UCSF Brain Tumor Center

“Building for everyone” within a high value low-cost healthcare system

NERVES Annual meeting
Los Angeles, CA
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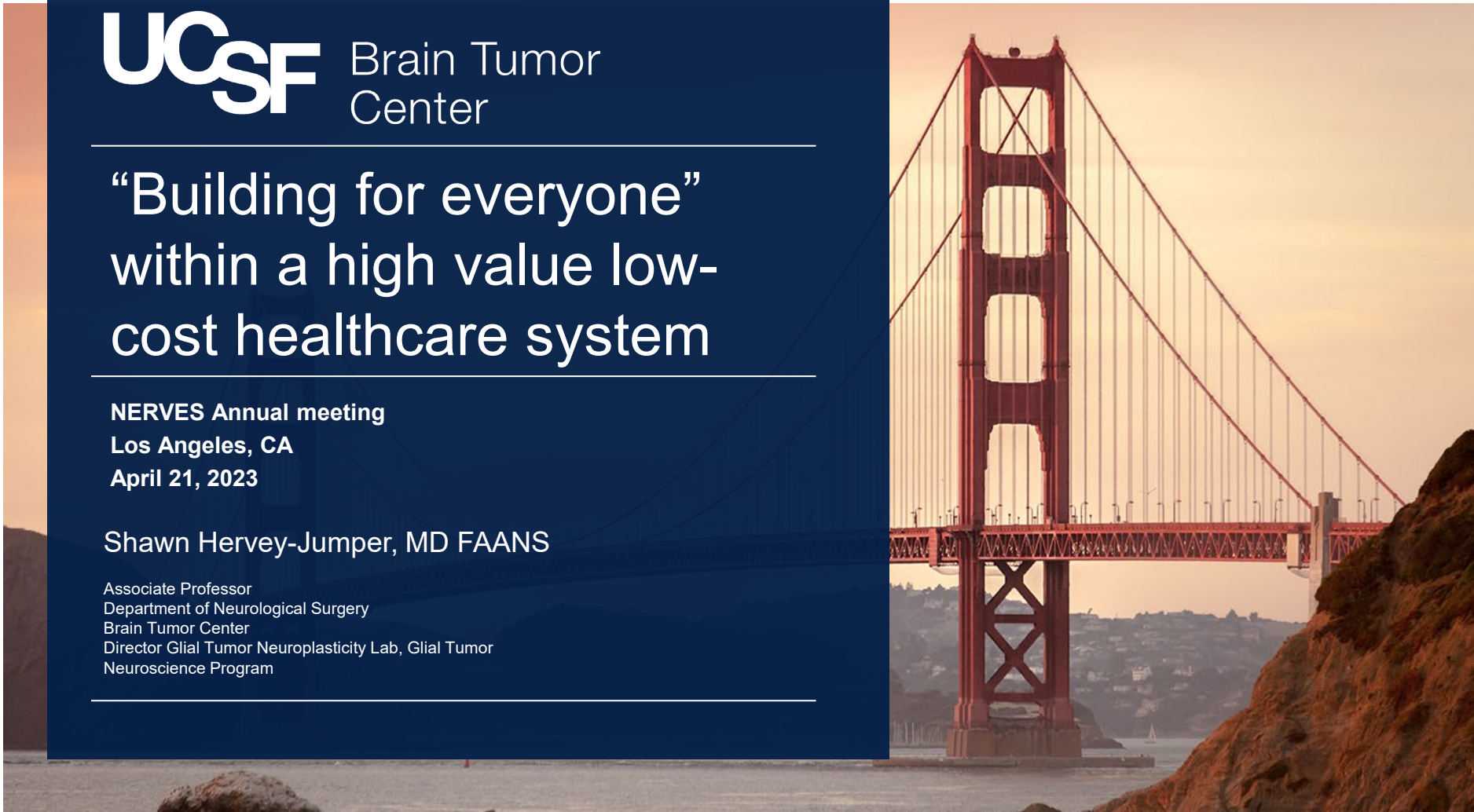

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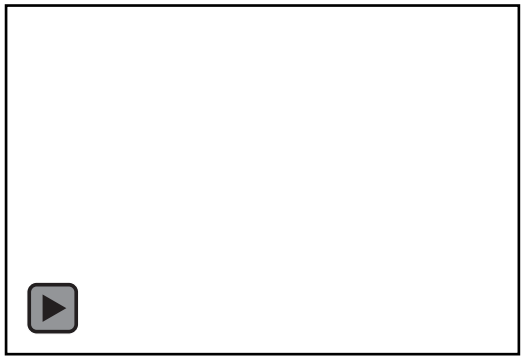
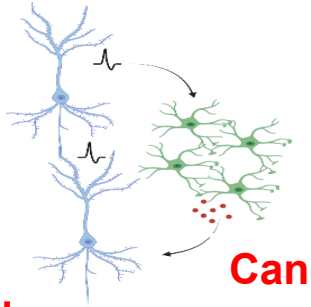
Cancer surgeon

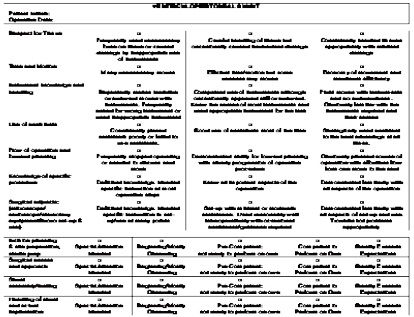


Neural regulation of cancer



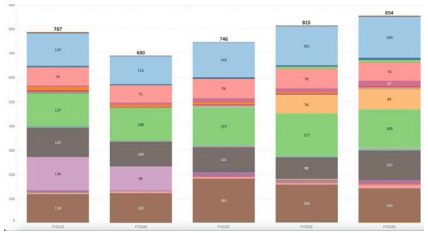
Associate Neurosurgery Residency Director

Index Case



Medical Director Neurosurgery

"Quality, safety, access, culture"

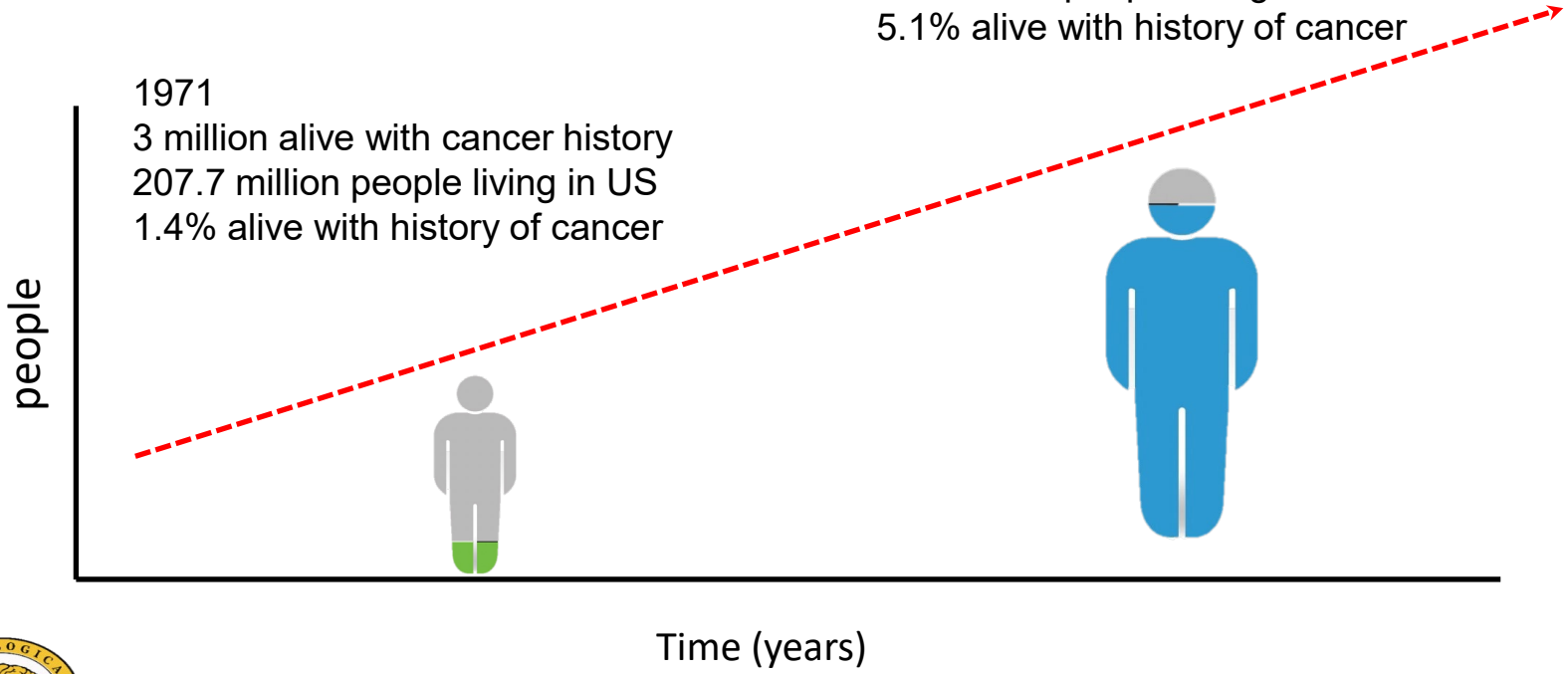


We need cancer therapies that work
We need to understand how they work
We need to build them for everyone

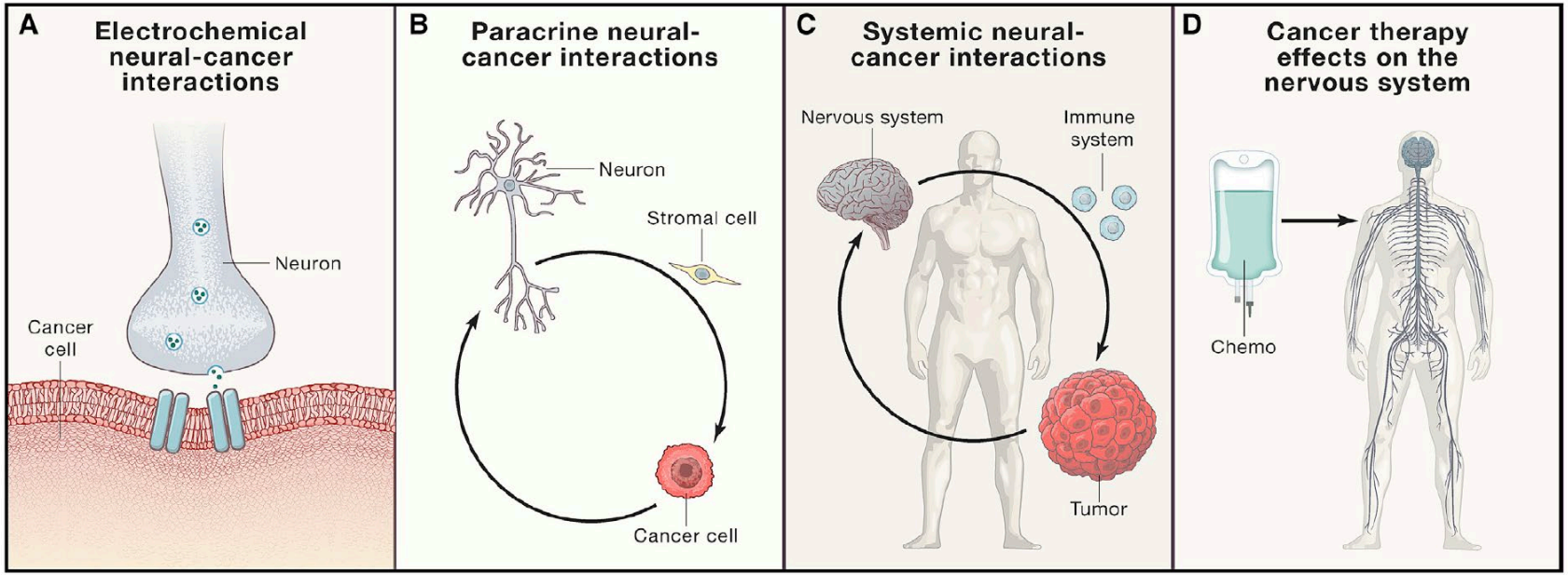
There are an increasing number of people diagnosed, living with, and dying from cancer

2019
16.9 million alive with cancer history
328 million people living in US
5.1% alive with history of cancer

1971
3 million alive with cancer history
207.7 million people living in US
1.4% alive with history of cancer



Interactions between the nervous system and cancer

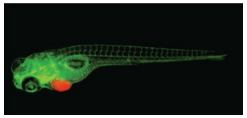


The brain is not a passive bystander…. “a brain tumor is not a marble”

Tumor models help us understand disease causes but only human application is truly relevant

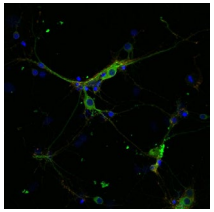
Dogs with disease

Mouse xenografts or engineered

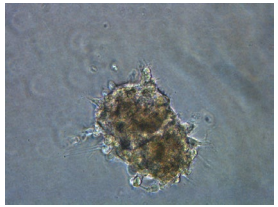


Zebra fish

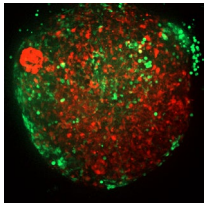
Fruit fly



2D cell culture



3D cell culture



Organoids

Model organisms

Humans

Physiologically relevant

Controlled environment quick results

Who are vulnerable patient populations in the US?

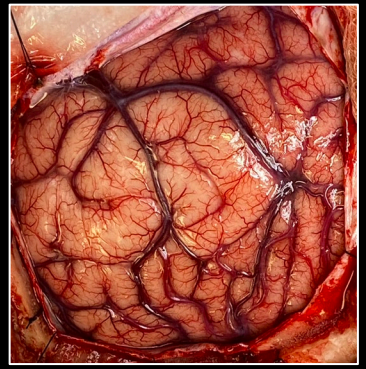
1. *Female gender*
2. *Ethnic/racial minority groups- Black, Latinx, Asian American/PI, Native*
3. *Urban underserved*
4. *Rural underserved*
5. *LGBTQ+*
6. *Elderly*

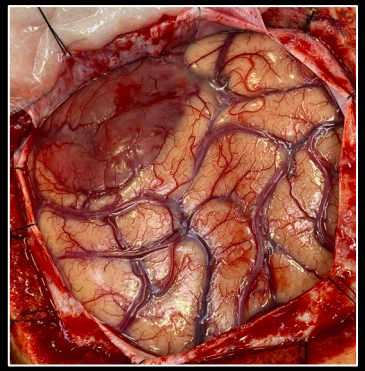
	Years	Women	Men
American Indians/Alaska Natives	78.4	81.1	75.8
Non-Hispanic whites	80.6	82.7	78.4

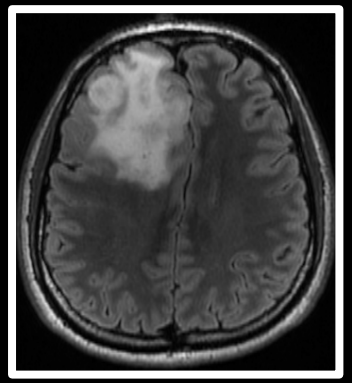
SOURCE: U.S. Department of Health and Human Services, Office of Minority Health, https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=3&lvlid=62.

Differences in health outcomes not known to be attributable to the disease process itself- gender, geography, race/ethnicity.

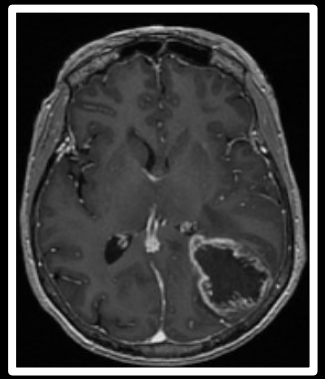
A journey through treatment





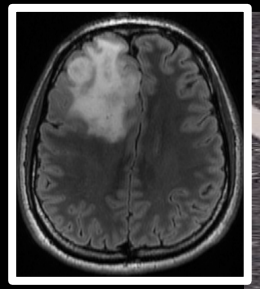


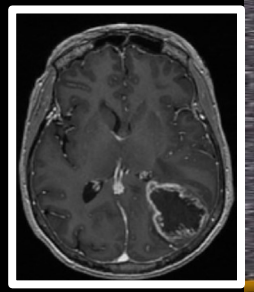
57 yo Woman

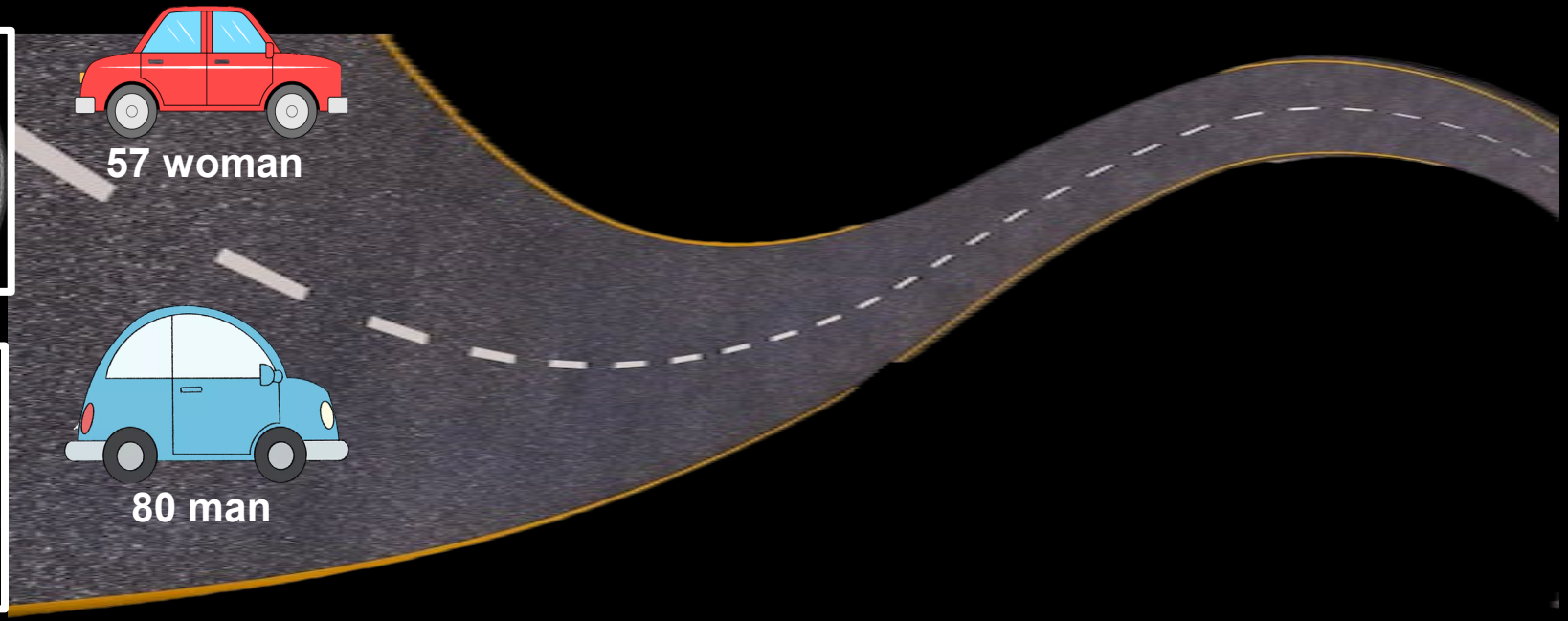


80 yo Man

Treatment is a multistep process

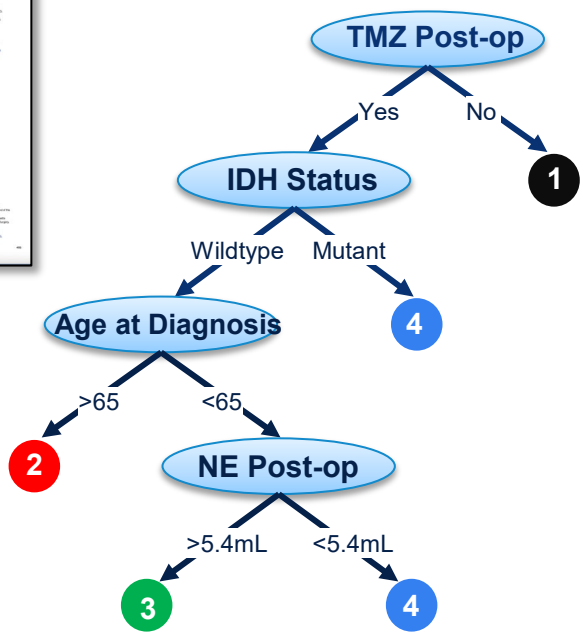




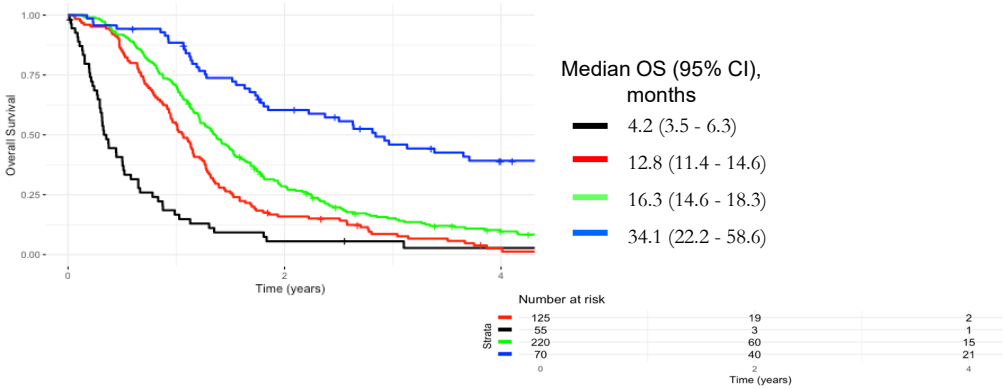


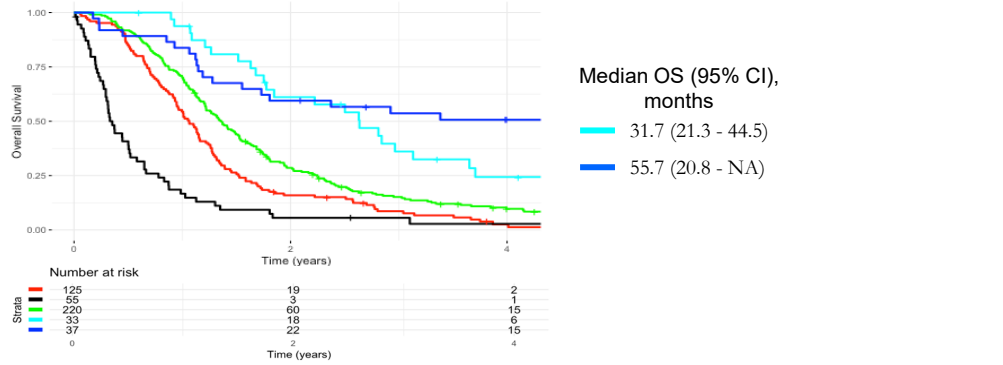
Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

Older age is one of the strongest predictors of shorter overall survival



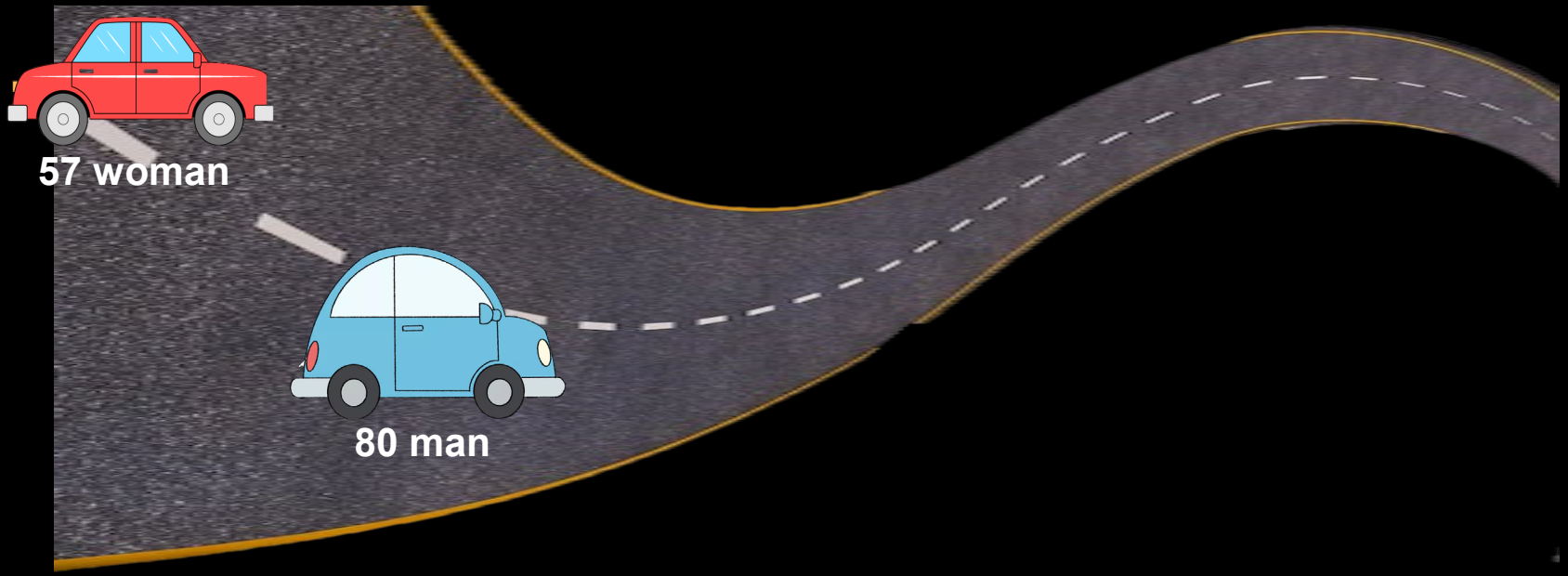
761 patients , 20 yrs. followed, 3 centers





Molinaro, Hervey-Jumper et al JAMA Oncology 2020

Age as a predictor of risk



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

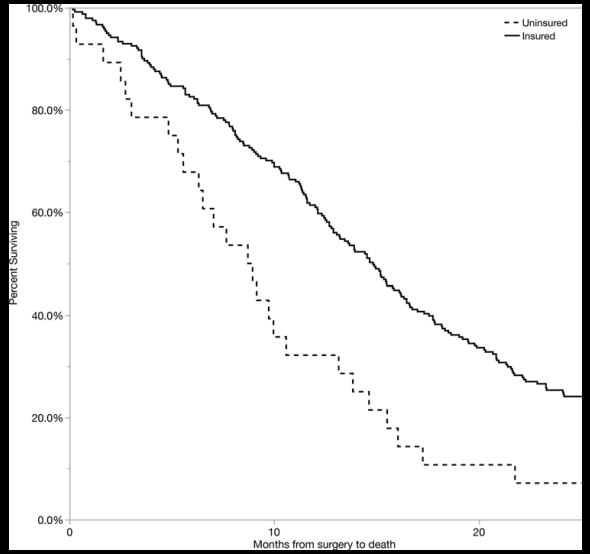
Symptoms and burden of disease varies- influenced by gender, socioeconomics, and race

Variable	No Insurance	Any Insurance	p Value
No. of patients	32	322	
Sex (no. female, %)	6 (18.75)	127 (39.44)	**0.0218**
Median age in yrs (range)	59 (19–83)	62 (18–88)	0.176
Median household income in $1000s (range)	45.37 (25–128.35)	52.43 (19.95–140.90)	0.676
PCP status (no., %)			
Yes	0 (0)	232 (72.05)	
No	32 (100)	90 (27.95)	**<0.001**
Tumor characteristics			
Mean diameter in cm (95% CI)	4.56 (3.96–5.26)	4.44 (4.26–4.62)	0.72
Extent of resection (no., %)			
Gross-total	15 (46.88)	115 (35.71)	0.40
Subtotal	16 (50)	200 (62.11)	
Biopsy	1 (3.13)	7 (2.17)	
Mean ± SD length of stay in days	4.30 ± 2.09	4.83 ± 3.30	0.39
Resp at first recurrence (no., %)	8 (25)	75 (23.29)	0.82
Comorbidities at diagnosis (no., %)	24 (75)	166 (51.55)	**0.01**
CCI score (no., %)			
0	17 (53.13)	218 (67.7)	0.23
1	8 (25)	63 (19.57)	
≥2	7 (21.88)	41 (12.73)	
Postop adjuvant treatment (no., %)			
Radiation therapy	18 (56.25)	255 (79.2)	**0.003**
TMZ	18 (56.25)	242 (75.16)	**0.02**
Clinical trials	9 (28.13)	86 (26.71)	0.86
Agents in addition to Stupp protocol	13 (40.63)	138 (42.86)	0.81
Median postop survival in mos (95% CI)			
Overall	8.82 (5.55–10.59)	15.22 (13.61–16.64)	**<0.0001**
XRT plus TMZ	9.14 (5.29–16.04)	16.34 (14.9–18.21)	**0.025**
Patients with comorbidities	7.35 (2.73–13.15)	13.18 (11.28–15.22)	**0.007**

9% uninsured 91% insured
More women, Latinx
Same median household income
More medical comorbidities
Lower rates of completion chemoradiation

Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

Symptoms and burden of disease varies- influenced by gender, socioeconomics, and race

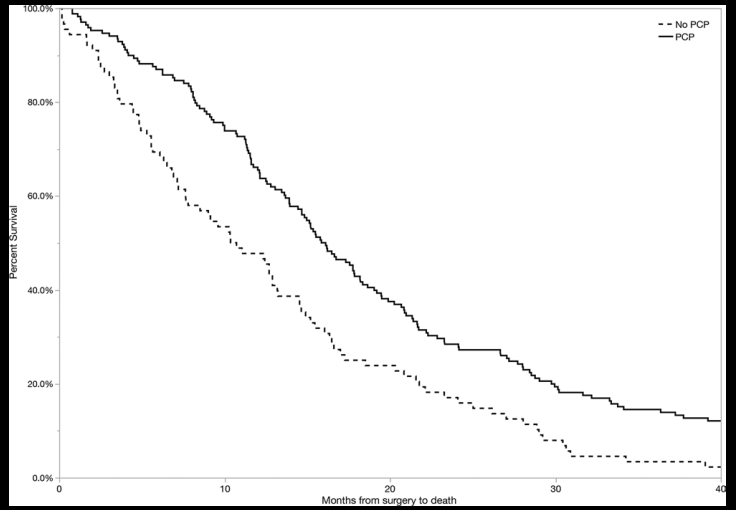


Shorter survival for uninsured patients

Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

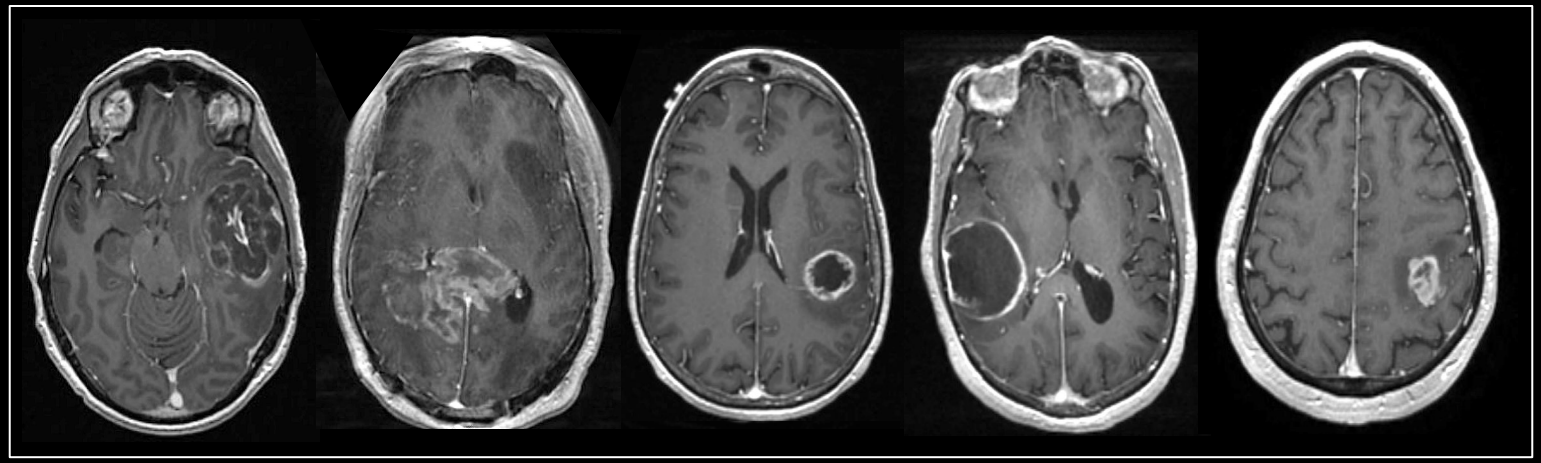
Disease specific mortality purely because of no PCP

Designated PCP improves survival by 50%
Over 60% improvement when insured w/PCP



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

When and why do we offer an operation?



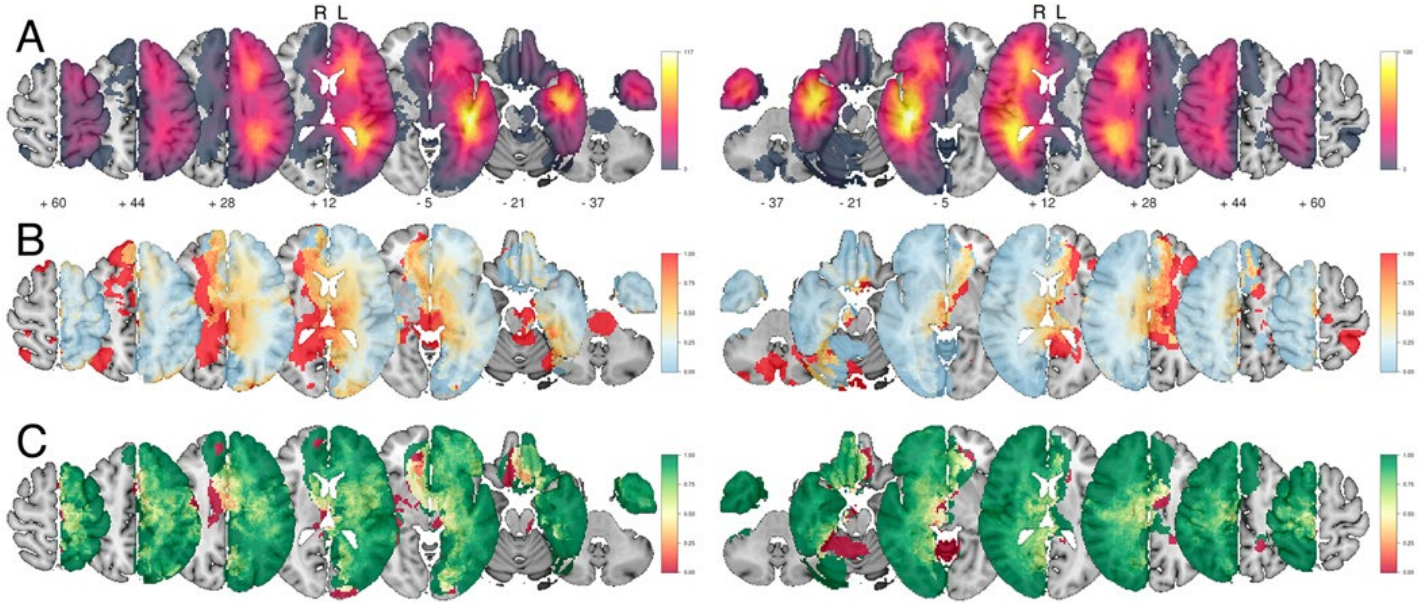
Volume, location, functional status (KPS/language/motor), comorbidities, social support, presumed molecular sub-classification

There is general agreement among neurosurgeons regarding which patients to offer surgery

Biopsy

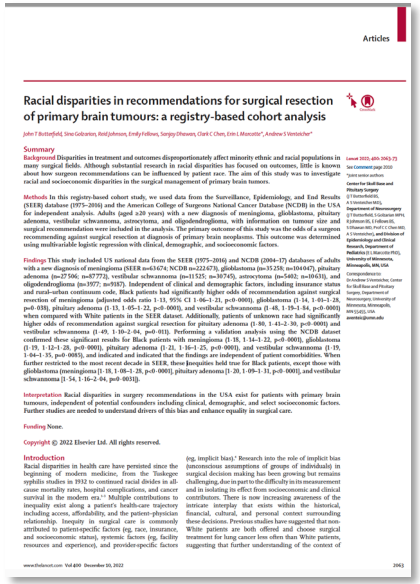
Resect

Both



Muller JNS 2021

How do we decide who gets surgery?
(when do surgeons decide against surgery)



Articles

Racial disparities in recommendations for surgical resection of primary brain tumours: a registry-based cohort analysis

John T Botterfield, Sina Gobarzan, Reid Johnson, Emily Follows, Sanjay Dhawan, Clark C Chen, Erin L Mazcotte*, Andrew S Venteicher*

Summary

Background Disparities in treatment and outcomes disproportionately affect minority ethnic and racial populations in many surgical fields. Although substantial research in racial disparities has focused on outcomes, little is known about how surgeon recommendations can be influenced by patient race. The aim of this study was to investigate racial and socioeconomic disparities in the surgical management of primary brain tumours.

Methods In this registry-based cohort study, we used data from the Surveillance, Epidemiology, and End Results (SEER) database (1975–2016) and the American College of Surgeons National Cancer Database (NCDB) in the USA for independent analysis. Adults (aged ≥20 years) with a new diagnosis of meningioma, glioblastoma, pituitary adenoma, vestibular schwannoma, astrocytoma, and oligodendroglioma, with information on tumour size and surgical recommendation were included in the analysis. The primary outcome of this study was the odds of a surgeon recommending against surgical resection at diagnosis of primary brain neoplasms. This outcome was determined using multivariable logistic regression with clinical, demographic, and socioeconomic factors.

Findings This study included US national data from the SEER (1975–2016) and NCDB (2004–17) databases of adults with a new diagnosis of meningioma (SEER n=63674; NCDB n=222673), glioblastoma (n=35258; n=104047), pituitary adenoma (n=27506; n=87772), vestibular schwannoma (n=11525; n=30745), astrocytoma (n=5402; n=10630), and oligodendroglioma (n=3977; n=9787). Independent of clinical and demographic factors, including insurance status and rural–urban continuum code, Black patients had significantly higher odds of recommendation against surgical resection of meningioma (adjusted odds ratio 1·13, 95% CI 1·06–1·21, p<0·0001), glioblastoma (1·14, 1·05–1·28, p=0·038), pituitary adenoma (1·13, 1·05–1·22, p<0·0001), and vestibular schwannoma (1·48, 1·19–1·84, p<0·0001) when compared with White patients in the SEER dataset. Additionally, patients of unknown race had significantly higher odds of recommendation against surgical resection for pituitary adenoma (1·80, 1·41–2·30, p<0·0001) and vestibular schwannoma (1·49, 1·10–2·04, p=0·011). Performing a validation analysis using the NCDB dataset confirmed these significant results for Black patients with meningioma (1·18, 1·14–1·22, p<0·0001), glioblastoma (1·19, 1·12–1·28, p<0·0001), pituitary adenoma (1·21, 1·16–1·25, p<0·0001), and vestibular schwannoma (1·19, 1·04–1·35, p=0·0085), and indicated and indicated that the findings are independent of patient comorbidities. When further restricted to the most recent decade in SEER, these inequities held true for Black patients, except those with glioblastoma (meningioma [1·18, 1·08–1·28, p<0·0001], pituitary adenoma [1·20, 1·09–1·31, p<0·0001], and vestibular schwannoma [1·54, 1·16–2·04, p=0·0031]).

Interpretation Racial disparities in surgery recommendations in the USA exist for patients with primary brain tumours, independent of potential confounders including clinical, demographic, and select socioeconomic factors. Further studies are needed to understand drivers of this bias and enhance equality in surgical care.

Funding None.

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Introduction

Racial disparities in health care have persisted since the beginning of modern medicine, from the Tuskegee syphilis studies in 1932 to continued racial divides in all-cause mortality rates, hospital complications, and cancer survival in the modern era.[1] Multiple contributions to inequality exist along a patient's health-care trajectory including access, affordability, and the patient–physician relationship. Inequity in surgical care is commonly attributed to patient-specific factors (eg, race, insurance, and socioeconomic status), systemic factors (eg, facility resources and experience), and provider-specific factors (eg, implicit bias).[2] Research into the role of implicit bias (unconscious assumptions of groups of individuals) in surgical decision making has been growing but remains challenging, due in part to the difficulty in its measurement and in isolating its effect from socioeconomic and clinical contributors. There is now increasing awareness of the intricate interplay that exists within the historical, financial, cultural, and personal context surrounding these decisions. Previous studies have suggested that non-White patients are both offered and choose surgical treatment for lung cancer less often than White patients, suggesting that further understanding of the context of

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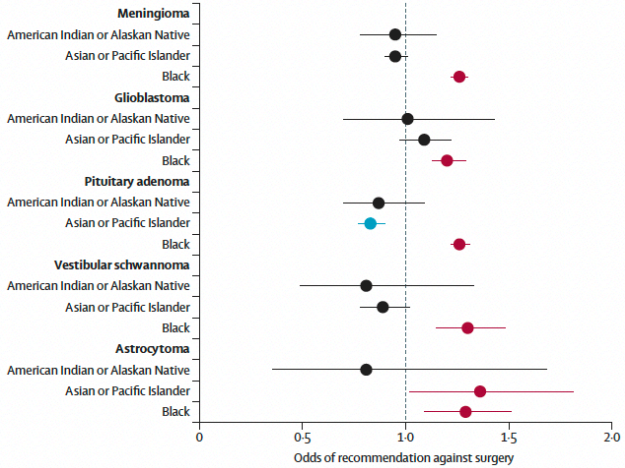
Insurance status
Rural-urban-continuum code
Black patients

… true for glioma, pituitary, vestibular schwannomas

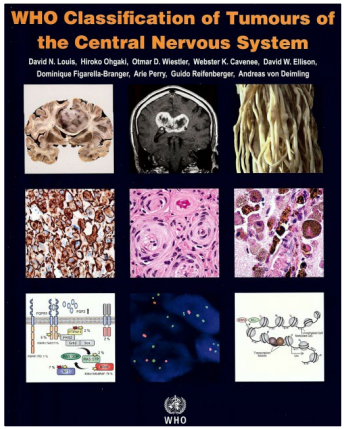


Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

Lancet Oncology 2022

Integrated diagnosis drives treatment

Molecular diagnostics



Diffuse astrocytic and oligodendroglial tumours – Introduction

Louis D.N.
von Deimling A.
Cavenee W.K.

This 2016 update of the 2007 WHO classification incorporates well-established molecular parameters into the classification of diffuse gliomas, and this nosological shift has impacted the classification in several ways. Most notably, whereas all astrocytic tumours were previously grouped together, now all diffuse gliomas (whether astrocytic or not) are grouped together, on the basis of not only their growth pattern and behaviours, but more pointedly of their shared *IDH1* and *IDH2* genetic status. From a pathogenetic point of view, this provides a dynamic classification based on both phenotype and genotype; from a prognostic point of view, it groups tumours that share similar prognostic markers; and from the eventual therapeutic point of view, it will presumably guide the treatment of biologically similar entities.

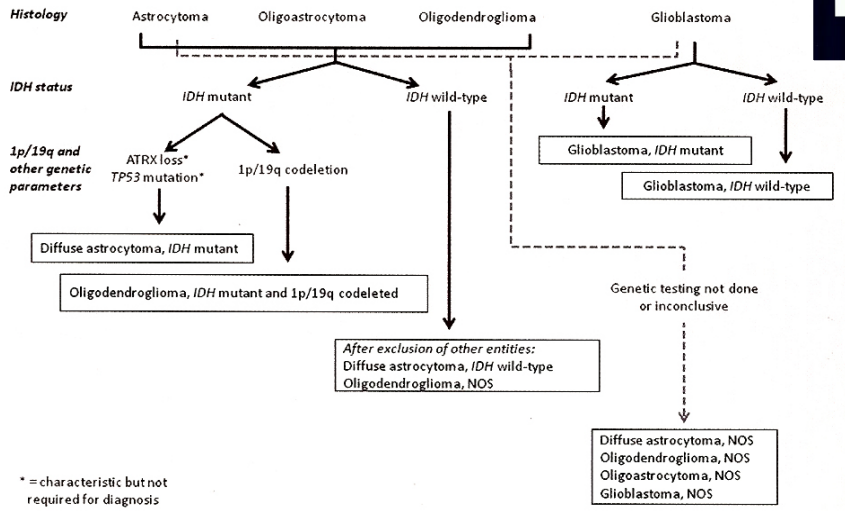
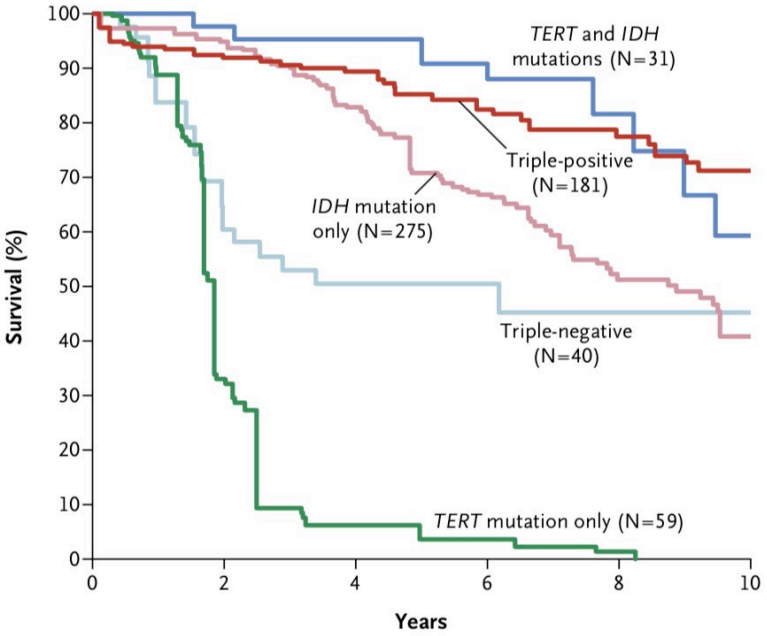


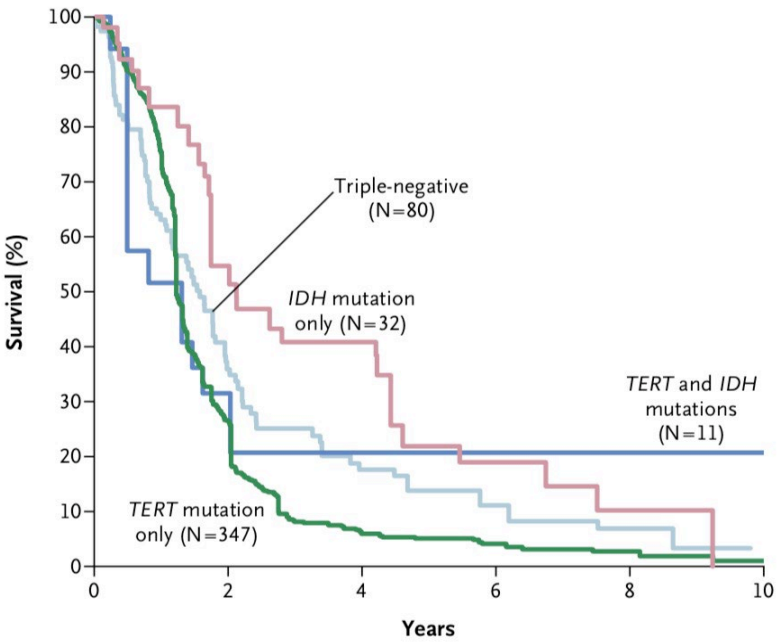
Fig. 1.01 Diffuse gliomas: from histology, IDH status, and other genetic parameters to WHO diagnosis.

Genomic: Molecular diagnostics

WHO 2-3 glioma



WHO 4 glioma



Data based almost entirely on European ancestry

Eckel-Passow et al Glioma groups based on 1p19q, IDH and TERT promoter mutation in tumors, NEJM 2015

Bench to Bedside: Molecular diagnostics

General Schema

Layer 1	**Final Integrated Diagnosis**
Layer 2	Histologic Classification
Layer 3	WHO Grade
Layer 4	Molecular Information

NEW

Specific Example

Layer 1	**Anaplastic oligodendroglioma**
Layer 2	Infiltrating glioma with oligodendroglial features by microscopy
Layer 3	WHO Grade III
Layer 4	Isocitrate dehydrogenase 1 mutation Whole-arm loss of both 1p and 19q

Johnson et al. 2016 Updates to the WHO brain tumor classification system: what the radiologist needs to know. 2017. Radiographics

Who gets molecular testing is influenced by socioeconomic status

Table 1. Factors Associated With *MGMT* Promoter Methylation Testing in Patients With Glioblastoma

Characteristic	Total No.	% With *MGMT* testing[a]	Testing % in 2016	Multivariable logistic regression of having *MGMT* testing[b]	
				aOR (95% CI)	*P* value
Age at diagnosis, y					
40-49	1258	61.5	81.2	1.27 (1.08-1.48)	.004
50-59	3437	58.3	74.3	0.98 (0.87-1.10)	.72
60-69	4251	57.3	74.2	1 [Reference]	
70-79	2875	55.2	70.9	0.95 (0.84-1.08)	.45
≥80	1009	50.0	69.0	0.83 (0.70-0.99)	.04
Primary payer					
Uninsured	386	42.8	60.9	1 [Reference]	
Private insurance	5841	60.8	76.1	1.78 (1.39-2.28)	<.001
Medicaid	802	53.9	74.9	1.30 (0.98-1.74)	.07
Medicare	5476	54.7	71.9	1.49 (1.14-1.93)	.003
Median household income by zip code, $					
<38 000	1693	49.7	63.5	1 [Reference]	
38 000-47 999	2775	53.2	69.9	1.11 (0.96-1.29)	.15
48 000-62 999	3523	57.2	74.5	1.23 (1.06-1.42)	.006
≥63 000	4819	61.4	78.5	1.31 (1.13-1.52)	<.001
Cancer program type					
Community	466	44.9	56.2	1 [Reference]	
Comprehensive community	3794	44.3	66.8	0.99 (0.80-1.23)	.94
Academic/NCI-designated	6532	65.0	79.8	2.21 (1.78-2.73)	<.001
Integrated network	2038	57.5	72.2	1.65 (1.31-2.08)	<.001

Testing most likely for…

40 and over 80-year-olds
Private insured
Median income over $63K
Academic/ integrated model

Bench to Bedside: Individualized targeted therapies

Precision medicine

41 year old woman

2 days of nausea and dizziness.

MRI shows 5 x 3 cm L frontal ring-enhancing lesion

Pathology: GBM, IDH wt, EGFR amplified, MGMT methylated (index 14)

XRT/TMZ +ABT 414/placebo

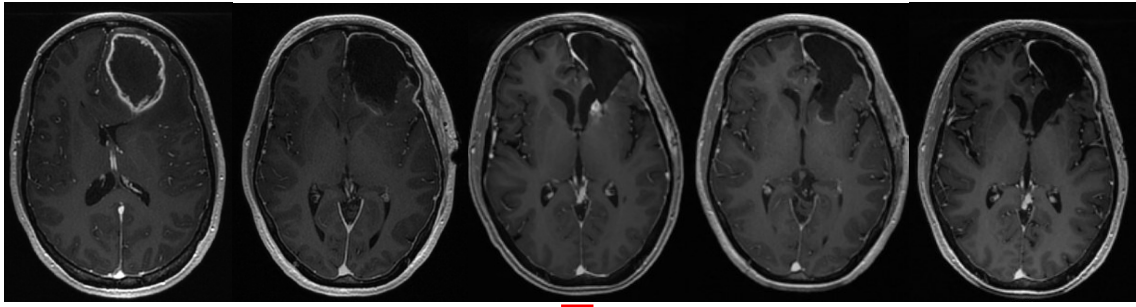
TMZ + ABT 414/placebo

Off study, followed

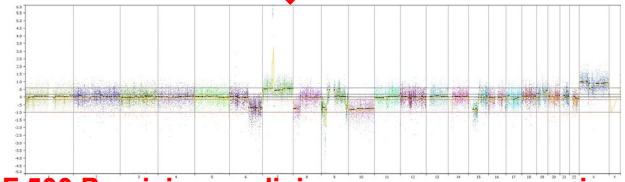
<u>Focal recurrence- precision medicine trial</u>

1. Dose reduced TMZ
2. Olaparib- Parp inhibitor
3. Afatinib- Tyrosine kinase/EGFR inhibitor
4. Everolimus- mTOR inhibitor

Stable disease- cycle 10



Sequence recurrent tumor

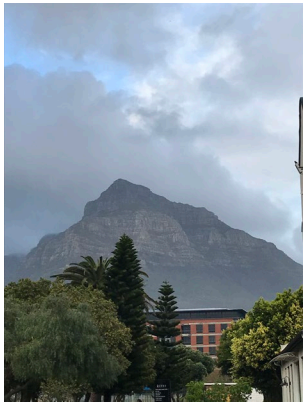


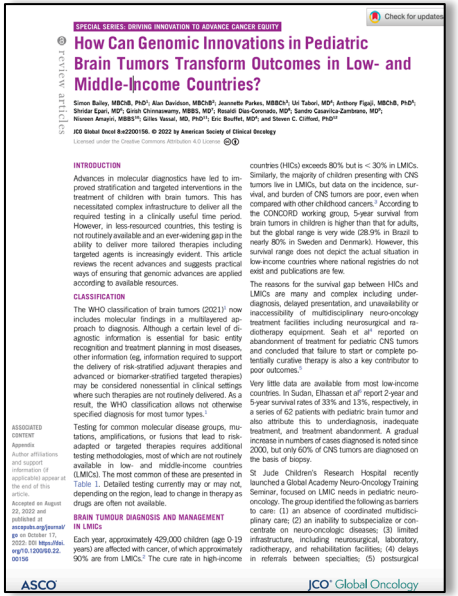
UCSF 500 Precision medicine program sequencing results

Pathogenic or Likely Pathogenic SOMATIC ALTERATIONS				
VARIANT	TRANSCRIPT ID	CLASSIFICATION	READS	MUTANT ALLELE FREQUENCY
CDKN2A, CDKN2B homozygous deletion	all	Pathogenic	N/A	N/A
EGFR high level amplification	all	Pathogenic	>30,000 (>50x)	N/A
PTEN p.Tyr177fs	NM_000314.4	Pathogenic	278	68%
TERT c.-146C>T	NM_198253.2	Pathogenic	368	45%
Trisomy 7; Monosomy 10	N/A	Pathogenic	N/A	N/A

Low- and middle-income settings end up with data which does not pertain adherence to international guidelines- cost/scientifically invalid

SNOSSA annual meeting 2019





review articles

SPECIAL SERIES: DRIVING INNOVATION TO ADVANCE CANCER EQUITY

Check for updates

How Can Genomic Innovations in Pediatric Brain Tumors Transform Outcomes in Low- and Middle-Income Countries?

Simon Bailey, MBChB, PhD[1], Alan Davidson, MBChB[2], Jeannette Parkes, MBBCh[3], Uri Tabori, MD[4], Anthony Figaji, MBChB, PhD[5], Shridar Ejeri, MD[6], Girish Chinnaswamy, MBBS, MD[7], Rosaldi Dias-Coronado, MD[8], Sandro Casavilca-Zambrano, MD[9], Nisreen Amayiri, MBBS[10], Gilles Vassal, MD, PhD[11], Eric Bouffet, MD[4], and Steven C. Clifford, PhD[12]

JCO Global Oncol 8:e2200156. © 2022 by American Society of Clinical Oncology

INTRODUCTION

Advances in molecular diagnostics have led to improved stratification and targeted interventions in the treatment of children with brain tumors. This has necessitated complex infrastructure to deliver all the required testing in a clinically useful time period. However, in less-resourced countries, this testing is not routinely available and an ever-widening gap in the ability to deliver more tailored therapies including targeted agents is increasingly evident. This article reviews the recent advances and suggests practical ways of ensuring that genomic advances are applied according to available resources.

CLASSIFICATION

The WHO classification of brain tumors (2021)[1] now includes molecular findings in a multilayered approach to diagnosis. Although a certain level of diagnostic information is essential for basic entity recognition and treatment planning in most diseases, other information (eg, information required to support the delivery of risk-stratified adjuvant therapies and advanced or biomarker-stratified targeted therapies) may be considered nonessential in clinical settings where such therapies are not routinely delivered. As a result, the WHO classification allows not otherwise specified diagnosis for most tumor types.[1]

Testing for common molecular disease groups, mutations, amplifications, or fusions that lead to risk-adapted or targeted therapies requires additional testing methodologies, most of which are not routinely available in low- and middle-income countries (LMICs). The most common of these are presented in Table 1. Detailed testing currently may or may not, depending on the region, lead to change in therapy as drugs are often not available.

BRAIN TUMOUR DIAGNOSIS AND MANAGEMENT IN LMICs

Each year, approximately 429,000 children (age 0-19 years) are affected with cancer, of which approximately 90% are from LMICs.[2] The cure rate in high-income countries (HICs) exceeds 80% but is < 30% in LMICs. Similarly, the majority of children presenting with CNS tumors live in LMICs, but data on the incidence, survival, and burden of CNS tumors are poor, even when compared with other childhood cancers.[3] According to the CONCORD working group, 5-year survival from brain tumors in children is higher than that for adults, but the global range is very wide (28.9% in Brazil to nearly 80% in Sweden and Denmark). However, this survival range does not depict the actual situation in low-income countries where national registries do not exist and publications are few.

The reasons for the survival gap between HICs and LMICs are many and complex including underdiagnosis, delayed presentation, and unavailability or inaccessibility of multidisciplinary neuro-oncology treatment facilities including neurosurgical and radiotherapy equipment. Seah et al[4] reported on abandonment of treatment for pediatric CNS tumors and concluded that failure to start or complete potentially curative therapy is also a key contributor to poor outcomes.[5]

Very little data are available from most low-income countries. In Sudan, Elhassan et al[6] report 2-year and 5-year survival rates of 33% and 13%, respectively, in a series of 62 patients with pediatric brain tumor and also attribute this to underdiagnosis, inadequate treatment, and treatment abandonment. A gradual increase in numbers of cases diagnosed is noted since 2000, but only 60% of CNS tumors are diagnosed on the basis of biopsy.

St Jude Children's Research Hospital recently launched a Global Academy Neuro-Oncology Training Seminar, focused on LMIC needs in pediatric neuro-oncology. The group identified the following as barriers to care: (1) an absence of coordinated multidisciplinary care; (2) an inability to subspecialize or concentrate on neuro-oncologic diseases; (3) limited infrastructure, including neurosurgical, laboratory, radiotherapy, and rehabilitation facilities; (4) delays in referrals between specialties; (5) postsurgical

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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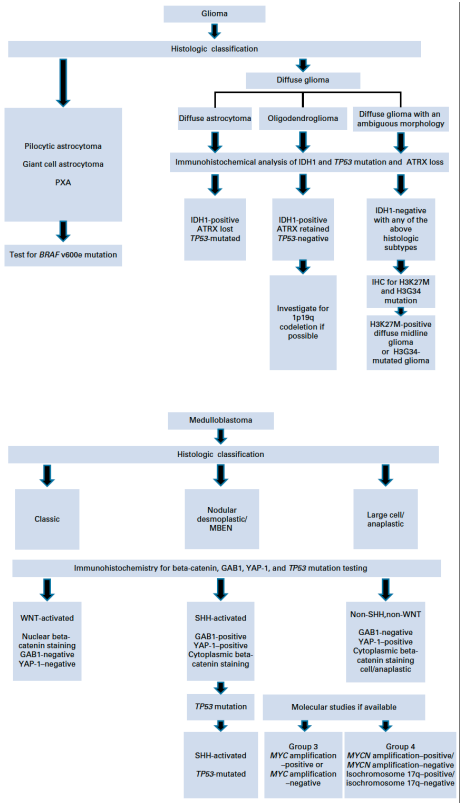
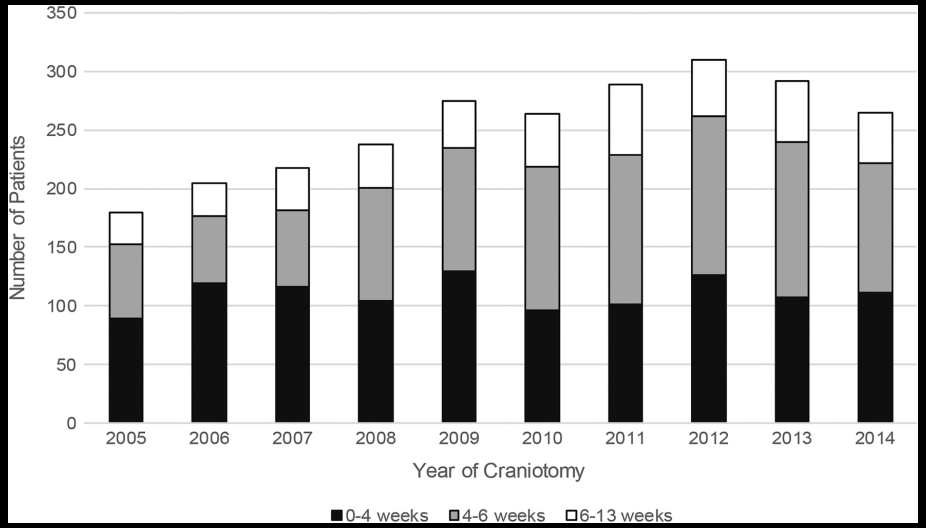
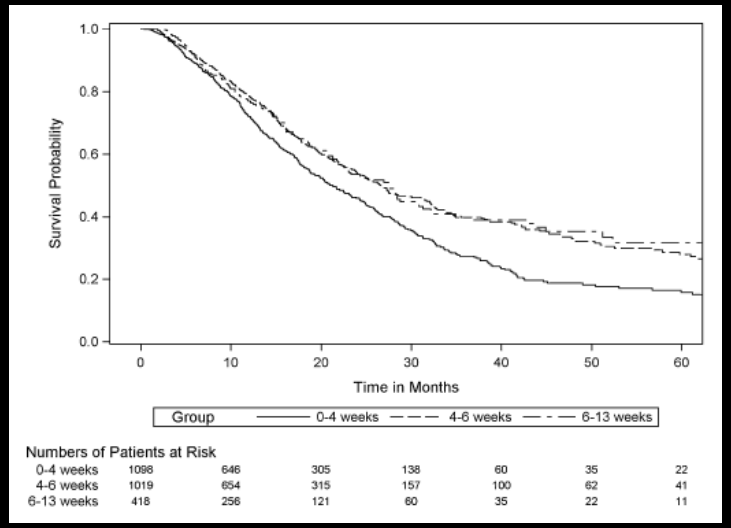


What about timing of treatment?

Only patient with commercial insurance- Black and Latinx 1.2 HR

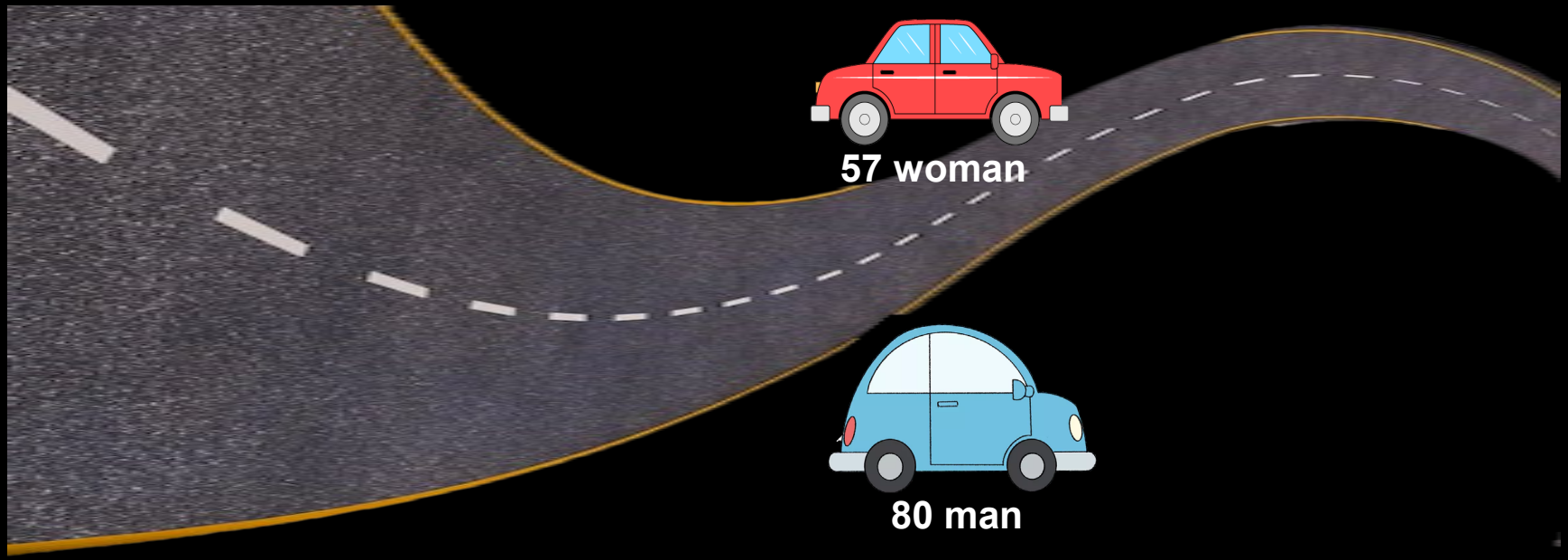




Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

Nathan J NeuroOncol 2017

Recurrence is universal with brain cancer



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What comes next when the tumor grows back?

1. Another chemotherapy drug (<10% respond)
2. Palliative care/hospice (most continue to have excellent functional status)
3. Clinical Trial/ experimental therapies

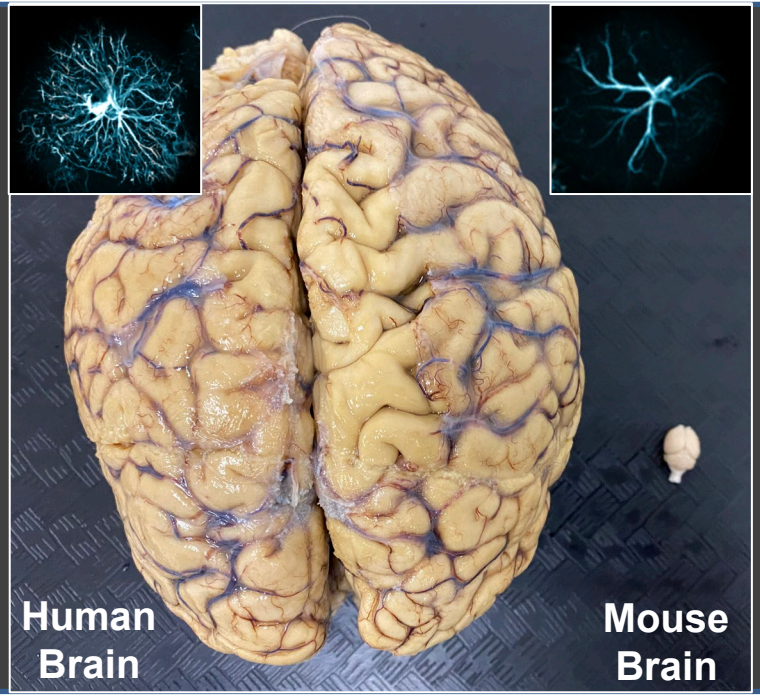
Mouse data doesn’t work in humans

How do we translate advances in cellular level analysis of the brain from model organisms of human brain/disease ?

Human experiments

1. Highly variable
2. No/low cell type specificity
3. Intralesional heterogeneity
4. Limited functional experimentation
5. Little genetic access

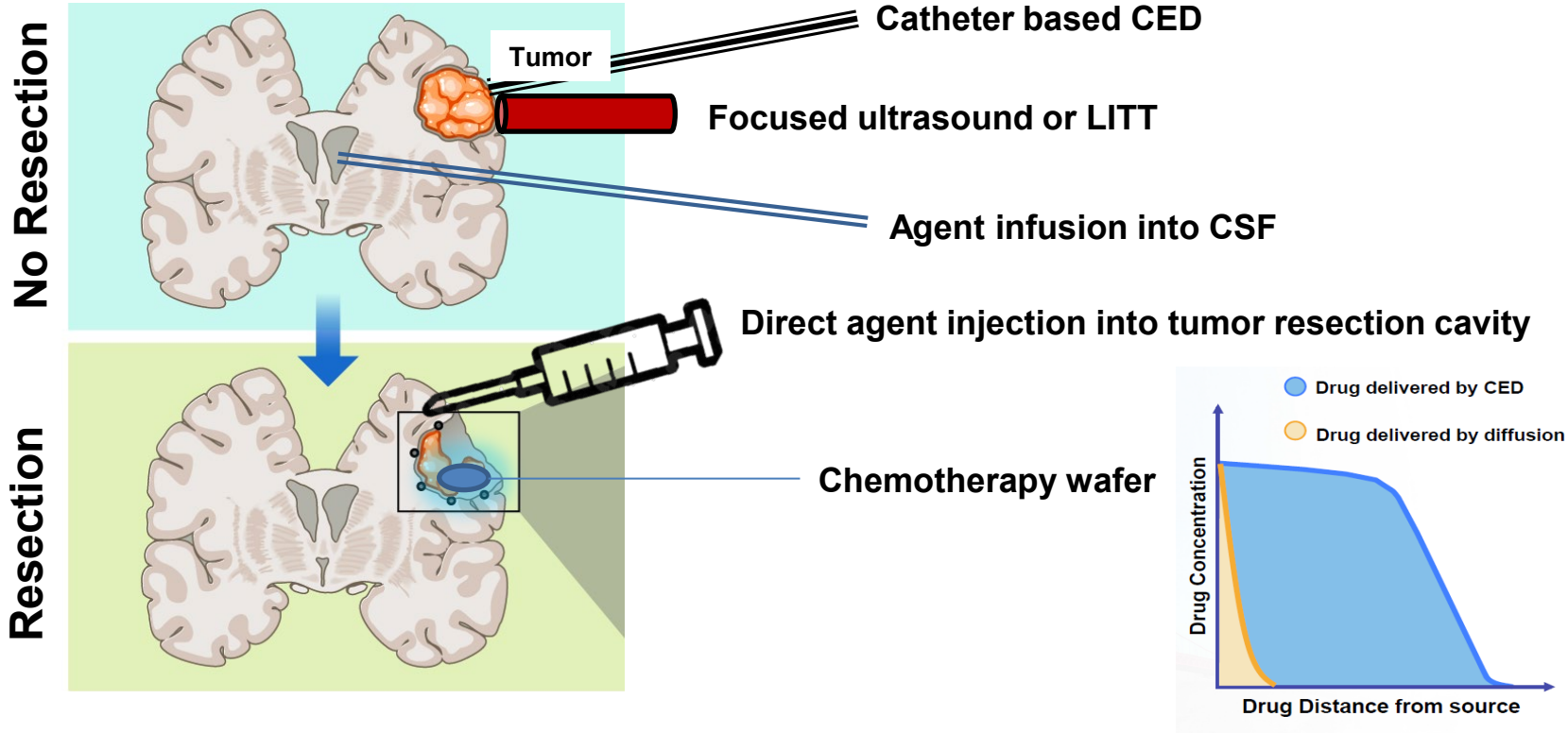
1 billion neurons
1 trillion network connections



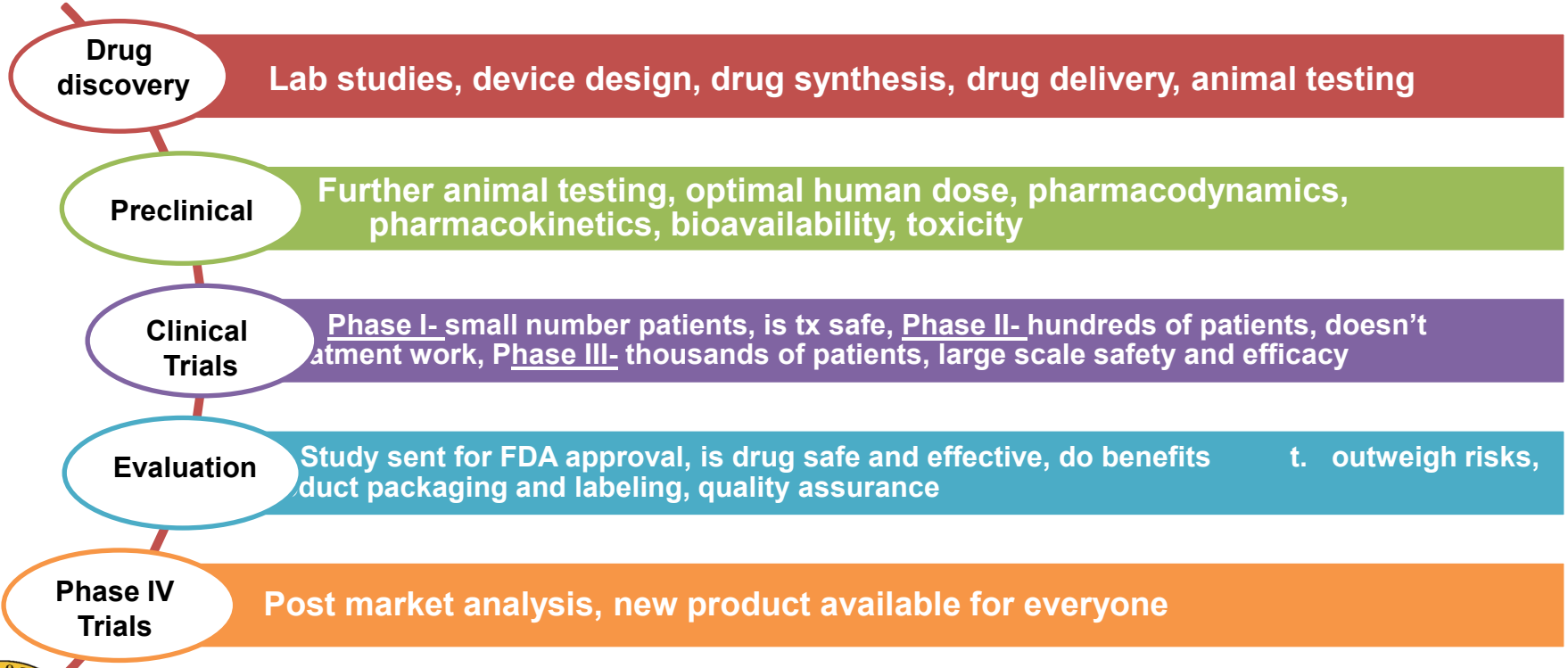
Mouse models

1. Highly controlled
2. Cell type specific
3. Functional experimentation
4. in vivo
5. little intralesional heterogeneity
6. Genetic access
7. Quick results

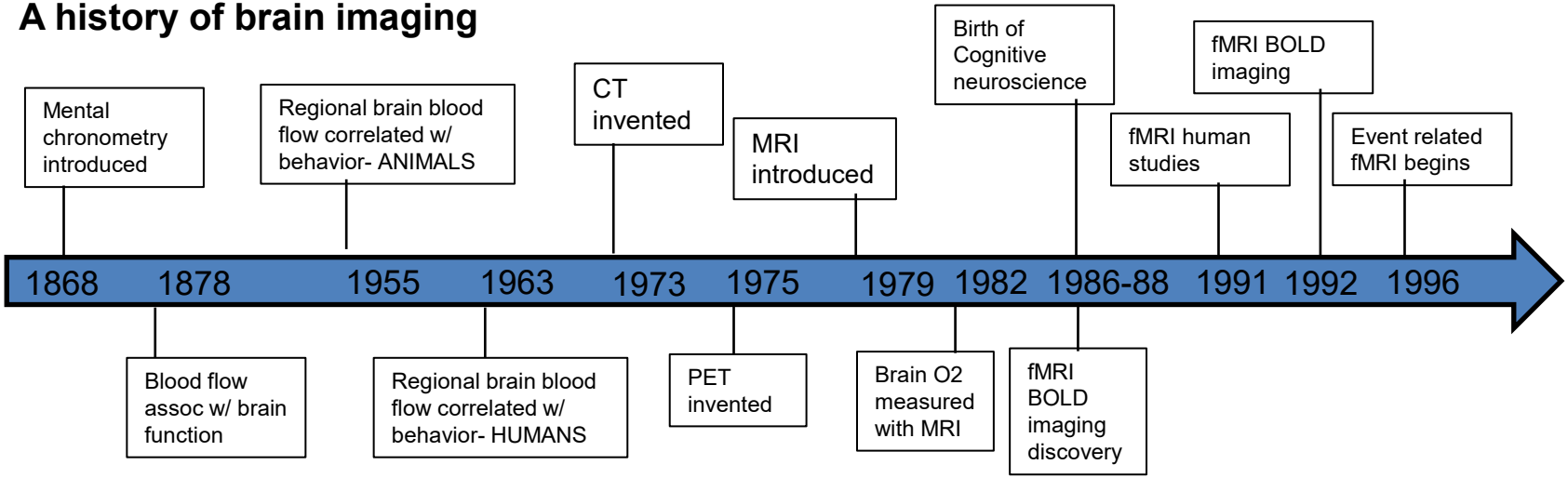
How we deliver therapies into the brain



It takes time for treatments to make their way from bench to bedside-What does FDA approval mean?

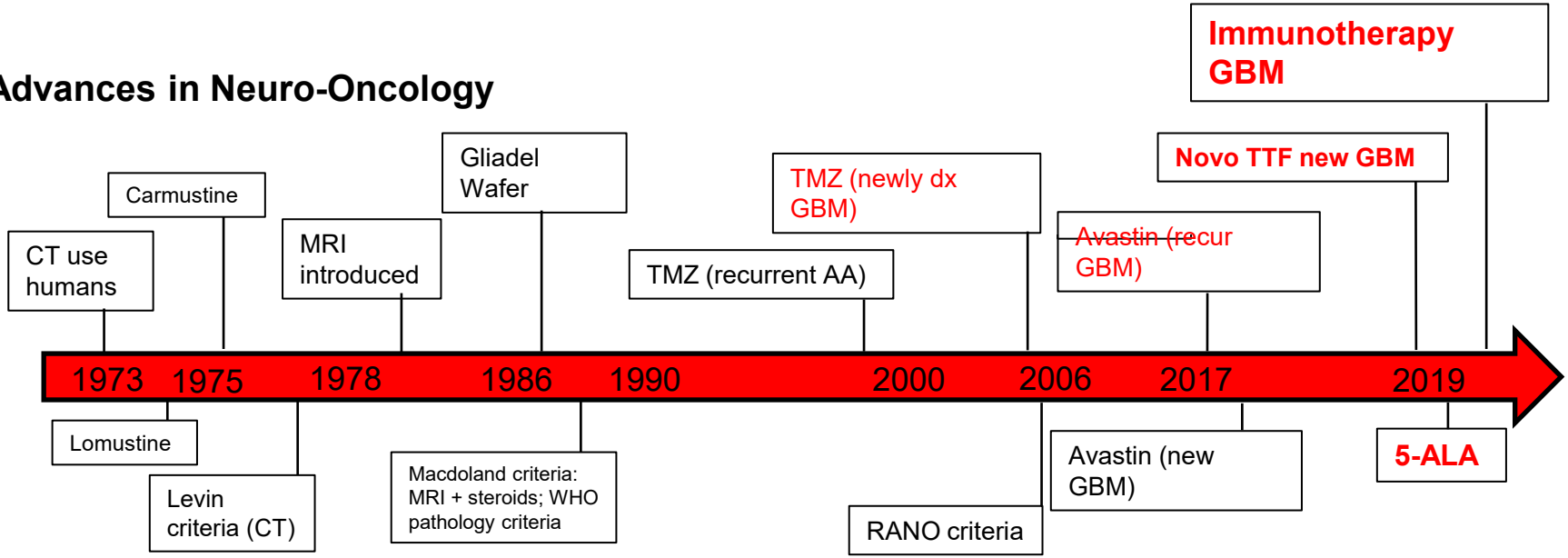


A history of brain imaging



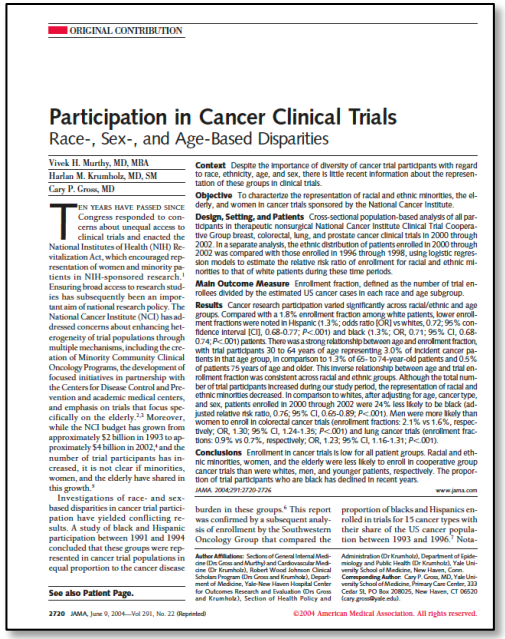
Raichle. Brief history of human brain mapping. Trends in Neurosciences. 2008, 32(2):118-126

Advances in Neuro-Oncology



Raichle. Brief history of human brain mapping. Trends in Neurosciences. 2008, 32(2):118-126

Where do new cancer drugs come from?



ORIGINAL CONTRIBUTION

Participation in Cancer Clinical Trials

Race-, Sex-, and Age-Based Disparities

Vivek H. Murthy, MD, MBA
Harlan M. Krumholz, MD, SM
Cary P. Gross, MD

Context Despite the importance of diversity of cancer trial participants with regard to race, ethnicity, age, and sex, there is little recent information about the representation of these groups in clinical trials.

Objective To characterize the representation of racial and ethnic minorities, the elderly, and women in cancer trials sponsored by the National Cancer Institute.

Design, Setting, and Patients Cross-sectional population-based analysis of all participants in therapeutic nonsurgical National Cancer Institute Clinical Trial Cooperative Group breast, colorectal, lung, and prostate cancer clinical trials in 2000 through 2002. In a separate analysis, the ethnic distribution of patients enrolled in 2000 through 2002 was compared with those enrolled in 1996 through 1998, using logistic regression models to estimate the relative risk ratio of enrollment for racial and ethnic minorities to that of white patients during these time periods.

Main Outcome Measure Enrollment fraction, defined as the number of trial enrollees divided by the estimated US cancer cases in each race and age subgroup.

Results Cancer research participation varied significantly across racial/ethnic and age groups. Compared with a 1.8% enrollment fraction among white patients, lower enrollment fractions were noted in Hispanic (1.3%; odds ratio [OR] vs whites, 0.72; 95% confidence interval [CI], 0.68-0.77; P<.001) and black (1.3%; OR, 0.71; 95% CI, 0.68-0.74; P<.001) patients. There was a strong relationship between age and enrollment fraction, with trial participants 30 to 64 years of age representing 3.0% of incident cancer patients in that age group, in comparison to 1.3% of 65- to 74-year-old patients and 0.5% of patients 75 years of age and older. This inverse relationship between age and trial enrollment fraction was consistent across racial and ethnic groups. Although the total number of trial participants increased during our study period, the representation of racial and ethnic minorities decreased. In comparison to whites, after adjusting for age, cancer type, and sex, patients enrolled in 2000 through 2002 were 24% less likely to be black (adjusted relative risk ratio, 0.76; 95% CI, 0.65-0.89; P<.001). Men were more likely than women to enroll in colorectal cancer trials (enrollment fractions: 2.1% vs 1.6%, respectively; OR, 1.30; 95% CI, 1.24-1.35; P<.001) and lung cancer trials (enrollment fractions: 0.9% vs 0.7%, respectively; OR, 1.23; 95% CI, 1.16-1.31; P<.001).

Conclusions Enrollment in cancer trials is low for all patient groups. Racial and ethnic minorities, women, and the elderly were less likely to enroll in cooperative group cancer trials than were whites, men, and younger patients, respectively. The proportion of trial participants who are black has declined in recent years.

JAMA. 2004;291:2720-2726 www.jama.com

burden in these groups.[4] This report was confirmed by a subsequent analysis of enrollment by the Southwestern Oncology Group that compared the proportion of blacks and Hispanics enrolled in trials for 15 cancer types with their share of the US cancer population between 1993 and 1996.[5] Nota-

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See also Patient Page.

37,635 patients

Relative to European ancestry participants
9.1% enrollment Latinx OR 0.72
10.8% enrollment Black OR 0.71
3.8% enrollment AAPI
0.7% enrollment Native

30-64 year olds 3%
65-74 year olds 1.3%
Over 75 year olds 0.5%

Characteristic	Trial Participants, No. (%)	Proportion of Incident Cancer Patients, %†	Proportion of US Population, %†
Race/ethnicity			
White non-Hispanic	64 355 (85.6)	83.1	75.7
Hispanic	2292 (3.1)	3.8	9.1
Black	6882 (9.2)	10.9	10.8
Asian/Pacific Islander	1446 (1.9)	2.0	3.8
American Indian/Alaskan Native	240 (0.3)	0.2	0.7
Type of cancer			
Breast	40 788 (54.2)	27.9	
Colorectal	15 406 (20.5)	20.3	
Lung	9416 (12.5)	24.6	
Prostate	9605 (12.8)	27.1	
Age, y			
30-64	51 145 (68.0)	37.5	78.5
65-74	17 851 (23.7)	31.4	11.3
≥75	6219 (8.3)	31.2	10.2
Sex			
Male	24 104 (32.1)	51.0	47.6
Female	51 111 (67.9)	49.0	52.4

Steady decline in women and minority patients

Review of clinical trial participation among vulnerable populations in trials supported by NIH

	2013 (%)	2014 (%)	2016 (%)	2017 (%)	2018 (%)
Female	44.3	47.2	54.1	47.9	52.4
American Indian	2.1	1.3	0.8	0.7	1.0
Asian	15.1	17.2	8.4	26.4	7.8
Black/African American	12.2	14.3	10.0	10.8	13.5
Native Hawaiian/Pacific Islander	0.3	0.3	0.6	0.1	0.2
White	52.9	49.5	49.6	49.9	60.0
More than 1 race	1.1	1.1	2.0	1.9	2.3
Unknown race	1.1	1.1	2.0	1.9	2.3
Hispanic	9.8	8.1	10.8	6.7	8.5
Non-Hispanic	86.1	89.6	62.6	81.8	76.2
Unknown ethnicity	4.1	2.3	22.4	9.8	12.0
Sum of all races	84.7	84.8	73.5	91.8	87.2
Sum of all ethnicities	100.0	100.0	95.8	98.3	96.7

NOTE: The full analysis is available in Appendix B.

Bibbins-Domingo et al 2022

Who gets screened and who gets enrolled into brain cancer trials?

Table 2 Minority versus non-minority rates of trial screening and enrollment

	Minority	Non-minority	OR[a]	p-value[b]
Initial diagnosis				
Trial screening pursued	94/261 (36.0%)	212/443 (47.9%)	0.61 [0.45–0.84]	0.002
Trial enrollment	37/261 (14.2%)	87/443 (19.6%)	0.68 [0.44–1.03]	0.07
Recurrence				
Trial screening pursued	80/164 (48.8%)	231/460 (50.2%)	0.94 [0.66–1.35]	0.75
Trial enrollment	46/164 (28.0%)	119/460 (25.9%)	1.12 [0.75–1.67]	0.59

	White/Caucasian	Black/African American	Asian/Pacific Islander	Hispanic/Latino	American Indian/Alaskan Native	Not Reported
New diagnosis						
Trial screening pursued	212/443 (47.9%)	13/39 (33.3%)	62/172 (36.1%)	17/40 (42.5%)	1/6 (16.7%)	1/4 (25.0%)
Trial enrollment	87/443 (19.6%)	4/39 (10.3%)	28/172 (16.3%)	4/40 (10.0%)	1/6 (16.7%)	0/4 (0%)
Recurrence						
Trial screening pursued	231/460 (50.2%)	6/19 (31.6%)	55/100 (55%)	14/34 (41.2%)	1/1 (100%)	4/10 (40%)
Trial enrollment	119/460 (25.9%)	4/19 (21.1%)	27/100 (27%)	12/34(35.3%)	0/1 (0%)	3/10 (30%)

Fewer minorities screened and therefore fewer enrolled

Morshed et al JNO 2020

Who is most likely to enroll?

Shorter distance to hospital
In-state
Privately insured
Higher median household income
employed

	Minority (n=320)	Non-minority (n=650)	p-value
Age at diagnosis	48.6 [46.9–50.3]	51.6 [50.5–52.8]	0.002
Sex			
Male	178 (55.6%)	388/650	0.23
Female	142 (44.4%)	262/650	
WHO grade			
II	95 (29.7%)	176/650	0.68
III	58 (18.1%)	126/650	
IV	167 (52.2%)	348/650	
Location			
In-state	279 (87.2%)	470 (72.3%)	<0.0001
Out-of-state	41 (12.8%)	180 (27.7%)	
Distance from UCSF (miles)[a]	71.9 [59.5–84.3]	104.4 [94.8–119.9]	<0.0001
Insurance type			
Private	182/314 (58.0%)	412/630 (65.4%)	<0.0001
Public	91/314 (29.0%)	190/630 (30.2%)	
None	41/314 (13.0%)	28/630 (4.4%)	
Employed[b]	57/149 (38.3%)	285/559 (51.0%)	0.006
Mean household income	85,476.30 [81,803–89,150]	78,259.30 [75,668–80,850]	0.002
Percent below poverty	11.9% [11.1–12.7%]	11.5% [10.9–12.0%]	0.46

Morshed J et al NeuroOncol 2020

Who have enrollment numbers changed over 20 year period post NIH revitalization act?- Women

Neuro-Oncology
24(8), 1341–1349, 2022 | https://doi.org/10.1093/neuonc/noac011 | Advance Access date 6 January 2022

A population study of clinical trial accrual for women and minorities in neuro-oncology following the NIH Revitalization Act

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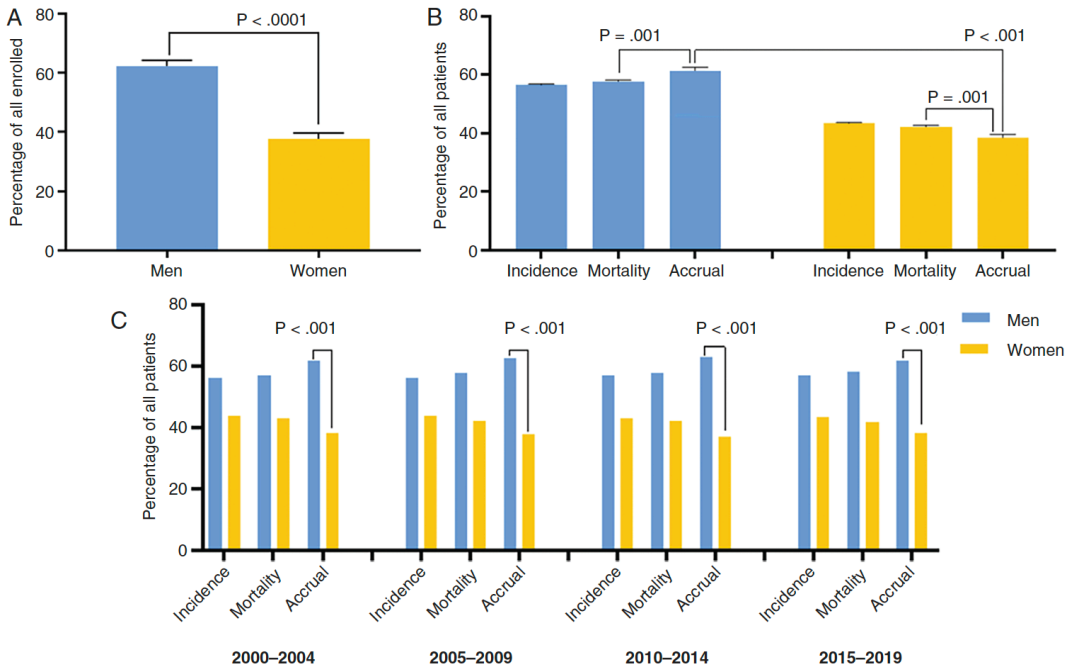
Abstract

Background. The NIH Revitalization Act, implemented 29 years ago, sot to improve the representation of women and minorities in clinical trials. In this study, we investigate progress made in all phase therapeutic clinical trials for neuroepithelial CNS tumors stratified by demographic-specific age-adjusted disease incidence and mortality. Additionally, we identify workforce characteristics associated with clinical trials meeting established accrual benchmarks.

Methods. Registry study of published clinical trials for World Health Organization defined neuroepithelial CNS tumors between January 2000 and December 2019. Study participants were obtained from PubMed and ClinicalTrials.gov. Population-based data originated from the CBTRUS for incidence analyses. SEER-18 Incidence-Based Mortality data was used for mortality analysis. Descriptive statistics, Fisher exact, and χ^2 tests were used for data analysis.

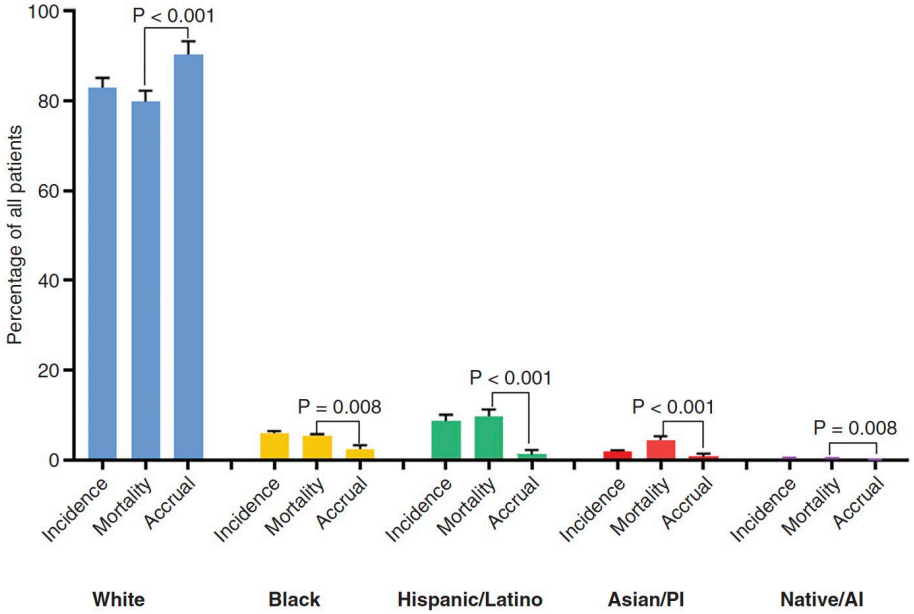
Results. Among 662 published clinical trials representing 49 907 participants, 62.5% of participants were men and 37.5% women ($P < .0001$) representing a mortality specific over-accrual for men ($P = .001$). Whites, Asians, Blacks, and Hispanics represented 91.7%, 1.5%, 2.6%, and 1.7% of trial participants. Compared with mortality, Blacks (47% of expected mortality, $P = .008$), Hispanics (17% of expected mortality, $P < .001$) and Asians (33% of expected mortality, $P < .001$) were underrepresented compared with Whites (114% of expected mortality, $P < .001$). Clinical trials meeting accrual benchmarks for race included minority authorship.

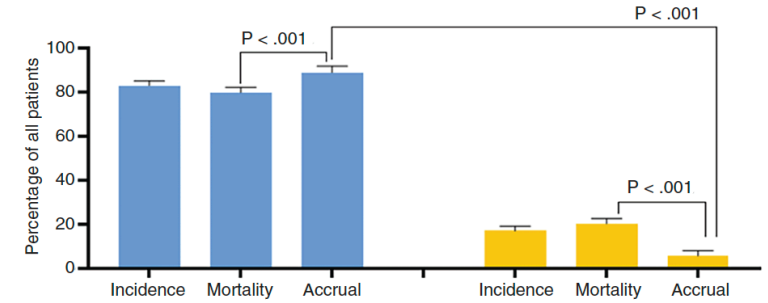
Conclusions. Following the Revitalization Act, minorities and women remain underrepresented in therapeutic clinical trials for neuroepithelial tumors, relative to disease incidence and mortality. Study accrual has improved with time. This study provides a framework for clinical trial accrual efforts and offers guidance regarding workforce considerations associated with enrollment of underserved patients.

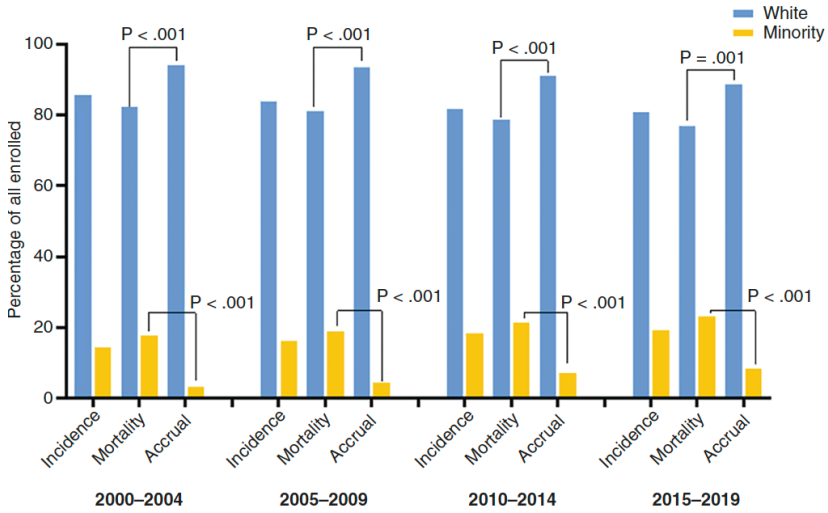


Reihl et al Neuro-Oncology 2022

Who have enrollment numbers changed over 20 year period post NIH revitalization act?- Minorities

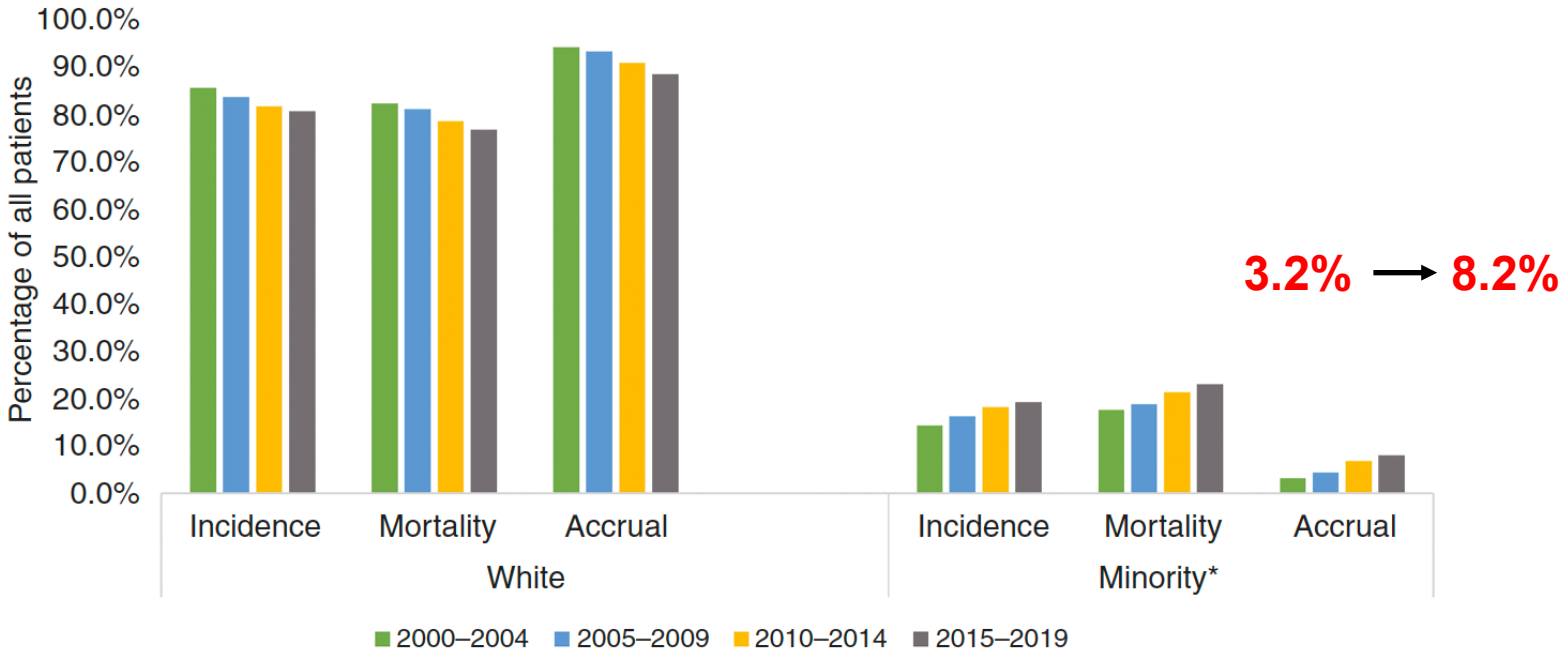






Reihl et al Neuro-Oncology 2022

Who have enrollment numbers changed over 20 year period post NIH revitalization act?- Minorities



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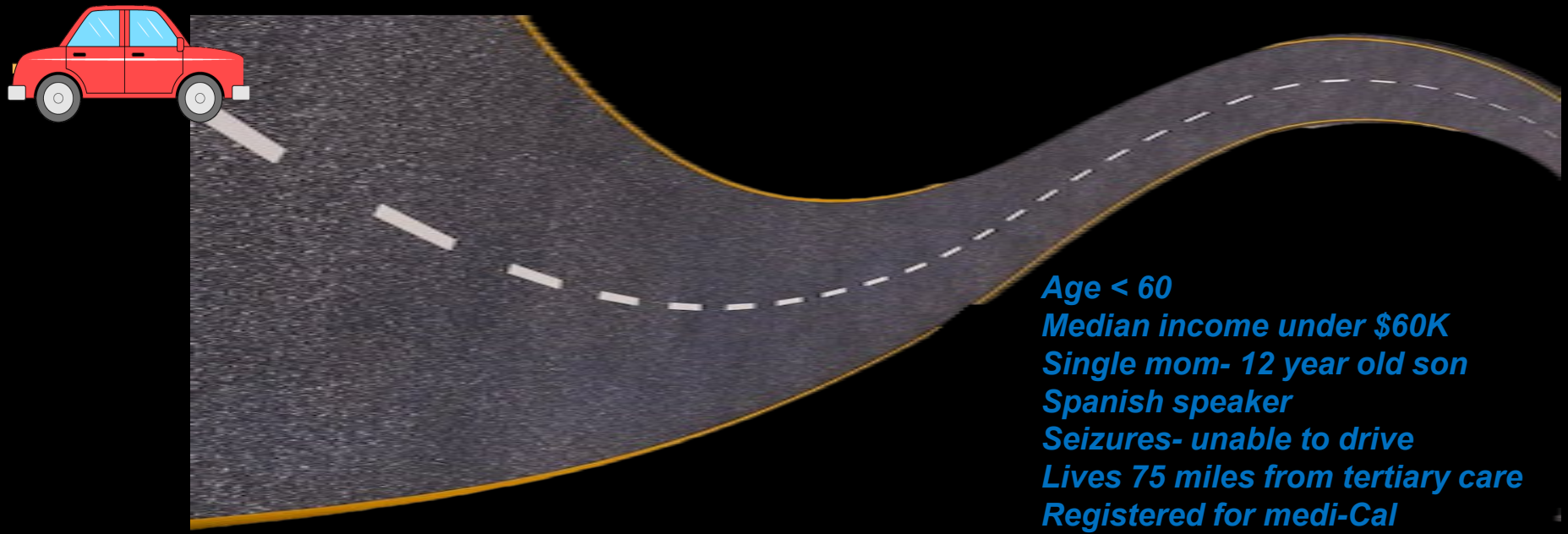
Which studies do enroll at benchmark levels?

Inclusive hiring practices matters

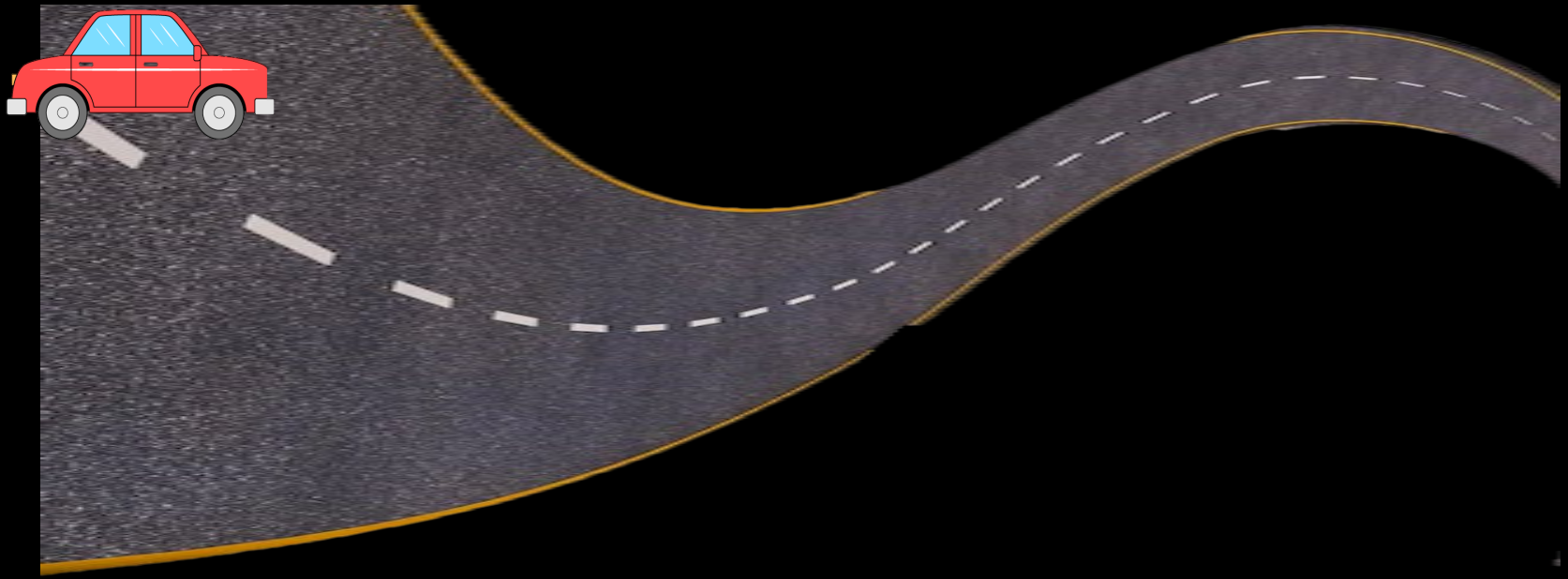
What did treatment look like for 57 yo woman



Age < 60
Median income under $60K
Single mom- 12 year old son
Spanish speaker
Seizures- unable to drive
Lives 75 miles from tertiary care
Registered for medi-Cal

Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 57 yo woman



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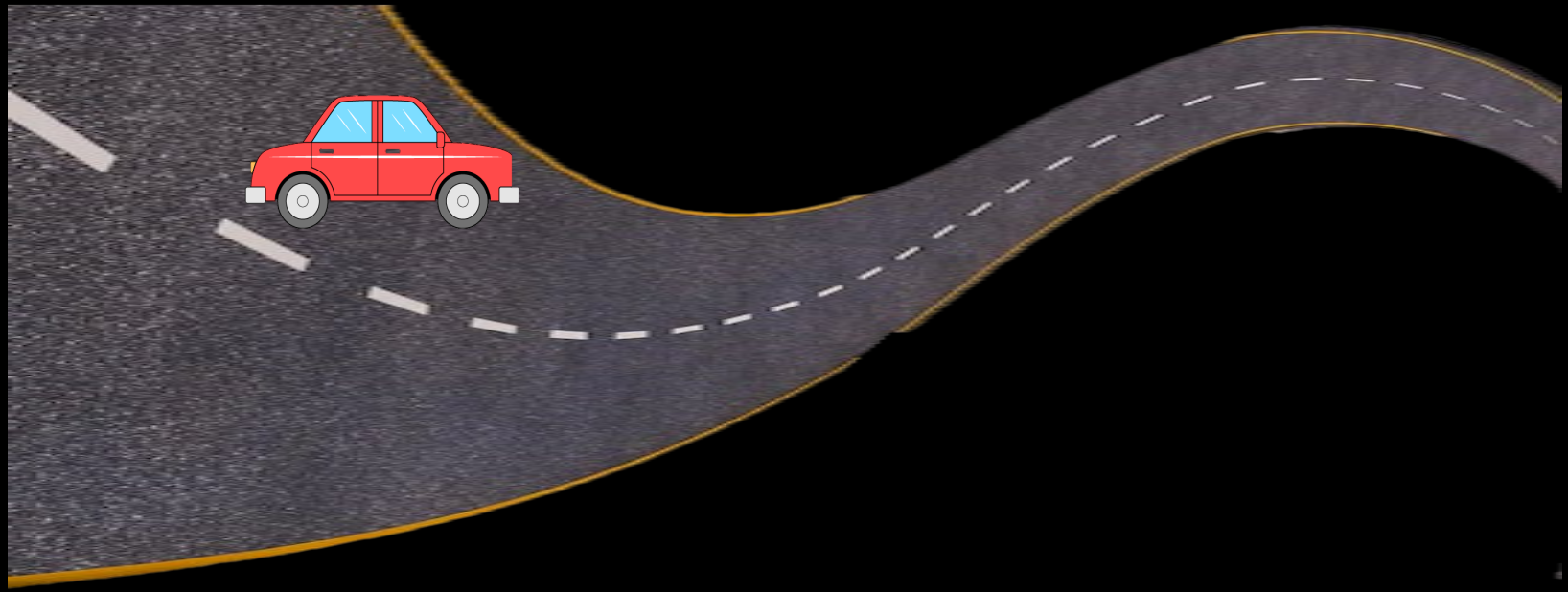
What did treatment look like for 57 yo woman



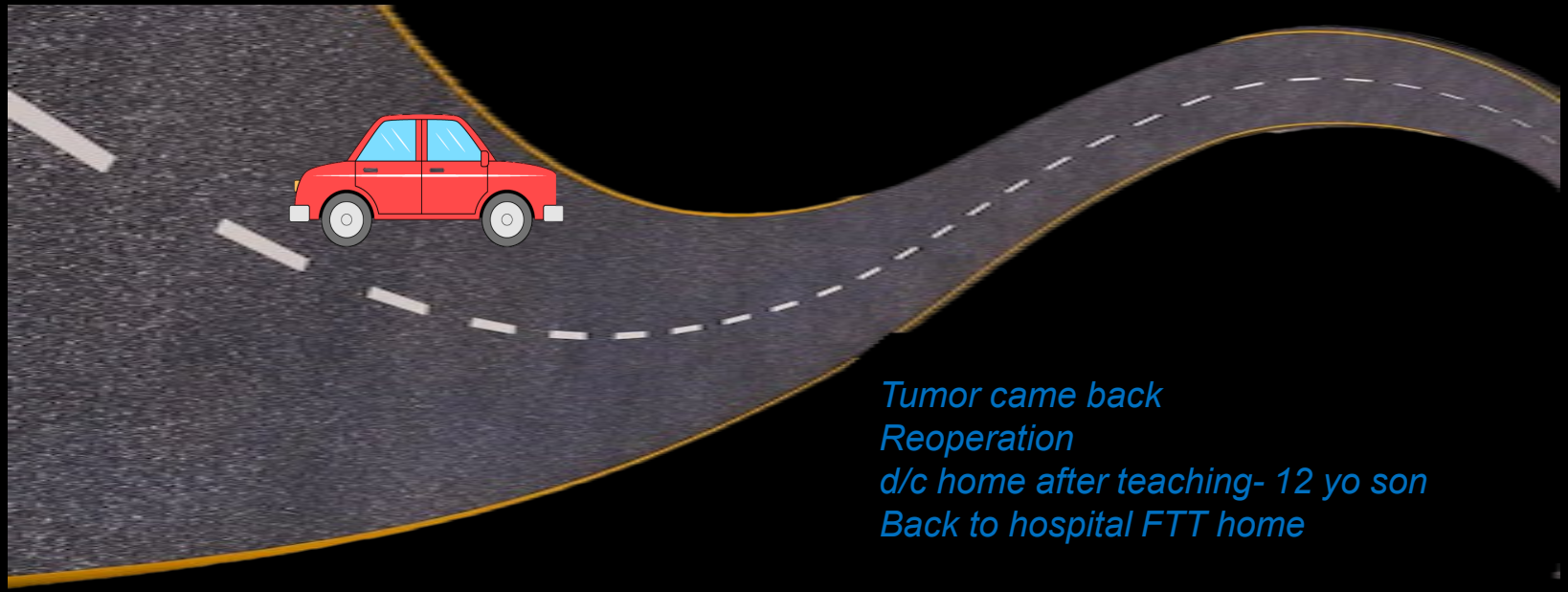
Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 57 yo woman

After 3 months unable to start XRT

Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 57 yo woman



Tumor came back
Reoperation
d/c home after teaching- 12 yo son
Back to hospital FTT home

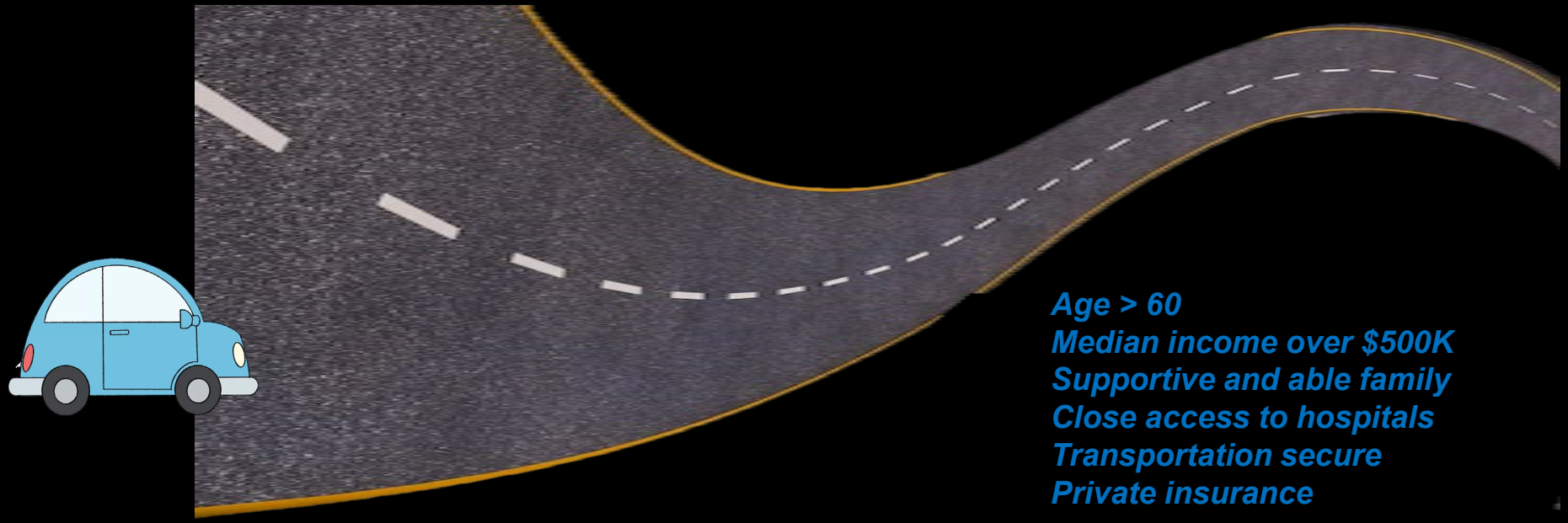
Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 57 yo woman

Missed labs
Thrombocytopenia
Passed 10 months post dx

Symptoms → ***Diagnosis*** → ***Surgery*** → ***Chemoradiation*** → ***Recurrence*** → ***Experimental therapies***

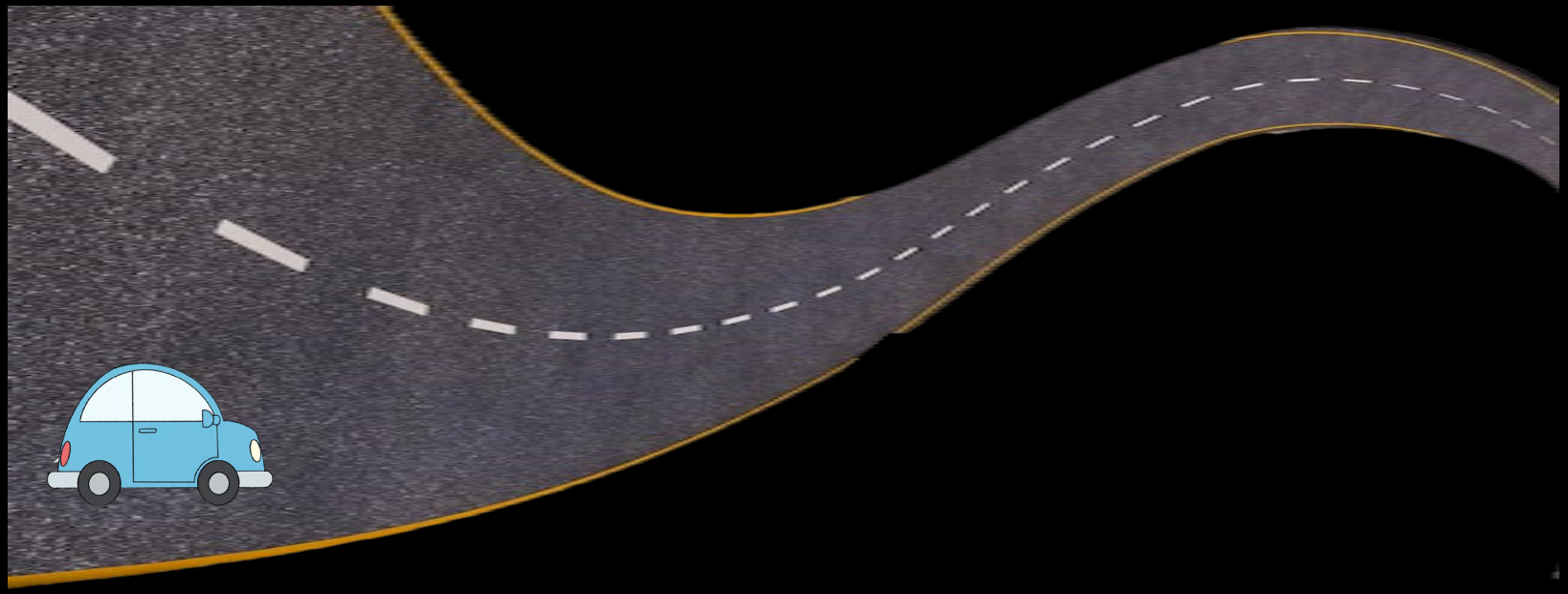
What did treatment look like for 80 yo man



Age > 60
Median income over $500K
Supportive and able family
Close access to hospitals
Transportation secure
Private insurance

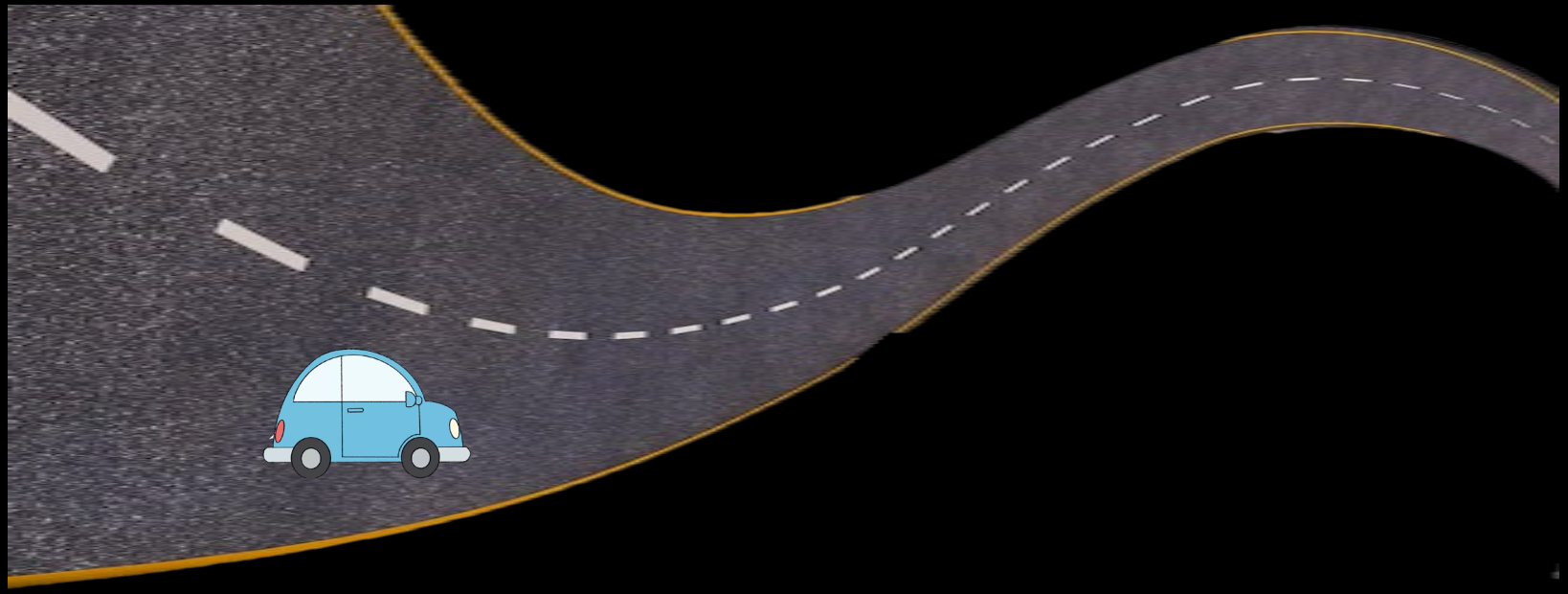
Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 80 yo man



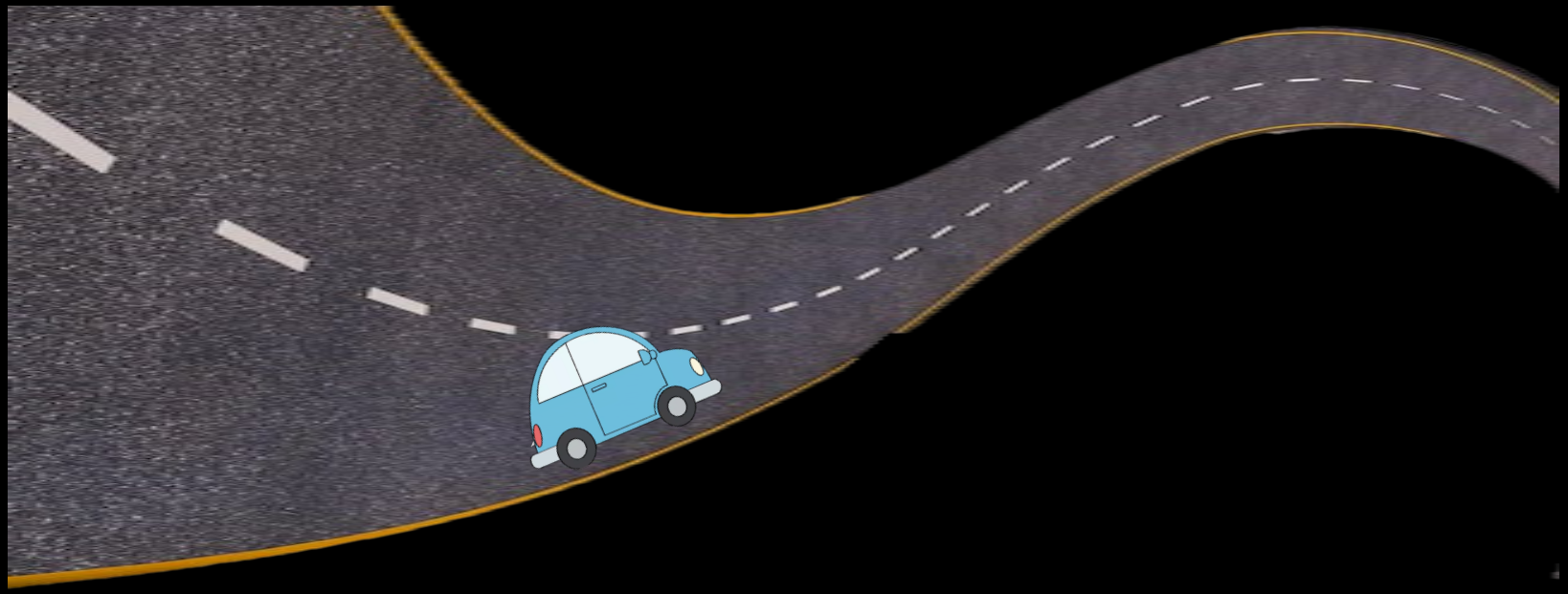
Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 80 yo man



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 80 yo man



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

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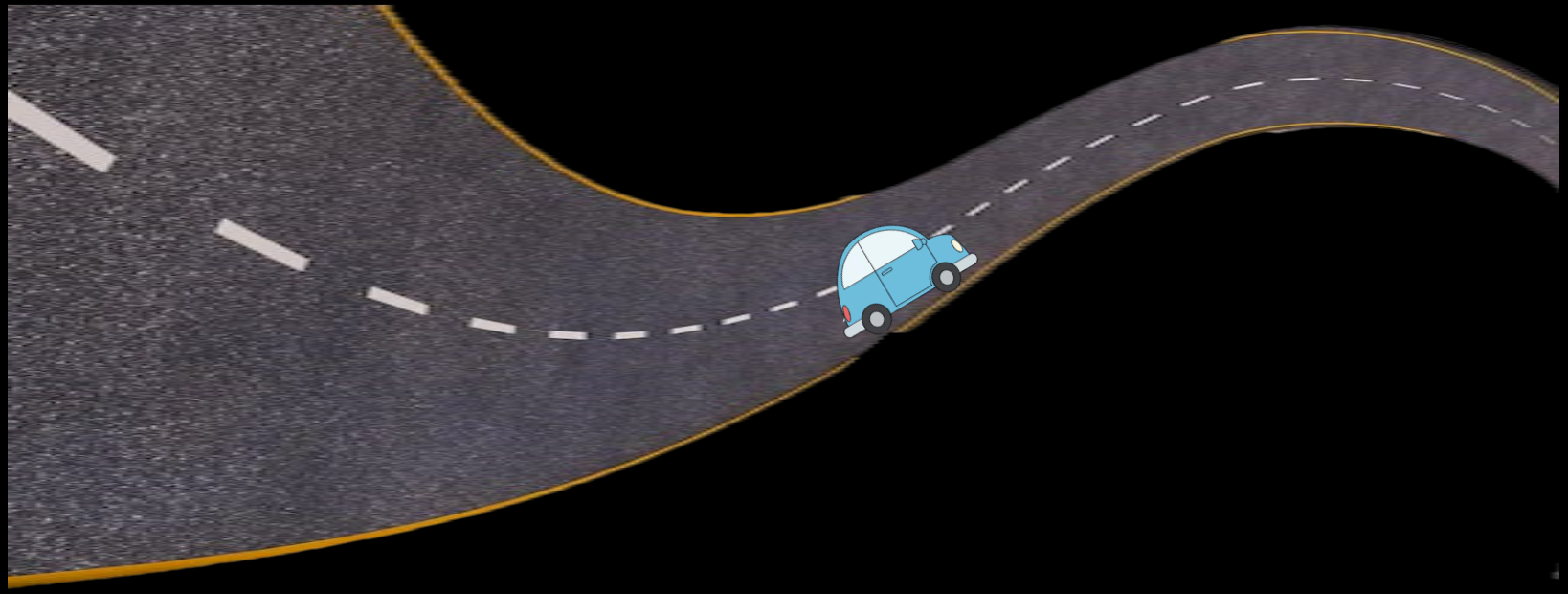
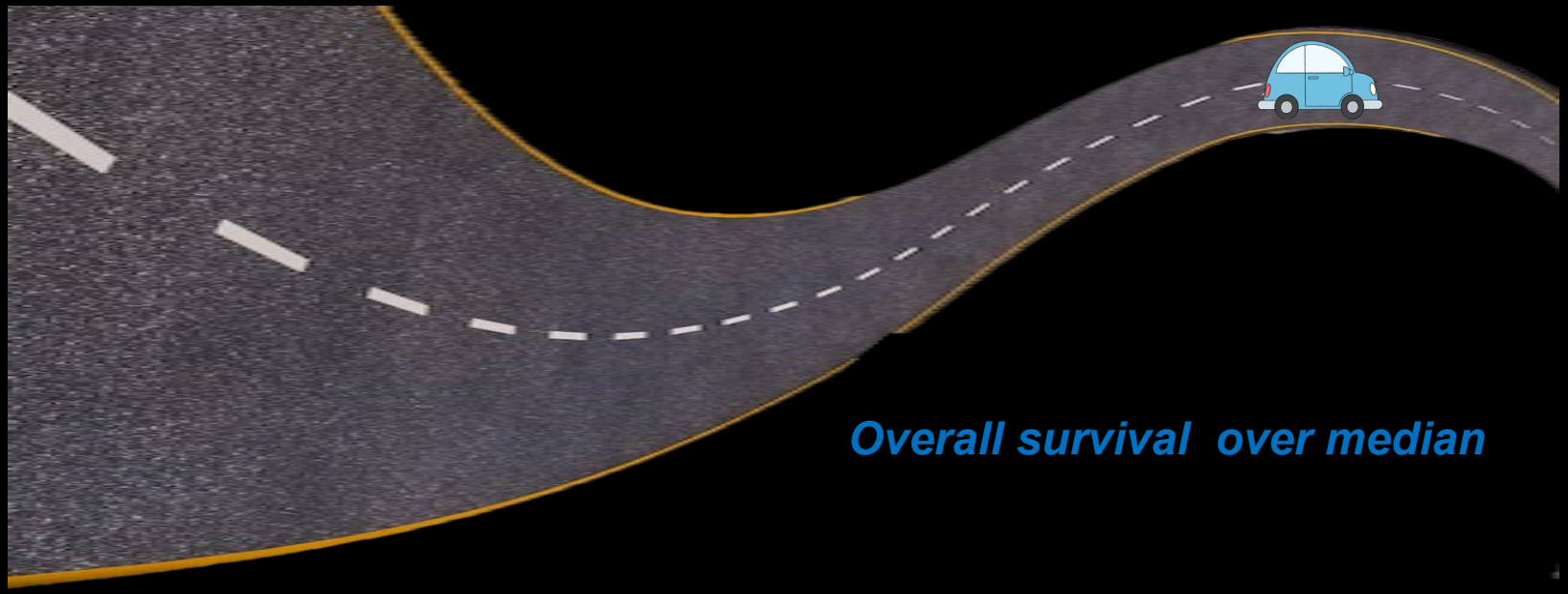


Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

What did treatment look like for 80 yo man



Symptoms → Diagnosis → Surgery → Chemoradiation → Recurrence → Experimental therapies

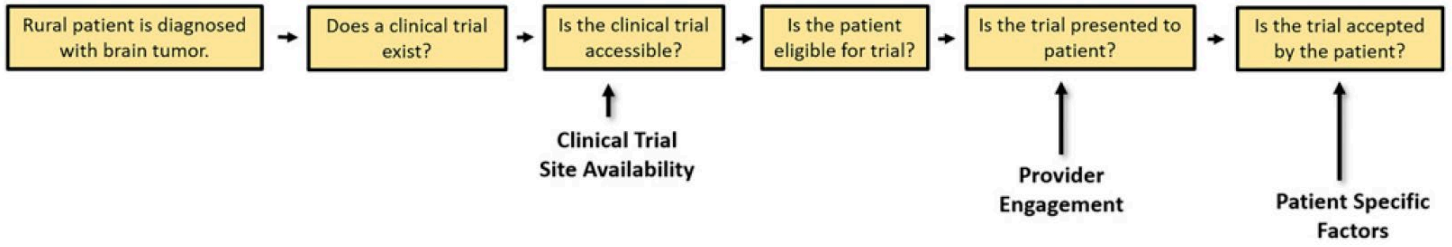
McCain hated Obamacare. He also saved it.

The Arizona senator, who died on Saturday, was driven less by his interest in health care policy than his disdain for bullies trampling the "little guy."

What can we do to built programs/research/clinical access for everyone?

1. *Community outreach and marketing*

Conceptual model of rural trial enrollment:



How many surgeries must a surgeon perform to be considered an expert- i.e. perioperative risk declines?

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Surgeon Case Volume and 30-Day Mortality After Carotid Endarterectomy Among Contemporary Medicare Beneficiaries

Before and After National Coverage Determination for Carotid Artery Stenting

Hiraku Kumamaru, Jessica J. Jalbert, Louis L. Nguyen, Marie D. Gerhard-Herman, Lauren A. Williams, Chih-Ying Chen, John D. Seeger, Jun Liu, Jessica M. Franklin and Soko Setoguchi

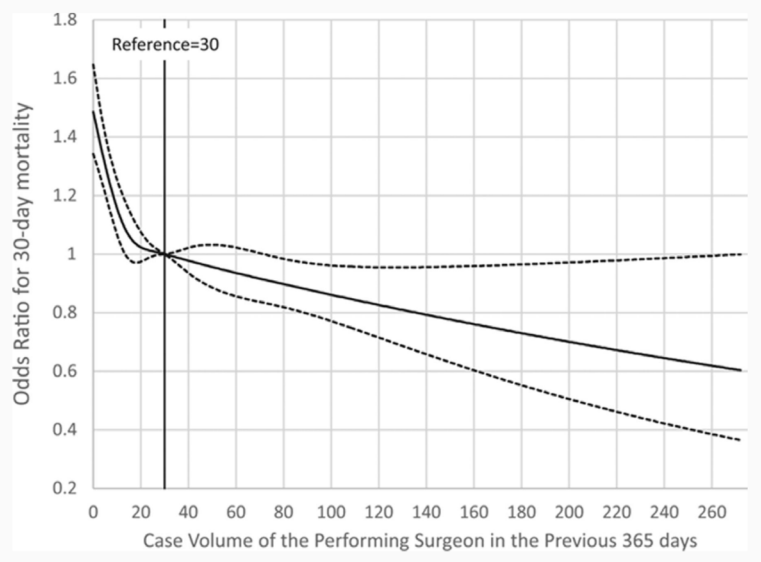
Originally published 19 Mar 2015 | https://doi.org/10.1161/STROKEAHA.114.006276 | Stroke. 2015;46:1288–1294

Other version(s) of this article

Abstract

Background and Purpose—

After the 2005 National Coverage Determination to reimburse carotid artery stenting (CAS) for Medicare beneficiaries, the number of CAS procedures increased and carotid endarterectomy (CEA) decreased. We evaluated trends in surgeons' past-year CEA case-volume and 30-day mortality after CEA, and their association before and after the National Coverage Determination.



10-20 cases per year associated with lowest surgical complications

How many surgeries must a surgeon perform to be considered an expert- i.e. perioperative risk declines?

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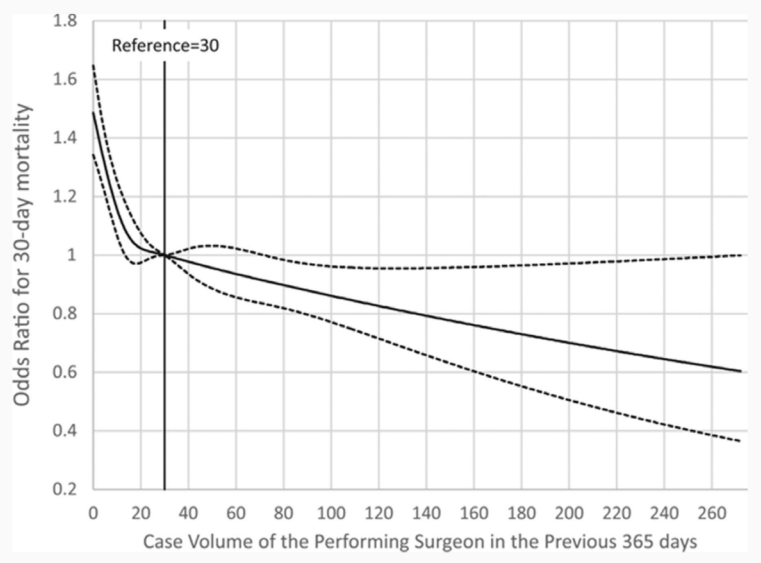
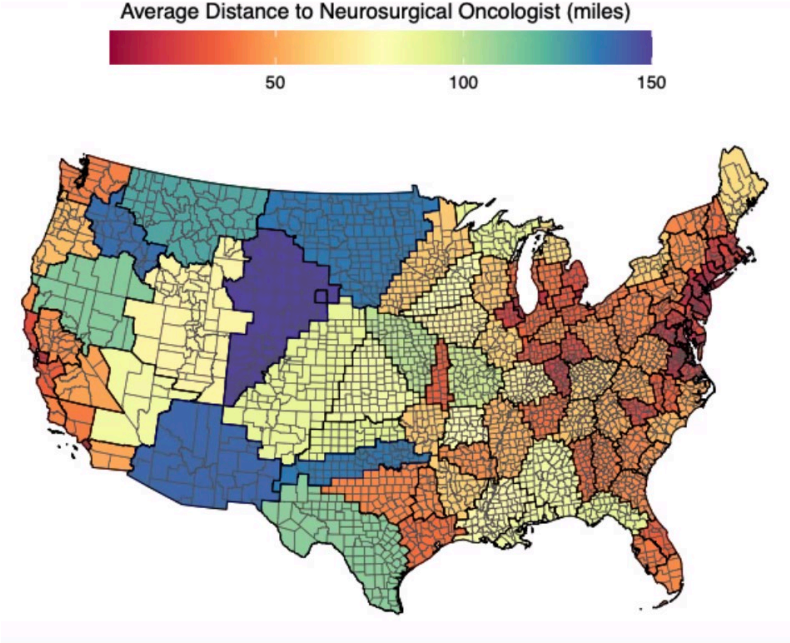
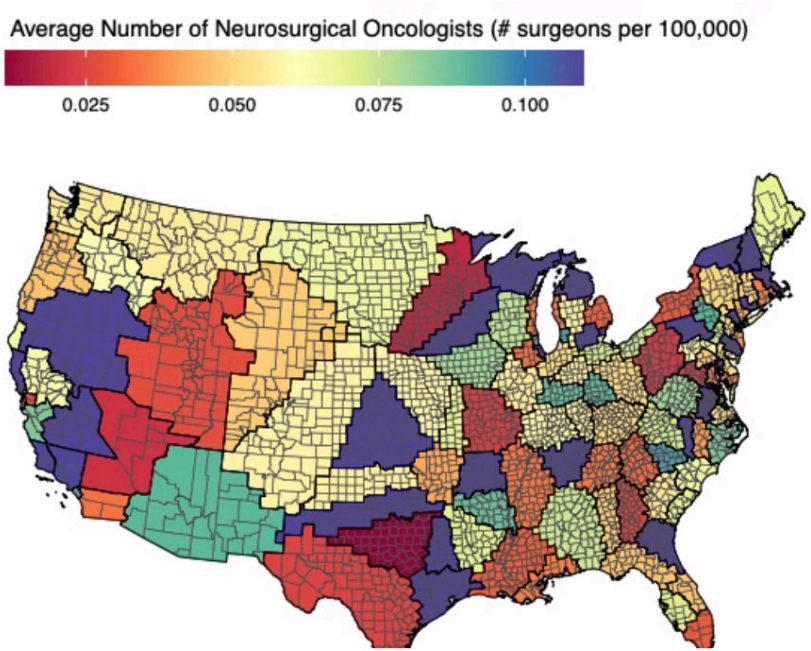


Community outreach- partnerships
Access to a neuro-oncologist varies greatly across the US





People want care in their community- how can we bridge this gap

What can we do to built programs/research/clinics for everyone?

1. *Community outreach and marketing*
2. *Education efforts for both patient and providers*
3. *Patient facing programs to increase access to surveillance and screening*
4. *Travel/ transportation resources*
5. *Treatment inequities education*
6. *Funding agency review of enrollment practices*

Guidance for improving access for vulnerable populations from National Academy of Medicine

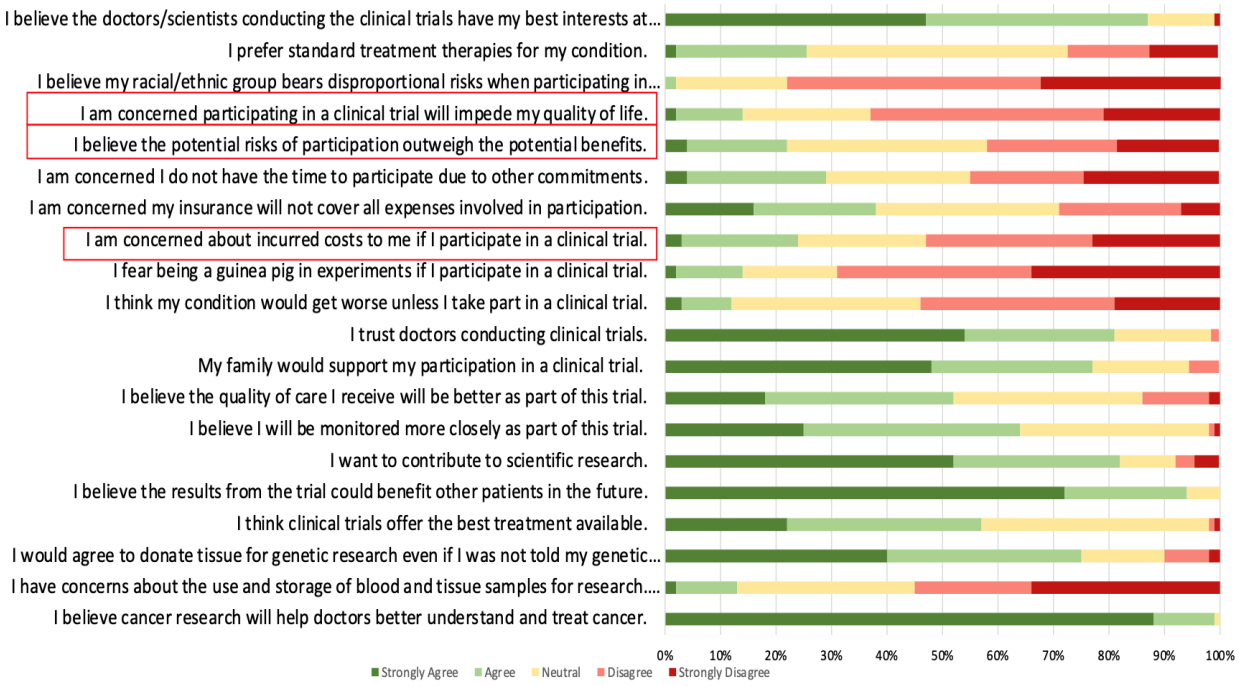
Bibbins-Domingo et al 2022

Factors Affecting Willingness to Participate in Therapeutic Clinical Trials for Minority Patients with Low and High-Grade Gliomas

- 82 trial participants (N=8, 10% minority) and 192 non-trial participants (N=44, 23% minority) completed the SPECIFIC questionnaire.

- Compared to non-trial participants, trials participants were more likely to be:
  - White (83%vs74%,p=.02)
  - Non NIH-designated minority (90%vs77%,p=.02),
  - Privately insured (83%vs66%,p < .001)
  - Higher income level (79%vs65%,p=.03)
  - Referred for a trial (29% vs 5%, p=<.001)

Perception Towards Clinical Trials Among Non-Trial Participants

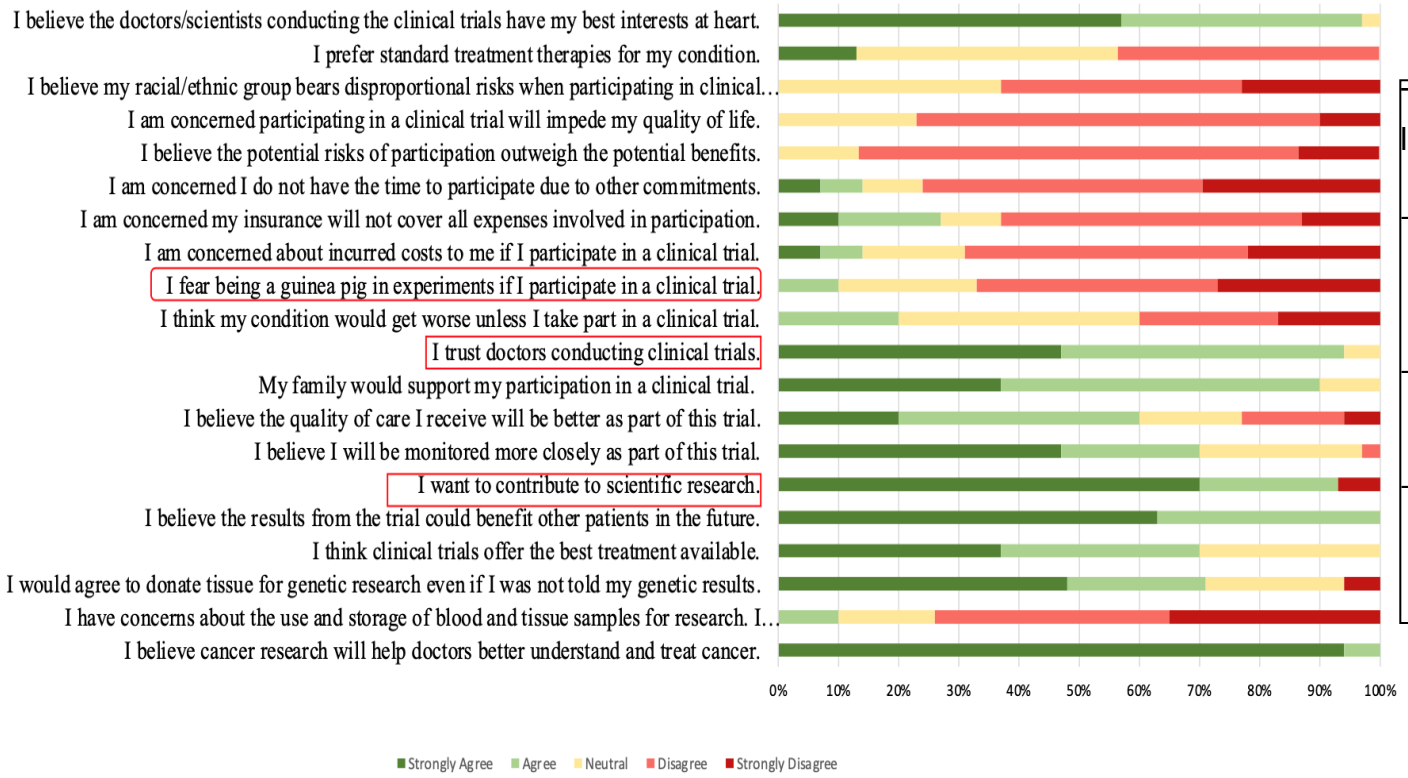


Results Summary

Non-trial participants were more likely to endorse:

- A fear that “risks outweigh benefits” (22%vs0%,p < 0.001)
- A fear of “burden to quality of life” (14%vs0%,p < 0.001).
- A concern for “costs of participation” (24%vs11%,p=0.01).

Perception Towards Clinical Trials Among Trial Participants

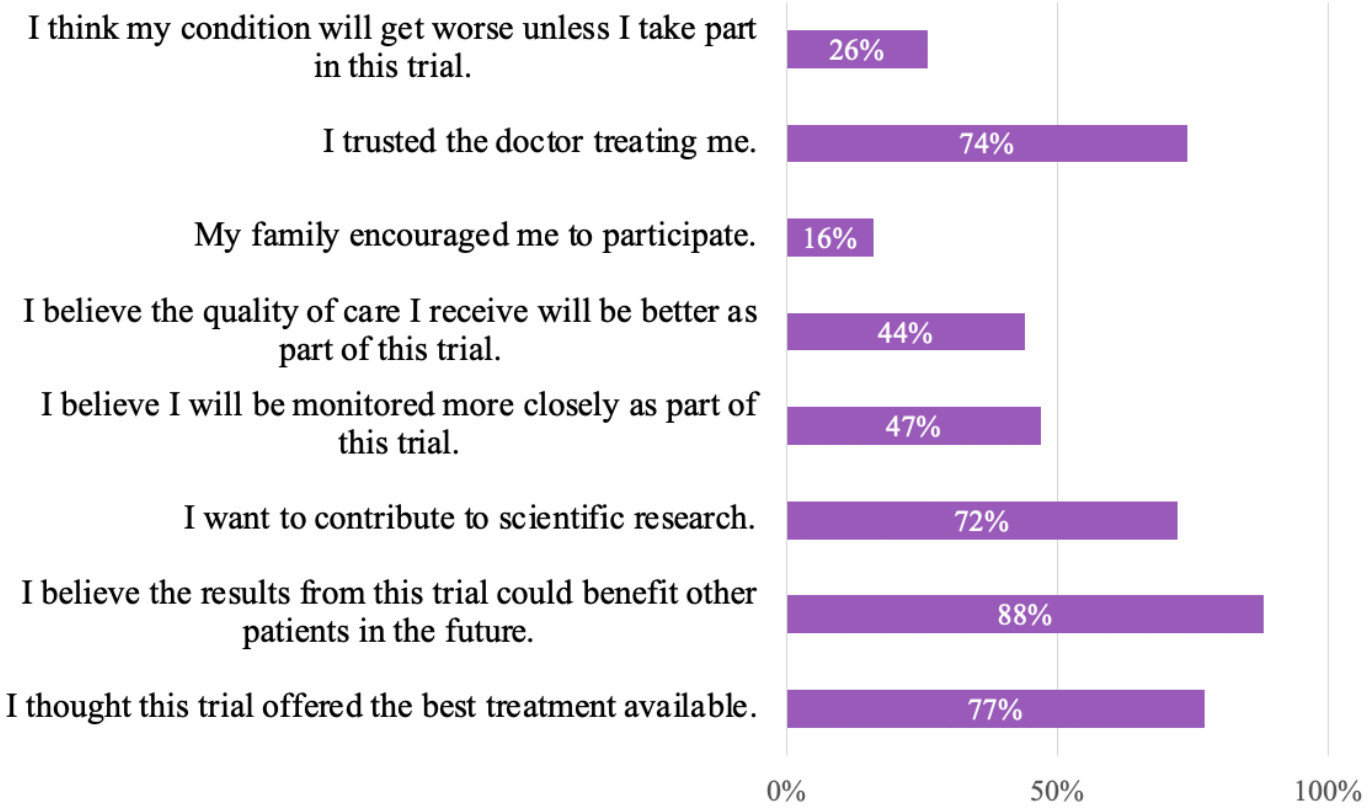


Results Summary

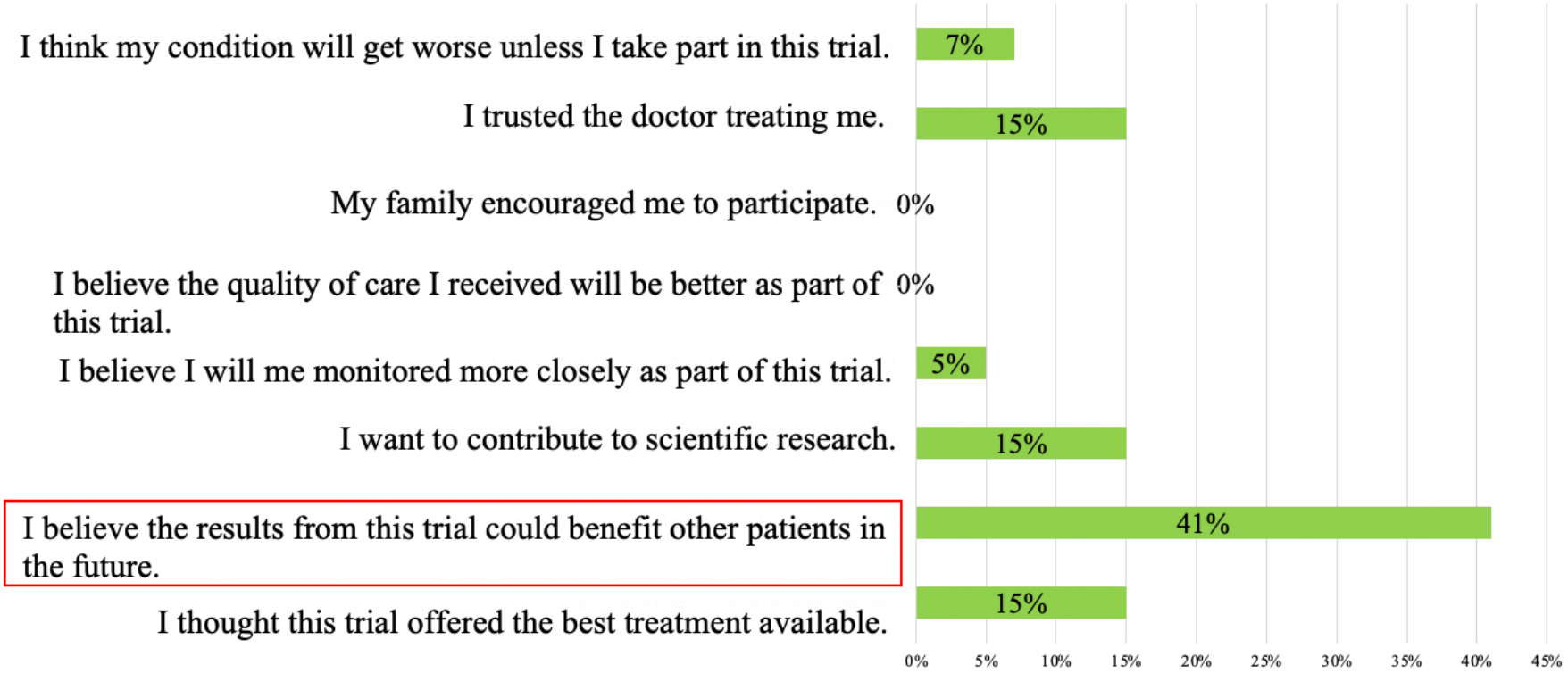
Trial participants were more likely to:

- "desire to contribute to scientific research" (95%vs82%,p=0.006)
- "trust physician investigators" (95%vs81%,p=0.005)
- "fear a worsening of their condition without clinical trial enrollment" (22%vs12%,p=0.02)

All Motivating Factors For Prospective Trial Participants



Most Significant Factor That Led to Positive Decision to Enroll



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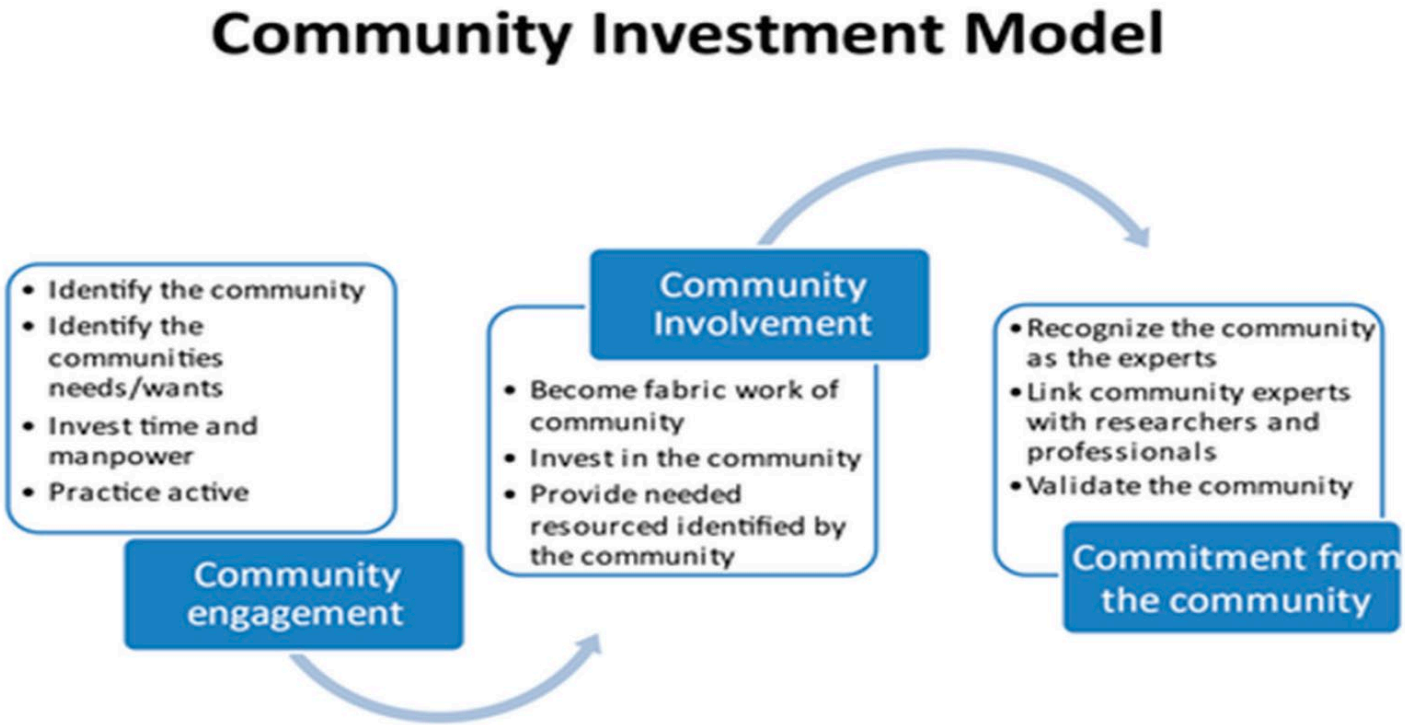

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loglio
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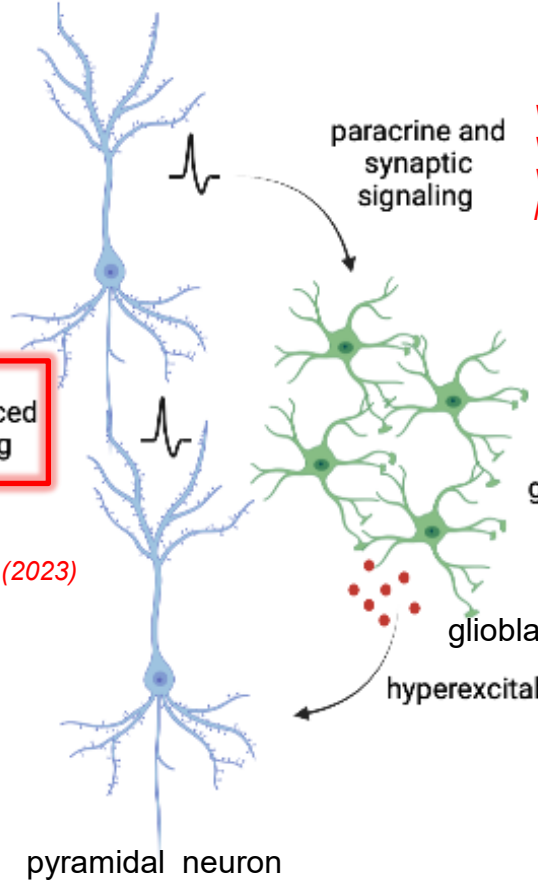
Thank you for the opportunity to speak!

@HerveyJumper

Shawn Hervey-Jumper, M.D., FAANS

Associate Professor
Department of Neurological Surgery
University of California San Francisco
Principal Investigator, Brain Tumor Research Center
Co-Director of the Sheri Sobrato Brisson Brain Cancer Survivorship Program

Bidirectional interactions between glioma cells and neurons



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