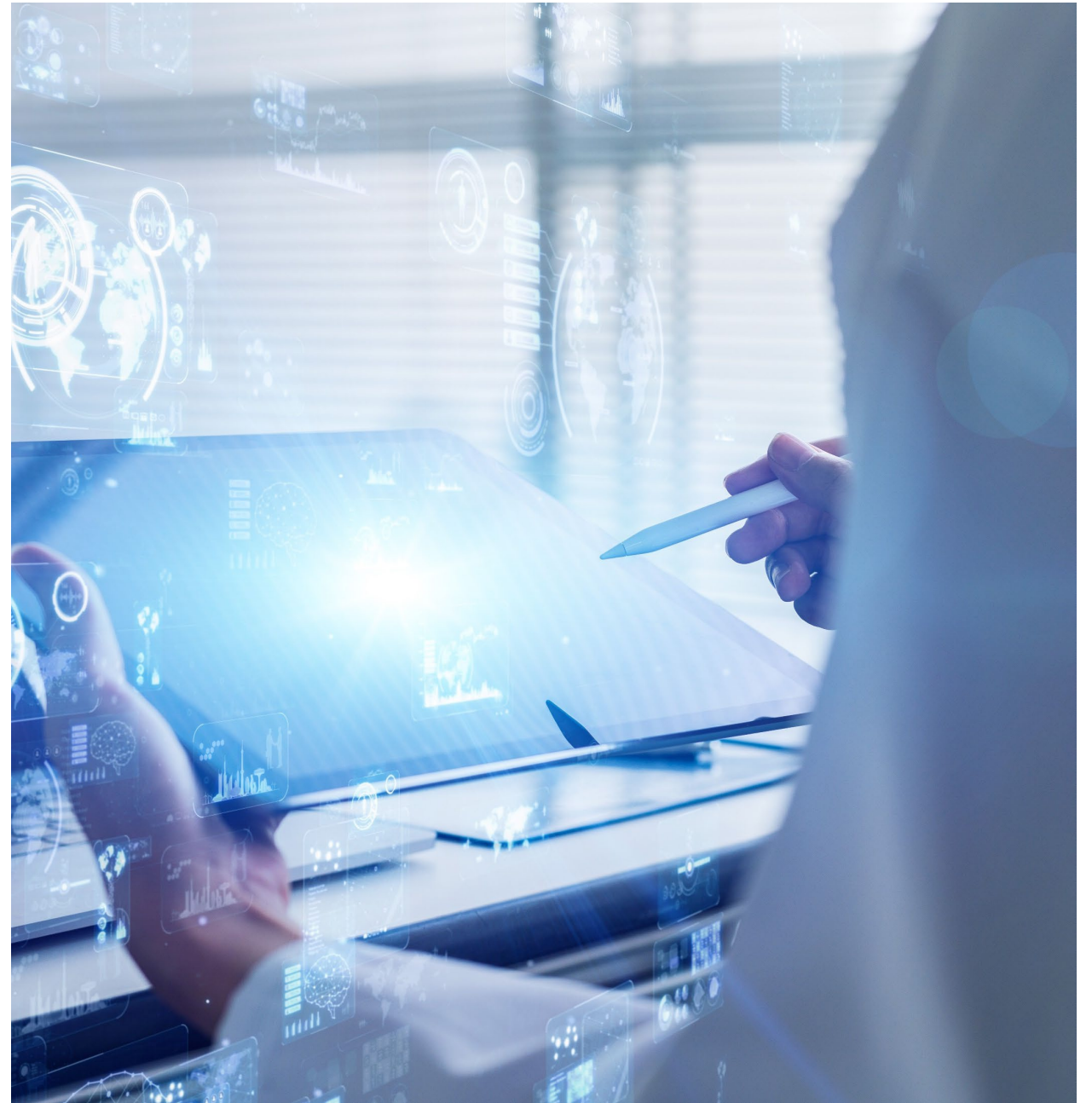


Clinical Trial Notifications Triggered by Artificial Intelligence–Detected Cancer Progression

Ken Kehl, MD, MPH
Dana-Farber Cancer
Institute



Can we use AI to find “clinical trial-ready” patients?

Historically, less than 10% of adults with cancer enroll in clinical trials

- Yet trials often struggle to reach their accrual goals

Many trials of novel therapies have specific molecular criteria

- Tools have been developed to match patients to trials based on these criteria

Computational clinical trial matching tools

Commercial

- IBM Watson (inactive)
- Tempus Link
- SYNERGY-AI (Massive Bio) – patient-directed/phone app
- OncoTrials (Flatiron)
- OncoLens
- Triomics / OncoLLM
- TrialinQ (ConcertAI)
- TriNetX
- IQVIA
- Antidote (patient-directed)

Academic / open

- TrialGPT (NIH): Retrieve, criterion match, trial-level ranking
- Clinical Trial Patient Matching (CTPM): Yale
- MatchMiner: Dana-Farber



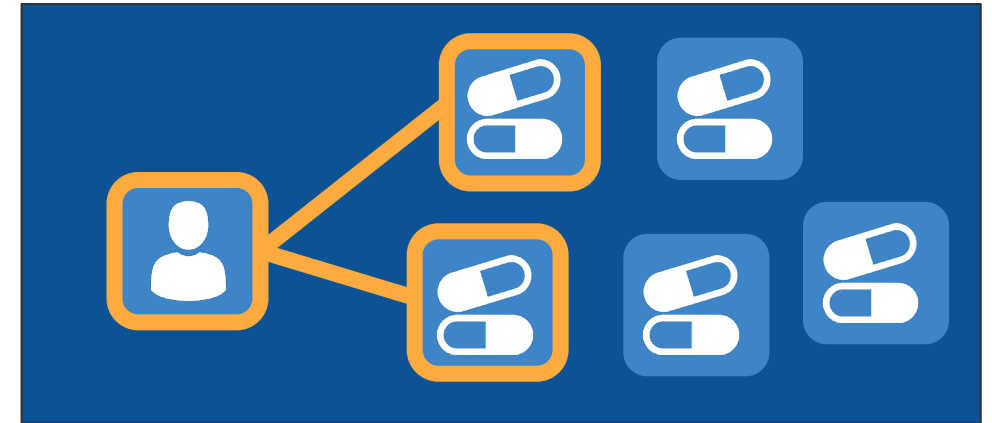
MatchMiner: Connecting Patients and Trials

Trial-centric mode



Recruit patients for a specific genomically-targeted trial

Patient-centric mode



Identify genomically-targeted trial options for an individual patient

MatchMiner interface

The screenshot displays the MatchMiner Patient-Centric Matching interface. On the left, the 'Patient' section shows details for TCGA-38-4627, including MRN, Date of Birth (23 Sep 1952), Primary Cancer Type (Lung Adenocarcinoma), Biopsy Site (Lung), Biopsy Site Type (Diagnosis Pending), Sample ID (TCGA-38-4627-01), and Report Date (6 Mar 2012). Below this is the 'Filters' section, which is annotated with a red box and the label 'Filter Matching Trials'. The filters include: Gene (Mutant), Gene (Wildtype), Tumor Type, Hormone Receptor, Age, Disease Status (with checkboxes for Advanced (6), Localized (1), Locally Advanced (5), Metastatic (5), and Recurrent (4)), Drug, and Phase. The main area is titled 'Clinical trial matches' and is annotated with a red box and the label '8 TRIAL MATCHES'. It shows a 'Total Number of Trial Matches' of 8. Below this, a 'Genomic rationale for match' section explains that MatchMiner has identified 8 potential precision medicine clinical trial matches based on genomic profiling results. The 'Results' section displays a table of trial matches. The first match is 'AZD9291 + NAVITOCCLAX IN EGFR-MUTANT NSCLC', with a 'Variant-Level Match Tier 3' for 'EGFR p.L858R'. The second match is 'NO EGFR p.T790M', also with a 'Variant-Level Match Tier 3'. Both matches are annotated with a red box and the label 'Clinical Trial Status'. The table columns are: Genomic match, Protocol #, Disease Center, Coordinating Center, and DFCI Trial Status. The 'DFCI Trial Status' column contains a green button labeled 'OPEN TO ACCRUAL' for each match. The interface also includes a 'Filters' section on the left, which is annotated with a red box and the label 'Filter Matching Trials'. The filters include: Gene (Mutant), Gene (Wildtype), Tumor Type, Hormone Receptor, Age, Disease Status (with checkboxes for Advanced (6), Localized (1), Locally Advanced (5), Metastatic (5), and Recurrent (4)), Drug, and Phase.

Total Number of Trial Matches

Genomic rationale for match

Clinical Trial Status

Filter Matching Trials

8 TRIAL MATCHES

EGFR p.L858R
Variant-Level Match
Tier 3

AZD9291 + NAVITOCCLAX IN EGFR-MUTANT NSCLC
Protocol No: 16-714
DFCI & Overall Principal Investigator: Oxnard, Geoffrey R

EGFR **Non-Small Cell Lung Cancer** **Adults**
Advanced **Metastatic** **AZD9291**
NAVITOCCLAX **Phase I**

NO EGFR
p.T790M
Variant-Level Match
Tier 3

NO EGFR
p.T790M
Variant-Level Match
Tier 3

EGFR **Non-Small Cell Lung Cancer** **Adults**
Untreated **Advanced** **Metastatic**
GEFITINIB **OSIMERTINIB** **Phase I**

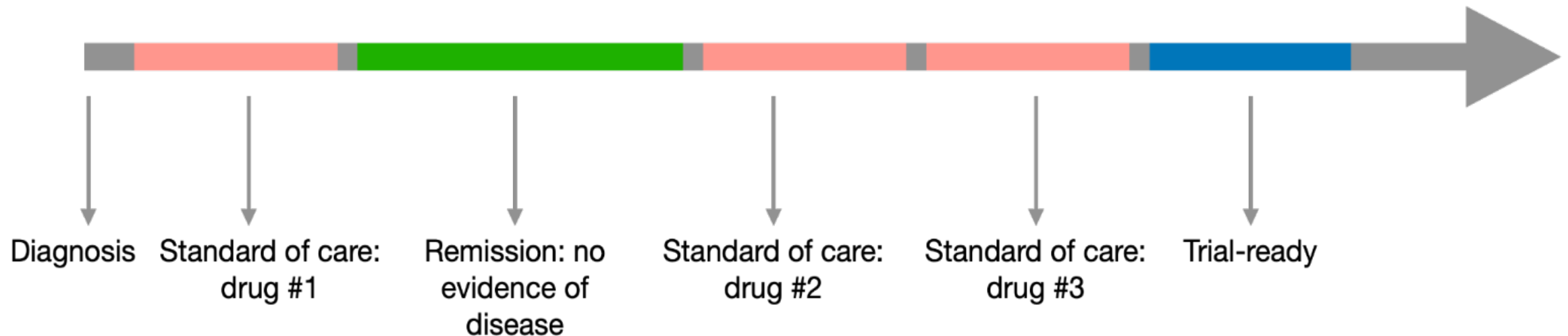
OPEN TO ACCRUAL

OPEN TO ACCRUAL

Screenshot of MatchMiner Patient-Centric Matching (Simulated data shown).

Trial Readiness: The Problem

- MatchMiner matches all living patients to genomic trials/filters
- However, patients are often not 'trial-ready'



Slide courtesy of Tali Mazor, PhD (DFCI Matchminer team)

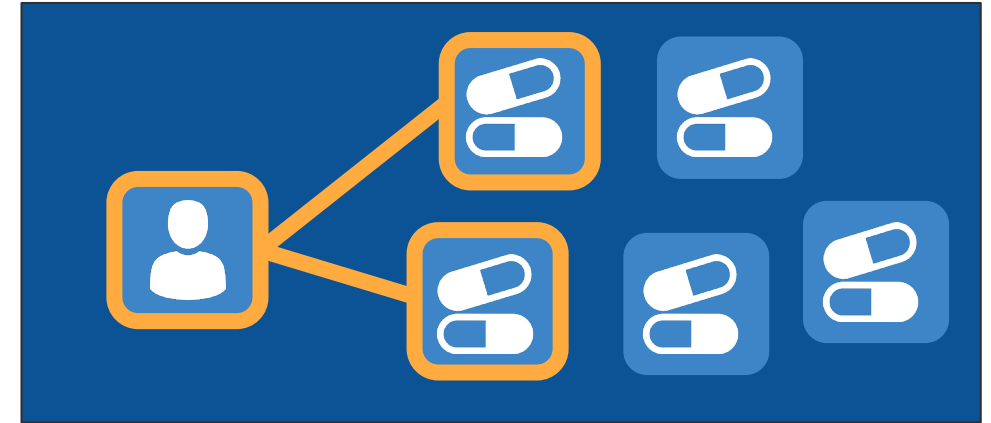
Trial readiness: The problem

Trial-centric mode



Too many patients: Filters return too many patients to review, most of whom are not trial-ready anyway.

Patient-centric mode



Notification overload: Attempts at 'push notifications' to providers mostly include patients that are not trial-ready, therefore providers ignore notifications (and get annoyed at us).

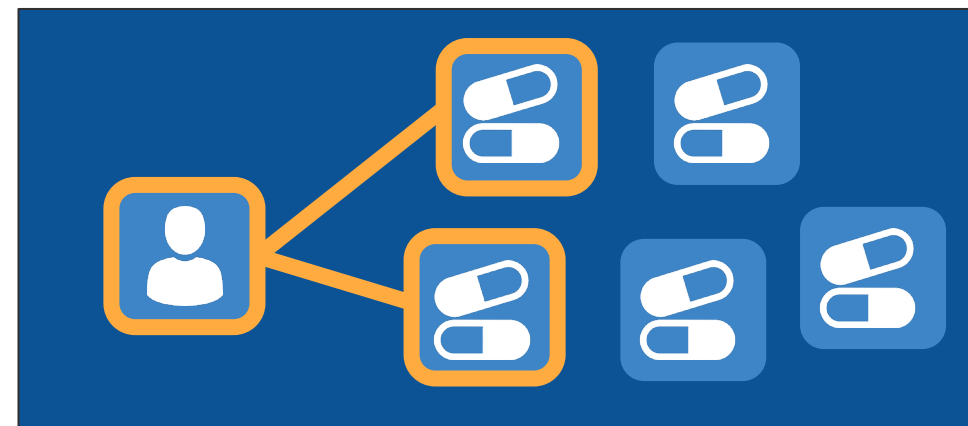
Trial readiness: The problem

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Patient-centric mode



Notification overload: Attempts at 'push notifications' to providers mostly include patients that are not trial-ready, therefore providers ignore notifications (and get annoyed at us).

We have AI models to extract clinical data from imaging reports

- Propensity to change treatment within 30 days
- Probability of mortality within 6 months
- Progression of disease
- Brain metastases

Clinical Inflection Point Detection on the Basis of EHR Data to Identify Clinical Trial–Ready Patients With Cancer

Kenneth L. Kehl, MD, MPH¹; Stefan Groha, PhD¹; Eva M. Lepisto, MA, MSc¹; Haitham Elmarakeby, PhD¹; James Lindsay, PhD¹; Alexander Gusev, PhD¹; Eliezer M. Van Allen, MD¹; Michael J. Hassett, MD, MPH¹; and Deborah Schrag, MD, MPH¹

Assessment of Deep Natural Language Processing in Ascertaining Oncologic Outcomes From Radiology Reports

Kenneth L. Kehl, MD, MPH^{1,2,3}; Haitham Elmarakeby, PhD³; Mizuki Nishino, MD, MPH⁴; [et al](#)

[» Author Affiliations](#) | [Article Information](#)

JAMA Oncol. 2019;5(10):1421-1429. doi:10.1001/jamaoncol.2019.1800

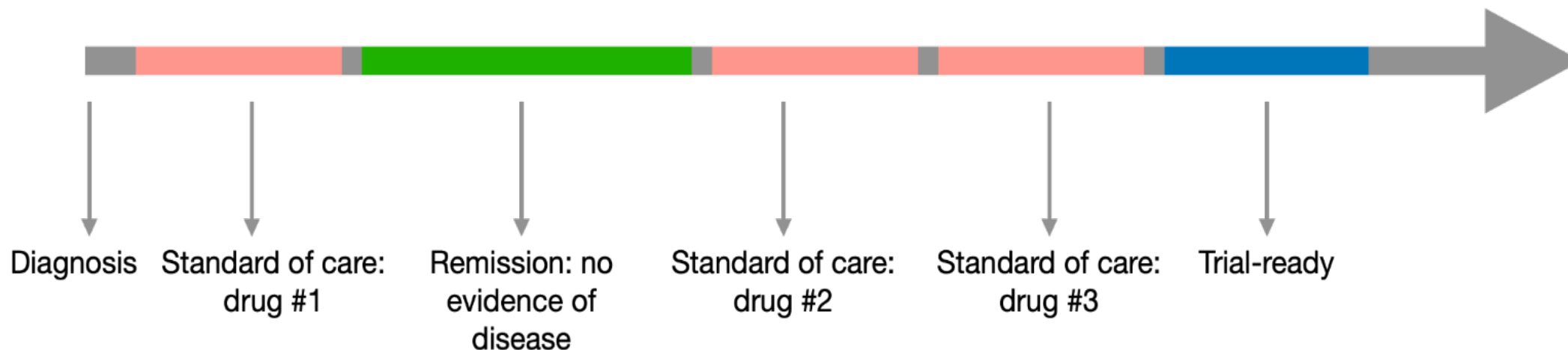
Artificial intelligence-aided clinical annotation of a large multi-cancer genomic dataset

[Kenneth L. Kehl](#) [✉](#), [Wenxin Xu](#), [Alexander Gusev](#), [Ziad Bakouny](#), [Toni K. Choueiri](#), [Irbaz Bin Riaz](#), [Haitham Elmarakeby](#), [Eliezer M. Van Allen](#) & [Deborah Schrag](#)

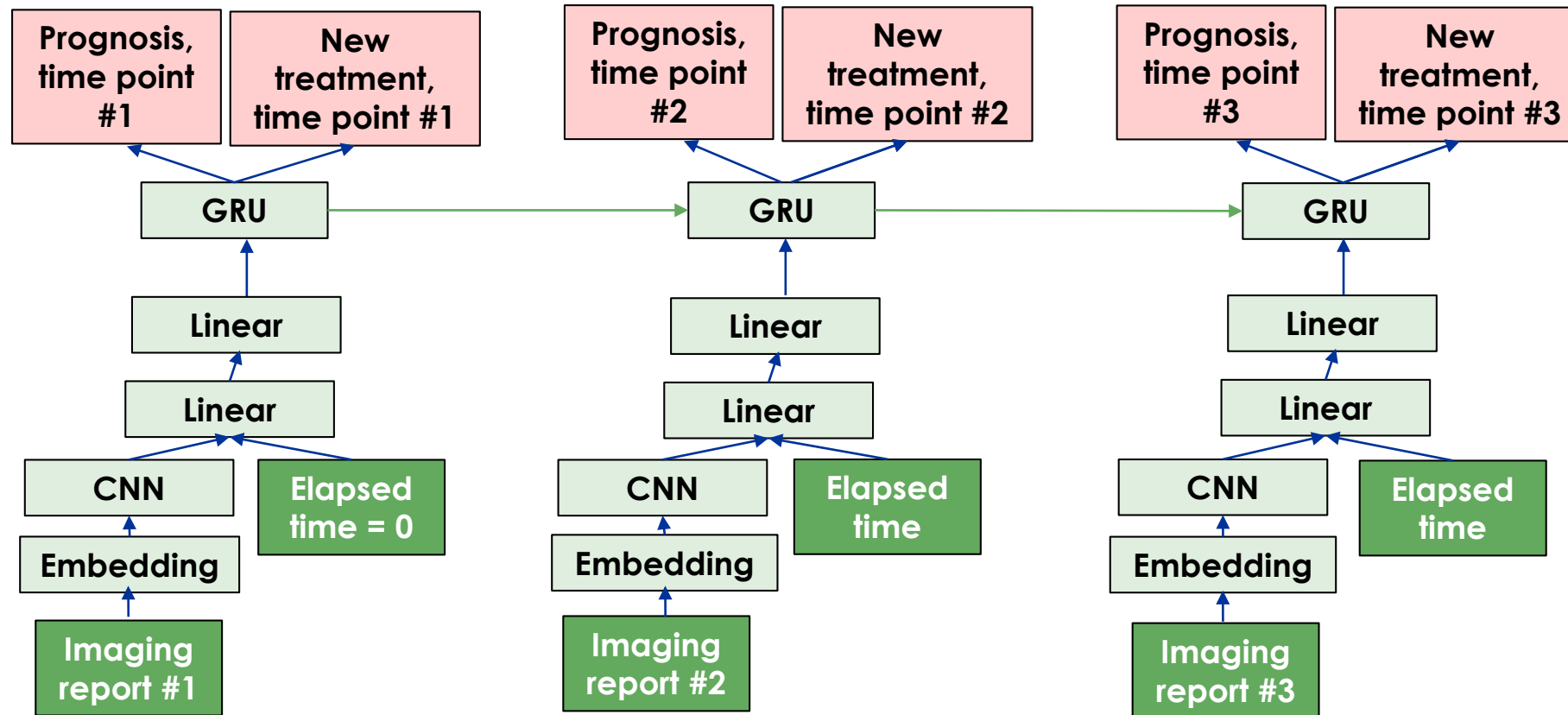
[Nature Communications](#) **12**, Article number: 7304 (2021) | [Cite this article](#)

Trial readiness: The Problem

- MatchMiner matches patients to trials based on genomics
- However, patients are often not “trial-ready.”
- Can we train an AI model to find “trial-ready” patients?



Modeling for one patient



Finding patients for trials: Implementation pilot

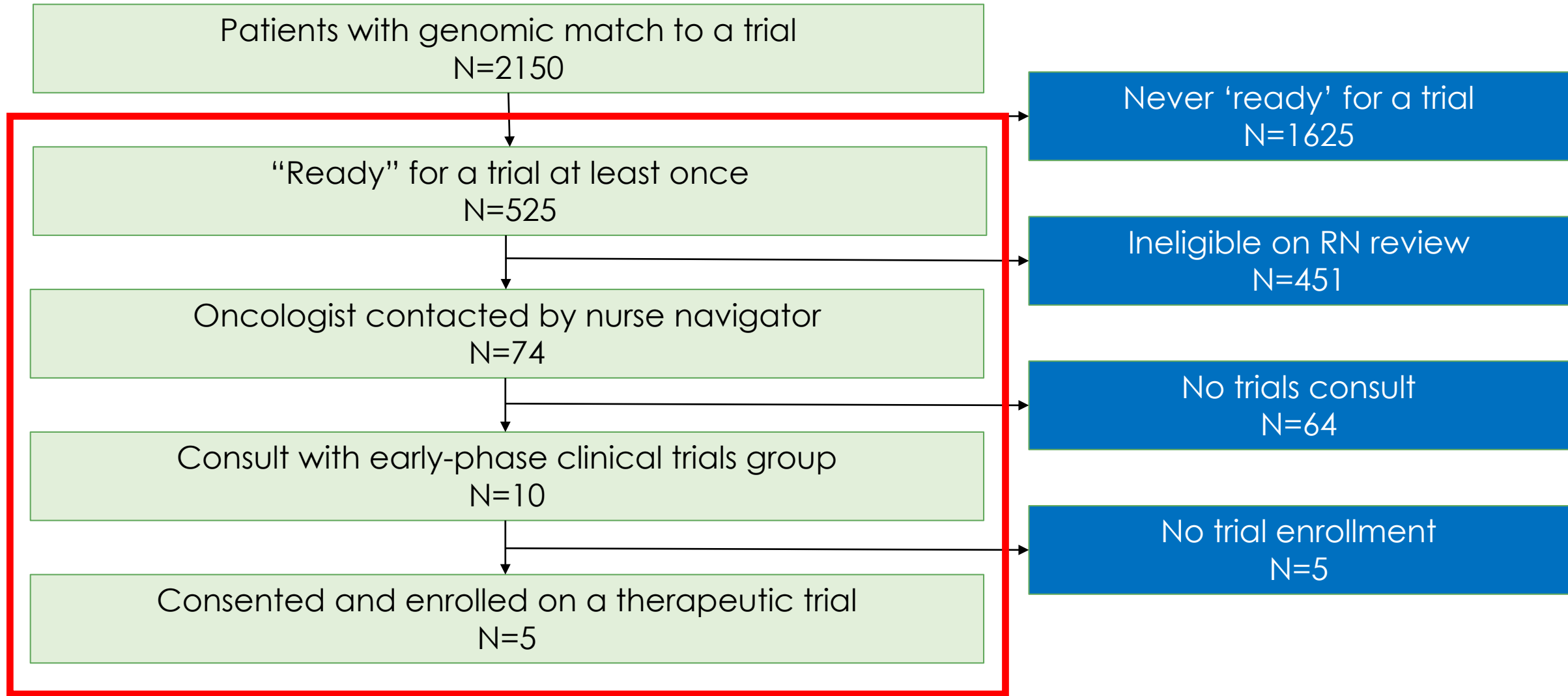
Disease center

- Center for Cancer Therapeutic Innovation
 - Early-phase studies

Intervention

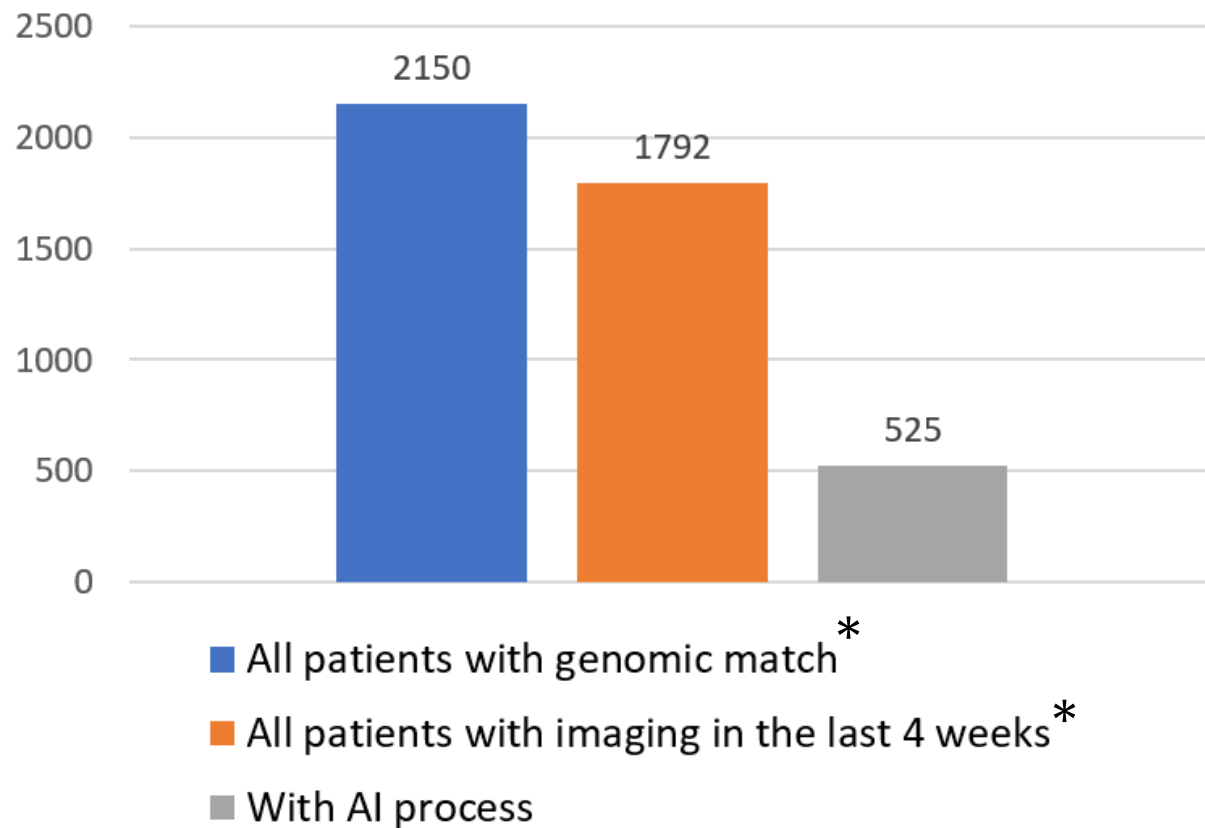
- Weekly spreadsheets providing predictions of clinical trial “readiness” based on propensity to initiate new treatment within 30 days
- Emailed to small group of clinicians and research staff in each disease center

Nine-month pilot results

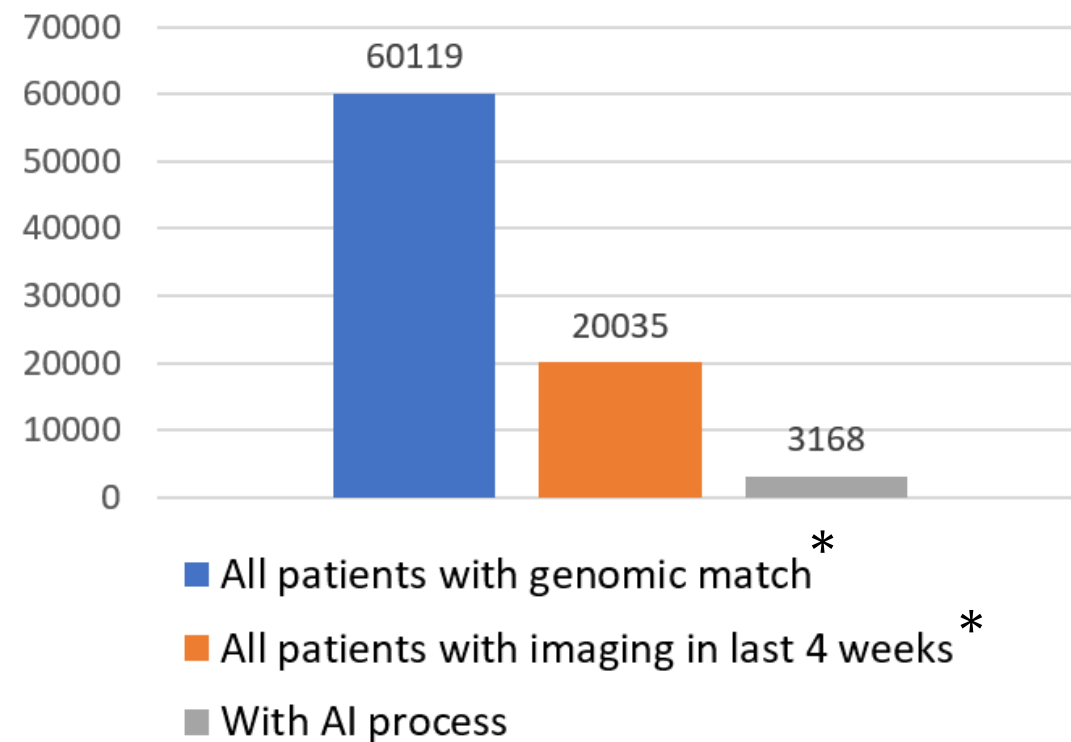


Volume of manual review required

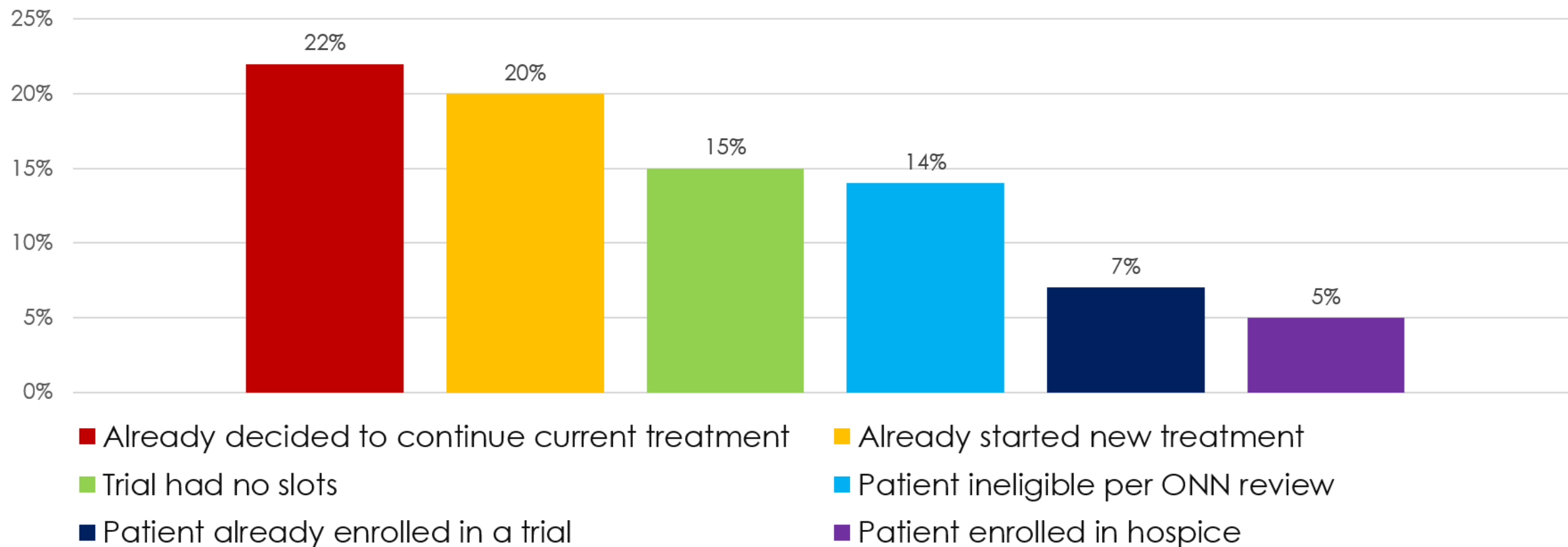
Patients ever requiring manual review



Patient-trial matches requiring manual review at a given time



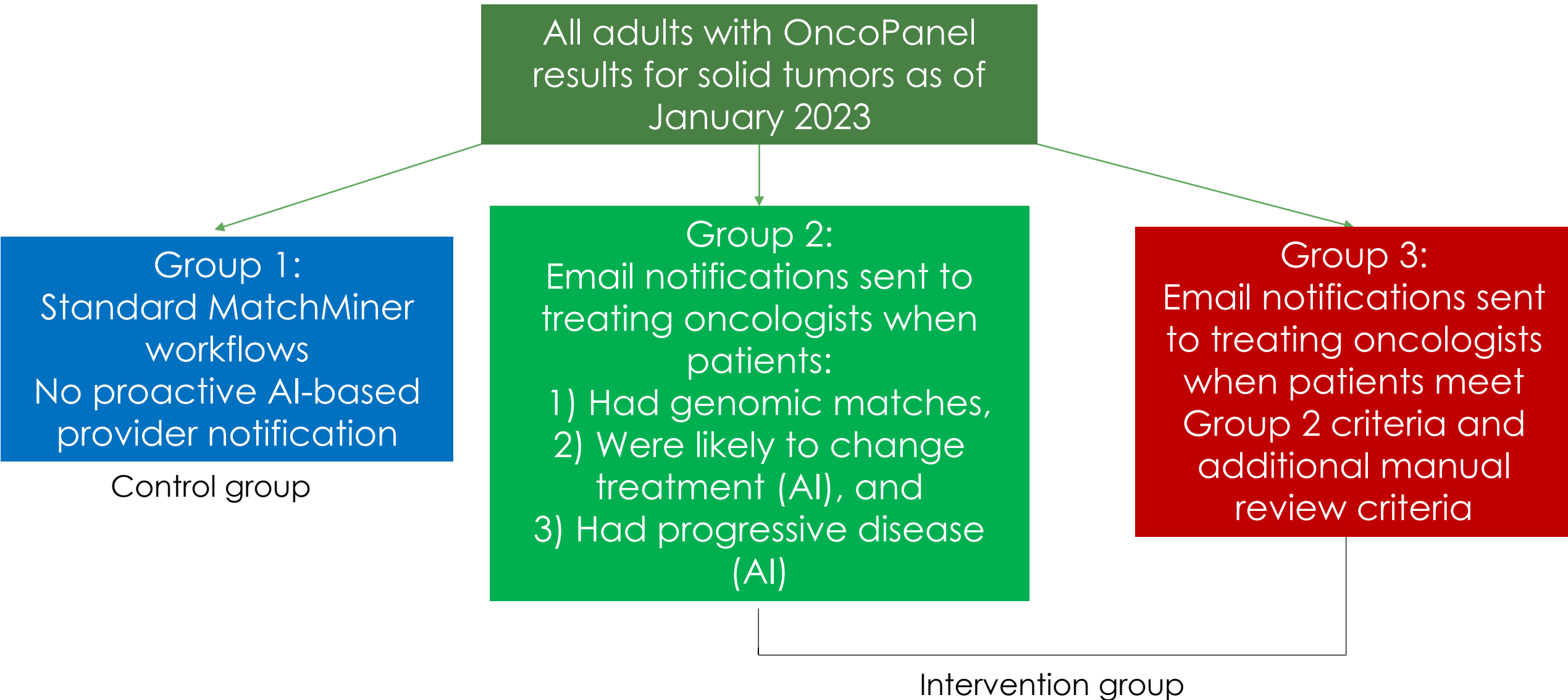
Reasons for oncologist non-contact



Kehl et al. JCO Precis Oncol. 2024 Mar;8:e2300507.

Finding trials for patients: OPTIONS

(Optimizing Precision Trials with an artificial Intelligence driven Oncologist Notification System)



Interlude: What is this study?

Research?

- Is it a clinical trial? What 'accrual' do I report?
 - Zero?
 - 50,000?

Operational?

- The operations of clinical research?
- What do we do when trial PI's ask for lists of patients with progressive disease who match their trials?

OPTIONS: Outcomes

Primary

- **Enrollment in any DFCI therapeutic (anti-cancer medicine) clinical trial by end of follow-up 7/1/24**
 - **Groups 2+3 versus group 1**

Secondary

- Enrollment in therapeutic trials across all three groups
- Consultations in Center for Cancer Therapeutic Innovation
- Consents to any therapeutic trial
- Consents and enrollments among patients deemed likely to change treatment
- Proportion of new treatments that were trials
- Clinician survey results

20707 Adults with solid tumors underwent NGS from 2013 to 2022 and were alive as of January 30, 2023

20707 Randomized 1:2

6905 Randomized to control
(no AI-assisted alert to oncologists)

13802 Randomized to intervention
(email notifications to treating oncologists when patients had genomic matches, were likely to change treatment [AI], and had progressive disease [AI])

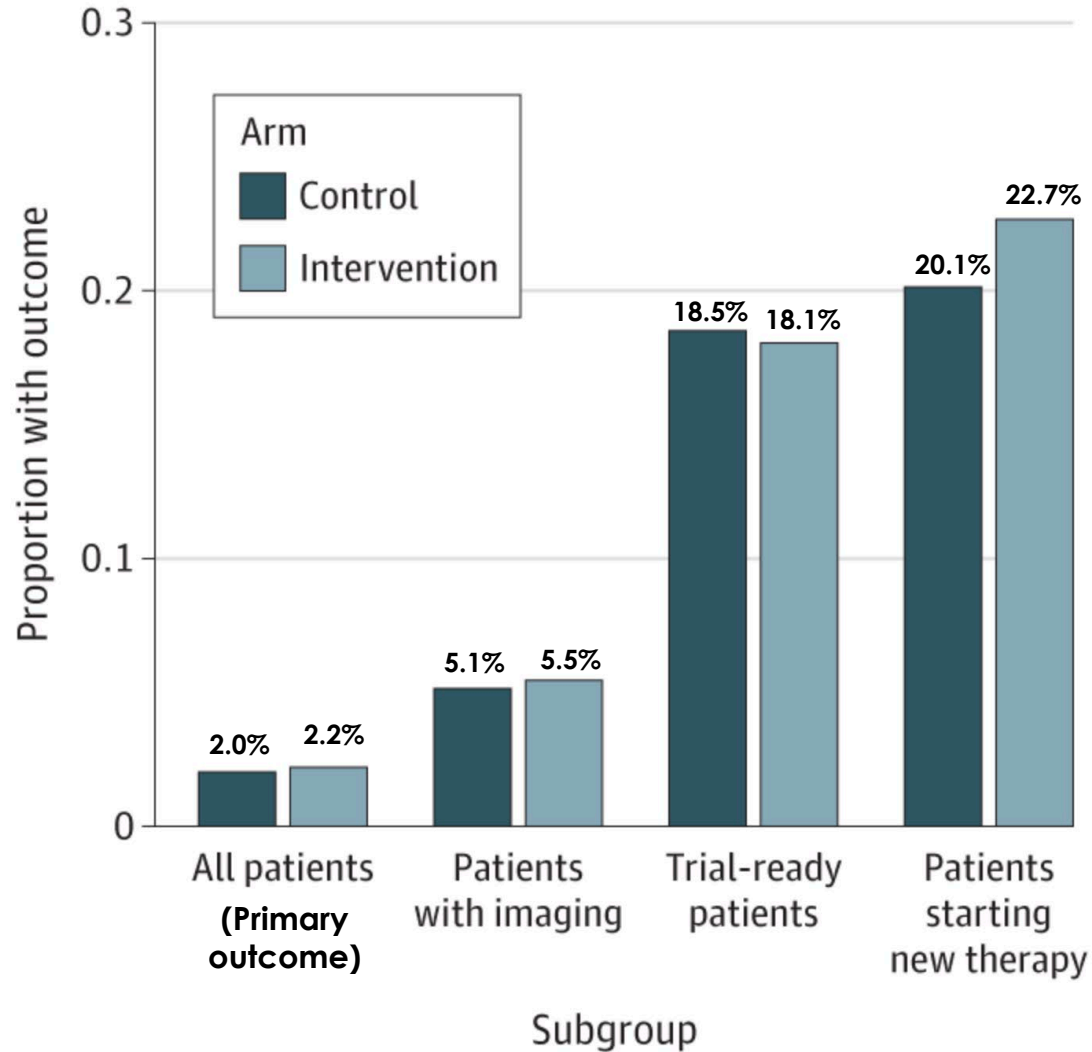
13802 Randomized 1:1

6932 Randomized to subgroup A
(no manual review before sending emails)

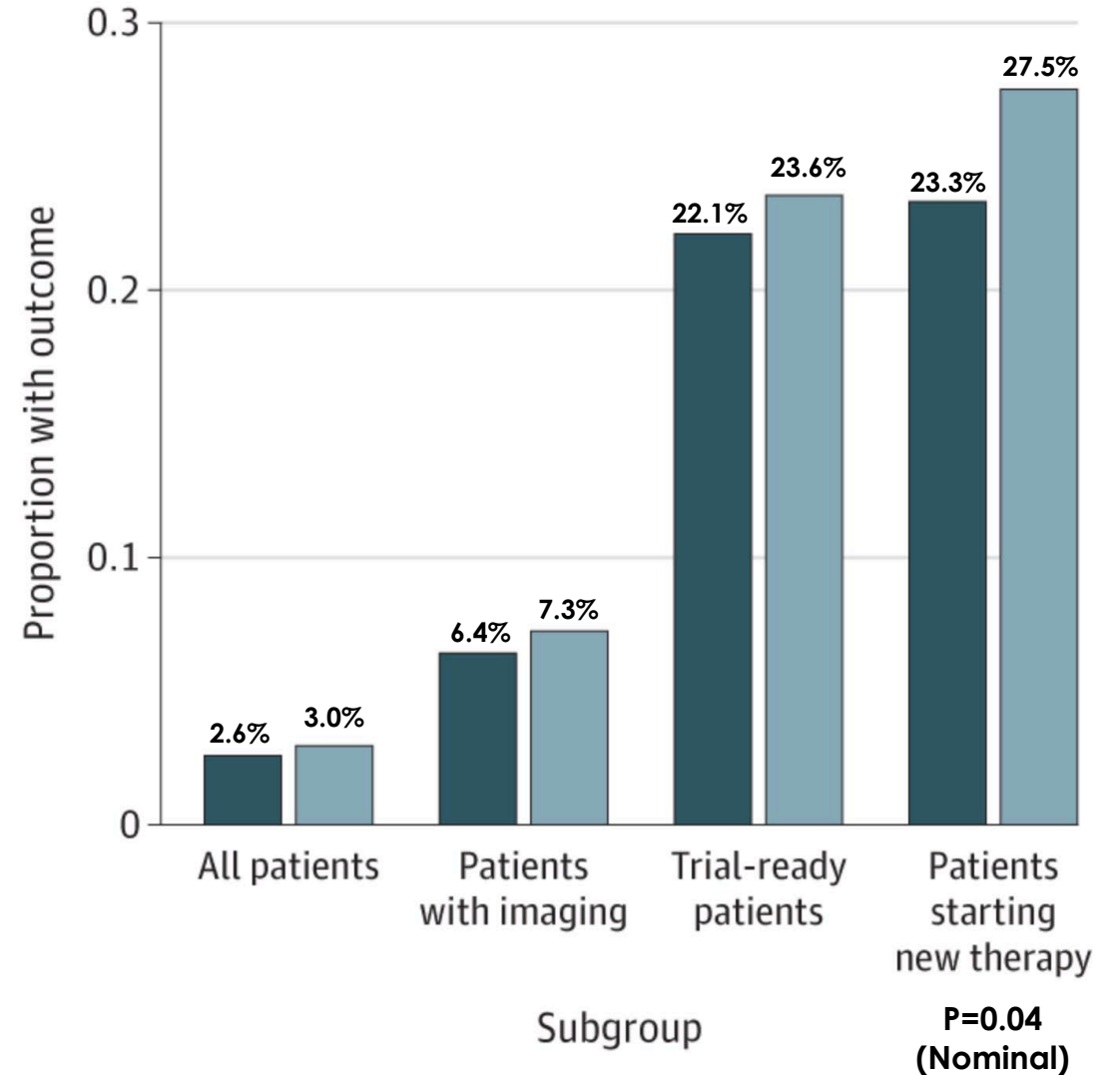
6870 Randomized to subgroup B
(manual review before sending emails)

OPTIONS results

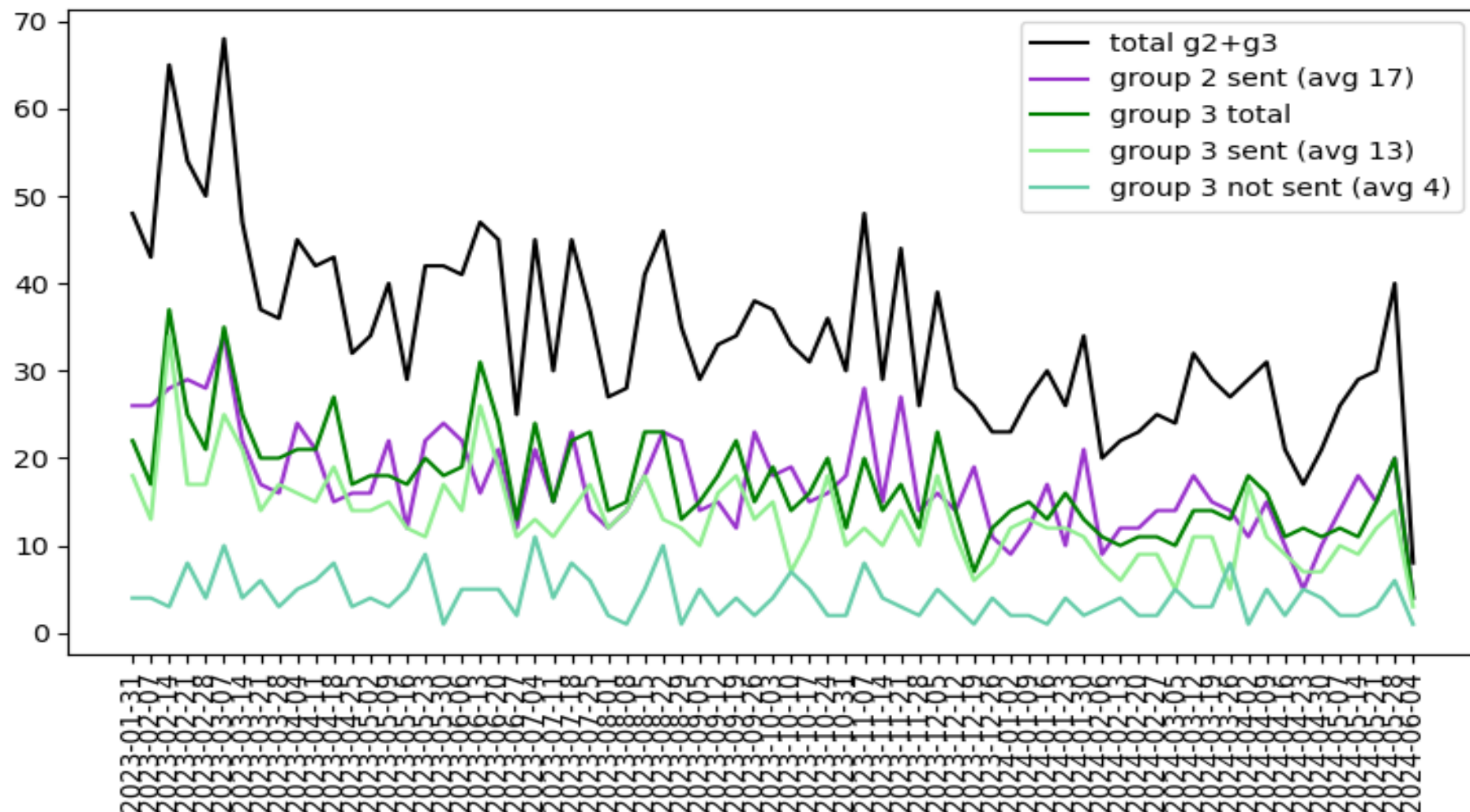
A Enrollment rate



B Consent rate



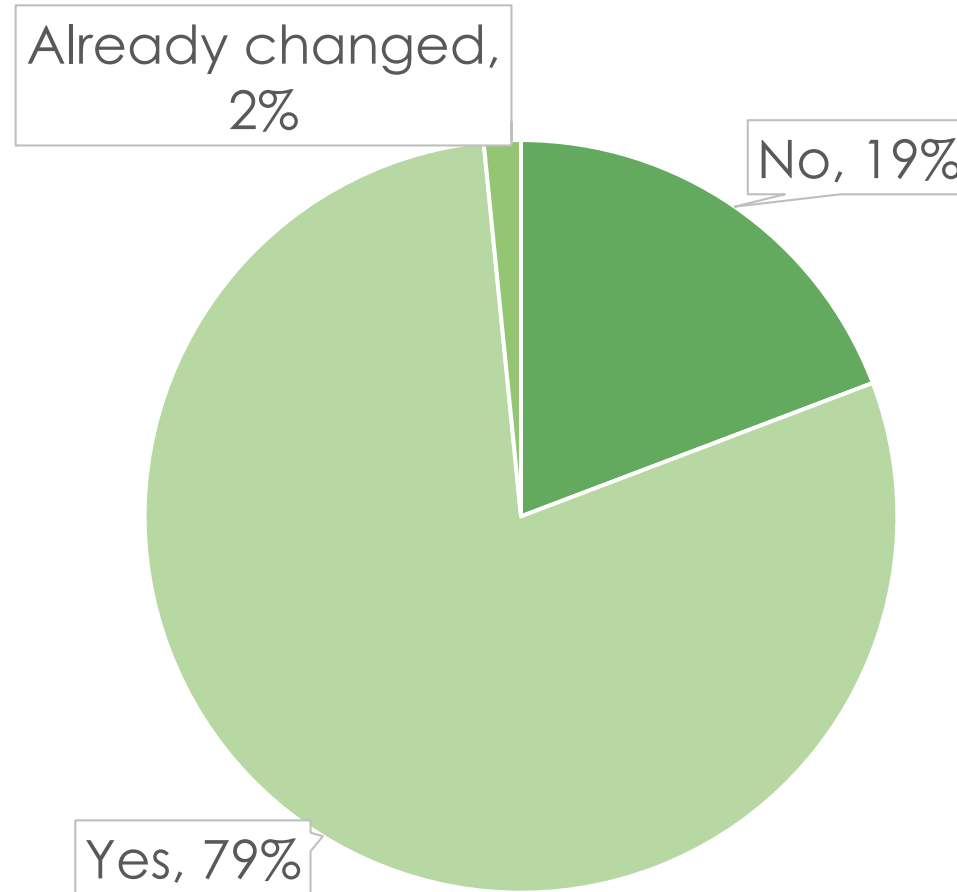
OPTIONS: Email counts



Data courtesy of Tali Mazor, PhD (DFCI Matchminer team)

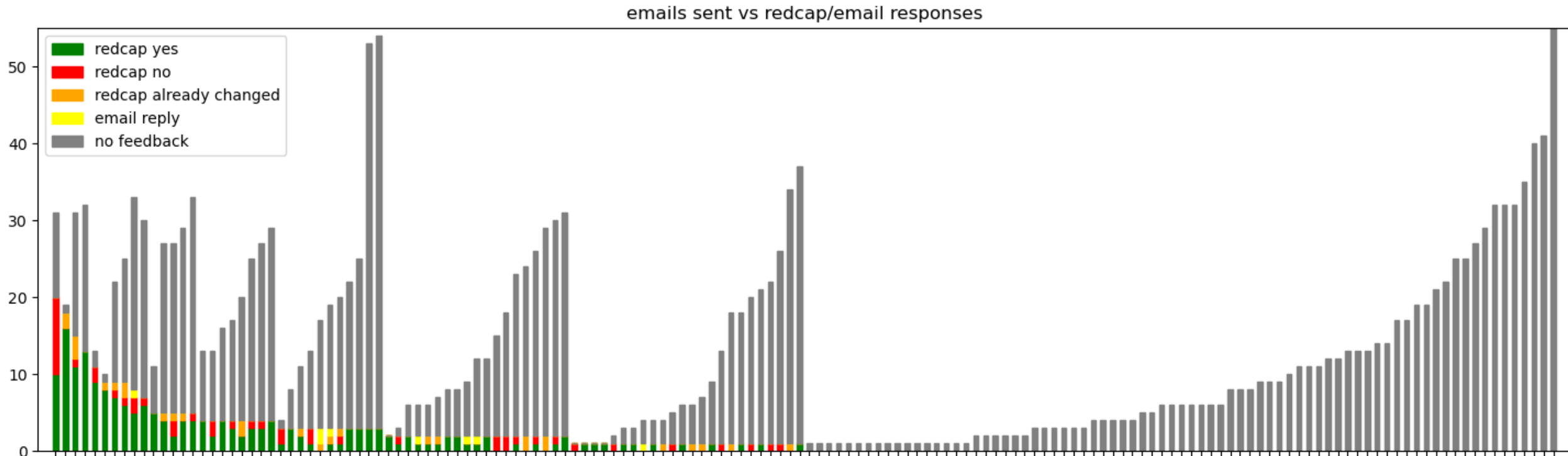
OPTIONS: Oncologist survey results

Do you agree that this patient is likely to change treatment in the next 30 days?



OPTIONS: Survey results by provider

Survey response rate on per-email basis: 12%
About half of email recipients responded at least once.

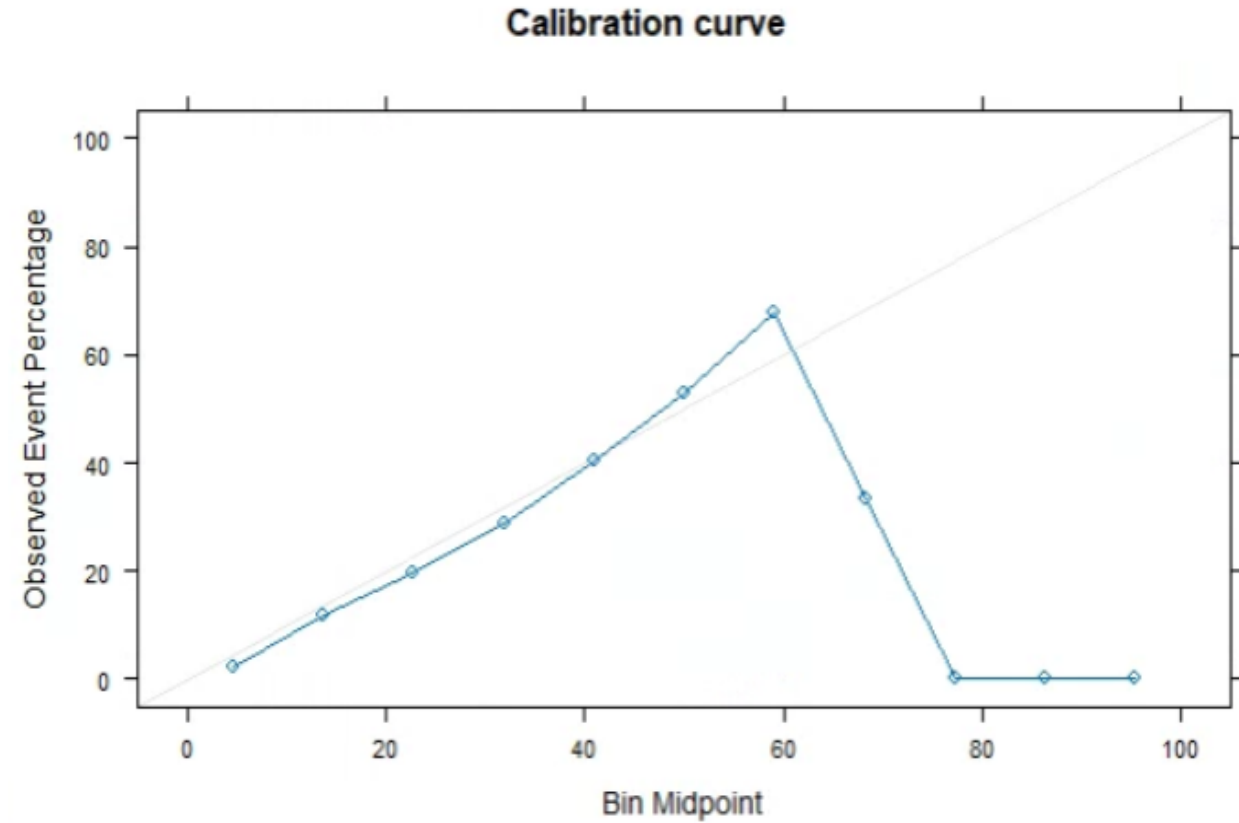
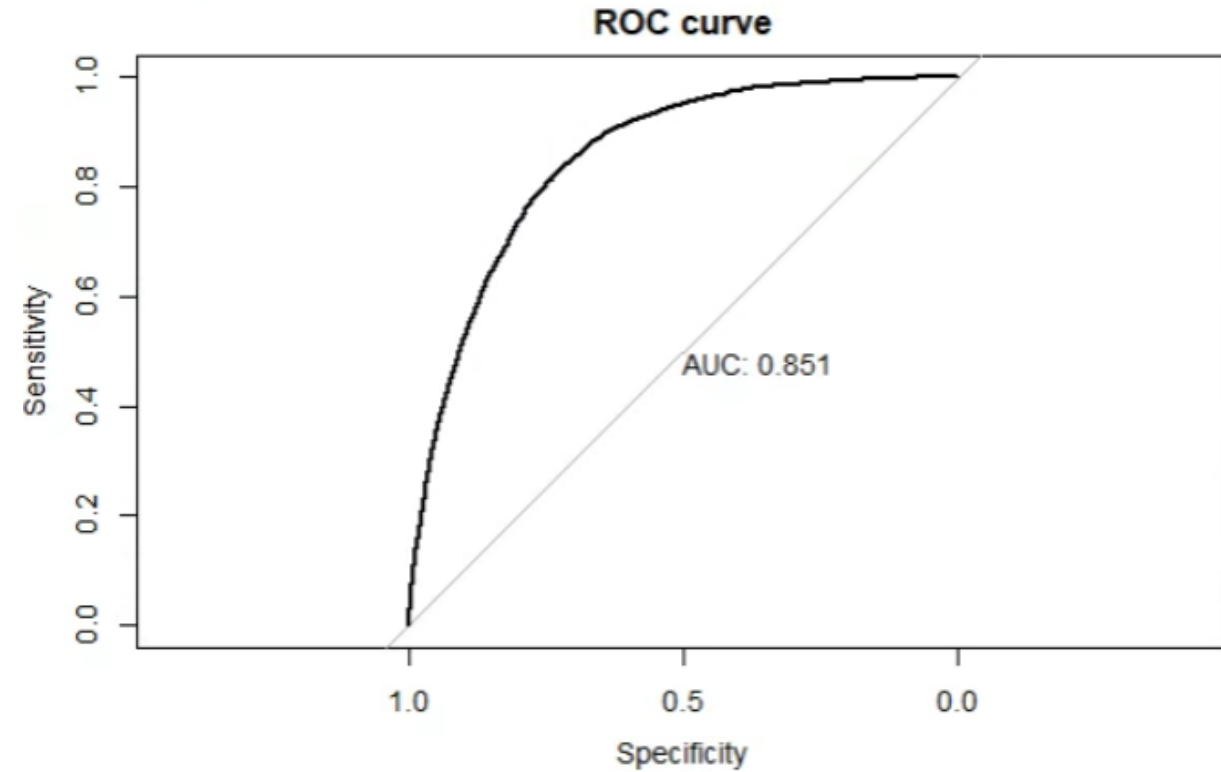


OPTIONS: Manual email rejection reasons

Of 1158 candidate clinician notifications manually reviewed for patients in group 3, 269 (23%) were rejected by our team and not sent.

Reason	N
Uncontrolled brain mets	96
No measurable disease	77
Model is wrong	46
Already changed treatment	30
ECOG	15
Hospice	11
Other	3
Multiple primary cancers	3

OPTIONS: AI model predicted treatment changes, as designed



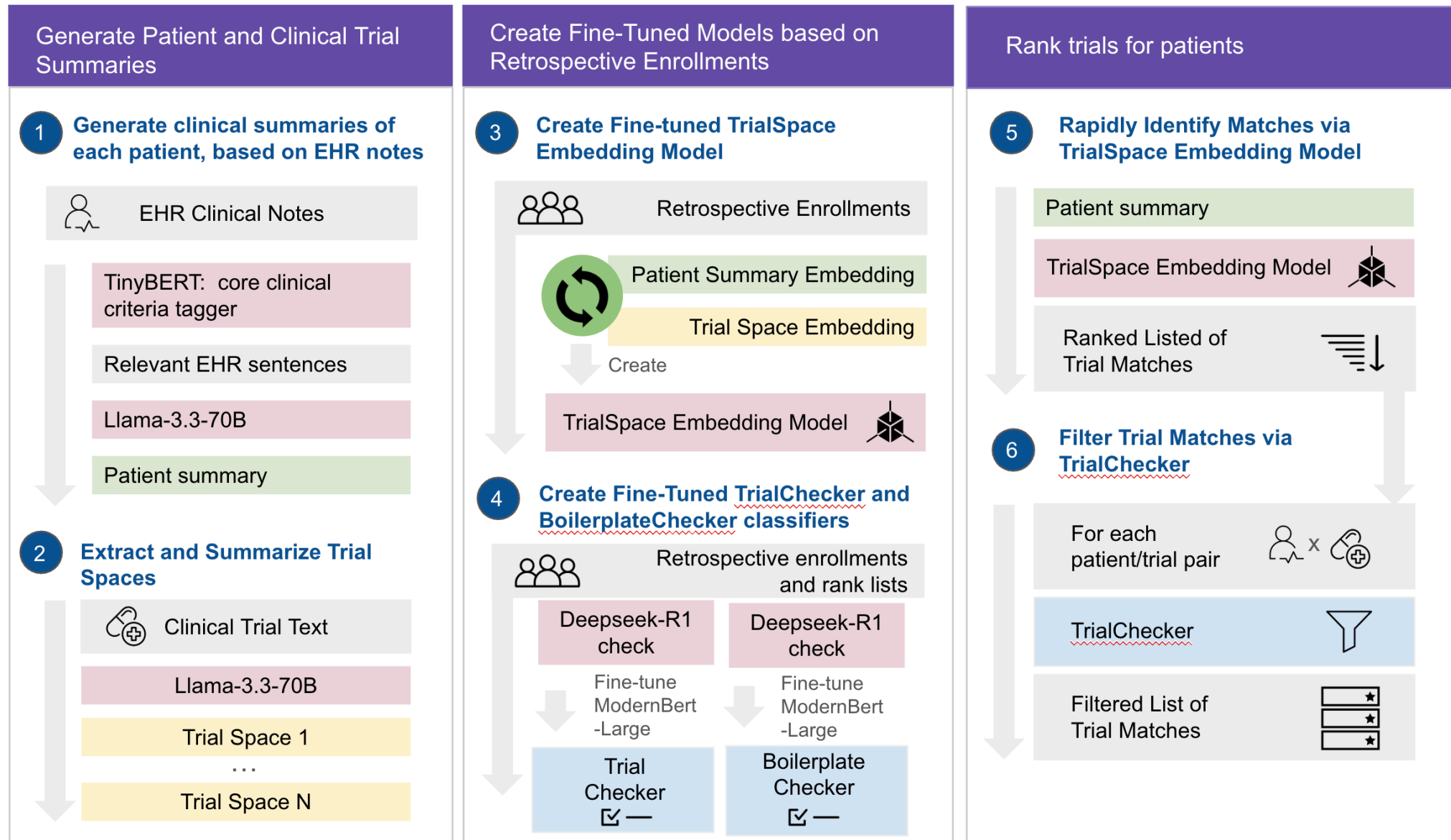
Notifying treating oncologists of trials: Conclusions to date

- Emailing academic oncologists with genomically matched trial information when their patients have progressive disease did not increase trial enrollment
- The AI models do reasonably well at finding patients with active/progressive cancer who may need treatment changes
- Our intervention addresses only one barrier to trial participation. Others may include:
 - Eligibility criteria beyond genomics and recent progression
 - Patient or oncologist preference/convenience
 - Is a trial an end in itself?
 - Complexity of trials
 - Biopsies for biomarker testing
 - Time toxicity

MatchMiner-AI: Trial matching for all

- MatchMiner selects specific trials based on genomic eligibility criteria.
- Our deployed AI pipeline can identify patients with progressive disease for whom genomic trial matches may be relevant.
- What if patients don't have genomic data or we don't have it in structured form?
- What about trials that do not select based on genomics?

MatchMiner-AI: Trial matching for all



MatchMiner-AI: Trial matching for all

Metric	Retrospective DFCI trial enrollment dataset (Patient test split; n=1582 patient summaries queried)			DFCI standard-of-care treatment start and external trials dataset (Patient test split; n=9477 patient summaries queried)		
	Stella baseline	TrialSpace alone	TrialSpace + TrialChecker	Stella baseline	TrialSpace alone	TrialSpace + TrialChecker
Precision @ 10	0.43	0.67	0.89	0.39	0.64	0.83
MAP @ 10	0.60	0.87	0.94	0.55	0.78	0.90
Median results returned per query (N)	10	10	7.0	10	10	7.0
Mean results returned per query (N)	10	10	7.0	10	10	7.0

MatchMiner-AI: Trial matching for all



MatchMiner AI Trial Search

Search

kk71

Enter a DFCI MRN or patient summary.*†



Cancer type: Non-small cell lung cancer
Histology: Adenocarcinoma
Cancer burden: Metastatic
Prior treatment: Pembrolizumab
Biomarkers: PD-L1 70%, KRAS G12C mutation

Clear

Submit

* Describe your patient in the style of an assessment and plan sentence.

Feedback helps us improve. The rating icons allow you to express us how you feel about AI generated trial matching content. In return you get results that are better tailored to your patients.

Rank ‡	Protocol	Phase ▽	Location ▽	Coordinating Center	Pre-screen **
	Trial Suggestion		 		
1	ZM008 as single agent and in combination with Pembrolizumab in advanced solid tumors	I	BWH DF Longwood	Hanna, Glenn, J Investigator DFCI/BWH Center for Cancer Therapeutic Innovation Managed By	✓
	24-403 Protocol No.				
	View trial details				

[Trial Summary](#)




Cancer type allowed: Non Small Cell Lung Cancer. Histology allowed: Not specified. Cancer burden allowed: Metastatic. Prior treatment required: Patients with tumors with actionable mutations should have progressed on all approved targeted therapies. Prior treatment excluded: None. Biomarkers required: None. Biomarkers excluded: None.

<https://arxiv.org/abs/2412.17228>

Caution!

Brief Communication | [Open Access](#) | [Published: 19 January 2023](#)

Racial and ethnic disparities in a real-world precision oncology data registry

[Alexander T. M. Cheung](#), [Elina L. Palapattu](#), [Isabella R. Pompa](#), [Christopher M. Aldrighetti](#), [Andrzej Niemierko](#), [Henning Willers](#), [Franklin Huang](#), [Neha Vapiwala](#), [Eliezer Van Allen](#) & [Sophia C. Kamran](#) 

npj Precision Oncology **7**, Article number: 7 (2023) | [Cite this article](#)

➤ [Cancer Epidemiol Biomarkers Prev.](#) 2023 Mar 6;32(3):344-352.
doi: 10.1158/1055-9965.EPI-22-0875.

Elucidating Analytic Bias Due to Informative Cohort Entry in Cancer Clinico-genomic Datasets

[Kenneth L Kehl](#) ¹, [Hajime Uno](#) ¹, [Alexander Gusev](#) ¹, [Stefan Groha](#) ¹, [Samantha Brown](#) ²,
[Jessica A Lavery](#) ², [Deborah Schrag](#) ³, [Katherine S Panageas](#) ²

Affiliations + expand

PMID: 36626408 PMCID: PMC9992002 (available on 2023-09-06)

DOI: [10.1158/1055-9965.EPI-22-0875](#)



Caution!

Original Investigation

August 14, 2019

Association Between Surgical Skin Markings in Dermoscopic Images and Diagnostic Performance of a Deep Learning Convolutional Neural Network for Melanoma Recognition

Julia K. Winkler, MD¹; Christine Fink, MD¹; Ferdinand Toberer, MD¹; [et al](#)

[» Author Affiliations](#) | [Article Information](#)

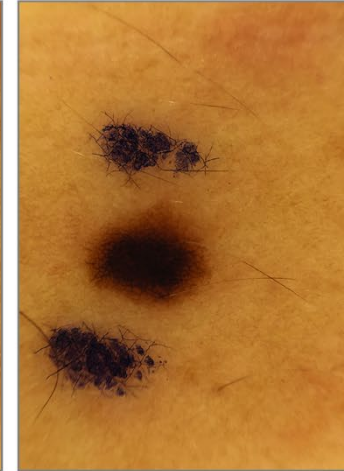
JAMA Dermatol. 2019;155(10):1135-1141. doi:10.1001/jamadermatol.2019.1735

FREE

A Unmarked benign nevus



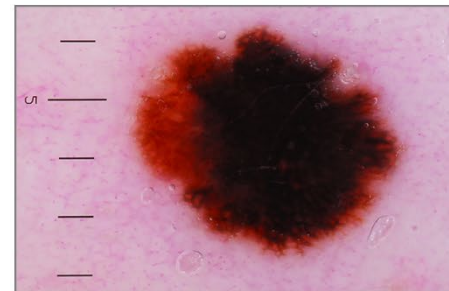
B Marked benign nevus



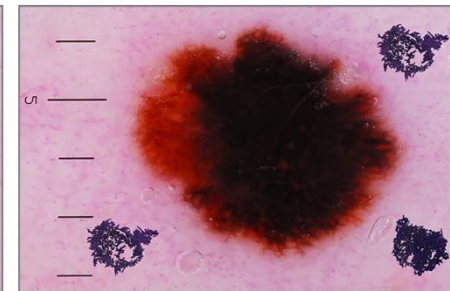
C Cropped benign nevus image



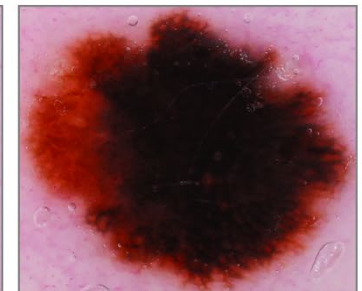
D Unmarked melanoma



E Marked melanoma



F Cropped melanoma image



Conclusions



Artificial intelligence can accelerate clinical cancer research by rapidly identifying clinical trial options for patients.



But impact requires integration.

Apply thoughtfully

Evaluate like any other technology

Beware of pitfalls and shortcuts