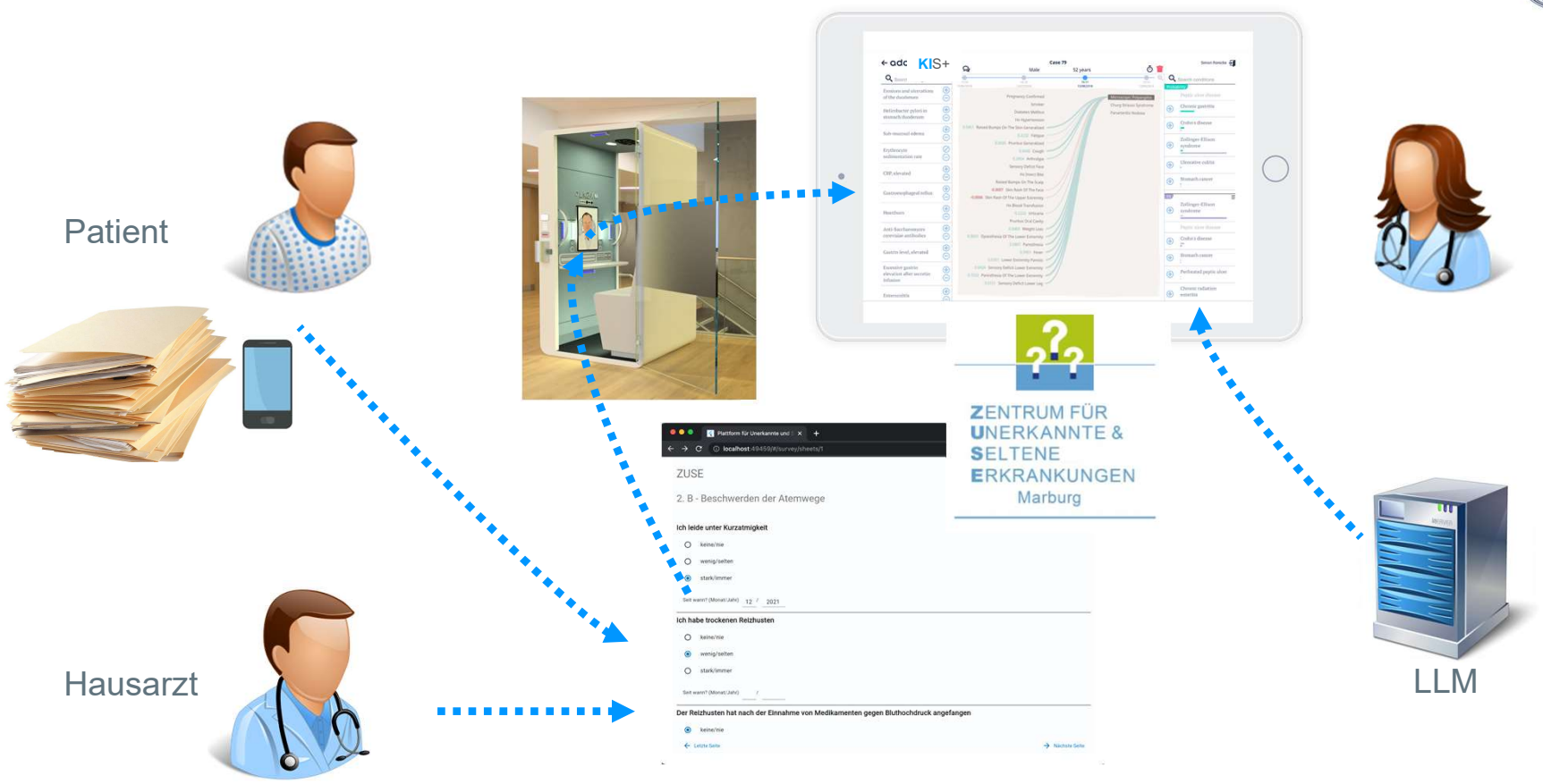
KI gestützte Anamnese und Falleinschätzung im ZusE



ZENTRUM FÜR
UNERKANNTE &
SELTENE
ERKRANKUNGEN
Marburg



KI gestützte Anamnese und Falleinschätzung im ZusE

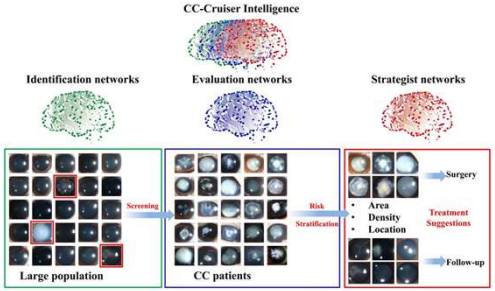


FAZIT | KI in der SE-Diagnostik

Ich sehe vor allem drei Möglichkeiten, Nutzen zu stiften:

Pre-diagnostic Hints & Patient Targeting

Erkennen von SEs in spezifischen Kontexten



Diagnostic Decision Support in SE-Zentren

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