



2ND CDDF MULTI-STAKEHOLDER WORKSHOP

THE USE OF REAL-WORLD DATA TO OPTIMISE ONCOLOGY DRUG
DEVELOPMENT AND ACCESS

21-22 November 2019
AMSTERDAM, NETHERLANDS

Clinician Perspective On Real World Data repositories

Jaap Verweij





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The first perspectives: Confusion and Despair





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Categories of RWD definitions and sources

- Category 1: Data collected in a **non-RCT** setting
- Category 2: Data collected in a **non-interventional**/non- controlled setting
- Category 3: Data collected in a **non-experimental** setting
- Category 4: Others

Categories of RWD sources

Category A: Datasources(e.g., databases and registries)

Category B: Study designs that generate RWD (e.g.,observational studies and pragmatic clinical trials[PCTs])



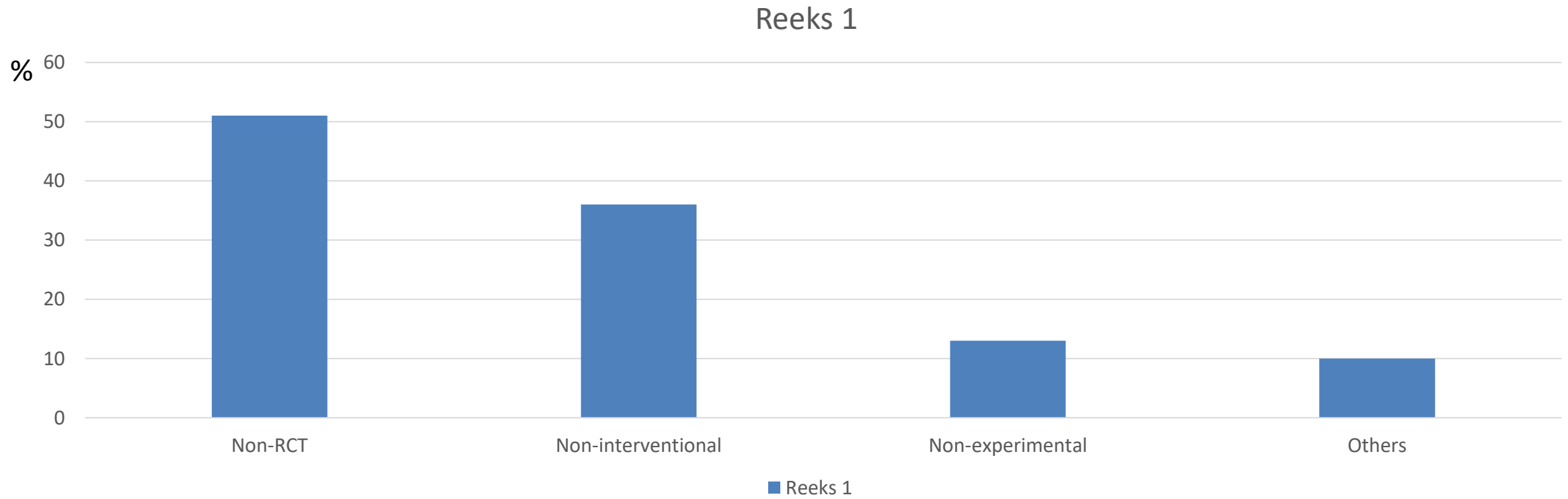


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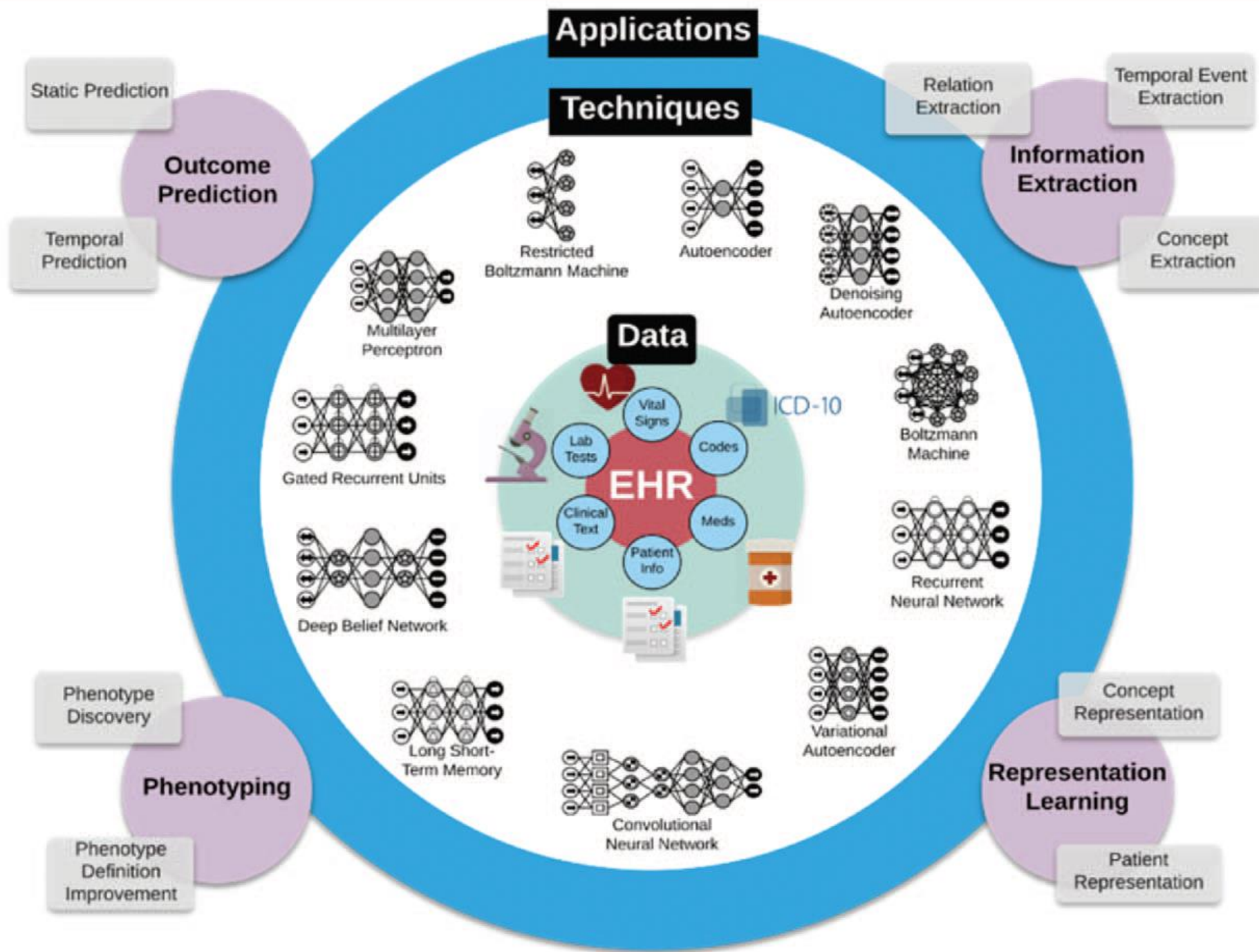
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Frequency of used definitions in literature



From Makady et al, Value Health 2017; 20:858-865





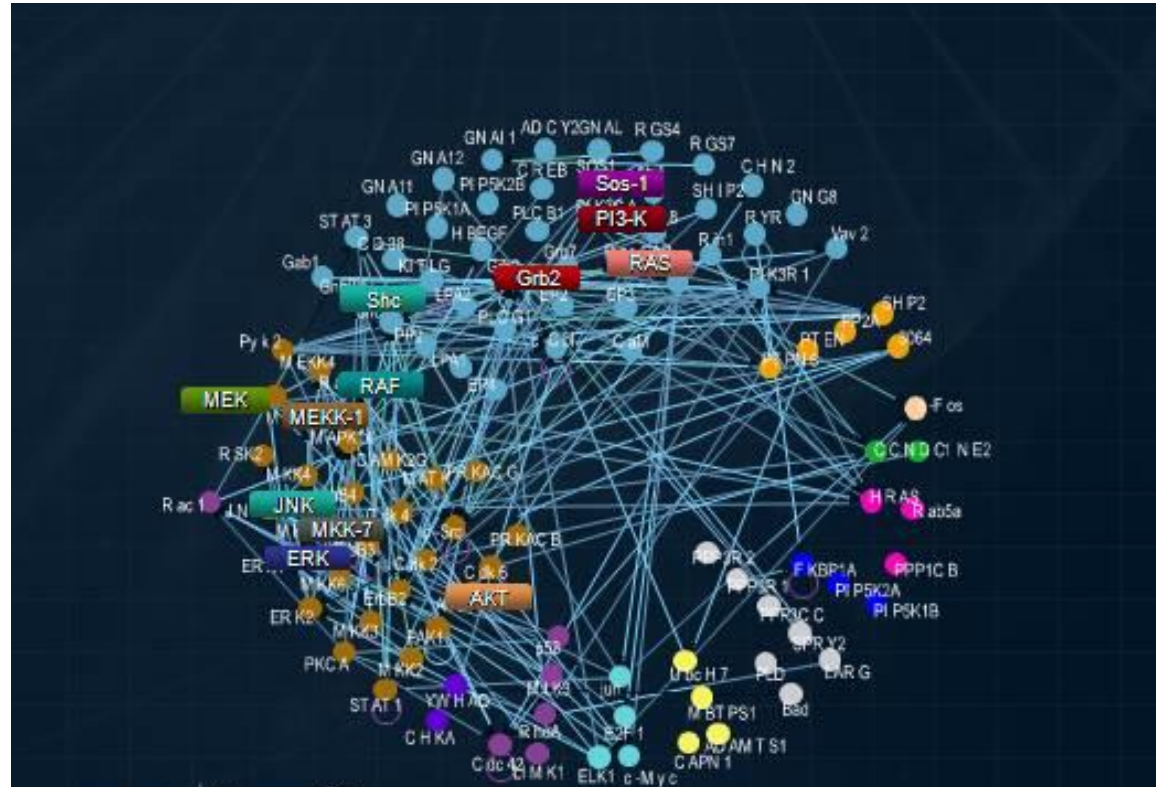
**RWD:
Machine
learning and
algorithm
development**



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The new world of clinicians





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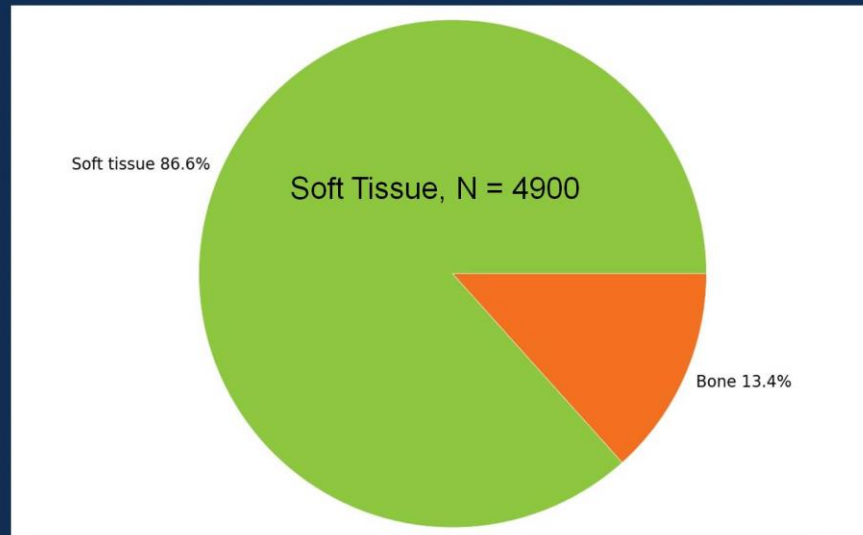
The challenges of the clinical investigator





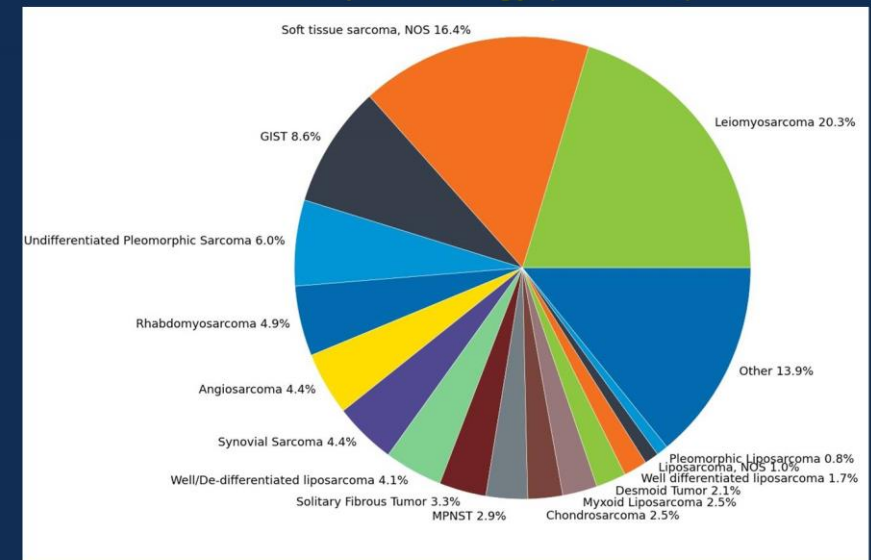
Subtyping a rare disease histologically

Distribution of Soft tissue versus Bone sarcoma (n = 5749)



PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Mrinal Gounder, MSKCC
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56 unique histology (n = 5749)



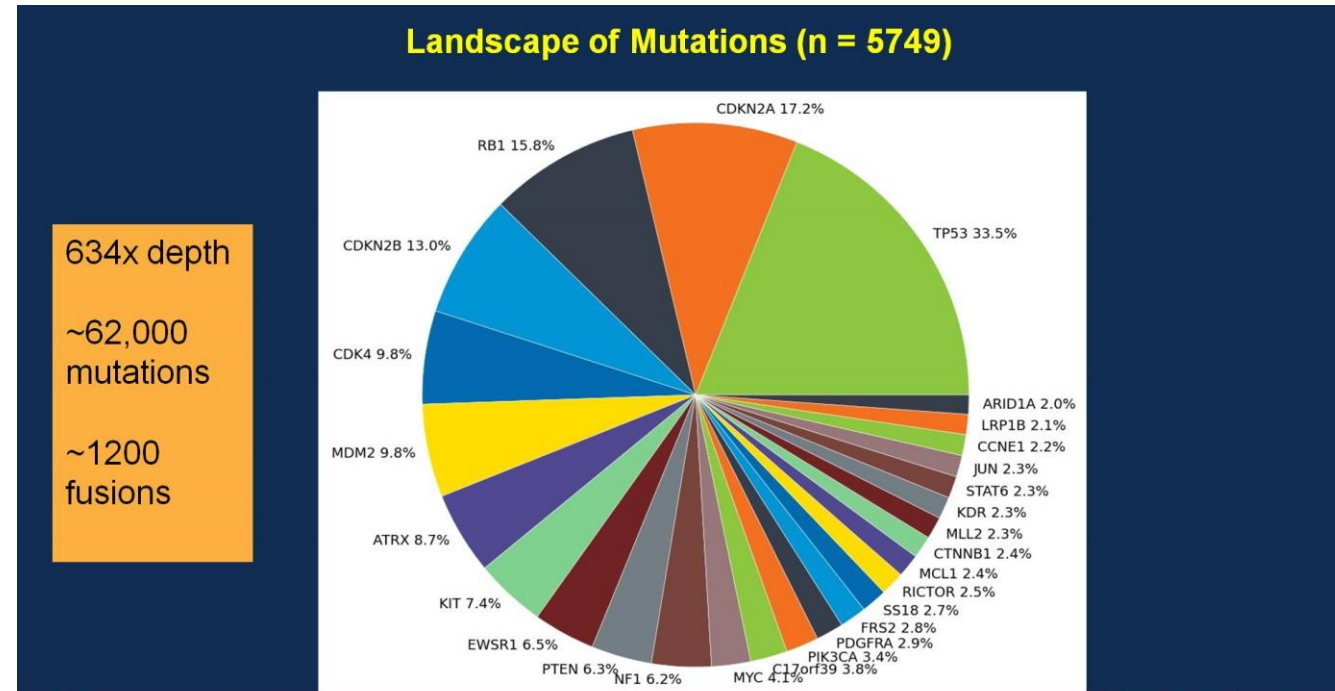
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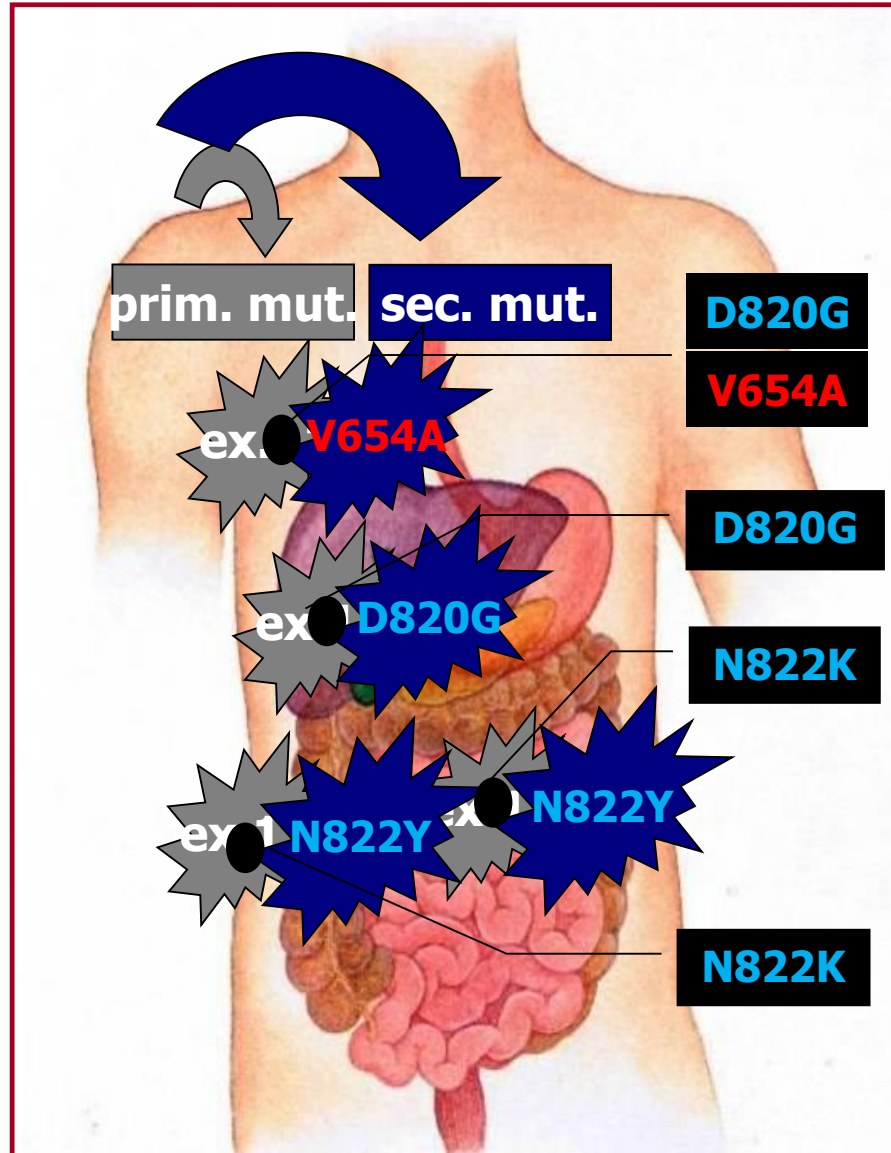


Subtyping subtypes genetically



Subtyping subtypes of subtypes:

GIST: Implications of Mutational Heterogeneity



Drug/ATP binding pocket
Imatinib resistant
Sunitinib sensitive

Kinase activation loop
Imatinib resistant
Sunitinib resistant

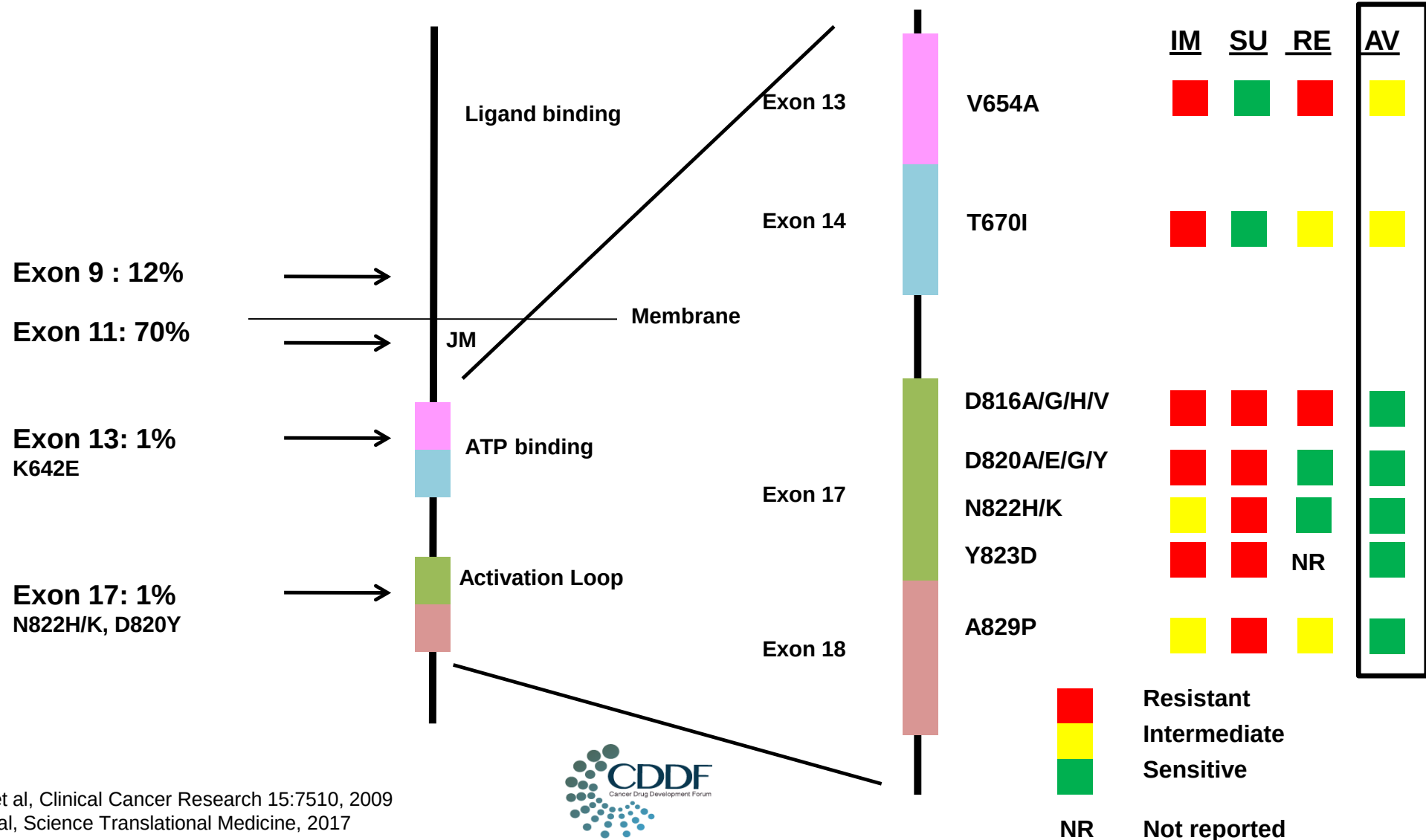


Primary Mutations

Protein Domain

Secondary Mutations

Drug Sensitivity





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The rationale for testing EGFR PKIs in non-small cell lung cancer (NSCLC)

- EGFR (aka HER1 or ErbB1) is a RTK, closely related to three other growth factor receptors: HER2 (neu, ErbB2), HER3 (Erb3), and HER4 (ErbB4)
- The viral oncogene, v-erbB, is a truncated and constitutively activated form of EGFR
- EGFR is expressed in multiple cancer types at elevated levels relative to normal tissues
- Targeting EGFR was predicted to be a novel way to treat EGFR-expressing cancer





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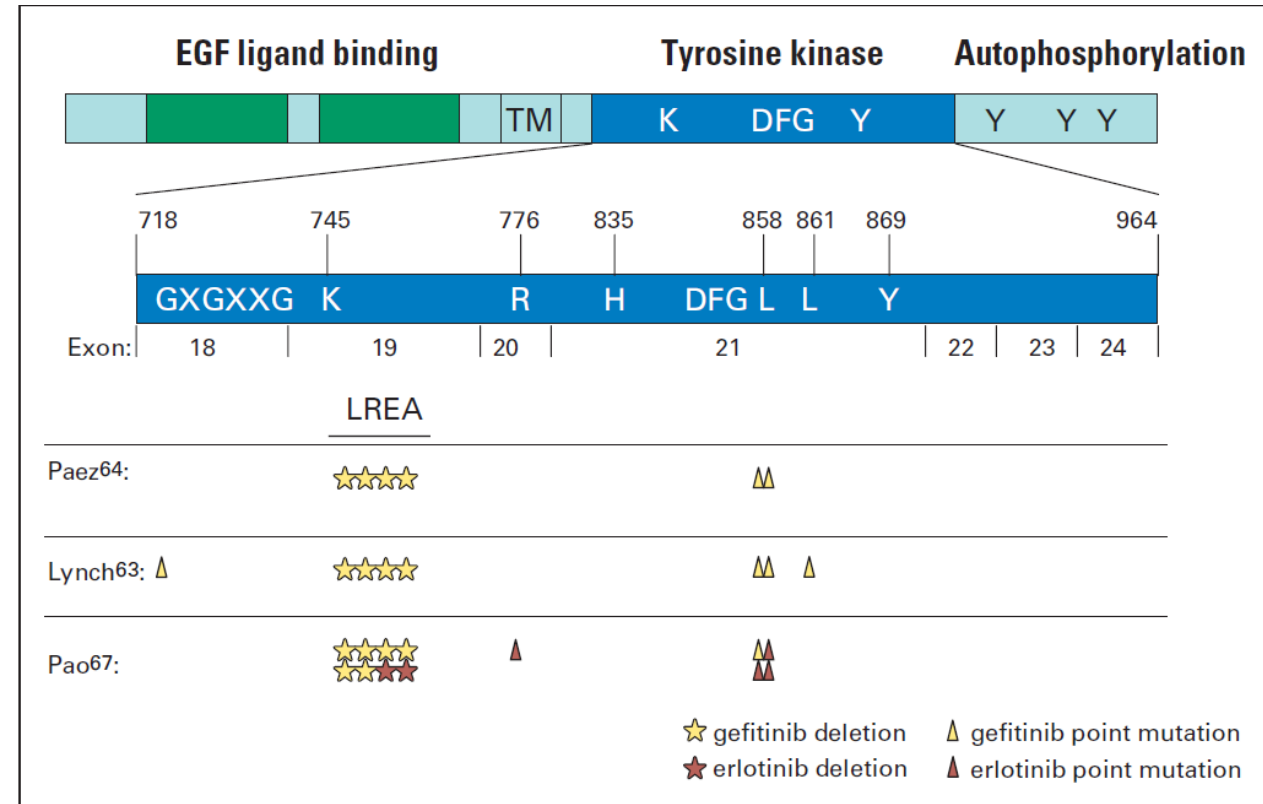
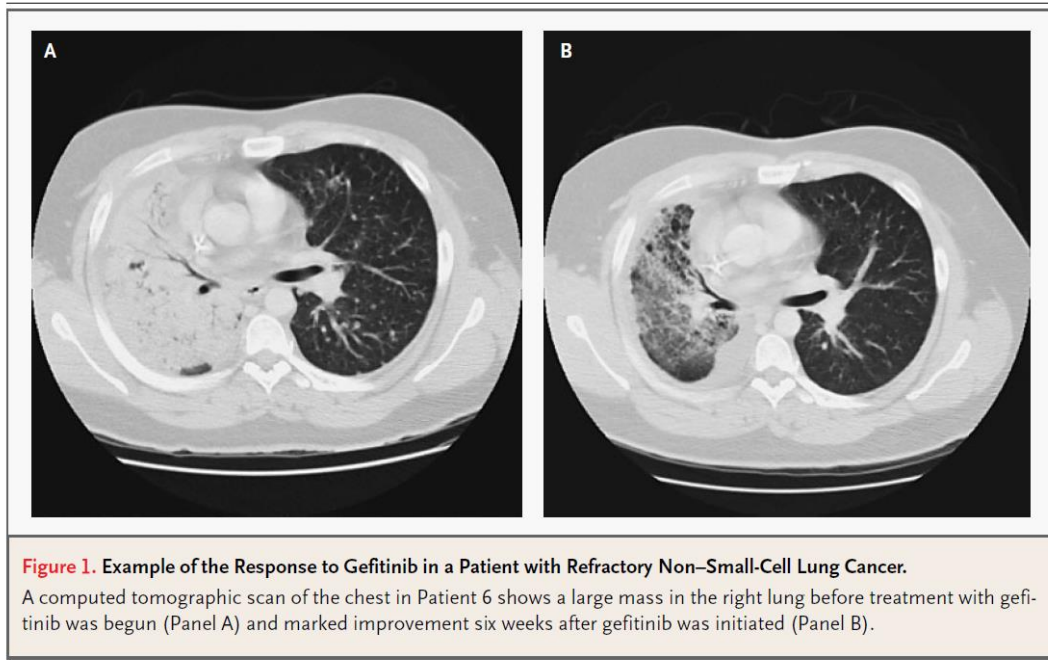
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Clinical activity of EGFR PKIs in NSCLC

- Testing of gefitinib or erlotinib in NSCLC yielded response rates of 9-18% in unselected populations
- **EGFR expression did not predict response**
- Response rates were higher in populations enriched for Asians, never smokers, adenocarcinoma histology, and women

Clinical activity of EGFR PKIs is strongly associated with gain-of-function EGFR mutations





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Clinical activity of EGFR PKIs is strongly associated with gain-of-function EGFR mutations

- 81% of tumors from individuals with partial responses to gefitinib or erlotinib were found to have EGFR mutations
- In contrast, none of 29 refractory tumors had such mutations
- Mutations were more prevalent in non-smokers (51 vs. 9%), females (38 vs. 13%), cases of adenocarcinoma (31 vs. 2%), East Asian (29 vs. 10% US)



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- The medical world is fragmenting into subsets
- So we will be dealing with very small groups of patients

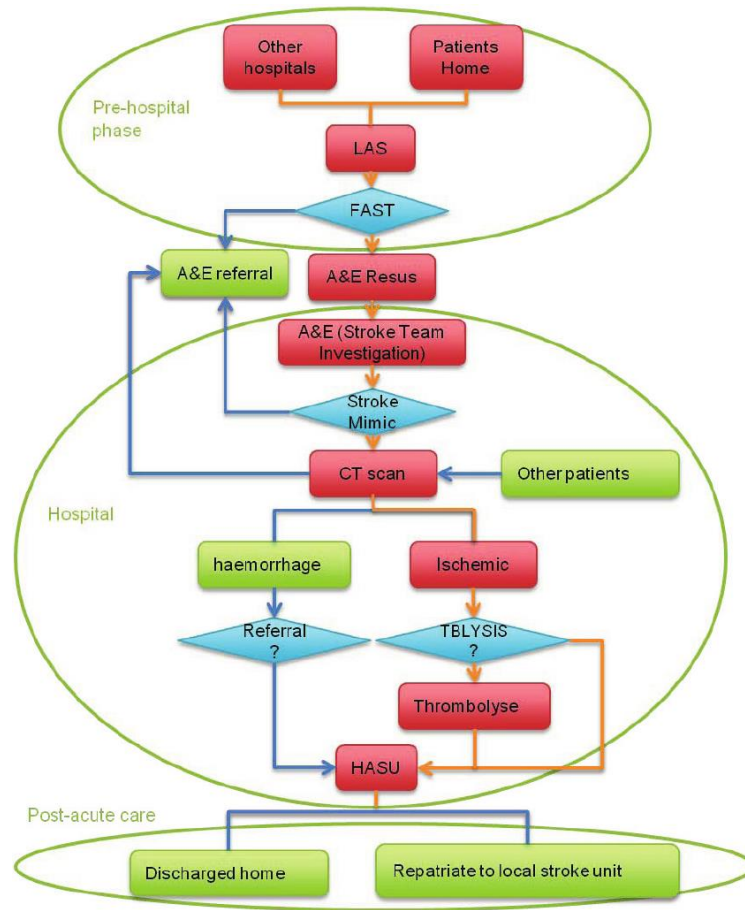


RWD/RWE





The challenges of the practicing clinician





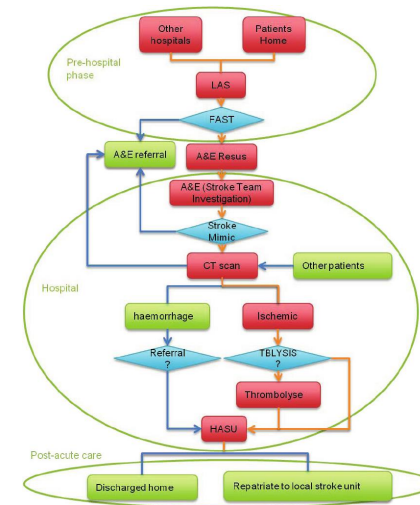
So what's the attraction of data-repositories for the clinician?

For doctors Practicing in hospitals and private clinics?

- Quality controls to pathway adherence
- Options for clinical decision making
- Financial controls
 - Input mostly done by practice assistants (Medical data quality?)

For clinical investigators?

- Options for research
- Concern on privacy and use of genetic data
- Input mostly done by datamanagers and nurses



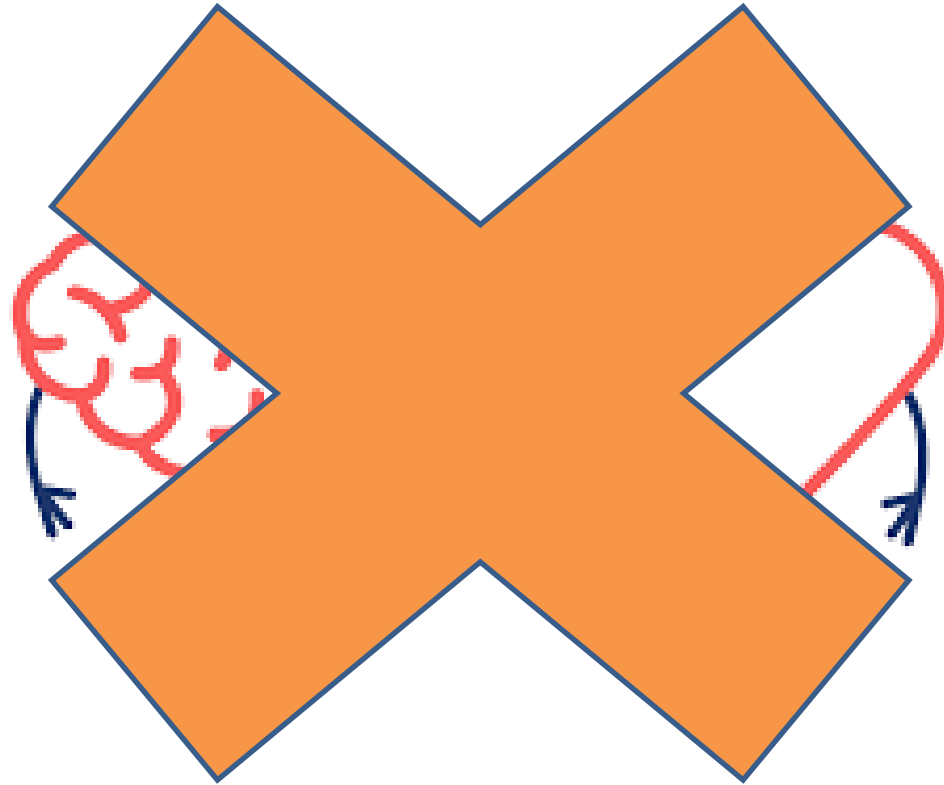


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But the empathy is missing



AND YET.....





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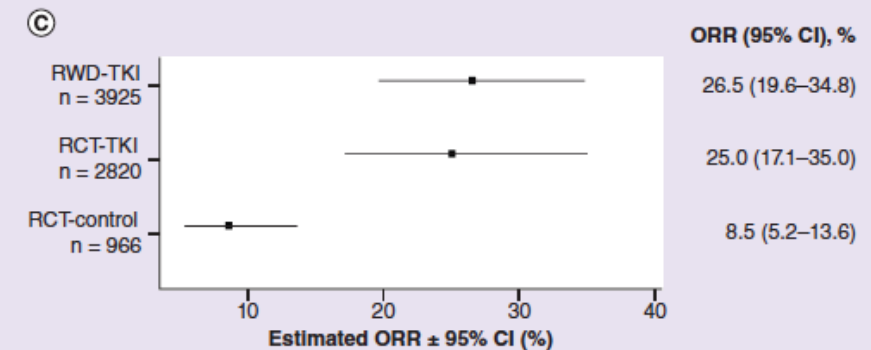
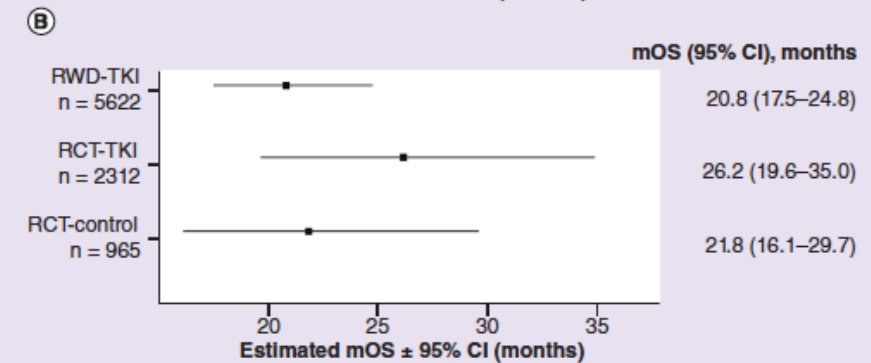
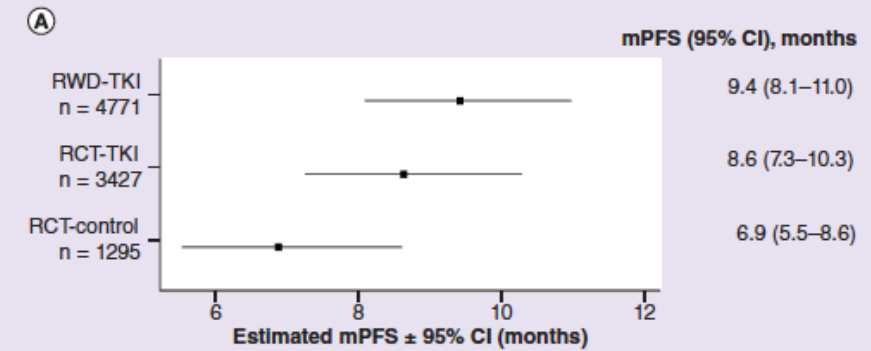
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Google/Ascension deal (Nov. 2019)

- > 2500 medical centers (all non-academic)
- Data use without patient permission?



RCT (N=13) vs RWD (N=22) in RCC





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Get the clinical world to embrace the options





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Challenges to convince clinicians

- Proper and clear definitions of what RWD and RWE means
- Simplify administrative procedures related to data
- Address the issues of quality, completeness, and bias when proposing RWD vs clinical trials



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Thank you for your attention