Rete Oncologica Veneta
Ricerca, innovazione, assistenza

Regione del Veneto
Coordinamento Regionale per le Attività Oncologiche
(CRAO)

Corso Formazione Esperti di Rete - Agenas

25 gennaio 2024 – Sede del CRAO

La Ricerca di Rete

Pierfranco Conte

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Oncology at the Cross Road

- Diagnostic-therapeutic Pathways: markers and outcomes
- Evidence- based medicine or Evidence-biased Medicine?
- RWD to provide RWE

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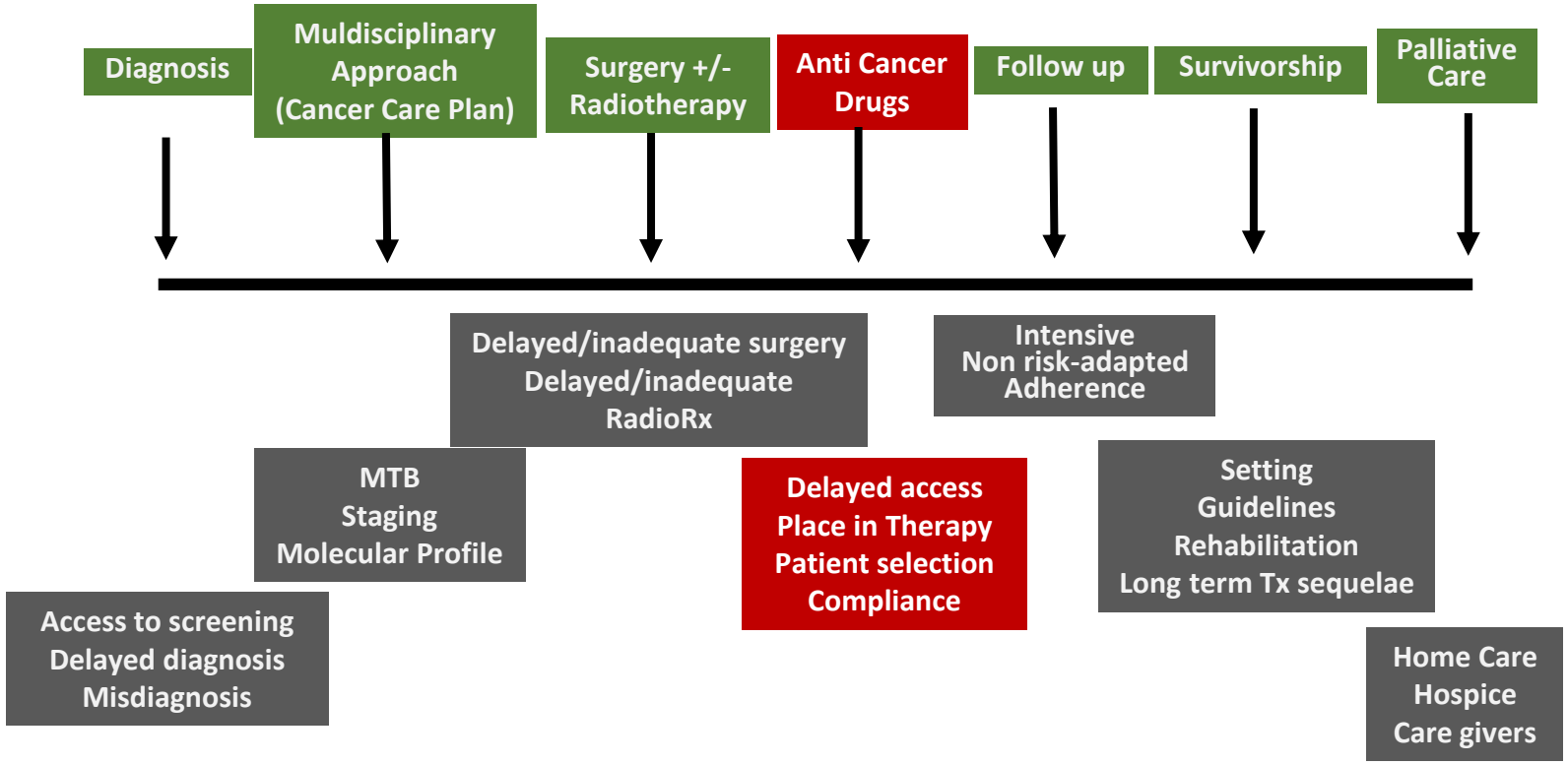
Patients' Journey in Oncology



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Time to adjuvant chemotherapy for eBC in five italian regions

original contribut

FOCUS ON QUALITY ReCAP

Use of Electronic Administrative Databases to Measure Quality Indicators of Breast Cancer Care: Experience of Five Regional Oncology Networks in Italy

Valentina Guarneri, PhD, MD[1,2]; Paolo Pronzato, MD[3,4]; Oscar Bertetto, MD[5]; Fausto Roila, MD[6]; Gianni Amunni, MD[7,8]; Alberto Bortolami, PharmD[2,9]; Sandro Tognazzo, MS[2,9]; Gaia Griguolo, MD[1,2]; Eva Pagano, MEcon[10]; Fabrizio Stracci, PhD, MD[11]; Fortunato Bianconi, PhD, MS[12]; Fabrizio Gemmi, MD[13]; Letizia Bachini, MS[13]; Giovannino Ciccone, MS[10]; Gabriella Paoli, MEng[14]; Laura Paleari, PhD, MS[14]; and Pier Franco Conte, MD[1,2] on behalf of the Periplo Association

Adjuvant therapy within 8 weeks from surgery % of patients					
Veneto	Liguria	Toscana	Piemonte	Umbria	Benchmark
73.7 %	66.7 %	NA	71.8 %	69.9 %	≥ *80%*

No data available on breast cancer subtypes

The VERO Study: The VEneto and ROmagna Breast project

IRST Meldola:
Ilaria Massa, Roberta Maltoni, Valentina Danesi, William Balzi, Andrea Roncadori

AUSL Romagna:
Mattia Altini, Roberto Grilli

Rete Oncologica Veneta:
Pierfranco Conte, Alberto Bortolami, Valentina Guarneri

Azienda Zero:
Manuel Zorzi

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163/544 trials with OS improvement
108,344 patients included in these trials
14.2 millions years of life gained

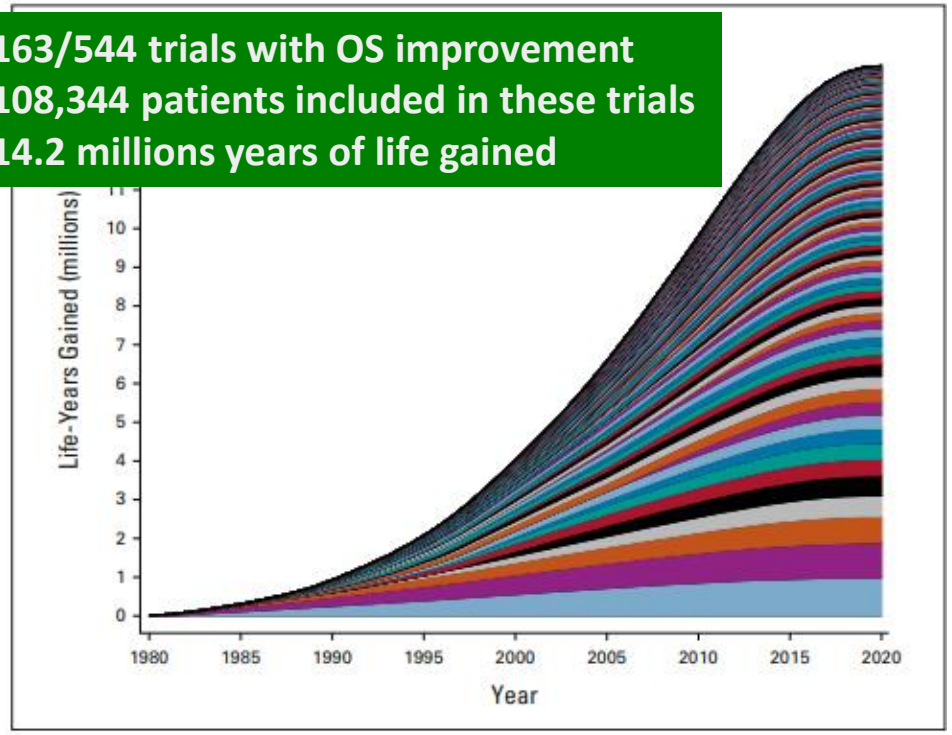
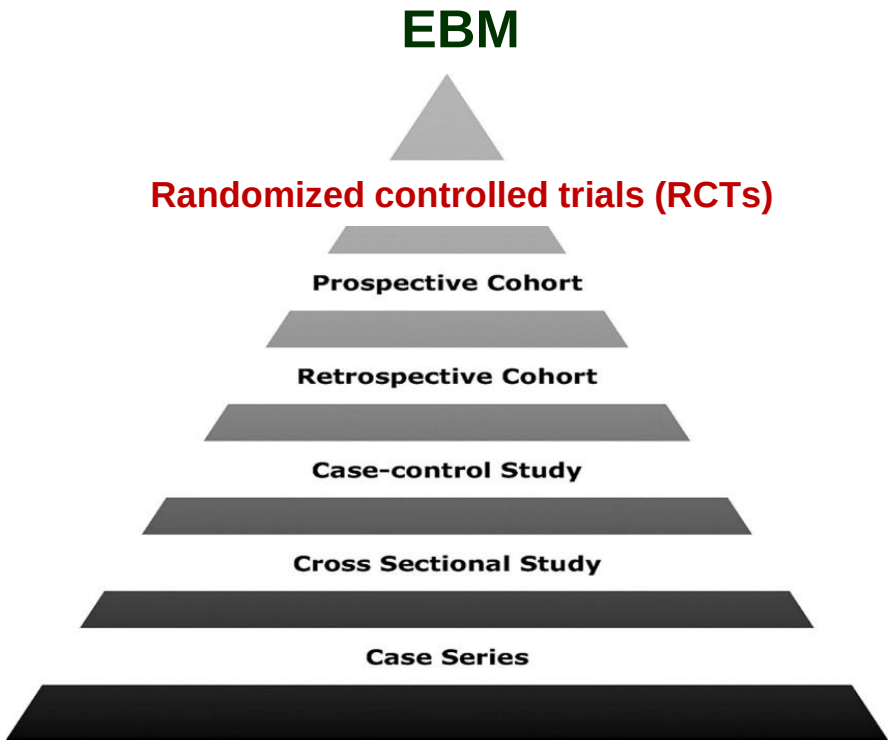


FIG 1. Cumulative life-years gained through 2020 by study. Each color-coded area represents cumulative life-years for 1 of 133 studies for which life-year gains were estimated.

Unger JM et al, JCO 2023



EBM is largely based on RCTs
RCTs are in large part conducted to apply for marketing authorization
Regulatory Agencies decide on the basis of the risk/benefit ratio
This judgement does not take into account:

- under-represented patients (elderly, unfit, with comorbidities, with comedications
- treatment duration (e.g. ICIs, antiHER2 drugs)
- treatment sequences
- rare & long term toxicities
- impact on diagnostic-therapeutic pathways
- budget impact

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The Oncologist®
Commentary

Real-World Evidence in Oncology: Opportunities and Limitations

Massimo Di Maio.[a] Francesco Perrone.[b] Pierfranco Conte[c]

Large proportion of new treatments only show a globally modest efficacy within RCTs

↓

Effect in clinical practice might be further diluted

↓

Real value of results may fall under an acceptable threshold of relevance

↓

Post marketing studies could be useful to **confirm or refute the drug's benefit** on survival in real-world populations

↓

RWE analysis may challenge the magnitude of the efficacy previously shown in RCTs

Di Maio, Perrone, Conte; The Oncologist *2020*

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JAMA Oncology | Original Investigation

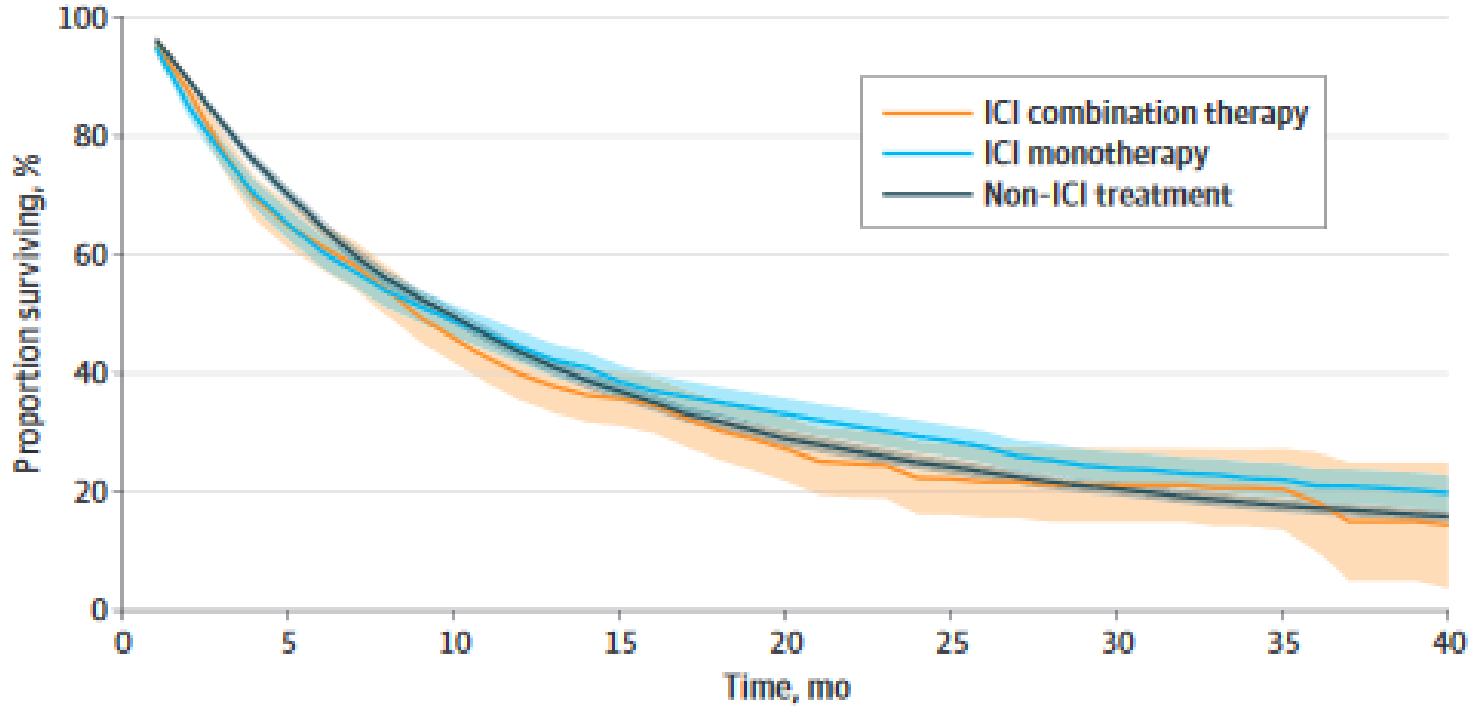
Uptake and Survival Outcomes Following Immune Checkpoint Inhibitor Therapy Among Trial-Ineligible Patients With Advanced Solid Cancers

Ravi B. Parikh, MD, MPP; Eun Jeong Min, PhD; E. Paul Wileyto, PhD; Fauzia Riaz, MD; Cary P. Gross, MD; Roger B. Cohen, MD; Rebecca A. Hubbard, PhD; Qi Long, PhD; Ronac Mamtani, MD, MSCE

JAMA Oncol. 2021 Dec 1;7(12):1843-1850.

- **34,131 patients with advanced non oncogene-driven NSCLC, urothelial cell, renal cell or hepatocellular carcinoma**
- **9,318 (27.3%) patients were trial-ineligible**
- **From january 2014 to december 2019, ICI monotherapy increased from 0.1% to 19.4% among trial-eligible patients and from 0% to 39.2% among trial-ineligible patients**
- **Among trial-ineligible patients there was no OS differences between ICI monotherapy, ICI combination therapy or non-ICI therapies**

Figure 2. Kaplan-Meier Curves of Overall Survival Among Trial-Ineligible Patients With Advanced Solid Tumors



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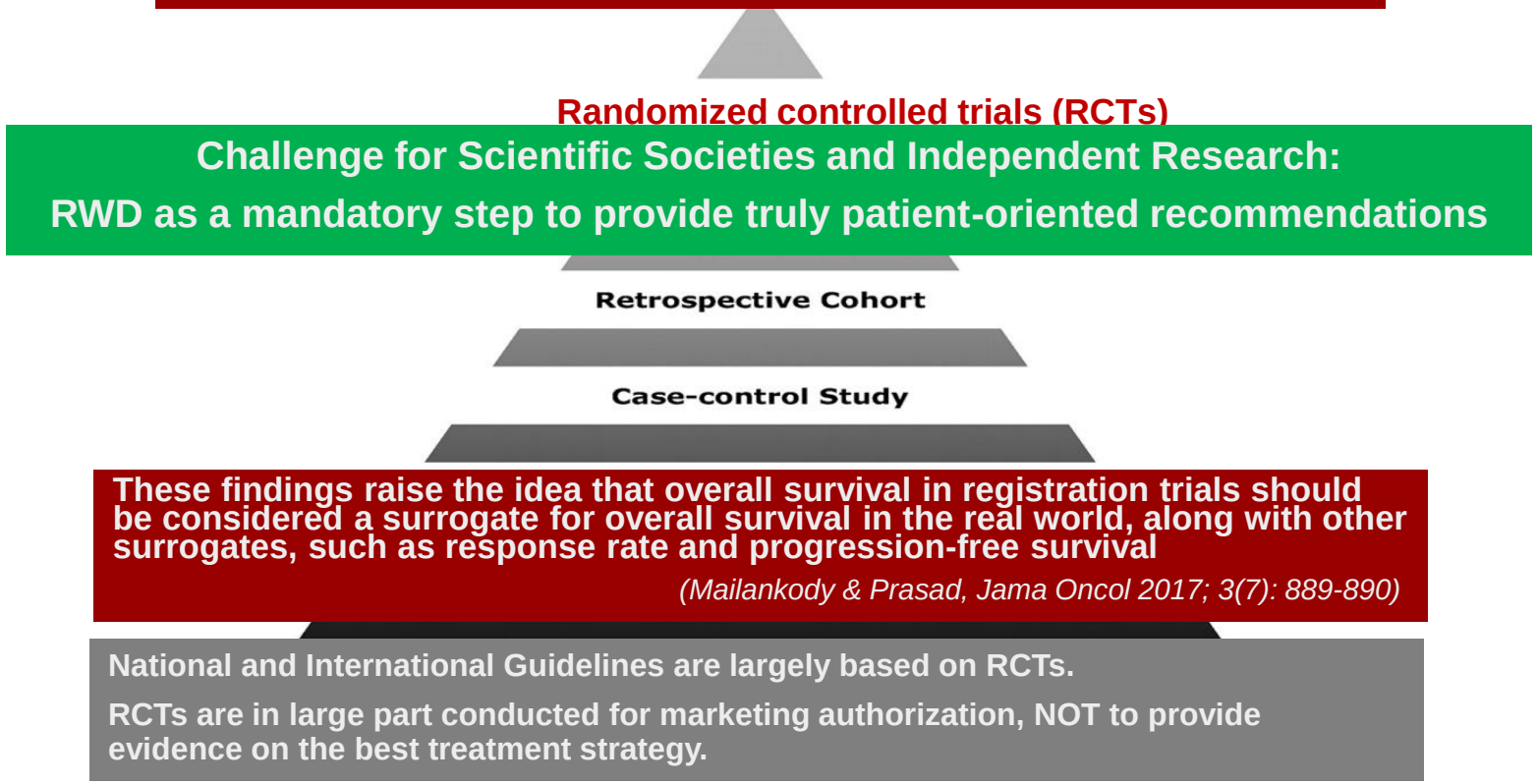
Evidence Based or Evidence Biased Medicine?



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The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

The Magic of Randomization versus the Myth of Real-World Evidence

Rory Collins, F.R.S., Louise Bowman, M.D., F.R.C.P., Martin Landray, Ph.D., F.R.C.P., and Richard Peto, F.R.S.

Targets of RWE

- Complement/provide data for Regulatory Authorities
- Comparative effectiveness data (rare populations, applicability, treatment sequences, rare&long term toxicities)
- Definition of diagnostic-therapeutic pathways
- Budget impact (whole disease model-bundled payments)
- Patient-oriented guidelines

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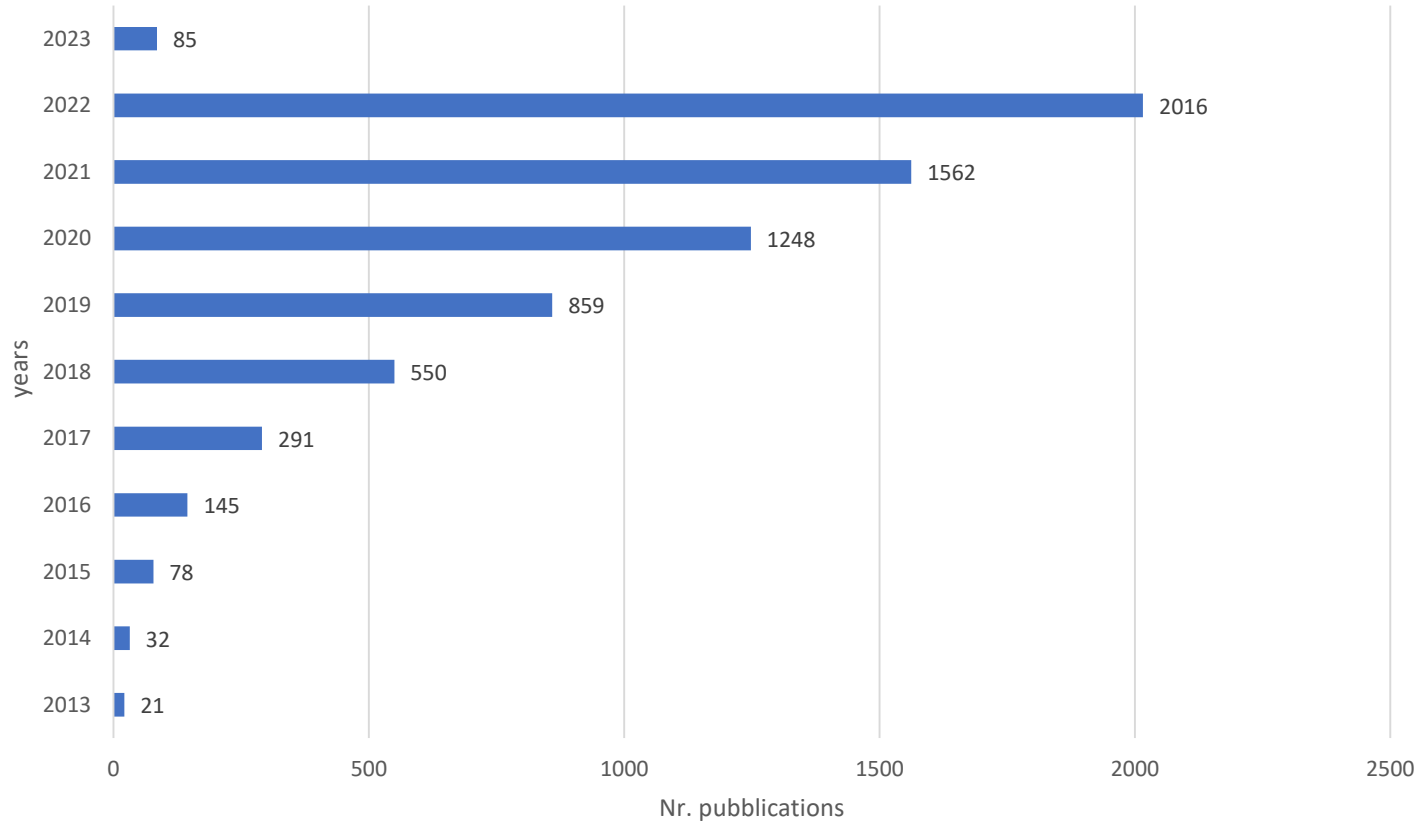
Real World Publications - Oncology



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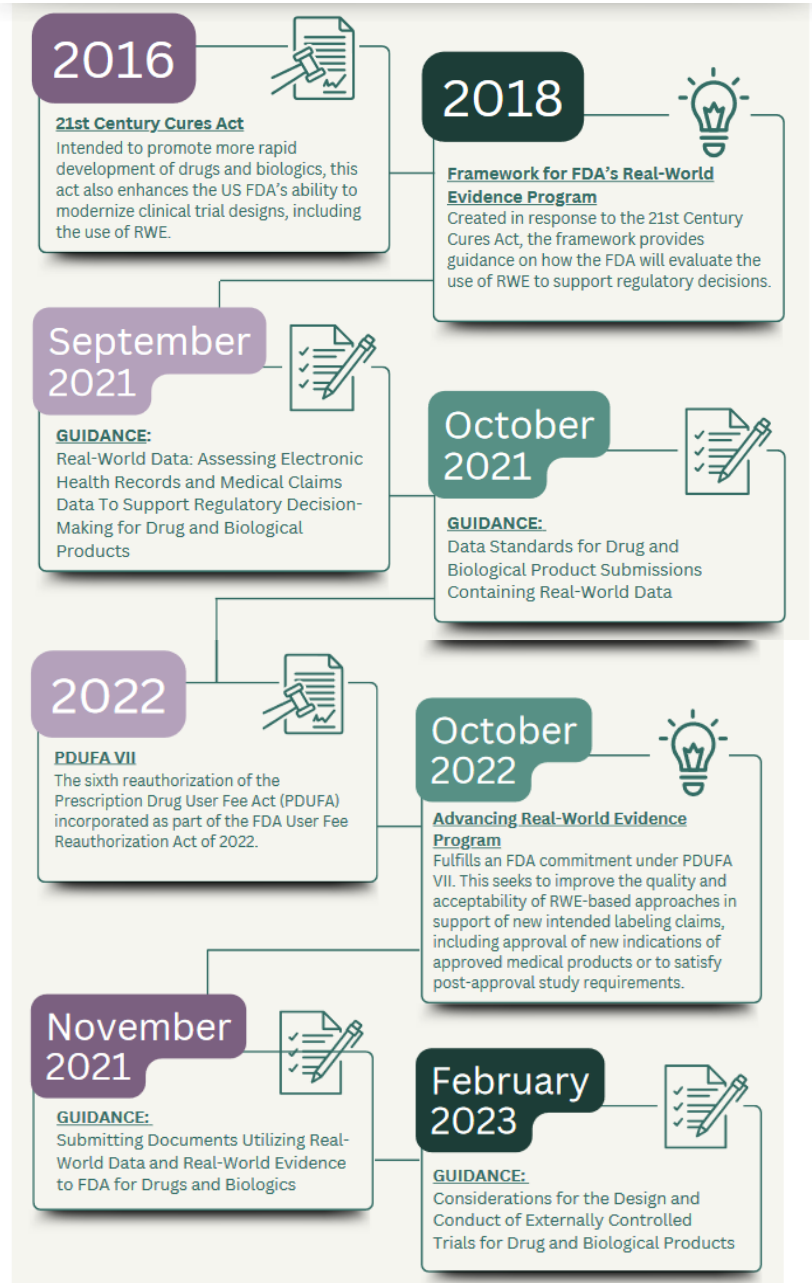
Milestones in the FDA's **Real-World Evidence** Activities

Real-world data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records, medical claims data, data from product or disease registries, and data gathered from other sources (such as digital health technologies) that can inform on health status.

Real-world evidence (RWE) is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

The Evidence Base®

https://www.evidencebaseonline.com/



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RWE must be based on good quality Real World Data

BARRIERS to good quality Real World Data

- Access to regional/national Data Bases (institutional data bases are NOT enough!)
- Data Availability (i.e. molecular characteristics/mutational profiles)
- Set of Data (i.e. proportion of patients; TTF, emergency room access, attrition rate)
- Quality of Data (EMR, source of data and data verification)
- Data interpretation (comparative effectiveness)
- Funding

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MINISTERO DELLA SALUTE

DECRETO 30 maggio 2023.

Istituzione dei *Molecular tumor board* e individuazione dei centri specialistici per l'esecuzione dei test per la profilazione genomica estesa *Next generation sequencing* (NGS).

"Istituzione dei Molecular Tumor Board e individuazione dei centri specialistici per l'esecuzione dei test per la profilazione genomica estesa Next Generation Sequencing (NGS)"

2.ISTITUZIONE DEI MOLECULAR TUMOR BOARD NELL'AMBITO DELLE RETI ONCOLOGICHE REGIONALI

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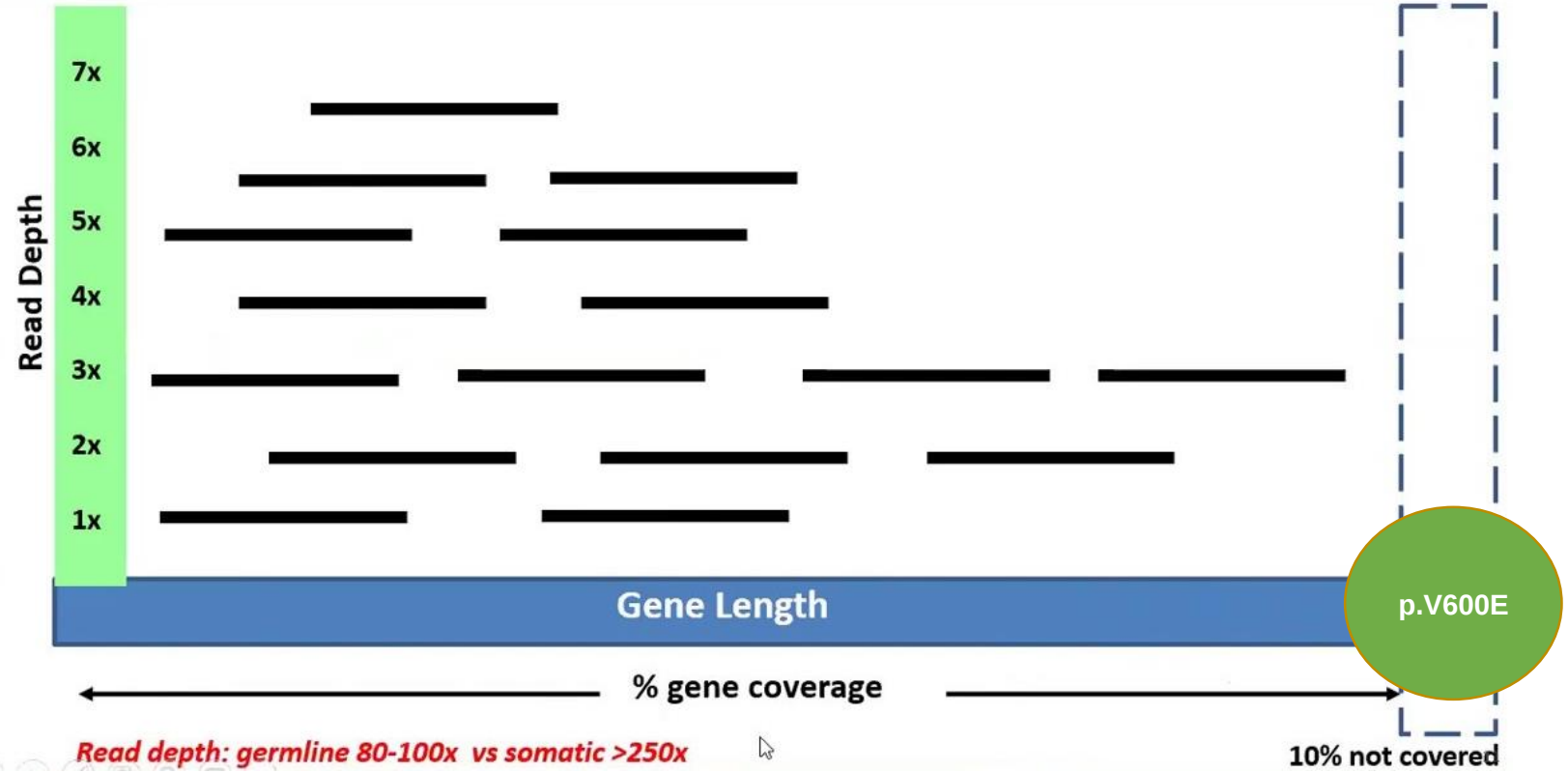
Diagnostic alternatives and interpretation

Real Time PCR
BRAF p.V600E

p.V600E

wt

NGS
BRAF wt



Courtesy of M Fassan

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Precision Oncology……still a long road ahead

Prevalence of specific dysregulations in the general population of cancer patients	**Largely unkown with the exception of «classic» dysregulations (PanRAS, PIK3CA,PTEN,BRCA,ALK,ROS,EGFR,HER2, BRAF,NTRK, MSI…) already included in routine molecular diagnostics**
Natural history of cancers from same organs and histologies with specific genetic dysregulations	**Largely unknown** (i.e. BRCAm vs PALB2m breast cancer; BRCAm vs BRCAwt breast cancer)
Sensitivity to «standard» treatments of tumors from same organs and specific dysregulations	**Some data indicate that BRCAm tumors respond better to platinum compounds and that oncogene-driven NSCLC is less responsive to ICI**
Sensitivity to «targeted» treatments of tumors from different organs and same dysregulations (agnostic approach)	**Largely unknown for most dysregulations. The clinical value of PARPi is significantly different according to tumor type and tumor stage.**
Relevance of concomitant mutations to dictate sensitivity/resistance to targeted treatments	**Largely unknown; not considered in ESCAT or OncoKB**

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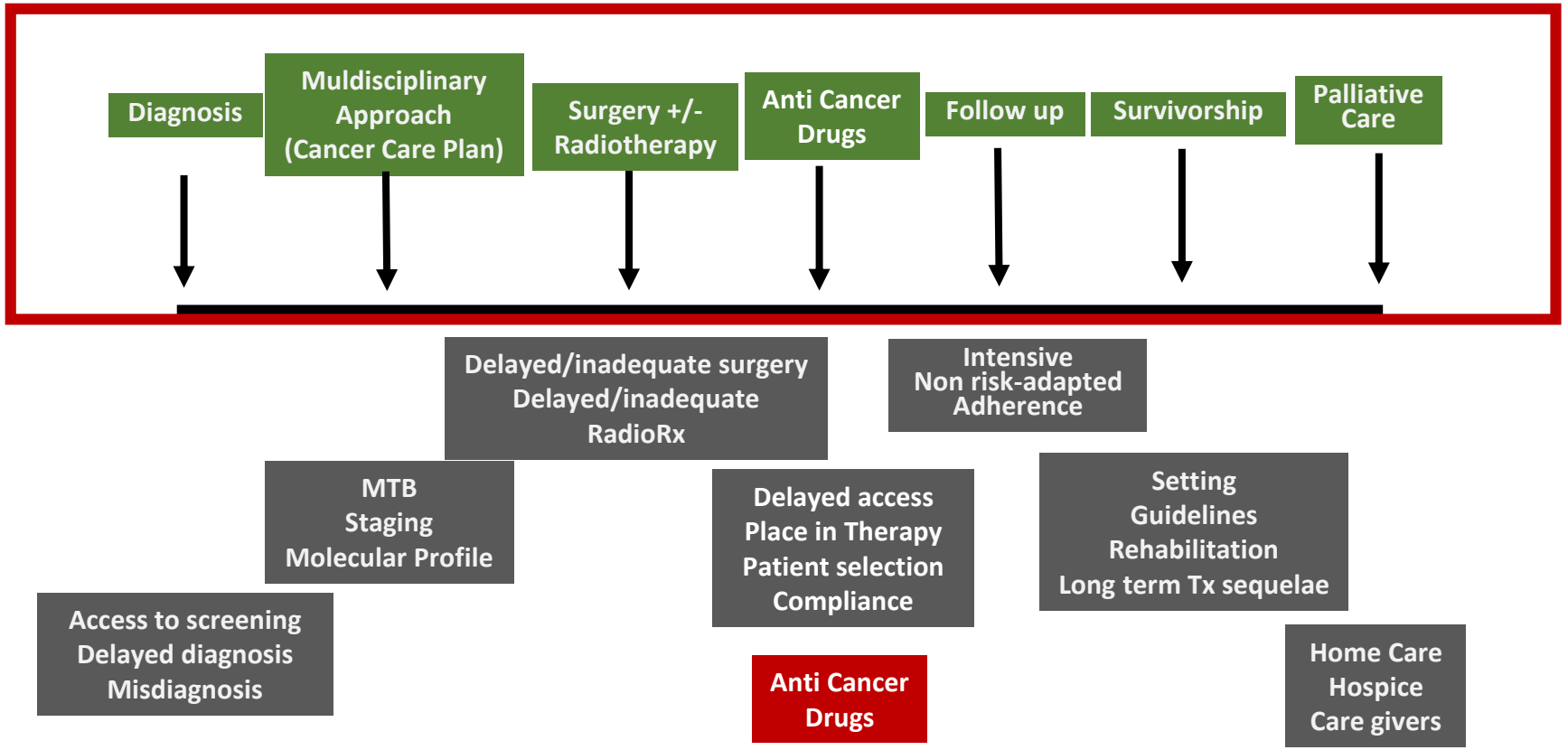
Patients' Journey in Oncology



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Sources of Data

Identificazione dei casi

Casi di tumore al polmone NSCLC

incidenti nel 2017

Registro Tumori Veneto

Fonti dei dati per il calcolo degli indicatori

Flussi amministrativi
SDO, SPS, Registro mortalità, farmaceutica, Hospice, Assistenza protesica, PS, Device, Assistenza domiciliare

Flusso di anatomia patologica
referti istologici, referti citologici

RTV - *Registro Polmone*
archivi di registro, collegamenti SIL delle ASL, cartelle cliniche

Data links and interpretation:
a multidisciplinay team including physicians, pathologists, pharmacists and epidemiologists

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PDTA per i pazienti affetti da tumore del polmone

Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Estimated direct costs of non-small cell lung cancer by stage at diagnosis and disease management phase: A whole-disease model

Alessandra Buja[1], Michele Rivera[1], Anna De Polo[1], Eugenio di Brino[6], Marco Marchetti[6], Manuela Scioni[2], Giulia Pasello[4], Alberto Bortolami[7], Vincenzo Rebba[3], Marco Schiavon[1], Fiorella Calabrese[1], Giovanni Mandoliti[5], Vincenzo Baldo[1] & PierFranco Conte[4,8]

Table 3 Estimates of average (and confidence interval) per-patient costs of care for NSCLC by disease stage (€) during the first year after diagnosis

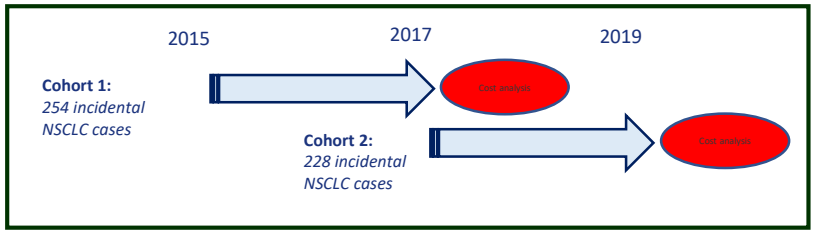
	Average total costs	Cost ratio vs. stage I
Stage I	16 291 (95% CI: 15 284–17 505)	1
Stage II	19 530 (95% CI: 18 263–21 091)	1.19
Stage III	21 938 (95% CI: 20 271–25 252)	1.34
Stage IV	22 175 (95% CI: 22 127–22 190)	1.36
Pancoast	28 711 (95% CI: 27 711–29 890)	1.79
TOTAL	21 328 (95% CI: -20 897–22 322)	

VALUE IN CANCER CARE ReCAP

Non–Small-Cell Lung Cancer: Real-World Cost Consequence Analysis

Alessandra Buja, MD, PhD[1]; Giulia Pasello, MD[2]; Giuseppe De Luca, MD[1]; Alberto Bortolami, PharmD[3]; Manuel Zorzi, MD[4]; Federico Rea, MD[1]; Carlo Pinato, MStat[3]; Antonella Dal Cin, BS[4]; Anna De Polo, MD[1]; Marco Schiavon, MD[1]; Andrea Zuin, MD[1]; Marco Marchetti, MD[4]; Giovanna Scroccaro, PharmD[5]; Vincenzo Baldo, MD[1]; Massimo Rugge, MD[4]; Valentina Guarneri, MD, PhD[2,6]; and PierFranco Conte, MD[2,6]; on behalf of Rete Oncologica Veneta

Buja A et al, JOP 2021



Regression models dependent variable	Coefficient 2017 (ref 2015)	95% CI	p-value
Hospitalization costs	343.9	383.7 ; 0.9	0.37
Outpatient visits costs	192.0	314.1 ; 0.6	0.541
Emergency room costs	39.8	27.6 ; 1.4	0.149
Hospice costs	-911.3	397.0 ; -2.3	0.022
Hospital delivered drugs costs	2976	1116.0 ; 2.7	0.008
Medical devices costs	522.6	371.9 ; 1.4	0.160
Other Drugs costs	-55.1	44.84; -1.2	0.219
Total costs	3006	1148.0 ; 2.6	0.009

- Total costs adjusted for age, stage at diagnosis, sex, cohort, at 2 yrs after cancer diagnosis
- significant **increase in the average costs** of patients in the 2017 cohort
- significant **decrease** in the average cost of **hospice care**
- significant **increase** in the average cost of **drugs**
- **Significant OS improvement at 2 yrs**

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Periplo Foundation
Outcome-COsts-CAncer Programme

OCOCA Lung

(evaluation of impact of the introduction of the clinical pathway on health outcome, costs and quality of care in NSCLC patients) – PI V Guarneri

Registro Tumori Veneto

Rete Oncologica Veneta

Università degli Studi di Padova

Studio osservazionale di coorte che prevede la raccolta di tutti i casi di NSCLC diagnosticati in Regione Veneto in tre anni differenti (2017,2019,2021) per valutare:

1) **Qualità delle cure**
2) **Costi della presa in carico globale**
3) **Esiti in termini di sopravvivenza globale**

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From Cancer Institutions to Oncology Networks for the benefit of our patients