VIII Simpósio International Câncer de PULMÃO

Inteligência Artificial e Oncologia: IBM Watson e os resultados na América Latina

Mehool Patel MD, MBA, FACP

March 13, 2020

IBM

São Paulo, Brazil

LEGAL DISCLAIMER

The information contained in this publication is provided for informational purposes only. While efforts were made to verify the completeness and accuracy of the information contained in this publication, it is provided AS IS without warranty of any kind, express or implied. In addition, this information is based on IBM's current product plans and strategy, which are subject to change by IBM without notice. IBM shall not be responsible for any damages arising out of the use of, or otherwise related to, this publication or any other materials. Nothing contained in this publication is intended to, nor shall have the effect of, creating any warranties or representations from IBM or its suppliers or licensors, or altering the terms and conditions of the applicable license agreement governing the use of IBM software.

References in this presentation to IBM products, programs, or services do not imply that they will be available in all countries in which IBM operates. Product release dates and/or capabilities referenced in this presentation may change at any time at IBM's sole discretion based on market opportunities or other factors, and are not intended to be a commitment to future product or feature availability in any way. Nothing contained in these materials is intended to, nor shall have the effect of, stating or implying that any activities undertaken by you will result in any specific sales, revenue growth or other results.

Performance is based on measurements and projections using standard IBM benchmarks in a controlled environment. The actual throughput or performance that any user will experience will vary depending upon many factors, including considerations such as the amount of multiprogramming in the user's job stream, the I/O configuration, the storage configuration, and the workload processed. Therefore, no assurance can be given that an individual user will achieve results similar to those stated here.

All customer examples described are presented as illustrations of how those customers have used IBM products and the results they may have achieved. Actual environmental costs and performance characteristics may vary by customer.

AGENDA

- Overview of Artificial Intelligence (AI) in Medicine/Oncology
  - *Machine Learning & Deep Learning*
  - *Advantages of AI in Medicine/Oncology*
  - *Challenges of AI use in Medicine/Oncology*

- AI Solutions answering Oncology challenges

- Research Findings of AI use

- Future of AI in Medicine/Oncology

Tabulating Systems Era

1900 – 1940s

Programmable Systems Era

1950s – Present

Artificial Intelligence Era

2011 –

IBM Leadership in **AI and Health**

1962
IBM developed and implemented an early EMR with Akron Children's Hospital

1981
Richard Feynman urges creating quantum computer at MIT/IBM conference

1997
IBM's Deep Blue beat the world chess champion Garry Kasparov in a six-game match

2005
The next **GRAND CHALLENGE**

2008
Cognitive test case results in creation of Watson.

2010
IBM enables an "evidence-based healthcare ecosystem"

2011
JEOPARDY!
CÚRAM SOFTWARE

2012
Cleveland Clinic
Memorial Sloan Kettering Cancer Center

2014
MAYO CLINIC

2015
explorys
PHYTEL
MERGE Healthcare

2016
The Weather Company
An IBM Business
TRUVEN HEALTH ANALYTICS

2017
MIT & IBM $240M collaboration

Today
7,000 employees
13,000+ clients & partners

QUANTITY AND TYPES OF INFORMATION RELEVANT IS EXPLODING

Data Explosion

Medical data is expected to **double every 73 days** by 2020[1]

300M books
How much health-related data each person will generate in a lifetime[2]

Physician shortage and burnout rising

12.9 Million
Expected global shortage of healthcare workers by 2035[3]

½ of the workday
Primary care physicians spend 6 hours interacting with the EHR during and after clinic hours[4]

Medical images growing and taking valuable time

60 Billion
Medical images generated in the US in 2015[5]

64% of Time
radiologists spend on non interpretive tasks[4]

Managing vulnerable populations is essential

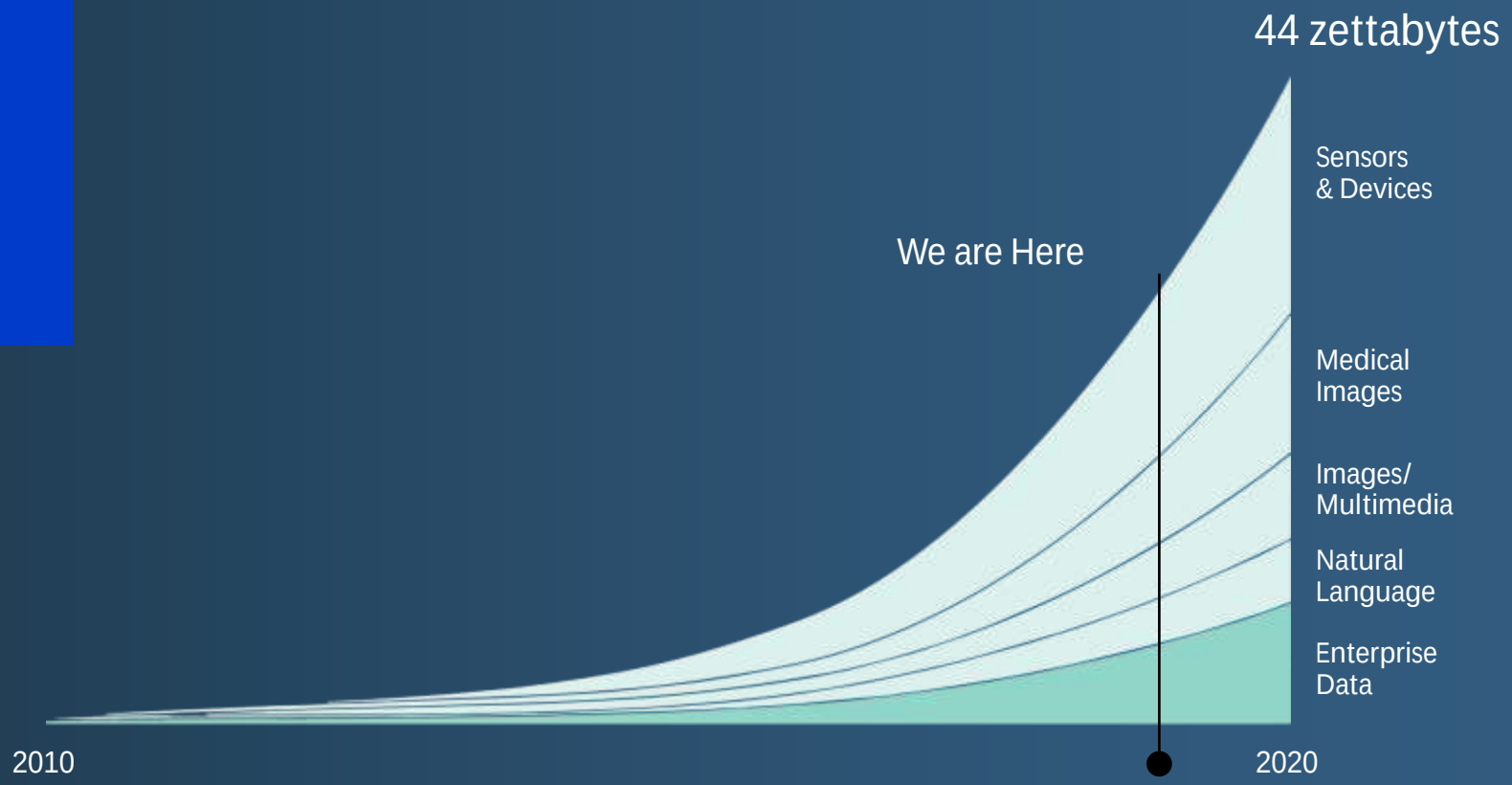
40% Growth
Expected from 2014-2030 for the US population age 65 and over[6]

$47 Trillion
Estimated global economic impact of chronic disease by 2030[7]

Sources:
1. IBM
2. IBM
3. WHO
4. Tethered to the EHR: Primary Care Physician Work-load Assessment using EHR Event Log Data and Time-Motion Observations
5. Journal of American College of Radiology
6. MedPac
7. WHO

Each factor that impacts health is increasing in volume and complexity

Each person will generate 300M books of health-related data in a lifetime[1]



1. IBM Study

IDC, Digital Universe Study, 2014

Scientific Evidence Says We Are Falling Short

Medical Errors
3rd leading cause of death[1]

Physician EHR and Desk Work
2 out of 3 minutes[2]

Recommended Care
55% of adults[3]

Waste
$760 - $935 billion [4]

Difficulty paying for healthcare within past 3 months
22%[5]

Deaths Due to Racial Disparity
83,000[6]

[1]Makery MA. *BMJ.* 2016; 353:i2139.
[2]Sinsky C et al. *Ann Intern Med.* 2016:165(11):753-760.
[3]McGlynn EA et al. *N Eng J Med.* 2003; 348(26):2635-45.

[4]Shrang WH et al. JAMA 2019.
[5]IBM Pulse Survey 2019.
[6]Satcher D et al. *Health Affairs.* 2005;24(2):459-464.

COGNITIVE SYSTEM ATTRIBUTES

Understanding

Measured by the ability to interpret and derive actionable information and knowledge

Reasoning

Ability to link together data and knowledge elements, draw connections from information resources and solve problems using the information

Learning

Extent the system improves over time with exposure to new data

Interacting

Recognition of and leveraging available content to fit naturally in workflow and provide interactions that work best for users

Humans + AI = augmented intelligence

Humans excel at:


common sense


imagination


morals


abstraction

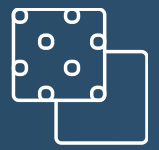

compassion


generalization

AI excels at:


natural language


machine learning


pattern identification


reducing bias


locating knowledge


repetition and consistency

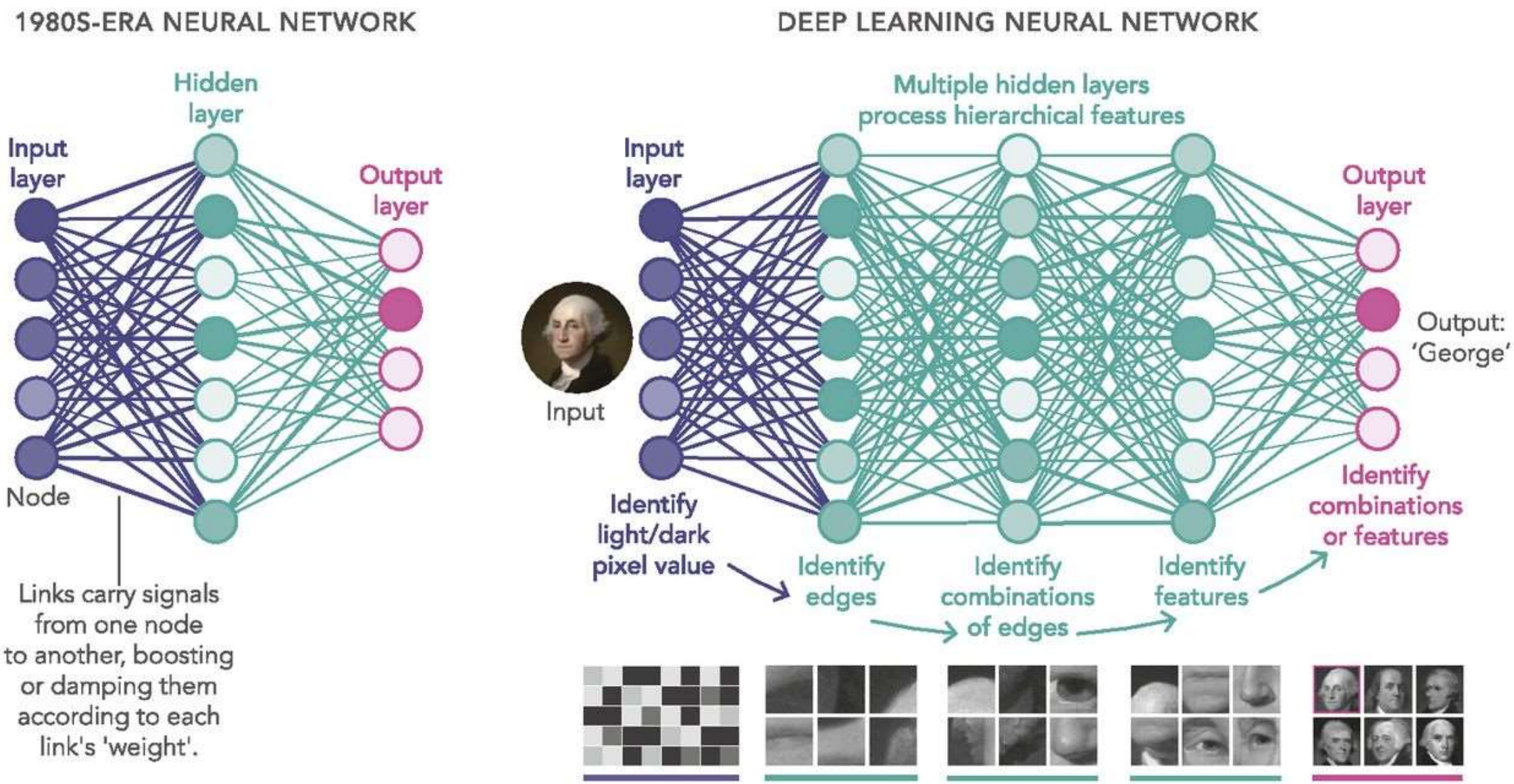
AI BACKGROUND

- Founded in 1950’s
  - Ability for machines to execute human behavioral tasks
  - Iterative process that ascertains data relationships allowing for speedier performance over time
- Prevalent use in transportation, communications, and social platforms
- 1980’s: Machine Learning (ML)
- 2000’s+: Deep Learning (DL)

AI Term Definitions

Algorithm	Unambiguous specification of how to solve a class of problems.
Artificial intelligence	The theory and development of computer systems able to perform tasks that normally require human intelligence.
Backpropagation	Algorithm for supervised learning of artificial neural networks using gradient descent.
Convolutional neural networks	A class of deep, feed-forward artificial neural networks typically applied to analyzing visual imagery.
Deep learning	Broader family of machine learning methods based on learning data representations, as opposed to task-specific algorithms.
Data science	Study of where information comes from, what it represents and how it can be turned into a valuable resource in support of business and IT strategies. Common tasks of a data scientist include data cleansing, wrangling, leveraging statistical and mathematical algorithms to build operationalized models.
Expert systems	Computer system that emulates the decision-making ability of a human expert.
Feature engineering	Process of using domain knowledge of the data to create features that make machine learning algorithms work.
Graph analysis	Network of interconnected objects and their relationships.
Knowledge representation	Field of artificial intelligence (AI) dedicated to representing information about the world in a form that a computer system can utilize to solve complex tasks.
Linear regression	Modeling the relationship between two variables by fitting a linear equation to observed data.
Machine learning	An application of artificial intelligence (AI) that provides systems the ability to automatically learn and improve from experience without being explicitly programmed.
Model	A structure and corresponding interpretation that summarizes or partially summarizes a set of data, for description or prediction.
Natural language processing	The ability of a computer program to understand human language as it is spoken.
Overfitting	Refers to a model that models the training data too well and negatively impacts the performance of the model on new data.
Perceptron	A probabilistic model for information storage and organization in the brain.
Quantum machine learning	Machine learning leveraging quantum computing.
Regression	A set of statistical processes for estimating the relationships among variables.
Scoring	A form of Newton's method used in statistics to solve maximum likelihood equations numerically.
Underfitting	Occurs when a statistical model cannot adequately capture the underlying structure of the data.

Steven Astorino Vice President of Development, IBM Analytics.
https://dzone.com/articles/navigating-the-ai-and-cognitive-maze12



Oleksii Kharkovyna. **The A-Z of AI and Machine Learning: Comprehensive Glossary. https://towardsdatascience.com/the-a-z-of-ai-and-machine-learning-comprehensive-glossary-fb6f0dd8230**

Natural Language Processing

Finds and breaks down language into concepts, while understanding the relationships between them.

Lung Cancer

A 52 year old man born in Cleveland, developed hip pain. He is a 28 pack year smoker who quit 7 years ago. PMH negative. A chest CT revealed bilateral lung and multiple lesions in ribs. A pelvis MRI revealed multiple bony lesions consistent with metastases. His exam in normal. KPS 70%. A core needle biopsy of a lung lesion revealed adenocarcinoma. Additional cores have been submitted for mutational testing. His pain is poorly controlled with ATC Percocet. You change to a fentanyl patch but nausea and dizziness result and pain is still not controlled.

DIFFERENT KINDS OF DATA

Table 1: Salt Concentration and Light Transmittance					
Salt Concentration (%)	Transmittance (%T)				
	Trial #1	Trial #2	Trial #3	Trial #4	Trial #5
0	77.23	74.50	64.88	75.27	54.66
3	85.23	92.82	78.91	60.71	57.96
6	88.39	100.05	73.66	66.51	64.54
9	80.71	100.05	68.29	64.91	52.96
12	82.66	117.18	71.01	56.91	46.95
15	72.55	115.40	65.72	66.03	55.38

CHAPTER 2

Synthesis of the Literature

Facility Design

Current roundabout and CTL design criteria are presented in documents such as the AASHTO Policy on Geometric Design of Highways and Streets (AASHTO 2004); the *Intersection Channelization Design Guide* (Neuman 1985); the FHWA's *Manual on Uniform Traffic Control Devices* (2009); the AASHTO Guide for Planning, Design, and Operation of Pedestrian Facilities (2004); the FHWA's *Pedestrian Facilities Users Guide* (Zegeer et al. 2002); the FHWA's *Signalized Intersections: Informational Guide* (2004); the FHWA's *Roundabouts: An Informational Guide* (2000); an updated version of the FHWA roundabout guide available as *NCHRP Report 672: Roundabouts: An Informational Guide*, Second Edition (Rodegerdts et al. 2010); and the research results and synthesis to come from NCHRP Project 3-72, "Lane Widths, Channelized Right Turns, and Right-Turn Deceleration Lanes in Urban and Suburban Areas" (Midwest Research Institute 2011), which will be available in 2011. These documents include provisions for determining the placement of crosswalks, signage, and other aspects of roundabout and CTL design. A key issue is that existing designs are intended to accommodate the majority of pedestrians, who have normal vision. Current designs were not developed specifically to support unassisted crossing of streets by pedestrians who are blind.

Geometric Design for Pedestrian Crossings at Roundabouts

Current practice in the United States (FHWA 2000) locates the pedestrian crosswalk approximately one car length back from the circulating lane, although this varies. The crosswalk is generally perpendicular to the travel lane and passes through an approach splitter island. This island is designed to separate opposing traffic streams, reduce wrong-way movements around the central island, and provide refuge to pedestrians before they cross the second leg of the approach. The presence of the splitter island serves to divide the pedestrian crossing task into two separate segments. Under low traffic volumes, a pedestrian may be able to cross in a single maneuver. Under higher traffic volumes, pedestrians may wait on the splitter island until a crossable opportunity is detected on the second leg of the crossing. In either case, the pedestrian crossing task is typically focused in one direction at a time. Figure 1 shows a schematic drawing of typical roundabout crosswalk geometry.

The actual alignment of the crosswalk can vary. Often there is no deviation in the orientation of the crosswalk, and the crosswalk proceeds straight from curb to curb. However, some crosswalks are designed with a bend at the splitter island, which may pose wayfinding challenges for blind travelers in the absence of additional tactile cues. There are a few crosswalks that use an offset or zigzag design that deflects pedestrian traffic onto an elongated splitter island before the second part of the crossing. The intent of this treatment is to reinforce two-stage crossing behavior and, to some extent, increase the distance between the crosswalk and the circulating lane.

For all crosswalks, pedestrian ramps at either curb are supposed to be perpendicular to the curb/gutter line. Due to the radius of the curve, they may not be in line with the direction of travel on the crosswalk and therefore may cause alignment difficulties for blind pedestrians. Curb ramps built after 2001 are supposed to have truncated dome detectable warning surfaces at the bottom of the ramp to alert the pedestrian who is blind that he or she has arrived at a street–sidewalk boundary. In the United States, few pedestrian crosswalks at roundabouts are signalized (either for pedestrian or traffic control purposes).

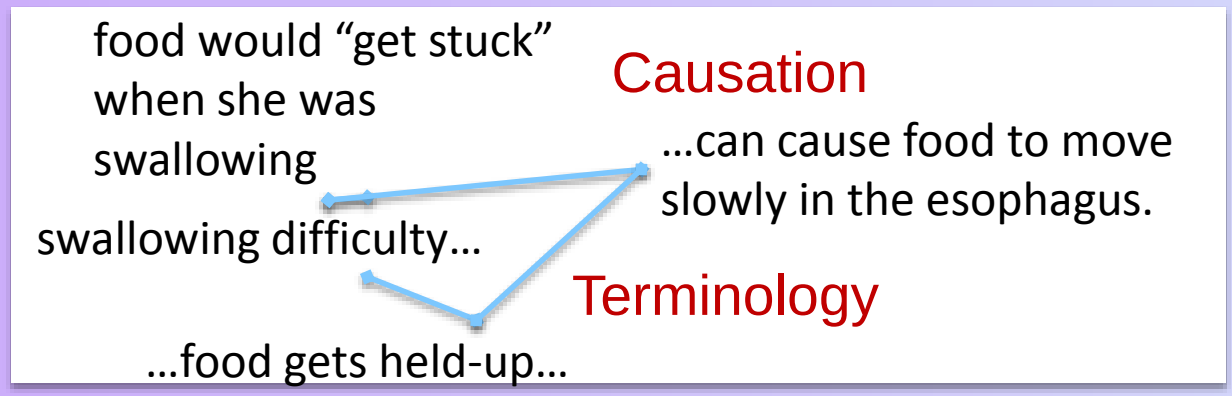
The Geometric Design for Pedestrian Crossings at Channelized Turn Lanes

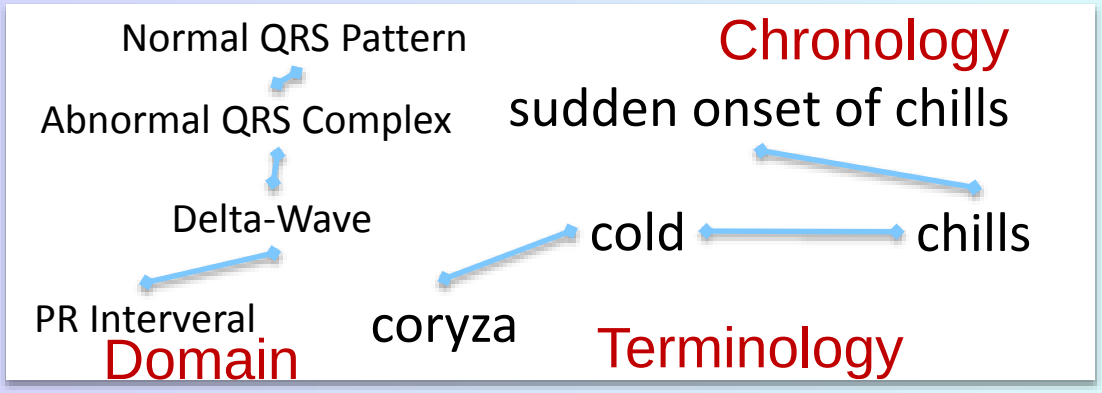
Channelized turn lanes are much more prevalent in the United States than roundabouts. Despite their increased prevalence, less attention has been given to the effects of treatments

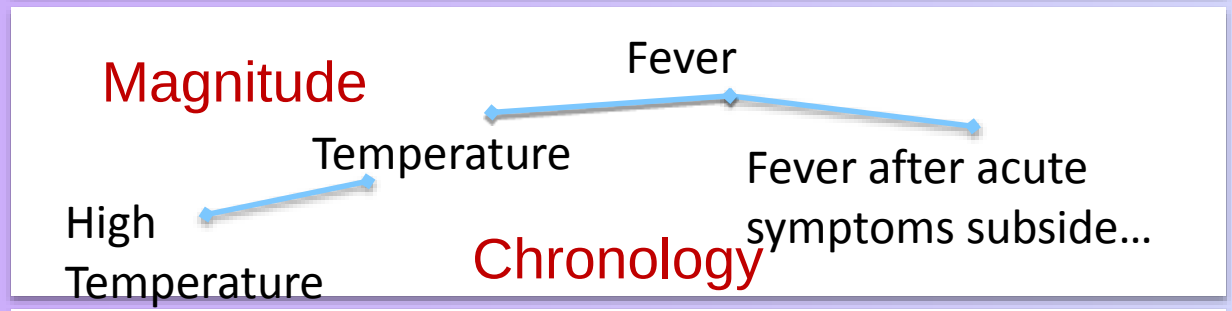
Structured

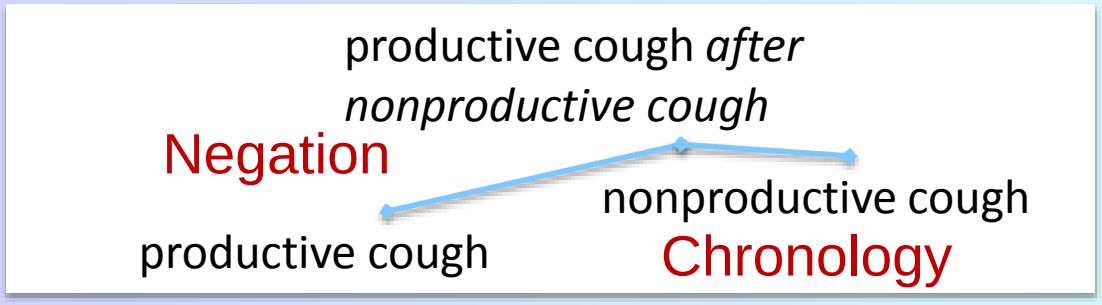
Unstructured

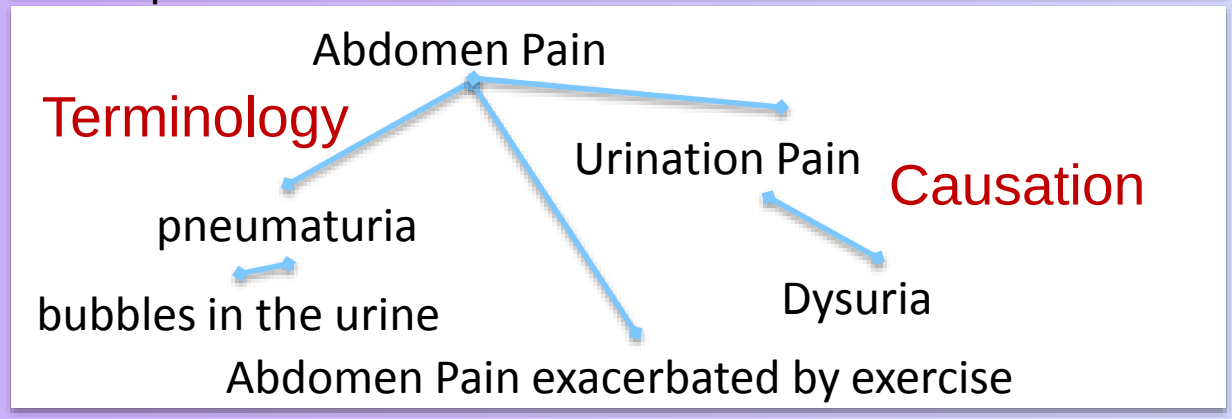
NLP ASSOCIATIONS

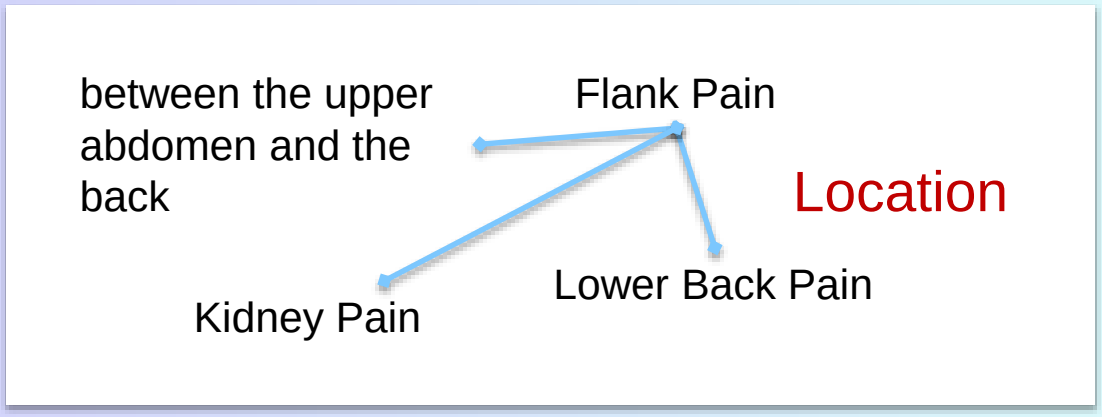






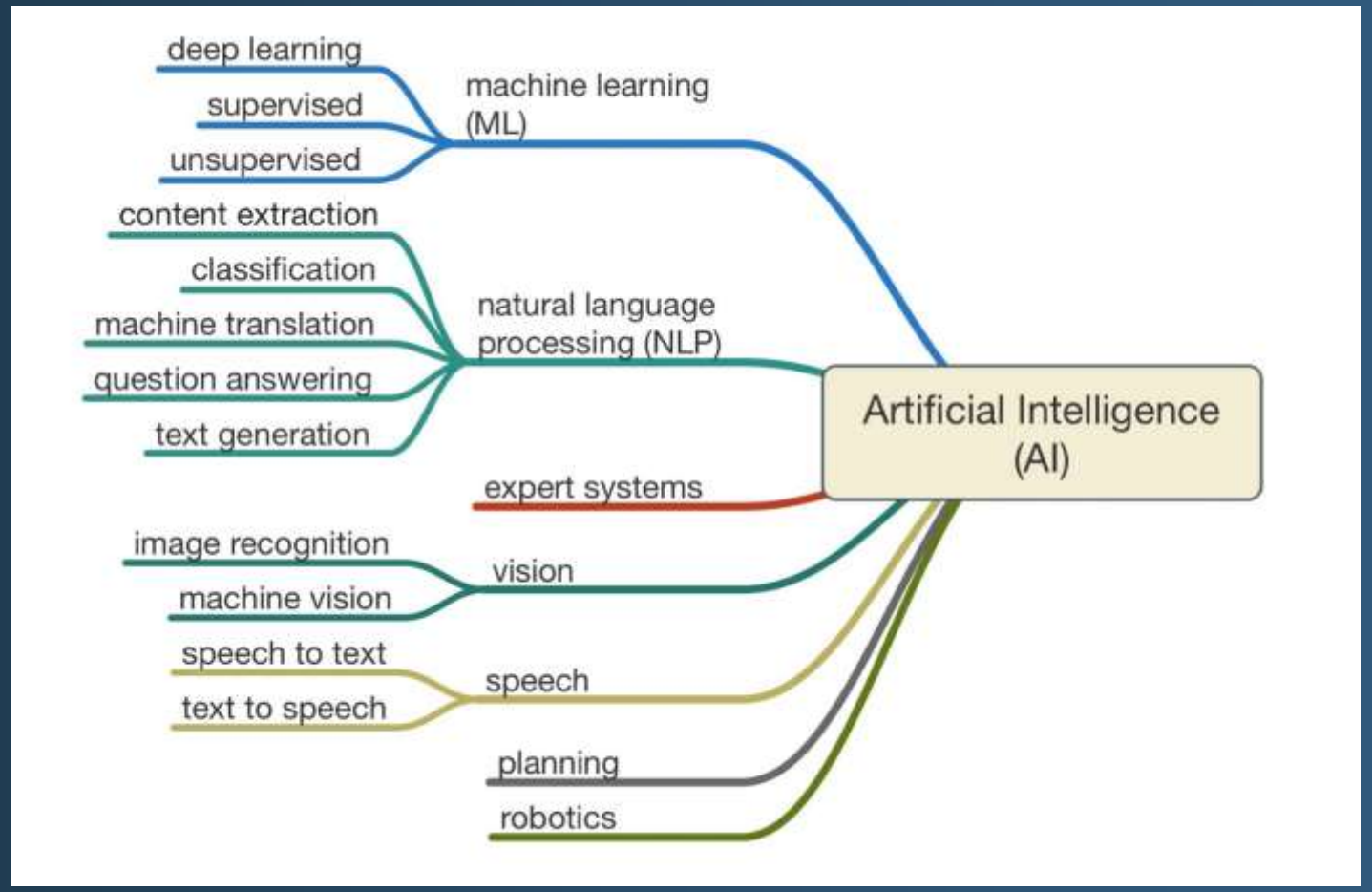






ARTIFICIAL INTELLIGENCE

Using Machines to perform human-level tasks



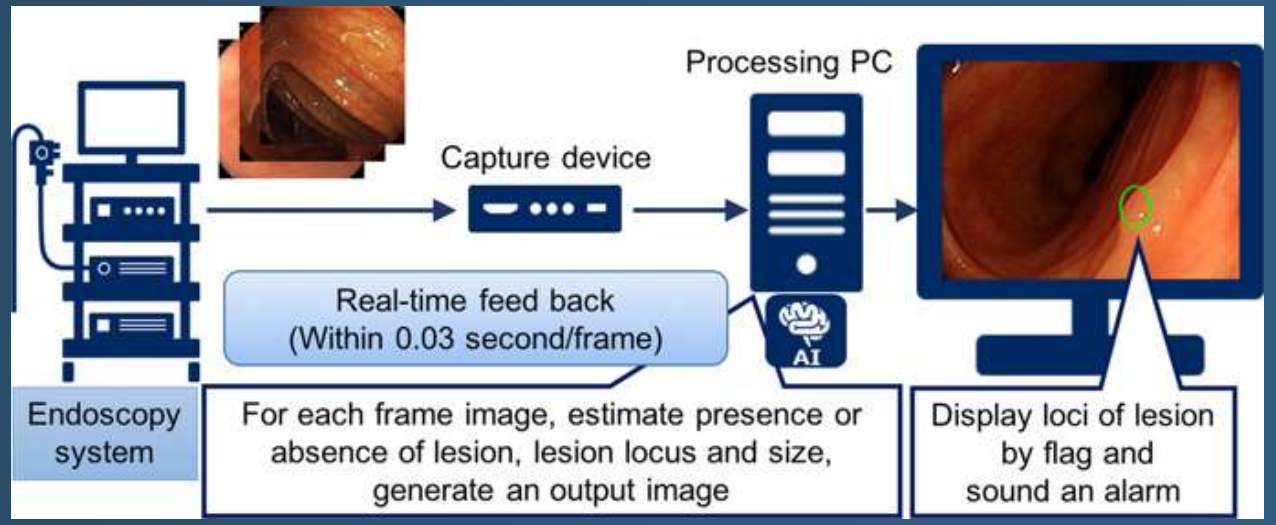
CHALLENGES IN AI & HEALTHCARE

- Unstructured Data remains challenging to capture
  - Pre-engineered data organization relied upon for input into structured datasets.
  - Deep Learning is nascent and evolving to handle this dilemma.
    - Imaging, Natural Language Processing (NLP), Sequence Prediction exemplify applications for DL
    - Allows for significant possibilities within Healthcare
      - Precision Medicine
      - Mobile Health Interfaces

AI & CANCER IMAGING

- Convolutional Neural Networks (CNN)
  - DL architecture that analyzes pixel-level information from images
  - Allows for delineation of lines, curves, and objects in the images
  - Studies show base equivalency to humans in classification and detection
    - Dermatological, Radiology, and Photographic images use CNN with high accuracy in several studies.

Yamada M et al.

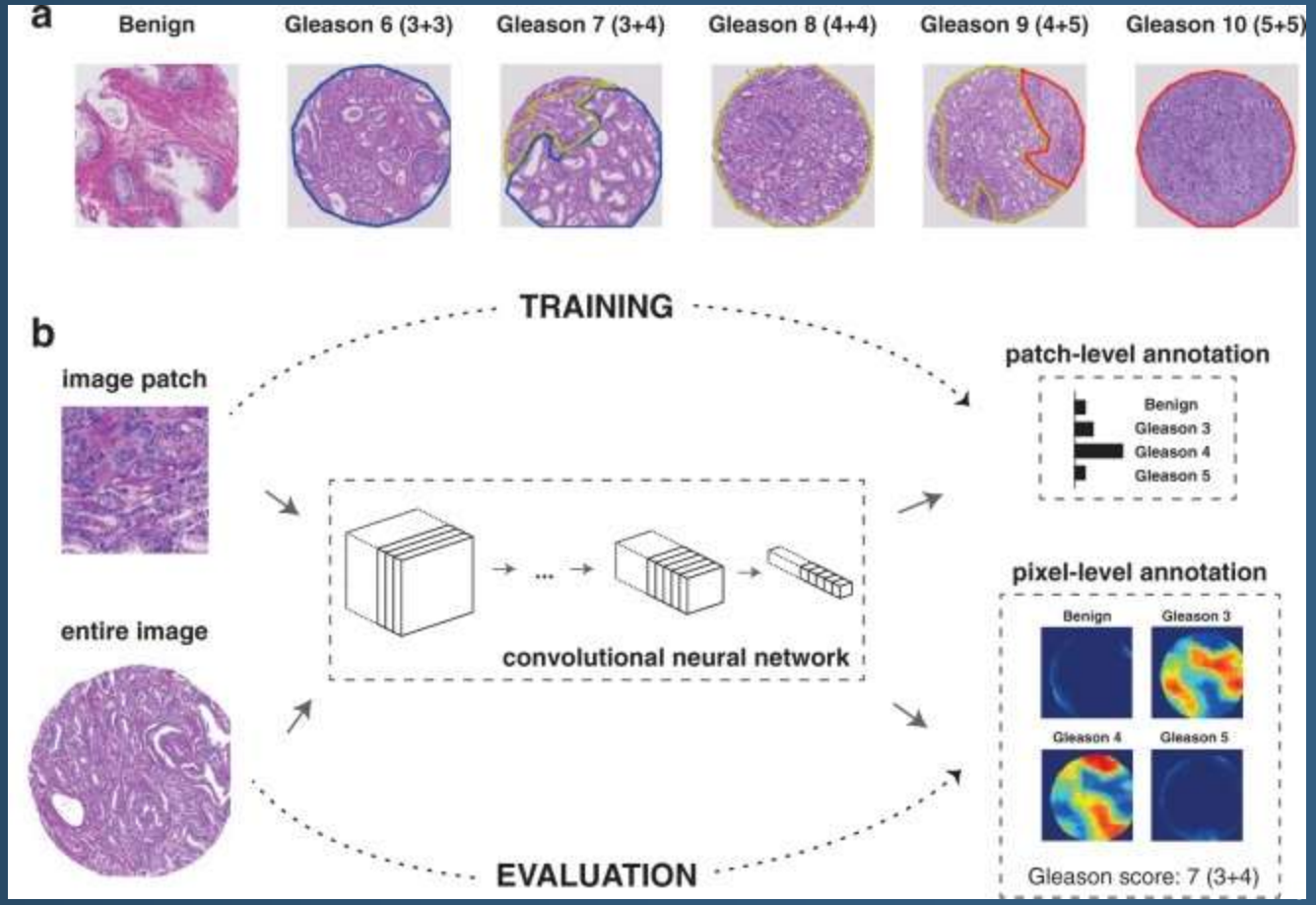


1. Webster DE, Suver C, Doerr M, et al. The Mole Mapper Study, mobile phone skin imaging and melanoma risk data collected using ResearchKit. Sci Data. 2017;4:170005
2. Yamade M, Saito Y, Imaoka H et al. Development of a real-time endoscopic image diagnosis support system using deep learning technology in colonoscopy. Sci Rep. 2019 Oct 8;9(1):14465. doi: 10.1038/s41598-019-50567-5.

AI & DIGITAL PATHOLOGY

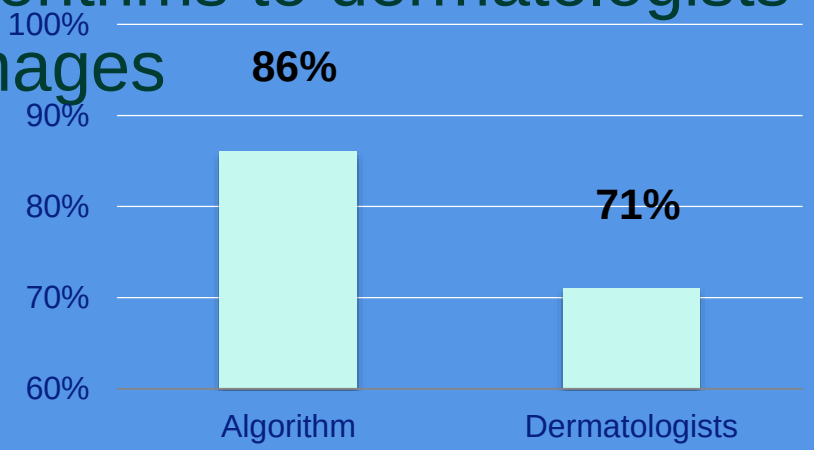
- DL shown in automated Gleason grading of prostate adenocarcinoma Hematoxylin and Eosin–stained (H&E) specimens to have 75% concordance between the algorithm and pathologists.

Arvaniti E, Fricker KS, Moret M, et al. Automated Gleason grading of prostate cancer tissue microarrays via deep learning. Sci Rep. 2018;8:12054. https://www.nature.com/articles/s41598-018-30535-1#rightslink



American Academy of Dermatology, September 2017

Comparison of the accuracy of computer algorithms to dermatologists for the diagnosis of melanoma from dermoscopic images



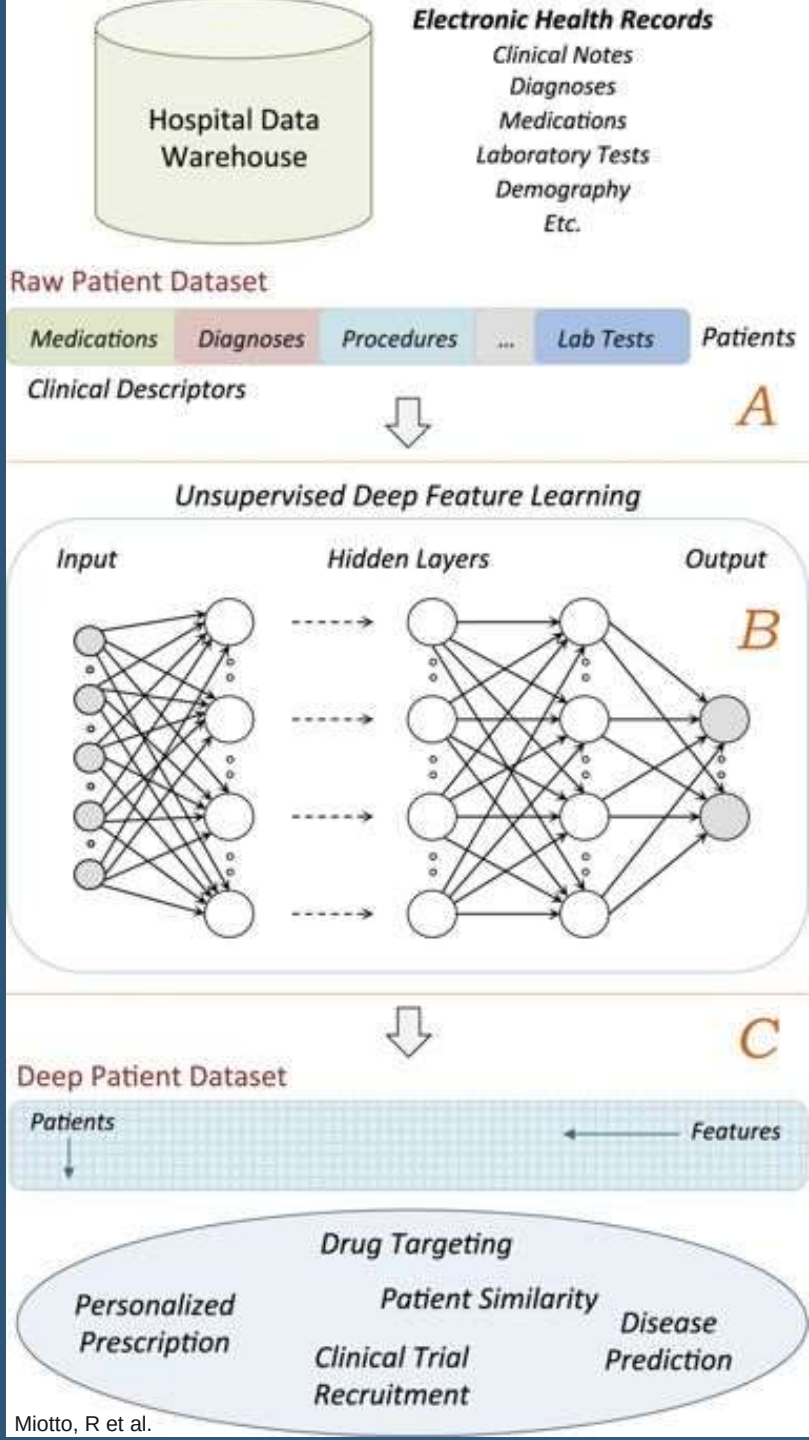
Fusion algorithm v. dermatologists (N=100)

"Deep learning computer vision systems classified melanoma dermoscopy images with accuracy that exceeded some but not all of the dermatologists."

J Am Acad Dermatol. 2018 Feb;78(2):270-277.e1. doi: 10.1016/j.jaad.2017.08.016. Epub 2017 Sep 29.
Results of the 2016 International Skin Imaging Collaboration International Symposium on Biomedical Imaging challenge: Comparison of the accuracy of computer algorithms to dermatologists for the diagnosis of melanoma from dermoscopic images.
Marchetti MA[1], Codella NCF[2], Dusza SW[1], Gutman DA[3], Helba B[4], Kalloo A[1], Mishra N[5], Carrera C[6], Celebi ME[7], DeFazio JL[1], Jaimes N[8], Marghoob AA[1], Quigley E[1], Scope A[9], Yélamos C[1], Halpern AC[10]; International Skin Imaging Collaboration.

AI & DATA OUTCOMES

- Electronic Health Records (EHR)/ Electronic Medical Records (EMR)
  - NLP being used to predict disease development in large healthcare systems
    - Mt. Sinai (US) used DL-AI algorithm with 93% accuracy
    - Included Cancers of Prostate, Rectum and Liver
  - Cancer Toxicity
    - Novel discovery of drug-drug interactions
    - Toxicity from prostate (urinary/rectal), liver (hepatobiliary), and cervical (rectal) radiotherapy using dosimetric data from EHR



Miotto, R et al.

1. Miotto R, Li L, Kidd BA, Dudley JT. Deep patient: an unsupervised representation to predict the future of patients from the electronic health records. Sci Rep. 2016;6:26094.
2. Zitnik M, Agrawal M, Leskovec J. Modeling polypharmacy side effects with graph convolutional networks. Bioinformatics. 2018;34:i457-i466.
CNN approach was used to predict side effects of polypharmacy combinations based on databases of protein-protein and drug-protein interactions.

AI & DATA OUTCOMES

- Using published research, clinical trial enrollment, drug development, and biomarker discovery opportunity for AI to assist in synthesizing this data and support/inform physician decision-making
  - Utilize DL and natural language processing to achieve this aim.
  - AI designed to link patient data to clinical trial databases and to match patients to appropriate clinical trials
  - AI utilizing ML to select appropriate investigational drugs in development for given patients
  - AI coupled with patient data, expert guidance, and national treatment guidelines to guide cancer management

CHALLENGES IN AI

- External validation and proving generalizability
  - Complexity of neural networks and the large number of parameters creates a tendency for detailed models unable to generalize across diverse populations.
  - Due to heterogeneity of medical data across institutions, several external validation sets required to prove accurate performance
- Data Restrictions
  - Lack of data for organizations to use AI algorithms
    - Privacy restrictions
  - Large amount of data needed for DL
    - Problematic in disease with less prevalence

CHALLENGES IN AI

- Opaque logic of the AI
  - Limited ability to determine precise logic behind DL-based predictions
  - Traditional ML algorithms (i.e. linear regression) are limited to model complex relationships, but offer easy interpretability
    - There is a set of pre-defined weighted features used to bring output
    - DL utilizes unstructured input data with the bulk of knowledge generation from hidden layers.
- Lack of data science training in Clinicians
  - Limits ability to adopt technology more readily
  - Data Scientist lack insight into appropriate clinical use cases

CHALLENGES IN AI

- Medical imaging relies heavily on deep learning architectures designed and trained on natural images
  - Medical images are also used to further fine-tune models enhancing ability to recognize image patterns in training data but not generalizable to new image patterns.
  - Additionally, training a new model architecture needs a large number of images that may not be readily available.

- Data challenges include differences in images from patients with different ethnicities
  - Light vs. dark skin produce disparities in AI model's decisions.
  - A model trained on lighter skin individuals will perform better on lighter skin patients than dark skin patients.

1. Henglin M, Stein G, Hushcha PV, Snoek J, Wiltschko AB, Cheng S. Machine learning approaches in cardiovascular imaging. Circ Cardiovasc Imaging 2017; 10 (10) e005614
2. Fei Wang and Anita Preininger. **AI in Health: State of the Art, Challenges, and Future Directions.** Yearb Med Inform 2019; 28(01): 016-026. DOI: 10.1055/s-0039-1677908

Our AI footprint

Human + machine = greater than the sum of its parts

118,000 patients
touched by IBM cognitive health applications

46,000 cancer patients
touched to date by Watson Health oncology offerings

40+ peer-reviewed publications, abstracts, and presentations on cognitive applications published by Watson Health

100+ journal publications
on deep learning applications in health published by IBM Research

295 million
clinical and claims data records

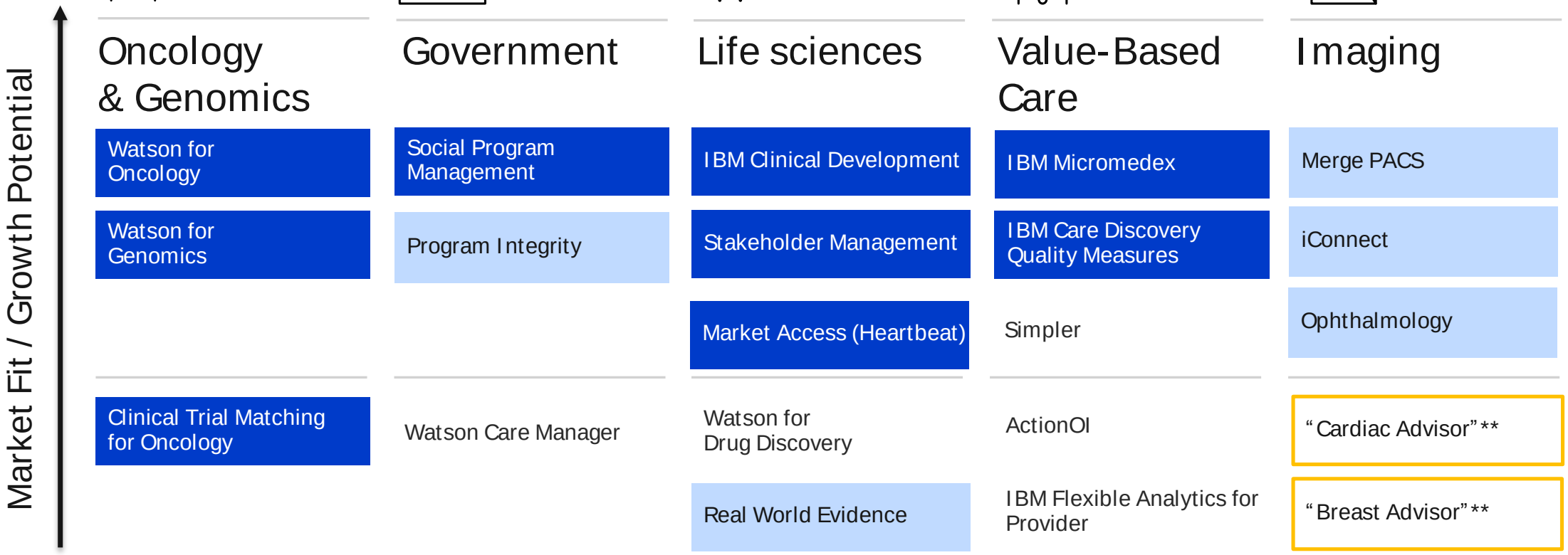
13,000+
clients and partners

IBM is **ranked 1st in US patents**

400+ patents
granted or pending for Watson Health

25+ patents
granted in deep learning applications for healthcare and life sciences

Watson Health Offerings by Pillar – Availability in Latin America



Watson Health is working to enhance the ability of cancer care specialists to make sense of health information with three powerful cognitive solutions:

Watson for Oncology

- Evidenced-based treatment recommendations based on individual patient profiles
- Recommendations derived from published guidelines and top cancer center expertise

Watson for Genomics

- Molecular profiling of tumors
- Automated translation into actionable insights of relevant genetic mutations and associated treatments

Watson for Clinical Trial Matching

- Research, guideline and patient record analysis
- Automated trial identification
- Trial comparison
- Trial management dashboards

HOW IT WORKS

2

Use those attributes to help identify candidate treatment options as determined by expert guidance

Expert Treatment Options from Memorial Sloan Kettering (MSK)

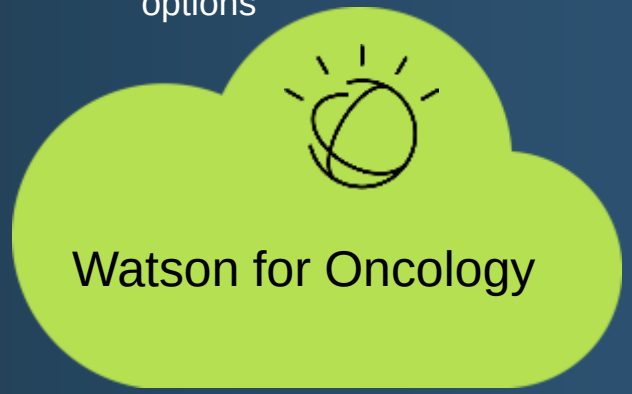
3

Search a corpus of evidence data to find supporting evidence for each option

Candidate treatment options

Patient case

61 y/o woman s/p mastectomy is here to discuss treatment options for a recently diagnosed 4.2 cm grade 2 infiltrating ductal carcinoma…



- Inclusion/exclusion criteria
- Co morbidities
- Contraindications
- FDA risk factors
- MSK preferred treatments
- Other guidelines
- Published literature-studies, reports, opinions from text books, journals, manuals, etc.

Key case attributes

Supporting evidence

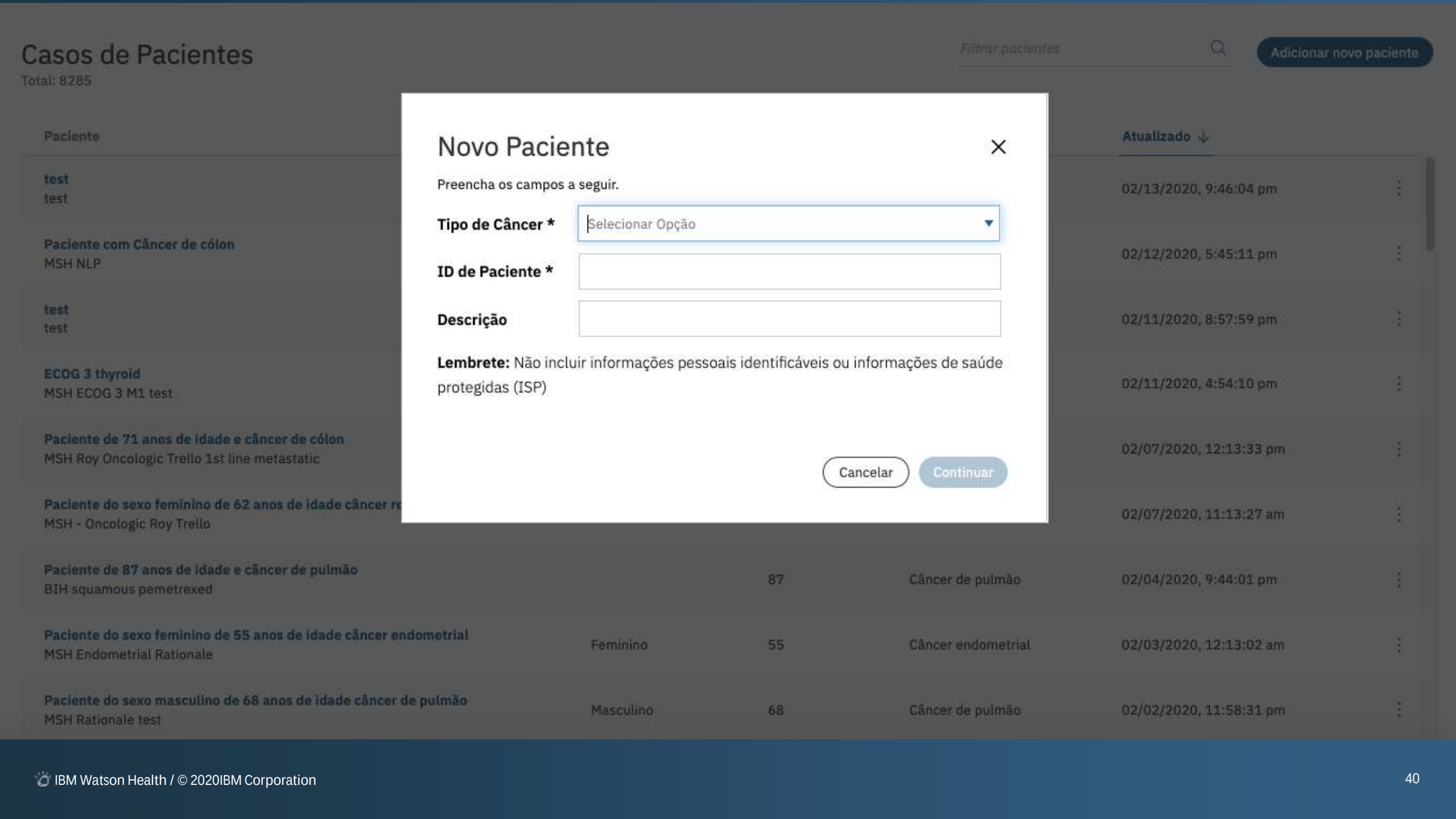
1

Extract key attributes from a patient's case

Prioritized Treatment Options
+
Evidence Profile

4

Use Watson's analytic algorithms together with expert guidance to help prioritize treatment options informed by- evidence.


Casos de Pacientes
Total: 8285
Filtrar pacientes
Adicionar novo paciente
Paciente
Atualizado
test
test
02/13/2020, 9:46:04 pm
Paciente com Câncer de cólon
MSH NLP
02/12/2020, 5:45:11 pm
test
test
02/11/2020, 8:57:59 pm
ECOG 3 thyroid
MSH ECOG 3 M1 test
02/11/2020, 4:54:10 pm
Paciente de 71 anos de idade e câncer de cólon
MSH Roy Oncologic Trello 1st line metastatic
02/07/2020, 12:13:33 pm
Paciente do sexo feminino de 62 anos de idade câncer r
MSH - Oncologic Roy Trello
02/07/2020, 11:13:27 am
Paciente de 87 anos de idade e câncer de pulmão
BIH squamous pemetrexed
87
Câncer de pulmão
02/04/2020, 9:44:01 pm
Paciente do sexo feminino de 55 anos de idade câncer endometrial
MSH Endometrial Rationale
Feminino
55
Câncer endometrial
02/03/2020, 12:13:02 am
Paciente do sexo masculino de 68 anos de idade câncer de pulmão
MSH Rationale test
Masculino
68
Câncer de pulmão
02/02/2020, 11:58:31 pm
Novo Paciente
Preencha os campos a seguir.
Tipo de Câncer *
Selecionar Opção
ID de Paciente *
Descrição
Lembrete: Não incluir informações pessoais identificáveis ou informações de saúde protegidas (ISP)
Cancelar
Continuar

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: Não especificado

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Não especificado

Biomarcadores preditivos
Alterações genéticas: Não especificado

Histórico do Tratamento
Cirurgia: Não especificado
Terapia sistêmica: Não especificado

Informações do Paciente

Buscar Atributos

Salvar

Ask Watson

Visualizar a lista de Todos os Atributos

Resumo 4

Observações Clínicas

Atributos Necessários:

Características do paciente

Idade *

Valor anos de idade

Performance status * ?

Selecionar

Status da doença

Histologia * ?

Selecionar

Recorrência do tumor localizado * ?

Selecionar

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Não especificado
Terapia sistêmica: Não especificado

Informações do Paciente

Buscar Atributos

Salvar | Ask Watson

Visualizar a lista de Todos os Atributos

Resumo | Observações Clínicas

Tratamentos prévios para câncer de pulmão

Biomarcadores preditivos

Alterações genéticas * ?

Nenhum fator oncogênico identificado

Medida da expressão PDL * ?

Expressão PD-L1 informada como <1% ou ≥1%

Intervalo PD-L1 informado * ?

<1% | ≥1%

Comorbidades

Especificar a gravidade de qualquer comorbidade presente.

Doença autoimune que requer terapia imunomoduladora sistêmica nos últimos 2 anos * ?

Sim | Não

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Informações do Paciente

Buscar Atributos

Salvar

Ask Watson

Visualizar a lista de Todos os Atributos

Resumo 9

Observações Clínicas

Atributos Necessários:

Comorbidades

Especificar a gravidade de qualquer comorbidade presente.

Pressupor que o restante está normal.

Grau de audição *

Selecionar

Grau da neuropatia *

Selecionar

Hemoptise *

Sim

Não

Tromboembolismo Arterial (por exemplo, infarto do miocárdio, infarto cerebral) *

Selecionar

Exames laboratoriais

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Planos de Tratamento

Expandir Todos Imprimir

NCCN

Recomendado (2) Outros planos (2)

Recomendado (2)

As seguintes terapias são recomendadas pelo Watson for Oncology treinado pelo Memorial Sloan Kettering:

Selecionar um estudo clínico

Terapia sistêmica →

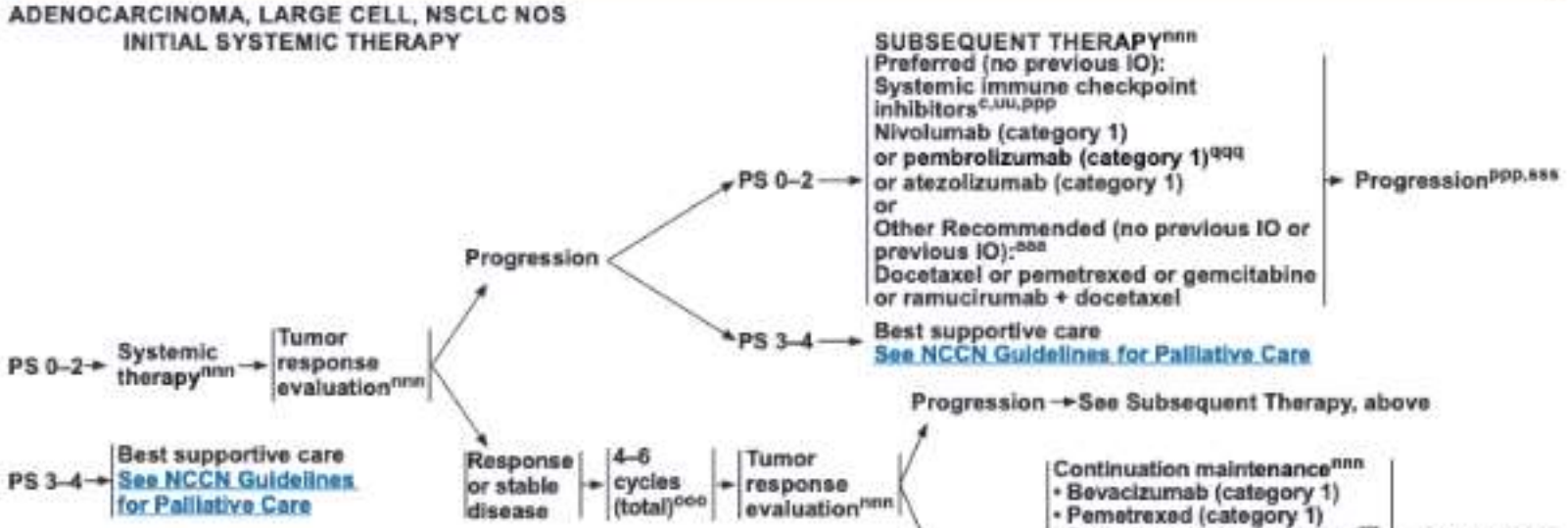
Outros planos (2)

Outros planos que podem ser aceitáveis para este paciente:

Radiação Paliativa →

Tratamento sintomático exclusivo →

NCCN Guidelines Version 1.2020
Non-Small Cell Lung Cancer



[c] Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. N Engl J Med 2010;363:733-742.

[uu] The data in the second-line setting suggest that PD-1/PD-L1 inhibitor monotherapy is less effective, irrespective of PD-L1 expression, in *EGFR+/ALK+* NSCLC.

[sss] If not previously given.

[ii] If pembrolizumab/carboplatin/pemetrexed or pembrolizumab/cisplatin/pemetrexed given.

[jj] If atezolizumab/carboplatin/paclitaxel/bevacizumab given.

[nnn] See Systemic Therapy for Advanced or Metastatic Disease (NSCL-J)

[ooo] In general, four cycles of initial systemic therapy (ie, with carboplatin or cisplatin) are administered prior to maintenance therapy. However, if patient is tolerating therapy well, consideration can be given to continue to 6 cycles.

[ppp] If progression on PD-1/PD-L1 inhibitor, switching to another PD-1/PD-L1 inhibitor is not recommended.

[qqq] Pembrolizumab is approved for patients with NSCLC tumors with PD-L1 expression levels ≥1%, as determined by an FDA-approved test.

[rrr] If bevacizumab was used with a first-line pemetrexed/platinum chemotherapy regimen.

[sss] If not already given, options for PS 0–2 include (nivolumab, pembrolizumab, or atezolizumab), docetaxel (category 2B), pemetrexed (category 2B), gemcitabine (category 2B), or ramucirumab + docetaxel (category 2B); options for PS 3–4 include best supportive care. Options for further progression are best supportive care or clinical trial.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Recomendado

As seguintes terapias são recomendadas pelo Watson for Oncology treinado pelo Memorial Sloan Kettering.

Platina (2): Cisplatina
Antimetabólito: Pemetrexede
Agente anti-PD1/PDL1 (6): Pembrolizumabe

Preferido — **Cisplatina / pemetrexede / pembrolizumabe →**

Platina (2): Carboplatina
Taxano (3): Paclitaxel
Agente anti-PD1/PDL1 (6): Atezolizumabe
Inibidor de VEGF (2): Bevacizumabe

Carboplatina / paclitaxel / atezolizumabe / bevacizumabe →

Outros tratamentos (30)

Não Recomendado (19)

Terapia sistêmica: Salvar no plano

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Outros tratamentos (30)

Outros tratamentos *refere-se a regimes listados em compêndios que se aplicam a cânceres de pulmão metastáticos. Os regimes listados em compêndios contra-indicados ou não indicados com base no tipo de doença estão listados em* ***Não recomendado****.*

Expandir Todos

- ▶ Platina / antimetabólito / inibidor de VEGF (2 opções)
- ▼ Platina / taxano / agente anti-PD1/PDL1 (4 opções)
  - ○ **Carboplatina / paclitaxel ligado a albumina / pembrolizumabe →**
  - ○ **Carboplatina / paclitaxel / pembrolizumabe →**
  - ○ **Cisplatina / paclitaxel ligado a albumina / pembrolizumabe →**
  - ○ **Cisplatina / paclitaxel / pembrolizumabe →**
- ▶ Platina / taxano / inibidor de VEGF (1 opção)
- ▶ Antimetabólito / taxano (1 opção)
- ▶ Antimetabólito / alcaloide da vinca (1 opção)
- ▶ Inibidor de CTLA-4 / agente anti-PD1/PDL1 (1 opção)
- ▶ Platina / antimetabólito (4 opções)
- ▶ Platina / taxano (5 opções)

Terapia sistêmica: ✓ Salvar no plano

Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Carboplatina / paclitaxel / atezolizumabe / bevacizumabe

Comparar a Outro Tratamento

Recomendado

Evidência | **Administração** | **Informações sobre o Fármaco**

Literatura Publicada

44 resultados

Imprimir Classificar por: Fonte da Curadoria

Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC.

Visualizar no PubMed

Visualizar Resumo do Artigo

Socinski,Mark A, Jotte,Robert M, Cappuzzo,Federico, Orlandi,Francisco, Stroyakovskiy,Daniil, Nogami,Naoyuki, Rodríguez-Abreu,Delvys, Moro-Sibilot,Denis, Thomas,Christian A, Barlesi,Fabrice, Finley,Gene, Kelsch,Claudia, Lee,Anthony, Coleman,Shelley, Deng,Yu, Shen,Yijing, Kowanetz,Marcin, Lopez-Chavez,Ariel, Sandler,Alan, Reck,Martin, IMpower150 Study Group. N. Engl. J. Med.. 2018-06-14. Pubmed PMID: 29863955.

Curado por MSK **Data:** 06/14/2018 **Qualidade:** Estudo de Controle Aleatório Fase III

Visualizar Mais

Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.

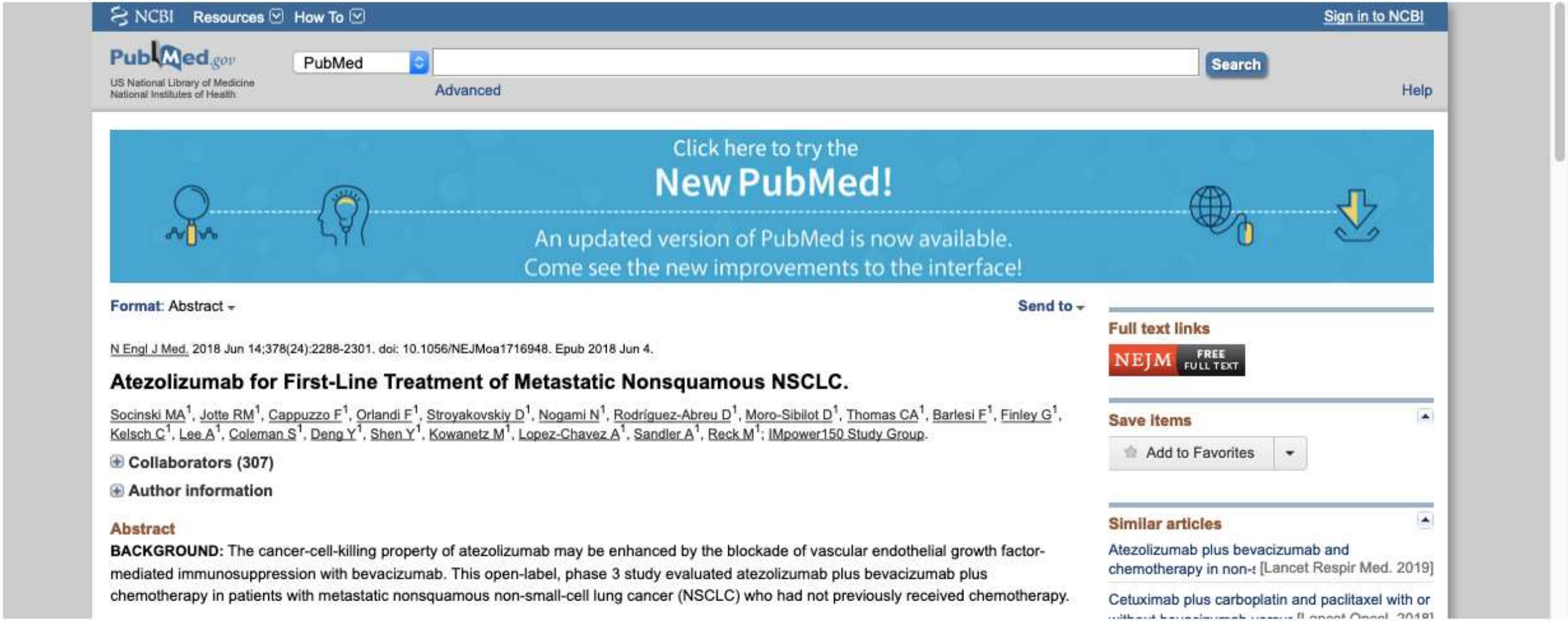
Visualizar no PubMed

Sandler,Alan, Gray,Robert, Perry,Michael C, Brahmer,Julie, Schiller,Joan H, Dowlati,Afshin, Lilenbaum,Rogerio, Johnson,David H. N. Engl. J. Med.. 2006-12-14. Pubmed PMID: 17167137.

Watson Correspondência parcial de terapia **Data:** 12/14/2006 **Qualidade:** Estudo de Controle Aleatório Fase III

Visualizar Mais

Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC.



Caso de Paciente
Francisco Oliveria (123456)

Dados Demográficos
Sexo: Não especificado
Idade: 67

Status da doença
Tipo de câncer: Câncer de pulmão
Histologia: Adenocarcinoma

Biomarcadores preditivos
Alterações genéticas: Nenhum fator oncogênico identificado

Histórico do Tratamento
Cirurgia: Nenhuma
Terapia sistêmica: Nenhuma

Carboplatina / paclitaxel / atezolizumabe / bevacizumabe

Comparar a Outro Tratamento

Recomendado

Evidência | Administração | Informações sobre o Fármaco

Opções de administração

Imprimir

Opções de dosagem do MSK

Informações sobre a administração de tratamento base são fornecidas pelo MSK apenas para fins de referência. Dosagens específicas do paciente devem ser determinadas com base na apresentação individual do paciente e calculadas separadamente.

AUC 6 carboplatin, 200mg/m2 paclitaxel, 1200mg Atezo 15mg/kg bevacizumab on day 1, repeated every 21 days.

Informações do Tratamento de Suporte da NCCN

Expandir Todos

PACLitaxel/CARBOplatin + Atezolizumab and Bevacizumab

- Emetic Risk
- Febrile Neutropenia Risk
- Supportive Care - Antiemetic Therapy

Growth Factors and Appendix C to the NCCN Templates.

Supportive Care - Other Supportive Therapy

- For atezolizumab:
  - Atezolizumab may cause severe, life-threatening immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated reactions are pneumonitis, colitis, hepatitis, hypophysitis, and endocrinopathy. While most of these reactions occur during treatment, some occur weeks to months after discontinuation of atezolizumab. In the setting of immune-mediated reactions, atezolizumab may be held, and for severe reactions, atezolizumab should be permanently discontinued. High-dose systemic corticosteroid therapy should be initiated for immune-mediated reactions according to specific recommendations in the drug package insert. The recommended corticosteroid dosing is:
    - PrednISONE (or equivalent) 1 - 2 mg/kg/day followed by a corticosteroid taper.
  - This agent may cause severe life-threatening diarrhea. Episodes of diarrhea should be monitored prior to each dose and as clinically indicated. Modification or discontinuation of therapy may be warranted. Review drug package insert for specific recommendations on antidiarrheal medication and/or systemic corticosteroids. Patients may require IV hydration and electrolyte replacement.
  - This agent may cause severe, life-threatening endocrinopathies. Systemic corticosteroids and appropriate hormone replacement therapy should be initiated in symptomatic patients.
  - This agent may cause new onset type 1 diabetes mellitus with ketoacidosis. Blood glucose should be monitored prior to each dose and as clinically indicated. Modification or discontinuation of therapy may be warranted. Patients may require insulin replacement therapy according to specific recommendations in the drug package insert.

Supportive Care - Premedications

- For PACLitaxel: Premedication for hypersensitivity is required:
  - **H2 antagonist**: Famotidine 20 mg IV/PO 30 - 60 minutes pre-PACLitaxel OR Ranitidine 50 mg IV or 150 mg PO 30 - 60 minutes pre-PACLitaxel**AND**
  - **H1 antagonist**: DiphenhydrAMINE 12.5 - 50 mg IV/PO 30 - 60 minutes pre-PACLitaxel**AND**
  - **Dexamethasone**: Dexamethasone 20 mg PO approximately 12 and 6 hours pre-PACLitaxel OR Dexamethasone 20 mg IV 30 minutes pre-PACLitaxel

Supportive Care - Safety Parameters and Special Instructions

Bevacizumab

Visualizar Incidência de Reação Adversa

Contraindicações/Precauções

Reações Adversas

Grave

- GI perforation
  0.3% a 3% de incidência
- **abdominal pain**
  <= 12% de incidência
- asthenia
  <= 10% de incidência

Diarrhea has been reported in 21% to 40% (grade 3 or 4, 18% or less) of patients treated with bevacizumab in combination with chemotherapy across clinical trials. Additional gastrointestinal adverse reactions include nausea (53% to 72%; grade 3 or 4, 12% or less), stomatitis (15% to 33%), mucosal inflammation (15% or less), oropharyngeal pain (16% or less), **abdominal pain** (33% or less; grade 3 or 4, 12% or less), vomiting (33% or less; grade 3 to 5, 11% or less), constipation (4% or less), and dehydration (grade 3 to 5, 10% or less); grade 3 to 5 ileus occurred in 4% of patients with metastatic colorectal cancer treated with bevacizumab plus FOLFOX4. Additionally, gingivitis (2.4%), gastroesophageal reflux disease (GERD) (2.4%), oral ulceration (1.8%), gastritis (1.5%), and gingival pain (1.5%) were reported 5-fold more frequently in patients with renal cell cancer treated with bevacizumab plus interferon-alfa compared to patients receiving placebo plus interferon-alfa. Gastrointestinal ulcer (peptic ulcer) and anastomotic ulceration have been reported in postmarketing experience with bevacizumab.[60402] [62350] [64400]

[60402] Avastin (bevacizumab) IV package insert. South San Francisco, CA: Genentech, Inc.; 2016 Dec.

- back pain
  <= 6% de incidência
- biliary fistula
  <= 1.79% de incidência
- bladder fistula
  <= 1.79% de incidência
- bleeding
  0.4% a 7% de incidência
- bronchopleural fistula
  <= 1.79% de incidência
- dehydration
  <= 10% de incidência
- diarrhea
  <= 18% de incidência
- dyspnea
  <= 4% de incidência
- epistaxis
  <= 5% de incidência

Idade: 67 | Histologia: Adenocarcinoma | oncogênico identificado | Terapia siste

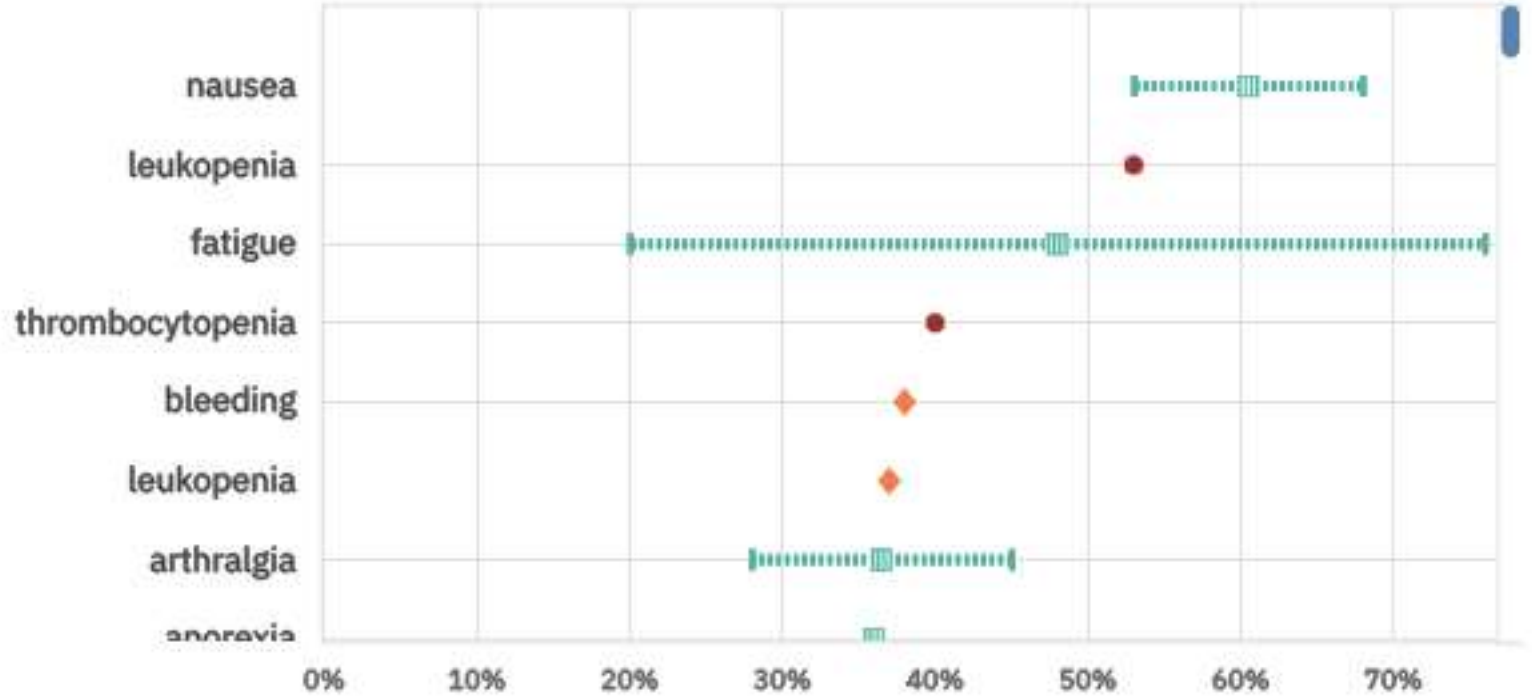
Visualizar

Incidência de Reação Adversa

Bevacizumab

Classificar por: Porcentagem de Incidência

Grave Moderado Leve



Fechar

Visualizar

Visualizar

IBM Watson Health™

IBM Watson™ for Oncology

Treinado pelo Memorial Sloan Kettering

Relatório de Tratamento

Francisco Oliveria

Plano de tratamento para diagnóstico: Câncer de pulmão
Sexo: Idade: 67 Id de paciente: 123456

Informações do Paciente

Características do paciente

Idade: 67 anos de idade

Performance status: ECOG 0 (Assintomático) ou KPS 90-100

Status da doença

Histologia: Adenocarcinoma

Recorrência do tumor localizado: Nenhuma

Estágio M: M1 - Metástase à distância

Características do estadiamento

Estágio do câncer: IV

Cenários de doença crítica

Cenários de doença crítica: Nenhum

Tratamentos prévios para câncer de pulmão

Tratamentos prévios para este câncer: Nenhum

Razão para mudança na terapia: Progressão da doença

Biomarcadores preditivos

Alterações genéticas: Nenhum fator oncogênico identificado

Medida da expressão PDL1: Expressão PD-L1 informada como <1% ou ≥1%

Intervalo PD-L1 informado: <1%

Comorbidades

Doença autoimune que requer terapia imunomoduladora sistêmica nos últimos 2 anos: Não

IBM Watson™ for Oncology Versão1.35 Impresso por: Unknown Última atualização: 02/15/2020, 7:03:06 pm Impresso: 02/15/2020, 7:08:25 pm

Recomendado

Carboplatina / paclitaxel / atezolizumabe / bevacizumabe

Evidência

Literatura Publicada

Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC.
Socinski,Mark A, Jotte,Robert M, Cappuzzo,Federico, Orlandi,Francisco, Stroyakovskiy,Daniil, Nogami,Naoyuki, Rodriguez-Abreu,Delvys, Moro-Sibilot,Denis, Thomas,Christian A, Barlesi,Fabrice, Finley,Gene, Kalach,Claudia, Lee,Anthony, Coleman,Shelley, Deng,Yu, Shen,Yijing, Kowanetz,Marcin, Lopez-Chavez,Ariel, Sandler,Alan, Reck,Martin, IMpower150 Study Group. N. Engl. J. Med.. 2018-06-14. Pubmed PMID: 29863955.

Curado por MS... **Data:** 06/14/2018 **Qualidade:** Estudo de Controle Aleatório Fase III

- Resultado de Sobrevida Positiva (sobrevida livre de progressão)
  Sobrevida melhor que "bevacizumab + carboplatin + paclitaxel" para os mesmos: age, diagnosis, histology, line of therapy, mutation, stage.
  The median progression-free survival was longer in the ABCP group than in the BCP group (8.3 months vs. 6.8 months; hazard ratio for disease progression or death, 0.62; 95% confidence interval [CI], 0.52 to 0.74; P<0.001); the corresponding values in the Teff-high WT population were 11.3 months and 6.8 months (hazard ratio, 0.51 [95% CI, 0.38 to 0.68]; P<0.001).
- Resultado de Sobrevida Positiva (sobrevida livre de progressão)
  Sobrevida melhor que "bevacizumab + carboplatin + paclitaxel" para os mesmos: age, diagnosis, histology, line of therapy, mutation, stage.
  Progression-free survival was also longer in the ABCP group than in the BCP group in the entire intention-to-treat population (including those with EGFR or ALK genetic alterations) and among patients with low or negative programmed death ligand 1 (PD-L1) expression, those with low Teff gene-signature expression, and those with liver metastases.
- Resultado de Toxicidade Positiva (segurança)
  Toxicidade positiva para os mesmos: age, diagnosis, histology, line of therapy, mutation, stage.
  The safety profile of ABCP was consistent with previously reported safety risks of the individual medicines.
- Resultado de Sobrevida Positiva (sobrevida livre de progressão)
  Sobrevida melhor que "bevacizumab + carboplatin + paclitaxel" para os mesmos: age, diagnosis, histology, line of therapy, mutation, stage.
  The addition of atezolizumab to bevacizumab plus chemotherapy significantly improved progression-free survival and overall survival among patients with metastatic non-squamous NSCLC, regardless of PD-L1 expression and EGFR or ALK genetic alteration status.
- Resultado de Sobrevida Positiva (sobrevida global)
  Sobrevida melhor que "bevacizumab + carboplatin + paclitaxel" para os mesmos: age, diagnosis, histology, line of therapy, mutation, stage.
  The addition of atezolizumab to bevacizumab plus chemotherapy significantly improved progression-free survival and overall survival among patients with metastatic non-squamous NSCLC, regardless of PD-L1 expression and EGFR or ALK genetic alteration status.

Este relatório deve ser utilizado apenas por um médico especializado no tratamento do câncer com acesso autorizado à solução Watson for Oncology (a "Solução"). A Solução e este relatório visam fornecer informações para auxiliar clínicos qualificados na tomada de decisões de assistência ao paciente. A IBM não tem nenhuma responsabilidade pela conduta do cuidado do paciente. O médico especializado no tratamento de câncer é o único responsável por todas as decisões de assistência ao paciente e o uso da Solução e deste relatório não diminui a responsabilidade do médico pelo cuidado do paciente.

Shared-decision Making in Prostate Cancer with Clinical Decision-support

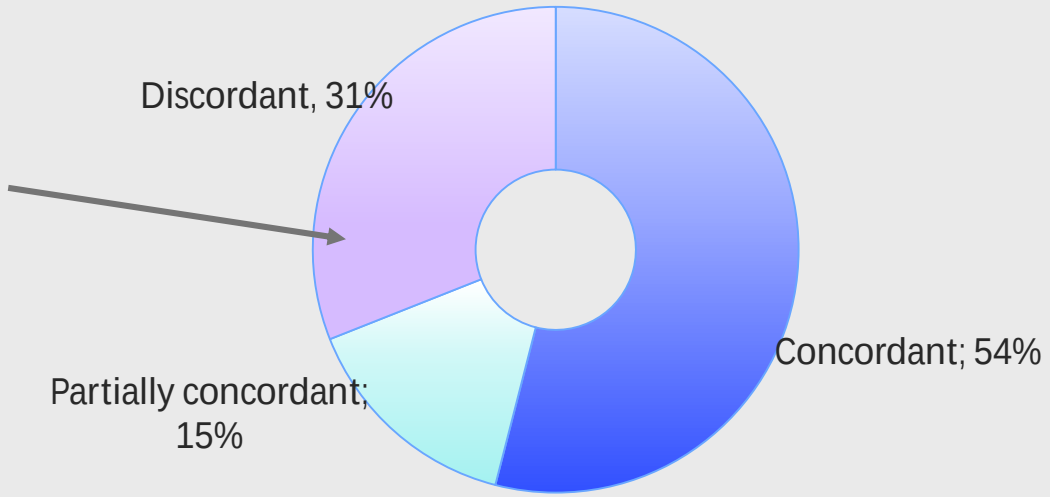
| Rocha HAL et al. *J Clin Oncol*. 2019; 37(suppl) abstract 16576.

Clinical decision-support systems may play a role in facilitating shared decision making when a single standard of care is lacking.

Watson for Oncology facilitated a shared decision-making process for 48 patients in Brazil.

53%

of discordant cases due to **patient preference** for treatment versus active surveillance



Concordance: WfO treatment option and chosen chosen treatment

"Variation in prostate cancer treatment exists. CDSS [clinical decisions-support systems] therapy options may be useful in quantifying and modifying unwarranted variations in prostate cancer treatment."

* Excerpt from abstract

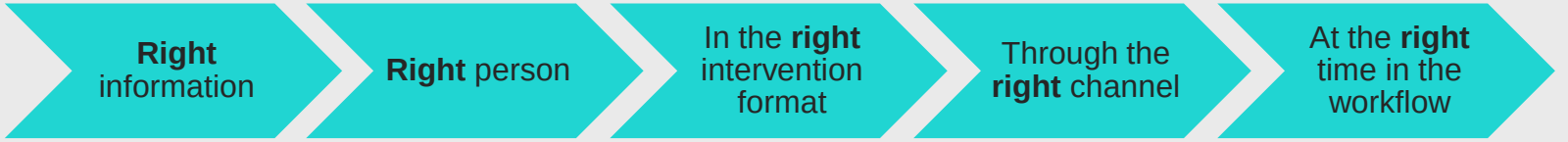
An Evaluation of Artificial Intelligence-based Clinical Decision Supports Use in Brazil

| Rocha HAL. et al. *J Clin Oncol*. 2019; 37(suppl): abstract e18081.

The goal of the study was to investigate how the implementation of Watson for Oncology (WfO) affects clinical decision-making and workflow at the Instituto do Câncer do Ceará in Brazil.

*AHRQ overview of CDS Five Rights

The Clinical Decision Support (CDS) Five Rights framework*:



The results from oncologists (n=7 oncologists; 903 cases) surveyed on the use of Watson for Oncology and the CDS Five Rights Framework found:

- **71.4%** Expressed **positive statements** pertaining to the use of WfO
- **86%** Agreed that WfO provides **actionable information** about treatment decisions
- **86%** Agreed that WfO provides information about treatment decisions **at the right time in a clinician's work flow**

"In this study base[d] on an established framework for evaluation, oncologists felt WfO met the 5 Rights for CDS. "

* Excerpt from abstract

A Systematic Review of Concordance Studies Using Watson for Oncology (WfO) to Support Breast Cancer Treatment Decisions: A Four-Year Global Experience

| Arriaga YE et al. Accepted for the December 10-14 2019 San Antonio Breast Cancer Symposium.

Study systematically reviewed the results of concordance studies for breast cancer measuring concordance between WfO therapeutic options and treatment recommendations by multidisciplinary tumor boards (MTBs) or individual clinicians (ICs).

Nine breast cancer concordance studies, from China, India and Thailand, with 4,427 patients were identified and reviewed. Five studies determined concordance with MTB and four with ICs.

70.8%	Mean concordance for all studies (range 55 – 98%)
90.7%	Mean concordance with MTBs (range 79 – 98%)
59.9%	Mean concordance with ICs (range 55 – 76%)

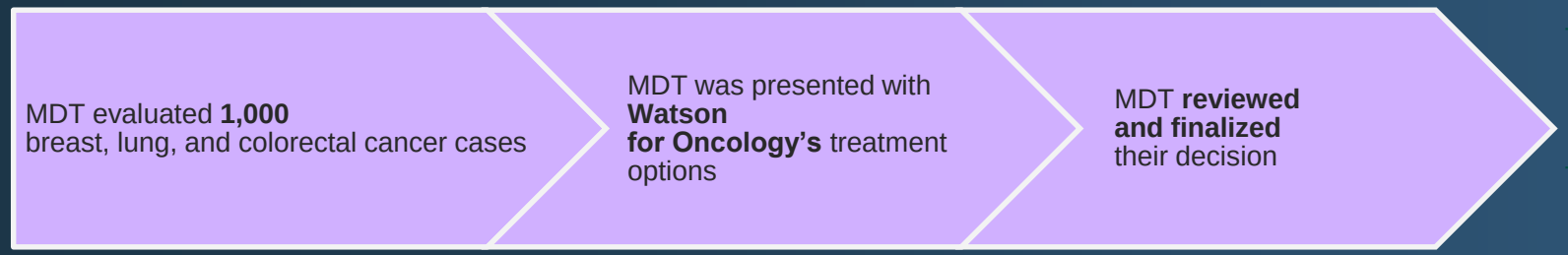
MTB/WfO concordance **was significantly higher** than ICs/WfO concordance ($P < .0001$)

"Higher concordance was observed between WfO and MTBs versus WfO and ICs, likely reflecting the multidisciplinary expertise having greater agreement with evidence and guideline-based recommendations of WfO than decisions of individual clinicians ."

A Prospective Blinded Study of 1000 Cases Analyzing Role of Artificial Intelligence. Watson for Oncology in Change of Decision Making of a Multidisciplinary Tumor Board (MDT) From a Tertiary Care Cancer Centre

| Somashekhar SP et al. ASCO 2019.

The MDT changed their decision in 13.6% of the cases.



Reason for Treatment Change	Percent
Evidence for newer treatment(s)	55%
More personalized treatment alternatives	30%
New genotypic, phenotypic and clinical insights	15%

"The study suggest[s] that cognitive computing decision support system[s] holds substantial promise to reduce cognitive burden on oncologist[s] by providing expert, updated, recent evidence-based [evidence-informed] insights for treatment-related decisions making."

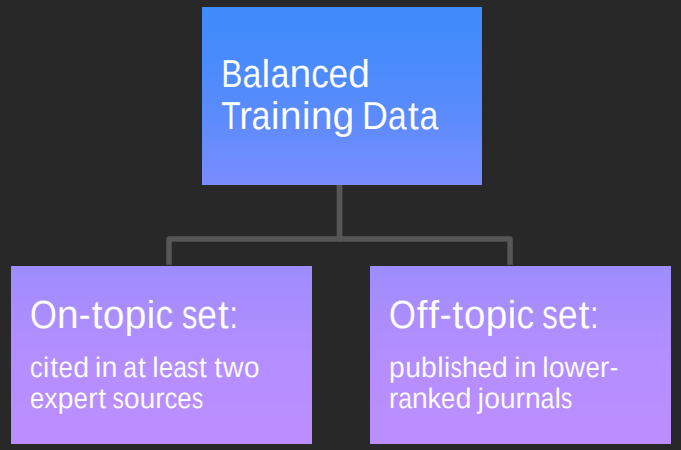
* Excerpt from abstract

Use of Machine Learning to Identify Relevant Research Publications in Clinical Oncology

| Suarez Saiz F, Sanders C et al. ASCO 2019.

A model was trained, using abstracts and titles from PubMed, to identify relevant clinical papers based on articles cited by 3 expert oncology sources.

- **NCCN**
- **NCI - PDQ**
- **Hemonc.org**



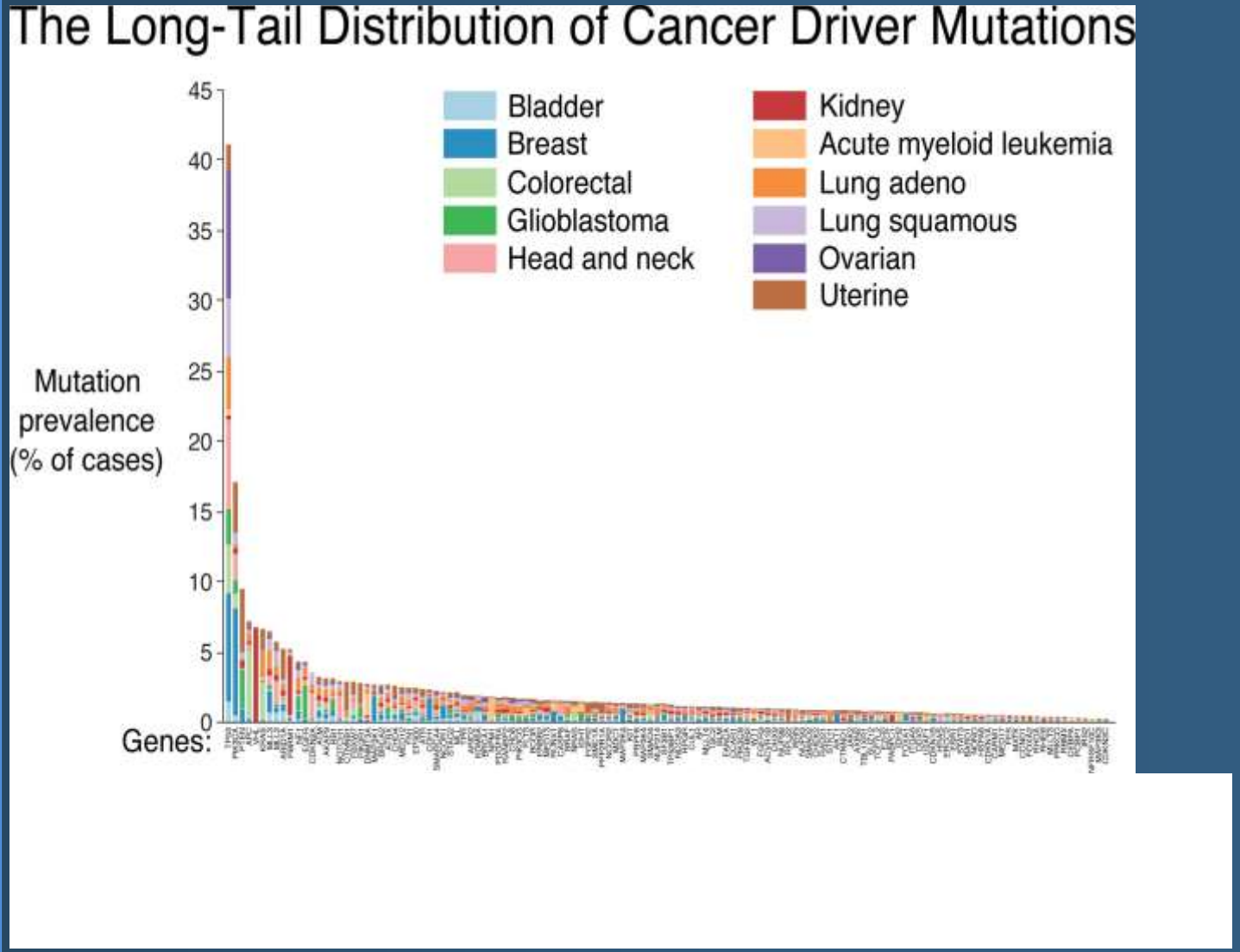
988 papers were classified with
0.93 accuracy
(95% CI, 0.9-0.96; $p \leq 0.0001$);
sensitivity 0.95 and
specificity 0.91

"The use of machine learning to identify relevant publications may reduce the time clinicians spend finding pertinent evidence for a patient."

* Excerpt from abstract

WATSON FOR GENOMICS

- Rapid “within minutes” interpretation
- Hence, accelerates the clinician’s access to information regarding therapeutic options
- Highly scalable – panels of varying sizes, whole exome, whole genome
- Increase the number of patients who can have access to individualized, precision cancer treatment by matching them with information related to molecular targeted therapies that are supported by evidence
- WFG excels at reading literature – thus is able to perform interpretation for known variants as well; the “long tail” of variants which manual/ semi-automated methods may not be capable of
- All cancers included in WFG interpretation
- Assist cancer care teams to keep up with the relevant literature published and available clinical trials



Courtesy: Dr. Warren Kibbe, Director of the Center for Biomedical Informatics and Information Technology (CBIIT) at the National Cancer Institute

Staying Current with Genomic Information Needs a New Approach

3 million
Average number of publications related to cancer[1]

9 times
NCCN Guidelines changed for NSCLC in 2017[2]

117
FDA-approved biomarker-based drugs for cancer[3]

~50%
Of new FDA-approved cancer therapies (2016-17) require specific molecular features[5]

600%
Increase from 2006 to 2018 in % of US patients with cancer estimated to benefit from genome-targeted therapy[6]

87%
Of Pharma pipe is biomarker driven drugs targeting late-stage cancer[4]

25%
The percent of variants of uncertain significance (VUS) that were reclassified[7]

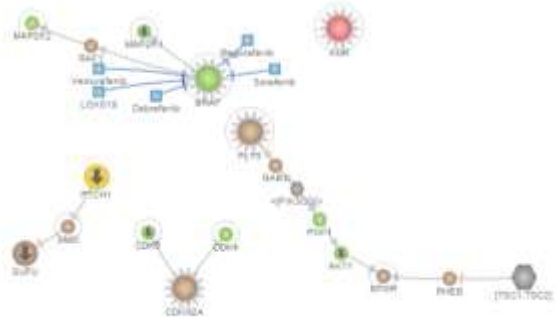
1. Reyes-Aldasoro CC. *PLoS ONE.* 2017;12(3):e0173671.
2. Reily GR. Lung Cancer IASLC News. Accessed August 9th, 2018
3. Julianne D et al. *Drug Resistance Updates.* 2017;30:48-62.
4. Aitken M et al. *Global Oncology Trends 2017.* (IQVIA, 2017).
5. Heymach J *et al.* *J Clin Oncol.* 2018; 36, 1020–1044.
6. Marquart J et al. *JAMA Oncol.* 2018;4(8):1093–1098.
7. Mersch J et al. *JAMA.* 2018;320(12):1266-1274.

WATSON FOR GENOMICS: How it Works

Case Sequenced

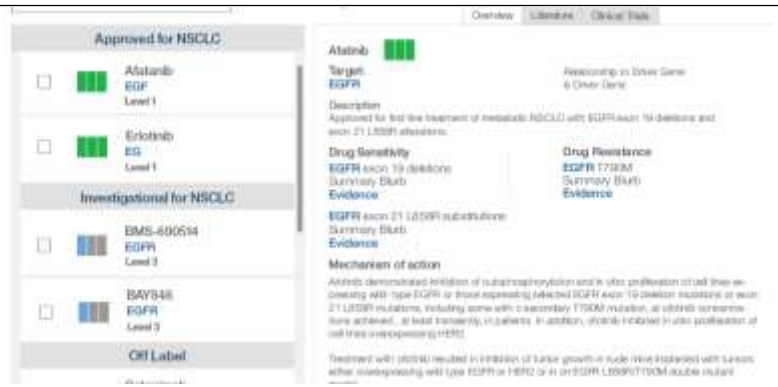
VCF / MAF, Log2, Dge, Fusion Encryption

Molecular Profile Analysis



Pathway Analysis

Drug Analysis



66

Performance and Validation of a Tumor Mutation Profiling, Based on Artificial Intelligence Annotation, to Assist Oncology Decision Making

| **Mitne-Neto M et al. *J Clin Oncol.* 2019; 37(suppl): abstract e13148.**

Tumor mutation profiling has become a key component for orienting the treatment of oncologic patients. A crucial step for this is the correct identification and classification of pathogenic and actionable variants.

Watson for Genomics (WfG) identified 1,219 variants from a hybrid capture panel evaluating 366 genes from **53 sequenced tumors.**

WfG classified 23% as **pathogenic, likely pathogenic, or actionable** and identified variants with the following indicators:

- **66%** Could **drive treatment** decisions
- **22.6%** Were **resistant** to targeted therapies
- **37.7%** Were **sensitive** to targeted therapies
- **86%** Had indication for a **clinical trial**

"The high percentage of samples that could benefit from mutational profiling highlights the importance of such approach in the clinical routine. Additionally, the high number of variants [indicated] the need for updated information for annotation."

* Excerpt from abstract

Clinical Insights for Hematological Malignancies from an Artificial Intelligence Decision-Support Tool

| Kim M et al. Accepted for publication ASCO 2019.

54 South Korean patient cases with hematological malignancies were analyzed by Watson for Genomics (WfG):

71% of cases had at least one clinically actionable therapeutic alteration

33% of cases had genes that were targeted by a US FDA approved therapy

20% of cases without therapeutic alterations, WfG identified additional diagnostic or prognostic insights

10 cases were randomly selected for **manual interpretation analysis:**

90% of cases were concordant with WfG analysis

WfG identified **9 more (33%) clinically actionable** variants not found in manual assessment

"WfG variant interpretation correlated well with manually curated expert opinion and identified clinically actionable insights missed by manual interpretation….WfG has obviated the need for labor-intensive manual curation of clinical trials and therapy, enabling our center to exponentially scale our NGS operations*"

* Excerpt from abstract

UNC Lineberger Comprehensive Cancer Center

Cognitive technology uncovers additional therapeutic options for cancer patients.

In a retrospective analysis of 1,018 cancer cases at UNC Lineberger Cancer Center, the molecular tumor board identified actionable genetic alterations in 703 cases, which Watson also confirmed. In addition, Watson for Genomics identified additional potential therapeutic options in 323 patients, or one third of the cases reviewed that the molecular tumor board hadn't identified. Of these, 96 were not previously identified as having an actionable mutation.[1]

1: Cancer Diagnostics and Molecular Pathology: Enhancing Next-Generation Sequencing-Guided Cancer Care Through Cognitive Computing. The Oncologist first published on November 20, 2017; doi:10.1634/theoncologist.2017-0170. Accessed at: http://theoncologist.alphamedpress.org/content/early/2017/11/20/theoncologist.2017-0170.full.pdf+html?sid=0703cdfd-db36-45fb-b561-a81544688384

Heightened Confidence

WATSON WAS

>99% accurate

in identifying tumor board findings

1,018 patients

were analyzed

WATSON IDENTIFIED ADDITIONAL OPTIONS IN

335 patients

(33% of the patients)

42 patients

with highly actionable mutations[1]

Comparing Sequencing Assays and Human-machine Analyses in Actionable Genomics for Glioblastoma

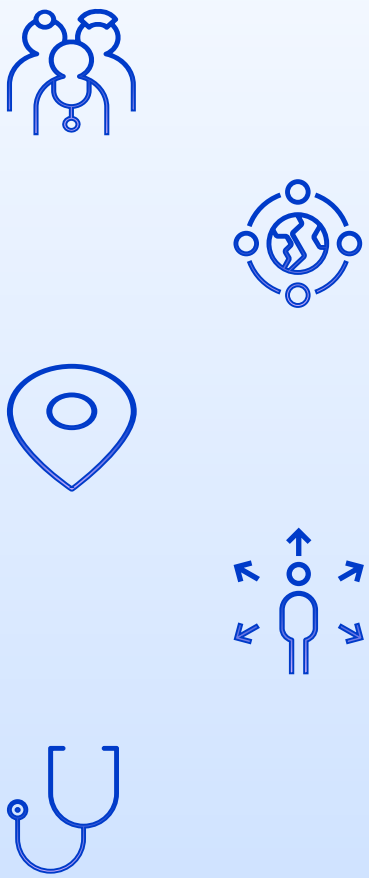
| Wrzeszczynski et al. Neurol Genet. 2017;3(4):e164.

Watson was applied in the analysis whole gene sequencing and RNA-sequencing of a single glioblastoma tumor in a 76-year-old patient.

Watson completed analysis of whole gene and RNA-sequencing results in 10 min vs 160 hours of person-time

“These findings suggest the unique role for cognitive computing in the detection of genetic alterations which may inform opportunities for investigational targeted cancer therapies.”

Clinical Trial Enrollment Presents Many Challenges



As of 10/11/19 there are 319,021 clinical trials registered in ClinicalTrials.gov for 2019[1]

A survey of 5,499 cancer patients found that only 40% discussed clinical trials with their physician and only 9% participated[2]

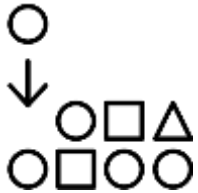
In a study of patient accrual into cancer clinical trials at a cancer center, of the 62% considered for participation only 53% had an appropriate protocol available for site and stage of disease[3]

1. ClinicalTrials.gov, Trends, Charts and Maps. Accessed October 11, 2019.
2. Unger JM et al. *Patient income level and cancer clinical trial participation.* https://www.ncbi.nlm.nih.gov/pubmed/23295802
3. Lara PN Jr. et all. Prospective evaluation of cancer clinical trial accrual patterns: identifying potential barriers to enrollment. https://www.ncbi.nlm.nih.gov/pubmed/11251003

Watson for Clinical Trial Matching (Point of Care)

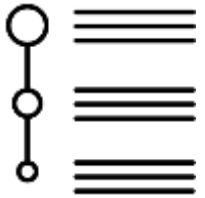
An overview of the Point of Care functionality of Watson for Clinical Trial Matching

Uses natural language processing to read and understand all the patient data, both unstructured and structured, in the medical record



Reads the eligibility criteria in all ingested clinical trial protocols, both from your institution and on www.clinicaltrials.gov

Returns a list of potentially eligible trials for a patient, ranked by highest relevance, with supporting evidence for why a patient did or did not meet criteria



Mayo Clinic

Advancing Medicine's future with more perfect patient matches

Despite Mayo Clinic's best efforts, just 5% of its patients take part in studies. Poor participation by patients, doctors cannot complete crucial clinical studies.

Watson CTM has enabled patients and clinical trial coordinators. Through Cognitive capabilities Watson CTM will provide preliminary patient matches, including a patient's proximity to a clinical trial. Clinicians trained the Watson technology on eligibility criteria and now receive suggestions of matches for trials in under 8 minutes versus a review process that used to take clinicians upward of 30 minutes per potential candidate.

Heightened Confidence

WATSON WAS

>73% faster

in identifying ideal clinical trial candidate patients (30 mins went down to 8 minutes)

94% Non-match

Omitted automatically for trials

CLINICAL TRIAL ENROLLMENT UP BY

80%

(approx. 4K~5K patients)

2620 visits

Lung and breast cancer cases processed

Upcoming Studies in Latin America

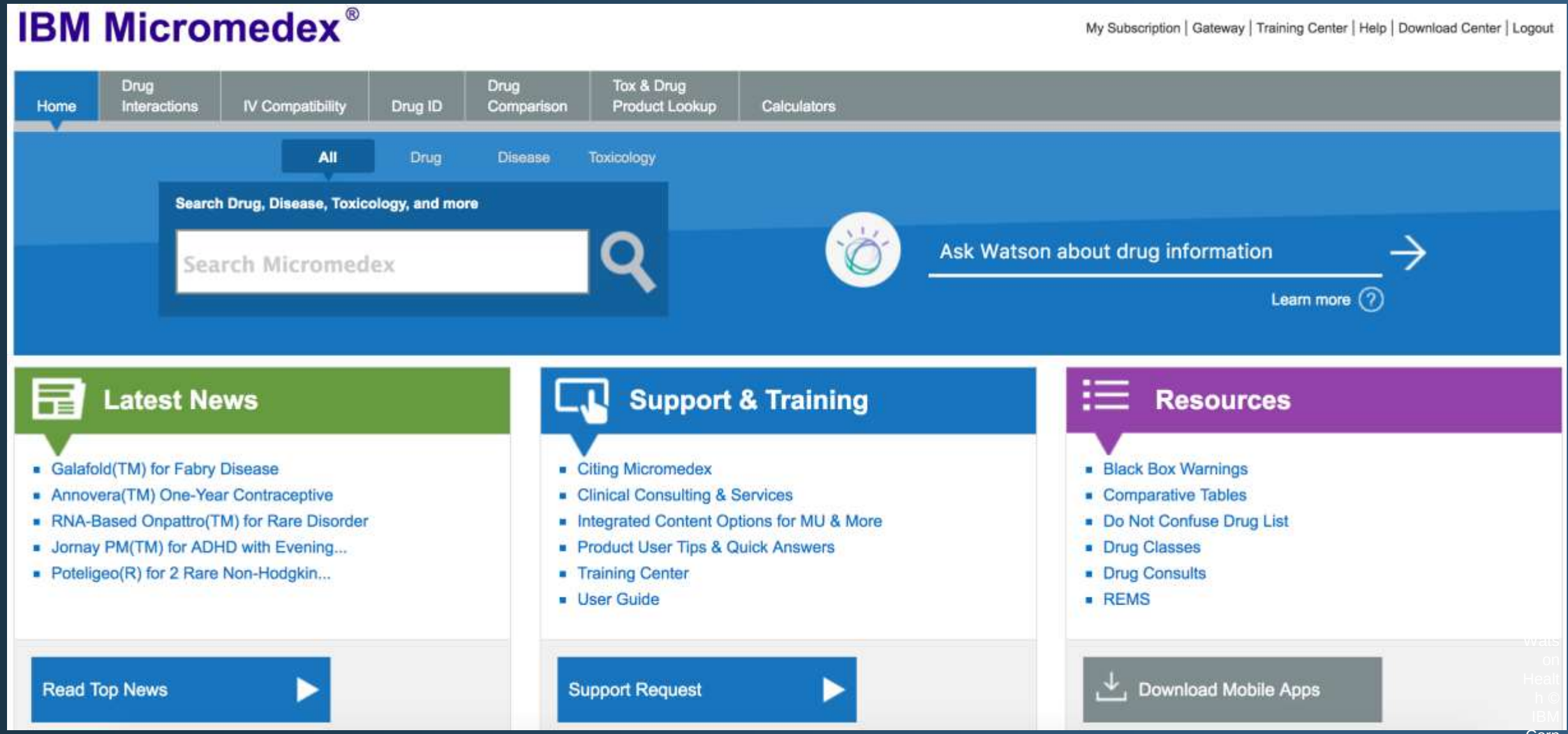
Planned for upcoming presentation at ASCO or in progress

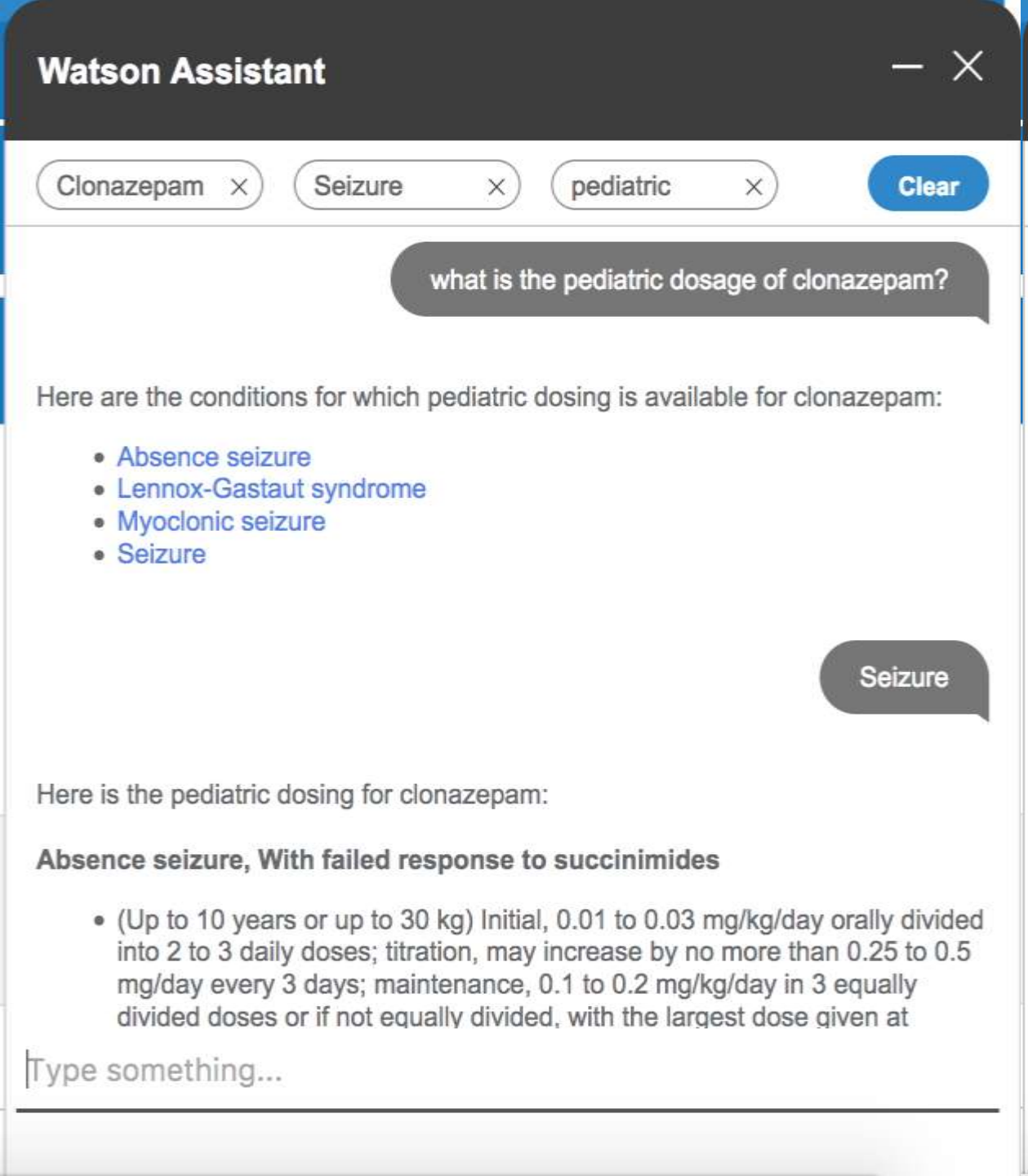
1) Variation of Care

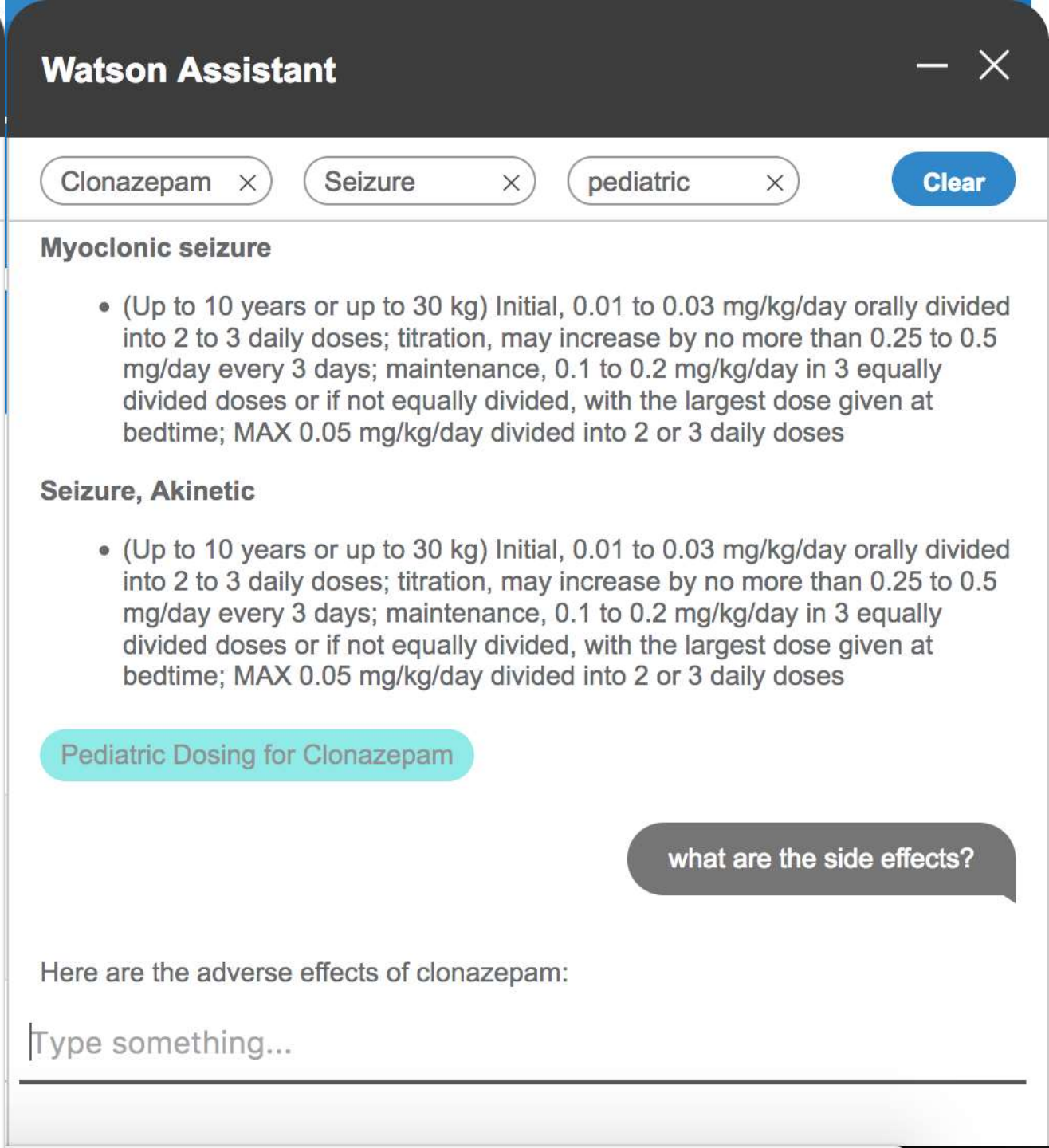
2) Qualitative Studies on Satisfaction with AI

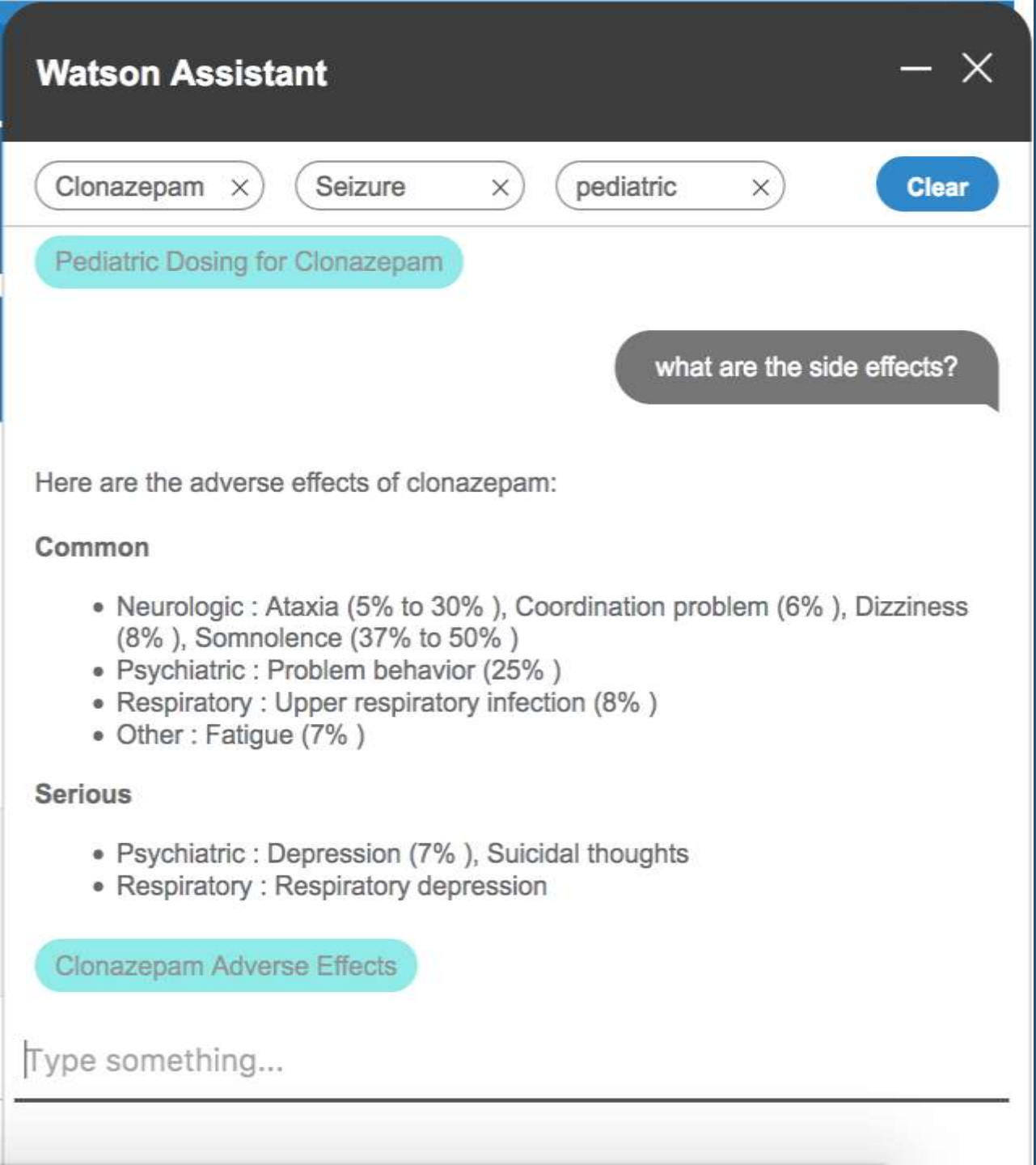
3) Cost of Care

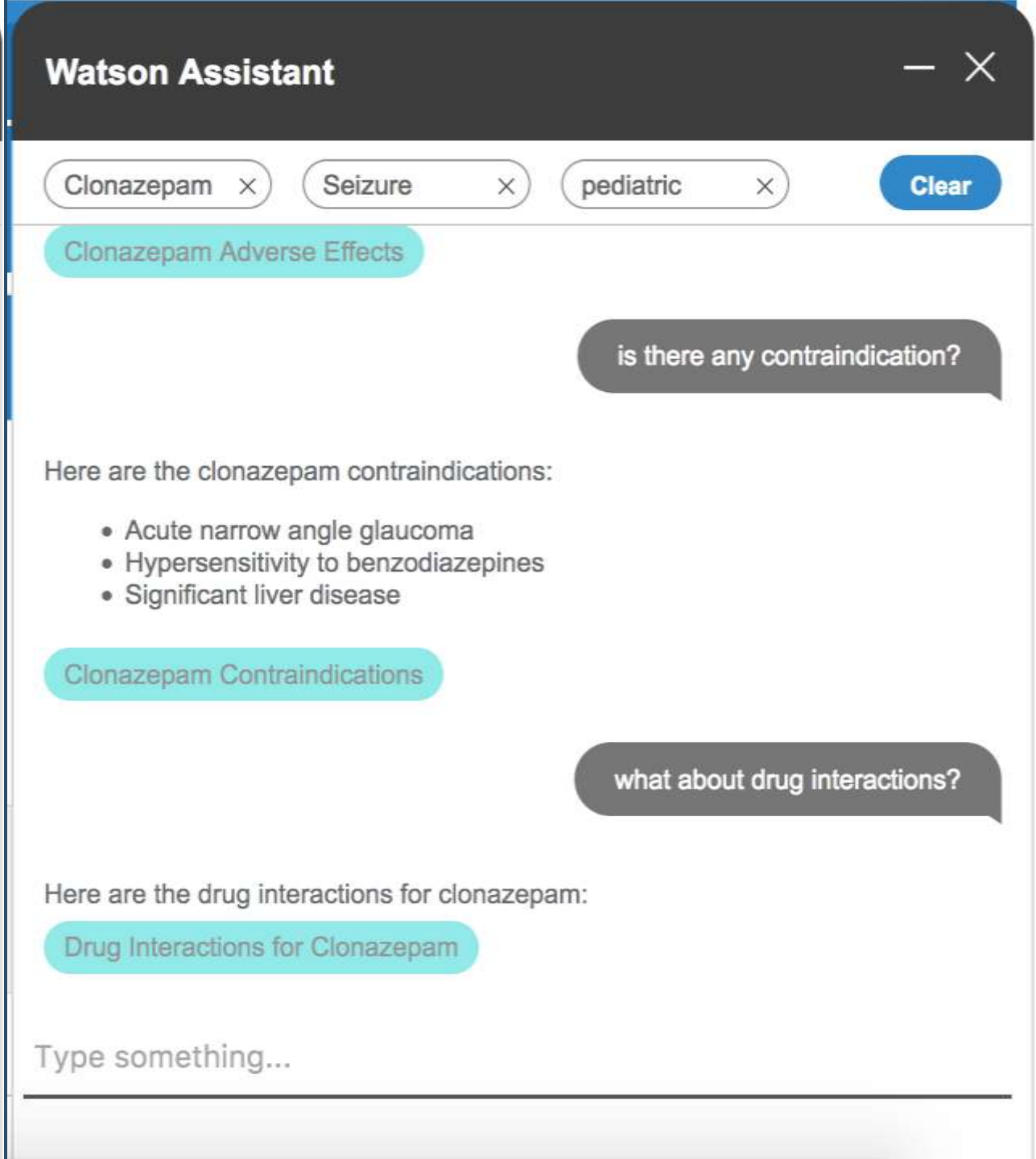
4) Health Equity



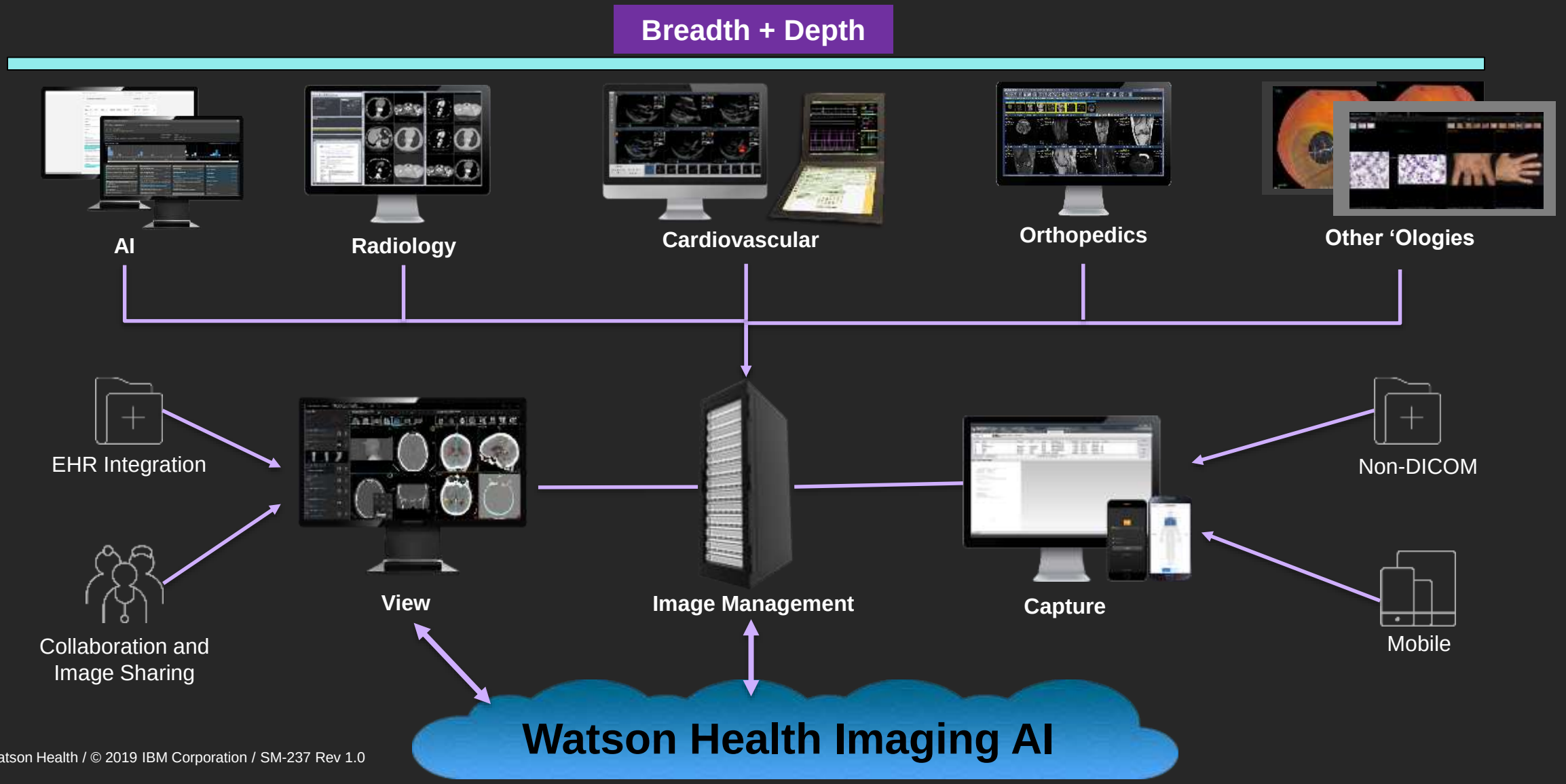

Watson Assistant
Clonazepam
Seizure
pediatric
Clear
what is the pediatric dosage of clonazepam?
Here are the conditions for which pediatric dosing is available for clonazepam:
Absence seizure
Lennox-Gastaut syndrome
Myoclonic seizure
Seizure
Seizure
Here is the pediatric dosing for clonazepam:
Absence seizure, With failed response to succinimides
(Up to 10 years or up to 30 kg) Initial, 0.01 to 0.03 mg/kg/day orally divided into 2 to 3 daily doses; titration, may increase by no more than 0.25 to 0.5 mg/day every 3 days; maintenance, 0.1 to 0.2 mg/kg/day in 3 equally divided doses or if not equally divided, with the largest dose given at
Type something...


Watson Assistant
Clonazepam
Seizure
pediatric
Clear
Myoclonic seizure
(Up to 10 years or up to 30 kg) Initial, 0.01 to 0.03 mg/kg/day orally divided into 2 to 3 daily doses; titration, may increase by no more than 0.25 to 0.5 mg/day every 3 days; maintenance, 0.1 to 0.2 mg/kg/day in 3 equally divided doses or if not equally divided, with the largest dose given at bedtime; MAX 0.05 mg/kg/day divided into 2 or 3 daily doses
Seizure, Akinetic
(Up to 10 years or up to 30 kg) Initial, 0.01 to 0.03 mg/kg/day orally divided into 2 to 3 daily doses; titration, may increase by no more than 0.25 to 0.5 mg/day every 3 days; maintenance, 0.1 to 0.2 mg/kg/day in 3 equally divided doses or if not equally divided, with the largest dose given at bedtime; MAX 0.05 mg/kg/day divided into 2 or 3 daily doses
Pediatric Dosing for Clonazepam
what are the side effects?
Here are the adverse effects of clonazepam:
Type something...


Watson Assistant
Clonazepam
Seizure
pediatric
Clear
Pediatric Dosing for Clonazepam
what are the side effects?
Here are the adverse effects of clonazepam:
Common
Neurologic : Ataxia (5% to 30%), Coordination problem (6%), Dizziness (8%), Somnolence (37% to 50%)
Psychiatric : Problem behavior (25%)
Respiratory : Upper respiratory infection (8%)
Other : Fatigue (7%)
Serious
Psychiatric : Depression (7%), Suicidal thoughts
Respiratory : Respiratory depression
Clonazepam Adverse Effects
Type something...


Watson Assistant
Clonazepam
Seizure
pediatric
Clear
Clonazepam Adverse Effects
is there any contraindication?
Here are the clonazepam contraindications:
Acute narrow angle glaucoma
Hypersensitivity to benzodiazepines
Significant liver disease
Clonazepam Contraindications
what about drug interactions?
Here are the drug interactions for clonazepam:
Drug Interactions for Clonazepam
Type something...

The Watson Health Imaging value proposition



Data explosion and industry challenges: Creating opportunities for AI

Misdiagnoses entail huge costs for organizations

$4 billion is spent on false-positive mammograms in the U.S. each year

Administrative tasks take up significant time

64% of radiologists' time spent on non-interpretive tasks

More physicians are experiencing burnout

51% of physicians experienced at least one symptom of burnout in 2016, a 25% increase in the last four years

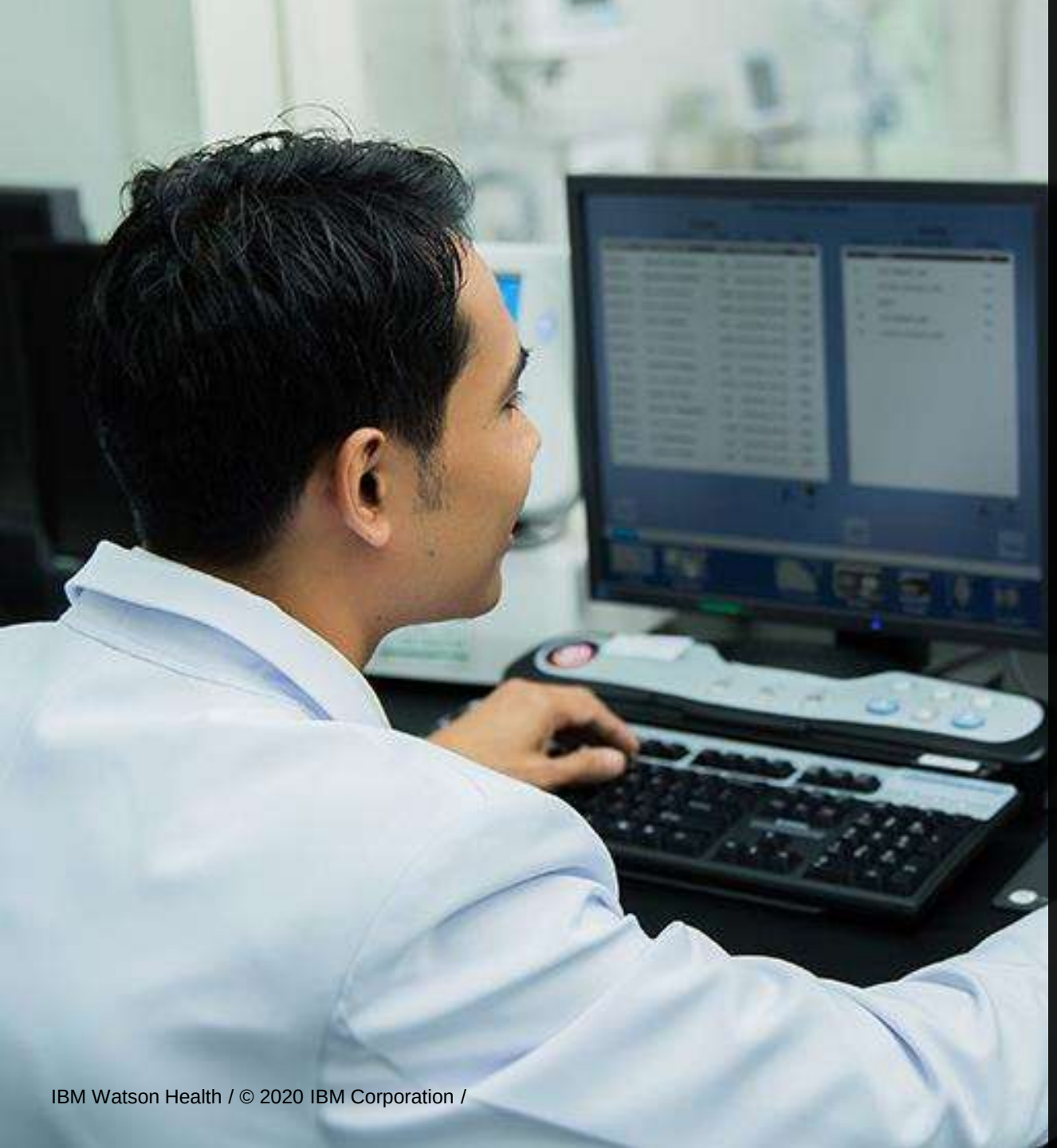
Imaging is generating a huge volume of data

60 billion medical images were generated in 2015 across the U.S.

Patient data is often unstructured

80% of patient data in organizations is unstructured, often lacking relevant context

Sources:
1. http://www.cnbc.com/2015/04/06/breast-cancer-misdiagnoses-cost-4-billion-study.html; http://content.healthaffairs.org/content/34/4/576.abstract
2. http://www.jacr.org/article/S1546-1440(15)00196-9/fulltext
3.http://www.medscape.com/features/slideshow/lifestyle/2017/overview
4-5. http://www.ibmbigdatahub.com/video/ibm-big-data-minute-transforming-unstructured-data-better-healthcare-outcomes



800M

Exams

94B

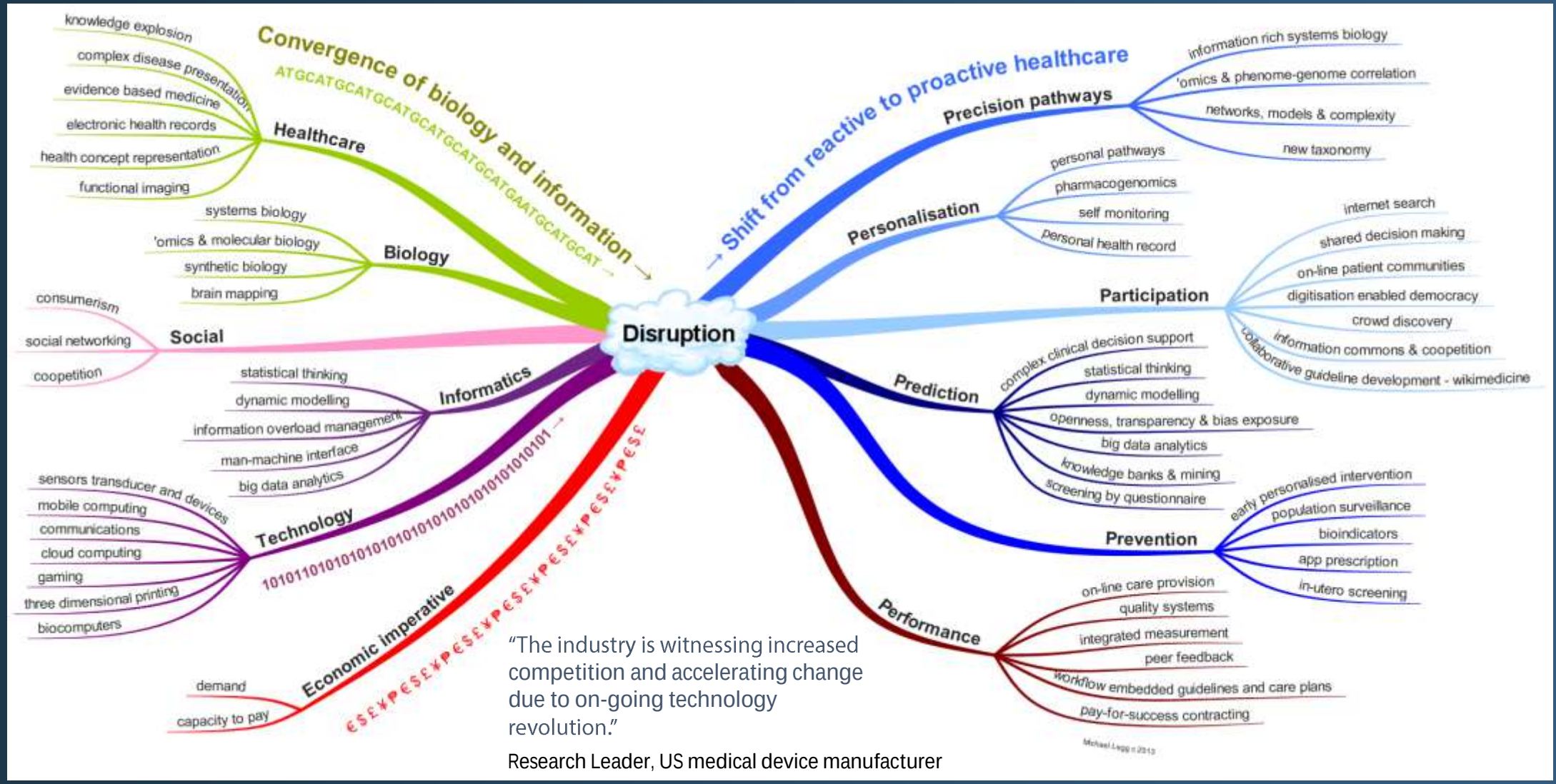
Images

31K

Radiologists

Source: The Advisory Board
The American College of Radiology

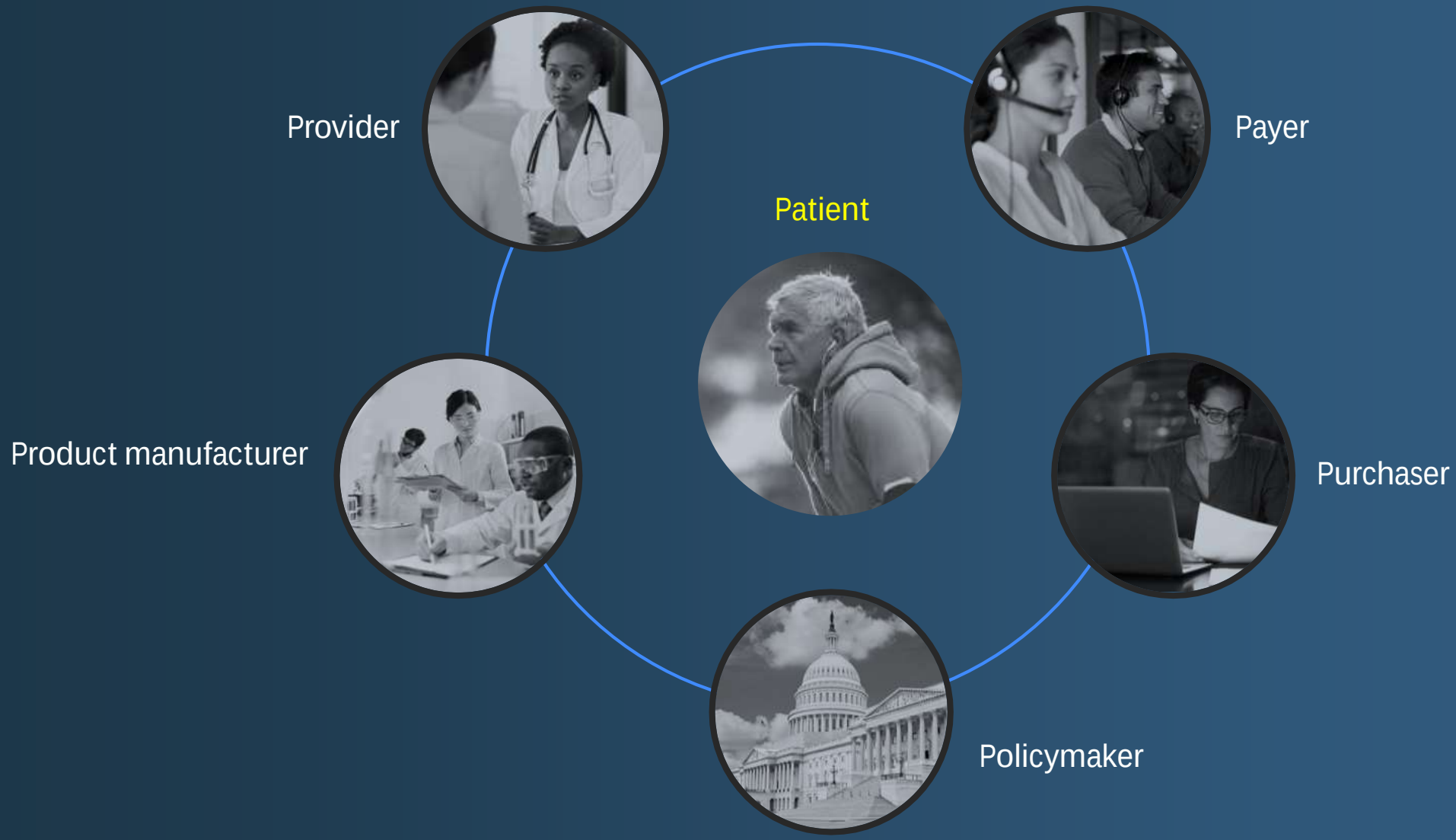
THE HEALTHCARE INDUSTRY NEEDS:
Harness the influx of data to meet the expectations of its constituents



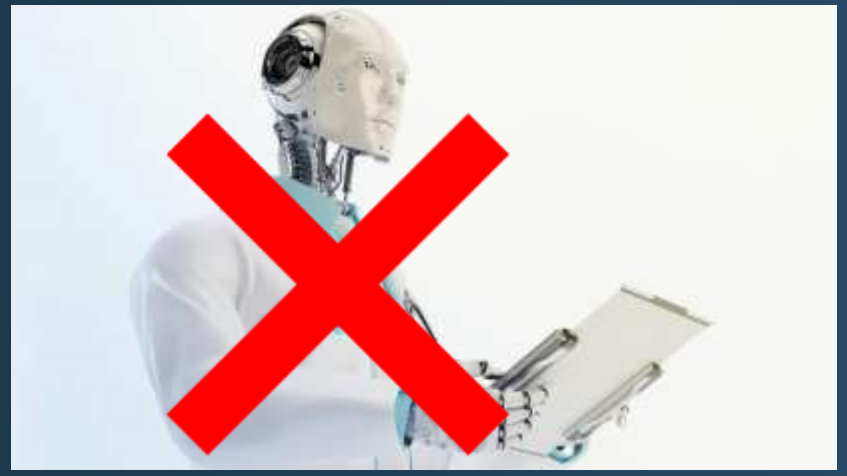
"The industry is witnessing increased competition and accelerating change due to on-going technology revolution."

Research Leader, US medical device manufacturer

AI for All Stakeholders in Health



Nosso futuro será assim?



Esse é nosso futuro em Oncologia


We believe the solutions to the world’s most challenging health issues are out there
Acreditamos que existem soluções para os problemas de saúde mais desafiadores do mundo