PERSONALIZED NUCLEAR MEDICINE: THE COST OF IT ALL

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DISCLOSURE STATEMENT

Sofie Biosciences: I am a founder and hold equity in the company and intellectual property invented by me and which has been patented by the University of California and has been licensed to Sofie Biosciences.

Trethera Therapeutics: I am a founder and hold equity in the company and intellectual property invented by me and which has been patented by the University of California and has been licensed to Trethera Therapeutics.

Commercial Interest:	Nature of Relationship:
Sofie Biosciences	Founder
Trethera Therapeutics	Founder
Point Biopharma	Scientific Advisor
Actinium	Scientific Advisor
Jubilant Radiopharma	Scientific Advisor
AMGEN	Scientific Advisor
Aktis Oncology	Scientific Advisor

Definitions of Cost in Health Care

- COST

Providers (e.g. Hospitals; outpatient clinics): the expense incurred to deliver health care services to patients.
Payers (e.g. Insurances): the amount they pay to providers for services rendered.
Patients: the amount they pay out-of-pocket for health care services.

- CHARGE or PRICE

The amount asked by a provider for a health care good or service, which appears on a medical bill.

- REIMBURSEMENT

A payment made by a third party to a provider. (Fee-for-service, per diem, for each episode of hospitalization (e.g., diagnosis-related groups, or DRGs), or for each patient considered to be under their care (capitation)).

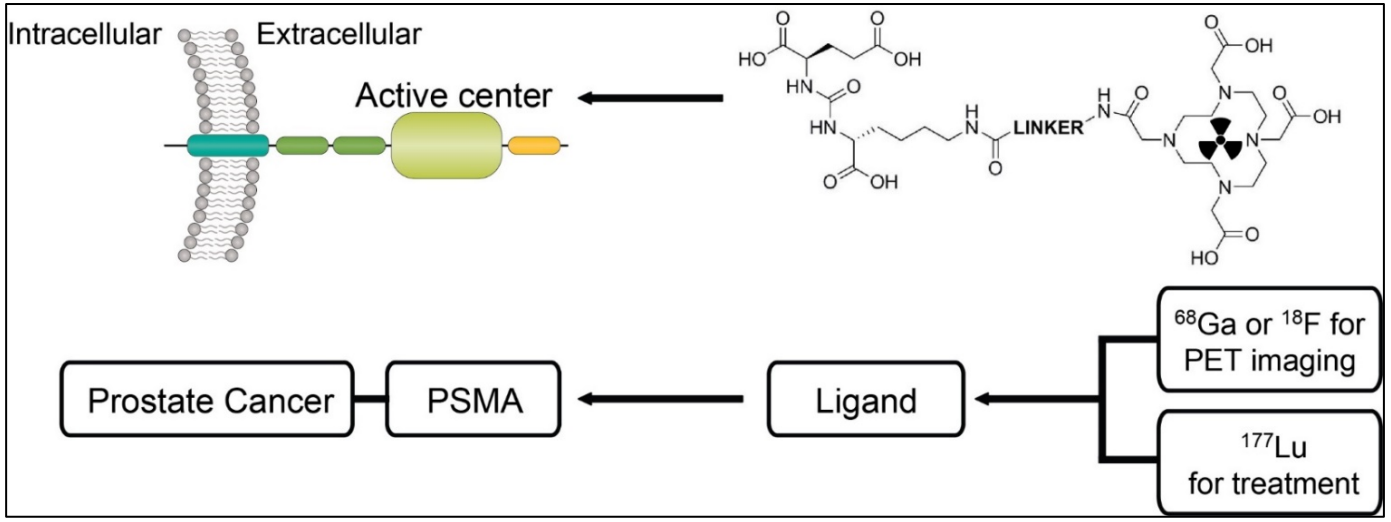
- **COST-EFFECTIVENESS**

Includes costs and effects of intervention in comparison to alternatives. Outcome: Cost per Quality Adjusted life-year

- COST EFFECTIVENESS ON A SOCIETAL/GLOBAL LEVEL

AMA J Ethics. 2015;17(11):1046-1052. doi: 10.1001/journalofethics.2015.17.11.stas1-1511.

LETS START WITH THERANOSTICS: A UNIQUE EXAMPLE OF PRECISION MEDICINE



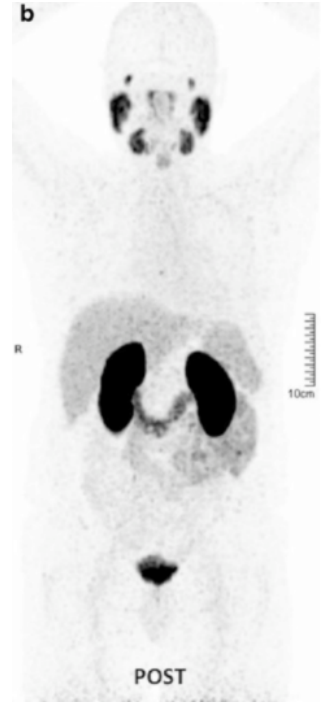
Diagnostic	Therapeutic	Target	Clinical Stage
$^{123/124}$ Iodine	^{131}Iodine	NaI-symporter	80 years..
^{68}Ga-DOTATATE *(Netspot)*	^{177}Lu-DOTATATE *(Lutathera)*	SSR2	Appr. 2016/2018
^{123}I-Iobenguane	^{131}I-Iobenguane *(Azedra)*	Norepinephrine Transporter	Appr. 2018
^{68}Ga-PSMA	^{177}Lu-PSMA617	PSMA	Phase 3 reported

YOU SEE THE TARGET

YOU TREAT

^{177}Lu-PSMA

YOU ASSESS RESPONSE



PSA *50 ng/ml* *0 ng/ml*

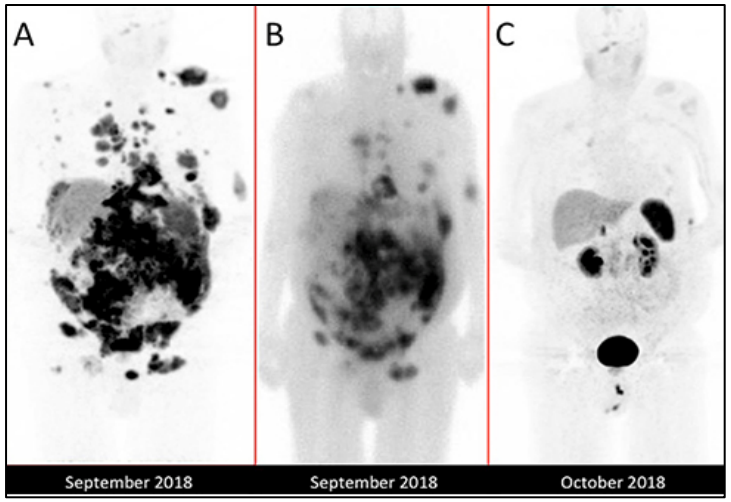
COST of PET + COST of Tx = ?

ADDING MEANINGFUL IMAGING REDUCES HEALTH CARE COSTS IN PRECISION NUCLEAR MEDICINE: ANECDOTAL EVIDENCE

THERAPY

$50 000 x 4

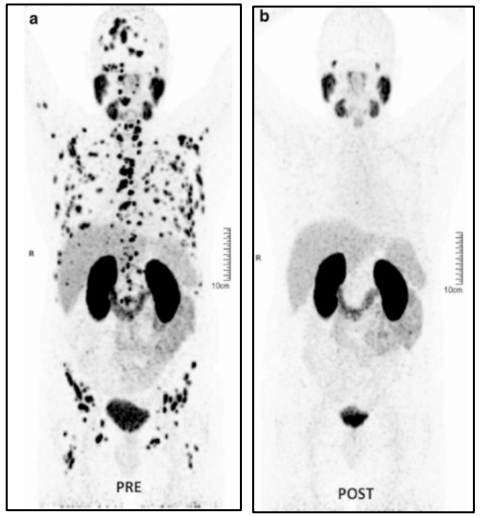
Pre **^{177}Lu-DOTATATE** *Post*



^{68}Ga-DOTATATE ^{68}Ga-DOTATATE

$50 000 x 3

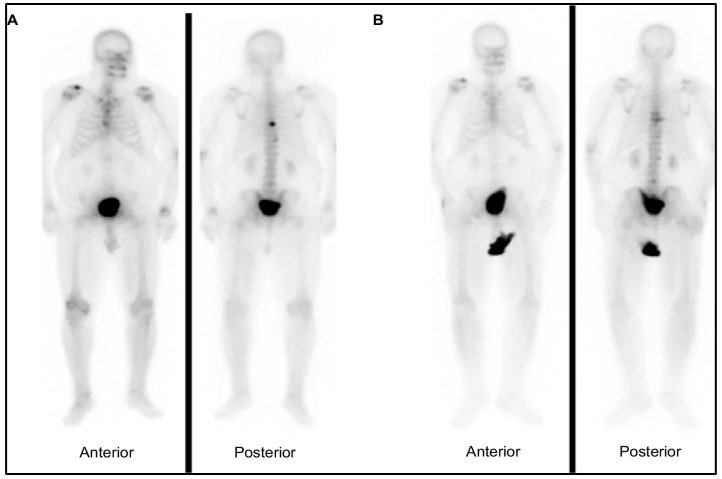
Pre **^{177}Lu-PSMA** *Post*



^{68}Ga-PSMA11 ^{68}Ga-PSMA11

$16 000 x 6

Pre **^{223}Ra (XOFIGO)** *Post*



^{99}Tc-MDP ^{99}Tc-MDP

IMAGING ***$5000*** ***$5000*** ***$300***

	Patients	PSMA scan ($5000/scan)	PSMA RLT ($/cycle)
No screening	40,000	$ 0	40,000 pts x $50,000 x 3 cycles = $6 Bill.
PSMA screening (-20%)	40,000	$200 Mil	32,000 pts x $50,000 x 3 cycles = $4.8 Bill.
		Adds $200 Mil. for IMAGING	**Reduces THERAPEUTICS by $1.2 Bill**

US Health Care Data

Health Care is #1 Employer in the USA

SOCIETAL BURDEN

- Health Care Costs
- Scarce resources

HC EXPENSE in 2018

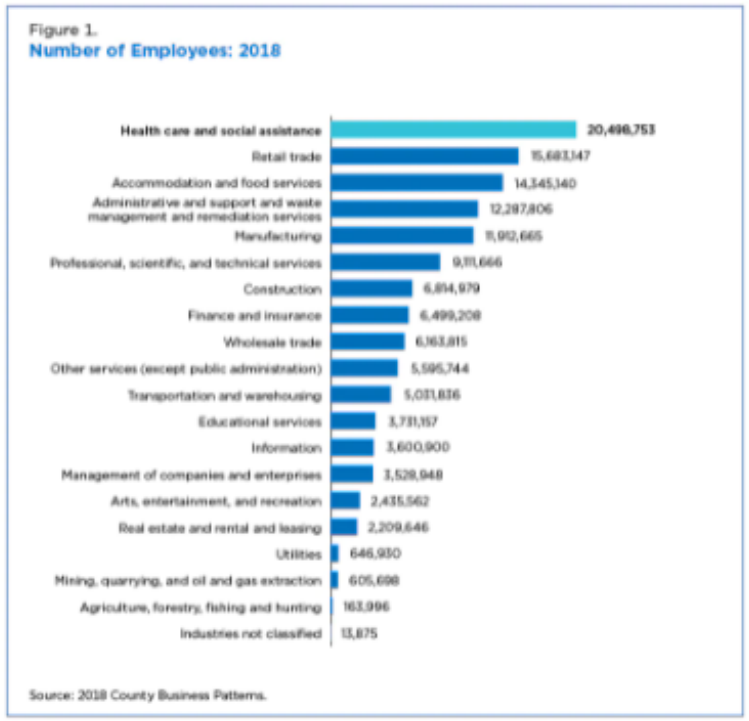
$3.8 trillion ($6.2 trillions in 2028)
24% of government spending

HC REVENUE in 2018

$1.853 trillion

TAX REVENUE?

Payroll tax, Sales, Corporate



PATIENT RELATED OUTCOMES

- *Improved QOL*
- *Improved PFS*
- *Improved OS*
- *Improved Life-time productivity*

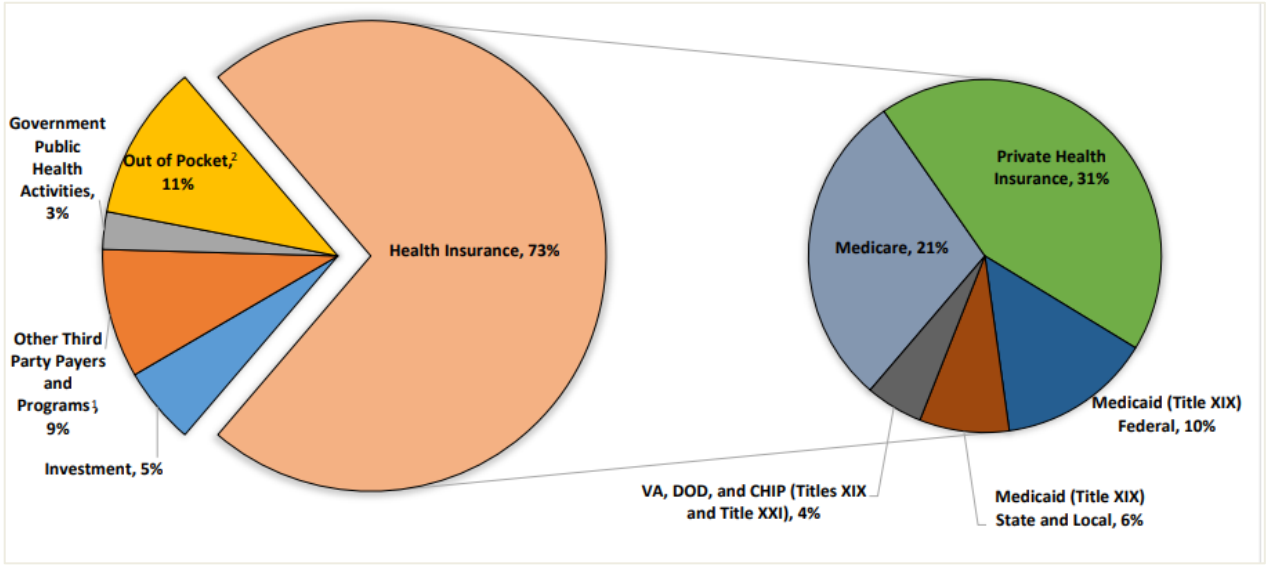
WORKFORCE

22 Mil; 14% of US workforce

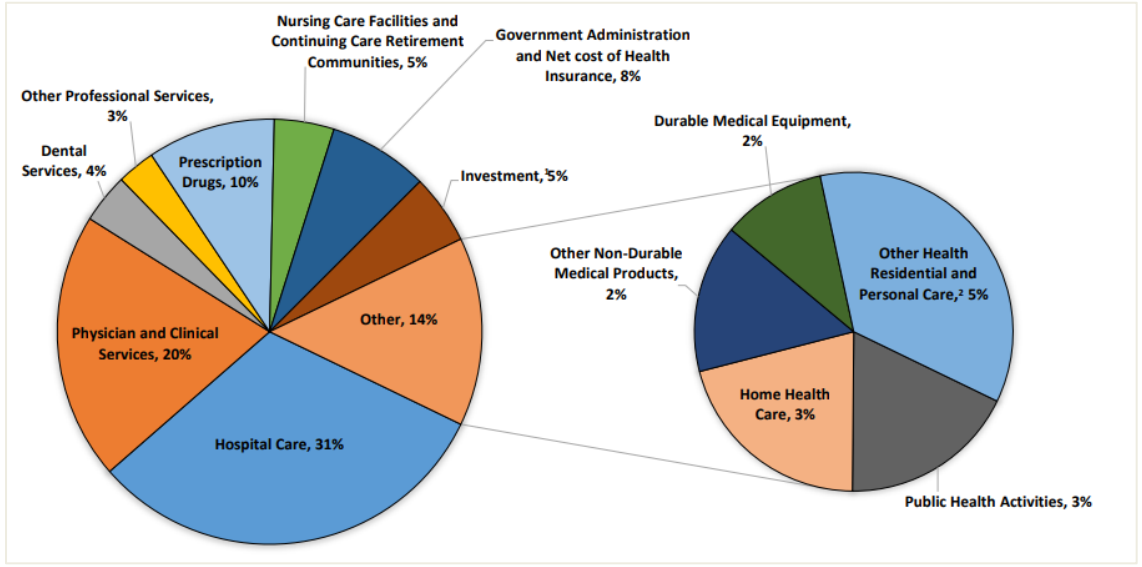
https://www.census.gov/library/stories/2020/10/health-care-still-largest-united-states-employer.html

THE NATIONS HEALTH EXPEDITURE IN 2019: $3.8 TRILLION

WHERE DID THE $3.8 TRILLION COME FROM

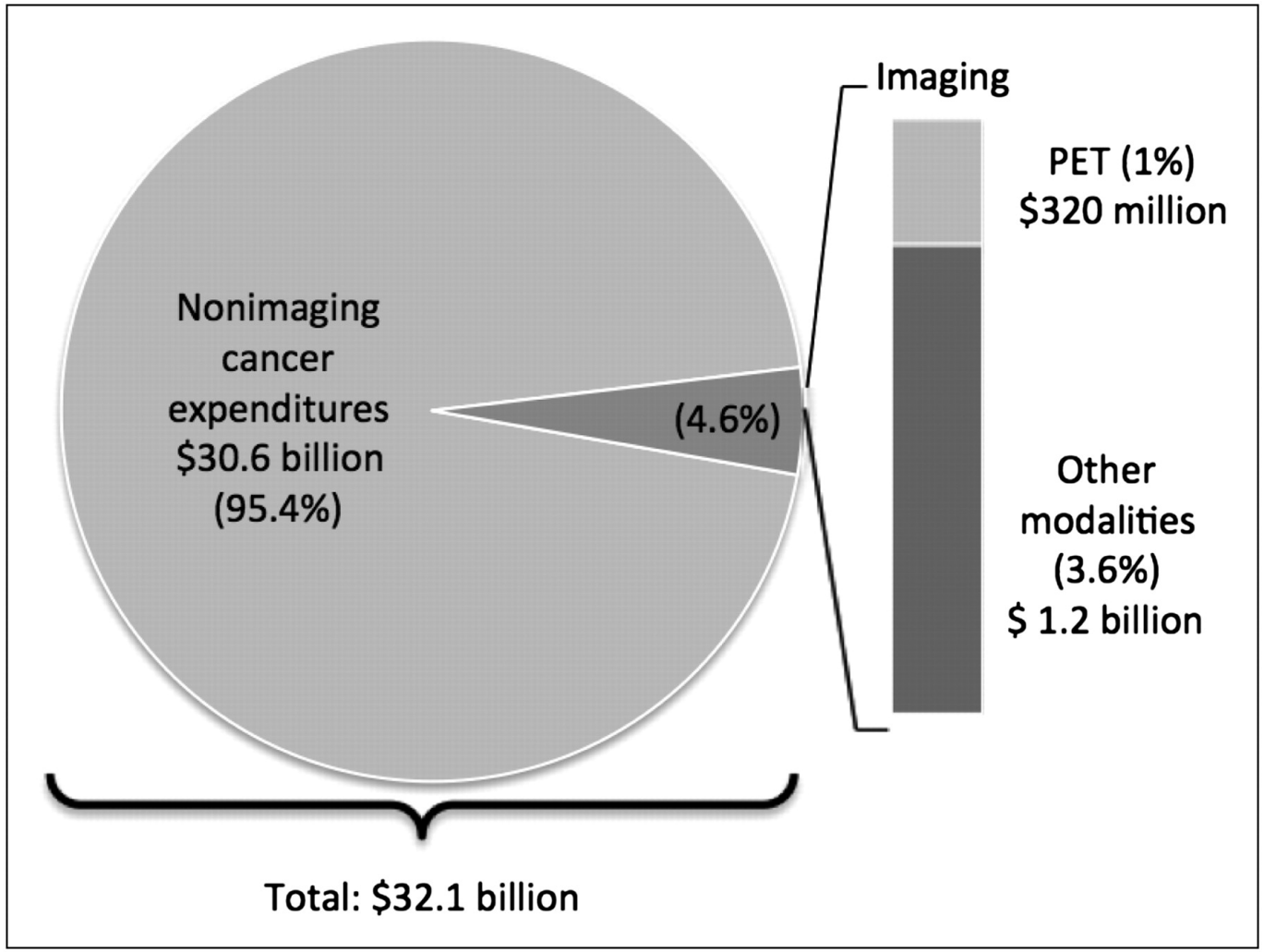


WHERE DID THE $3.8 TRILLION GO?



National Health Expenditures 2019 Highlights: CMS.gov; https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical

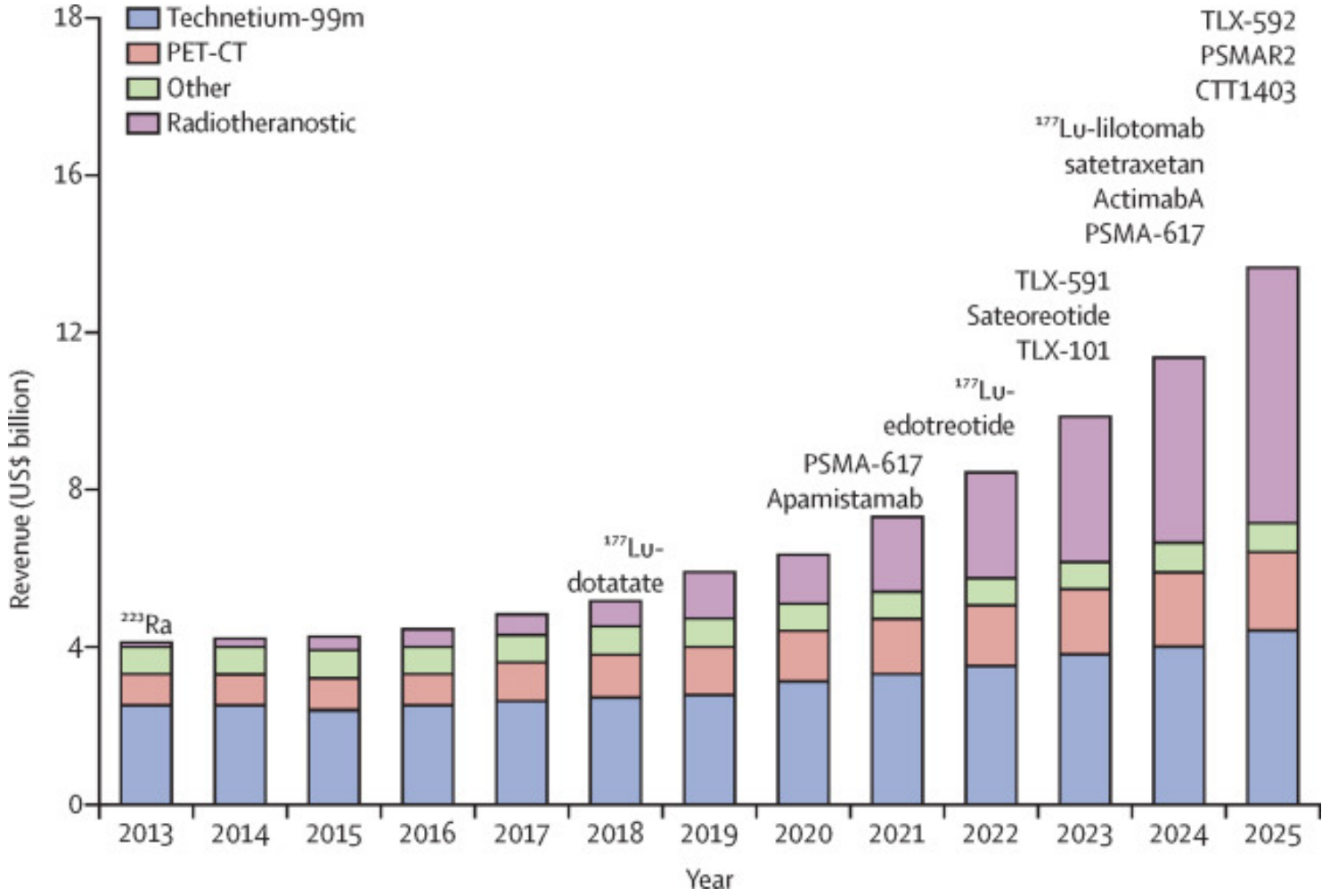
ONCE UPON A TIME WHEN IT WAS FDG IMAGING ONLY….



- Costs of imaging are overstated
- Nuclear Medicine imaging represents a small fraction of radiology imaging
- Cost assessments are blind. Cost effectiveness assessments are needed

Contribution of Imaging to Cancer Care Costs: Yang Yang and Johannes Czernin; J Nucl Md 2011, 52 (Supplement 2)

WHAT ABOUT NUCLEAR MEDICINE? Market will grow to >$13 billions in 2025



Theranostics

PET/CT

99mTc

Herrmann et al; Lancet Oncology, 2020 Adapted from Paul-Emmanuel Goethals and Richard Zimmermann (July 2019)

The World is changing: THE NEW PRECISION MOLECULAR IMAGING AND THERAPY MARKET

ESTABLISHED

Probe	Therapeutic	Target	Clinical Stage
$^{123/124}$Iodine	^{131}Iodine	NaI-symporter	80 years..
^{99}Tc-MDP/^{18}F-NaF	^{223}Radium *(Xofigo)*	Calcimimetic	Appr. 2013
^{99}Tc-MDP/^{18}F-NaF	^{153}Samarium EDTMP (Quadramet)	Calcimimetic	Appr. 1997
^{68}Ga-DOTATATE *(Netspot)*	^{177}Lu-DOTATATE *(Lutathera)*	SSR2	Appr. 2016/2018
^{123}I-Iobenguane	^{131}I-Iobenguane *(Azedra)*	Norepinephrine Transporter	Appr. 2018
^{68}Ga-PSMA	^{177}Lu-PSMA617	PSMA	Appr. 2020 Phase 3 completed

NEXT WAVE

Probe	Therapeutic	Target	Clinical Development
^{68}Ga-FAPi*	^{90}Y-FAPi*	FAP	In patients *
^{68}Ga-Pentixafor*	^{177}Lu-Petixather*	CXCR4*	Phase 1; In pts *
^{68}Ga-BOMBESIN	^{177}Lu-NeoBOMB1	Gastrin Releasing Peptide Receptors	IND; Phase 2
^{68}Ga-Lu-3B-227	^{177}Lu-3B-227	NTSR1	Phase 1
^{89}Zr-girentuximab*	^{177}Lu-girentuximab	CAIX	Imaging Phase 3

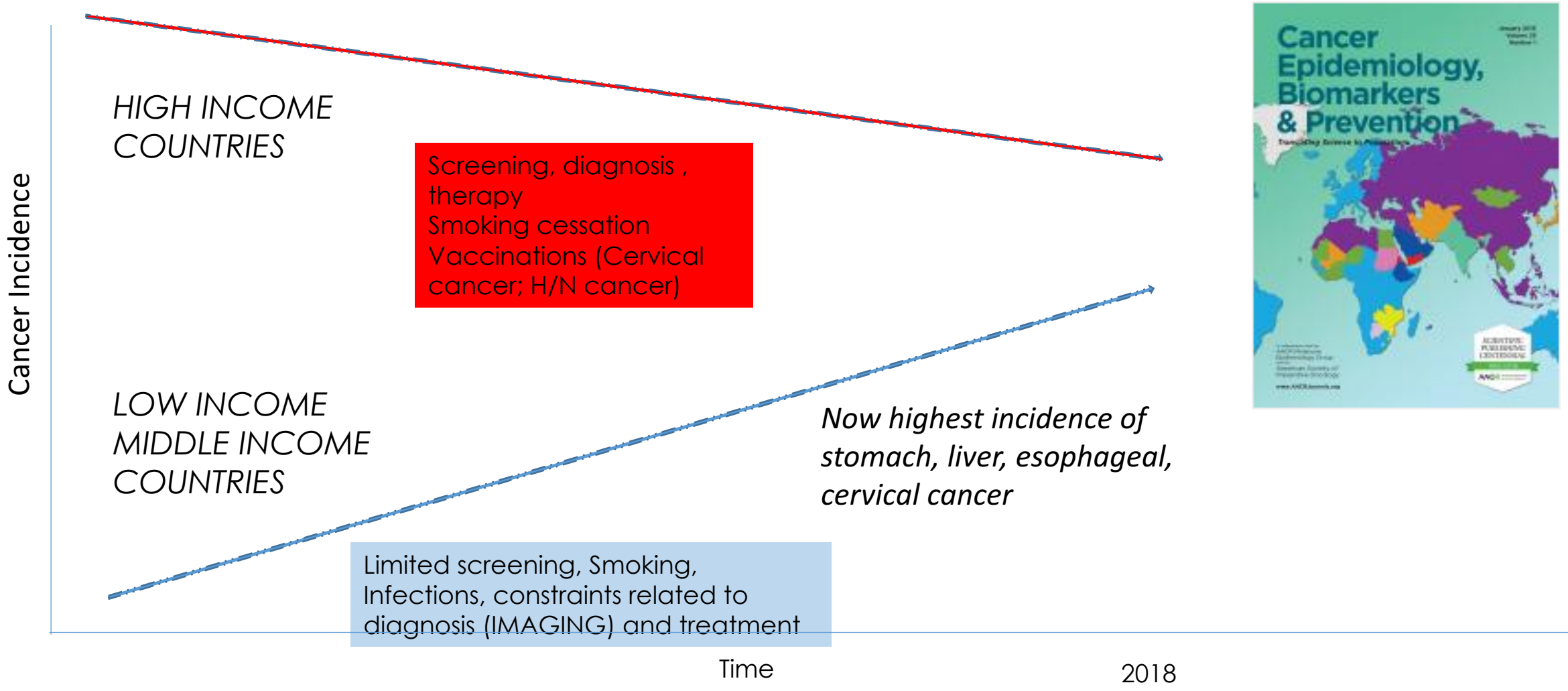
EMERGING

Brandname (if available)	Target	Disease	Company
APAMISTAMAB	CD45	BONE MARROW COND.	ACTINIUM
EDOTREOTIDE	SSTR 2 agonist	NET	ITM
SATEOREOTIDE	SSTR 2 antagon.	NET	IPSEN
^{131}I IODO-PhAI	LAT1	GBM	TELIX
^{68}GA-PSMA KIT	PSMA	PROSTATE CANCER	TELIX
^{225}Ac PSMA AB	PSMA	PROSTATE CANCER	TELIX
^{225}Ac-Lintuzumab	CD 33 AB	AML	ACTINIUM
^{177}Lu-lilotomab	CD20 AB	LYMPHOMA	NORDIC
^{177}Lu-PSMA	PSMA	PROSTATE CANCER	CTT

IS IT JUST ADDING COST?
HOW EXPENSIVE IS IT?
WHAT IS THE BENEFIT?

Adapted by Herrmann et al (Lancet oncology 2020) from Goethals and Zimmermann; adapted by JCz Nuclear Medicine MEDraysintell Report &Directory 2019)

CANCER INCIDENCE, MORTALITY AND AVAILABILITY OF THERAPY AND DIAGNOSTICS



GLOBAL CANCER INCIDENCE AND MORTALITY RATES AND TRENDS—AN UPDATE Lindsey A. Torre, Rebecca L. Siegel, Elizabeth M. Ward and Ahmedin Jemal

DOI: 10.1158/1055-9965.EPI-15-0578 Published January 2016

ESTIMATING THE IMPACT OF TREATMENT AND IMAGING MODALITIES ON 5-YEAR NET SURVIVAL of 11 CANCERS in 200 COUNTRIES

THE LANCET Oncology
Volume 21, Issue 8, August 2020, Pages 1077-1088

	Stage I		Stage II		Stage III		Stage IV	
	Percentage of cases	5-year net survival	Percentage of cases	5-year net survival	Percentage of cases	5-year net survival	Percentage of cases	5-year net survival
Global	19·6% (15·4–24·1)	76·9% (70·2–82·7)	26·6% (21·5–32·5)	59·4% (53·1–65·4)	28·5% (24·5–33·1)	34·8% (30·2–40·6)	25·4% (21·4–29·4)	7·1% (5·9–8·5)
Low income	11·8% (4·6–23·5)	8·4% (0·6–23·5)	22·6% (13·5–33·3)	4·6% (0·6–13·3)	37·4% (27·9–47·6)	2·8% (0·4–7·6)	28·3% (20·4–36·4)	2·5% (0·3–6·0)
Lower-middle income	10·5% (5·0–17·7)	36·8% (11·9–66·7)	28·0% (21·1–37·4)	29·0% (7·6–54·0)	37·5% (29·8–46·8)	17·8% (6·1–29·6)	24·4% (17·2–30·8)	6·4% (3·7–9·3)
Upper-middle income	15·1% (9·5–21·1)	72·6% (62·3–80·0)	26·4% (18·3–35·2)	59·1% (50·4–67·4)	31·8% (25·2–41·2)	37·0% (31·2–44·1)	26·7% (19·8–33·8)	6·4% (4·9–8·0)
High income	29·3% (22·8–35·4)	87·2% (85·0–89·9)	26·4% (18·6–31·9)	76·6% (70·1–81·9)	20·3% (16·9–24·5)	48·1% (39·8–57·3)	24·0% (20·7–26·6)	8·9% (7·2–11·4)

Data are mean (95% uncertainty interval).

Table 2: **Overall stage distribution and 5-year net survival for all 11 cancers combined, globally and by country income group**

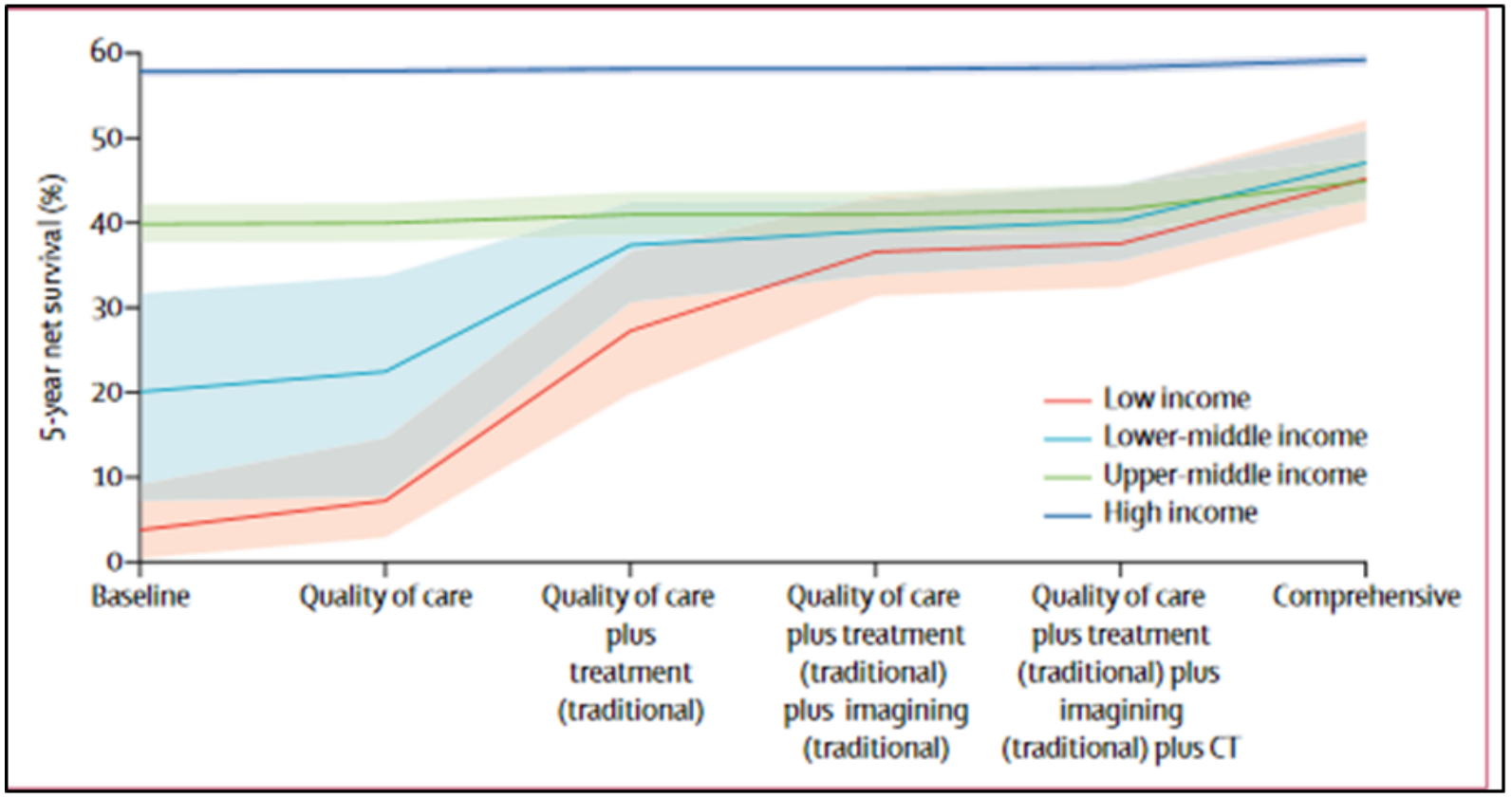
"Even after accounting for stage at diagnosis, we find large differences in survival by income group, with 5-year net survival an average of 12 x higher in high-income than in low-income countries"

Ward et al; Lancet Oncology 2020

CAN HIGH END IMAGING AFFECT CANCER PATIENT OUTCOMES

Estimating the impact of treatment and imaging modalities on 5-year net survival of 11 cancers in 200 countries:
A simulation based Analysis *ZJ Ward, et al;* ***Lancet Oncol* 2020; 21: 1077–88**

5-year cervical CA net survival with cumulative scale-up of treatment and imaging



Ward et al; Lancet Oncol 2020

➢ Misconceptions

Dr. Mike Sathegke:..Its wrong to say "we don't need CT and other techniques; It's the wrong message"
J Nucl Med 2021

Lancet Oncol 2021; 22: e136–72

Medical imaging and nuclear medicine: a *Lancet Oncology* Commission

Hedvig Hricak, May Abdel-Wahab*, Rifat Atun*, Miriam Mikhail Lette, Diana Paez, James A Brink, Lluís Donoso-Bach, Guy Frija, Monika Hierath, Ola Holmberg, Pek-Lan Khong, Jason S Lewis, Geraldine McGinty, Wim J G Oyen, Lawrence N Shulman, Zachary J Ward, Andrew M Scott*

Net return of $179.19 per $1 invested

SCALE UP OF IMAGING
-3.2% (2.46 Mil) CA deaths 2020-2030

→ COST : + US$6·84 billion
LIFETIME PRODUCTIVITY GAIN: $1·23 trillion

SCALE UP OF IMAGING, THERAPY, CARE QUALITY -12.5% (9.55 Mil) CA deaths 2020-2030

→ **LIFETIME PRODUCTIVITY GAIN $2.66 trillion**

Net return of $12·43 per $1 invested

Costs versus health and economic benefits of scaling up diagnostic imaging for cancer— A case for investment

SUMMARY AND CONCLUSIONS

- Itemizing individual procedure or therapy costs provides limited insights into the economic impact of health systems.
- Health Care is a Complex System that cannot be analyzed by simply adding or subtracting itemized expenses for individual procedures. A holistic view is needed
- Scaling up medical imaging and access to nuclear medicine can induces substantial health benefits for patients. Imaging alone results in markedly improved health care outcomes in developing and developed countries.
- Scaling up quality of care, diagnostics and therapeutics in developing and developed countries may be the best investment socially and economically as lifetime productivity will increase substantially.