MRO . ART
INNOVATIVE TREATMENTS AND PATIENTS COMPLIANCE
31° RESIDENTIAL COURSE

Compliance between innovation & clinical experience: *health economics perspective.*

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ESTRO
UZ GENT
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innovation

clinical experience

practice

health economics perspective

services

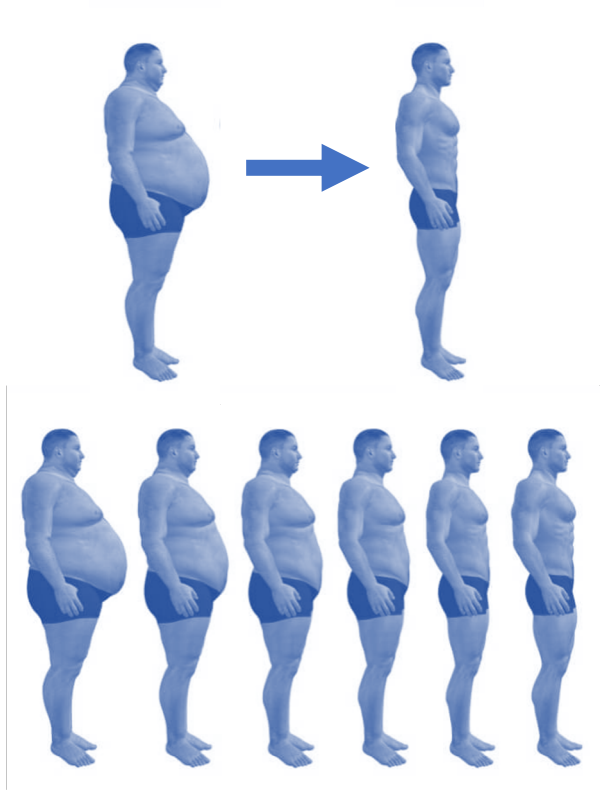
compliance

access, patients' value

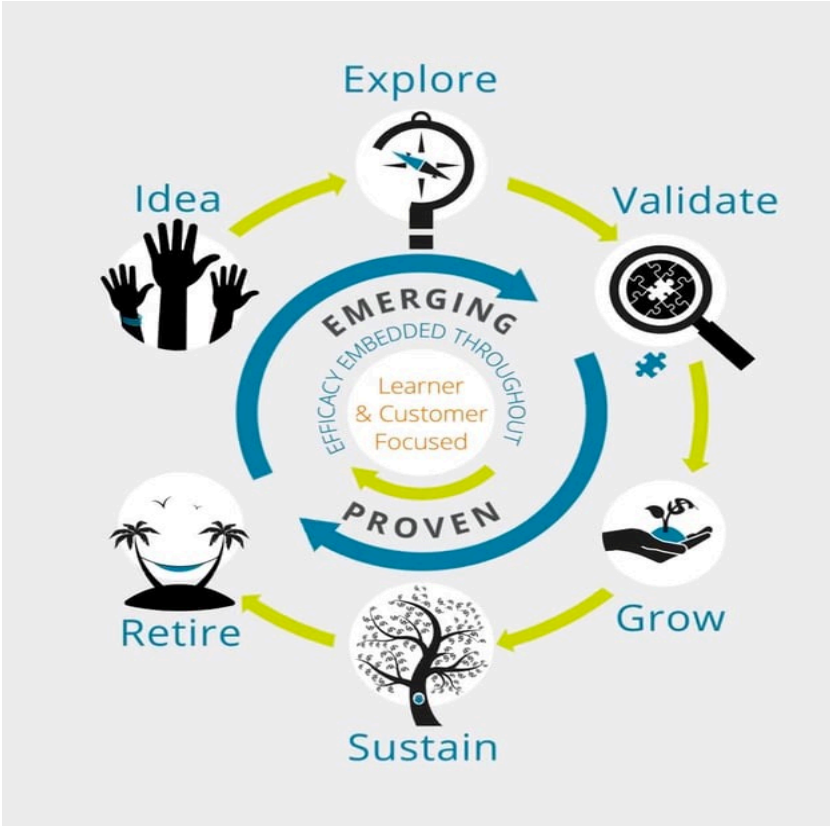
innovation

ESTRO HERO

stepwise *vs.* incremental



emerging *vs.* proven



Lievens et al, Lancet Oncol 2019
Borras et al, Radiother Oncol 2021

innovation

ESTRO HERO

technologies

vs.

techniques

vs.

treatments

Ex.

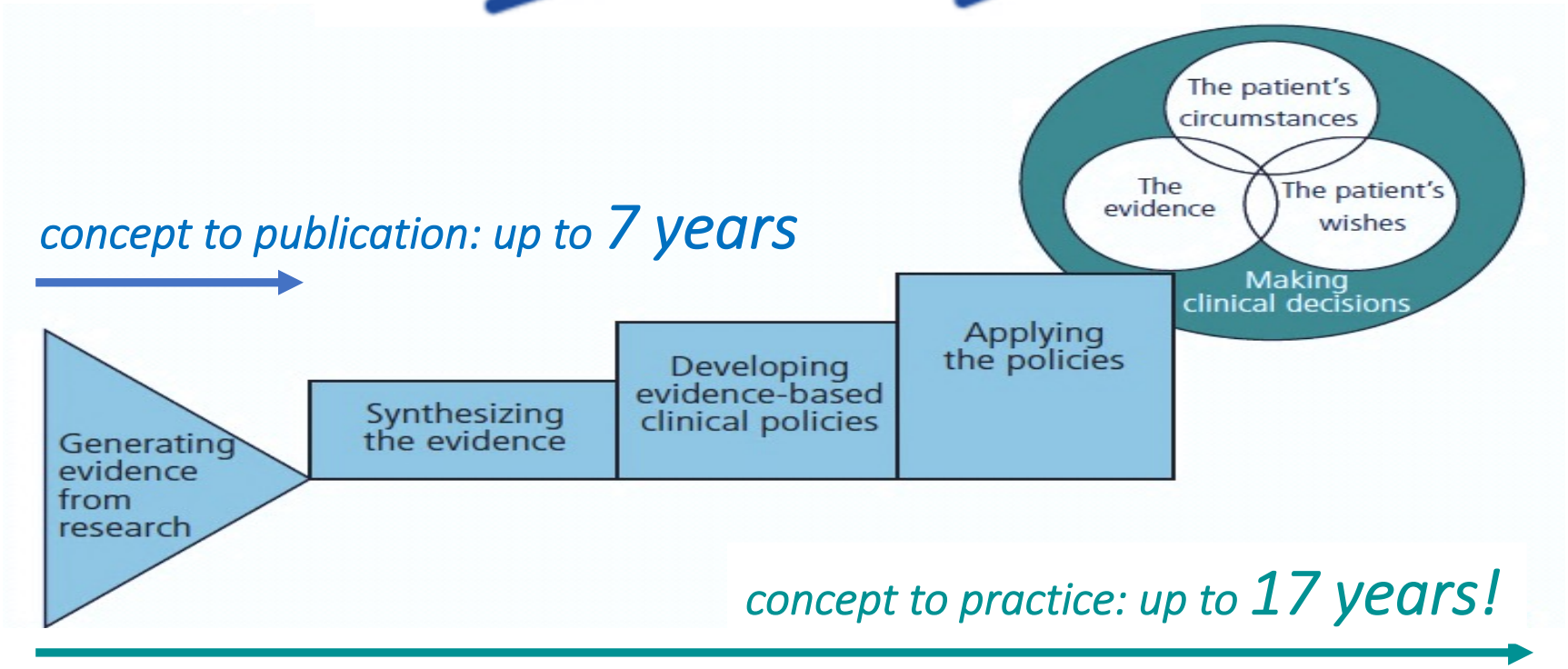
- Particle Therapy
- MR-based Radiotherapy
- FLASH Radiotherapy

- Stereotactic Body Radiotherapy / SBRT
- Adaptive Radiotherapy / ART

- Combinations with New Drugs
- Hypofractionation / Accelerated Radiotherapy
- Radical Treatment of Oligometastases (OMD)

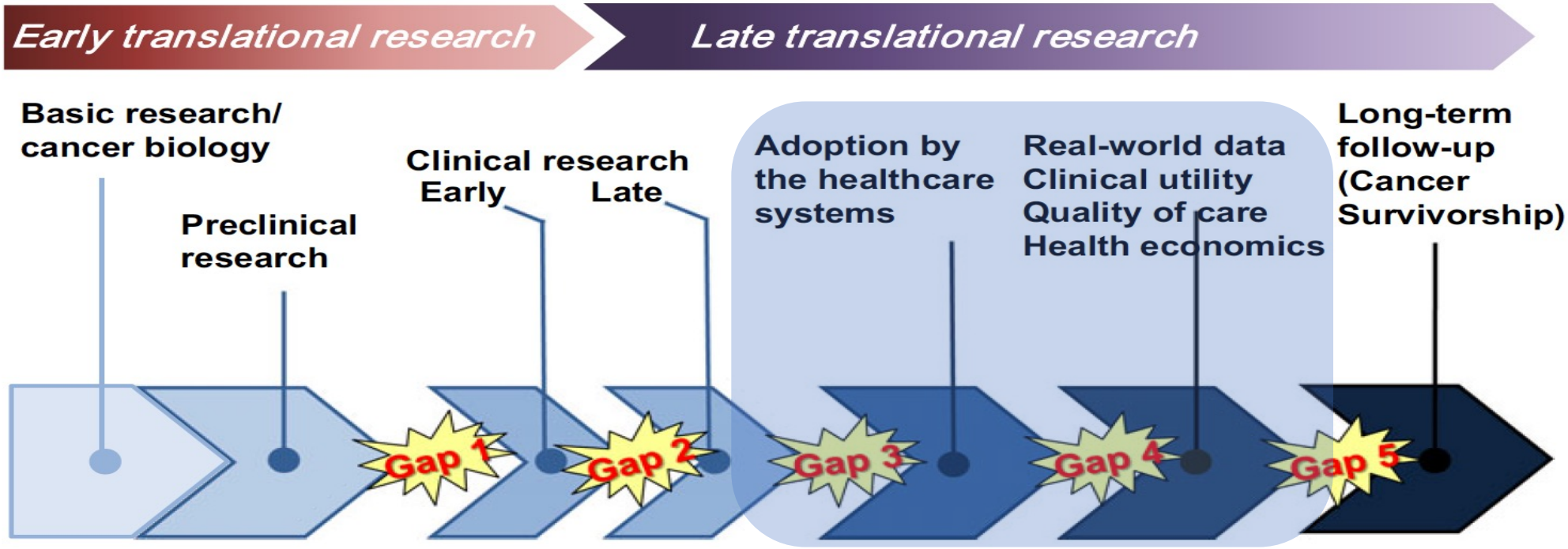
Lievens et al, Lancet Oncol 2019
Borras et al, Radiother Oncol 2021

innovation ⇄ clinical practice



Balas et al, Yearbook of medical informatics 2000
Morris et al, R Soc Med 2011
Haines et al, Bulletin of the World Health Organization, 2004

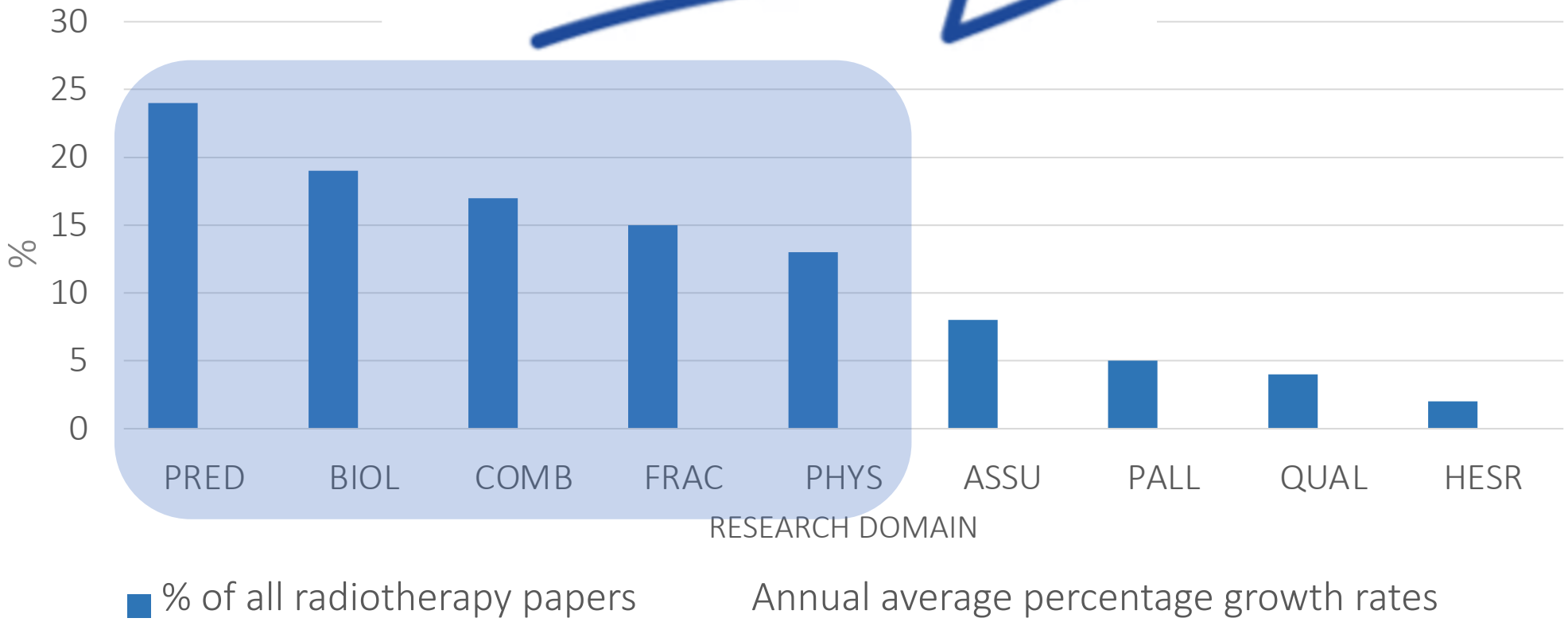
innovation ⇄ clinical practice



Ringborg U. Mol Oncol 2019

innovation

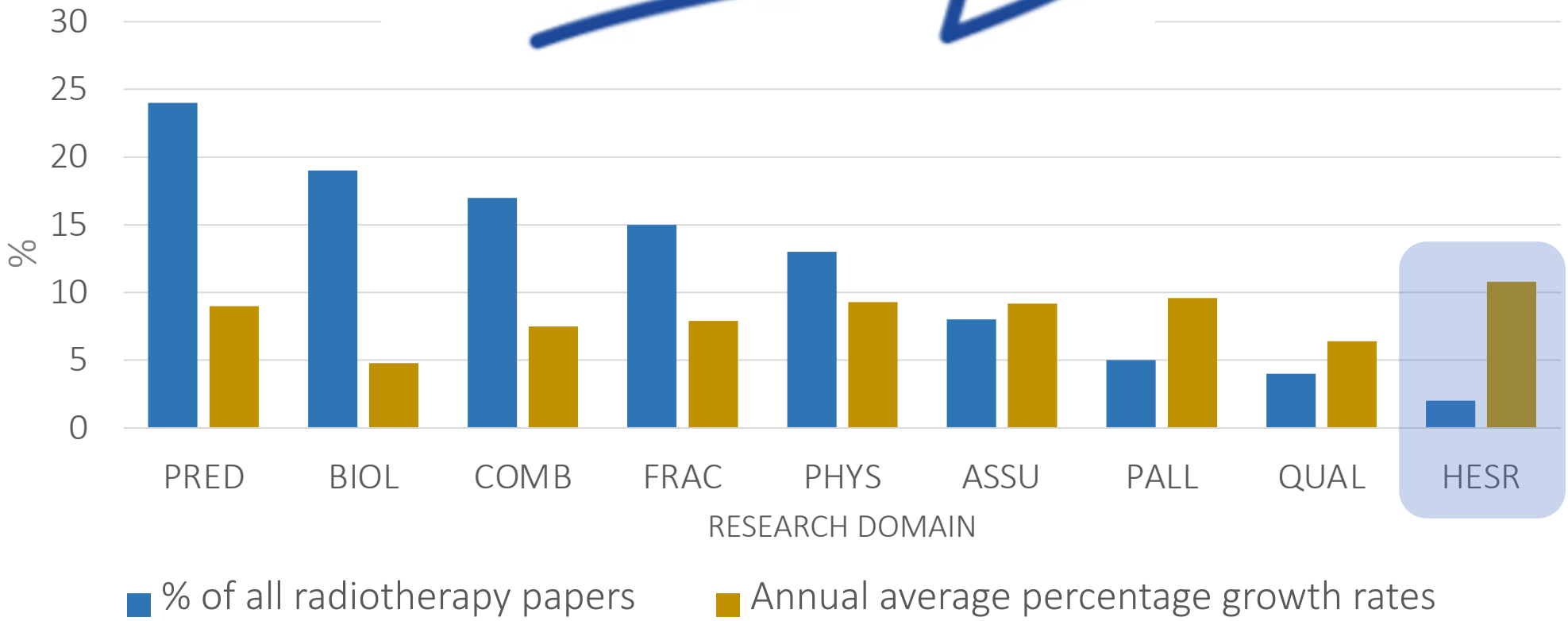
clinical practice



Aggarwal et a, IJROBP 2018

innovation

clinical practice



Aggarwal et a, IJROBP 2018

health services perspective

value-based healthcare

cost-effectiveness

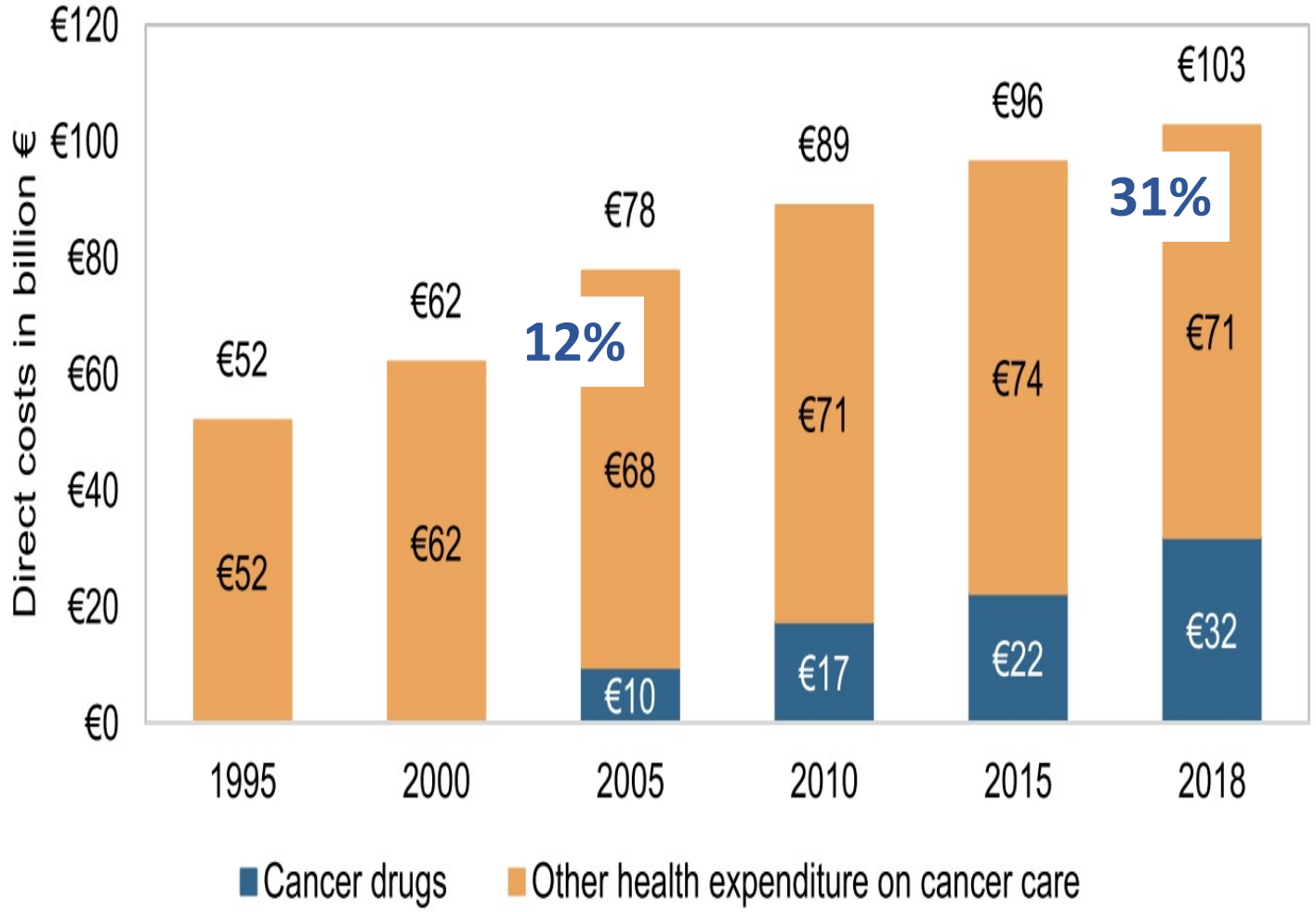
budget

cost

societal perspective
reimbursement

provider perspective
resource cost

the cost of cancer care



direct cancer care costs doubled
(4-7% total HC expenditure)

direct cost of cancer drugs tripled

radiotherapy costs

7,8% (4,3-12,3%)
total cancer care budget

0,42% (0·24%-0·67%)
total health care budget

Hofmarcher, Eur J Cancer 2020
Lievens et al, Lancet Oncol 2020

access to innovation

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY

NCCN National Comprehensive Cancer Network®

cost-effectiveness

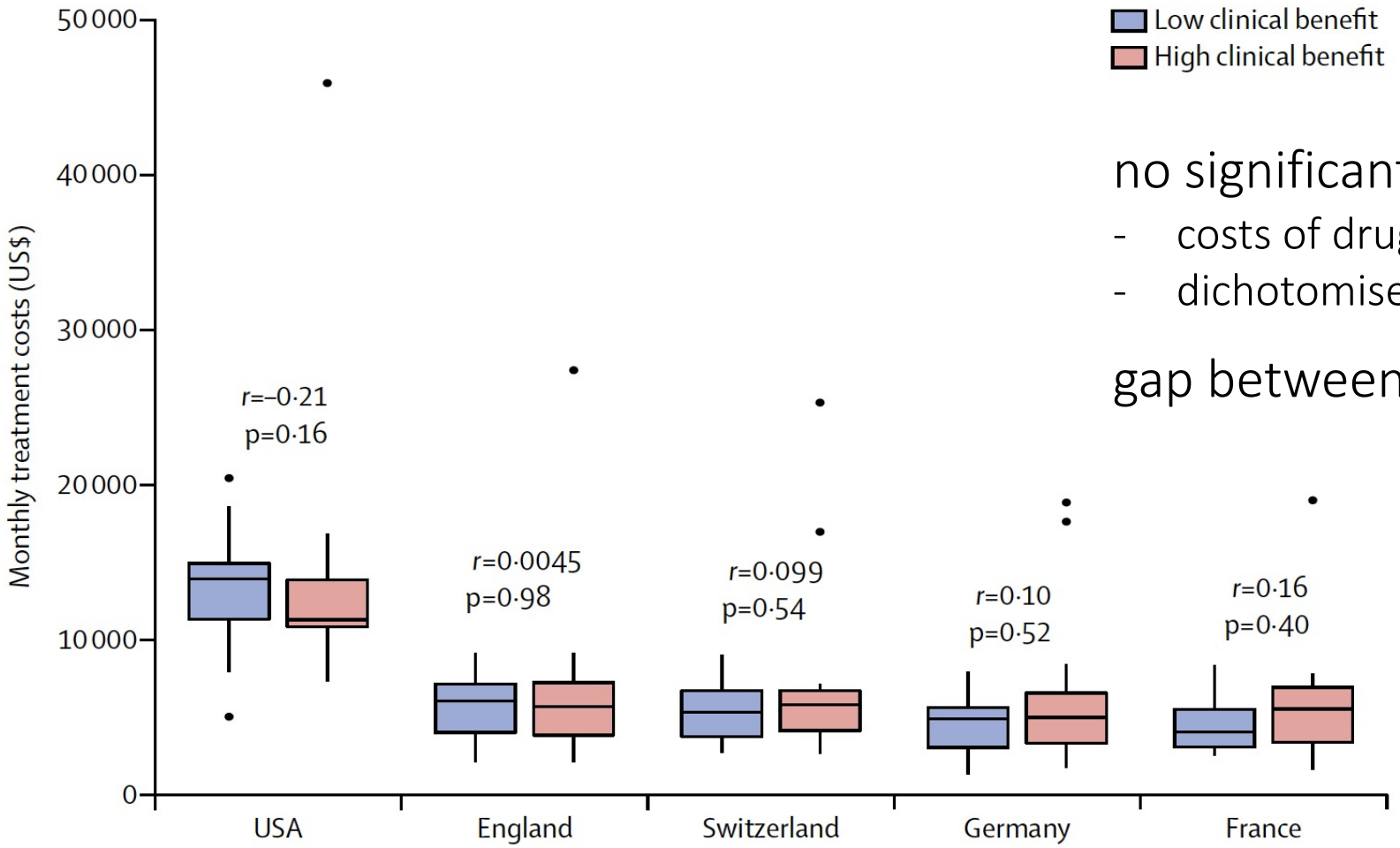
$$ICER = \frac{\text{incremental costs of new treatment}}{\text{incremental outcome of new treatment}}$$

value

$$\frac{\text{health outcomes that matter to } \textit{patients}}{\text{costs of delivering these outcomes}}$$

M. Porter, N Engl J Med 2010

value-based implementation of new cancer drugs?



GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

no significant association between

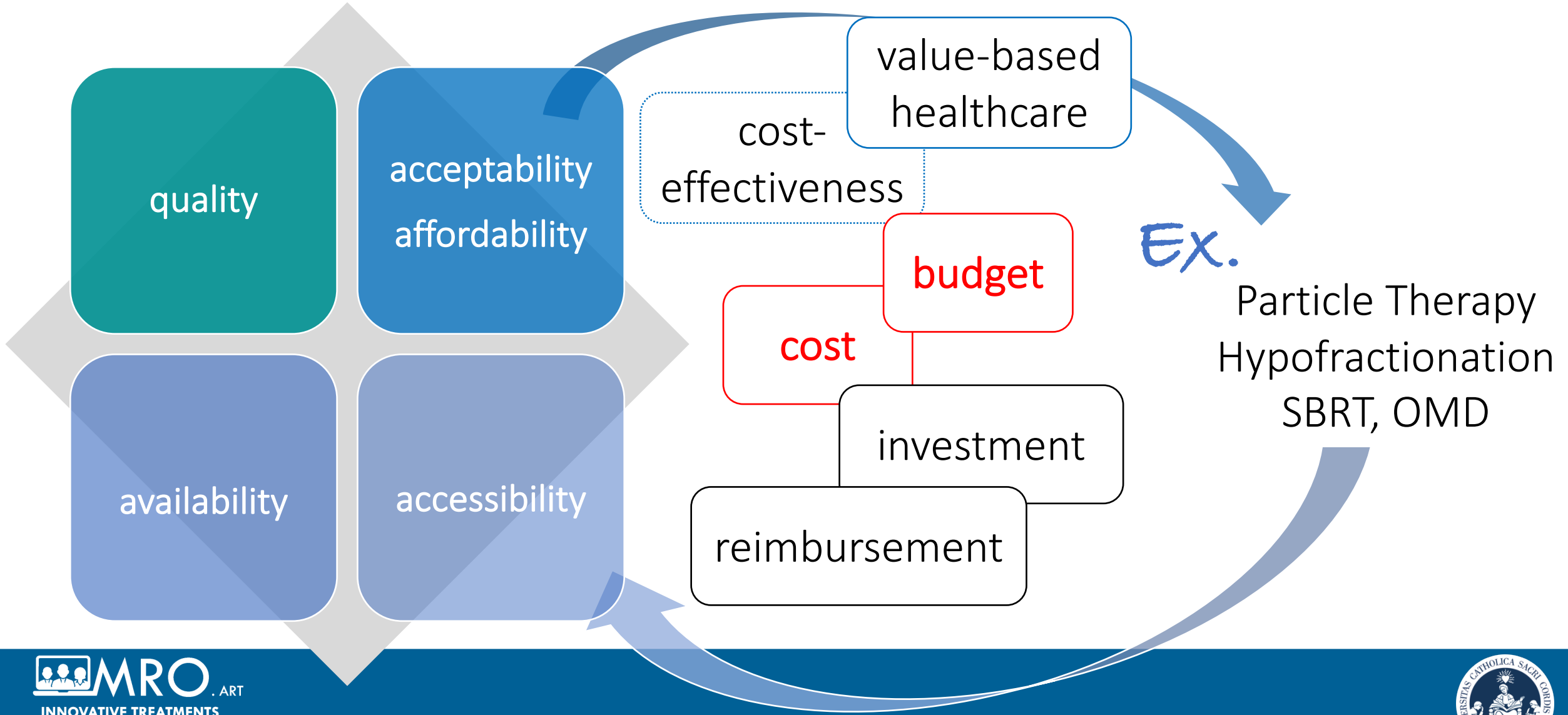
- costs of drugs approved for solid tumours
- dichotomised ESMO-MCBS scores

gap between value of innovation & practice

monthly pharmaceutical cost

Vokinger et al. Lancet Oncol, 2020

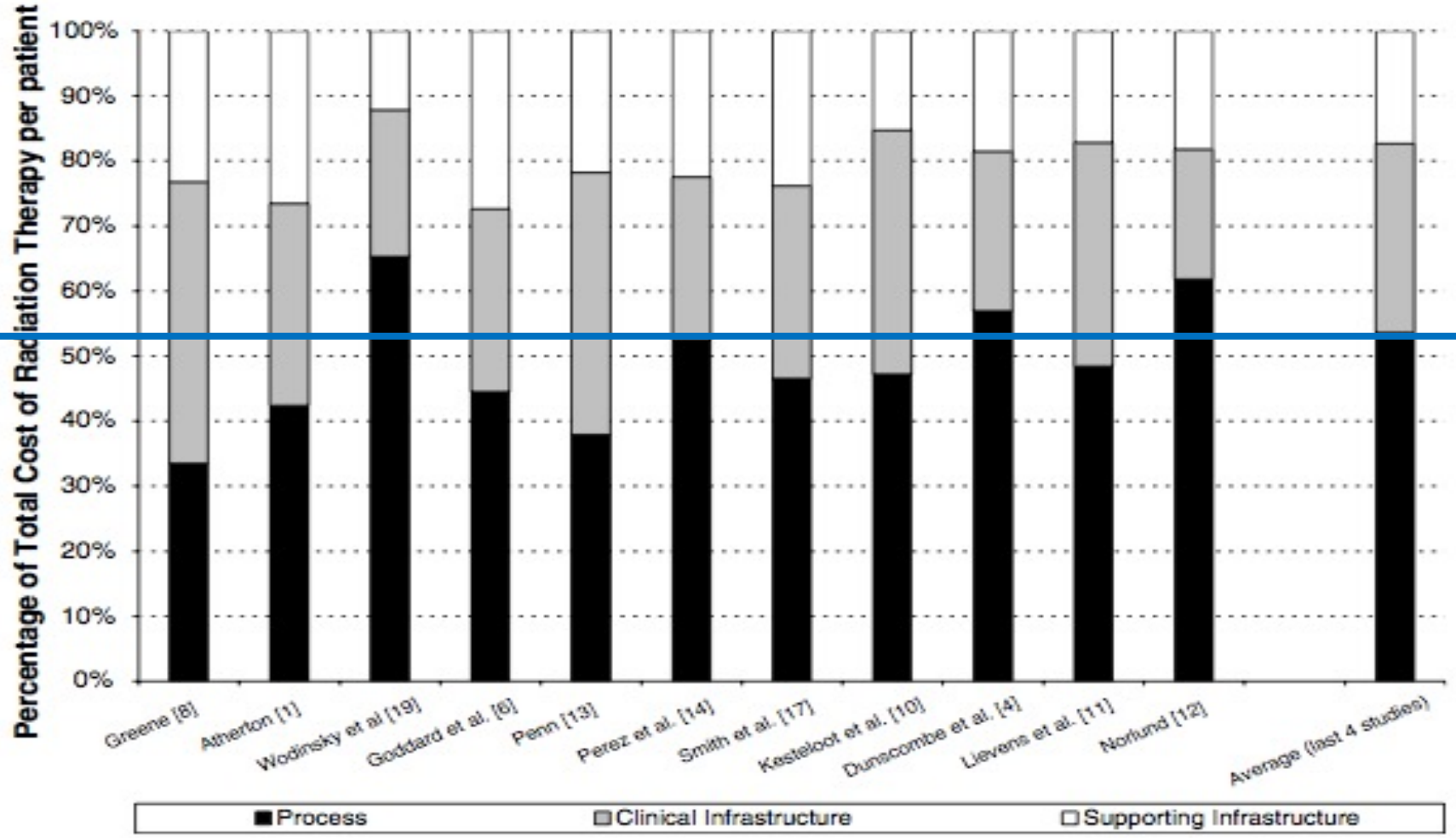
health services in radiotherapy



From investment over cost to implementation

Example of particle therapy

investment is important part of radiotherapy cost

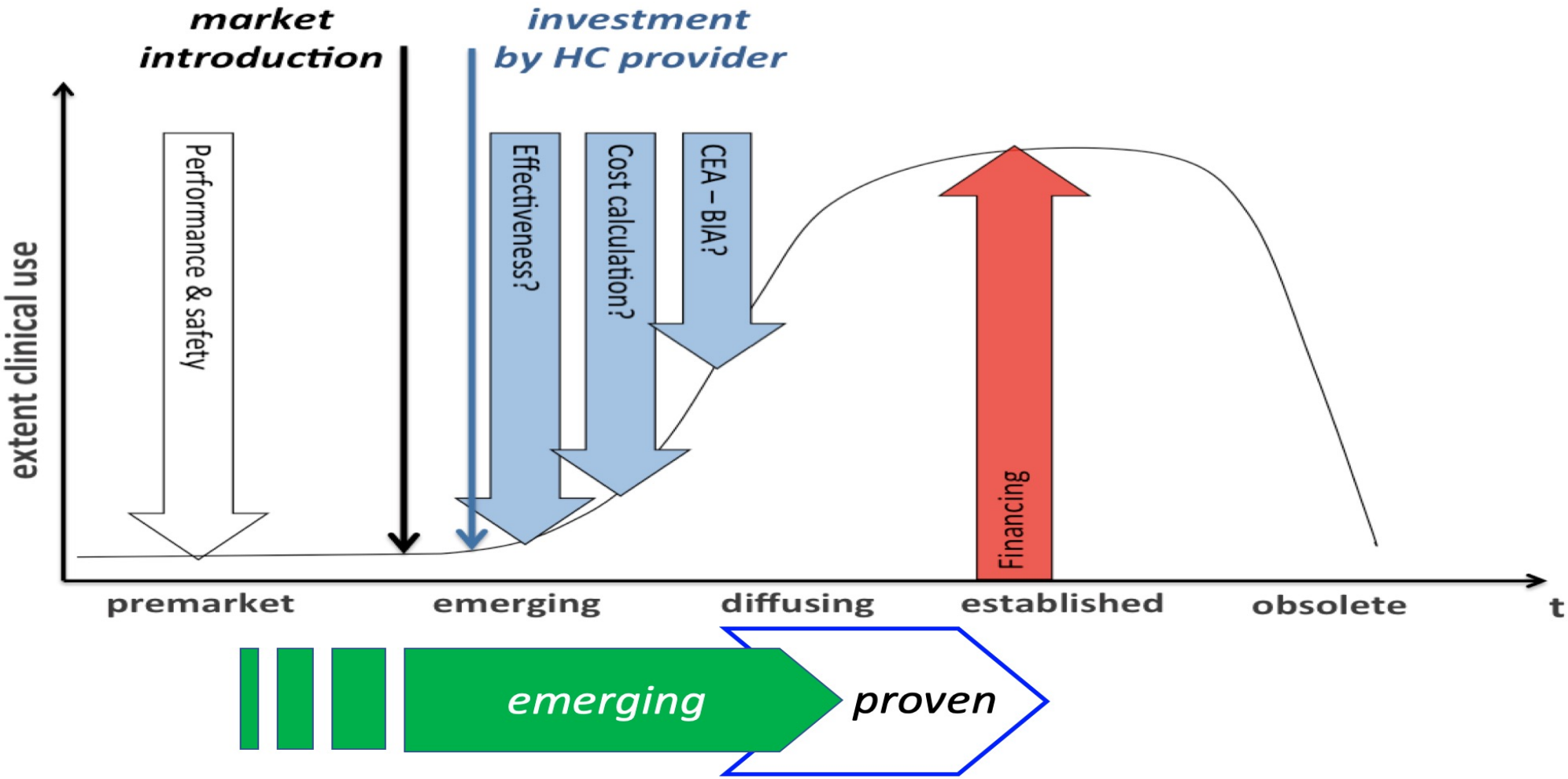


investment cost

operational cost

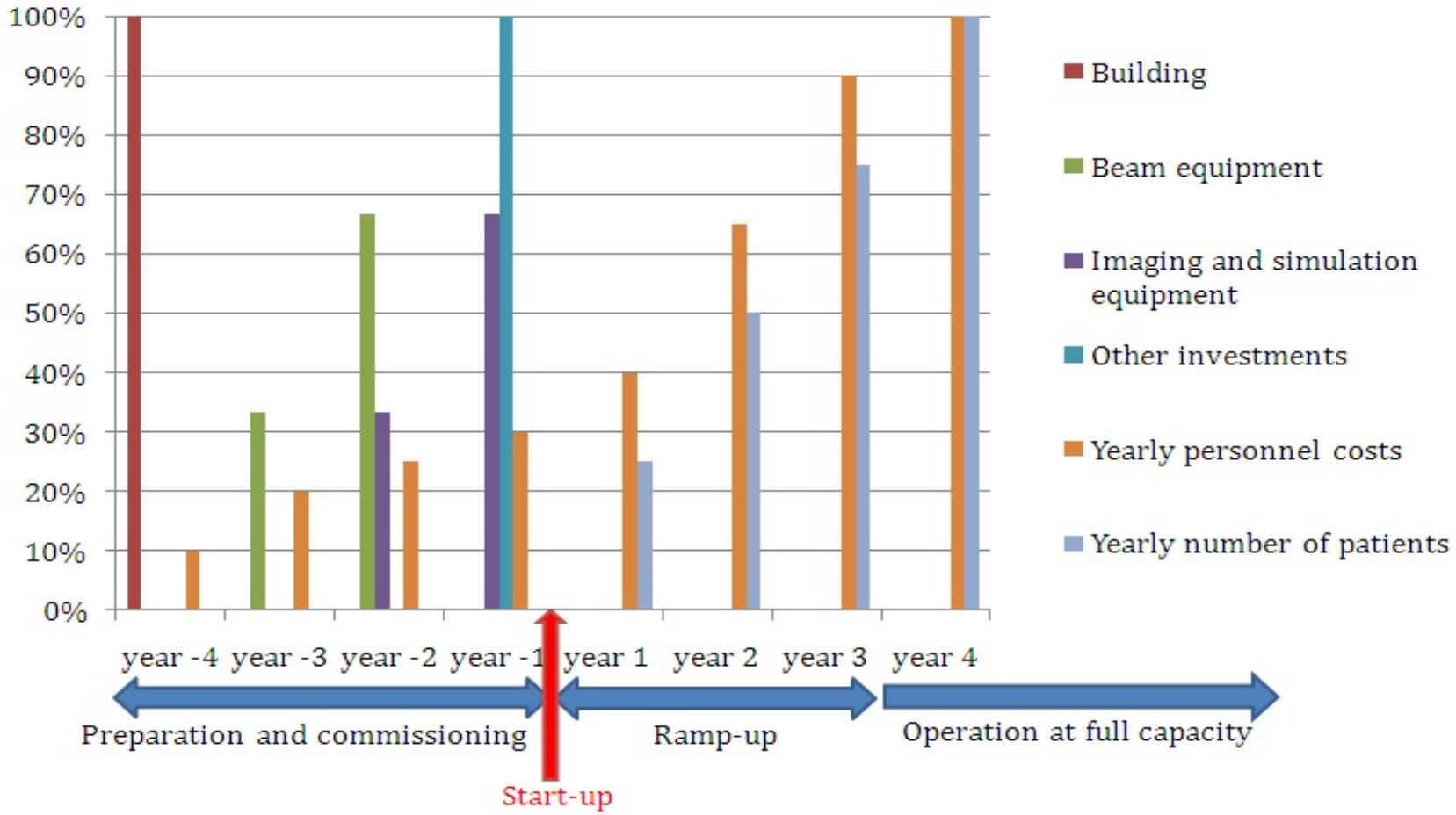
Ploquin and Dunscombe, R&O 2008

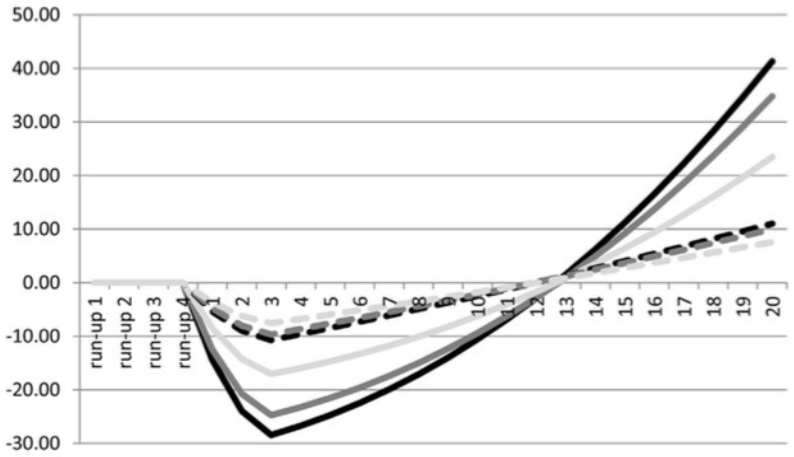
investment precedes financing



Lievens et al, Acta Oncol 2015

investment may threaten access





For-profit,
debt-laden,
poorly located.
"Endangered centres"

Vanderstraeten et al, IJROBP 2014
Johnstone & Kerstiens. IJROBP 2016

impact of investment on treatment cost

Type of technical solution and financing	Required reimbursement rate (€/patient)									
		SA total investment cost					SA total personnel cost	SA delay in commissioning and ramp-up		
	Baseline	−25%	+25%	+50%	+75%	+100%	−30%	1 y	2 y	3 y
CC										
Private financing	51,150	42,800	59,500	67,850	76,200	84,550	47,791	55,650	60,900	67,200
Public sponsoring	27,550	24,750	30,350	33,150	35,950	38,750	24,191	29,950	32,750	36,000
COC										
Private financing	32,400	27,400	37,400	42,400	47,400	52,400	30,040	35,250	38,600	42,500
Public sponsoring	18,400	16,750	20,050	21,700	23,350	25,000	16,040	19,950	21,800	23,950
POC										
Private financing	51,200	44,400	58,000	64,800	71,600	78,400	46,384	55,750	61,100	67,300
Public sponsoring	32,300	30,000	34,600	36,900	39,200	41,500	22,484	35,150	38,450	42,350

Vanderstraeten et al, IJROBP 2014

choice for therapy driven by outcome and cost

Table 1 Method to calculate toxicity for the *IMPT if efficient* strategy: Illustrated for xerostomia 6 months after radiation therapy

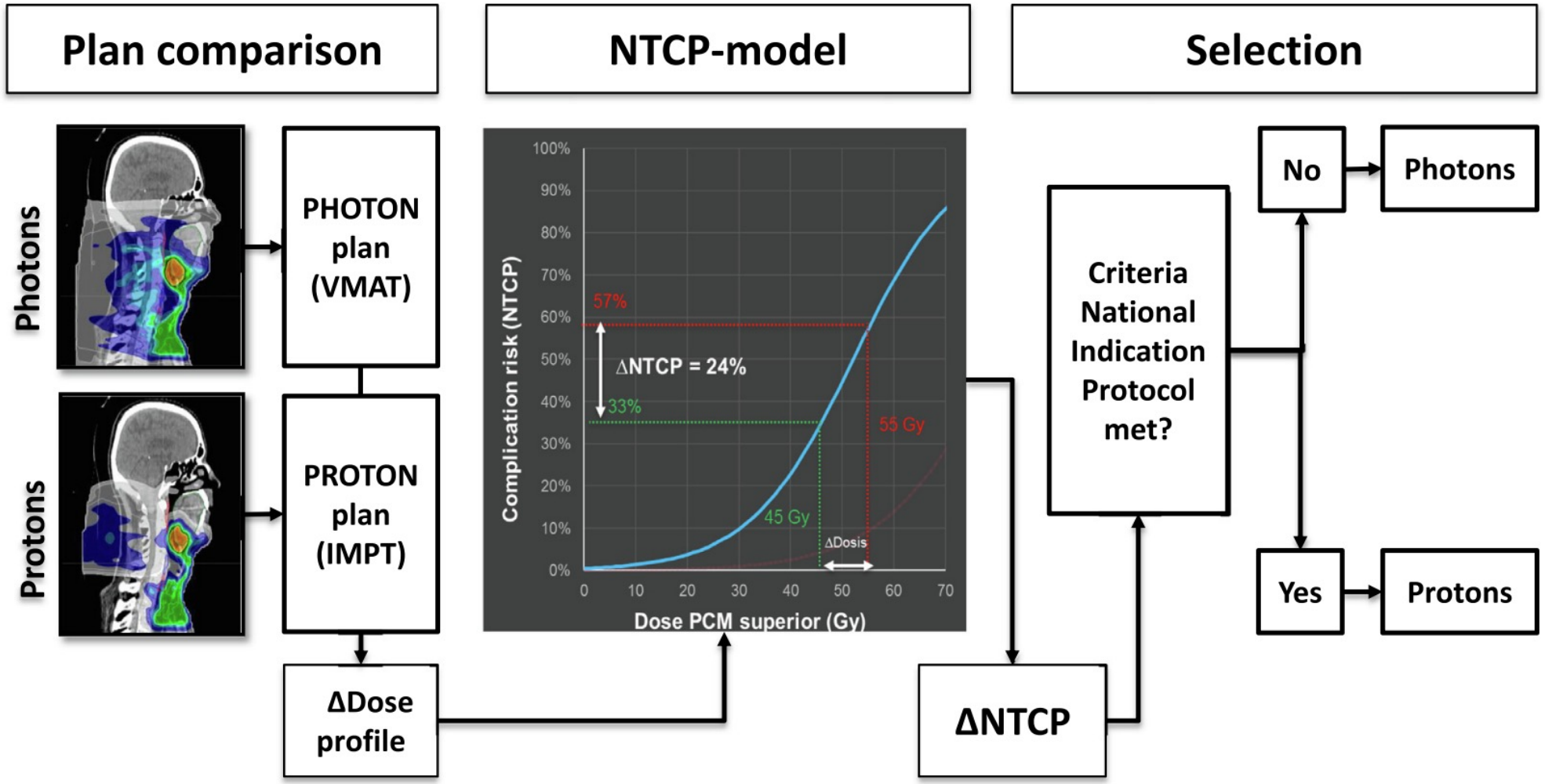
	Probability of xerostomia (%)		ICER	Preferred	Probability of xerostomia (%)
Patient	IMPT	IMRT	IMPT vs IMRT (€)	IMPT/IMRT	*IMPT if efficient**
1	25.5	41.3	93,302	IMRT	41.3
2	18.9	36.6	169,448	IMRT	36.6
3	23.6	55.2	44,358	IMPT	23.6
4	26.7	37.2	150,041	IMRT	37.2
↓	↓	↓	↓	↓	↓
25	25.8	45.1	89,593	IMRT	45.1
Mean probability of xerostomia for the IMPT if efficient strategy					37.1%

Table 2 Base case results of the cost-effectiveness analyses (sorted by QALY)

	Expected outcomes (95% CI*)			Increments (95% CI*)		ICER
Treatment strategy	QALY/DTFLY†	Costs (€)	Comparator	Incremental QALY/DTFLY†	Incremental costs (€)	€ per QALY/ DTFLY†
IMRT for all patients	6.520 (5.781 to 7.018)	41,038 (38,878 to 44,158)				
IMPT if efficient	6.563 (5.818 to 7.059)	43,650 (41,523 to 46,949)	IMRT for all patients	0.043 (0.014 to 0.073)	2612 (2008 to 3306)	60,278
IMPT for all patients	6.620 (5.869 to 7.115)	50,989 (48,227 to 54,852)	IMPT if efficient	0.057 (0.016 to 0.102)	7339 (6001 to 8744)	127,946

Ramaekers et al. IJROPB 2013

model-based selection of proton therapy



Tambas et al, Radiother Oncol 2020

Cost versus reimbursement

Example of hypofractionated breast radiotherapy

utilisation of hypofractionation varies

"Moving Forward Fast with FAST-Forward"

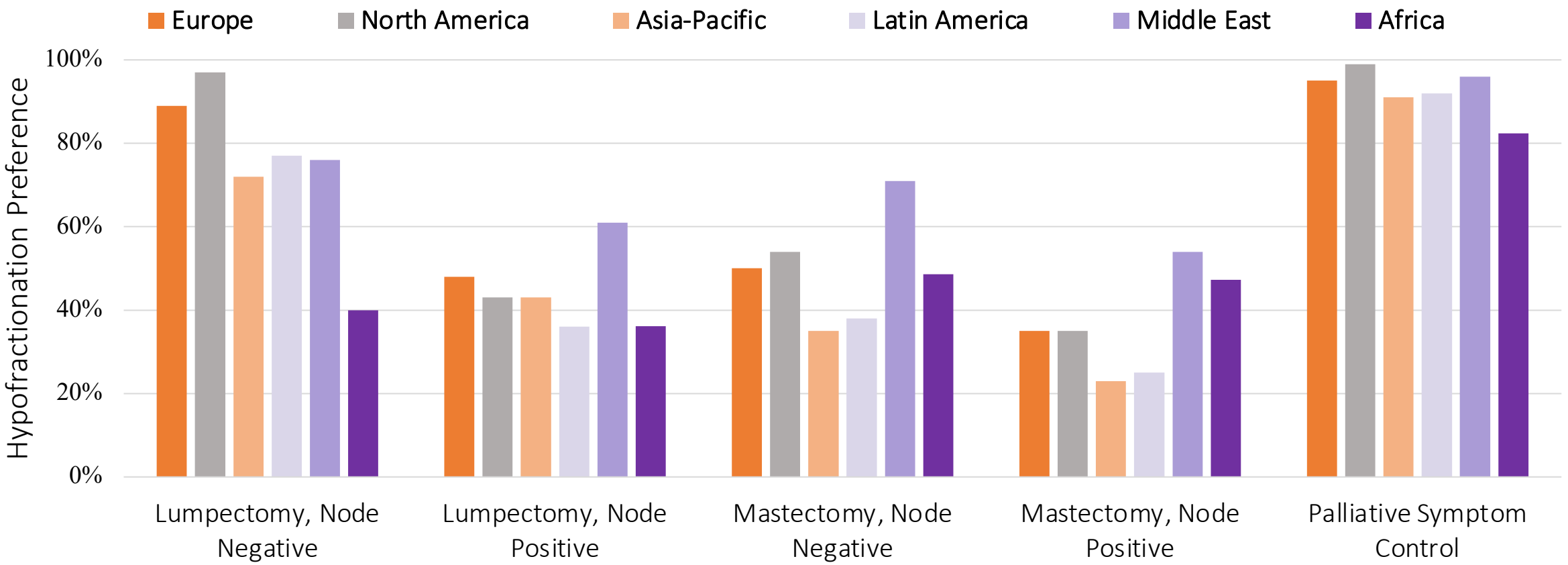
Royal College of Radiologists' breast cancer radiotherapy consensus statements 2021

Offer 26 Gy/5 fractions over 1 week for whole breast radiotherapy	Very strongly supported
Offer 26 Gy/5 fractions over 1 week for chest wall radiotherapy	Very strongly supported
Consider 26 Gy/5 fractions over 1 week for chest wall radiotherapy with reconstruction	Strongly supported
Offer 26 Gy/5 fractions over 1 week for partial breast radiotherapy	Very strongly supported
Consider 28.5 Gy/5 fractions over 5 weeks instead of 26 Gy/5 fraction over 1 week for patients with significant comorbidity and/or frailty that make daily radiotherapy difficult	Very strongly supported
Consider 26 Gy/5 fractions for nodal radiotherapy (excluding internal mammary chain) only for patients with significant comorbidities while awaiting the 2-year normal tissue results of the FAST-Forward nodal substudy	Strongly supported
For patients requiring a boost, offer: 26 Gy/5 fractions whole breast radiotherapy plus either a sequential normofractionated boost or a hypofractionated boost (delivered in no more than 5 fractions) or 15 fractions simultaneous integrated boost, e.g. 48 Gy to boost volume and 40 Gy to rest of breast all over 3 weeks	Strongly supported

15 fractions over 3 weeeks is the current standard of care for breast node RT

Lewis et al, Clin Oncol 2021
RCR Consensus Statements

utilisation of hypofractionation varies



Rodin et al, Radiother Oncol 2021

what impacts hypofractionation use?

	Europe		Asia Pacific		Africa		Latin America		North America		Middle East	
Justifications	**N=1654**	**No (%)**	**N=464**	**No (%)**	**N=63**	**No (%)**	**N=332**	**No (%)**	**N=231**	**No (%)**	**N=125**	**No (%)**
Clinical Evidence	Equivalent local control	1441 (87·1%)	Equivalent local control	384 (82·8%)	Equivalent local control	38 (60·3%)	Equivalent local control	279 (84·0%)	Equivalent local control	218 (94·4%)	Equivalent local control	106 (84·8%)
	Equivalent toxicity	1170 (70·7%)	Equivalent toxicity	309 (66·6%)	Equivalent toxicity	30 (47·6%)	Equivalent toxicity	235 (70·8%)	Equivalent toxicity	184 (79·7%)	Equivalent toxicity	80 (64·0%)
	Evidence	1528 (92·4%)	Evidence	382 (82·3%)	Evidence	52 (82·5%)	Evidence	295 (88·9%)	Evidence	160 (69·3%)	Evidence	115 (92·0%)
Economic and Resource Impact	Resource optimization: machine	1126 (68·1%)	Resource optimization: machine	264 (56·9%)	Resource optimization: machine	42 (66·7%)	Resource optimization: machine	234 (70·5%)	Resource optimization: machine	179 (77·5%)	Resource optimization: machine	102 (81·6%)
	Resource optimization: expense	869 (52·5%)	Resource optimization: expense	226 (48·7%)	Resource optimization: expense	40 (63·5%)	Resource optimization: expense	179 (53·9%)	Resource optimization: expense	178 (77·1%)	Resource optimization: expense	82 (65·6%)
	Reimbursement	76 (4·6%)	Reimbursement	38 (8·2%)	Reimbursement	2 (3·2%)	Reimbursement	11 (3·3%)	Reimbursement	0 (0·0%)	Reimbursement	13 (10·4%)
Professional Culture	Prior clinical experience	688 (41·6%)	Prior clinical experience	200 (43·1%)	Prior clinical experience	30 (47·6%)	Prior clinical experience	114 (34·3%)	Prior clinical experience	153 (66·2%)	Prior clinical experience	53 (42·4%)
	Personal preference	870 (52·5%)	Personal preference	196 (42·2%)	Personal preference	16 (25·4%)	Personal preference	144 (43·4%)	Personal preference	172 (74·5%)	Personal preference	63 (50·4%)
	Peer-accepted	749 (45·3%)	Peer-accepted	208 (44·8%)	Peer-accepted	29 (46·0%)	Peer-accepted	107 (32·2%)	Peer-accepted	190 (82·3%)	Peer-accepted	63 (50·4%)
Patient Considerations	Patient preference	581 (35·1%)	Patient preference	153 (33·0%)	Patient preference	13 (20·6%)	Patient preference	96 (28·9%)	Patient preference	159 (68·8%)	Patient preference	43 (34·4%)
	Patient convenience	1176 (71·1%)	Patient convenience	311 (67·0%)	Patient convenience	36 (57·1%)	Patient convenience	211 (63·6%)	Patient convenience	213 (92·2%)	Patient convenience	86 (68·8%)
Barriers	**N=1265**	**No (%)**	**N=551**	**No (%)**	**N=72**	**No (%)**	**N=413**	**No (%)**	**N=95**	**No (%)**	**N=119**	**No (%)**
Clinical Evidence	Lack of long-term data	516 (40·8%)	Lack of long-term data	243 (44·1%)	Lack of long-term data	13 (18·1%)	Lack of long-term data	150 (36·3%)	Lack of long-term data	37 (38·9%)	Lack of long-term data	72 (60·5%)
	Inferior local control	214 (16·9%)	Inferior local control	123 (22·3%)	Inferior local control	16 (22·2%)	Inferior local control	58 (14·0%)	Inferior local control	19 (20·0%)	Inferior local control	38 (31·9%)
	Acute toxicity	410 (32·4%)	Acute toxicity	204 (37·0%)	Acute toxicity	21 (29·2%)	Acute toxicity	98 (23·7%)	Acute toxicity	22 (23·2%)	Acute toxicity	59 (49·6%)
	Late toxicity	588 (46·5%)	Late toxicity	230 (41·7%)	Late toxicity	22 (30·6%)	Late toxicity	120 (29·1%)	Late toxicity	35 (36·8%)	Late toxicity	67 (56·3%)
Economic and Resource Impact	Technology	144 (11·4%)	Technology	87 (15·8%)	Technology	14 (19·4%)	Technology	100 (24·2%)	Technology	3 (3·2%)	Technology	27 (22·7%)
	Reimbursement	103 (8·1%)	Reimbursement	83 (15·1%)	Reimbursement	0 (0·0%)	Reimbursement	59 (14·3%)	Reimbursement	4 (4·2%)	Reimbursement	2 (1·7%)
Professional Culture	Personal preference	218 (17·2%)	Personal preference	104 (18·9%)	Personal preference	19 (26·4%)	Personal preference	56 (13·6%)	Personal preference	9 (9·5%)	Personal preference	18 (15·1%)
	Peer preference	173 (13·7%)	Peer preference	100 (18·1%)	Peer preference	14 (19·4%)	Peer preference	45 (10·9%)	Peer preference	14 (14·7%)	Peer preference	18 (15·1%)
Patient Considerations	Patient preference	91 (7·2%)	Patient preference	72 (13·1%)	Patient preference	5 (6·9%)	Patient preference	21 (5·1%)	Patient preference	5 (5·3%)	Patient preference	14 (11·8%)

Legend

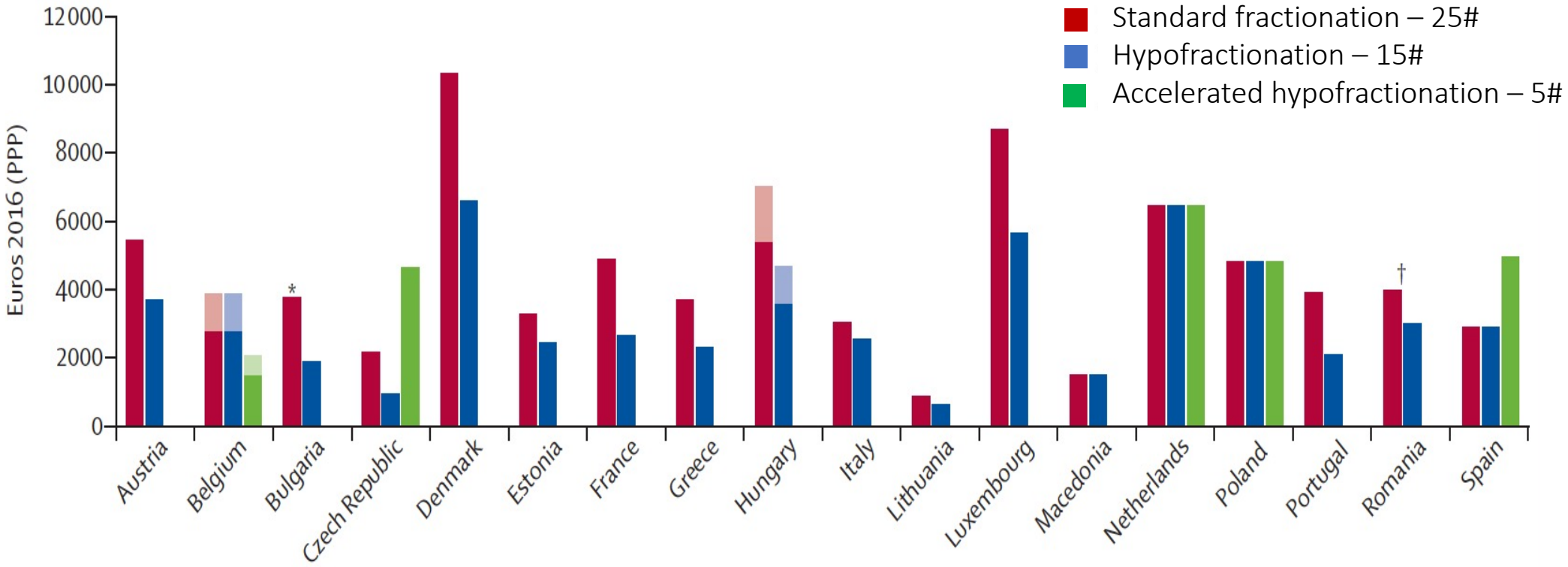
Colour Scale (%)
90-100
80-90
70-80
60-70
50-60
40-50
30-40
20-30
10-20
0-10

Rodin et al, Radiother Oncol 2021

practice is impacted by reimbursement

"In order to attain the general objectives of health care - quality, efficiency and accessibility - different tools can be used, amongst which financial incentives."

breast cancer reimbursement



Jegers et al, Health Policy 2002
Lievens et al, Lancet Oncol 2020

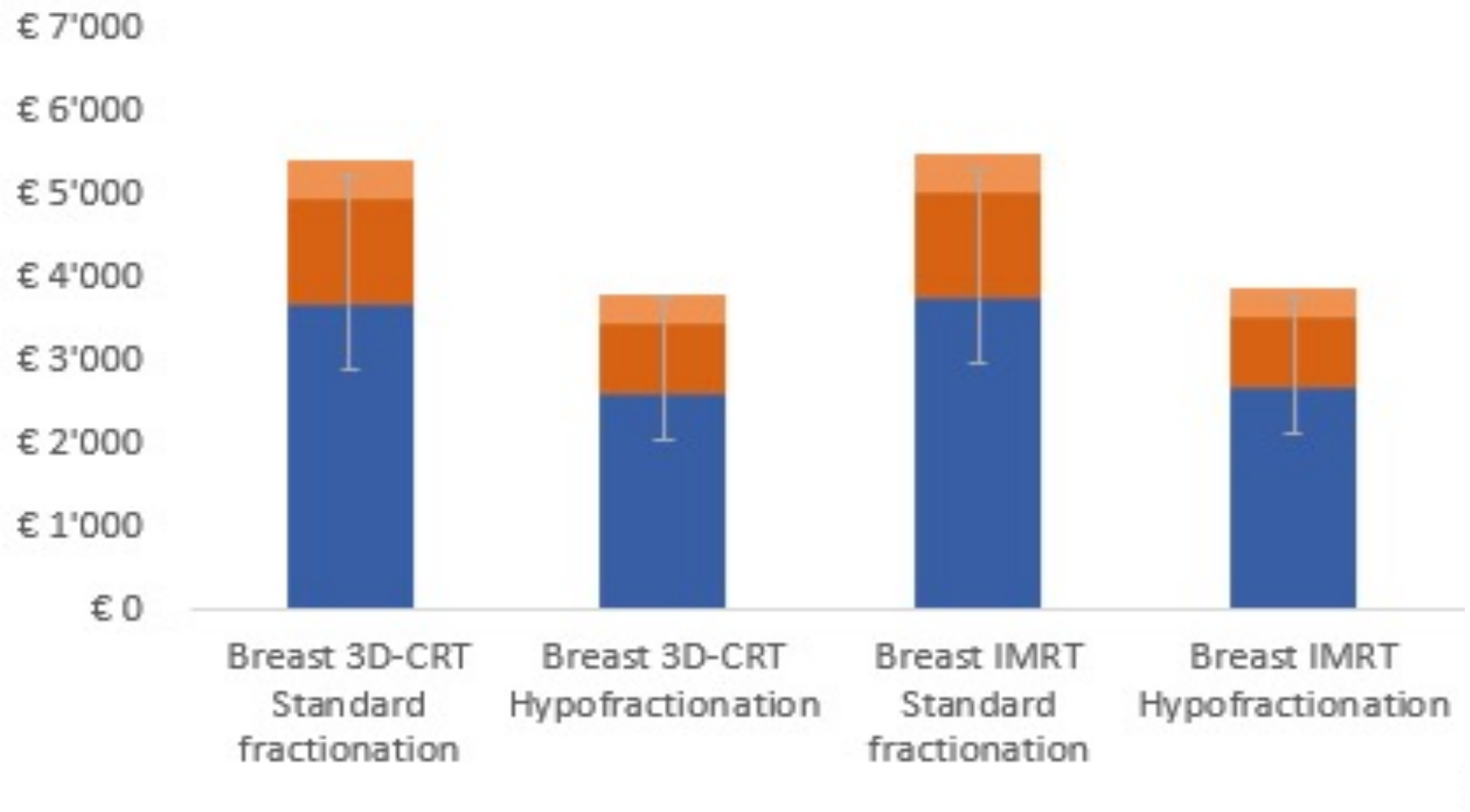
financing is impacted by hypofractionation

Basis of reimbursement and the potential influence of moderately hypofractionated radiation schedules on revenue

Country	Perspective	Base of reimbursement	Is there an influence of the total number of fractions on reimbursement?	Economic deficit generated by the reduction in income per-patient from applying a hypofractionation-based schedule
Denmark	Public practice	Separate fees per activity	Yes	30–40%
	Private Practice	NA	NA	NA
France	Public practice	Separate fees per activity	Yes	30–40%
	Private Practice	Separate fees per activity	Yes	30–40%
Israel	Public practice	Separate fees per activity	Yes	30–40%
	Private practice	Separate fees per activity	Yes	NA
Italy (Tuscany Region)	Public practice	Separate fees per activity	Yes	30–40%
	Private Practice	Separate fees per activity	Yes	30–40%
Italy (Lombardy)	Public practice	Separate fees per activity	Yes	30–40%
	Private Practice	Separate fees per activity	Yes	30–40%
The Netherlands	Public practice	Lump sum for the entire treatment (fixed fee)	No	No
	Private Practice	NA	NA	NA
Spain	Public practice	Lump sum for the entire treatment (fixed fee)	No	NA
	Private practice	Lump sum for the entire treatment (fixed fee)	No	NA
UK	Public practice	Separate fees per activity	Yes	30–40%
	Private Practice	Separate fees per activity	Yes	30–40%
USA	Public practice	Separate fees per activity	Yes	20–30%
	Private Practice	Separate fees per activity	Yes	20–30%

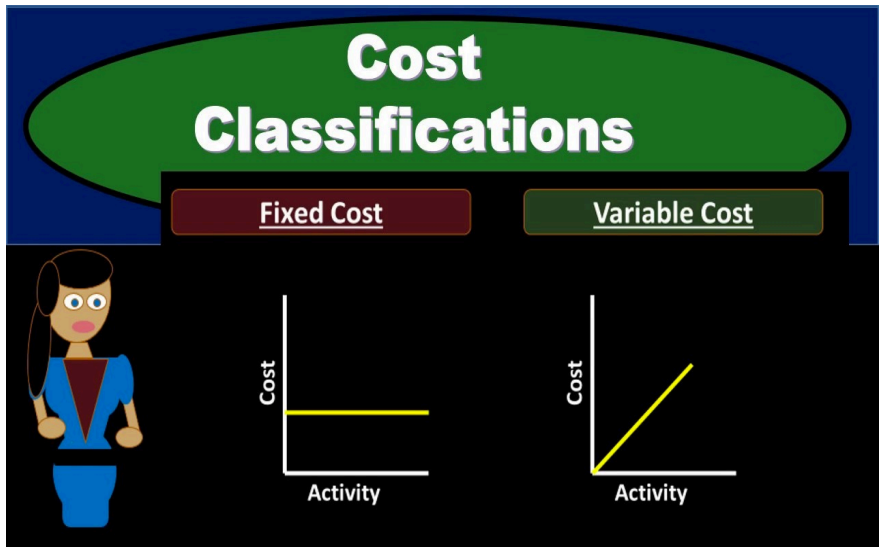
Marta et al, Clin Oncol 2021

provider cost is impacted by hypofractionation

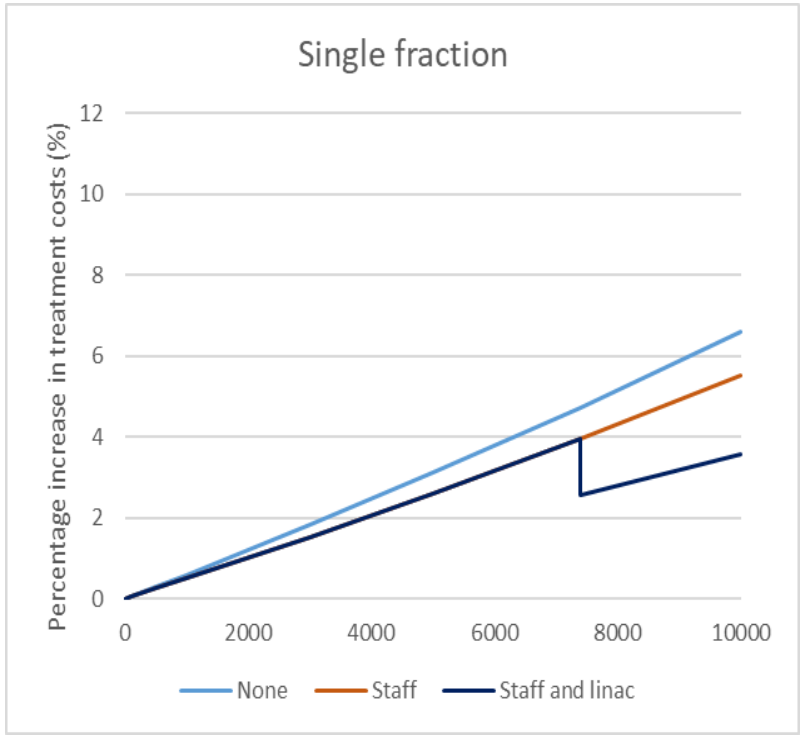


Defourny et al, Radiother Oncol 2019

impact of hypofractionation on provider cost is complex



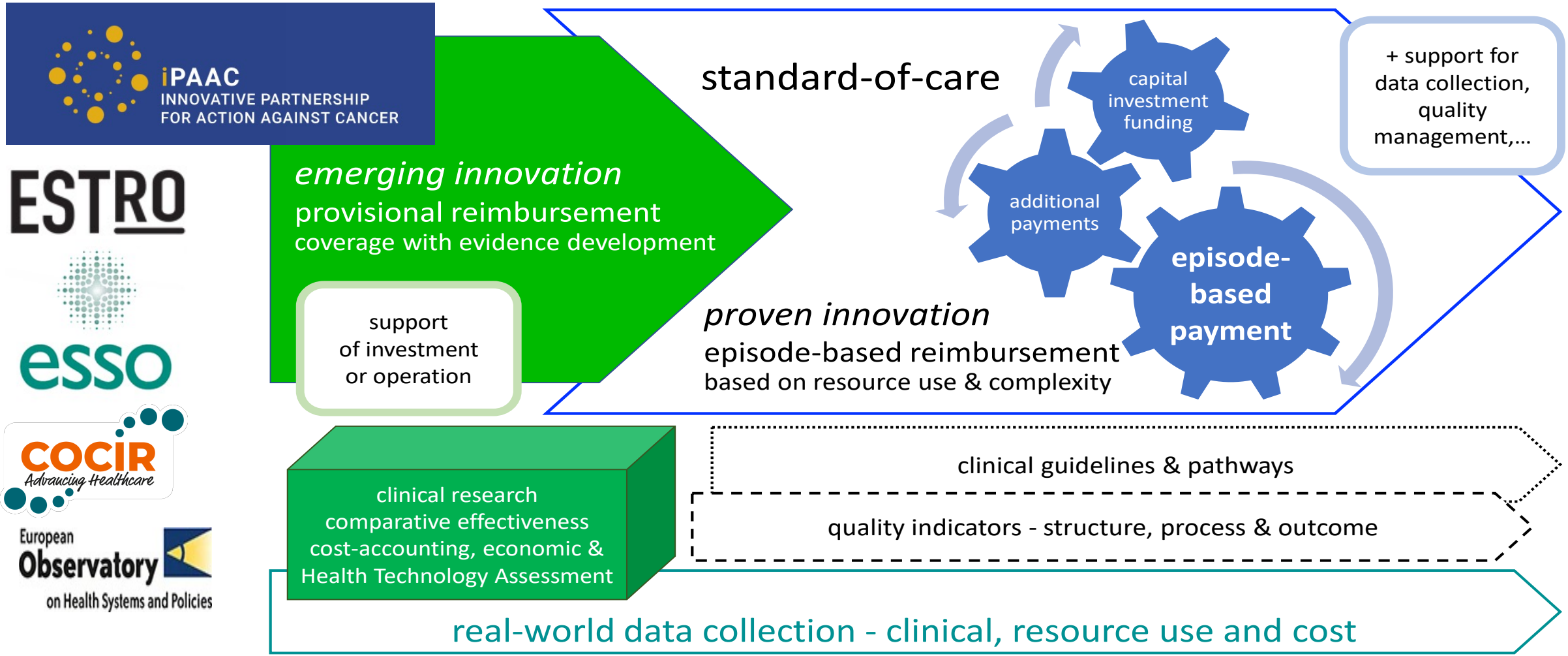
large majority of radiotherapy
resource costs are fixed/stepped



- higher treatment numbers or disinvestment
- imbalances between demand and capacity will initially result in **higher treatment costs**

Spencer et al, accepted Radiother Oncol 2021

financing should be tailored to support access



Borras et al, Radiother Oncol 2021

Coverage with evidence development

Example of SBRT in oligometastatic disease

The Convention for Innovative Radiotherapy, Belgium

Belgian Cancer Registry

INAMI-RIZIV

KCE

BeSTRO

College van Geneesheren Radiotherapie-Oncologie

Collège des Médecins Radiothérapie-Oncologie

- no SBRT reimbursement in Belgium, **Coverage with Evidence Development program**
- **agreement** participating radiotherapy centres & compulsory health insurance
- pre-defined target populations, but **no minimum criteria** for patient selection
- registration of clinical/technical data through **Belgian Cancer Registry**

indications and data collection

maximum 3 metastases: lung, hepatic, paravertebral and “non-standard”

data collection 10/2013 until 12/2019

- patient characteristics (age, gender, WHO)
- tumor characteristics (stage of primary, location OMD, number and size of lesions,…)
- treatment characteristics (RT type, motion management, image guidance,...)
- outcome: survival

link with administrative data sets feasible

6,296 SBRT registrations; **5,675 SBRT courses** withheld for analysis

- 2,885 (51%) primary tumors: mainly lung
- 2,790 (49%) metastases: lung: 53%; (para)spinal: 19%; liver: 12%; ‘non-standard’: 16%

patient selection and survival

2790 SBRT cases for OMD

WHO status:
43% WHO 0; 39% WHO 1

most frequent primary tumours:
Colorectal (23%) - Prostate (22%) – Lung (17%)
Breast (9%) – Kidney (6%)

average N lesions per patient: 1,2

lesion size:
17mm (lung), +/- 30mm others

SBRT in Belgian **reimbursement system** as of 1/1/2020

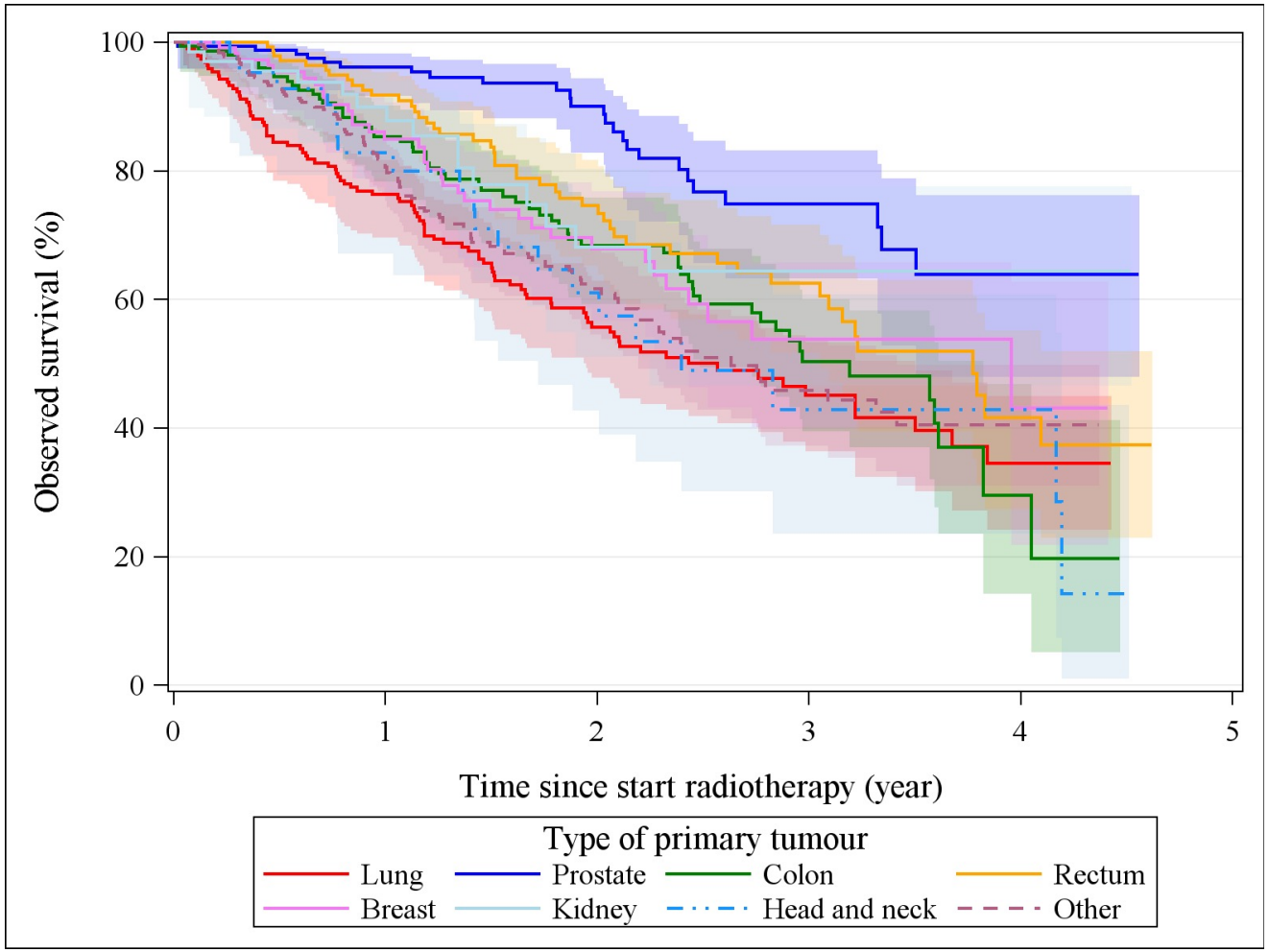


figure on first 1468 patients

patterns-of-care in the United Kingdom

Commissioning through Evaluation

selection criteria

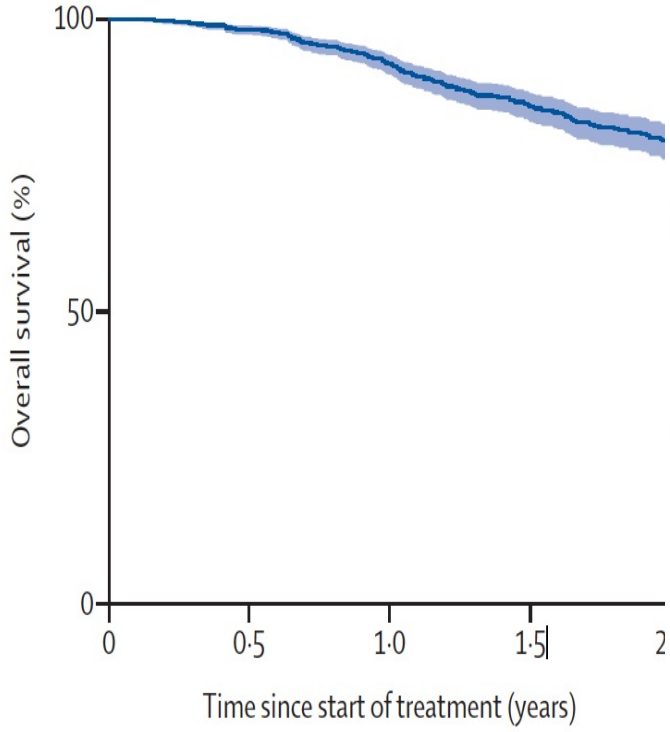
- 1 to 3 extracranial metastatic lesions
- disease-free interval of 6 months

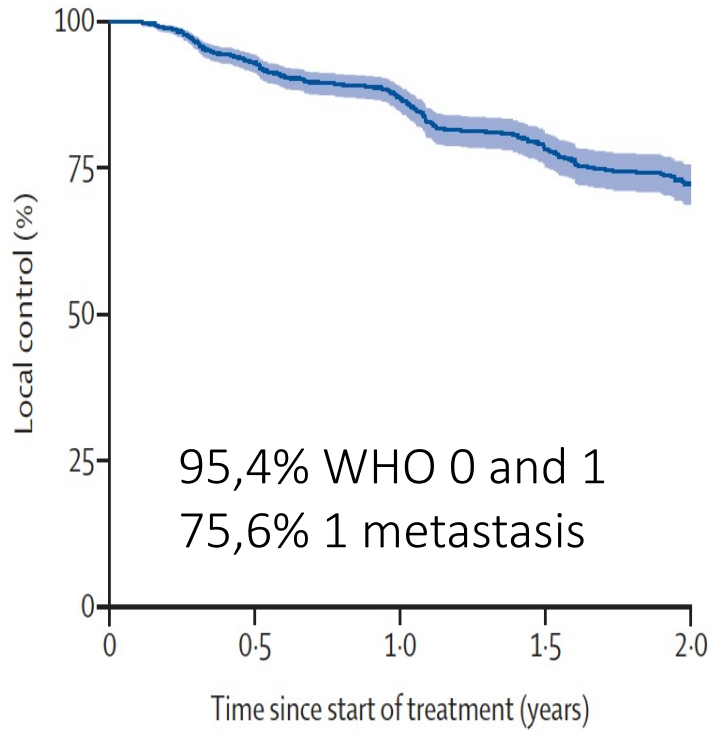
(except synchronous colorectal liver M+)

- WHO performance status 2 or lower
- life expectancy of at least 6 months

June 2015 – Jan 2019

SABR **commissioned for OMD** by NHS England in March, 2020





95,4% WHO 0 and 1

75,6% 1 metastasis

survival: prostate, breast, renal and colon better than lung

adverse events: gr 3: fatigue (2·0%); gr 4: increased liver enzymes (0·6%); no gr 5

Chalkidou et al, Lancet Oncol 2021

innovation  clinical practice

health services perspective

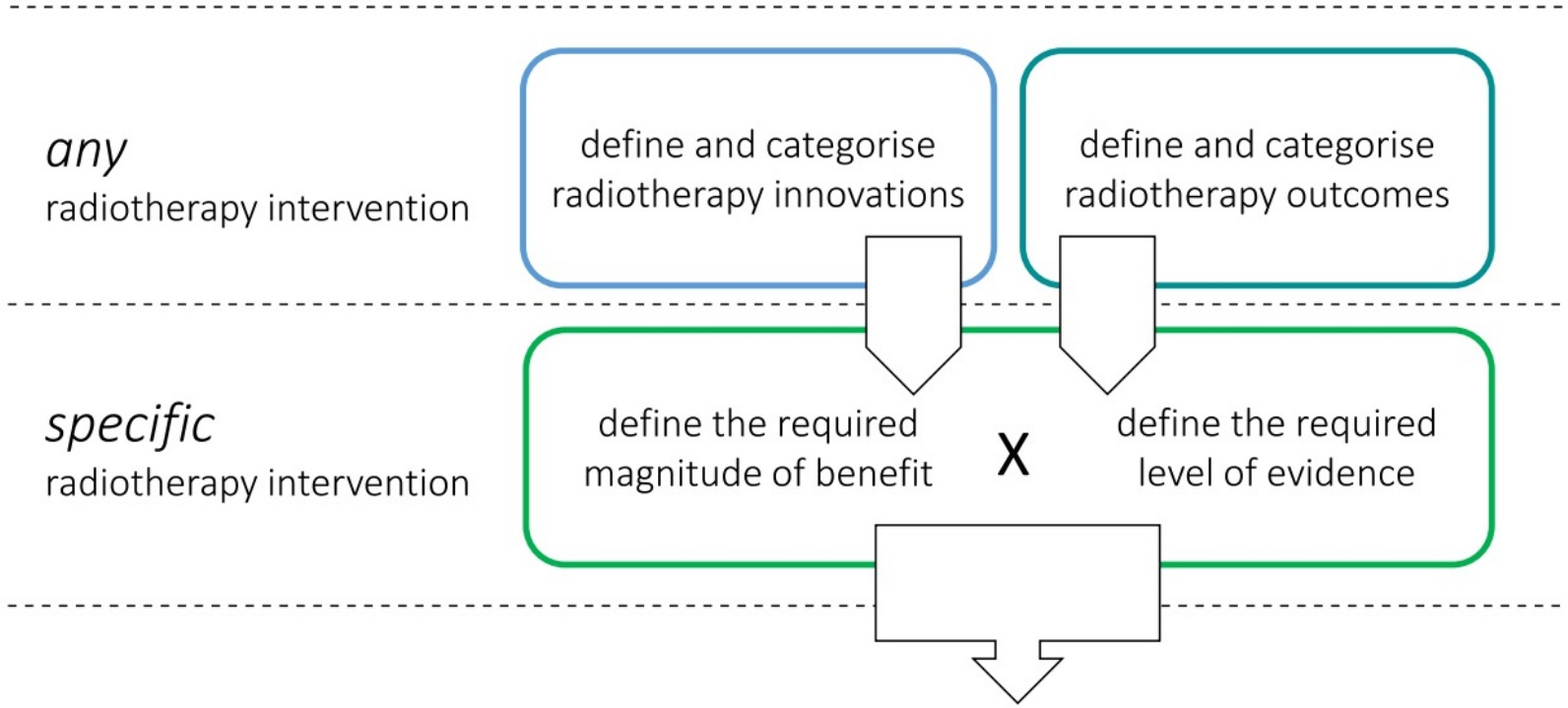
access, patients' value

innovation

clinical practice

ESTRO HERO

Value-Based Radiation Oncology



Value-Based Framework for Radiation Oncology

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Thank you for your attention !