Innovation: Changing the experience of serious illness

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Acknowledgement

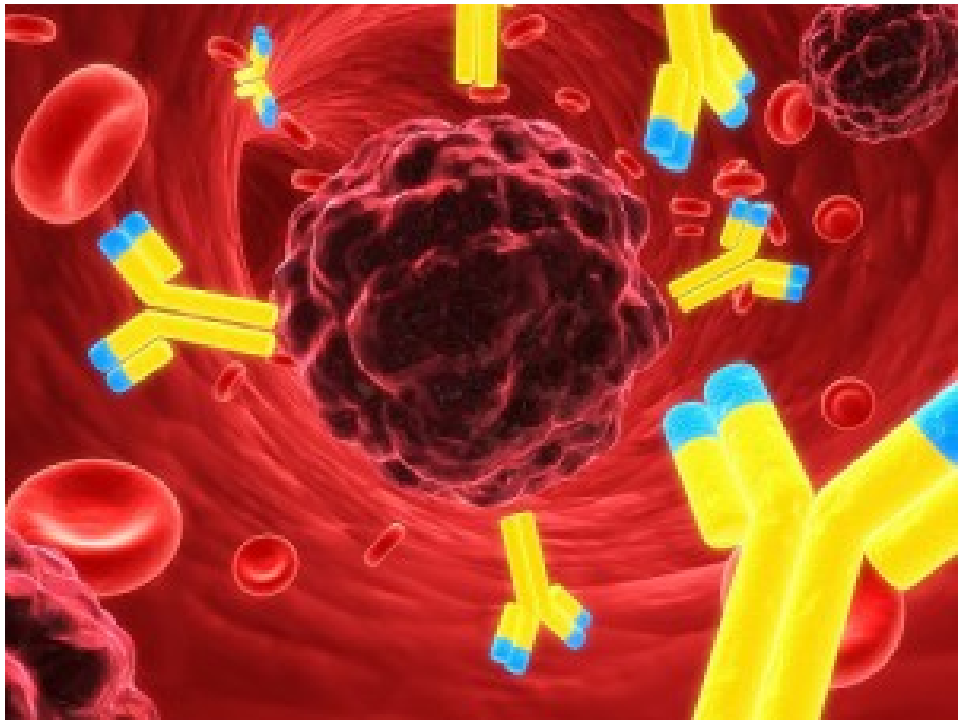
- A number of these slides have been provided by PhRMA, the US research-based industry association:

  Pharmaceutical Research and Manufacturers of America®950 F Street, NW Suite 300, Washington, DC 20004 - See more at: http://www.phrma.org/innovation/meds-in-development#sthash.yd3uB8vk.dpuf

An innovation explosion

Immuno-therapies

Personalized medicine

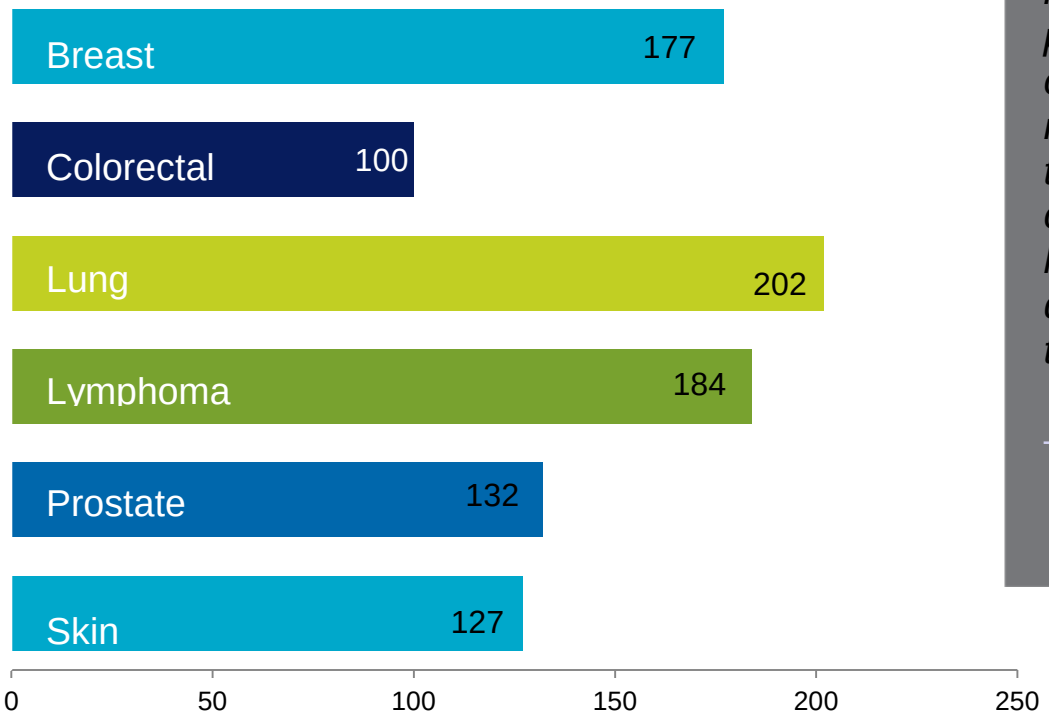


Application of big data to R&D

Novel drug delivery mechanisms

More than 1,000 Medicines in Development for Various Cancers

Number of Medicines in Development in the United States 2015, Selected Cancer Types*



"Scientifically, we have never been in a better position to advance cancer treatment. … We now understand many of the cellular pathways that can lead to cancer. We have learned how to develop drugs that block these pathways."

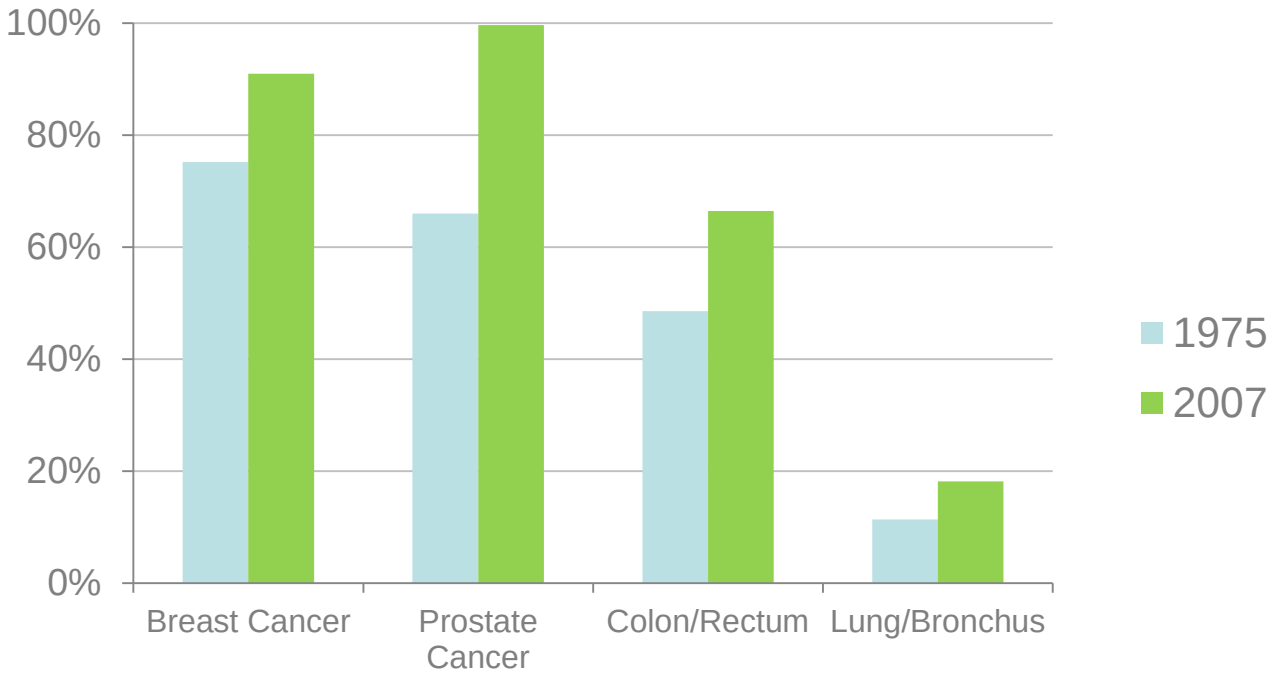
— Richard L. Schilsky, MD, Professor, University of Chicago

- Sources: Adis R&D Insight Database, 15 May 2015; American Society of Clinical Oncology, "Clinical Cancer Advances 2008: Major Research Advances in Cancer Treatment, Prevention and Screening," *Journal of Clinical Oncology,* 22 December 2008.

Five-Year Survival is Increasing for Many Types of Cancer

- The chances that a cancer patient will live 5 years or more has increased by 39% across cancers.

5-Year Survival Rates for Selected Cancers, 1975-2007



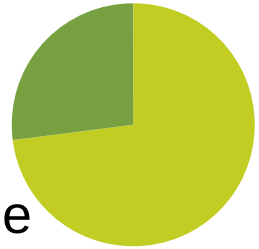
***83%** of survival gains in cancer are attributable to new treatments — including medicines.*

- Sources: E. Sun, et al., "The Determinants of Recent Gains in Cancer Survival: An Analysis of the Surveillance, Epidemiology, and End Results (SEER) Database," *Journal of Clinical Oncology,* May 2008 Suppl (Abstract 6616); American Cancer Society, "Cancer facts & Figures 2015," http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf; National Cancer Institute, Surveillance Epidemiology and End Results, Fast Stats: An interactive tool for access to SEER cancer statistics, http://seer.cancer.gov/faststats .

Personalized Medicine is Transforming Cancer Care

- **Biopharmaceutical companies focusing on personalized medicine has resulted in several recent approvals and a growing number of new medicines in the pipeline.**

12-50%



Of new drugs in the pipeline are reportedly personalized medicines (across all diseases)

73% of **cancer medicines** in the pipeline have the potential to be **personalized medicines**

"Oncology is on fire with [personalized medicine], with treatment selections based on individual molecular characteristics. This is also happening with chronic infectious diseases, and genetic diseases are not far behind."

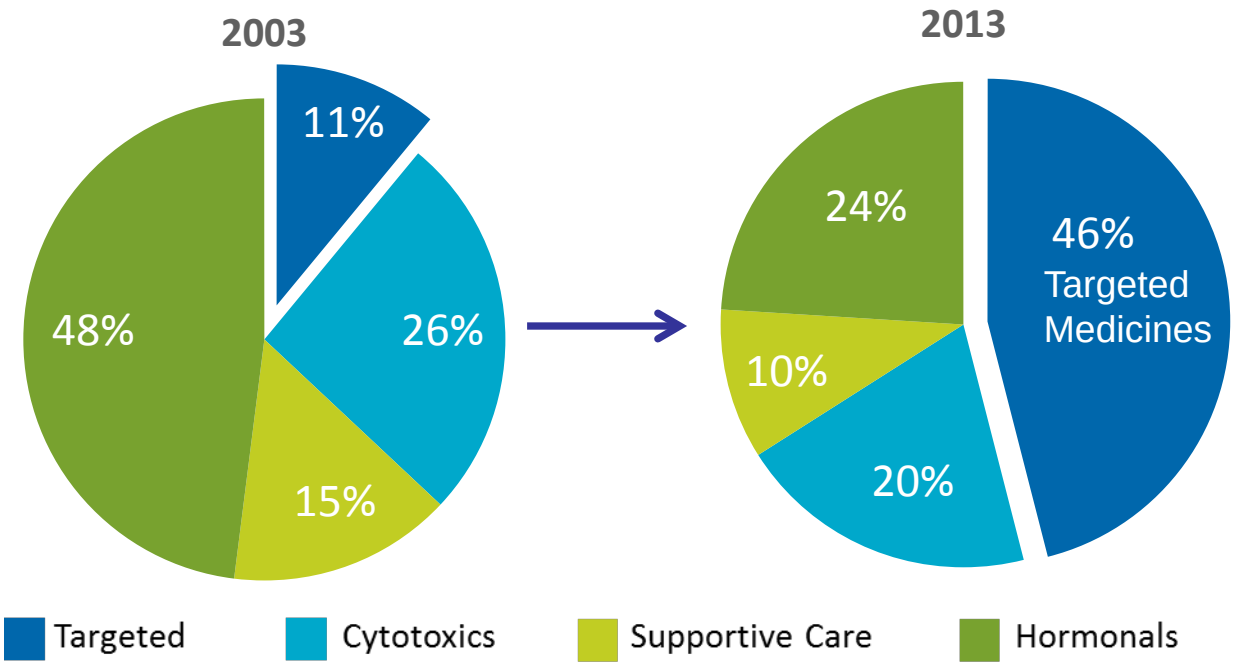
— Janet Woodcock, Director
Center for Drug Evaluation and Research,
U.S Food and Drug Administration

- Sources: Tufts Center for the Study of Drug Development, "Impact Report," Volume 17, No.3, May/June 2015; J.T. Aquino, "Personalized Medicine: Targeted Therapies Said Now Mainstream; Reimbursement, Clinical Trial Hurdles." *Life Sciences Law and Industry Report*, 31 May 2013. Available at www.personalizedmedicinecoalition.org/sites/default/files/files/BloombergBNA.pdf.

The Role of Personalized Medicines Has Grown in the Last Decade

Personalized medicines provide effective and efficient care by targeting the right medicine to the right patient.

Oncology Treatment Modalities in Top Pharmaceutical Markets, 2003-2013



- Source: IMS Institute for Healthcare Informatics, “Innovation in Cancer Care and Implications for Health Systems: Global Oncology Trend Report,” May 2014.

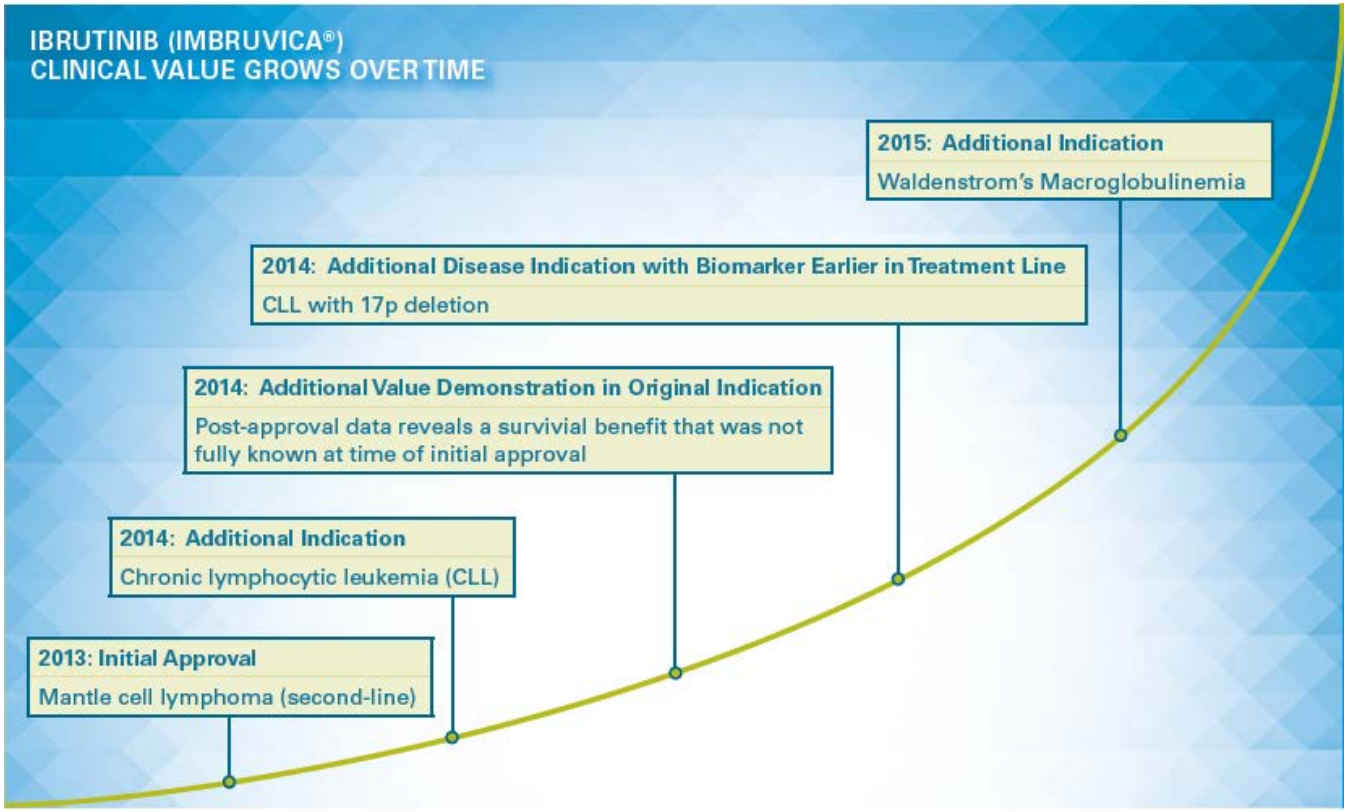
Changing the prognosis for malignant melanoma

- In 2010, ipilimumab became the first drug ever shown to extend survival for patients with metastatic melanoma in a large phase III trial. Ipilimumab reduced the risk of death by 32% and nearly doubled the likelihood of patients surviving to 1 and 2 years, with some patients experiencing complete and durable clinical regressions. Based on these results, ipilimumab was approved by the FDA as first-line therapy for advanced melanoma in 2011.

- The combination of ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) has been tested in patients with advanced melanoma in several trials, with impressive results. A phase I trial of the combination showed that the 2-year survival rate for all dose cohorts was 79%. At the best-responding dose level (nivolumab 1 mg/kg and ipilimumab 3 mg/kg), the 2-year survival rate was even more impressive—88%. This is compared to a 2-year survival rate of about 15% for patients treated with conventional chemotherapy.
http://www.cancerresearch.org/cancer-immunotherapy/impacting-all-cancers/melanoma

Clinical Value Evolves Over Time: Ibrutinib

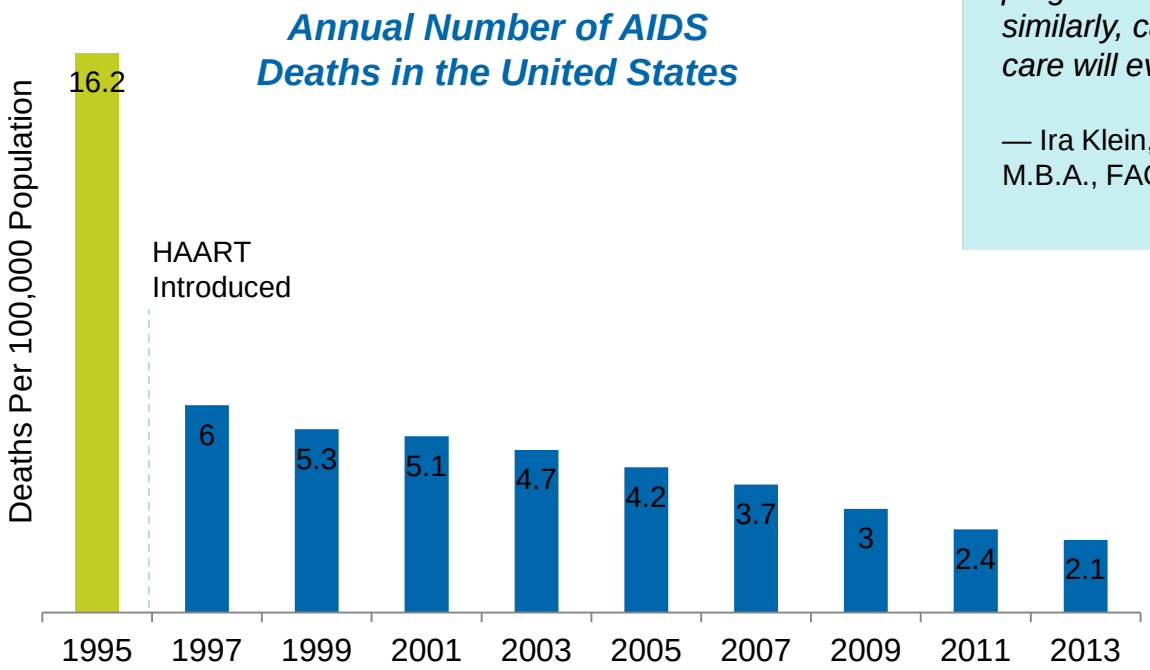
- In November 2013, the FDA granted accelerated approval to ibrutinib for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. The approval of ibrutinib was an important milestone for patients with this rare cancer, but continuing research has revealed additional benefits of ibrutinib not recognized at initial approval.



- Source: Boston Healthcare Associates, "The Value of Innovation in Oncology: Recognizing Emerging Benefits Over Time," Boston Healthcare Associates, Inc., May 2015.

Innovations in Cancer Treatment Could Echo HIV/AIDS Successes

- As HIV/AIDS treatments improved, spending became more sustainable.



"We used to think HIV costs would overwhelm us….but we figured it out and let drug development progress… similarly, cancer care will evolve."

— Ira Klein, M.D., M.B.A., FACP, Aetna

"Remember HIV?.... thanks to a wave of new discoveries that came both from academic centers and the pharmaceutical industry, the HIV crisis was transformed into a stable condition which is managed very differently by society where good drugs are available. They are controlling the disease, and society has been saving an enormous amount of money as a result of these innovative drugs by providing better care out of hospitals."

— Hervé Hoppenot, President, Incyte Pharmaceuticals

- Sources: National Center for Health Statistics. Health, United States, 2014: With Special Feature on Adults Aged 55–64. Hyattsville, MD. 2015. http://www.cdc.gov/nchs/data/hus/hus14.pdf page 125 http://www.cdc.gov/nchs/hus/contents2014.htm#029; M Kean, T Lessor (Eds.), "Sustaining Progress Against Cancer in an Era of Cost Containment Discussion Paper," June 2012, available at: www.TurningTheTideAgainstCancer.org.

Lilly & Hanmi Collaboration - Autoimmune Conditions

Lilly and Hanmi Announce an Exclusive License and Collaboration Agreement for the Development and Commercialization of an Immunological Therapy (March 19,2015).

- Exclusive license and collaboration agreement for the development and commercialization of Hanmi's oral Bruton's tyrosine kinase (BTK) inhibitor, HM71224, for the treatment of autoimmune and other diseases.

- Molecule is ready to enter Phase II and will be investigated for the potential treatment of rheumatoid arthritis, lupus, lupus nephritis, Sjögren's syndrome, and other related conditions.

"Lilly is committed to changing patient expectations in some of the world's most debilitating disease areas, and we're building a portfolio of potential advances in immunology through our own research and key collaborations such as with Hanmi. We're highly encouraged by the potential of HM71224 to deliver an innovative, first-in-class treatment option."

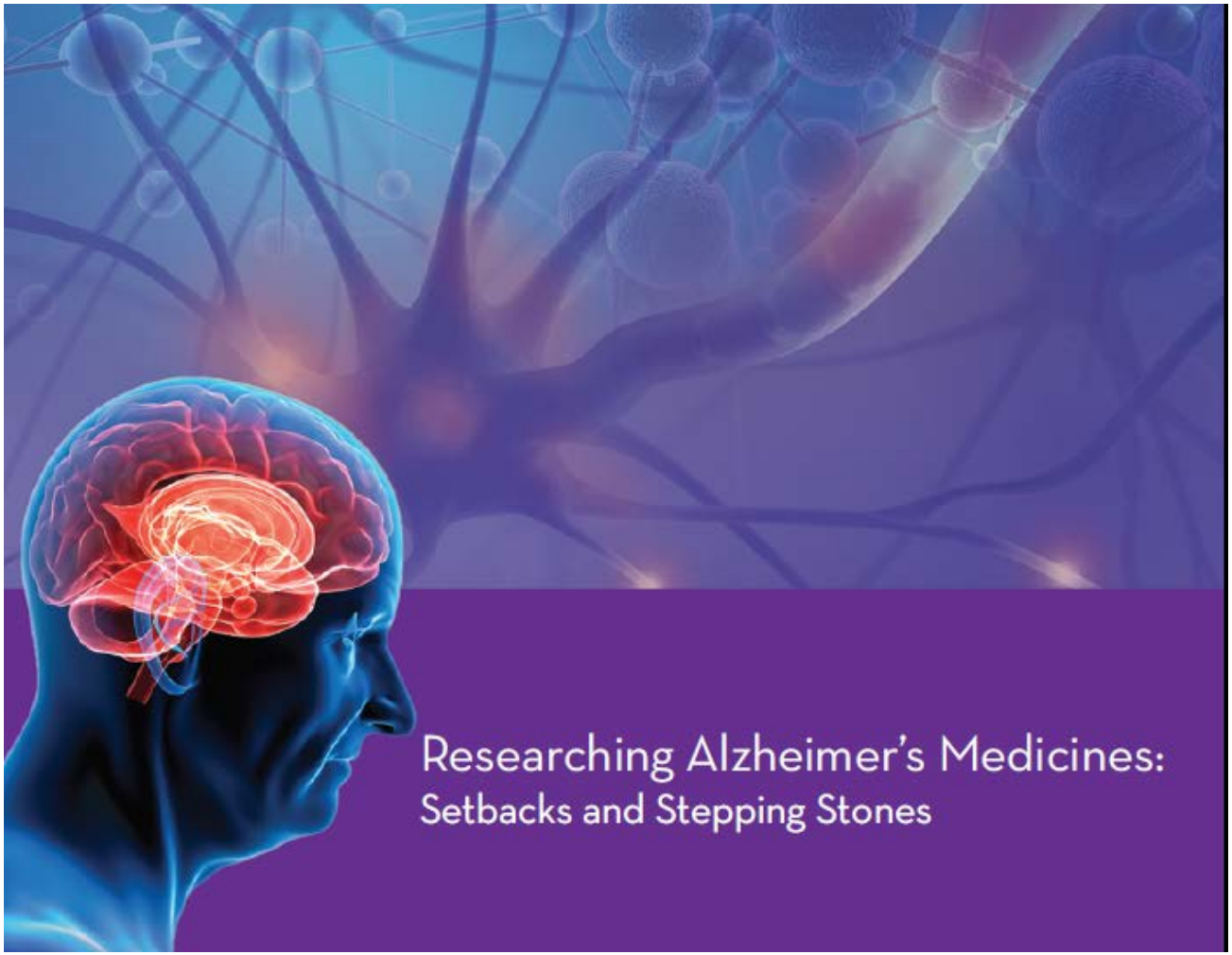
-Thomas Bumol, Ph.D., senior vice president, biotechnology and immunology research at Lilly

"We are very pleased to be collaborating with Lilly on HM71224, and through this agreement and R&D collaborations, we are excited to drive the joint project forward with the ultimate aim to offer new medical treatment options to patients with autoimmune disorders and related conditions."

- Dr. Gwan Sun Lee, CEO/President of Hanmi Pharmaceutical

Hanmi Pharmaceutical is a Korea-based global pharmaceutical company focused on the development and commercialization of new pharmaceutical products. More information on Hanmi is available at www.hanmipharm.com.

Alzheimer's disease: a difficult challenge

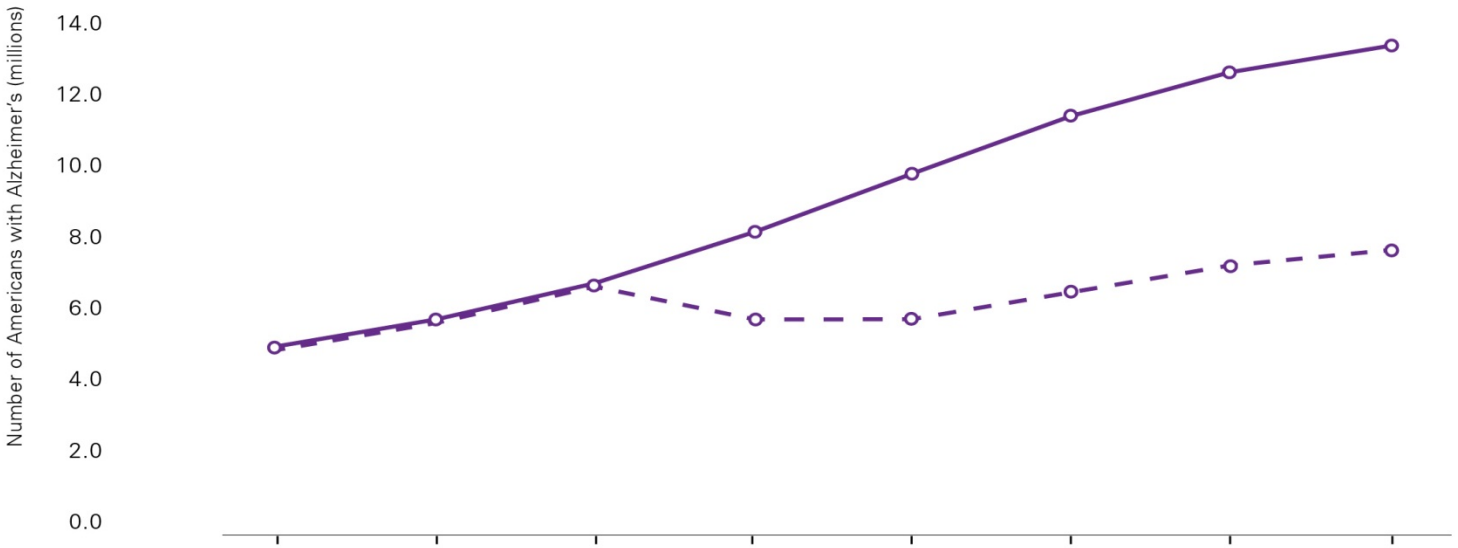


A recent report from PhRMA that highlights the challenges of achieving real progress in treating Alzheimer's disease (available from the PhRMA website)

The potential to change the trajectory of Alzheimer's disease

FIGURE 4

Impact of a Treatment That Delays Onset by Five Years on the Number of Americans Age 65 and Older Living with Alzheimer's Disease, 2015-2050



	2015	2020	2025	2030	2035	2040	2045	2050
Current trajectory	5.1	5.8	6.8	8.2	9.9	11.6	12.8	13.5
Delayed onset	5.1	5.8	6.8	5.8	5.9	6.6	7.3	7.8
Decrease	0.0	0.0	0.0	2.5	4.0	5.0	5.5	5.7

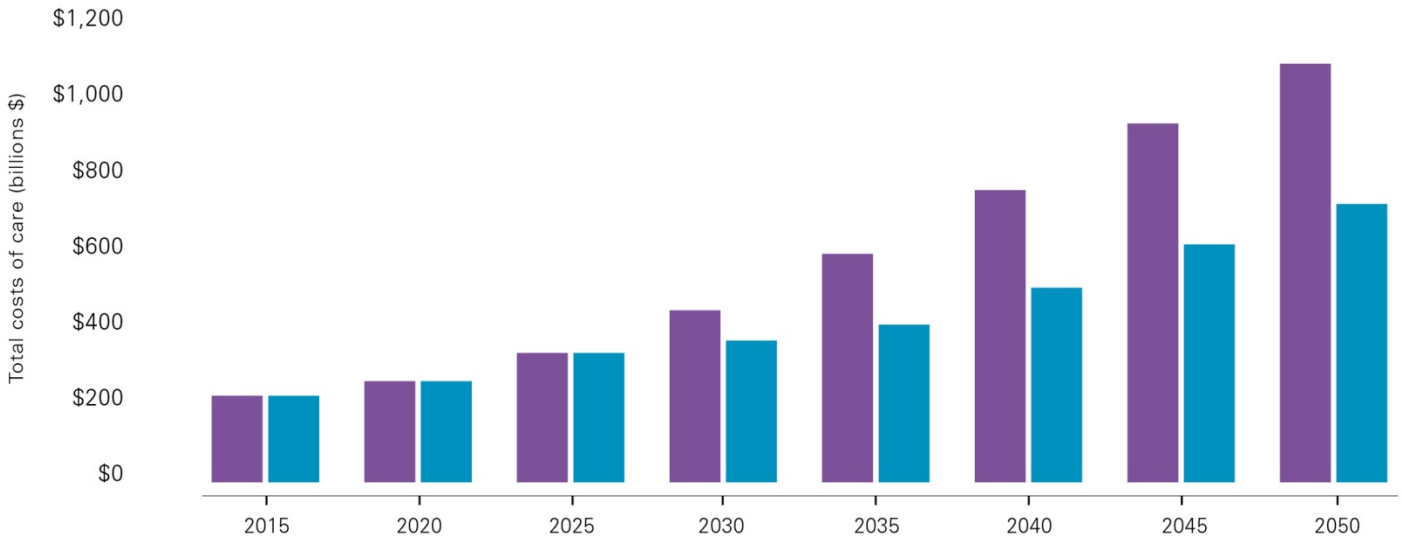
*Totals may not add due to rounding.

Source: A report to the Alzheimer's Association of America, completed by The Lewin Group, Washington DC in 2010. With permission.

The potential to change the trajectory of Alzheimer's disease

FIGURE 6

Impact of a Treatment That Delays Onset by Five Years on Total Costs, 2015-2050



	2015	2020	2025	2030	2035	2040	2045	2050
Current trajectory	$226	$267	$340	$451	$596	$767	$942	$1,101
Delayed onset	$226	$267	$340	$368	$417	$509	$622	$734
Savings	$0	$0	$0	$83	$180	$259	$320	$367

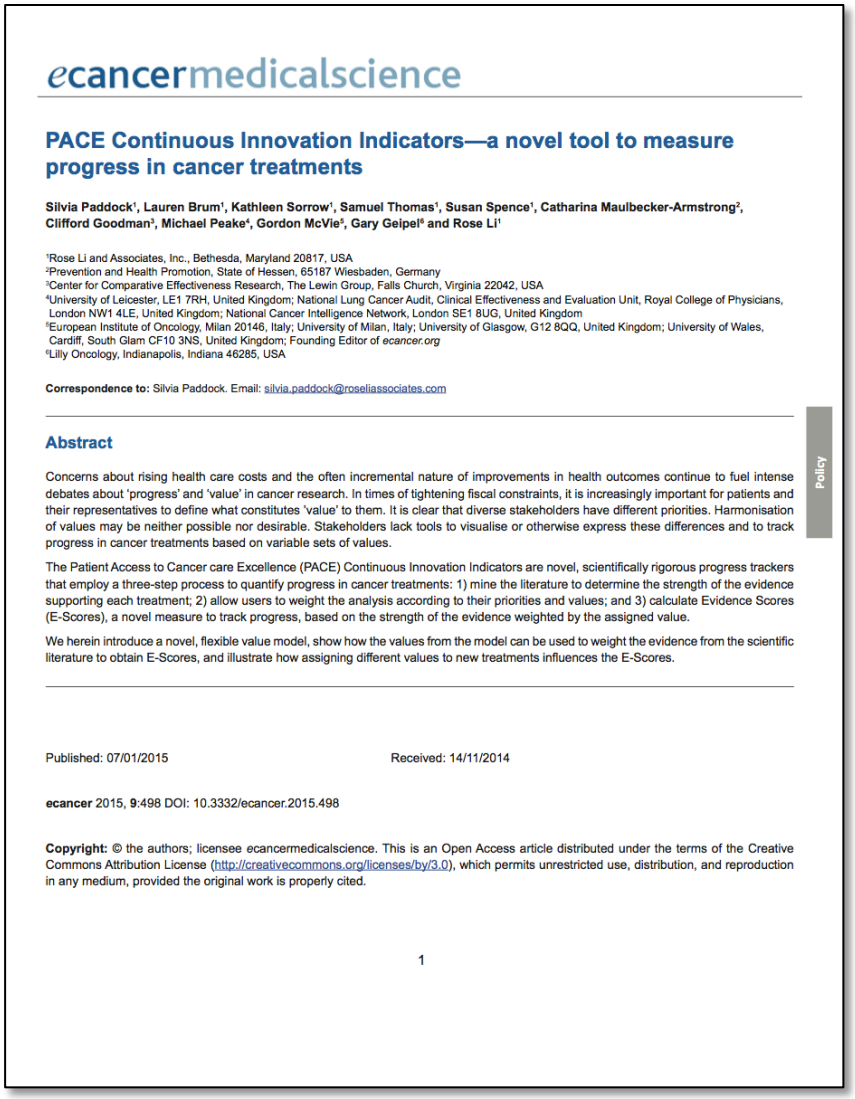
*All cost figures are reported in 2015 dollars. Totals may not add due to rounding.

Source: A report to the Alzheimer's Association of America, completed by The Lewin Group, Washington DC in 2010. With permission.

However, not all important innovation is “breakthrough”

- Innovation and progress in oncology has most often come in small steps
- While this has led to important gains in survival in many cancers, the rate of progress is too slow
- That is why Eli Lilly and Company developed its PACE initiative
  (Patient Access to Cancer Care Excellence)
- One specific project of PACE has been to develop a tool to illustrate the continuous nature of innovation in cancer and to help identify the gaps and needs

PACE Continuous Innovation Indicators



ecancermedicalscience

PACE Continuous Innovation Indicators—a novel tool to measure progress in cancer treatments

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Policy

Abstract

Concerns about rising health care costs and the often incremental nature of improvements in health outcomes continue to fuel intense debates about 'progress' and 'value' in cancer research. In times of tightening fiscal constraints, it is increasingly important for patients and their representatives to define what constitutes 'value' to them. It is clear that diverse stakeholders have different priorities. Harmonisation of values may be neither possible nor desirable. Stakeholders lack tools to visualise or otherwise express these differences and to track progress in cancer treatments based on variable sets of values.

The Patient Access to Cancer care Excellence (PACE) Continuous Innovation Indicators are novel, scientifically rigorous progress trackers that employ a three-step process to quantify progress in cancer treatments: 1) mine the literature to determine the strength of the evidence supporting each treatment; 2) allow users to weight the analysis according to their priorities and values; and 3) calculate Evidence Scores (E-Scores), a novel measure to track progress, based on the strength of the evidence weighted by the assigned value.

We herein introduce a novel, flexible value model, show how the values from the model can be used to weight the evidence from the scientific literature to obtain E-Scores, and illustrate how assigning different values to new treatments influences the E-Scores.

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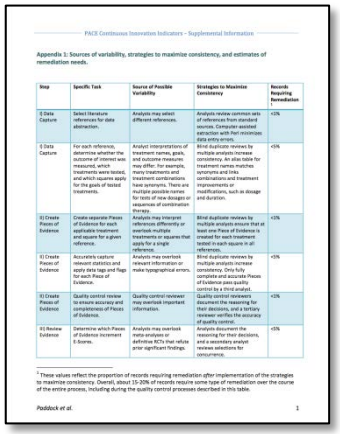
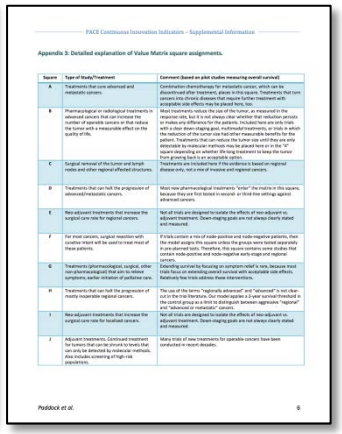
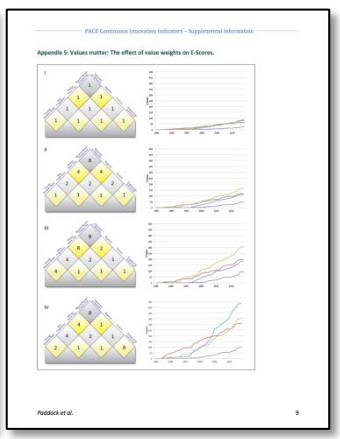
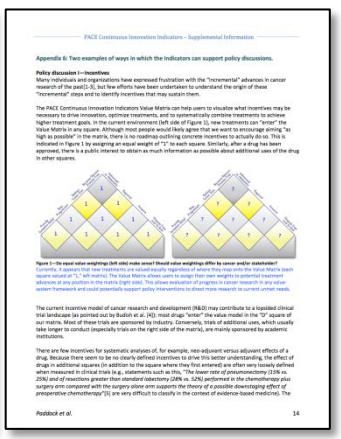


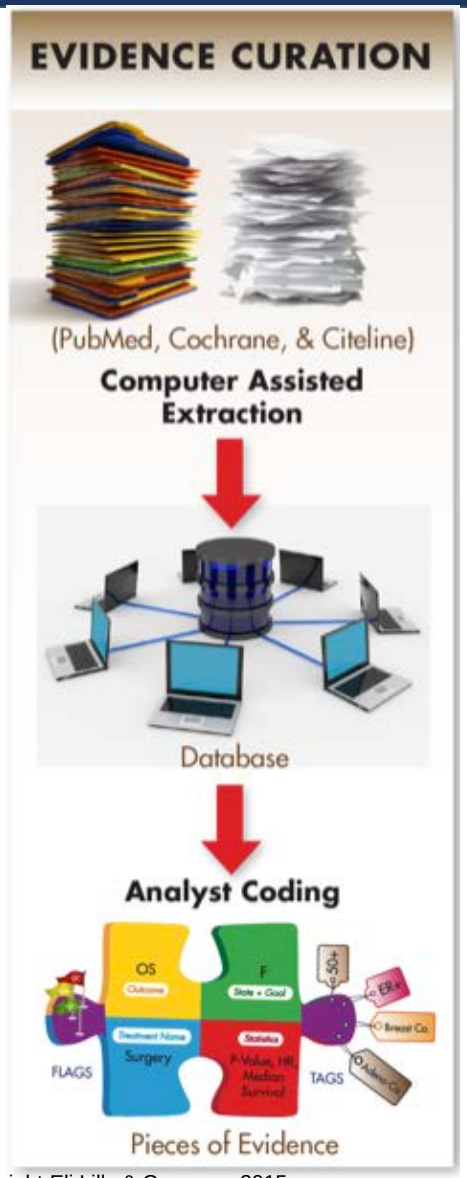






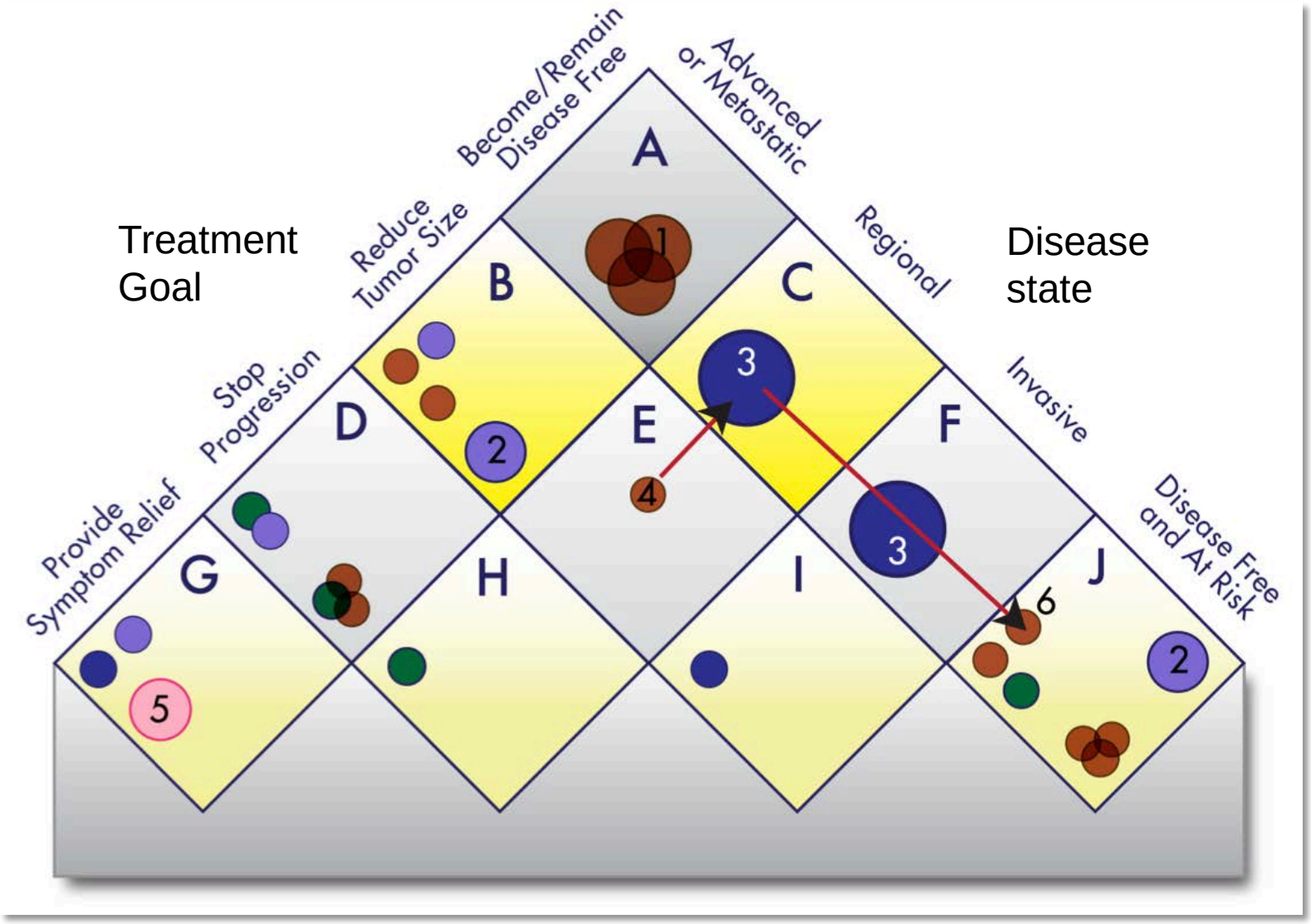
Paddock et al. *ecancermedicalscience* Jan. 2015
Policy paper; details on methodology provided in the supplemental information

PACE Innovation Indicators – Method



Database Name	Data Type	Number of Records	Comment
PubMed	Phase 2/3 clinical trial results in PubMed	4015	All records for 12 cancers of interest that mention “overall survival”
Oncology Reference (DeVita 9th Edition)	All PubMed references exported electronically	3325	Includes meta-analyses, register studies, etc. not covered in dataset above
Cochrane Library Database	Evidence Reviews	457	Only publicly accessible information is included
National Cancer Institute Physician Data Query (PDQ)	PubMed References quoted in the Health Professional Treatment Summaries	1549	We included all PDQ references, not only those associated with evidence ratings
PubMed and Books	Historic records	~25	Some innovation predates the above sources and has to be extracted from historical papers manually.
Citeline Pharmaprojects	Approval/Launch Data	120	Each of these compounds may be used in multiple cancers; the total number of data points is 524
Total		9491	

Scientific Value



Color codes:

Surgery

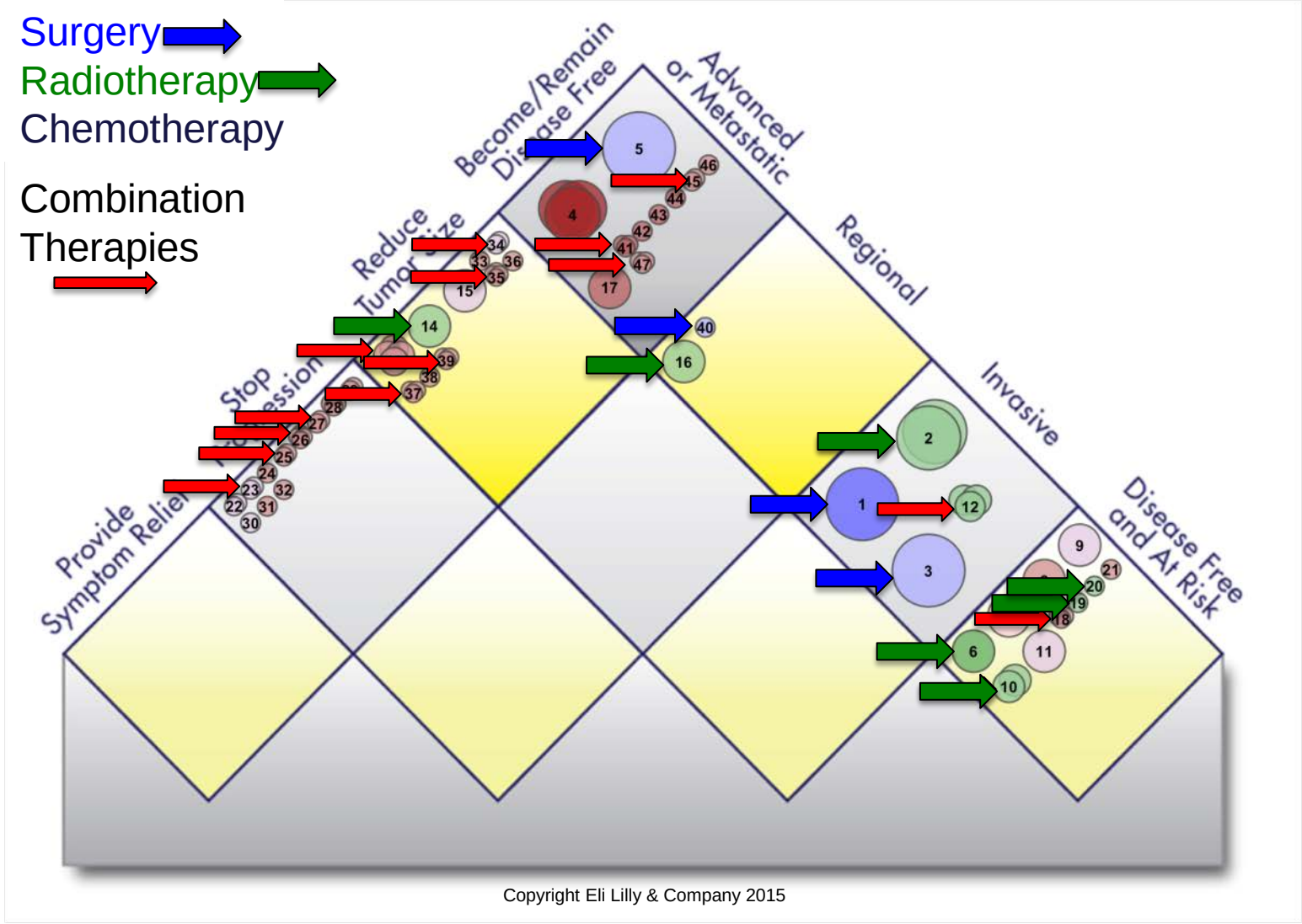
Radiotherapy

Chemotherapy

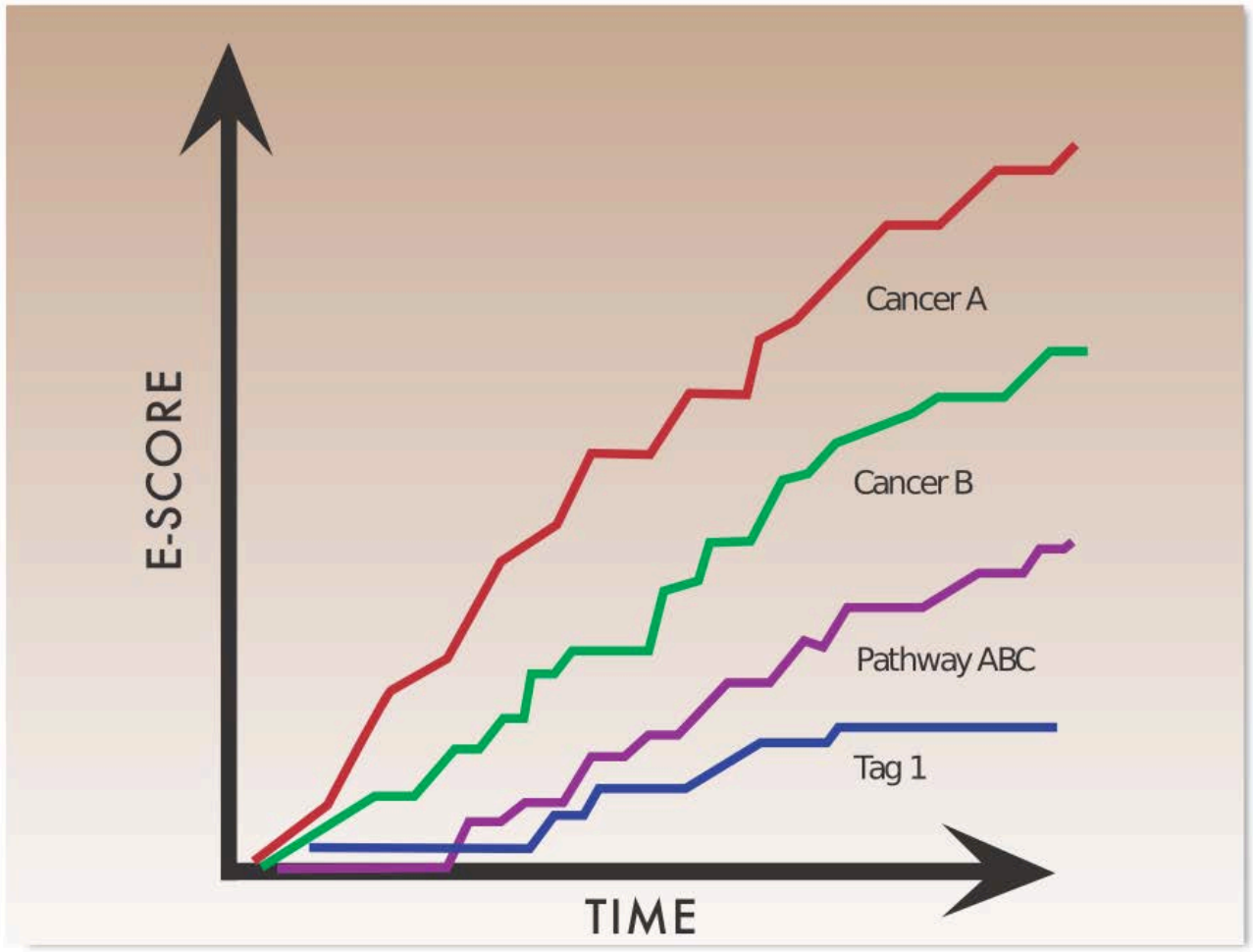
Treatment class evidence

Other (e.g., palliative care)

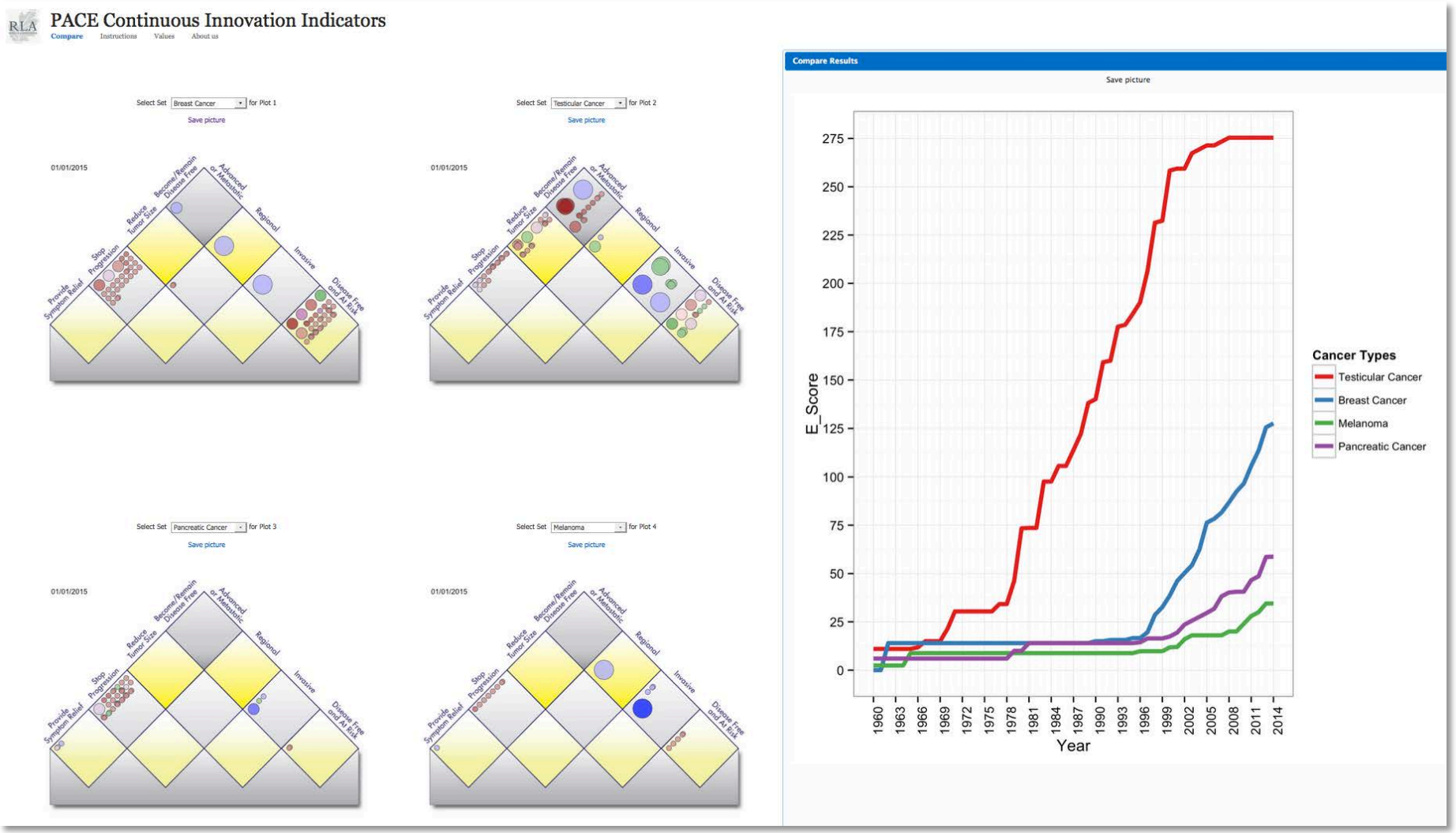
Testicular Cancer – PACE Value Matrix



Evidence (E)-Scores as a new measure of progress

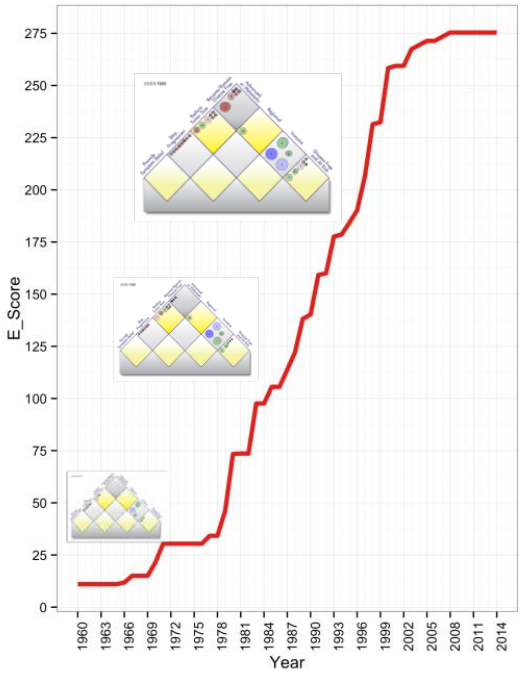


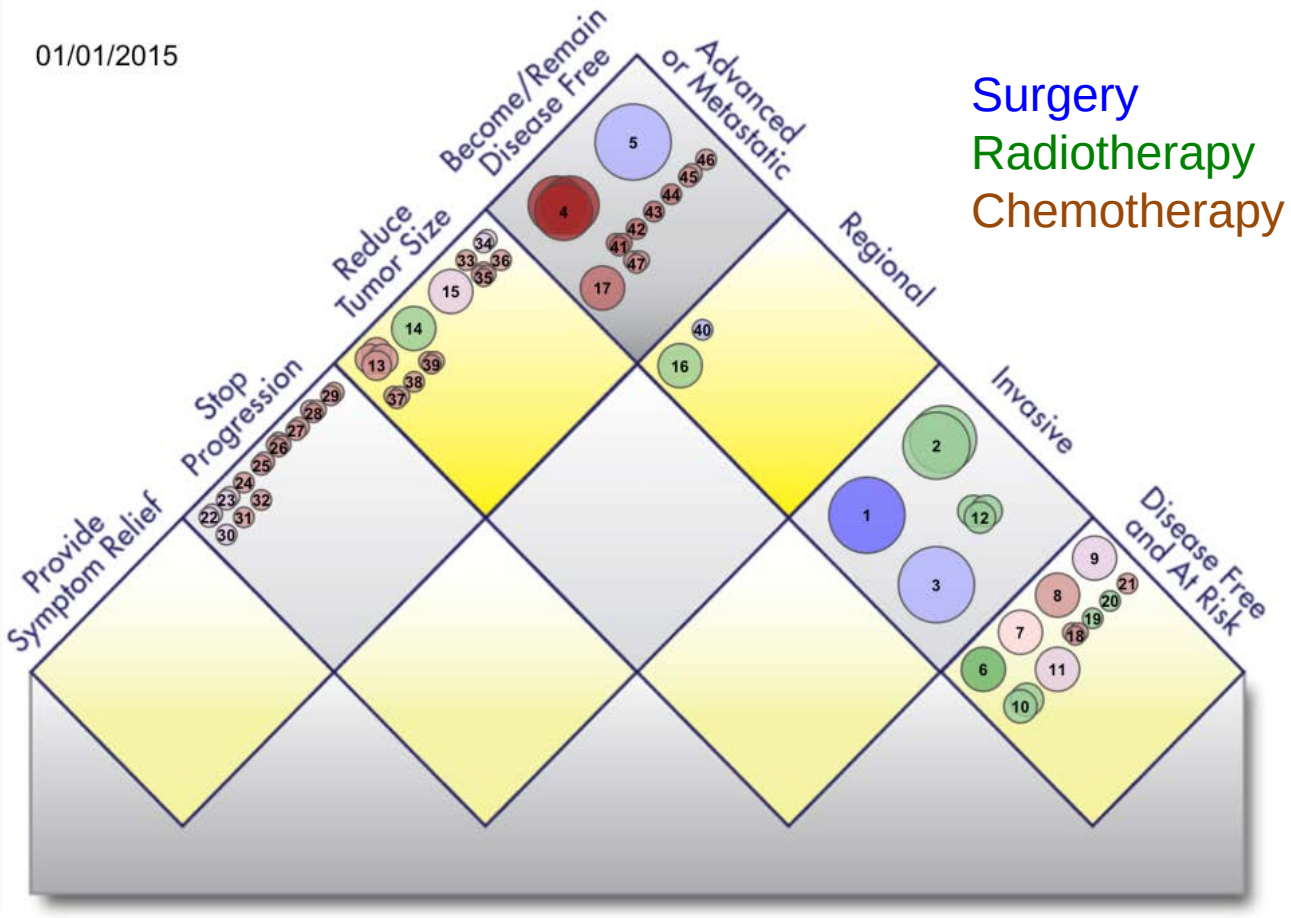
Platform Overview



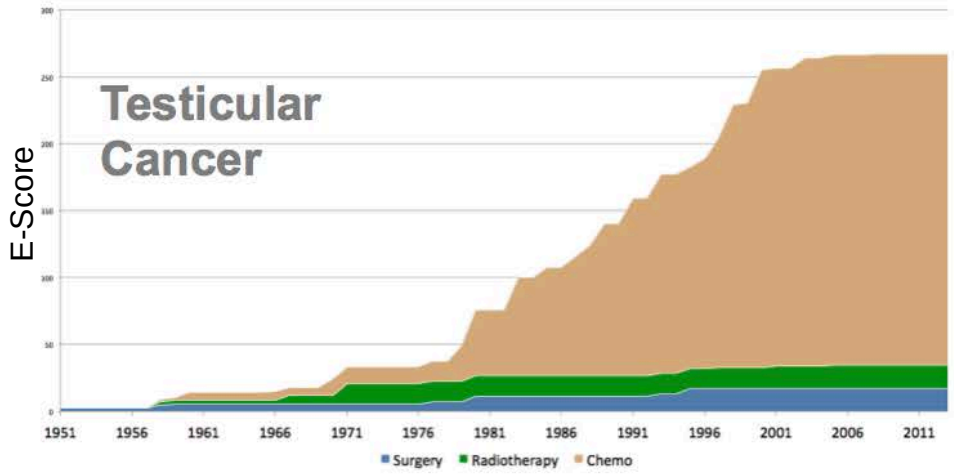
Testicular Cancer – Today

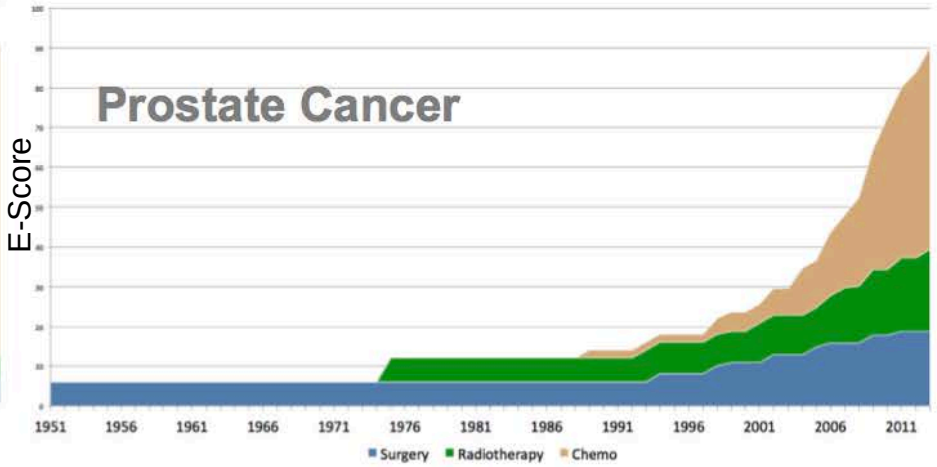
Progress Tracker

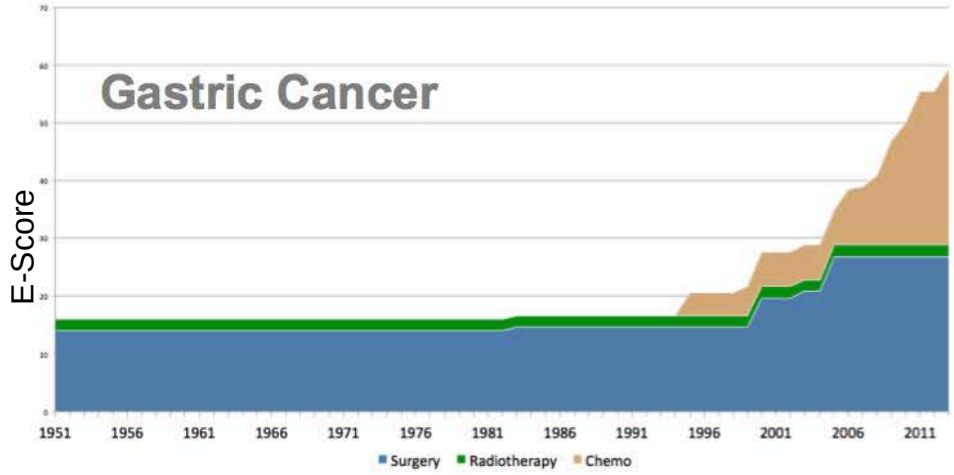


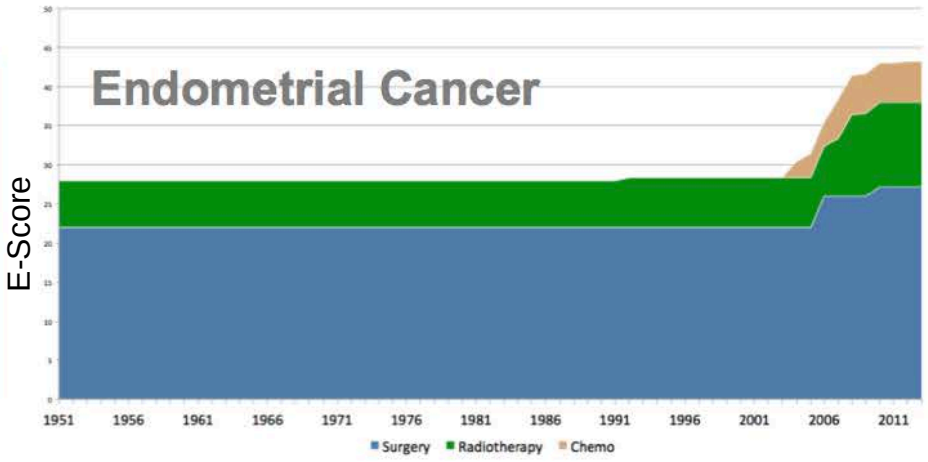


Results by Treatment Type









Getting the policy settings right

- An ecosystem that supports pharmaceutical innovation needs to ensure:
  - availability of excellent human resources,
  - access to government investment, private and venture capital,
  - protection of intellectual property rights,
  - predictable and transparent government policies.
- In addition, tomorrow's innovation requires additional conditions such as:
  - drug pricing policies that recognize and reward innovation, including the continuous nature of innovation in oncology,
  - overall regulatory, HTA and pricing processes that ensure patients' rapid accessibility to treatments.
  - increased investment in health system data that can support risk-sharing and related reimbursement agreements

Conclusions

- The innovation pipelines of the bio-pharmaceutical industry are delivering some exciting advances.

- Many of these have the potential to transform health outcomes (survival, functional ability and quality of life) in ways that change the experience of acute treatment. More patients may live longer with chronic, manageable illnesses and / or avoid progression to more severe illness.

- However, not all innovation is “breakthrough” and regulatory, HTA and reimbursement policies need to recognize this.