FLATIRON

Big Data & Precision Medicine

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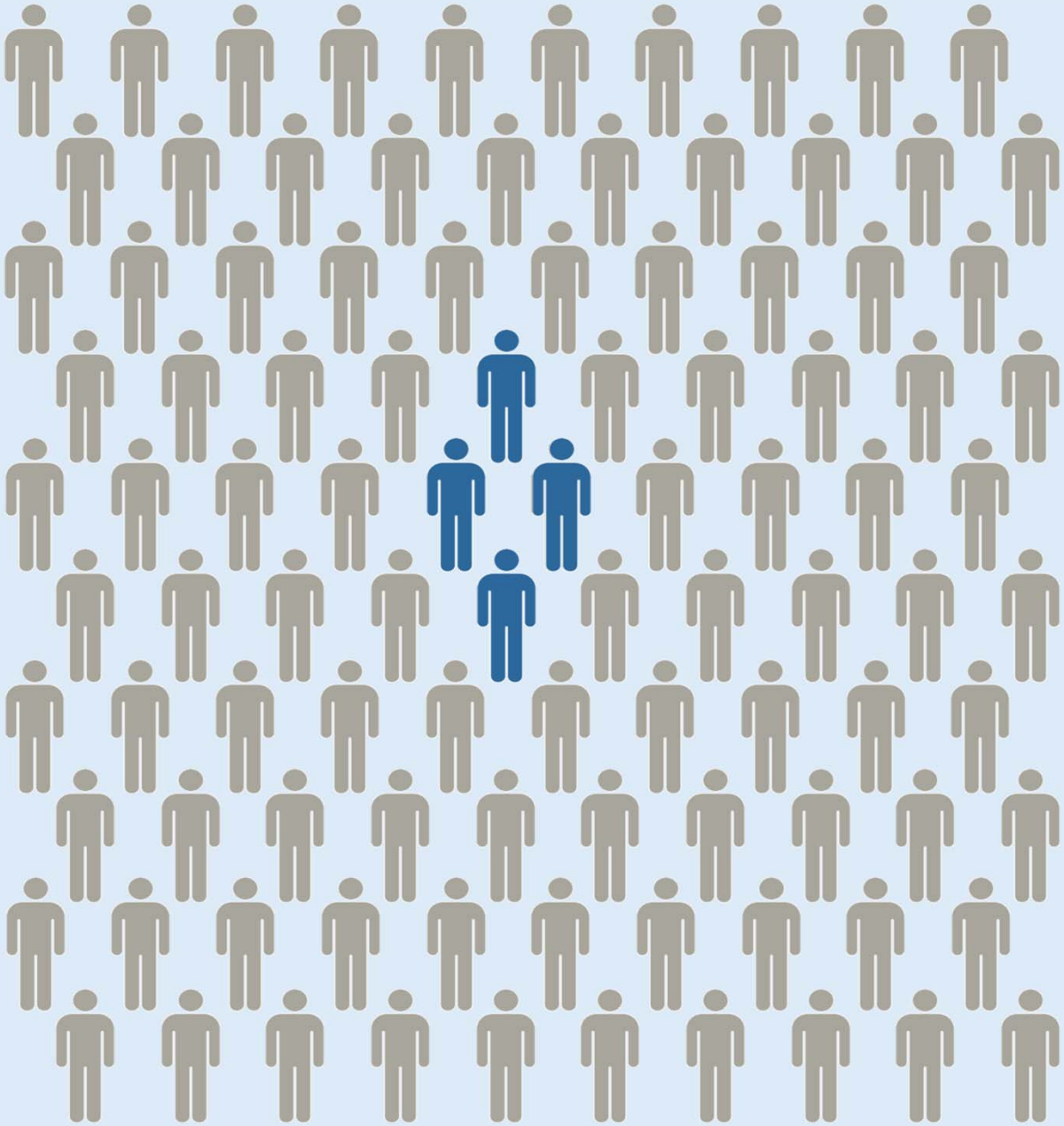
Big Data?


Notes
Ancillary Services
Notes
Surgery
Rad Onc
Treatment Plans
Family History
Demographics
Sites of Metastases
Labs
Pathology
Lab Values
Hospitalizations
Staging
Patient Reported Outcomes
Therapy
Biomarkers
Molecular Data
Comorbidities

4%

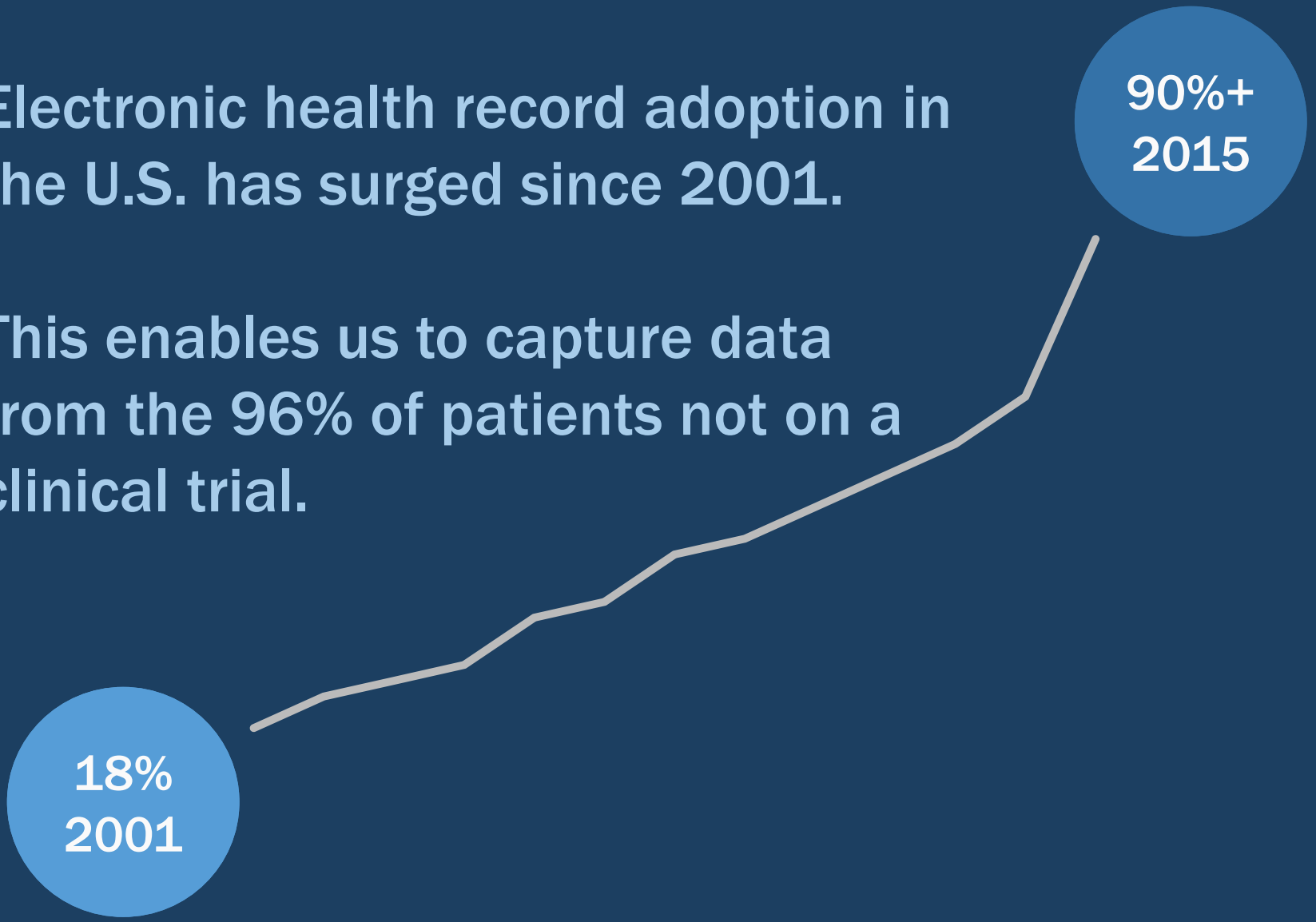
vs.

96%



Electronic health record adoption in the U.S. has surged since 2001.

This enables us to capture data from the 96% of patients not on a clinical trial.



Frustrations faced:

1. Clinical data is really messy and unreliable
2. Instrumentation data (including genomics) is really “big”
3. It’s incredibly hard to follow a patient’s complete journey
4. There is a lack of “real-world” evidence, which makes it difficult to talk with patients about expected outcomes

How can we leverage data in a meaningful way to enhance patient care and learn from their experiences?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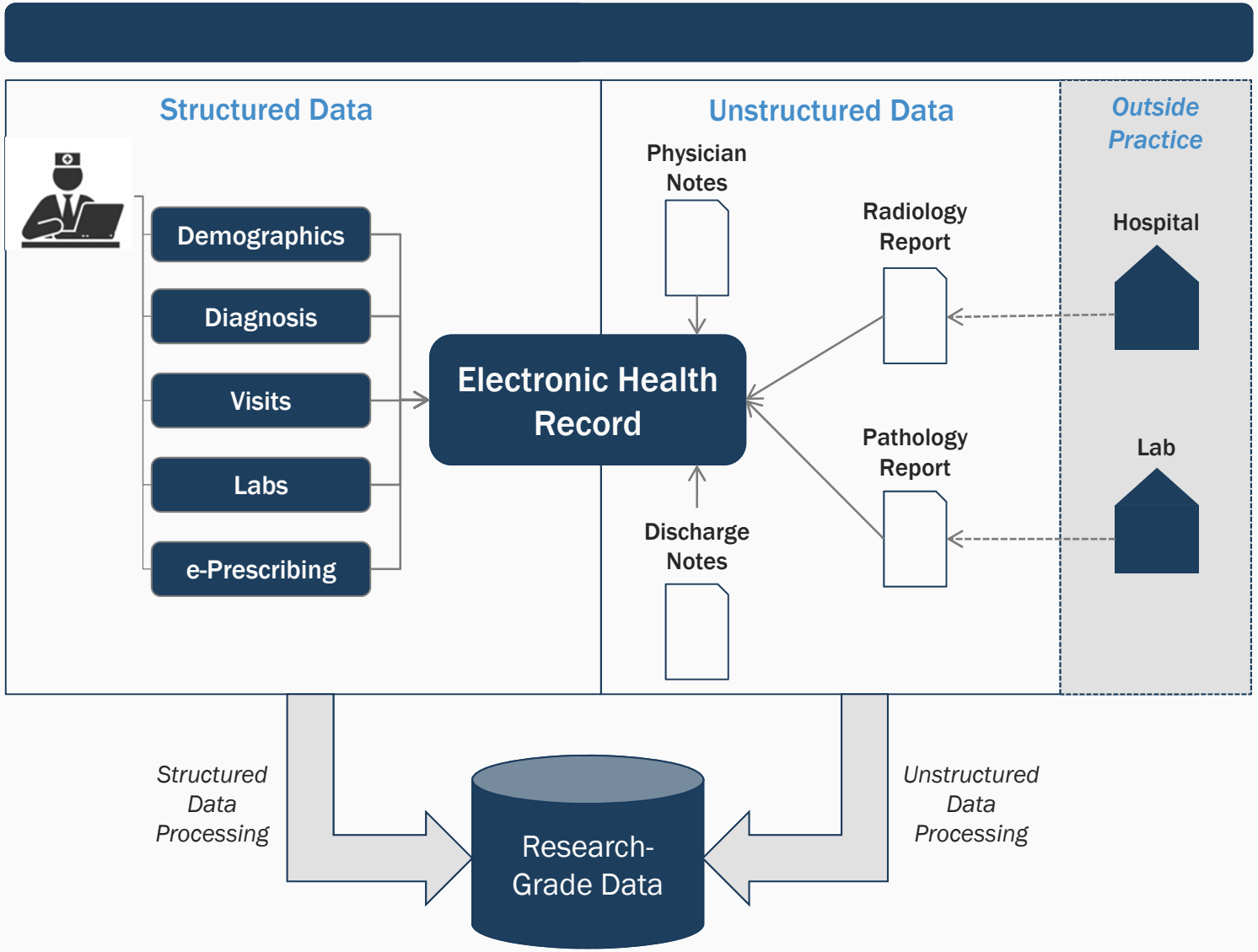
Processing the Electronic Health Record



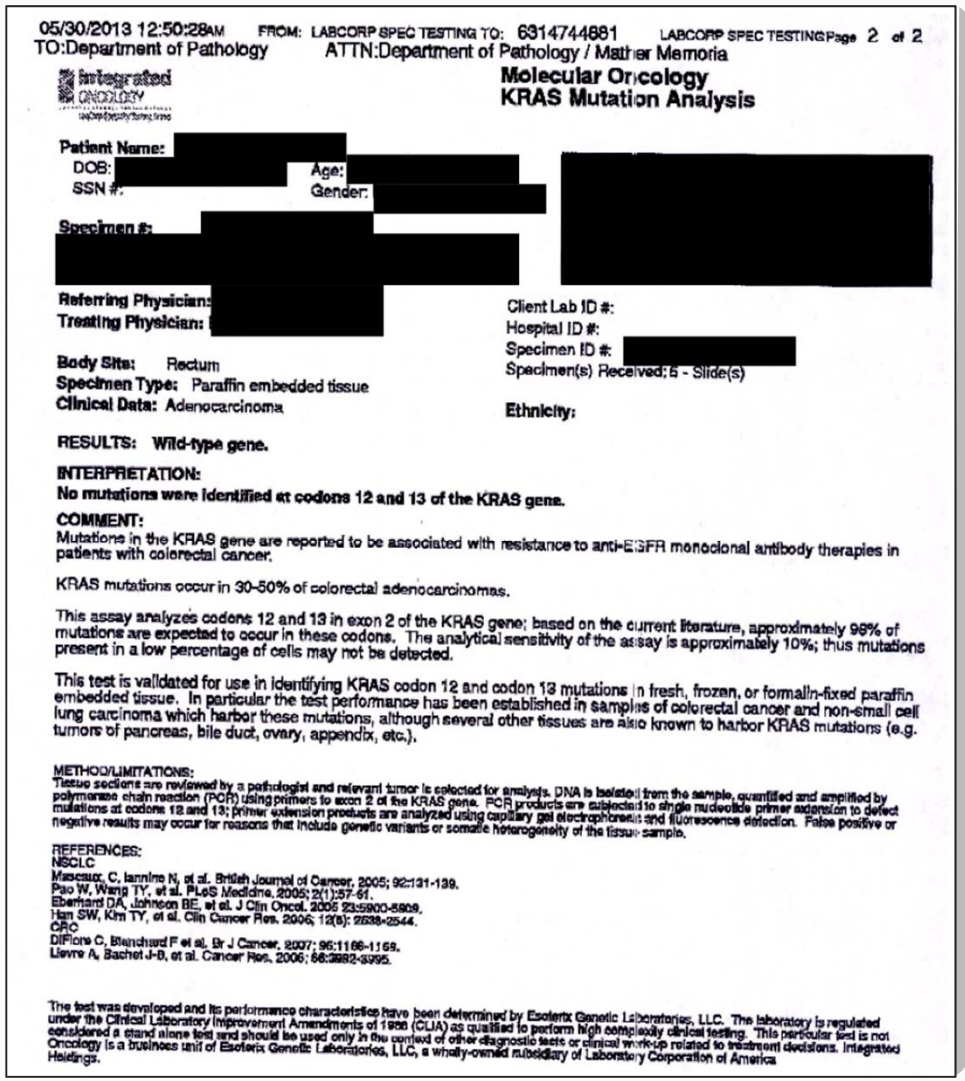
Structured Data Processing

2220	Blood Serum Albumin	g/dL
QD25001600	ALBUMIN/GLOBULIN RATIO QD	(calc)
QD25001400	ALBUMIN QD	g/dL
QD50058600	ALBUMIN	%
QD50055700	ALBUMIN	g/dL
CL3215104	Albumin % (EPR)	%
LC001081	ALBUMIN, SERUM (001081)	g/dL
LC003718	Albumin, U	%
LC001488	Albumin	g/dL
LC133751	Albumin, U	%
CL3215162	Albumin%, Urine	%
CL3215160	Albumin, Urine	mg/24hr
3234	ALBUMIN SS	g/dL
LC133686	Albumin, U	%
QD50060710	MICROALBUMIN	mg/dL
QD50061100	MICROALBUMIN/CREATININE RATIO, RANDOM URINE	mcg/mg creat
QD85991610	ALBUMIN	relative %
50058600	ALBUMIN UPEP RAND	%
CL3210074	ALBUMIN LEVEL	g/dL
QD86008211	ALBUMIN/GLOBULIN RATIO	(calc)
LC149520	Albumin	g/dL
QD45069600	PREALBUMIN	mg/dL
QD900415245	ALBUMIN, SERUM	mg/dl
QD900429745	ALBUMIN	g/dL
CL3215124	Albumin Electrophoresis	g/dL
LC016931	Prealbumin	mg/dL
QD50060900	MICROALBUMIN, 24 HOUR UR	mcg/min
QD85994821	ALBUMIN,SERUM	g/dL
CL3213320	PREALBUMIN	mg/dL
QD85995225	PROTEIN ELECTROPHORESIS ALBUMIN	g/dL

- All terms are mapped to a common vocabulary, standard across all centers
- Matching algorithms can predict matches for ~90% of terms
- Data processing engine transcodes terms in real-time
- Any unmatched term is flagged for clinical review by Flatiron MD/RN

1751-7	**Albumin [Mass/volume] in Serum or Plasma**	**g/dL**

Capturing Key Data From Unstructured Notes



05/30/2013 12:50:28AM FROM: LABCORP SPEC TESTING TO: 6314744881 LABCORP SPEC TESTING Page 2 of 2
TO:Department of Pathology ATTN:Department of Pathology / Mather Memoria

Integrated ONCOLOGY

Molecular Oncology
KRAS Mutation Analysis

Patient Name: [redacted]
DOB: [redacted] Age: [redacted]
SSN #: Gender: [redacted]

Specimen #: [redacted]

Referring Physician: [redacted]
Treating Physician:

Client Lab ID #:
Hospital ID #:
Specimen ID #: [redacted]
Specimen(s) Received: 5 - Slide(s)

Body Site: Rectum
Specimen Type: Paraffin embedded tissue
Clinical Data: Adenocarcinoma

Ethnicity:

RESULTS: Wild-type gene.

INTERPRETATION:
No mutations were identified at codons 12 and 13 of the KRAS gene.

COMMENT:
Mutations in the KRAS gene are reported to be associated with resistance to anti-EGFR monoclonal antibody therapies in patients with colorectal cancer.

KRAS mutations occur in 30-50% of colorectal adenocarcinomas.

This assay analyzes codons 12 and 13 in exon 2 of the KRAS gene; based on the current literature, approximately 98% of mutations are expected to occur in these codons. The analytical sensitivity of the assay is approximately 10%; thus mutations present in a low percentage of cells may not be detected.

This test is validated for use in identifying KRAS codon 12 and codon 13 mutations in fresh, frozen, or formalin-fixed paraffin embedded tissue. In particular the test performance has been established in samples of colorectal cancer and non-small cell lung carcinoma which harbor these mutations, although several other tissues are also known to harbor KRAS mutations (e.g. tumors of pancreas, bile duct, ovary, appendix, etc.).

METHOD/LIMITATIONS:
Tissue sections are reviewed by a pathologist and relevant tumor is selected for analysis. DNA is isolated from the sample, quantified and amplified by polymerase chain reaction (PCR) using primers to exon 2 of the KRAS gene. PCR products are subjected to single nucleotide primer extension to detect mutations at codons 12 and 13; primer extension products are analyzed using capillary gel electrophoresis and fluorescence detection. False positive or negative results may occur for reasons that include genetic variants or somatic heterogeneity of the tissue sample.

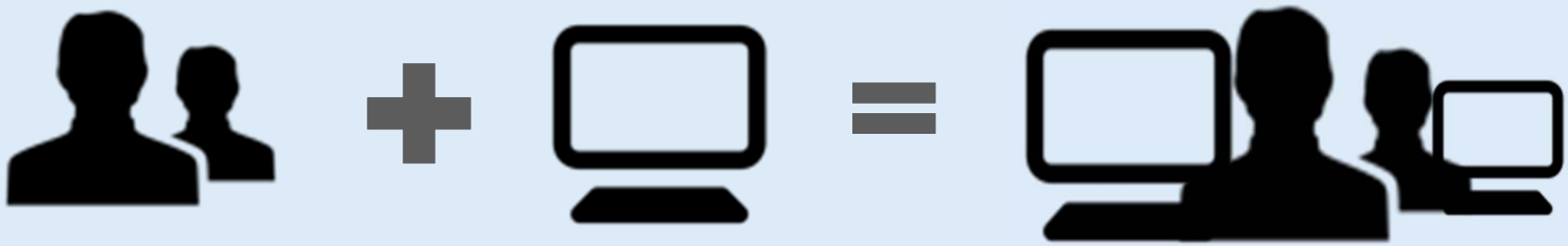
REFERENCES:
NSCLC
Massacc, C, Iannino N, et al., British Journal of Cancer, 2005; 92:131-139.
Pao W, Wang TY, et al. PLoS Medicine. 2005; 2(1):57-61.
Eberhard DA, Johnson BE, et al. J Clin Oncol. 2005 23:5900-5909.
Han SW, Kim TY, et al. Clin Cancer Res. 2006; 12(8): 2538-2544.
CRC
DiFiore C, Blanchard F et al, Br J Cancer, 2007; 96:1166-1169.
Lievre A, Bachet J-B, et al. Cancer Res. 2006; 66:3992-3995.

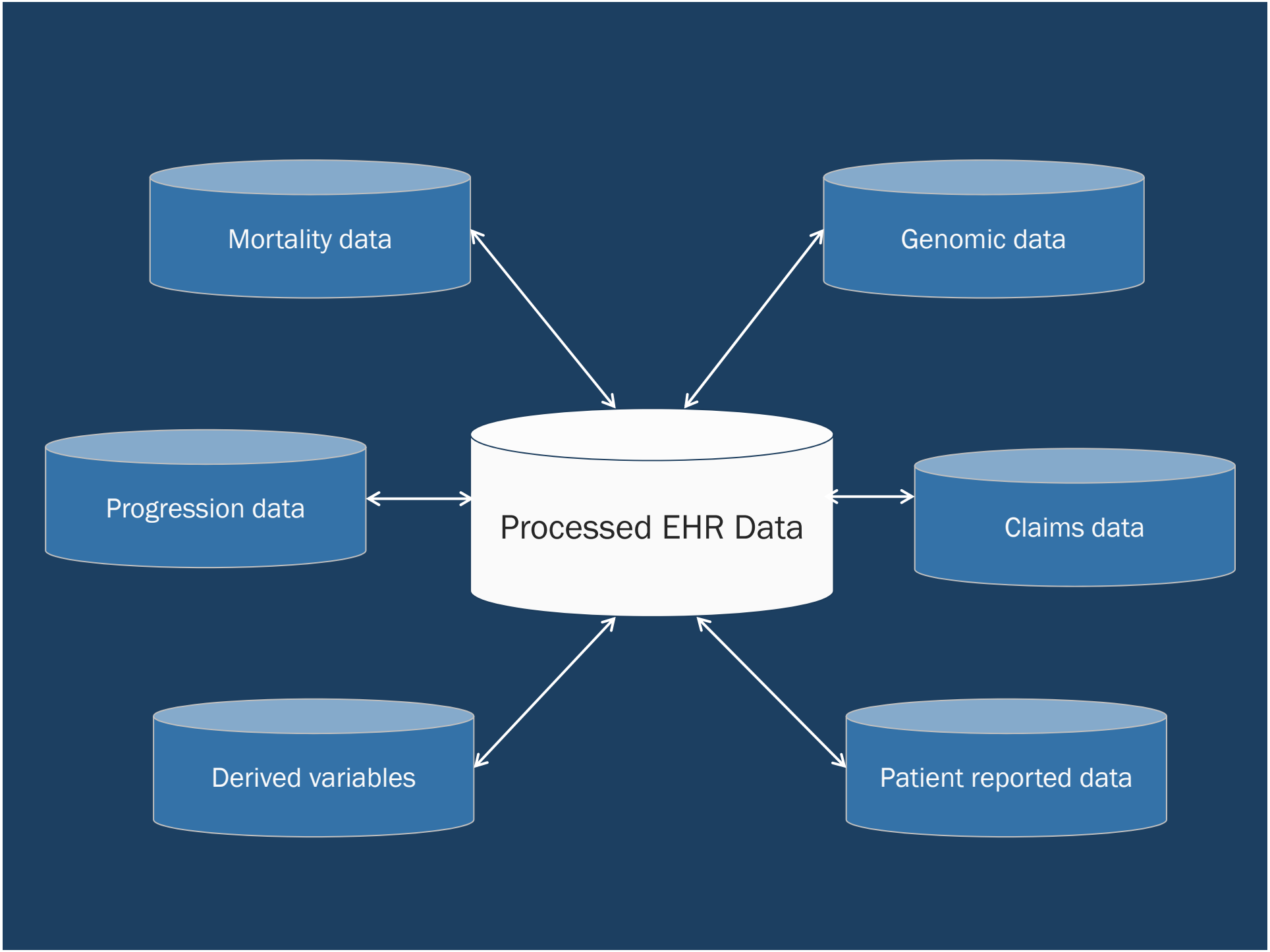
The test was developed and its performance characteristics have been determined by Esoterix Genetic Laboratories, LLC. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. This particular test is not considered a stand alone test and should be used only in the context of other diagnostic tests or clinical work-up related to treatment decisions. Integrated Oncology is a business unit of Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

Leverage unstructured data processing to drive accuracy and completeness of data elements

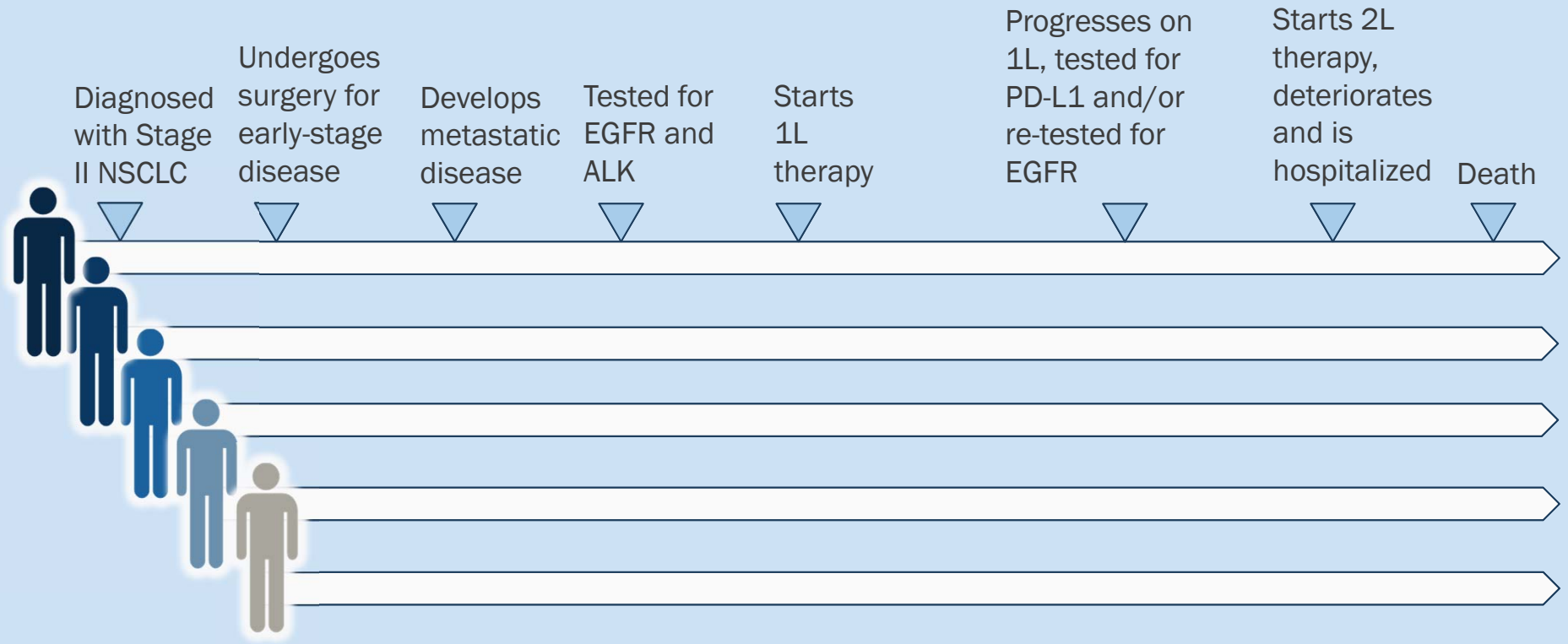
- KRAS testing status
- KRAS test result
- Date sample was collected
- Date sample was received in lab
- Date result was provided to physician

Technology leverages people & capabilities

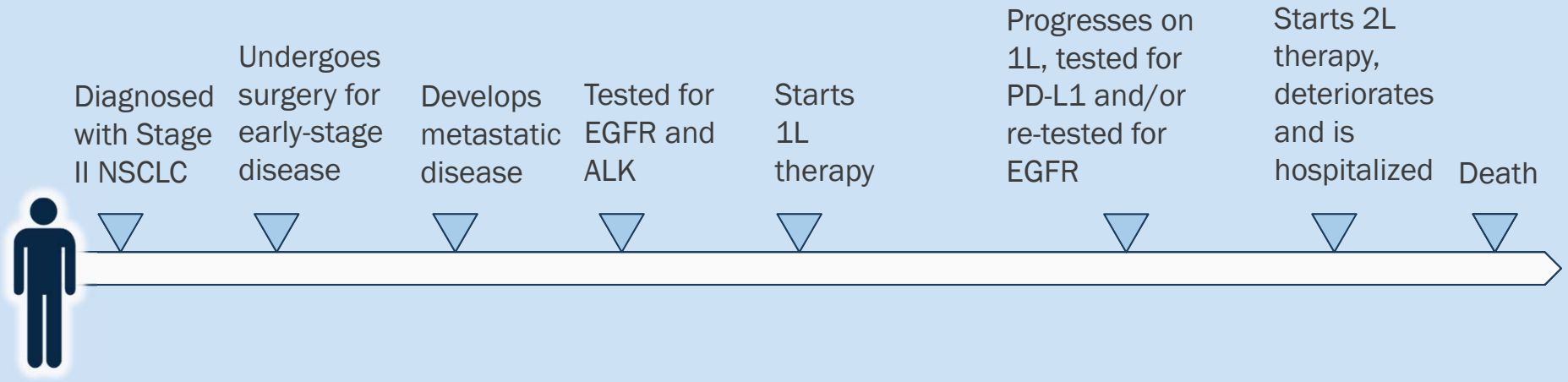



Mortality data
Genomic data
Progression data
Processed EHR Data
Claims data
Derived variables
Patient reported data

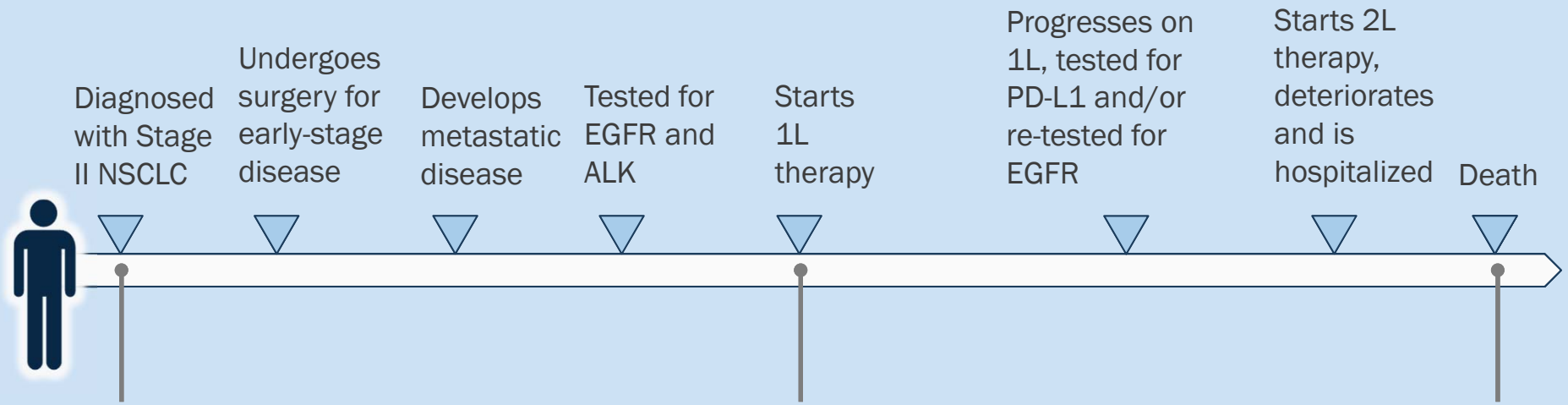
A dataset is an amalgamation of many patient stories



Organize datasets around patient stories

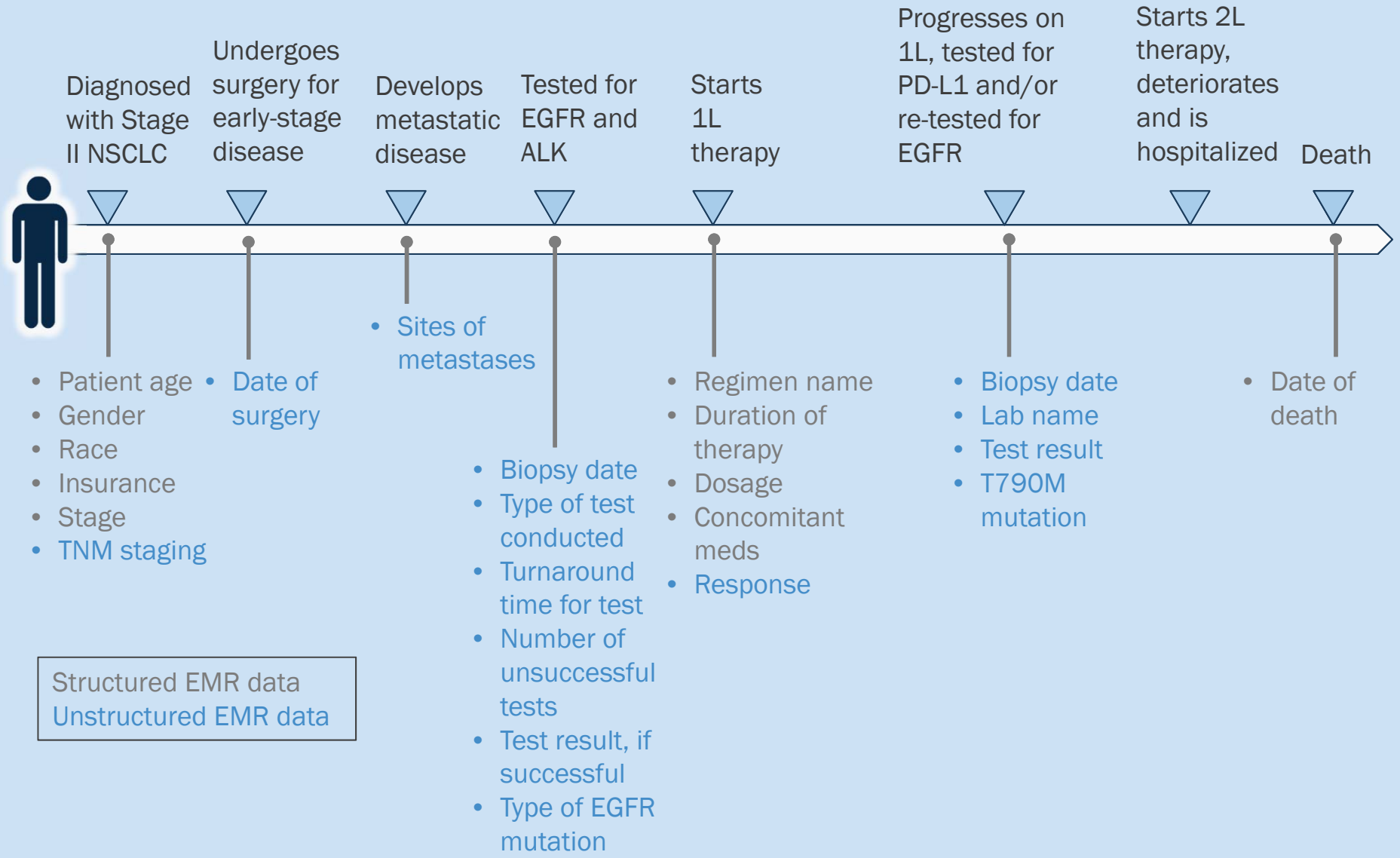


Organize datasets around patient stories

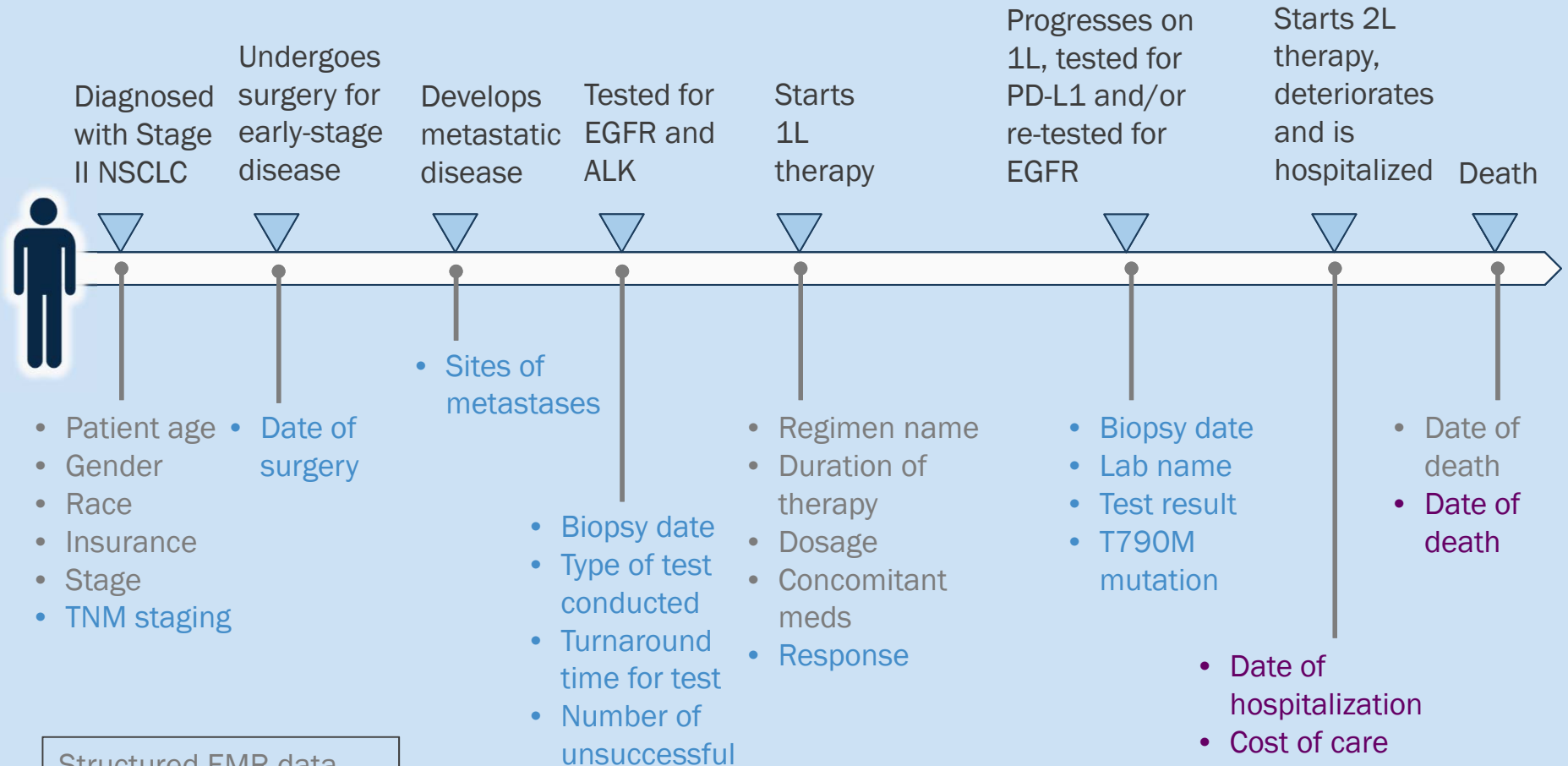


Structured EMR data

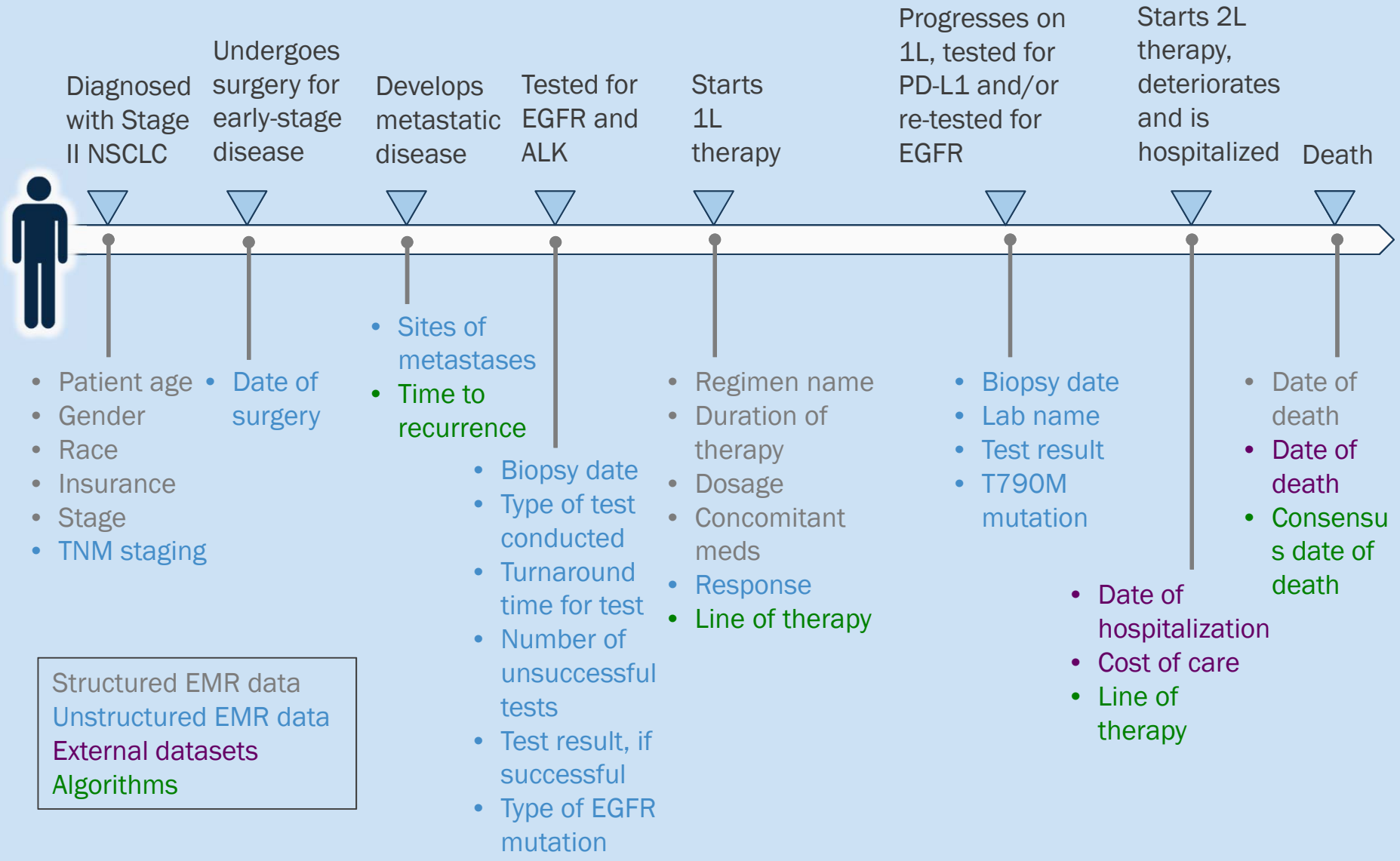
Organize datasets around patient stories



Organize datasets around patient stories



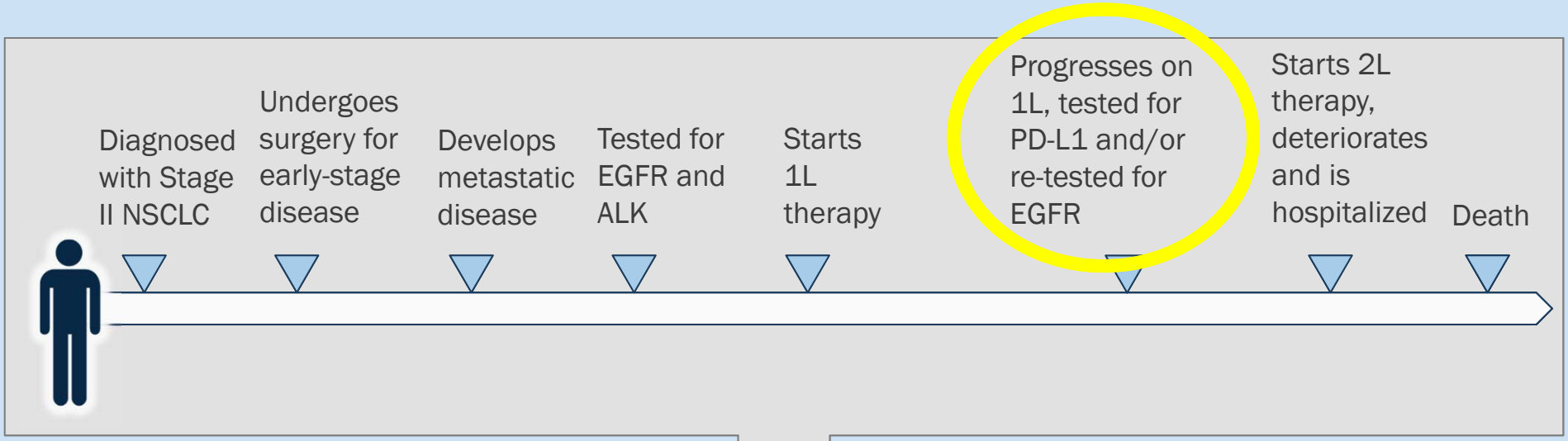
Organize datasets around patient stories



Curating the complete picture

Patient	Demographics	Stage	Diagnosis Date	Biomarkers	Treatment	Response	Hospital admissions	Mortality
A								
B								
C								
D								

Curating the complete picture



Patient	Demographics	Stage	Diagnosis Date	Biomarkers	Treatment	Response	Hospital admissions	Mortality
A				EGFR				
B								
C								
D								

Data quality must be a focus

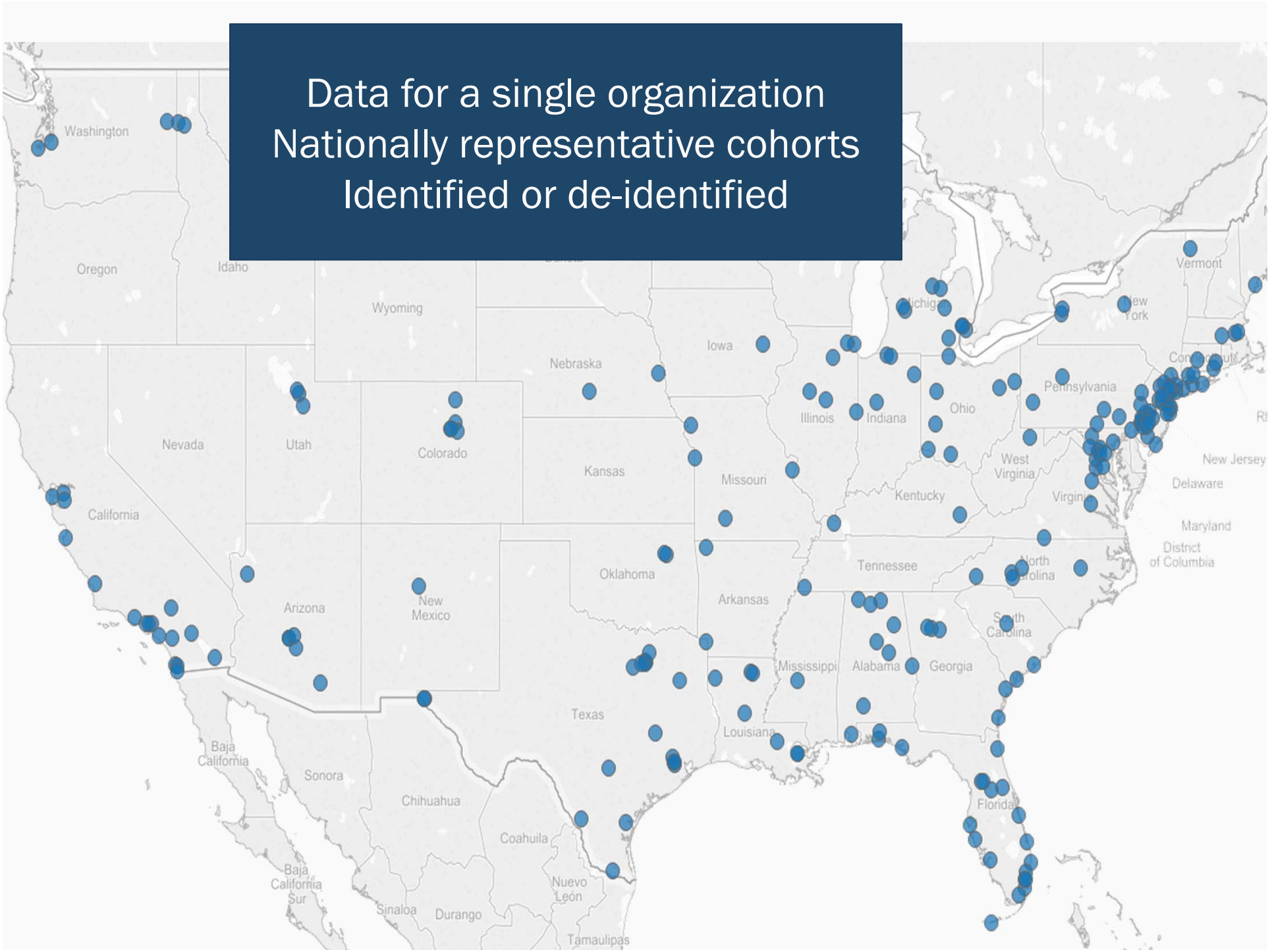
Variable	Structured data only	Flatiron data completeness
Smoking status	0%[1]	94%
Histology	37%	99%[2]
Stage	61%	95%
ALK results (of those tested)	9%	100%[3]
EGFR results (of those tested)	11%	99%[3]

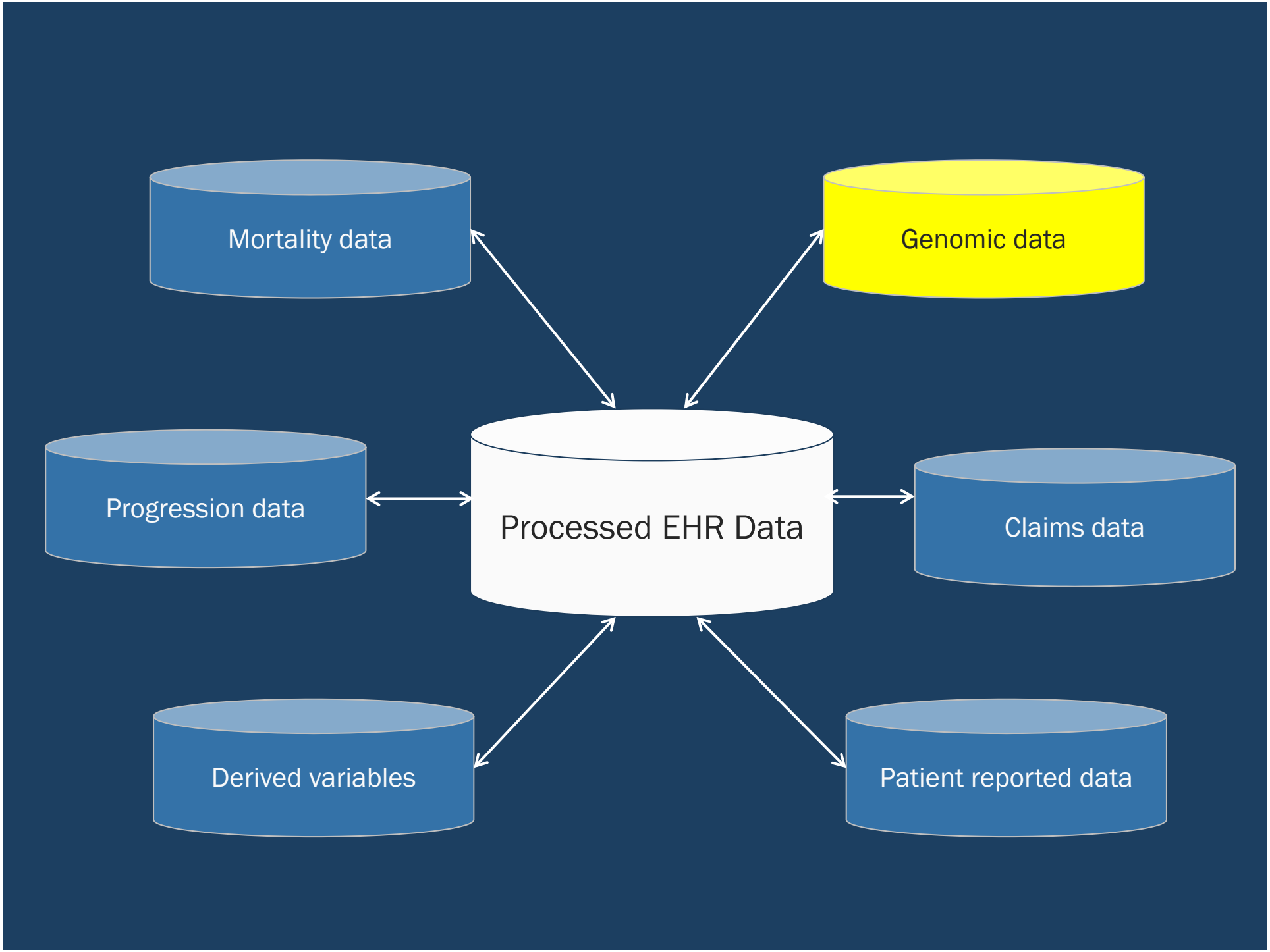
Site of Met	Inter-abstractor Agreement	Kappa
Bone	97%	0.93
Brain	96%	0.91
Liver	92%	0.83
Lung	94%	0.87

1.1M+

Always on

Up to date


Data for a single organization
Nationally representative cohorts
Identified or de-identified
Washington
Oregon
Idaho
Wyoming
Nevada
Utah
Colorado
California
Arizona
New Mexico
Kansas
Nebraska
Iowa
Missouri
Oklahoma
Arkansas
Texas
Louisiana
Illinois
Indiana
Ohio
Kentucky
Tennessee
Mississippi
Alabama
Georgia
Florida
Pennsylvania
West Virginia
Vermont
New Jersey
Delaware
Maryland
District of Columbia
Baja California
Sonora
Chihuahua
Coahuila
Baja California Sur
Sinaloa
Durango
Nuevo León
Tamaulipas


Mortality data
Genomic data
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Processed EHR Data
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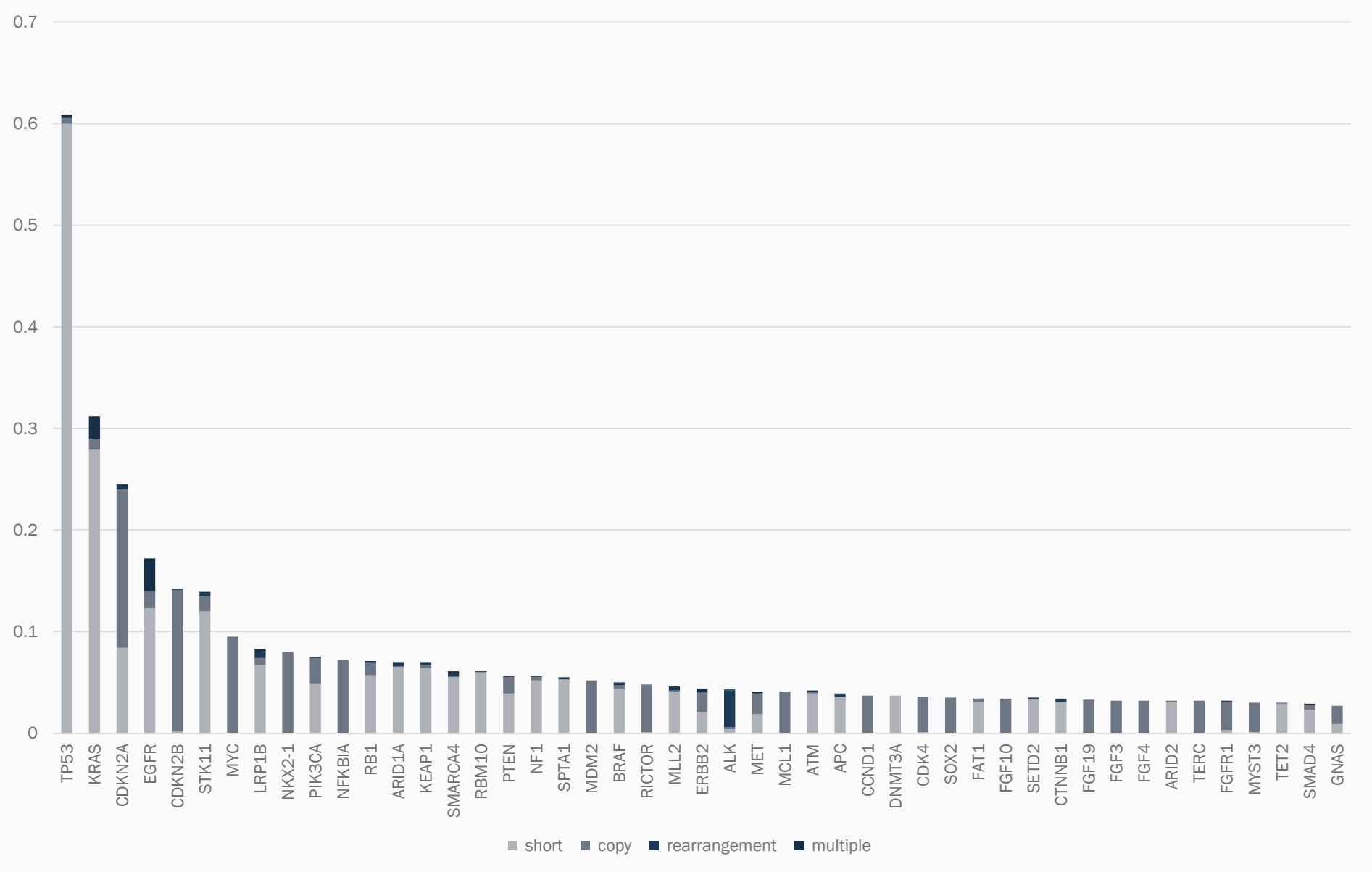
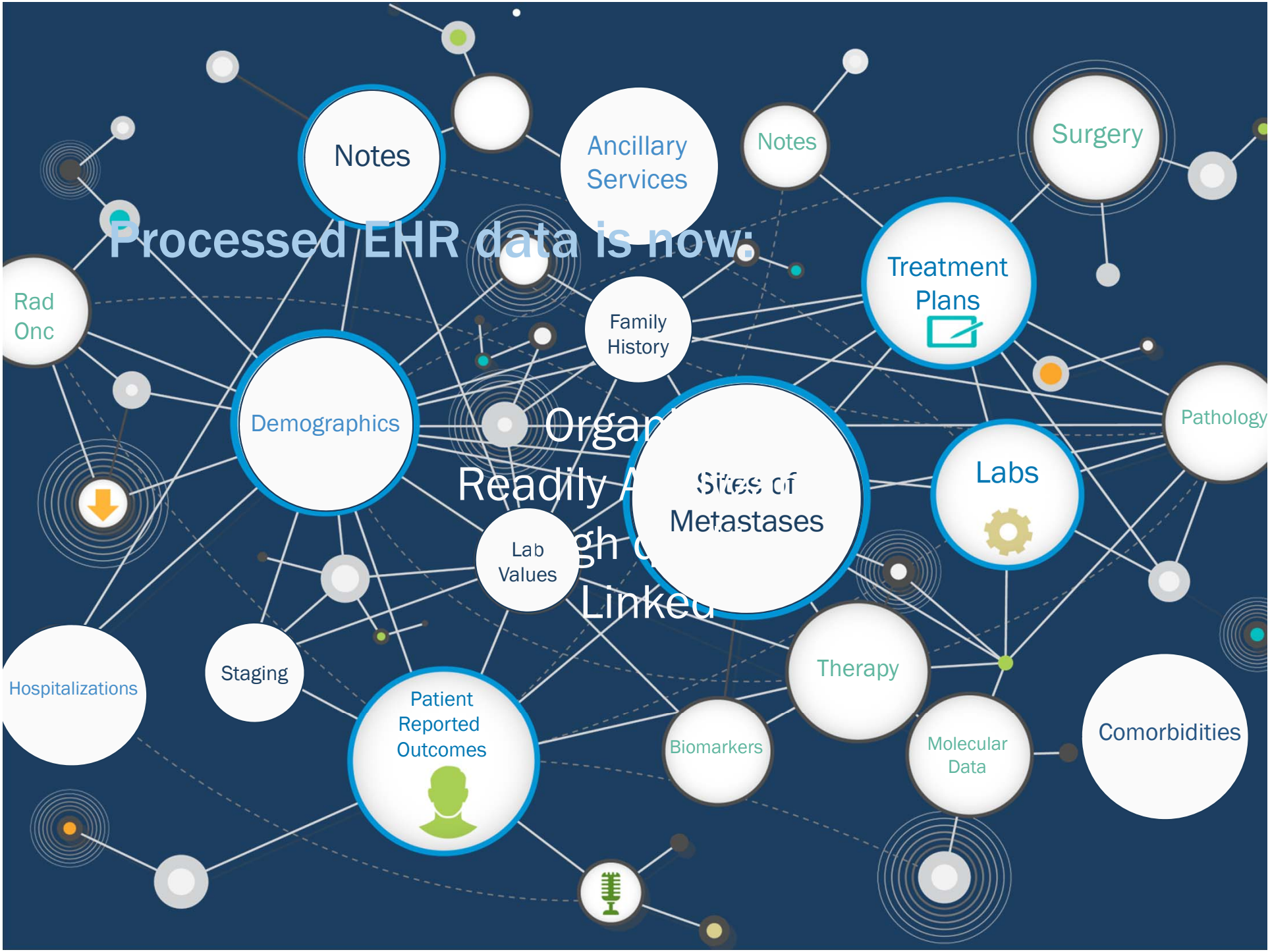
Derived variables
Patient reported data

Distribution of Most Commonly Altered Genes




Processed EHR data is now:
Notes
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Molecular Data
Comorbidities

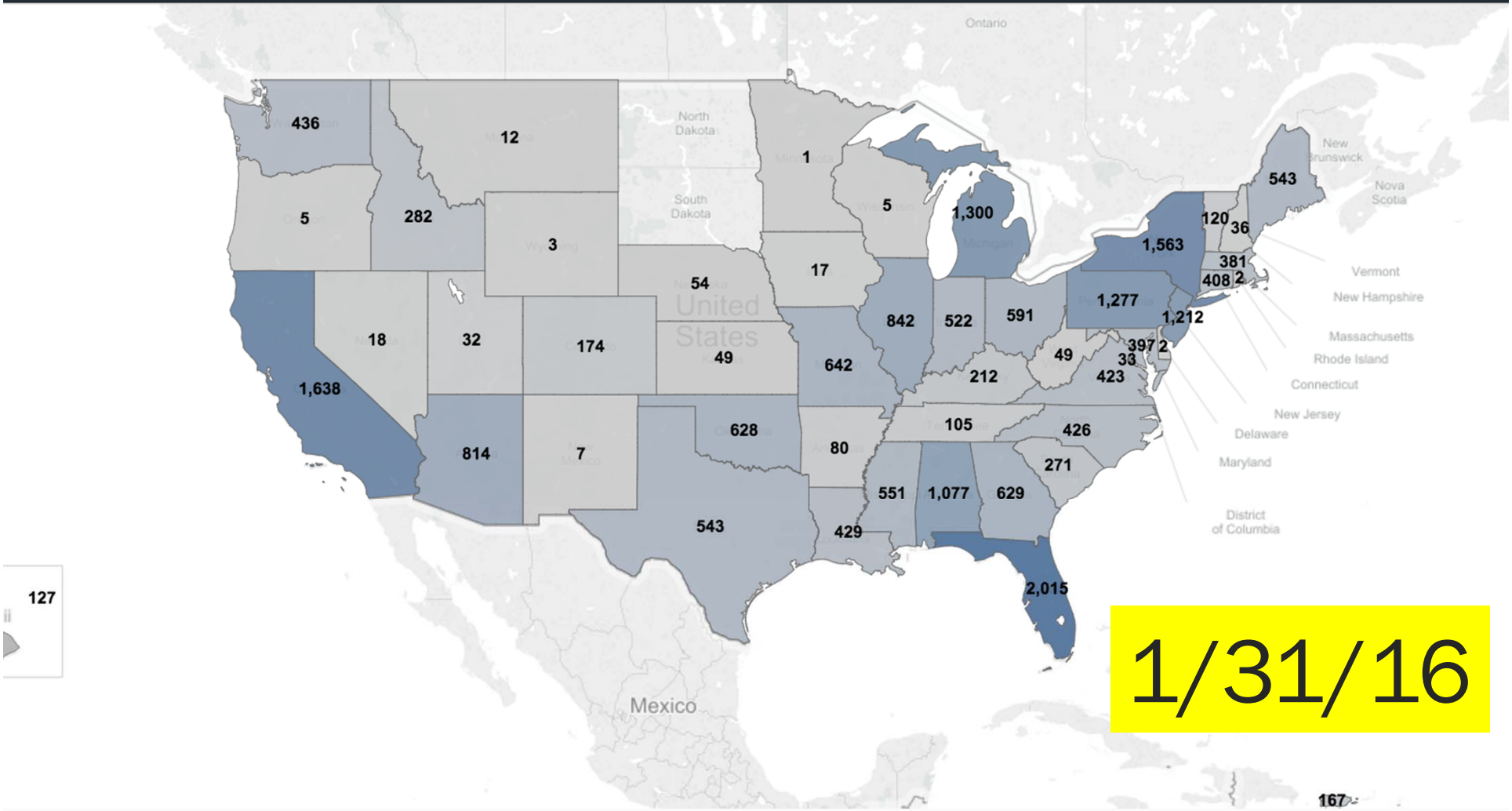
So….what's next?

The Evolving Landscape in Lung Cancer

How can we leverage data to better understand our patient population, monitor changes and document outcomes?

Current NSCLC Cohort

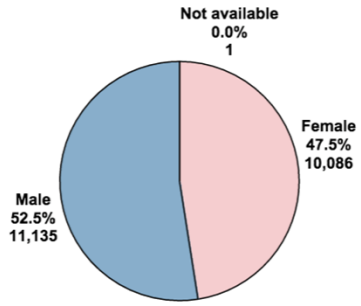
Total Patients: 22,762 (Community: 21,222, Academic: 1,540)
Number of Clinics Represented: 171



1/31/16

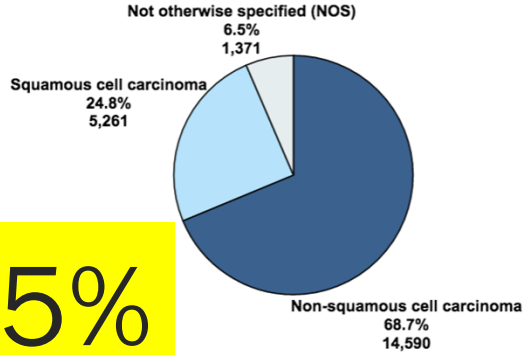
Cohort Demographics
(Number of Patients in Cohort: 21,222)

Gender

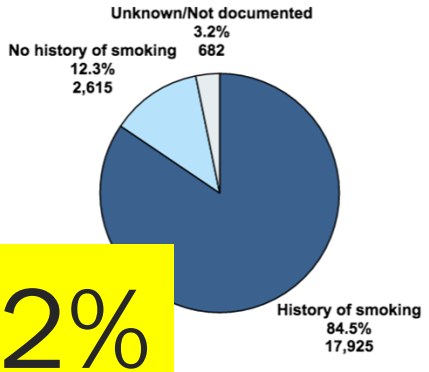


25%

Histology

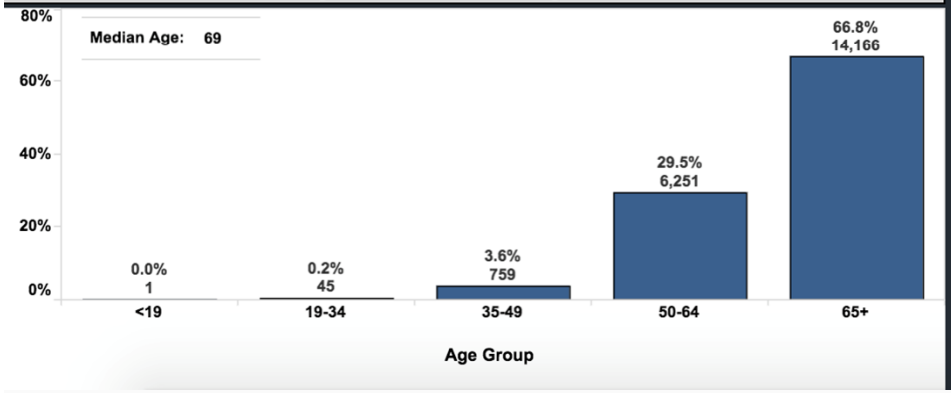


Smoking Status

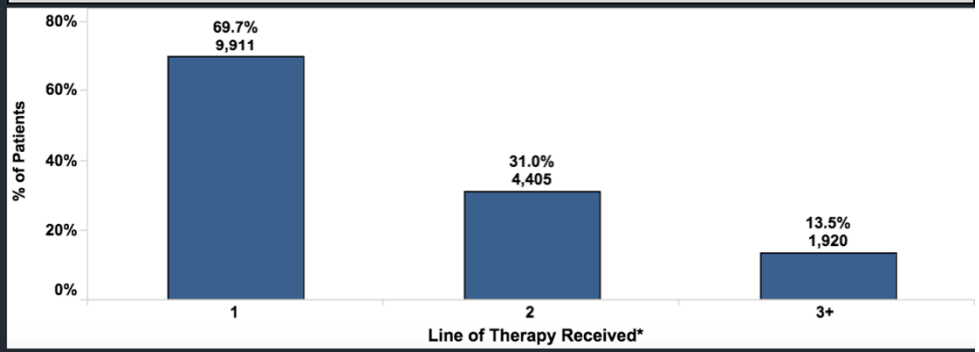


12%

Age at Advanced Diagnosis



Line of Therapy

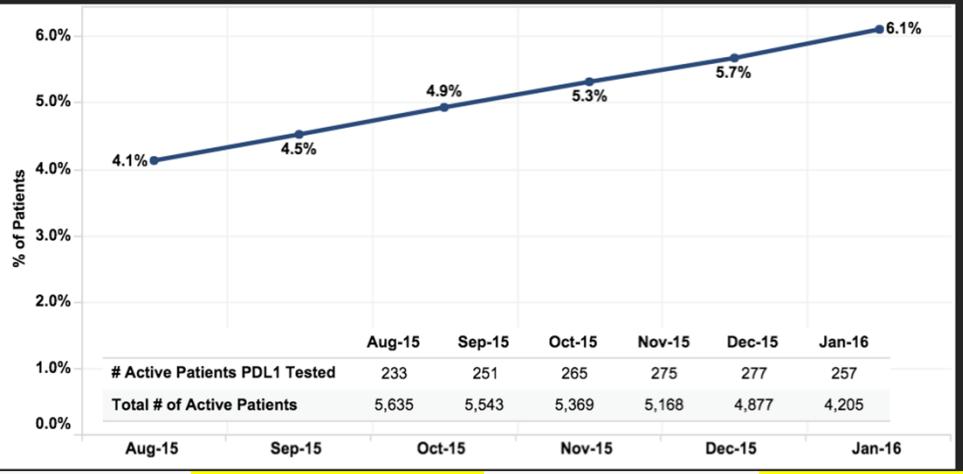


*Lines of ther hart represents the total number of patients that received any line of therapy after their advanced dia

70%

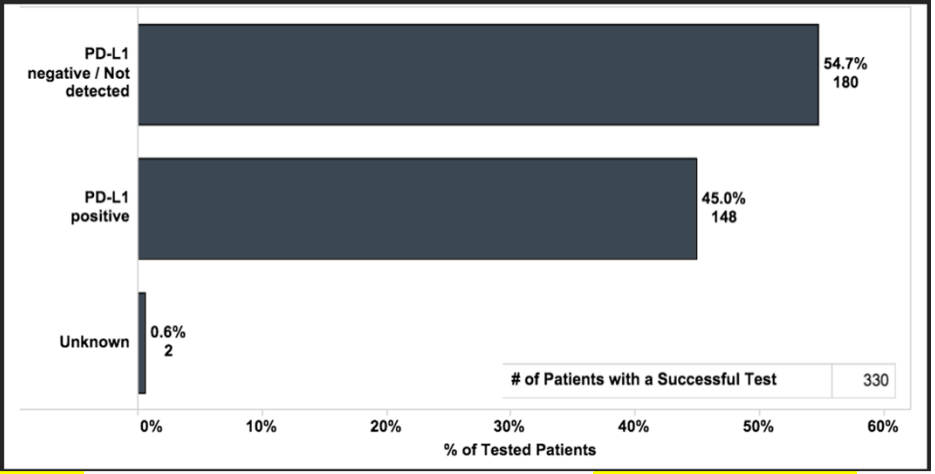
PDL1 Biomarker Test Overview

PDL1 Test Rate Among Active Patients



	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Jan-16
# Active Patients PDL1 Tested	233	251	265	275	277	257
Total # of Active Patients	5,635	5,543	5,369	5,168	4,877	4,205

PDL1 Test Results of First Successful Test



3.5% → 6.1%

45%

Patient Share by Therapy Class

Therapy Class
- Other therapies
- Clinical study drug-based th
- Non-platinum-based chemo
- ALK inhibitors
- PD-1/PD-L1-based therapies
- EGFR TKIs
- Anti-VEGF-based therapies
- Single agent chemotherapies
- Platinum-based chemo com

By Month or Quarter: Month

By Line Number: (All)

By Histology: (All)

By EGFR Status: (All)

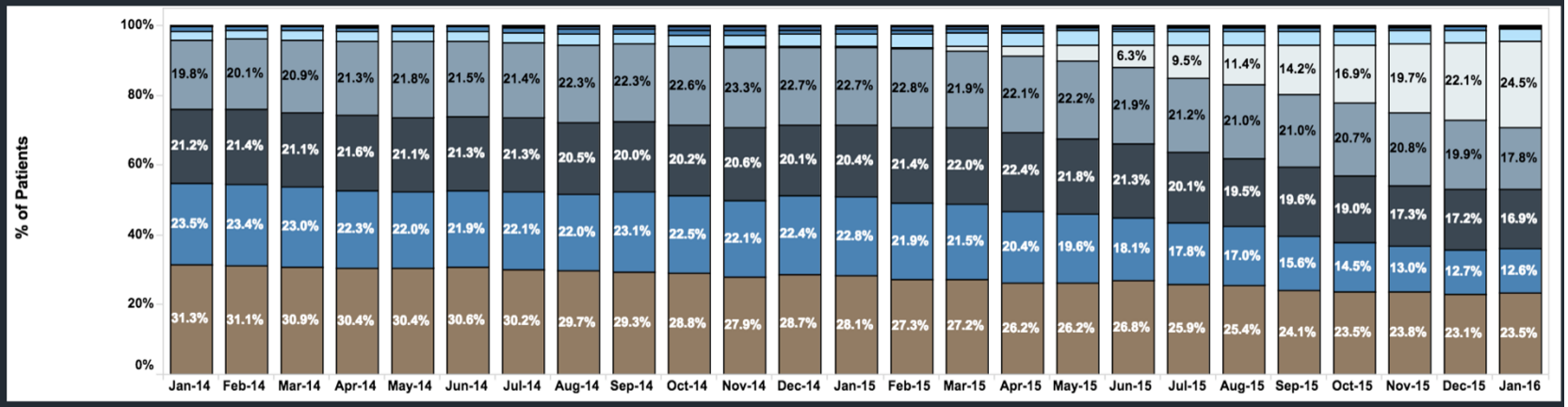
By ALK Status: (All)

By PDL1 Status: (All)

New or Continuing: (All)

Advanced Dx Date: Jan-11 – Jan-16

Patient Share



Number of Treated Patients

	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Ja..
PD-1/PD-L1-based therapies											2	3	3	5	39	80	132	185	282	340	429	513	579	642	687
Platinum-based chemo combos	769	776	806	808	810	821	848	826	837	825	766	795	771	734	766	751	739	782	772	759	726	714	697	673	659
EGFR TKIs	486	501	546	567	582	577	601	621	637	648	640	628	622	614	617	633	624	639	632	630	635	627	610	578	501
Anti-VEGF-based therapies	520	535	549	575	562	571	598	570	572	578	565	557	559	575	621	642	615	620	600	585	591	576	507	501	475
Single agent chemotherapies	576	585	600	593	587	587	622	612	662	644	608	621	626	589	606	585	551	529	530	510	472	439	381	369	353
ALK inhibitors	61	61	67	72	75	76	83	82	85	91	95	98	97	104	105	111	112	111	117	122	117	118	120	112	101
Non-platinum-based chemo combos	32	28	31	32	36	37	43	45	38	41	34	34	37	31	30	26	21	25	27	26	23	27	23	22	15
Clinical study drug-based therapies	6	7	8	10	10	9	11	20	22	30	36	30	20	31	30	30	20	23	20	19	22	15	13	10	12
Other therapies	3	2	1	3	2	1	3	6	8	5	3	3	6	5	3	3	2	3	2	2	2	5	3	3	4
# of patients	2,453	2,495	2,608	2,660	2,664	2,679	2,809	2,782	2,861	2,862	2,749	2,769	2,741	2,688	2,817	2,861	2,816	2,917	2,982	2,993	3,017	3,034	2,933	2,910	2,807

1.4% → 24.5%

687/2807

Patient Share by Therapy Class

Therapy Class

- Other therapies
- Clinical study drug-based th ...
- Non-platinum-based chemo ...
- PD-1/PD-L1-based therapies
- ALK inhibitors
- Single agent chemotherapies
- EGFR TKIs
- Anti-VEGF-based therapies
- Platinum-based chemo com ...

By Month or Quarter

Month

By Line Number

1L

- (All)
- 1L
- 1L maintenance
- 2L
- 3L+

By EGFR Status

(All)

By ALK Status

(All)

By PDL1 Status

(All)

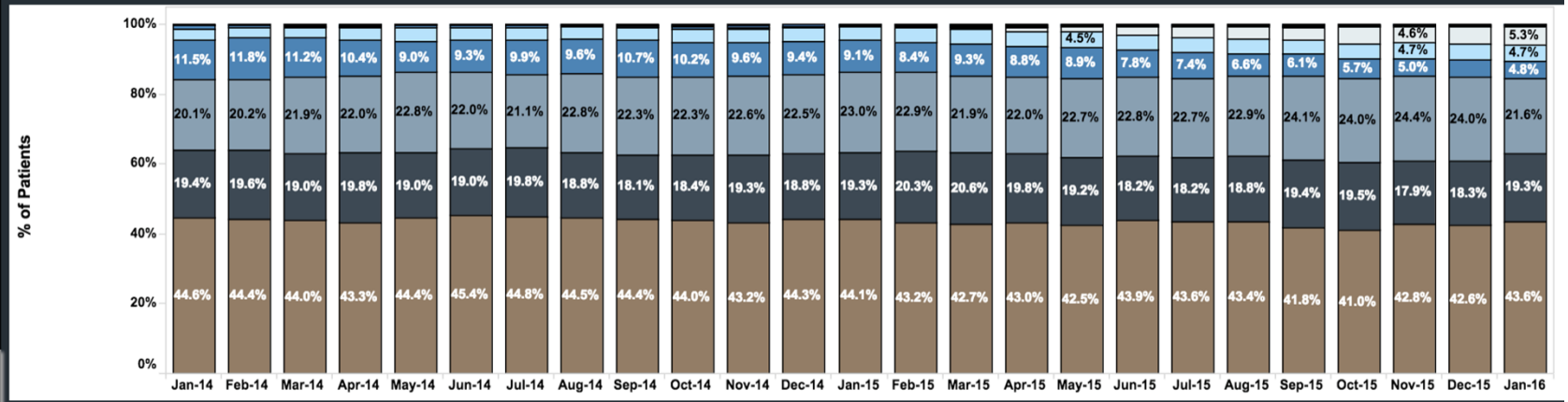
New or Continuing

(All)

Advanced Dx Date

Jan-11 Jan-16

Patient Share



Number of Treated Patients

	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Ja..
Platinum-based chemo combos	592	610	634	631	638	653	683	655	666	656	609	619	604	582	602	611	600	648	648	641	611	592	584	563	550
EGFR TKIs	267	278	315	320	328	316	321	335	335	332	319	314	315	308	309	313	320	337	338	338	352	347	333	318	272
Anti-VEGF-based therapies	257	270	274	289	273	273	301	277	271	275	272	262	264	274	290	282	271	268	271	278	284	282	244	242	244
PD-1/PD-L1-based therapies															8	15	22	36	45	51	56	67	63	64	67
Single agent chemotherapies	153	162	161	152	130	134	151	141	161	152	136	132	124	113	131	125	125	115	110	97	89	82	68	67	61
ALK inhibitors	43	41	46	50	52	51	54	52	53	55	54	54	53	60	58	63	64	62	64	62	59	63	64	61	59
Clinical study drug-based therapies	5	6	6	6	4	4	4	4	5	10	11	10	6	6	8	8	6	7	6	5	6	4	3	3	5
Non-platinum-based chemo combos	11	8	4	7	11	8	9	7	8	10	9	6	4	3	4	3	3	3	4	4	3	6	5	5	4
Other therapies			1	2	1		1	1	2	1	1			1	1	2				1	1	2	1		
# of patients	1,328	1,375	1,441	1,457	1,437	1,439	1,524	1,472	1,501	1,491	1,411	1,397	1,370	1,347	1,411	1,422	1,411	1,476	1,486	1,477	1,461	1,445	1,365	1,323	1,262

1st line 5%

Patient Share by Therapy Class

Therapy Class
- Other therapies
- Clinical study drug-based th
- ALK inhibitors
- Non-platinum-based chemo
- Anti-VEGF-based therapies
- EGFR TKIs
- Platinum-based chemo com
- PD-1/PD-L1-based therapies
- Single agent chemotherapies

By Month or Quarter
Month

By Line Number
(Multiple values)
- (All)
- 1L
- 1L maintenance
- 2L
- 3L+

By EGFR Status
(All)

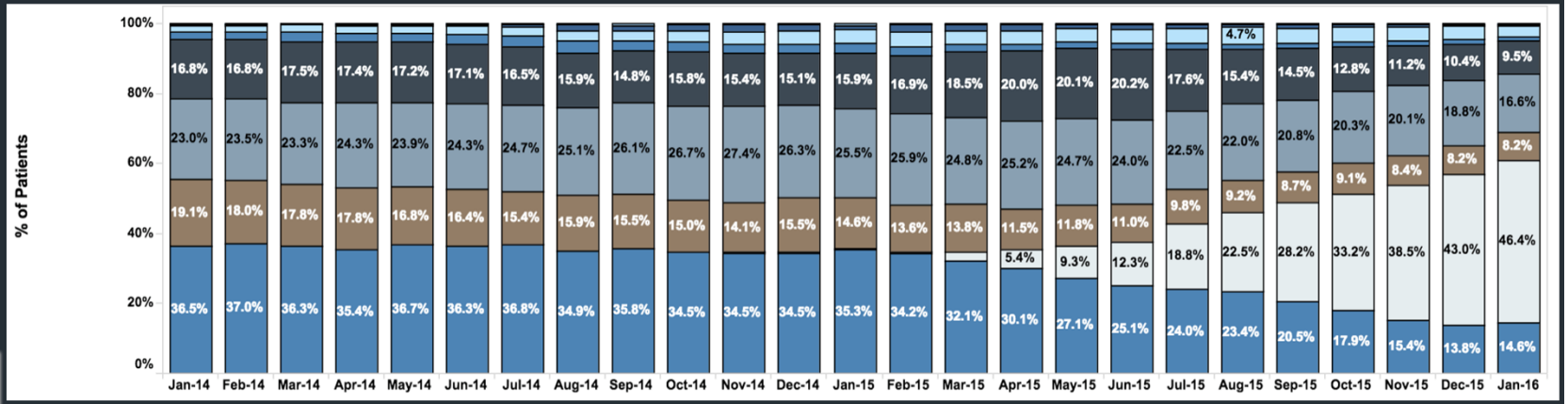
By ALK Status
(All)

By PDL1 Status
(All)

New or Continuing
(All)

Advanced Dx Date
Jan-11 Jan-16

Patient Share



Number of Treated Patients

	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Ja..
PD-1/PD-L1-based therapies											2	3	3	5	31	65	110	149	237	289	373	446	516	578	620
EGFR TKIs	213	217	225	242	245	250	265	270	287	302	306	298	292	290	294	306	292	291	284	283	275	272	270	252	222
Single agent chemotherapies	339	341	351	353	376	373	395	376	394	390	385	391	404	383	381	365	320	304	303	301	271	240	206	186	195
Anti-VEGF-based therapies	156	155	169	173	176	176	177	171	163	178	172	171	182	189	219	243	237	245	222	198	192	172	150	140	127
Platinum-based chemo combos	177	166	172	177	172	168	165	171	171	169	157	176	167	152	164	140	139	134	124	118	115	122	113	110	109
ALK inhibitors	18	20	21	22	23	25	29	30	32	36	41	44	44	44	47	48	48	49	53	60	58	55	56	51	42
Non-platinum-based chemo combos	21	20	27	25	25	29	34	38	30	31	25	28	33	28	26	23	18	22	23	22	20	21	18	17	11
Clinical study drug-based therapies	1	1	2	4	6	5	7	16	17	20	25	20	14	25	22	22	14	16	14	14	16	11	10	7	7
Other therapies	3	2		1	1	1	2	5	6	4	2	3	6	4	2	1	2	3	2	1	1	3	2	3	4
# of patients	928	922	967	997	1,024	1,027	1,074	1,077	1,100	1,130	1,115	1,134	1,145	1,120	1,186	1,213	1,180	1,213	1,262	1,286	1,321	1,342	1,341	1,344	1,337

2nd line+

2.6% → 46%

Kaplan-Meier Survival Analysis

Stratify By

- (•) All Patients
- ( ) Gender
- ( ) Histology
- ( ) Smoking Status

Advanced dx date

1/1/2013 — 6/1/2015

Follow-up time (days)

0 — 1608

First Line Therapy

(All)

Histology

- [x] Non-squamous cell carc…
- [x] NSCLC histology NOS
- [x] Squamous cell carcinoma

Smoking status

(All)

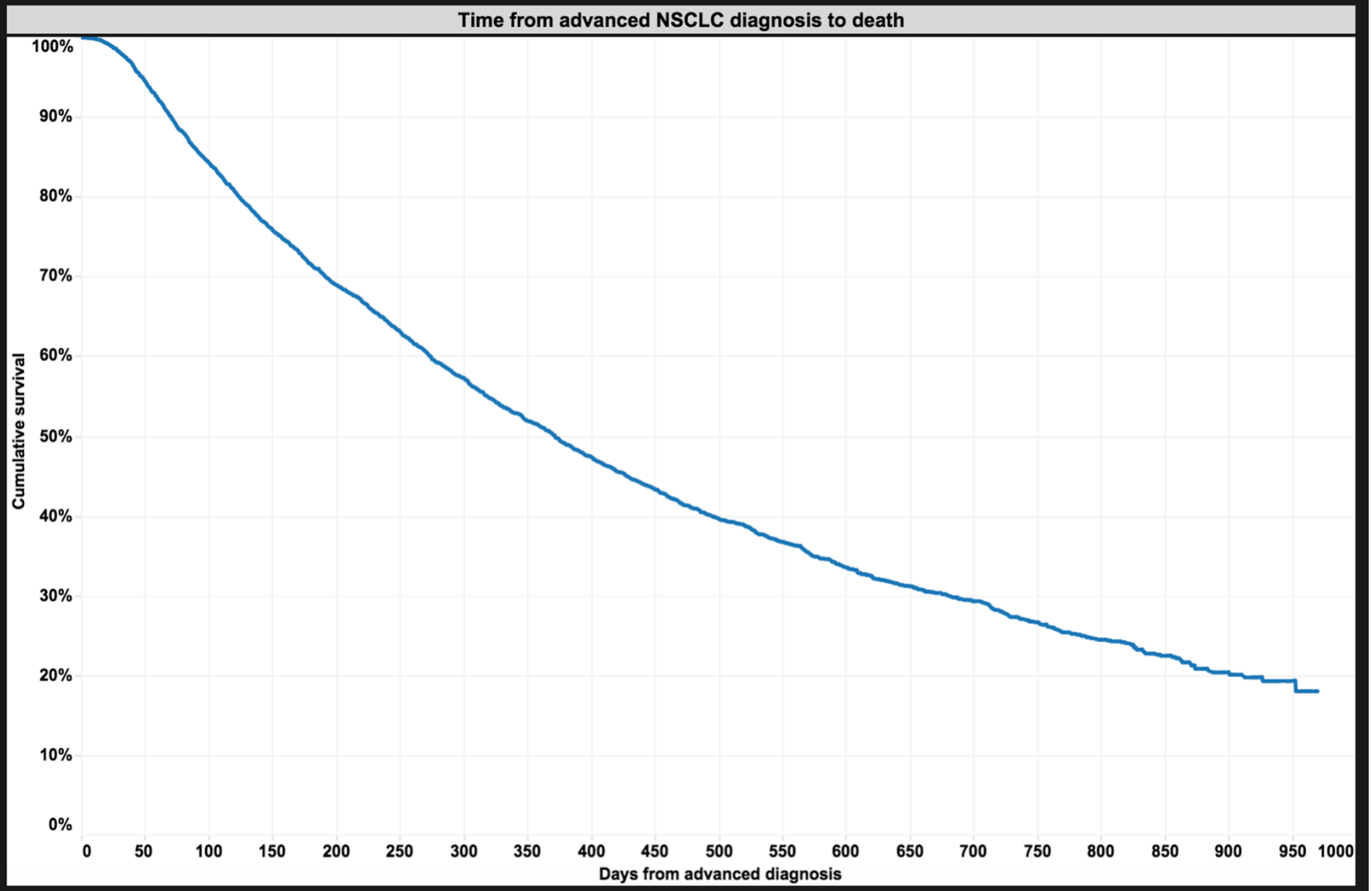
By EGFR status

(All)

By ALK status

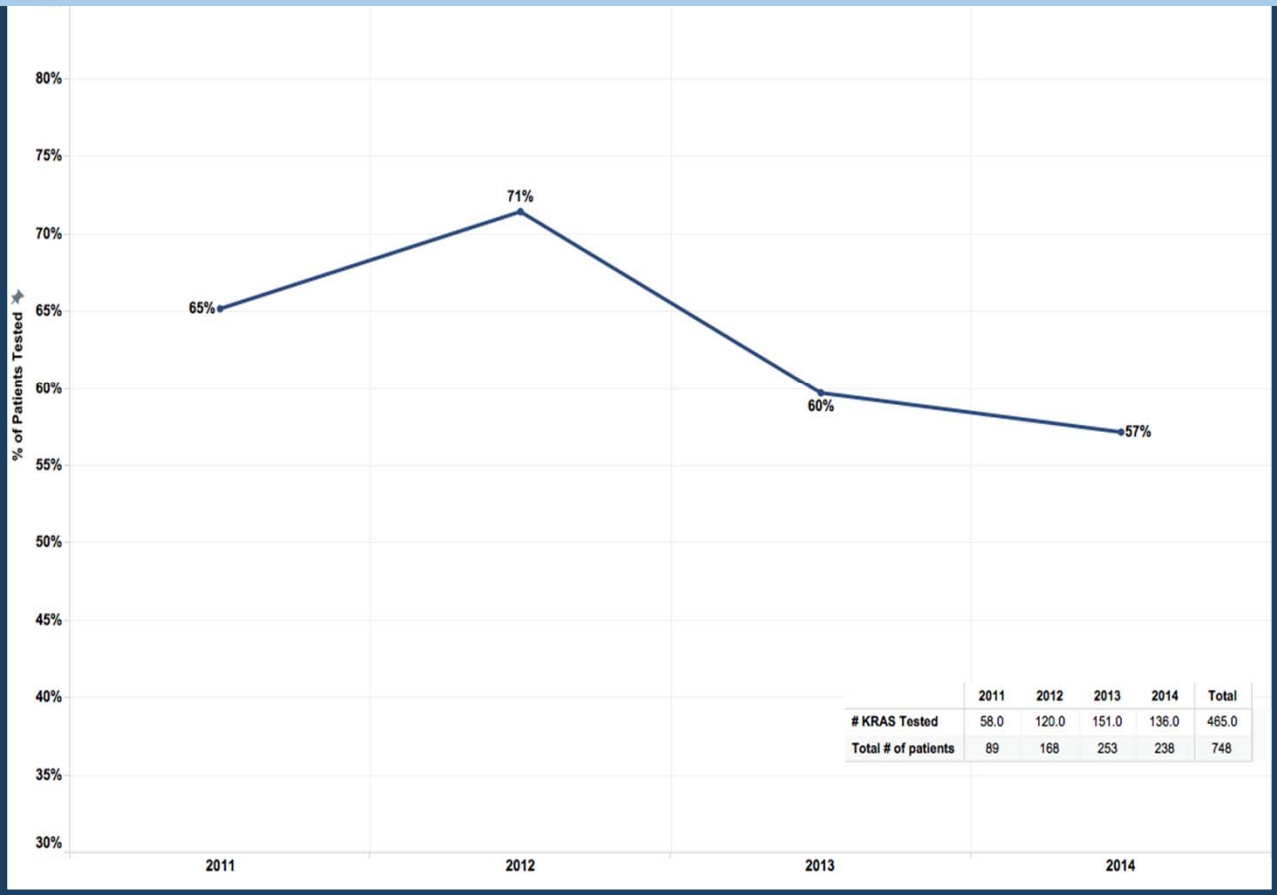
(All)

All Patients



How likely are patients to receive KRAS testing?

Metastatic colorectal cancer: KRAS testing rate by year of metastatic diagnosis (evaluated in June 2015)

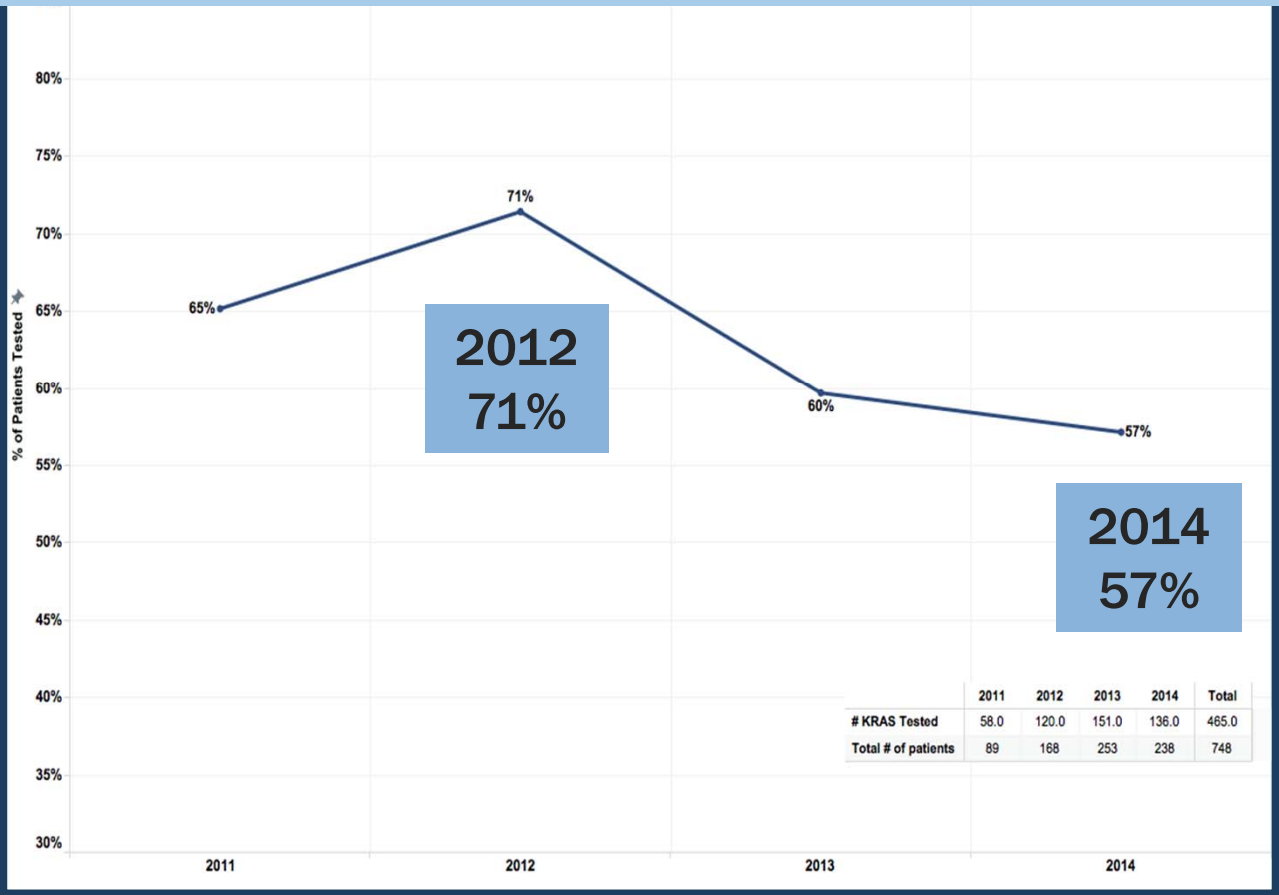


	2011	2012	2013	2014	Total
# KRAS Tested	58.0	120.0	151.0	136.0	465.0
Total # of patients	89	168	253	238	748

** Line of treatment is determined at Flatiron through a series of disease-specific business rules based on review of real-world data by oncologists*

How likely are patients to receive KRAS testing?

Metastatic colorectal cancer: KRAS testing rate by year of metastatic diagnosis (evaluated in June 2015)



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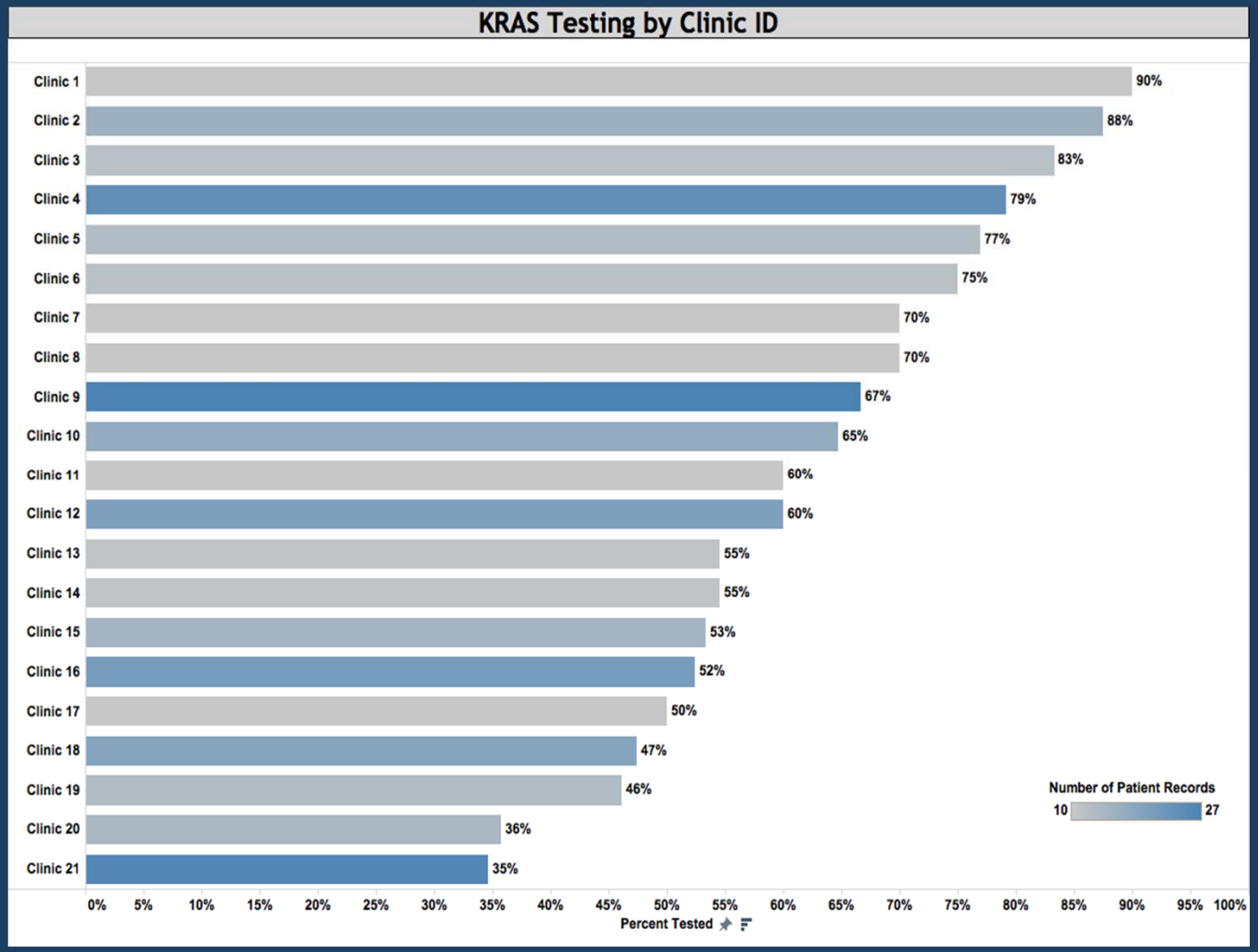
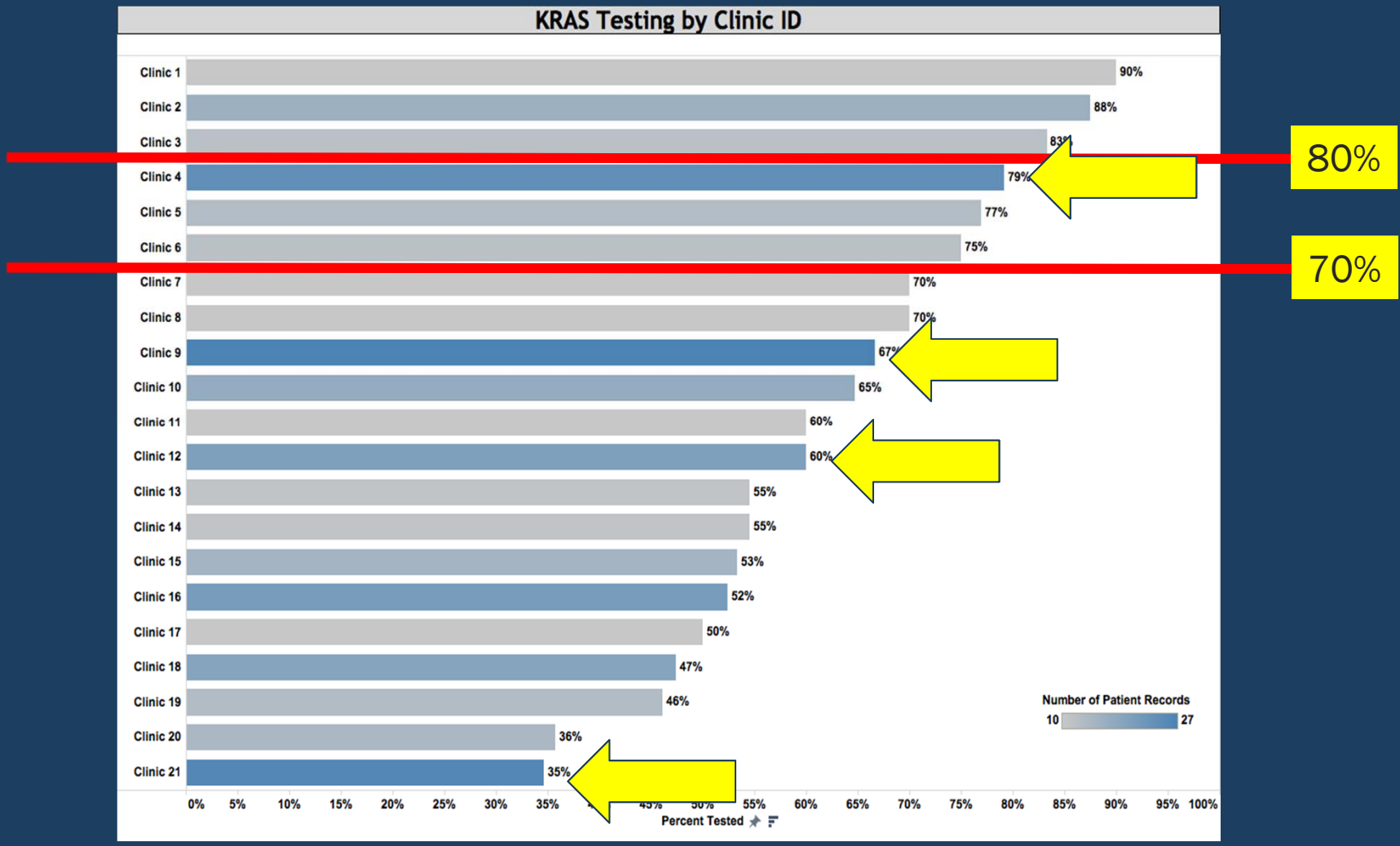
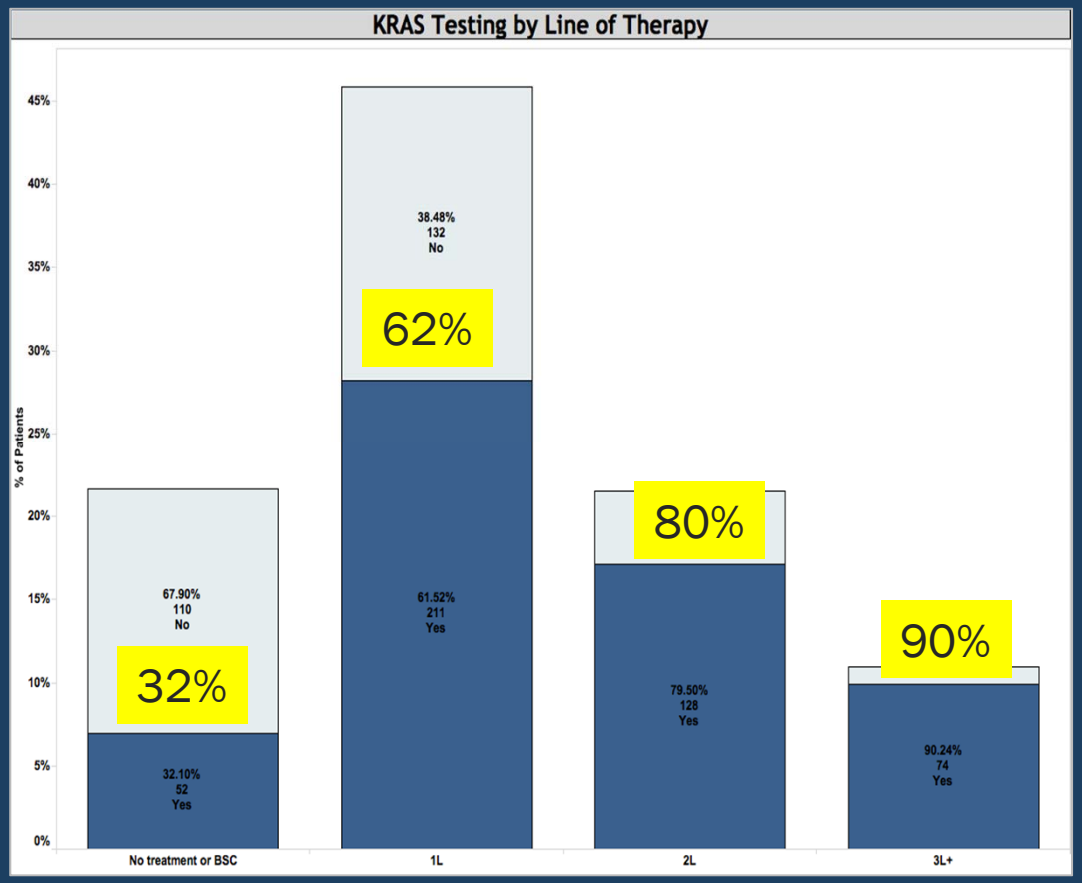
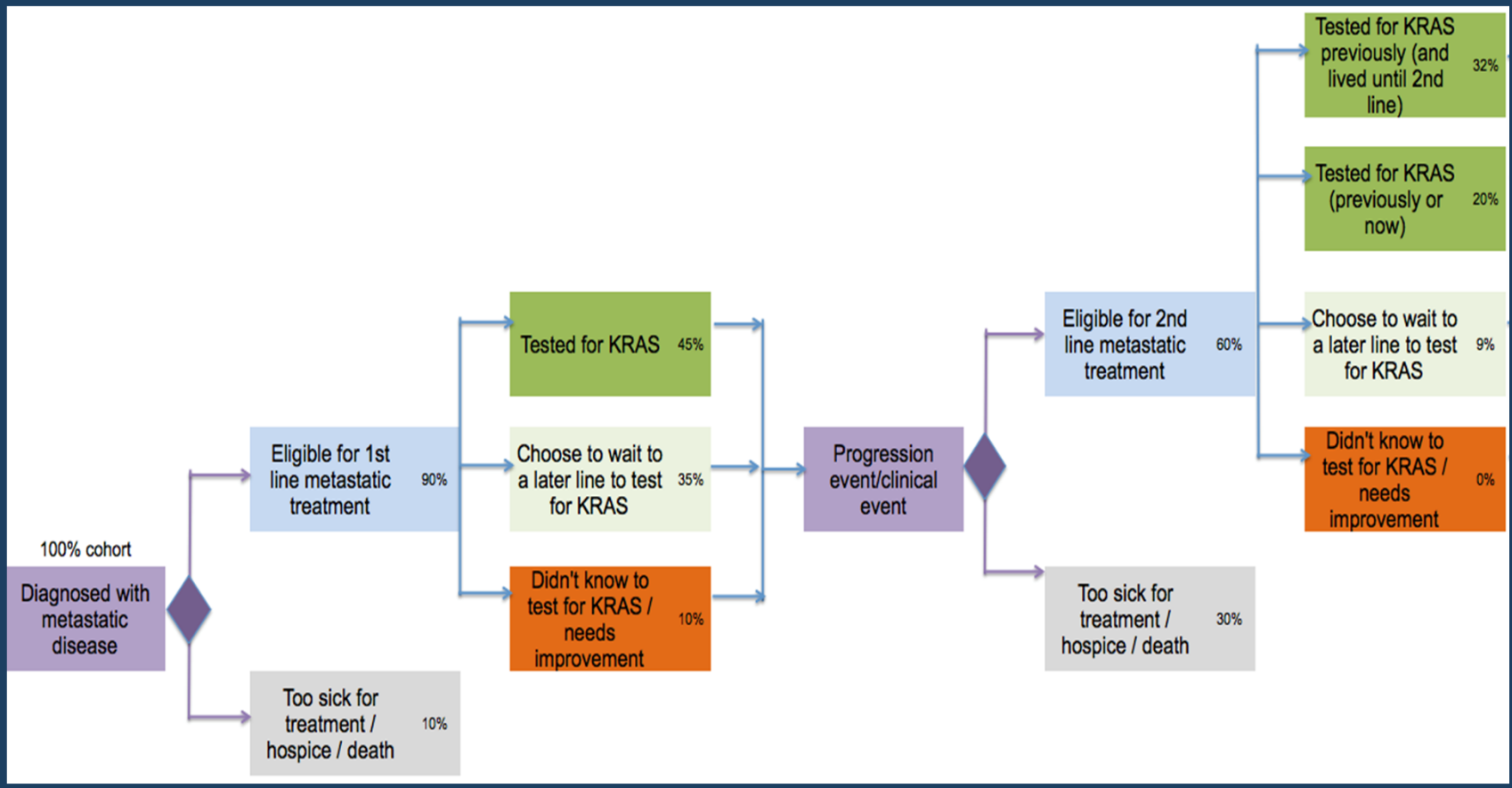

KRAS Testing by Clinic ID
Clinic 1
Clinic 2
Clinic 3
Clinic 4
Clinic 5
Clinic 6
Clinic 7
Clinic 8
Clinic 9
Clinic 10
Clinic 11
Clinic 12
Clinic 13
Clinic 14
Clinic 15
Clinic 16
Clinic 17
Clinic 18
Clinic 19
Clinic 20
Clinic 21
90%
88%
83%
79%
77%
75%
70%
70%
67%
65%
60%
60%
55%
55%
53%
52%
50%
47%
46%
36%
35%
Number of Patient Records
10
27
0%
5%
10%
15%
20%
25%
30%
35%
40%
45%
50%
55%
60%
65%
70%
75%
80%
85%
90%
95%
100%
Percent Tested

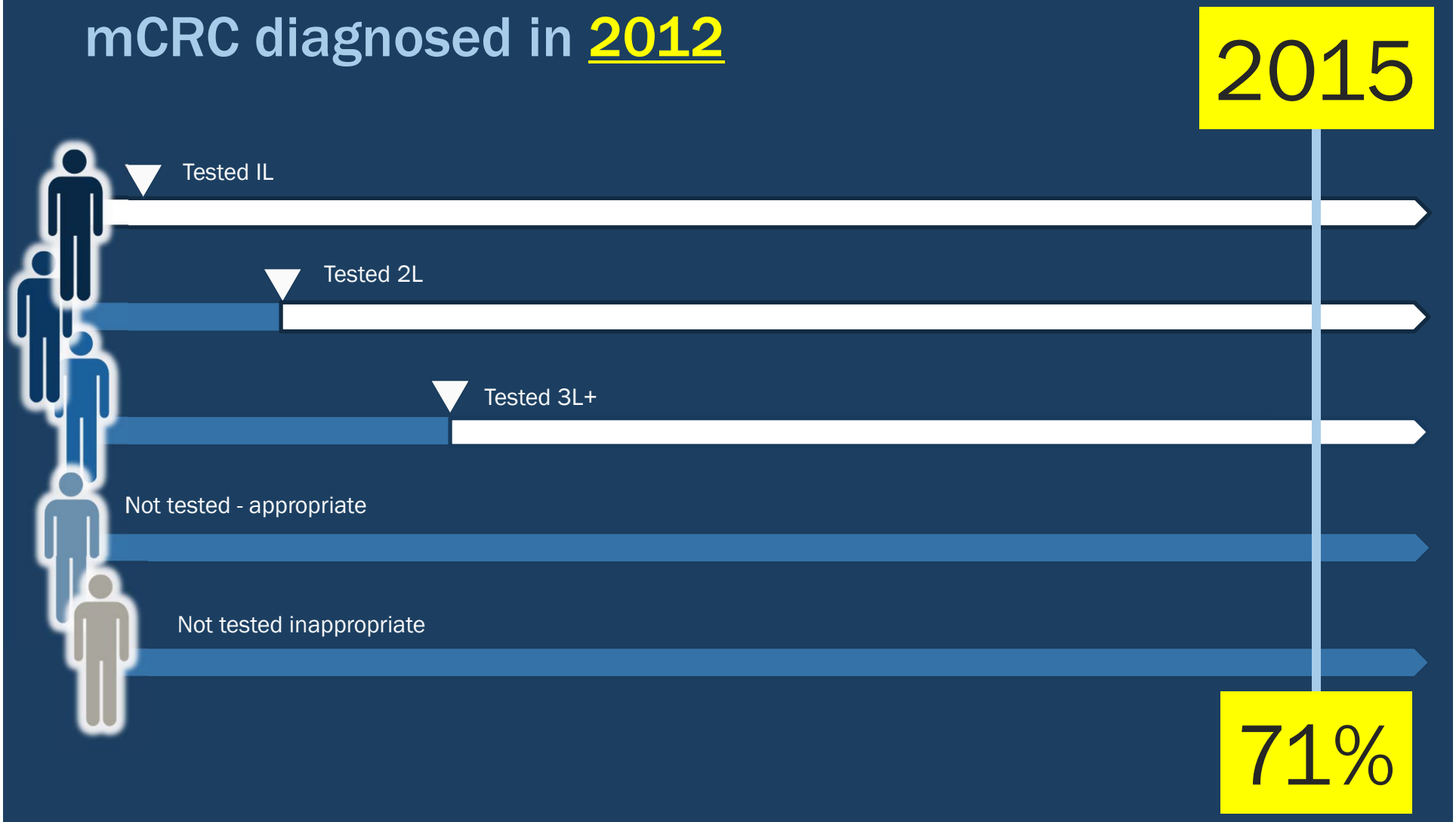

KRAS Testing by Clinic ID
Clinic 1
Clinic 2
Clinic 3
Clinic 4
Clinic 5
Clinic 6
Clinic 7
Clinic 8
Clinic 9
Clinic 10
Clinic 11
Clinic 12
Clinic 13
Clinic 14
Clinic 15
Clinic 16
Clinic 17
Clinic 18
Clinic 19
Clinic 20
Clinic 21
90%
88%
79%
77%
75%
70%
70%
65%
60%
60%
55%
55%
53%
52%
50%
47%
46%
36%
35%
80%
70%
Number of Patient Records
10
27
0%
5%
10%
15%
20%
25%
30%
35%
55%
60%
65%
70%
75%
80%
85%
90%
95%
100%
Percent Tested



Later lines of therapy are associated with a higher probability of KRAS testing

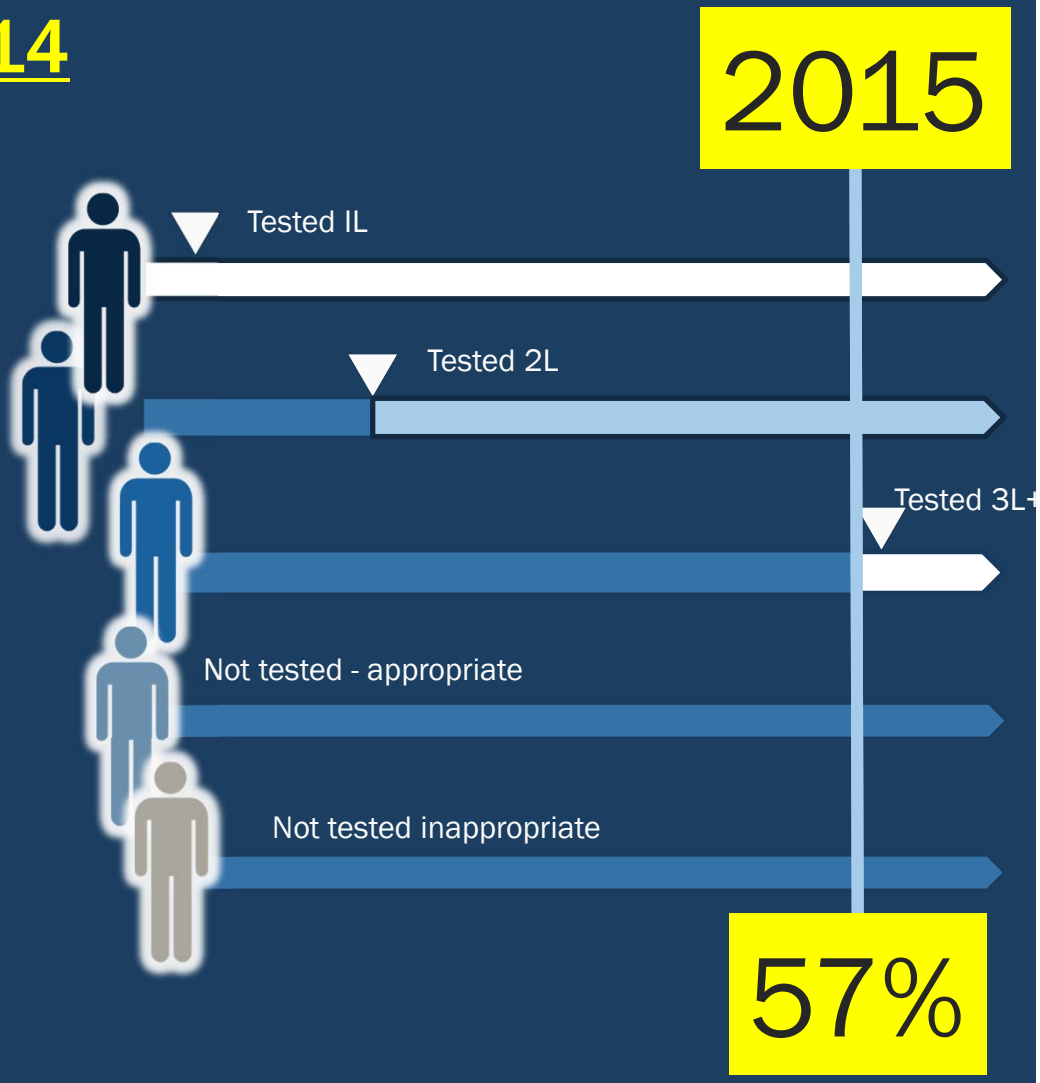

100% cohort
Diagnosed with metastatic disease
Eligible for 1st line metastatic treatment
90%
Too sick for treatment / hospice / death
10%
Tested for KRAS
45%
Choose to wait to a later line to test for KRAS
35%
Didn't know to test for KRAS / needs improvement
10%
Progression event/clinical event
Eligible for 2nd line metastatic treatment
60%
Too sick for treatment / hospice / death
30%
Tested for KRAS previously (and lived until 2nd line)
32%
Tested for KRAS (previously or now)
20%
Choose to wait to a later line to test for KRAS
9%
Didn't know to test for KRAS / needs improvement
0%

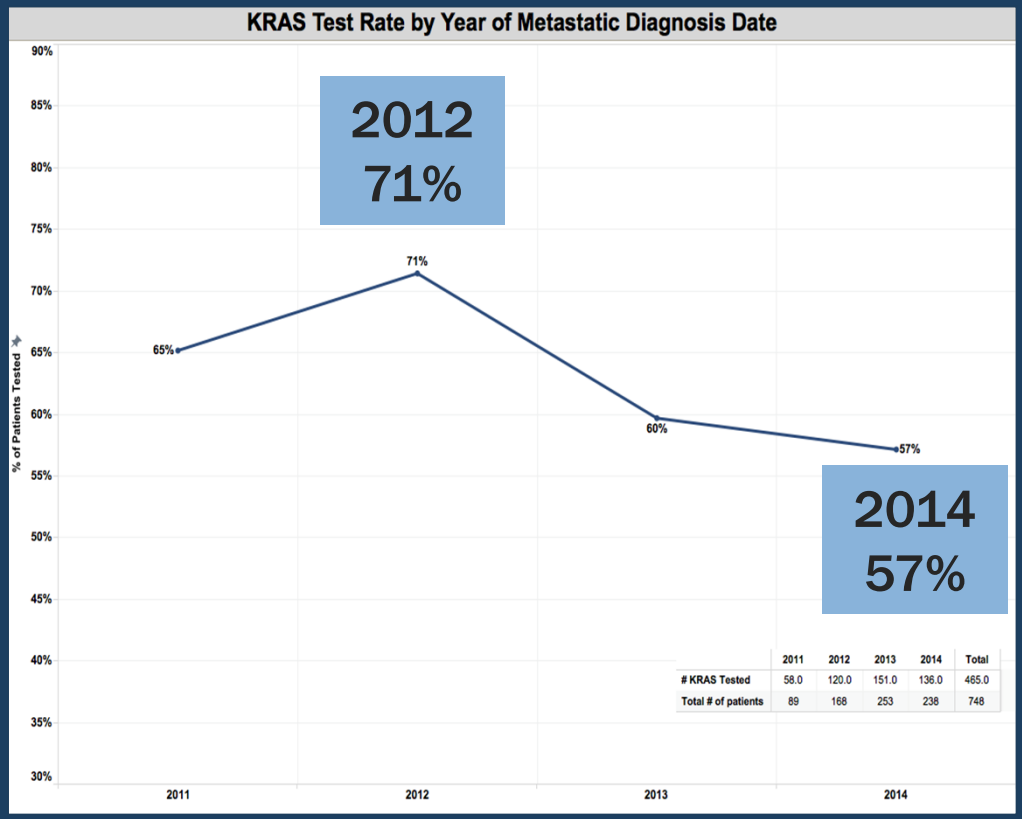
Use our understanding of patient journeys…



Use our understanding of patient journeys…

mCRC diagnosed in 2014



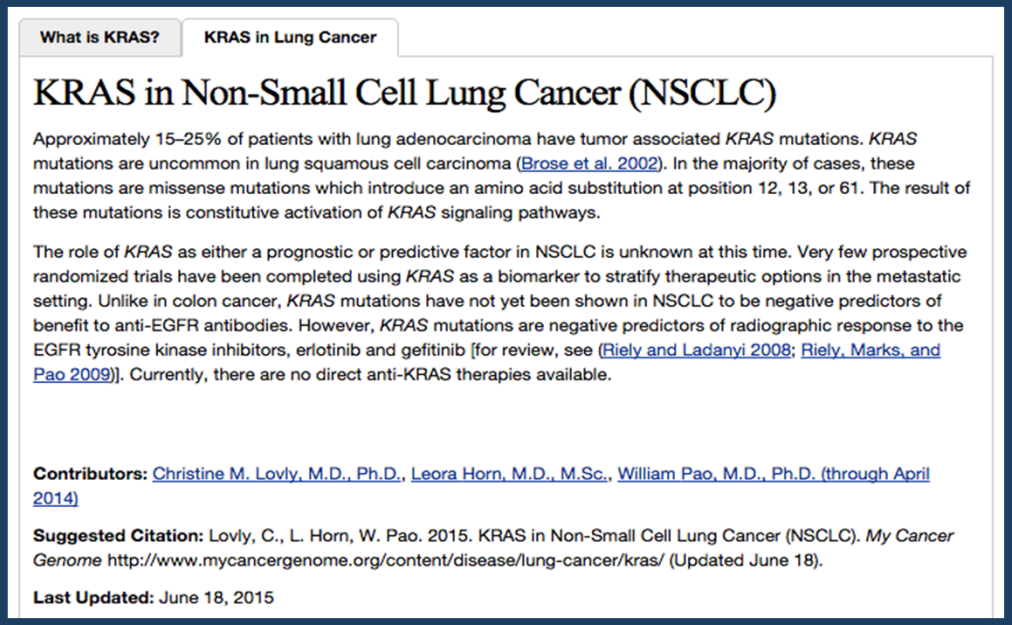

KRAS Test Rate by Year of Metastatic Diagnosis Date
% of Patients Tested
90%
85%
80%
75%
70%
65%
60%
55%
50%
45%
40%
35%
30%
2011
2012
2013
2014
65%
71%
60%
57%
2012
71%
2014
57%
2011 2012 2013 2014 Total
KRAS Tested 58.0 120.0 151.0 136.0 465.0
Total # of patients 89 168 253 238 748

Take care!

Addressing questions in precision medicine

How do I manage my lung cancer patient with a KRAS mutation?

MY CANCER GENOME®
GENETICALLY INFORMED CANCER MEDICINE



What is KRAS? | KRAS in Lung Cancer

KRAS in Non-Small Cell Lung Cancer (NSCLC)

Approximately 15–25% of patients with lung adenocarcinoma have tumor associated *KRAS* mutations. *KRAS* mutations are uncommon in lung squamous cell carcinoma (Brose et al. 2002). In the majority of cases, these mutations are missense mutations which introduce an amino acid substitution at position 12, 13, or 61. The result of these mutations is constitutive activation of *KRAS* signaling pathways.

The role of *KRAS* as either a prognostic or predictive factor in NSCLC is unknown at this time. Very few prospective randomized trials have been completed using *KRAS* as a biomarker to stratify therapeutic options in the metastatic setting. Unlike in colon cancer, *KRAS* mutations have not yet been shown in NSCLC to be negative predictors of benefit to anti-EGFR antibodies. However, *KRAS* mutations are negative predictors of radiographic response to the EGFR tyrosine kinase inhibitors, erlotinib and gefitinib [for review, see (Riely and Ladanyi 2008; Riely, Marks, and Pao 2009)]. Currently, there are no direct anti-KRAS therapies available.

Contributors: Christine M. Lovly, M.D., Ph.D., Leora Horn, M.D., M.Sc., William Pao, M.D., Ph.D. (through April 2014)

Suggested Citation: Lovly, C., L. Horn, W. Pao. 2015. KRAS in Non-Small Cell Lung Cancer (NSCLC). *My Cancer Genome* http://www.mycancergenome.org/content/disease/lung-cancer/kras/ (Updated June 18).

Last Updated: June 18, 2015

KRAS is among the most commonly altered gene in our lung cancer cohort, yet **the implications of KRAS mutations are not yet understood**

Journey of a Patient on Targeted Therapy After NGS

ABOUT THE TEST:
FoundationOne® is a next-generation sequencing (NGS) based assay that identifies genomic alterations within hundreds of cancer-related genes.

PATIENT RESULTS

- 3 genomic alterations
- 3 therapies associated with potential clinical benefit
- 0 therapies associated with lack of response
- 15 clinical trials

TUMOR TYPE: LUNG ADENOCARCINOMA

Genomic Alterations Identified†

KRAS Q61H
PTEN loss
CDKN2A/B loss

Additional Disease-relevant Genes with No Reportable Alterations Identified†

RET
ALK
BRAF
ERBB2
MET
EGFR

†For a complete list of the genes assayed and performance specifications, please refer to the Appendix
※See Appendix for details

THERAPEUTIC IMPLICATIONS

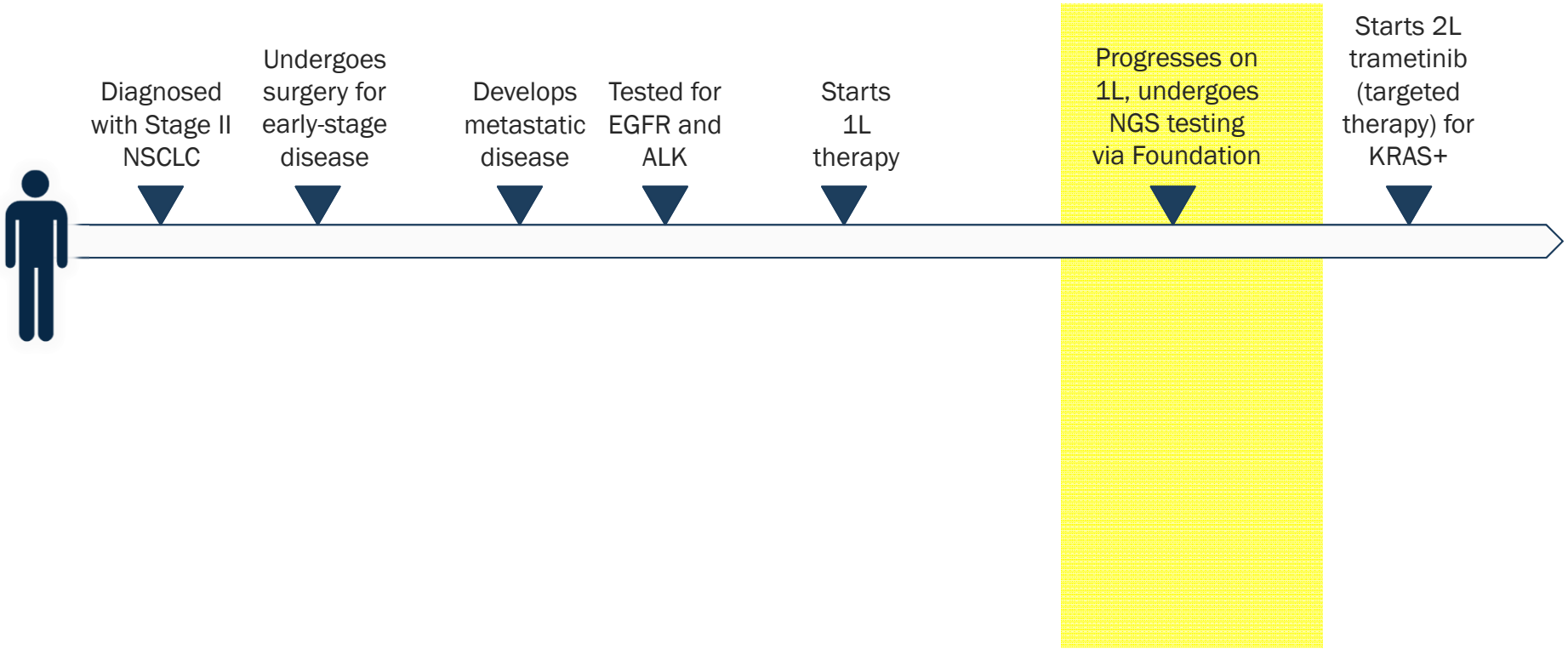
Genomic Alterations Detected	FDA Approved Therapies (in patient's tumor type)	FDA Approved Therapies (in another tumor type)	Potential Clinical Trials
KRAS Q61H	None	Trametinib	Yes, see clinical trials section
PTEN loss	None	Everolimus Temsirolimus	Yes, see clinical trials section
CDKN2A/B loss	None	None	Yes, see clinical trials section

Note: Genomic alterations detected may be associated with activity of certain FDA approved drugs; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type.

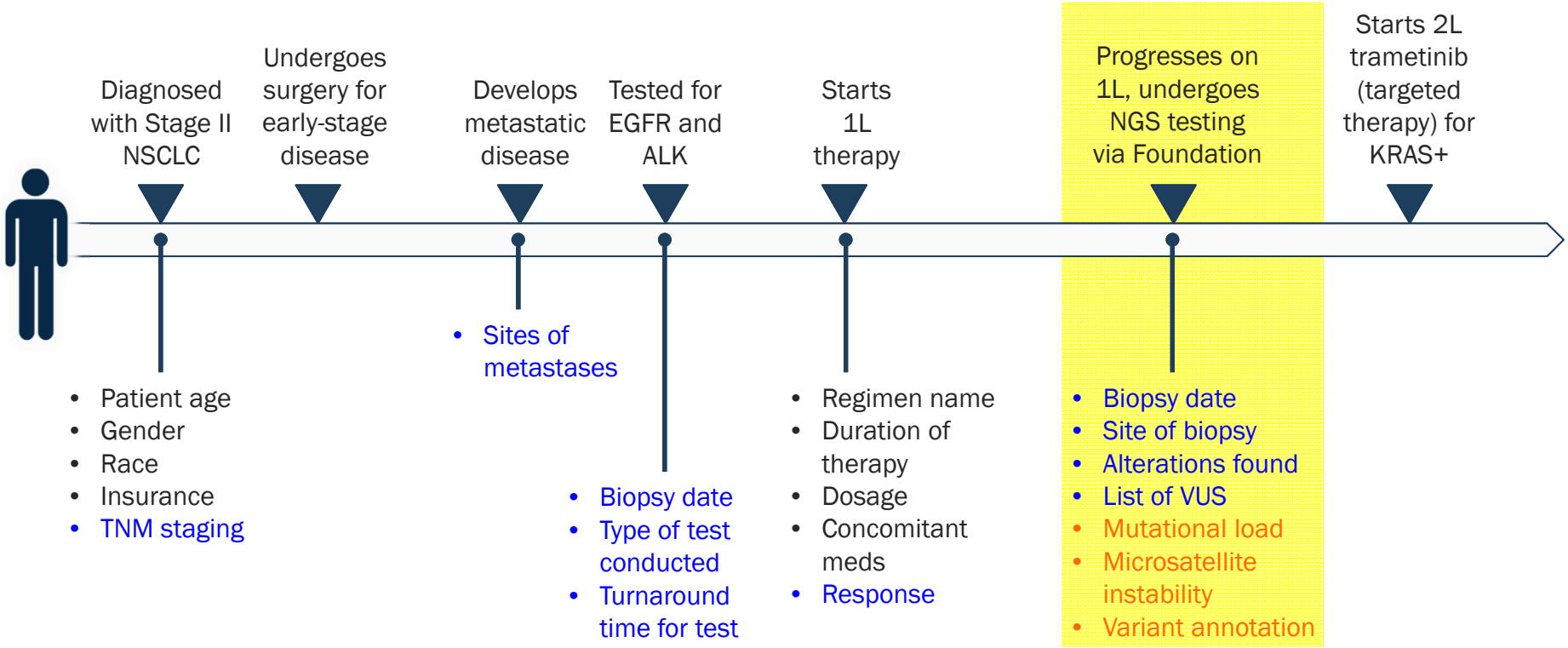
Based on NGS testing, patient underwent treatment with **trametinib** in 2L

FLATIRON

Journey of a Patient on Targeted Therapy After NGS



Journey of a Patient on Targeted Therapy After NGS



Structured EMR data
Unstructured EMR data
FMI Genetic Data

FLATIRON

What About Outcomes For Other KRAS+ Patients?

PFS for NGS-Tested Patients

Design your cohort. Plot

Clinical Endpoint

- ○ OS
- ◉ PFS

Start Date For PFS

- ○ Initial Diagnosis Date
- ◉ Advanced Diagnosis Date
- ○ 1st Line of Therapy Start Date

Add/Remove a second cohort

Filter Cohort 1 by:

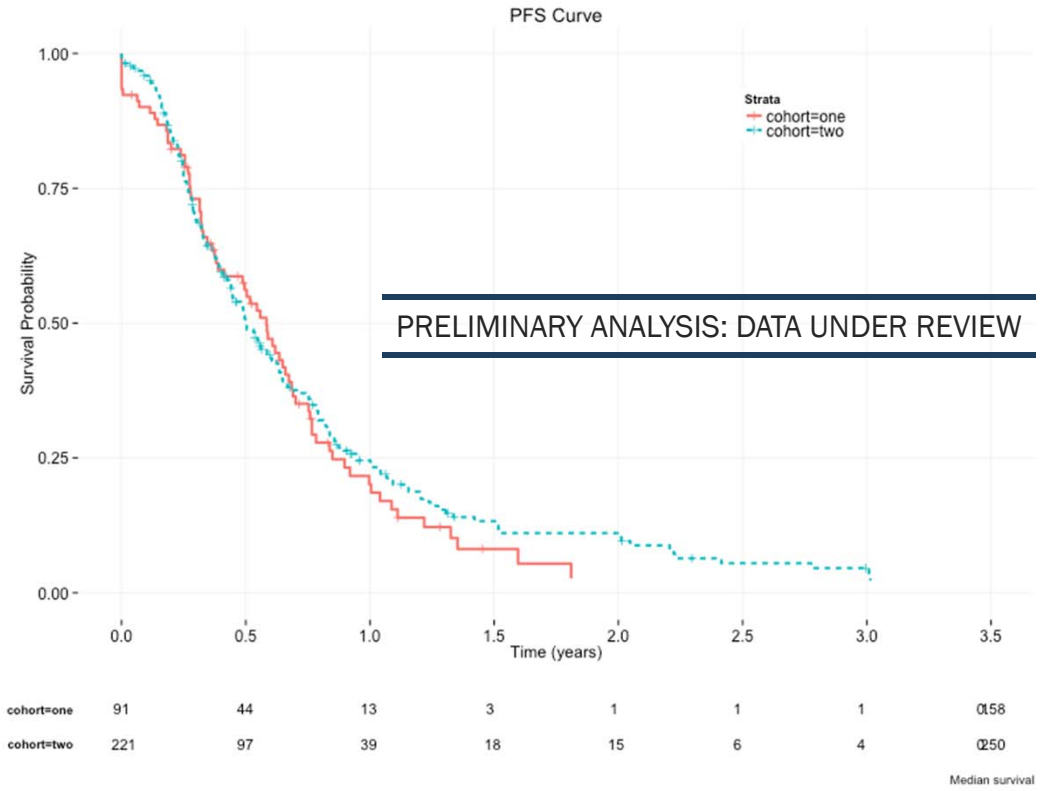
- ☐ Gender
- ☑ Gene Alteration

Gene Name	Alteration Status
KRAS	Altered

Filter Cohort 2 by:

- ☐ Gender
- ☑ Gene Alteration

Gene Name	Alteration Status
KRAS	WT



PRELIMINARY ANALYSIS: DATA UNDER REVIEW

FLATIRON

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