

Oncology Value Frameworks: A US Perspective

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DISCLOSURE SLIDE

- CVS Health consulting (<\$5000)
- JAMA associate editor consulting (>\$5000)

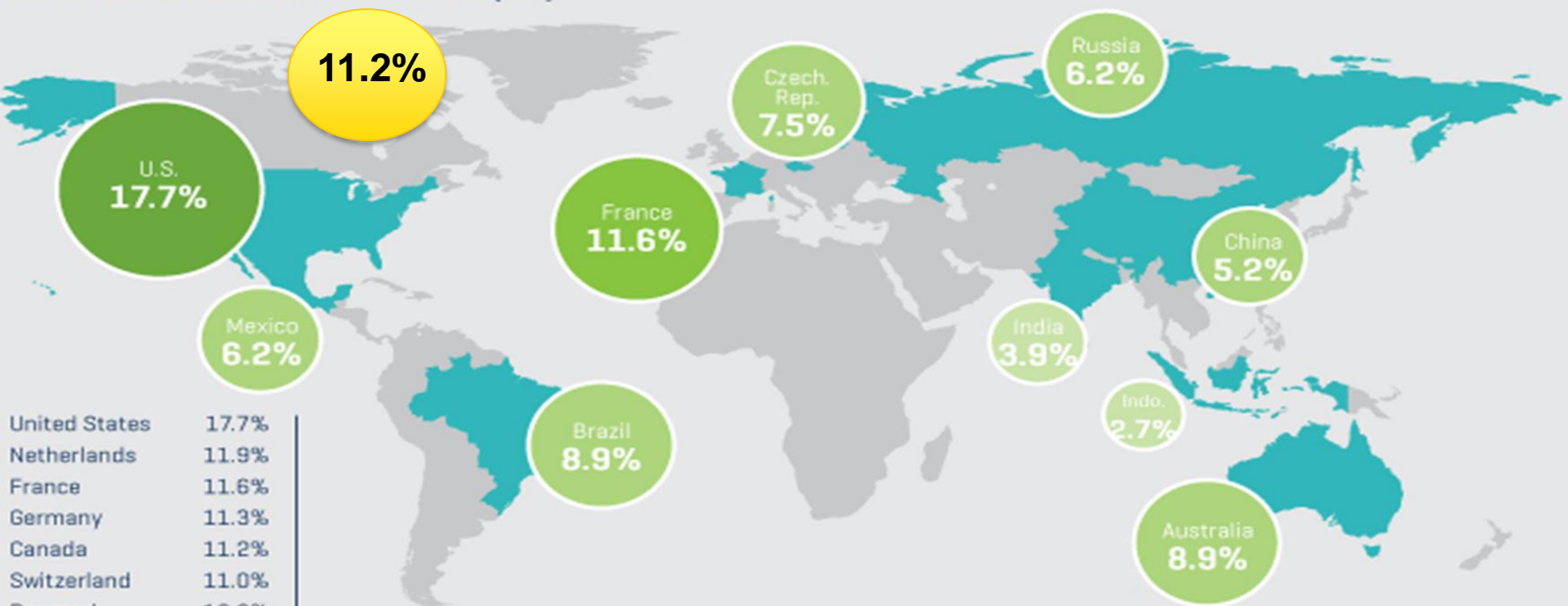
- Funding
 - ASCO
 - NIH, NCI
 - PCORI
 - Commonwealth of MA, State of NY
 - DOD

Value Frameworks in the Context of US Healthcare

- Genesis of Value Frameworks
- Overview of frameworks
- ASCO value framework
- Challenges and limitations
- Future of Value Frameworks

GLOBAL HEALTH CARE SPENDING

AS A PERCENT OF GROSS DOMESTIC PRODUCT (GDP)



United States	17.7%
Netherlands	11.9%
France	11.6%
Germany	11.3%
Canada	11.2%
Switzerland	11.0%
Denmark	10.9%
Austria	10.8%
Belgium	10.5%
New Zealand	10.3%
Portugal	10.2%
Japan	9.6%
Sweden	9.5%

United Kingdom	9.4%
Spain	9.3%
Norway	9.3%
Italy	9.2%
Greece	9.1%
Ireland	9.0%

Finland	9.0%
Australia	8.9%
Ireland	8.9%
Brazil	8.9%
Slovenia	8.9%
Hungary	7.9%

Israel	7.7%
Chile	7.5%
Czech Republic	7.5%
South Korea	7.4%
Poland	6.9%
Luxembourg	6.6%

Russian Fed.	6.2%
Mexico	6.2%
Turkey	6.1%
China	5.2%
India	3.9%
Indonesia	2.7%

What is Value? What Do We Value?

- Value: worth, usefulness, benefit
- Valuation: process of determining the magnitude of benefit
- Values: judgments, core beliefs about what matters

Value

vs

Values

$$\text{Value} = \frac{\text{Health Outcomes}}{\text{Costs}}$$

Values:

- Autonomy & Respect
- Compassion & Beneficence
- Fairness & Equality

➔ Possible, but hard to quantify

➔ Impossible to quantify

Why Are We Even Having This Conversation?

Many interventions in cancer medicine provide:

very small extra benefit

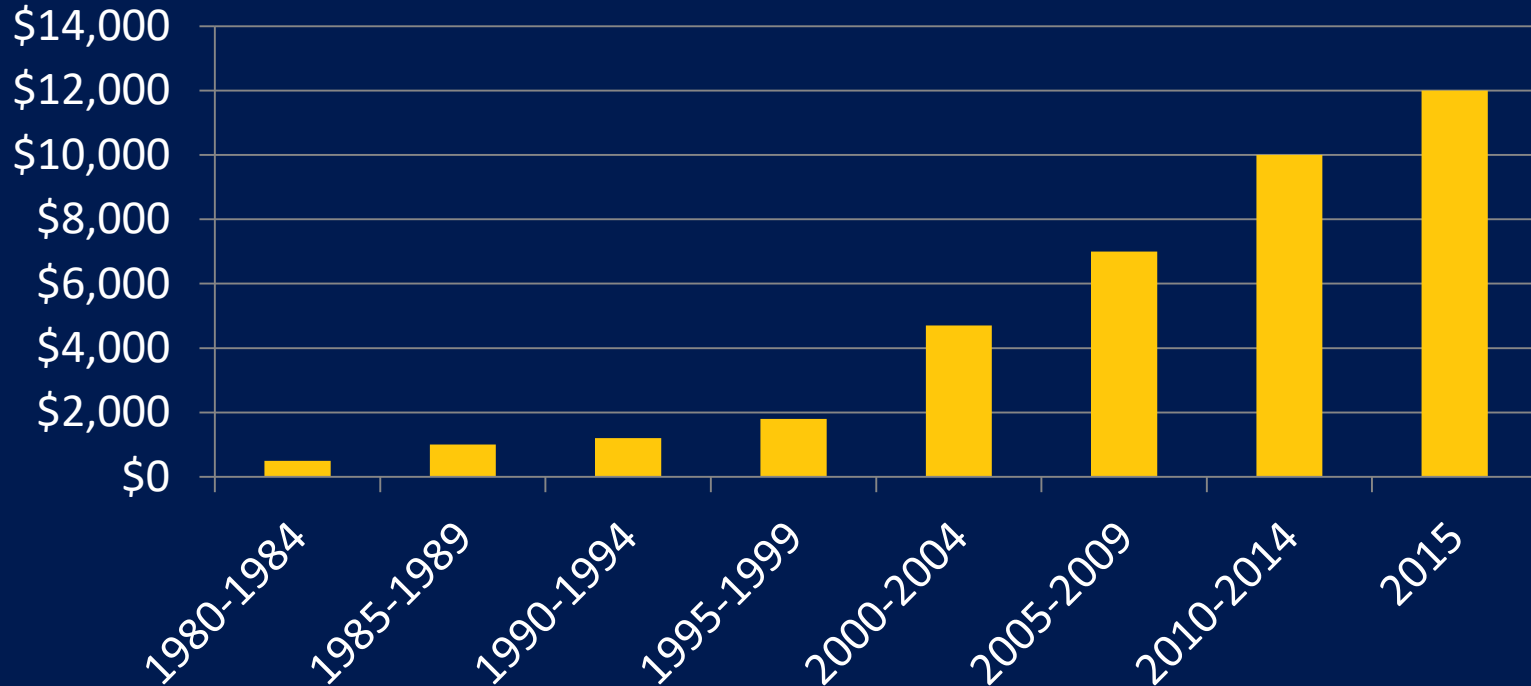
enormous additional costs

US Drug Development Process

FDA	CMS and other insurers	Physicians, Researchers	Health Care Systems	Society
Can this drug work?	Is it reasonable and necessary? Should we cover it?	Should we recommend it? Is it effective?	What efforts should we make to implement utilization?	How do we value this treatment intervention?

Cost is not an explicit component of US drug development

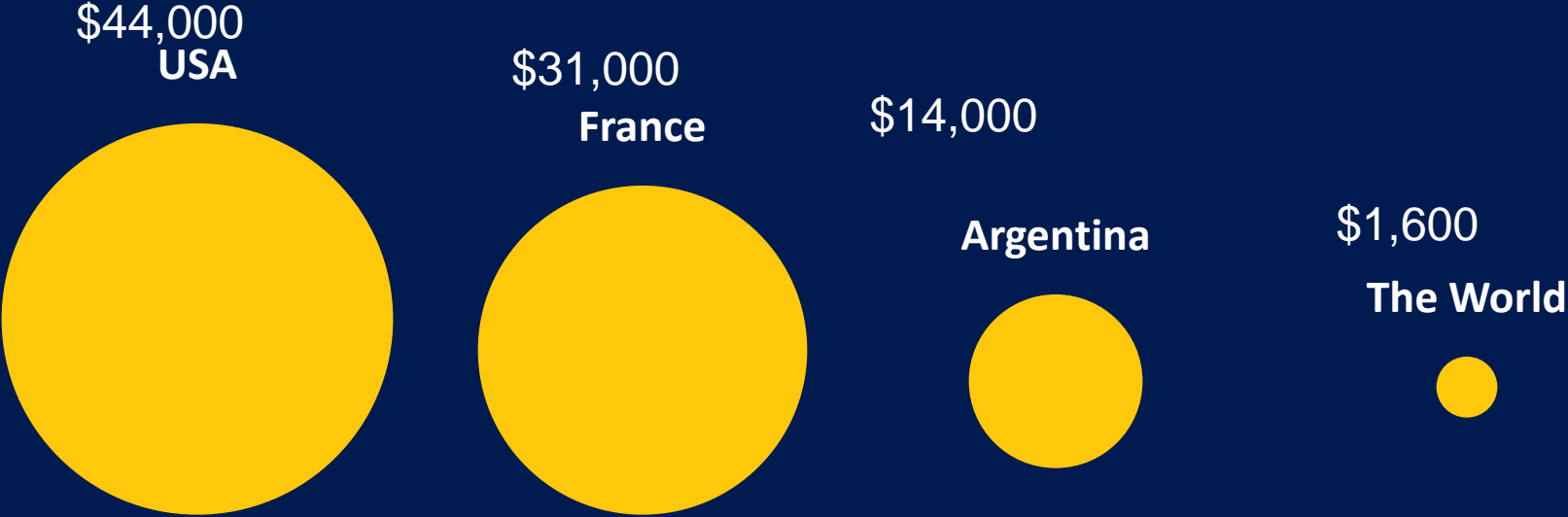
Soaring Cost of New Cancer Drugs



US costs in constant 2015 US\$ based on FDA approved monthly drug costs inflation adjusted

Valued but Unaffordable

Cancer is a financial catastrophe if costs of treatment exceed median annual household income



Estimates from 2006-2012 PPP constant \$US

How Does Low Value Healthcare Hurt Individuals & Families with Cancer?

↑↑ Costs
Cancer Treatment



- ↓ Access
- ↓ Adherence
- ↓ Effectiveness
- ↓ Recovery
- ↑ Suffering (stress & bankruptcy)

How Does Low Value Health Care Hurt Society?



Value and Our Conflicting Values



Alive: Jimmy a 91 year old from US with metastatic melanoma whose chemo costs exceed \$100,000/year



Dead: Oliver a 9 y/o with NHL from South America- potentially curative chemo was unaffordable

Five Value Frameworks in Oncology

2015-2016

	ABACUS-MSKCC	ICER	NCCN	ESMO	ASCO
The Core Question	What is the just price for a cancer drug?	What is the societal value?	How do expert clinicians rate a treatment's value?	What is the clinical value?	What is the clinical benefit in relation to cost?

ASCO's Goal

“Value and cost are among the biggest issues in healthcare today, but there are few tools to help doctors and patients objectively assess benefits, side effects and costs”

“Our goal is to help oncologists and their patients weigh potential treatment options based on high-quality scientific evidence and a thoughtful assessment of each patient's needs and goals”

“This is just the beginning of the process, we hope to drive discussion and debate about a critically important issue.”

-ASCO President Julie M. Vose, MD, MBA, FASCO 2015.

ASCO's value framework

- “Our goal is to help oncologists and their patients weigh potential treatment options based on high-quality scientific evidence and a thoughtful assessment of each patient’s needs and goals”
—J. Vose
- Applies only to interventions compared directly in RCTs
- Distinct frameworks for adjuvant and advanced disease
- Net Health Benefit (NHB): Scored on point system—
 - Max of 130 for advanced
 - Max of 100 for curative intent (adjuvant)
- Costs and NHB displayed side by side: no ratio
- Considers only 2 components of cost
 - Monthly drug acquisition cost (practice perspective)
 - Patient out of pocket (patient perspective)

Advanced Disease ASCO Framework:

Step 1: Determine Clinical Benefit

1.A. Is hazard ratio (HR) for death reported?	<p>YES. Assign an <u>HR Score for death</u> by subtracting the HR from 1, and then multiplying the result by 100. Write this number in the box labeled “HR Score (death).” Proceed to 1.F.</p> <p>No. Proceed to 1B.</p>	HR Score (death)
1.B. If HR for death is not reported, is median overall survival (OS) reported?	<p>YES. Assign an <u>OS Score</u> by calculating the percentage (ie, fractional) difference in median overall survival between the two regimens and multiply the result by 100. Write this number in the box labeled “OS Score.” Proceed to 1.F.</p> <p>NO. Proceed to 1.C.</p>	OS Score
1.C. If OS data are not reported, is hazard ratio (HR) for disease progression reported?	<p>YES. Assign an <u>HR Score for disease progression</u> by subtracting the HR from 1, multiplying the result by 100, and then multiplying this number by 0.8. Write this number in the box labeled “HR Score (progression).” Proceed to 1.F.</p> <p>NO. Proceed to 1.D.</p>	HR Score (progression)
1.D. If HR for disease progression is not reported, is median progression-free survival (PFS) reported?	<p>YES. Assign a <u>PFS Score</u> by calculating the percentage (ie, fractional) difference in median progression-free survival between the two regimens and multiply the result by 100. Multiply this number by 0.8. Write this number in the box labeled “PFS Score.” Proceed to 1.F.</p> <p>NO. Proceed to 1.E.</p>	PFS Score
1.E. If median PFS is not reported, is response rate (RR) reported?	<p>YES. Assign an <u>RR Score</u> by adding the complete response (CR) and partial response (PR) rates, multiply by 100, then multiply this number by 0.7. Write this number in the box labeled “RR Score.” Proceed to 1.F.</p>	RR Score
1.F. Calculate the Clinical Benefit Score	<p>Insert the score for HR death, HR PFS, median OS, or median PFS.</p> <p>Note: You should have a score for only 1 of the clinical benefit scales above.</p> <p>Write the total in the box labeled “Clinical Benefit Score.” Proceed to Step 2.</p>	Clinical Benefit Score

Advanced dz framework

Applies a hierarchy of outcomes

Overall survival (1)

Progression free survival (0.8)

Response rate (0.7)

Advanced Disease ASCO Framework:

Step 2: Determine Toxicity

Toxicity points:

- More points for more severe or more frequent toxicity
- Add points if new regimen is less toxic
- Subtract if new regimen is more toxic
- More points for persistent toxicity
- Total of 20 points
- Requires careful review of toxicity tables in RCT

Does the new regimen represent an improvement in toxicity over the standard of care/comparator?

For each of the regimens being assessed, compare the number and frequency of clinically relevant toxicities, and assign a Toxicity Score as shown below. Each clinically meaningful toxicity (ie, exclude laboratory results only) is assigned a score between 0.5 and 2.0 based on grade and frequency: For every grade 1 or 2 toxicity with a frequency < 10%, record 0.5 points. For every grade 1 or 2 toxicity with a frequency ≥ 10%, record 1.0 points. For every grade 3 or 4 toxicity with a frequency < 5%, record 1.5 points. For every grade 3 or 4 toxicity with a frequency ≥ 5%, record 2.0 points.

Calculate the total number of toxicity points for each regimen. Calculate the percentage difference in total toxicity points between the two regimens, then multiply by 20 to obtain a toxicity score. If the regimen being evaluated is more toxic than the comparator, subtract the toxicity score of the regimen from the clinical benefit score. If the regimen is less toxic than the comparator, add the toxicity score of the regimen to the clinical benefit score. **If there are unresolved symptomatic treatment-related toxicities at 1 year after completion of treatment, subtract 5 additional points from the clinical benefit score.** The maximum points that can be awarded is 20. **Proceed to Step 3.**

Toxicity Score

Advanced Disease ASCO Framework:

Step 3: Consider Bonus Points: “Tail of the Curve”

3.A. TAIL OF THE CURVE. Identify the time point on the survival curve that is 2X the median OS (or PFS) of the comparator regimen. Is there a 50% or greater improvement in proportion of patients alive with the test regimen at this time point (assuming > 20% surviving with standard)?

YES. If yes, award 20 points if the improvement is in OS, and 16 points (0.8 x 20) if the improvement is in PFS, and place this number in the box labeled “Tail of the Curve Bonus Points.”

Proceed to Step 3.B.

NO. No bonus points are awarded.

Proceed to Step 3.B.

Tail of the Curve Bonus Points

How durable is the benefit of the intervention?

Metric: At 2x the median OS for the comparator arm is the benefit >50%?

Example: If median survival is 4 months for comparator rx, then survival at 8 months must exceed 75% for new treatment in order to accrue tail of the curve bonus

Up to 20 tail points

Advanced Disease ASCO Framework:

Step 3: Consider Bonus Points:

3.B. PALLIATION BONUS. Is an improvement in cancer- related symptoms reported?	YES. If a statistically significant improvement in cancer-related symptoms is reported for the regimen being evaluated, award 10 points, and place this number in the box labeled “Palliation Bonus.” Proceed to Step 3.C.	Palliation Bonus
	NO. No bonus points are awarded. Proceed to Step 3.C.	
3.C. QoL BONUS. Is an improvement in QoL reported?	YES. If a statistically significant improvement in QoL is reported for the regimen being evaluated, award 10 points, and place this number in the box labeled “QoL Bonus.” Proceed to Step 3.D.	QoL Bonus
	NO. No bonus points are awarded. Proceed to Step 3.D.	
3.D. TREATMENT-FREE INTERVAL BONUS. Are data related to <u>treatment-free interval</u> reported?	YES. If a statistically significant improvement in treatment-free interval is reported for the regimen being evaluated, multiply the percentage improvement by 20 and award points. Proceed to 3.E.	Treatment-Free Interval Bonus
	NO. No bonus points are awarded. Proceed to Step 3.E.	
3.E. Calculate Total Bonus Points	Add the Palliation Bonus Points (Step 3.A), the Treatment-Free Interval Bonus Points (Step 3.B), and the QoL Bonus Points (Step 3.C.). Write this number in the box labeled “Total Bonus Points.” The maximum points available for Bonus Points is 60. Proceed to Step 4.	Total Bonus Points

Other Bonus points for

- Palliation
- Quality of Life
- Treatment free interval

The ASCO Value Framework: Net Health Benefit

Domain	Scoring Algorithm: Advanced Disease
Clinical Benefit	Score 1 metric (hierarchical order) <ol style="list-style-type: none"> HR Score: $(1 - \text{HR for OS}) * 100$ % change in median survival * 100 PFS Score: $(1 - \text{HR for PFS}) * 0.8 * 100$ Response: $(\% \text{ Response (CR+PR)}) * 0.7 * 100$
Toxicity	Assign toxicity points Treatment toxicity (+ if ↓, - if ↑ up to 20) Late toxicity (-5 if present at 1 year)
Tail of Curve	OS → 50% better at 2x median of control (20)
Palliation	Significant decrease in symptom burden (10)
Quality of Life	Significant increase in QoL (10)
Rx Free Interval	% improvement in Rx-free interval * 20

Total # of Points = Net Health Benefit Maximum Score = 130 (advanced disease)

Advanced Disease ASCO Framework: Considers Drug Acquisition Costs and Patient payment

Step 4: Determine the regimen's NET HEALTH BENEFIT			
Calculate the <u>Net Health Benefit</u>	Add the Clinical Benefit Score (Step 1), Toxicity Score (Step 2), and Bonus Points (Step 3). This yields a Net Health Benefit Score. Write this number in the box labeled "Net Health Benefit." Proceed to Step 5 .		Net Health Benefit
Step 5: Determine the regimen's COST			
Insert the drug acquisition cost (DAC) and patient co-pay based on how much the treatment regimen costs per month.		Cost (per month) DAC:	Patient Payment:
Step 6: Summary Assessment: Advanced Disease Framework			
Clinical Benefit	Bonus Points	Net Health Benefit	Cost (per month)
			DAC: Patient Payment:

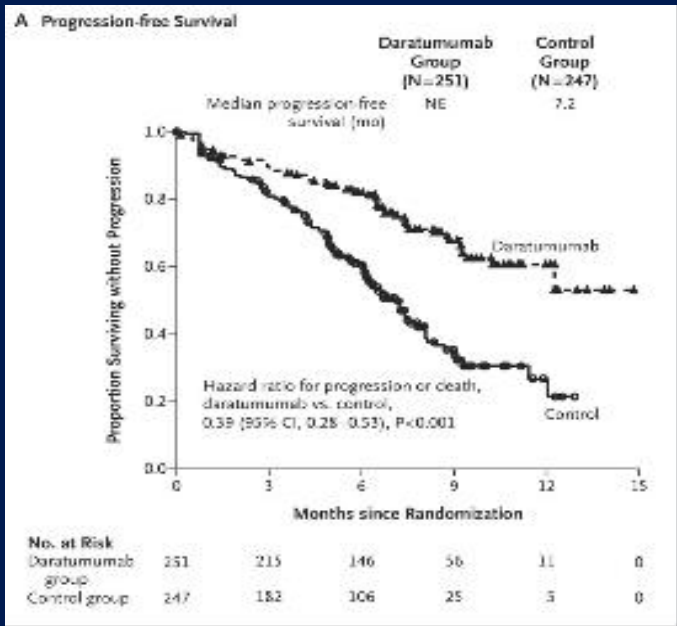
Net health benefits juxtaposed with drug acquisition costs and patient cost-share

Challenging to interpret without knowledge of scores for other interventions

Requires knowledge of drug acquisition costs and patient OOP share

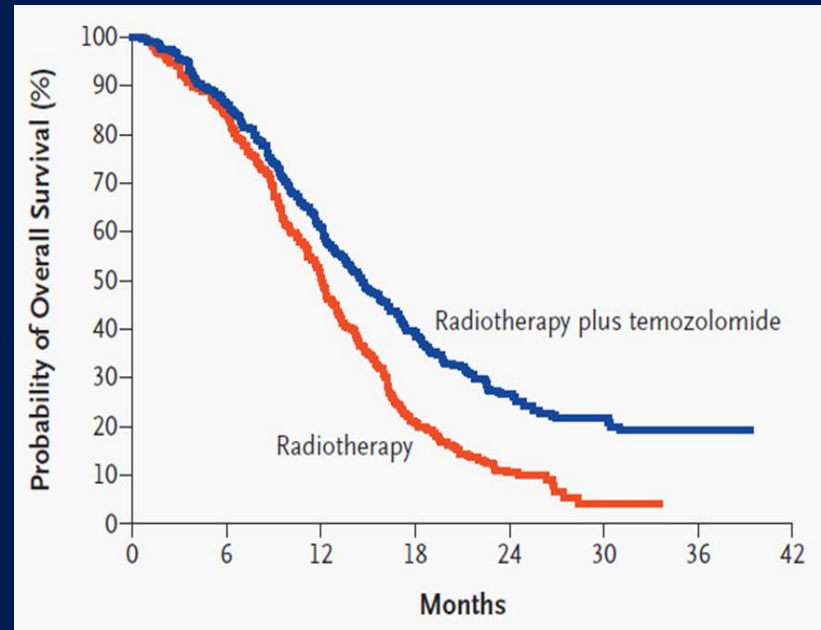
2 Examples: RCTs in Advanced Cancer: ASCO Plenary Abstracts 2016

12 month PFS of 61% vs. 27%
Median not reached



Daratumumab for Multiple Myeloma
Palumbo et al NEJM 2016 and ASCO Plenary

Median Overall Survival of 9.3 vs.
7.6 months, HR=0.67



XRT + or - temozolomide in glioblastoma
Perry et al NCI-Canada Group ASCO Plenary 2016

ASCO Value Framework: Advanced Disease

Scoring Domain	Daratumumab in Multiple Myeloma	Temozolomide with XRT in GBM
Clinical Benefit	HR for PFS=0.39; 1-.39=.61; .61*.8=49 49	HR for OS=0.67; 1-0.67=0.33 33
Toxicity (acute & late)	0	0
Bonus		
Tail of the Curve	0	10
Palliation	0	0
Quality of Life	0	0
Treatment Free Interval	0	0
Net Health Benefit	49	43
Patient cost/mo (USA estimates at 20% co-pay)	\$4680 (mo 1-2) \$2340 (mo 3-6) \$1170 (mo 6-12)	\$380 (mo 1) \$260 (mo 2-12)
Drug Acquisition Cost/month (USA estimates at ASP)	\$23400 (mo 1-2) \$11700 (mo 3-6), \$5850 (mo 6-12)	\$1900 (mo 1) \$1300 (mo 2-12)

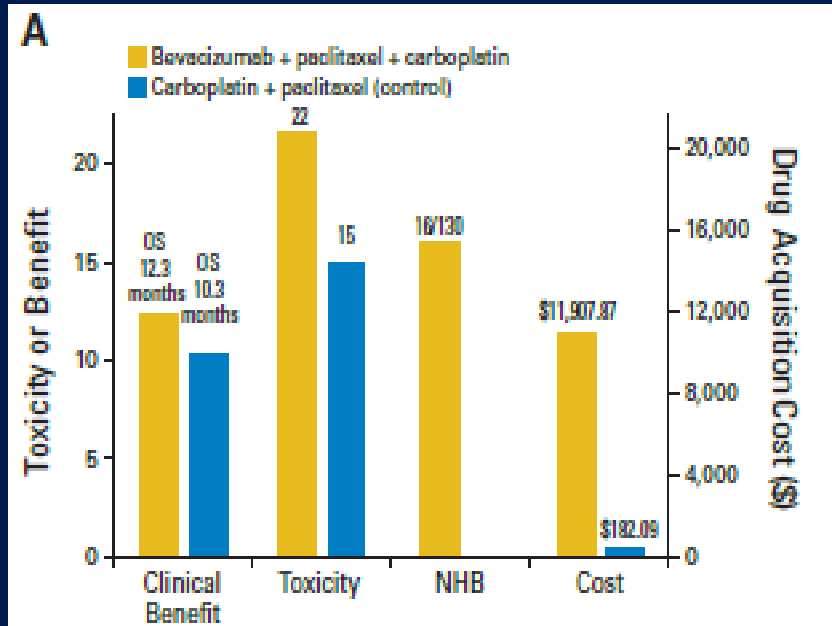
Drug costs estimated from CMS part B for BSA=1.7 and mid tier Silver Part D plan

ASCO Value Framework in Advanced NSCLC

Low Value

Adding Bev to Carbo/Tax

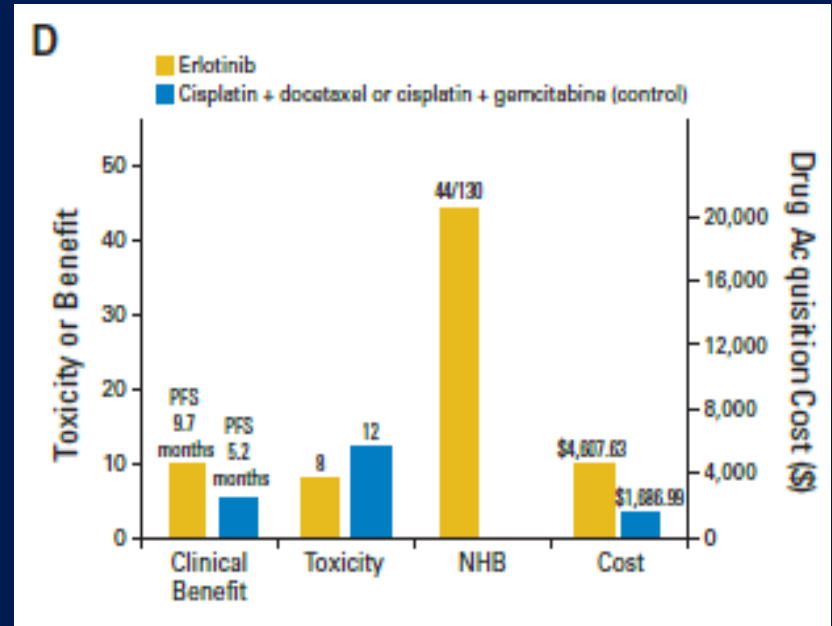
- NHB=16 points, DAC: >\$10K/month
- Small extra benefit, big extra costs



Moderate value:

Erlotinib versus Cis-Doublets

- NHB=44 points DAC: \$3000
- Big extra benefit, moderate extra costs



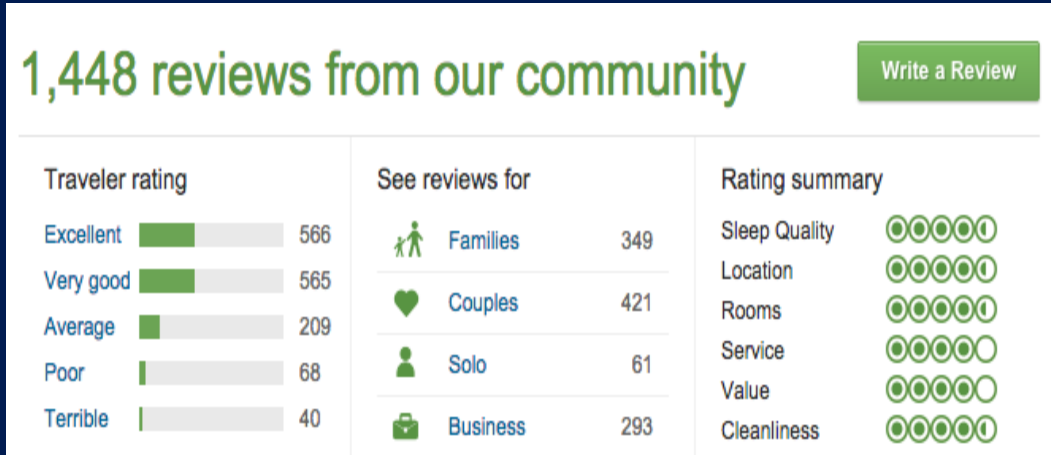
ASCO's Framework: Challenges for Implementation

- VALIDITY of INTRA TRIAL COMPARISONS: POSSIBLY
- VALIDITY OF INTER-TRIAL COMPARISONS: ABSOLUTELY NOT
- Complexity
- Time constraints
- Entrenched cultural traditions
- Lack of transparent information about costs and their variation over time
- Uncertain role of value discussions at “bedside”

Personal Values: Access to Information

Trip Advisor: Quest for a nice 4-star hotel in Rome

Ratings Data



Anecdotes

“You have to be small and thin”

Reviewed 1 week ago

Stayed at this hotel for 2 nights, the single room was not larger than Ikea closet. The bed was half the size of a normal bed, preventing you to chose which side you will get off. It was a sofa. The bathroom you kept on knocking on things, as it was so small. The sho small, that it would have fit a small child of 5 years old. The ventilations

“Great Location and rooms”

Reviewed 2 weeks ago

This hotel is in a great location. Steps away from the Trevi fountain and in the heart of a great little neighborhood with many places to eat and relax. Just a quick cab ride away from the train station, the Vatican and almost anywhere in Rome. The rooms was spacious clean and the

Patients Like Me

The Power of Patient Social Networks: More users, better info







Why patients stopped taking Lenalidomide

Multiple reasons could be selected

Reason	Patients
Side effects too severe	5
Course of treatment ended	4
Doctor's advice	3
Did not seem to work	2
Other	1

Cost per month

Cost per month	Patients	Percentage
\$200+	5	14%
\$100-199	0	0%
\$50-99	3	8%
\$25-49	4	11%
< \$25	14	38%
Not specified	11	30%

Treatment name(s)	Perceived effectiveness	Side effects	How many evaluations	Tried for
Stem Cell Transplant (Autologous CD34+ Stem Cell Transplant)	 for Multiple Myeloma (22 evaluations)	 Hospitalization, Diarrhea ▶ 24 more	22	Multiple Myeloma
Bortezomib- cyclophosphamide- dexamethasone (VcD or CyBorD)	 for Multiple Myeloma (22 evaluations)	 Peripheral Neuropathy, Fatigue ▶ 15 more	22	Multiple Myeloma
Lenalidomide (Revlimid)	 for Multiple Myeloma (49 evaluations)	 Diarrhea, Fatigue ▶ 27 more	49	Multiple Myeloma

Communicating Value: Treatment Benefits

Died, no Breast CA



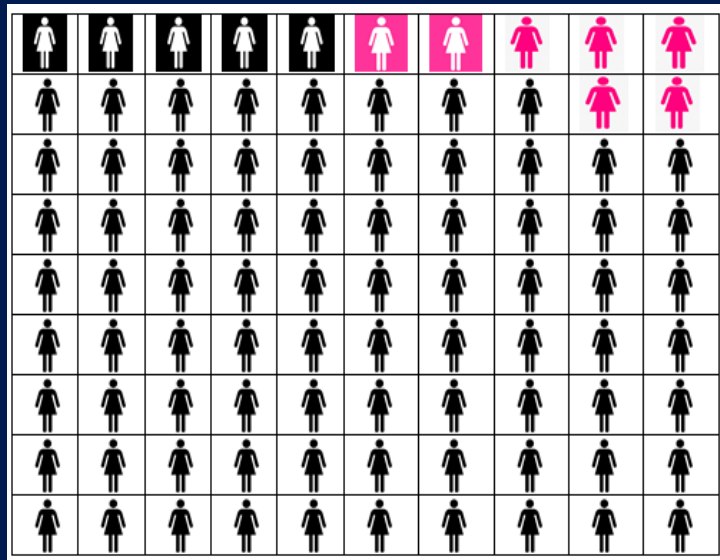
Died of Breast CA



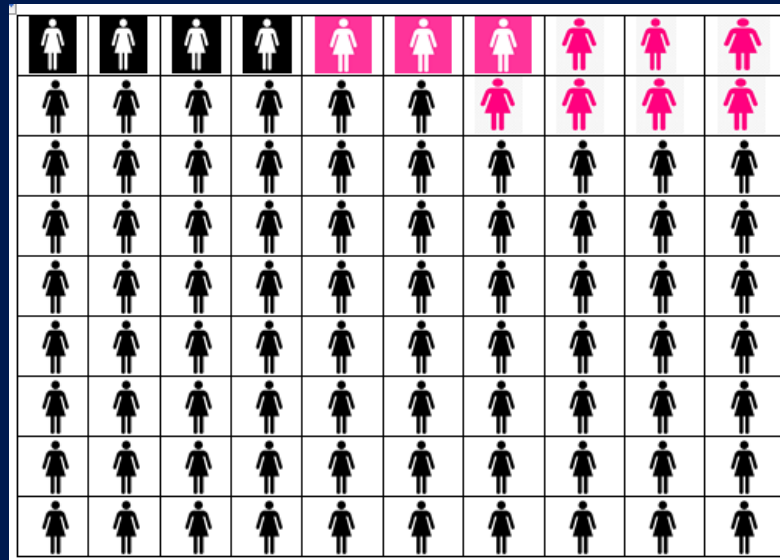
Alive with Breast CA



Alive without Breast CA



5 more years of Letrozole



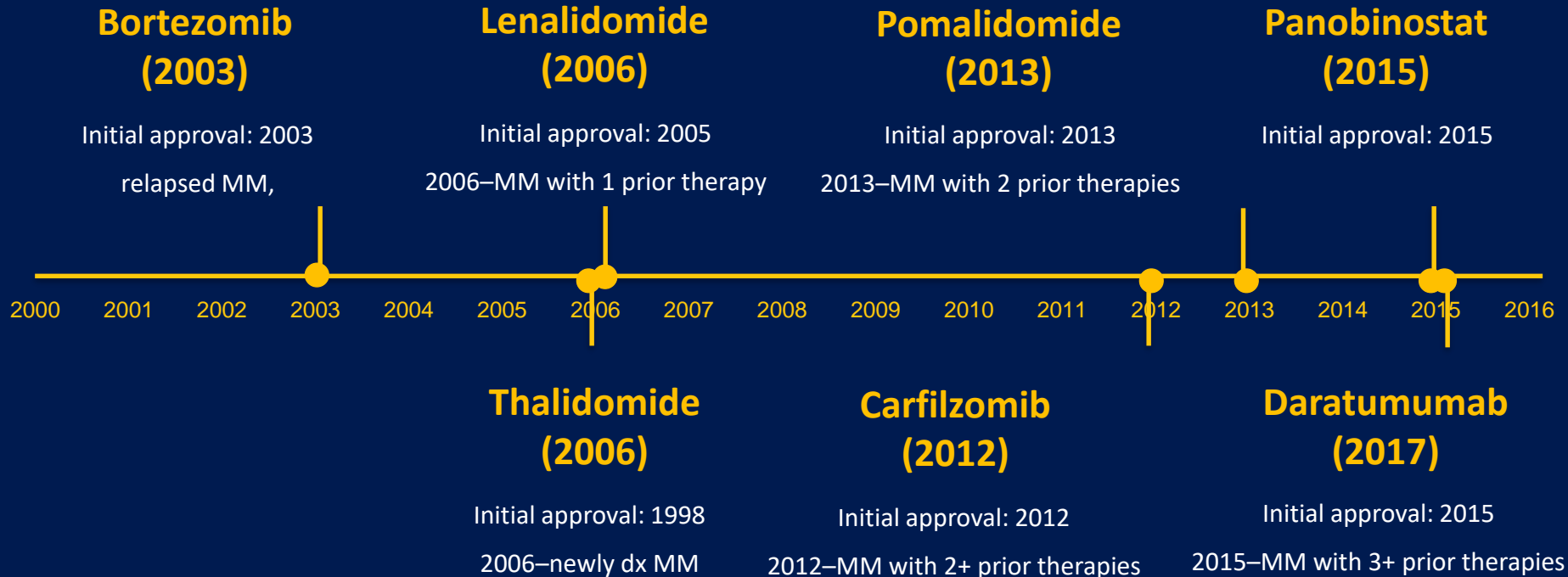
No Letrozole

Future of ASCO's Framework

- Less emphasis on estimating value “at the bedside”
- Shift to focus on valuing strategies in pathways/guidelines
- Value based pricing and tiering
- Clearer communication about “bottom line” clinical benefit
- Push for greater cost transparency
- Embedding value into reimbursement and coverage decisions
- New payment models
- Principles, not specifics

Will More Options Lead to Greater Price Competition?

Recent FDA approvals for Multiple Myeloma Drugs



Drug Approval Process is Changing

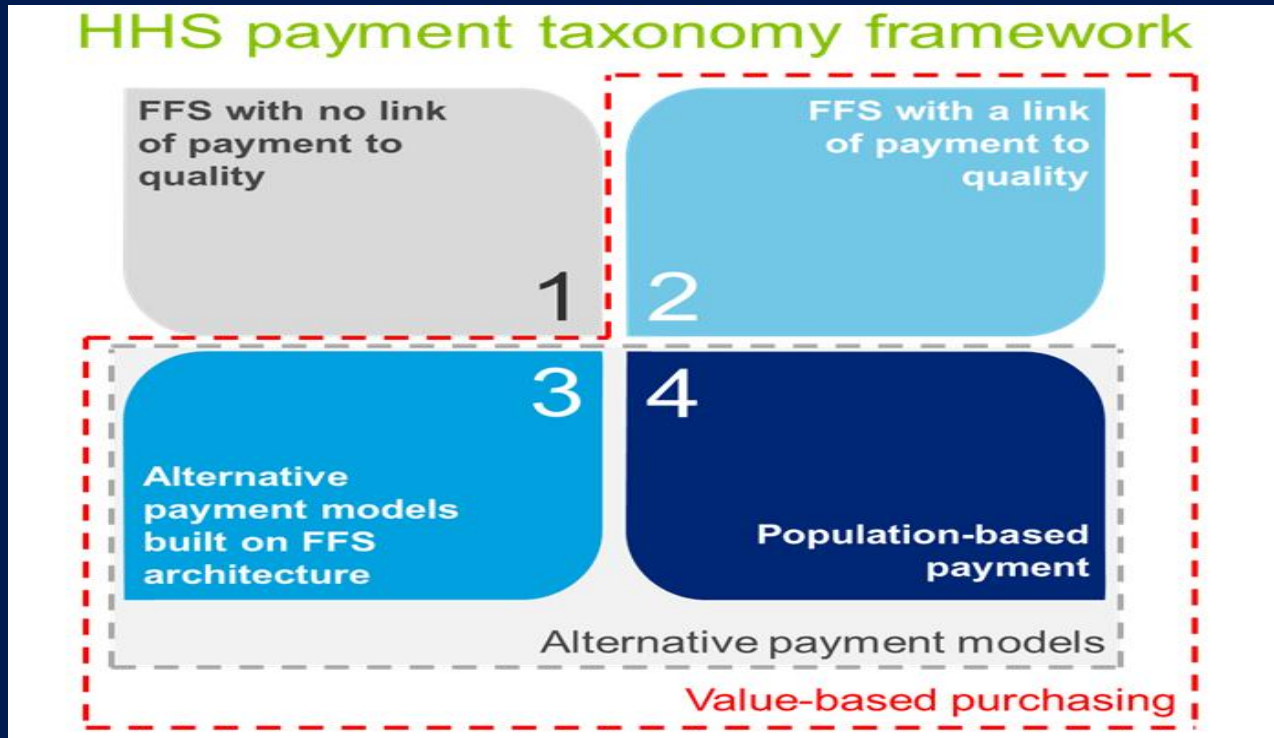
- Pembrolizumab FDA approved this week for MSI cancer
- First time drug has received approval based on a molecular marker, not specific to a particular cancer type
- Highly efficacious in a small targeted subset of patients
- Need to value the drug and companion diagnostic as a “bundle” ----challenge of precision medicine

DRUG payment: Taxonomy Framework: STALLED

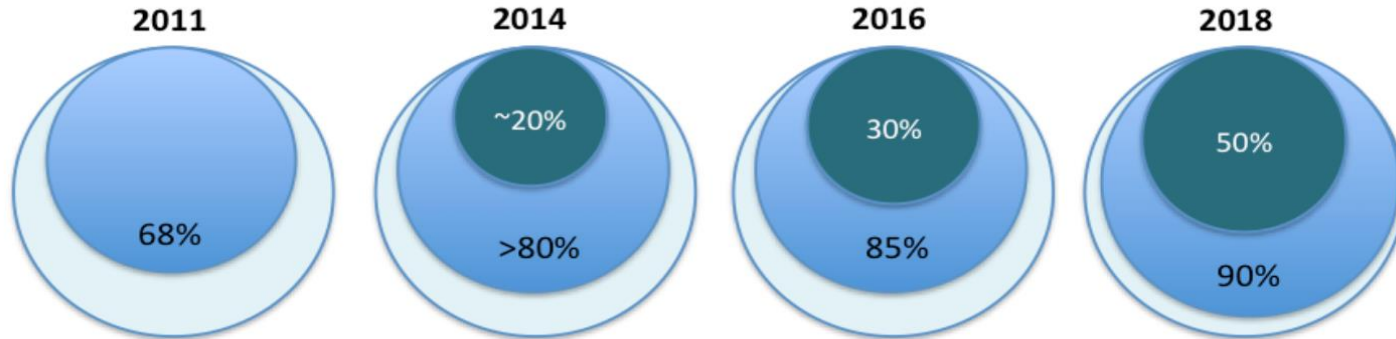
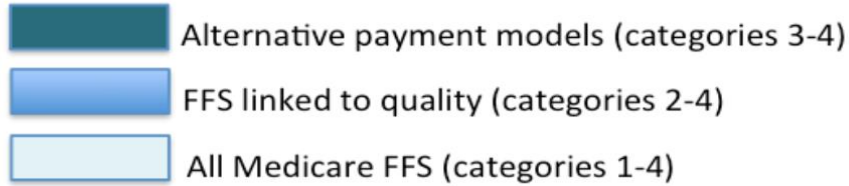
Category 1 FFS no link to quality	Category 2 FFS link to quality	Category 3 Alternative payment models on FFS platform	Category 4 Population based payments
Payments based on <u>volume</u> not linked to quality or efficiency	Some % of payment linked to performance metrics	Some % of payment tied to episode-based care Episodes triggered by events in FFS system	Payment not triggered by service delivery—follow a defined population for an extended period
Historical Medicare FFS	MD/Hospital-value based purchasing Readmission reduction	ACOs Medical Homes	Pioneer ACOs

CMS's Ambitious Goal: ON HOLD

P4Volume to P4Value



CMS's Goal WAS to Move Fast!



How to Better Align Value with Our Values?

- Make valuation a deliberate transparent process
- Innovation:
 - Design clinical trials that test high value innovations
 - Use an explicit framework to decide which innovations to test
- Implementation:
 - Incentivize adoption of high value innovations
 - Measure progress and reward success

Oncology Value Frameworks---

- A provocative beginning
 - Not yet practical for clinical decision making
 - Treatment costs vary enormously, hard to obtain and change
- Implementation: ASCO's shift in direction (Nov 2016)

Utilization of ASCO's Value framework and:

- Treatment decisions “at the bedside”
- Guidelines/pathways
- Coverage tiering by public and private insurance
- Drug pricing
- Guidelines

Thank you!

QUESTIONS

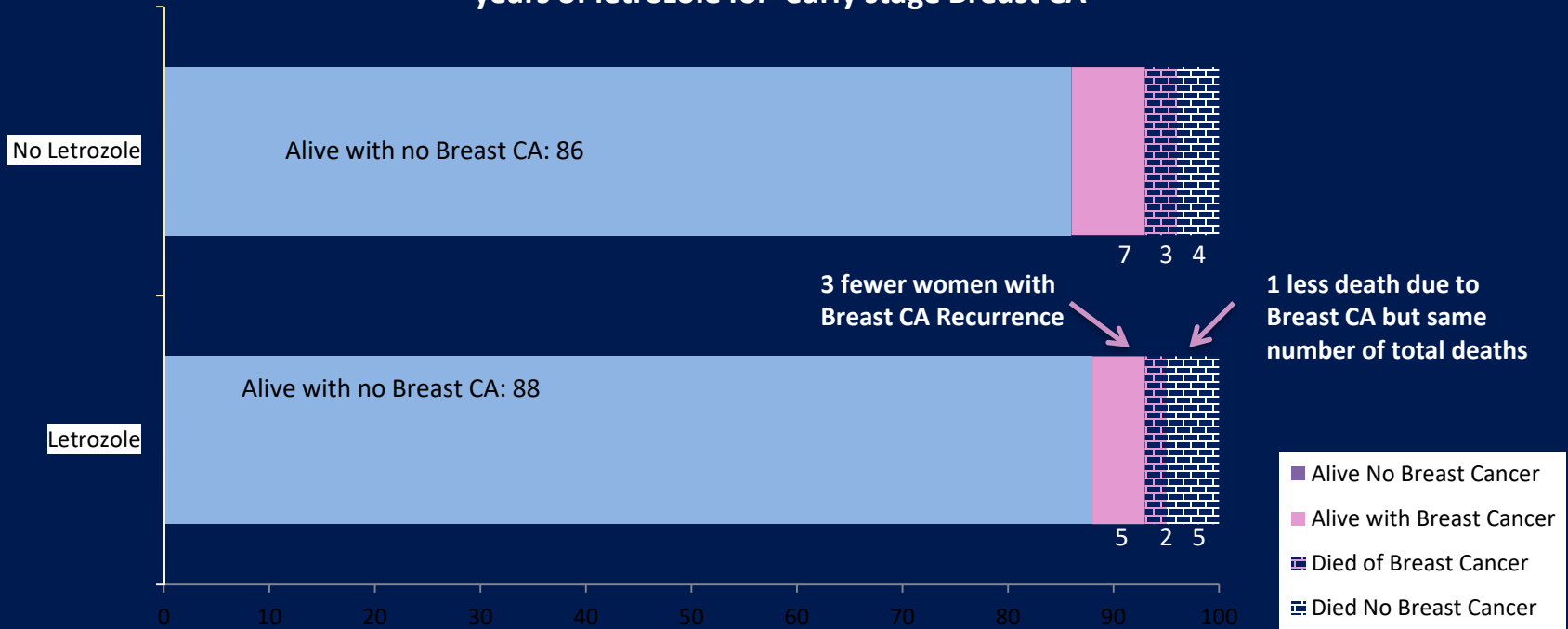
Presented by:

Summary: Value Frameworks Near Future

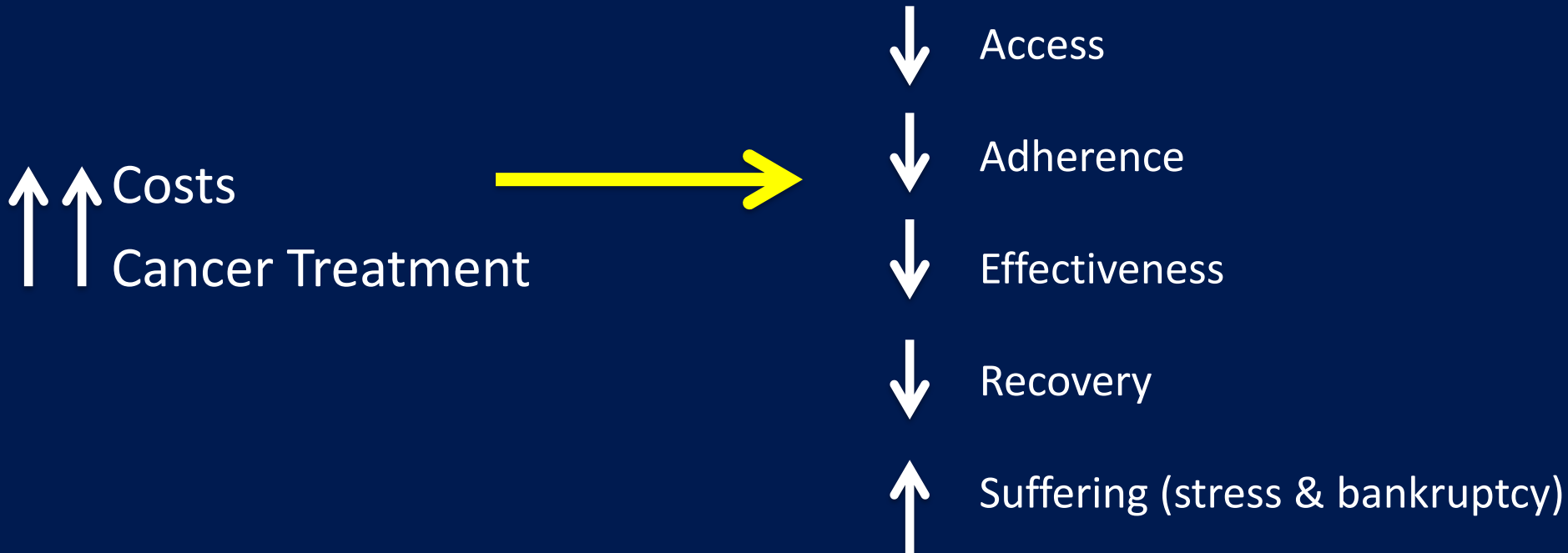
- Many opportunities for improvement
 - Frameworks are crude estimates not careful CEAs
 - Emphasis on speed, dynamic flexibility over accuracy
 - Opportunities to make frameworks significantly more robust
 - Need nimble models for each RCT (and for each payer)
 - Dynamic tools that allow variation of model inputs
 - Ability to evaluate alternative time horizons
 - Understanding of framing/decision theory constructs
 - Expertise in risk communication
- Near term in US, provocative discussion > specific policy

Communicating Value: Treatment Benefits

Expected outcomes for 100 Women who do or do not take 5 extra years of letrozole for early stage Breast CA



How Does Low Value Healthcare Hurt Individuals & Families with Cancer?



Curative Intent Treatment: ASCO Framework:

Step 1: Determine Clinical Benefit

Step 1: Determine the regimen's CLINICAL BENEFIT		
1.A. Is hazard ratio (HR) for death reported?	YES. Assign an <u>HR Score for death</u> by subtracting the HR from 1, and multiplying the result by 100. Write this number in the box labeled "HR Score (death)." Proceed to 1.E.	HR Score (death)
	NO. Proceed to 1.B.	
1.B. If HR for death is not reported, is median overall survival (OS) reported?	YES. Assign an <u>OS Score</u> by calculating the percentage (ie, fractional) difference in median OS between the two regimens and multiplying the result by 100. Write this number in the box labeled "OS Score." Proceed to 1.E.	OS Score
	NO. Proceed to 1.C.	
1.C. If OS data are not reported, is HR for disease-free survival (DFS) reported?	YES. Assign an HR score for <u>DFS Score</u> by subtracting the HR from 1, and multiplying the result by 100. Write this number in the box labeled "DFS Score." Proceed to 1.E. NO. Proceed to 1.D.	HR Score (DFS)
	NO. Proceed to 1.C.	
1.D. If HR for DFS is not reported, is median DFS reported?	YES. Assign a <u>DFS Score</u> by calculating the percentage (i.e., fractional) difference in median DFS between the two regimens and multiplying the result by 100. Write this number in the box labeled "Median DFS Score." Proceed to 1.E.	Median DFS Score
	NO. Proceed to 1.E.	
1.E. Calculate the <u>Clinical Benefit Score</u>	Insert the score for HR death, HR DFS, median OS, or median DFS. Note: You should have a score for only 1 of the clinical benefit scales above. Write the total in the box labeled "Clinical Benefit Score." Proceed to Step 2.	Clinical Benefit Score

Advanced dz framework hierarchy:

- Overall survival (1)
- Progression free survival (0.8)
- Response rate (0.7)

Adjuvant framework considers:

- Overall Survival (1)
- Disease free survival (0.9)

Selected Drugs That Have Received Accelerated Approval since 2011 and Their Listed Cost.*

Approval Year	Drug (Brand Name)	Initial Indication	Surrogate Measure Used for Approval	Current Cost (\$/mo)
2011	Crizotinib (Xalkori)	Anaplastic lymphoma kinase (ALK)-positive locally advanced or metastatic non-small-cell lung cancer	Overall response rate based on Response Evaluation Criteria in Solid Tumors	14,353
2012	Bedaquiline (Sirturo)	In combination therapy for pulmonary multidrug-resistant tuberculosis	Time to sputum culture conversion	6,000
2013	Pomalidomide (Pomalyst)	Multiple myeloma that has progressed despite receipt of two prior therapies	Overall response rate, based on European Group for Blood and Marrow Transplant criteria	14,165
2014	Blinatumomab (Blincyto)	Philadelphia chromosome-negative relapsed or refractory B-cell acute lymphoblastic leukemia	Complete remission or complete remission with partial hematologic recovery rate	56,262
2014	Pembrolizumab (Keytruda)	Unresectable or metastatic melanoma with disease progression	Overall response rate based on Response Evaluation Criteria in Solid Tumors	9,252
2014	Ceritinib (Zykadia)	ALK-positive locally advanced or metastatic non-small-cell lung cancer with disease progression or intolerance to crizotinib	Overall response rate based on Response Evaluation Criteria in Solid Tumors	14,628
2015	Panobinostat (Farydak)	Multiple myeloma that has progressed despite receipt of two prior therapies	Progression-free survival based on European Group for Blood and Marrow Transplant criteria	10,625
2015	Palbociclib (Ibrance)	Postmenopausal women with metastatic estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer	Progression-free survival based on Response Evaluation Criteria in Solid Tumors	11,224
2016	Eteplirsen (Exondys 51)	Duchenne's muscular dystrophy in patients with confirmed mutation amenable to exon 51 skipping	Increase in dystrophin in skeletal muscle	57,600

* Initial indications and surrogate measures were obtained from drug labeling (www.accessdata.fda.gov/scripts/cder/daf/index.cfm). Costs of drugs were obtained from DrugAbacus (run by the Memorial Sloan Kettering Cancer Center) in November 2016, except for the cost of bedaquiline, which is based on the average wholesale price (AWP) of \$36,000 for 24 weeks of treatment (as reported in UpToDate), and the cost of eteplirsen, which is based on the AWP of \$1,920 per 100 mg (assuming a patient weighing 25 kg and a dose of 30 mg per kilogram of body weight once weekly), or \$691,000 per year. Publicly reported estimates of \$300,000 included presumed discounts.

ABACUS Value Framework

The Core Question	What is the just price for a cancer drug?
Factors Considered	<ul style="list-style-type: none"> • Efficacy • Cost • Toxicity • Treatment Novelty • Costs of development • Rarity of disease • Population burden of condition
What evidence?	Phase II and III Drug Trials
Who judges?	Each user can customize own inputs
Whose perspective?	Manufacturer setting launch price, health insurer, concerned citizen

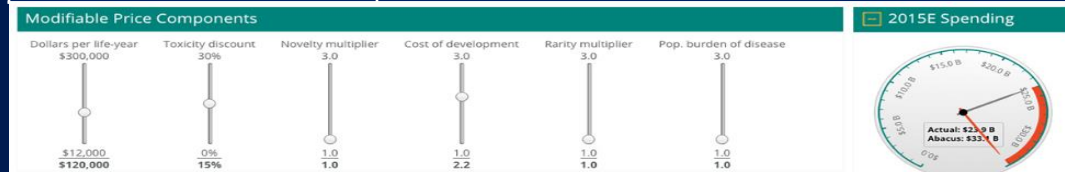
Daratumumab for Myeloma

✓✓✓ High efficacy

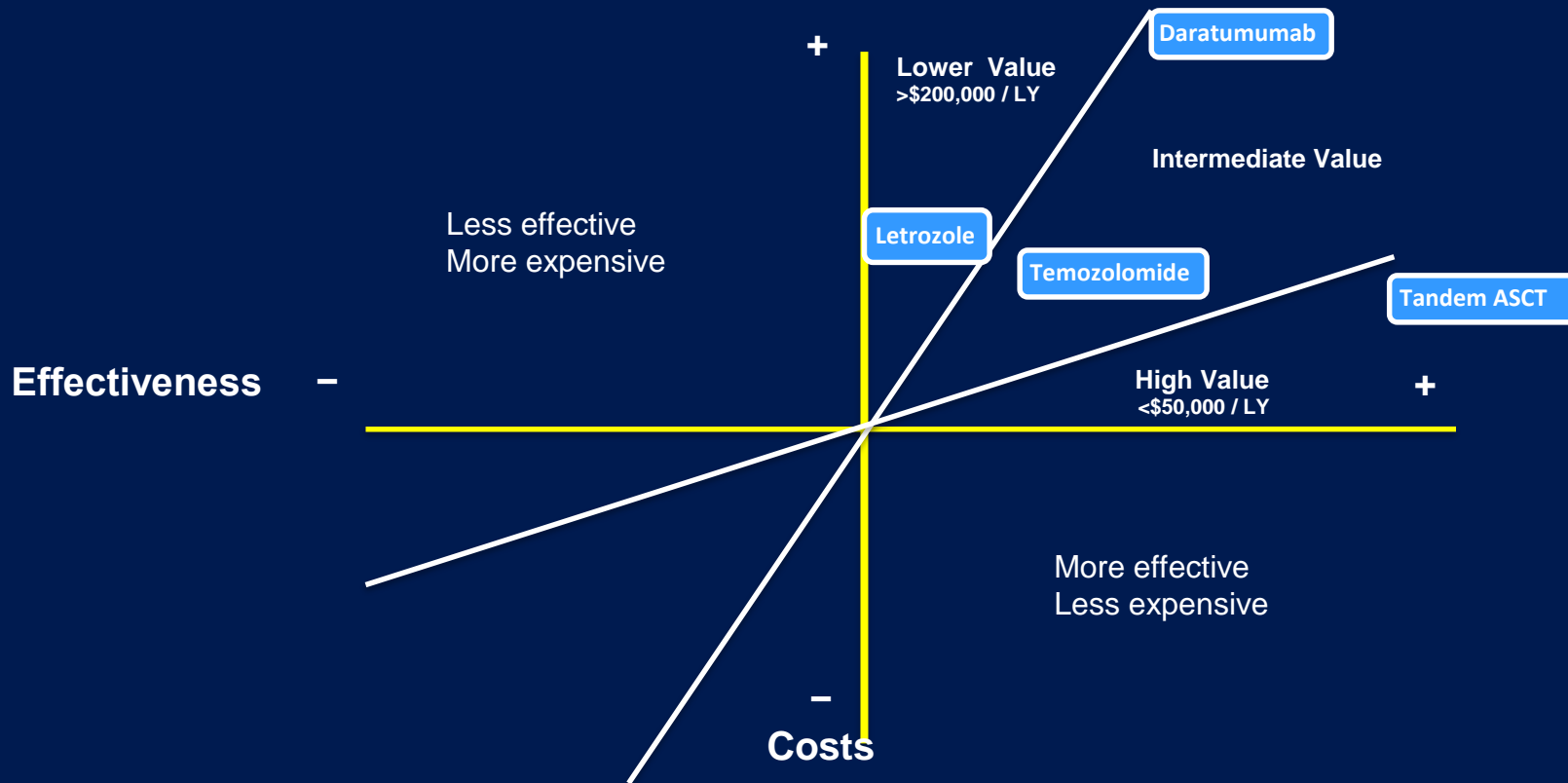
✓✓✓ Novel mechanism

What is a fair launch price?

Can the >\$10,000 per month be justified?



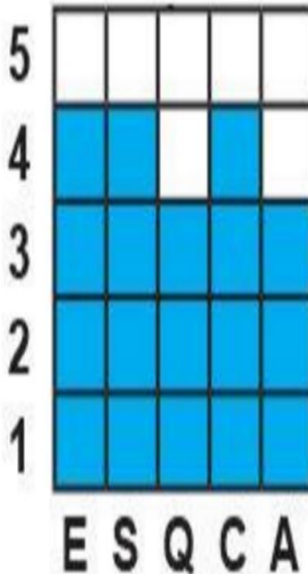
ICER Framework: Cost Effectiveness Modeling and “Expert” Input



Estimates based on regimen specific dosing
CMS and redbook drug prices

NCCN “Evidence Blocks”

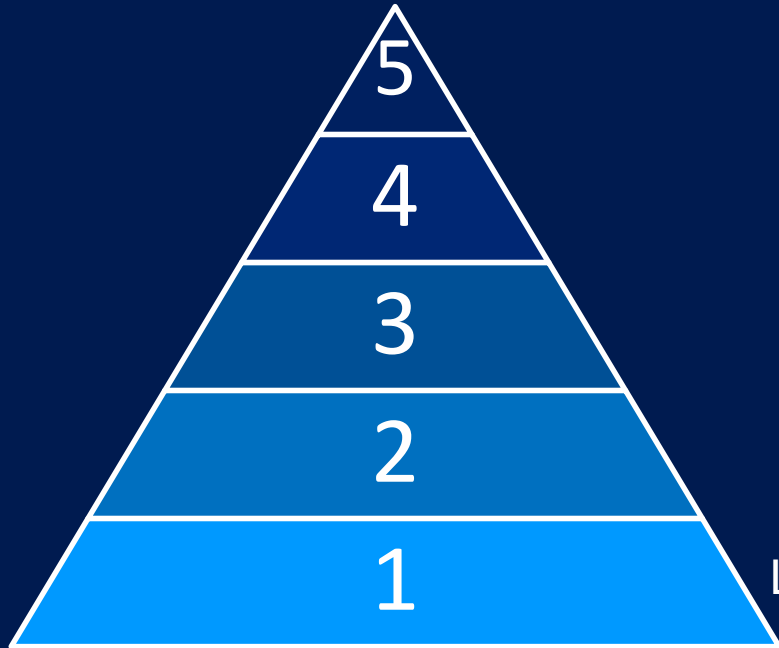
- Clinical Experts on Guideline Panels Rate Treatments on 5 Dimensions
- Not just RCTs
- Affordability varies and depends on perspective



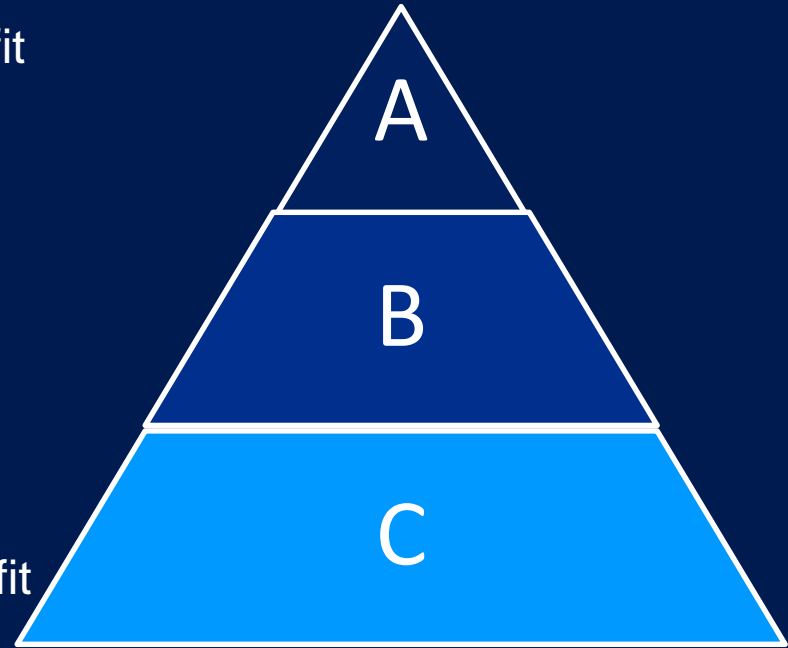
E = Efficacy of Regimen/Agent
S = Safety of Regimen/Agent
Q = Quality of Evidence
C = Consistency of Evidence
A = Affordability of Regimen/Agent

ESMO Magnitude of Clinical Benefit Scale

Palliative Treatment Setting



Curative Treatment Setting



Most Benefit
↑
↓
Least Benefit

ESMO Framework: Palliative Treatment

Grade	Benefit Criterion for non-curative Rx with OS endpoint	XRT+/-Temozolomide for Glioblastoma
4	HR \leq 0.65 and Gain \geq 3 months Increase in 2 year OS alone \geq 10%	No No
3	HR $<$ 0.65 AND median OS Gain 2.5-2.9 months Increase in 2 year survival 5- $<$ 10%	No (1.7 months) Yes
2	HR $>$ 0.65-0.7 OR Gain 1.5-2.4 months Increase in 2 yr survival 3- $<$ 5%	- -
1	HR $>$ 0.7 OR Gain $<$ 1.5 months Increase in 2 year survival $<$ 3%	- -
Bonus point?	Does QOL endpoint show benefit? Is there less Grade 3-4 toxicity?	No No
Summary	Highest Grade +/- Bonus point Magnitude of Clinical Benefit Score:	Grade 3

ESMO Value Framework: Curative Intent Treatments

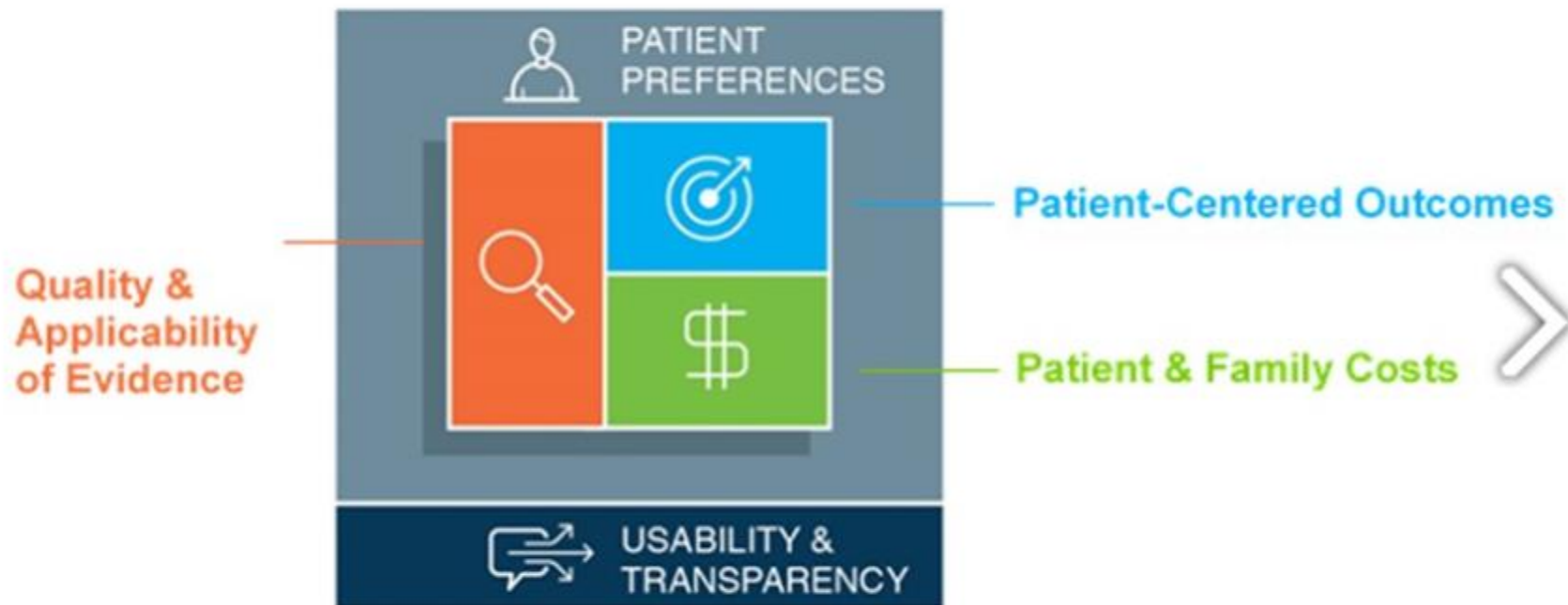
Grade	Benefit Criterion for non-curative Rx with OS endpoint	Extended Letrozole in Adjuvant Breast Cancer	Tandem ASCT in Neuroblastoma
A	>5% better OS at 3 years DFS better with HR<0.65	No No	No, but close (4.9%) Yes
B	3-<=5% better OS at 3 years DFS better with HR=.65-0.8	No YES (HR=0.66)	
C	<3% better OS at 3 years DFS with HR >0.8		
Summary	Highest Grade	Grade B	Grade A

The ASCO Value Framework (2016 Revision)

Domain	Scoring Algorithm: Advanced Disease
Clinical Benefit	Score 1 metric (hierarchical order) <ol style="list-style-type: none">1. HR Score: $(1 - \text{HR for OS}) * 100$2. % change in median survival * 1003. PFS Score: $(1 - \text{HR for PFS}) * 0.8 * 100$4. Response: $(\% \text{ Response (CR+PR)}) * 0.7 * 100$
Toxicity	Assign toxicity points Treatment toxicity (+ if ↓, - if ↑ up to 20) Late toxicity (-5 if present at 1 year)
Tail of Curve	OS → 50% better at 2x median of control (20)
Palliation	Significant decrease in symptom burden (10)
Quality of Life	Significant increase in QoL (10)
Rx Free Interval	% improvement in Rx-free interval * 20

Total # of Points = Net Health Benefit

The Five Domains of the Patient-Perspective Value Framework Version 1.0



Patient-Perspective Value Framework Steering Committee



PATIENT
GROUPS



LIFE
SCIENCES
COMPANIES



PAYERS



POLICY
AND RESEARCH
EXPERTS

- Aetna
- American Heart Association/American Stroke Association (AHA/ASA)
- America's Health Insurance Plans (AHIP)
- Amgen
- Astellas Pharma US
- Better Medicare Alliance (BMA)
- Bristol-Myers Squibb (BMS)
- Biogen
- Cancer Support Community (CSC)
- CVS Health
- Gilead Sciences
- GlaxoSmithKline (GSK)
- Johnson & Johnson (J&J)
- Leukemia & Lymphoma Society (LLS)
- Michael J Fox Foundation (MJFF)
- National Health Council (NHC)
- National Multiple Sclerosis Society (NMSS)
- Partnership to Improve Patient Care (PIPC)
- Patient-Centered Outcomes Research Institute (PCORI)

Value-Based Frameworks: Using Evidence and Values to Inform Policy and Practice

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Disclosure

I have no actual or potential conflict of interest in relation to this topic or presentation.

BACKGROUND AND CURRENT STATE FOR DRUG DECISION MAKING

What is priority setting?

- Given that we can't do everything, choices must be made about what to fund and what not to fund
- Priority setting is about making these choices:
 - *Health authorities*
 - *Hospitals*
 - *Program areas (including drugs)*
 - *Individual services*

Mitton and Donaldson CERA 2004

Health Technology Assessment

- **WHO defines Health technology assessment as:**
 - the the systematic evaluation of properties, effects, and/or impacts of health technology
 - multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology

Clarification: HTA vs. PE

- HTA is NOT synonymous with PE
- HTA can be seen as the the information capture that leads to decision making
- HTA should and almost always does include more than 'just' PE
- However many jurisdictions focus on PE as the key lever for the decision

Typical HTA process

- Review of clinical and economic literature
- Environmental scan of other jurisdictional practices
- Economic evaluation (typically using QALYs)
- Analysis of clinical and/or administrative data
- Primary data collection of local practices/context
- Assessment of costs in budget impact analysis (BIA)

A simple decision rule

ICER for new program \leq \$50,000/QALY

Decision: **adopt new program**

ICER for new program $>$ \$50,000/QALY

Decision: **do not adopt new program**

Limitations in one slide

- QALYs and the cost per QALY approach are only informing the decision maker about some of the potential benefit of a given technology
- Simple decision rule does not recognize concept of local opportunity cost as even a 'favourable' ICER will require an increase in budget to achieve some additional gain (aka opportunity cost often ignored)

SO IS THERE AN ALTERNAIVE?

What is needed?

- Need for a broader values based framework for decision making that moves away from simplistic cost per QALY assessment and one off decisions
- Application of a multi-criteria approach set within a values framework will ensure full range of benefit is being considered in drug decision making whilst achieving greater gains in terms of value overall
- Ideally based on public values which then inform the criteria that decisions will be based on

Priority setting in health care

- Identify stakeholder values
- Use this to construct decision criteria
- Determine costs and ‘benefits’ of options
- Explicitly assess trade-offs
- Validate and communicate
- Accept winners and losers



Broader tools required

- The decision making around the coverage of HTs is a complex process. The need for more comprehensiveness in decision-making, the movement toward expanding the decision-making criteria and the requisite to have more transparent decisions have changed the priorities of decision makers and HTA doers. Otherwise said, most pressing needs in HTA and reimbursement decisions are to develop tools that will allow investing in most valuable and disinvesting in least valuable interventions – thus a value index that is complete, meaningful, and comparable such as MCDA is needed.

Diaby and Goeree (Expert Reviews in Pharmacoeconomic Outcomes Research 2014)

Iterative steps of MCDA (Yoe 2002)

- Explicitly describe objectives
- Identify options for assessment
- Define and weight criteria
- Assess each option against decision criteria
- Compile initial assessment and validate results
- Decision making guided by MCDA results

Possible list of criteria (Dowie)

- Severity of disease
- Impact on population health
- Ease of implementation
- Urgency of condition
- Burden of disease
- Economic impact
- Vulnerable populations
- Budget impact
- Equity/ equal opportunity
- Cost-effectiveness

Reasons for 'special consideration'

- Severity of the underlying illness
- End of life treatments
- Stakeholder persuasion
- Significant innovation
- Disadvantaged populations
- Children

Rawlins et al. 2009

Value judgments

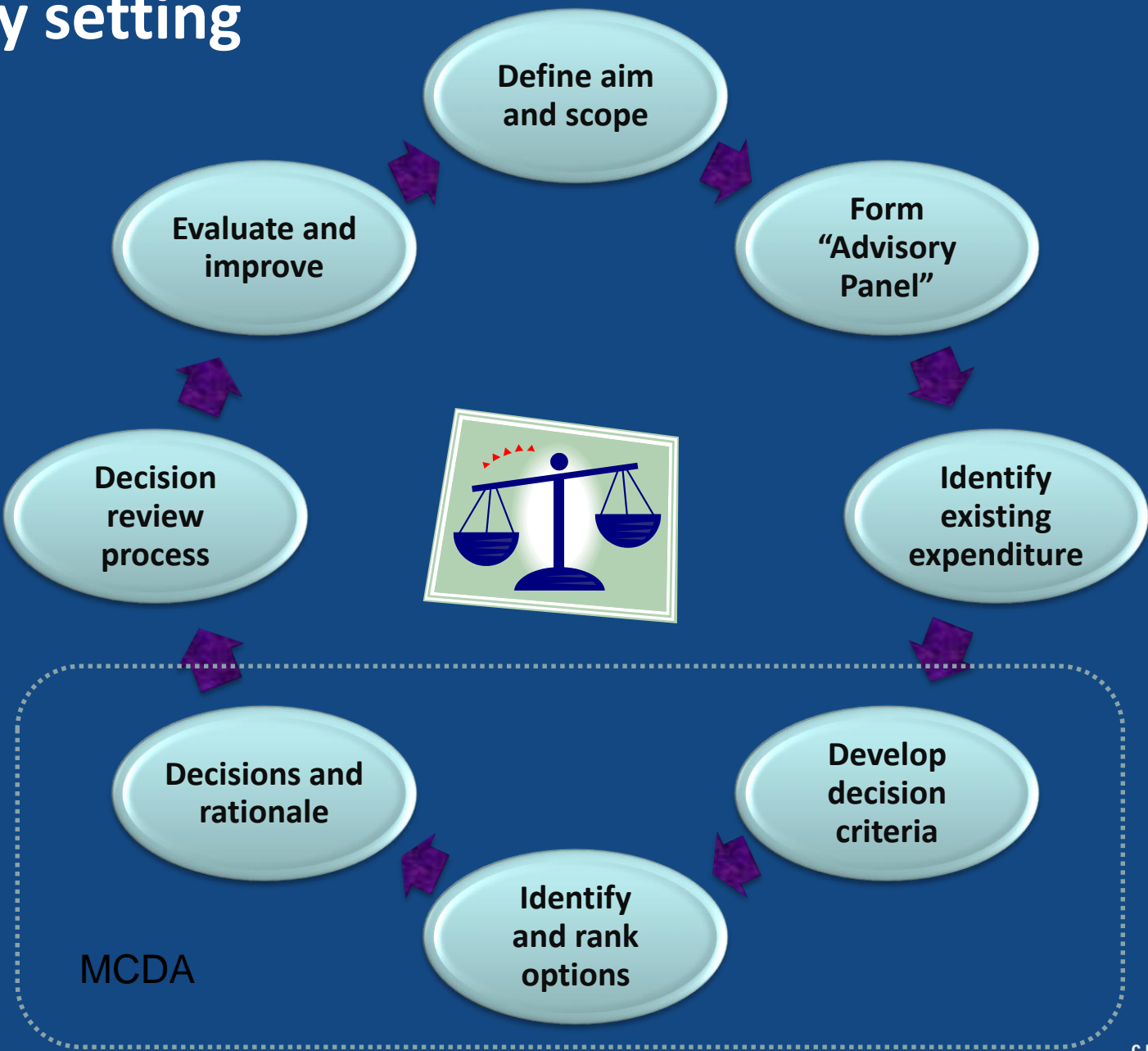
Devlin and Sussex 2010

- MCDA does not:
 - Decide which criteria to include
 - Decide what weight to place on each criterion
 - Replace decision-making
- Decision making in health care is value based
 - MCDA output can inform the final decision but should not be the final decision
 - Consensus model in decision making - MCDA results as starting point for discussion

Key concepts in one slide

- Broad set of criteria for drug decision making set within an overarching values framework
 - Public consultation and investment in new approach to HTA
- Both criteria and underlying principles need to be identified and the process itself needs to be made public
 - This is ‘just’ a tool to support decision making
- Focus on BIA and assessing opportunity cost of given spend
 - Incorporate notion of disinvestment as part of assessment process

Priority setting



[Peacock et al. 2006]

Discussion



Valuing the patient experience

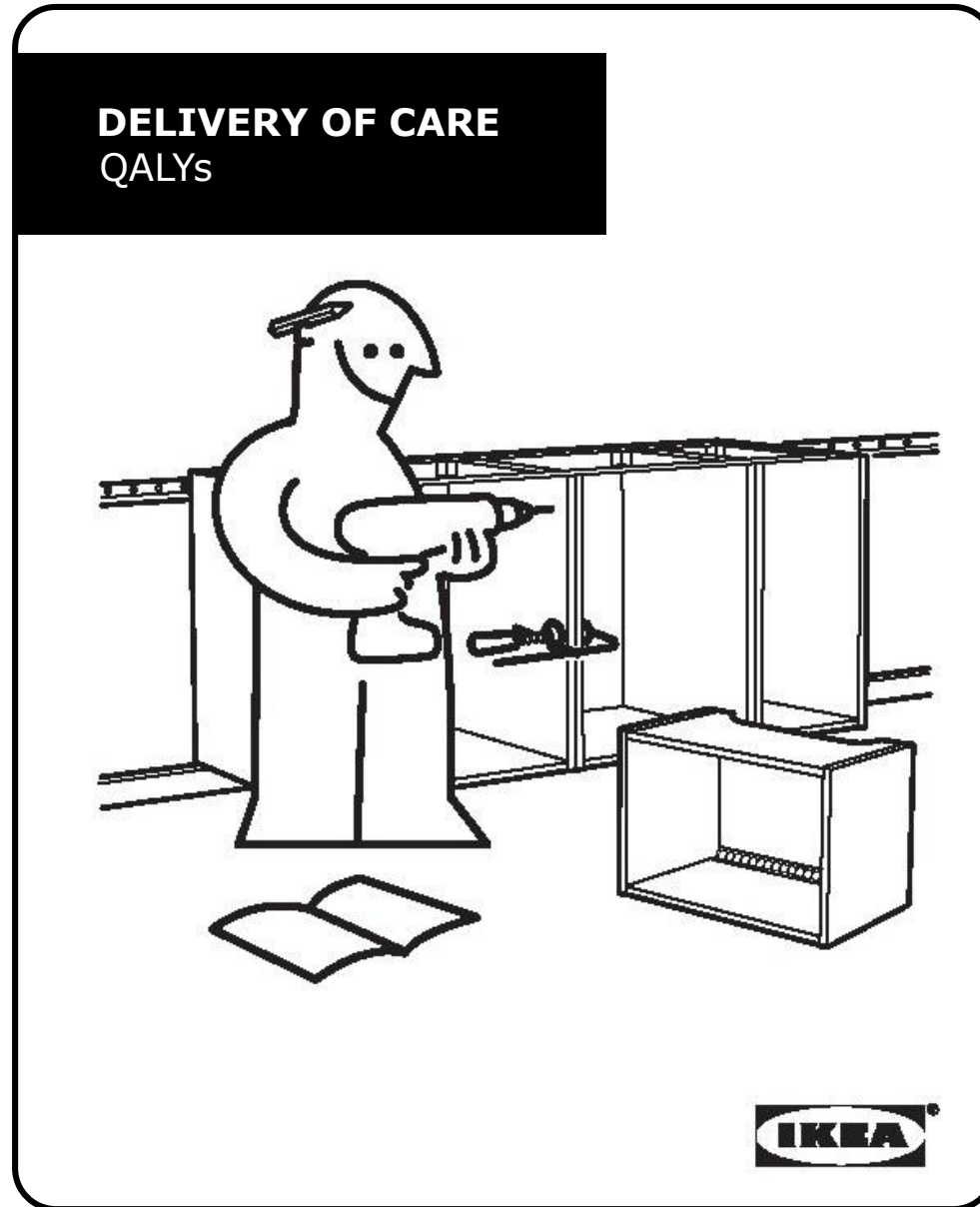
Reflections of a health economist.....and patient...

MandyRyan

May2017

The presenter has no conflict of interests

What matters to you in the delivery of health care?



Reflections of a Health Economist.....



Buying a puppy?



designed by  freepik.com

Breed

Dog Breeder

Size

Price

Care Needed

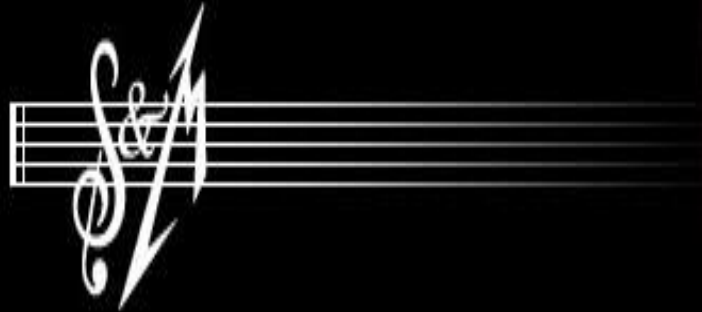
Personality

Life Span



METALLICA

WITH **MICHAEL KAMEN** CONDUCTING
THE SAN FRANCISCO SYMPHONY ORCHESTRA



Choosing a pharmacy?



Location



Car park?



Waiting time?



Who do you see?
Are they friendly?

Do they ask questions?
Do you understand?



Cost of trip and
medicine?

$$\int R(x, \sqrt{\frac{ax+b}{cx+d}}) dx \quad e^2 - xyz = e; A[0; e; 1] \quad x^3 + x^2 + y^3 + z^3 + xyz - 6 = 0 \quad \frac{2x}{x^2 + 2y^2} = 2$$

$$C = \begin{pmatrix} 0, 1 \\ 1, 0 \end{pmatrix} \quad \frac{\sin x}{x} \leq \frac{x}{x} = 1 \quad \text{grad} f = \left(\frac{\partial f}{\partial x}; \frac{\partial f}{\partial y} \right) \quad \frac{\partial z}{\partial x} = 2; \frac{\partial z}{\partial y} = 0$$

$$y = \sqrt[3]{x+1}; x = \text{tg} t \quad B = \begin{pmatrix} 2 & 1 & -1 & 0 \\ 3 & 0 & 1 & 2 \end{pmatrix} \quad \vec{n} = (F_x'; F_y'; F_z') \quad A = [1; 0; 3] \quad X_1 = \begin{pmatrix} \alpha + \beta + \gamma \\ \alpha \\ \beta \end{pmatrix}$$

$$A+B+C=8 \quad -3A-7B+2C=-10,3 \quad \int 3x^7 + 1,66x^{-0,17} dx \quad \lim_{n \rightarrow +\infty} \left(1 + \frac{3}{n}\right)^n \quad X \in \mathbb{R} \quad \cos \varphi = \frac{(1,0) \cdot \left(\frac{1}{2\sqrt{3}}; \frac{1}{4\sqrt{3}}\right)}{\sqrt{\frac{1}{12} + \frac{1}{48}}}$$

$$\lim_{n \rightarrow +\infty} \frac{\sqrt[n]{n^3+1+n}}{\sqrt[n]{3n^2+2n-1}} \quad \lambda_2 = i\sqrt{14} \quad \delta(p_2) = \sqrt{0,16} \quad z = \frac{1}{x} \arcsin \frac{\sqrt{2}}{2} \quad y \left(\frac{\partial f}{\partial x} \right) = 16 - x^2 + 16y^2 - 4z > 0$$

$$\lim_{x \rightarrow 0} \frac{e^{2x} - 1}{5x} = \frac{2}{5} \quad X_2 = \begin{pmatrix} -\kappa \\ \beta \\ -\delta \end{pmatrix} \quad \eta_1 = \lambda_1^2 - 3\lambda_1 + 1 \neq 0 \quad 2 \arctg x - x = 0, I = (1, 10) \quad \lambda x - y + z = 1$$

$$(1+e^x)yy' = e^x \quad y(t) = 1 \quad A = \begin{pmatrix} x & 1+x^2 & 1 \\ y & 1+y^2 & 1 \\ z & 1+z^2 & 1 \end{pmatrix} \quad x=0, y=1, z=2 \quad F_z' = 2xyz - 1 = 1 \quad x + \lambda y + z = \lambda^2$$

$$X_1 = \begin{pmatrix} 2p \\ -p \\ 0 \end{pmatrix} \quad \alpha, \beta, \gamma \in \mathbb{C} \quad \cos^2 \alpha + \cos^2 \beta + \cos^2 \gamma = 1 \quad \sum_{i=1}^n (p_2(x_i) - y_i)^2 \quad y' - \frac{\sqrt{y}}{x+2} = 0; y(0) = 1 \quad \frac{x^2}{a^2} + \frac{y^2}{b^2} + \frac{z^2}{c^2} = 0$$

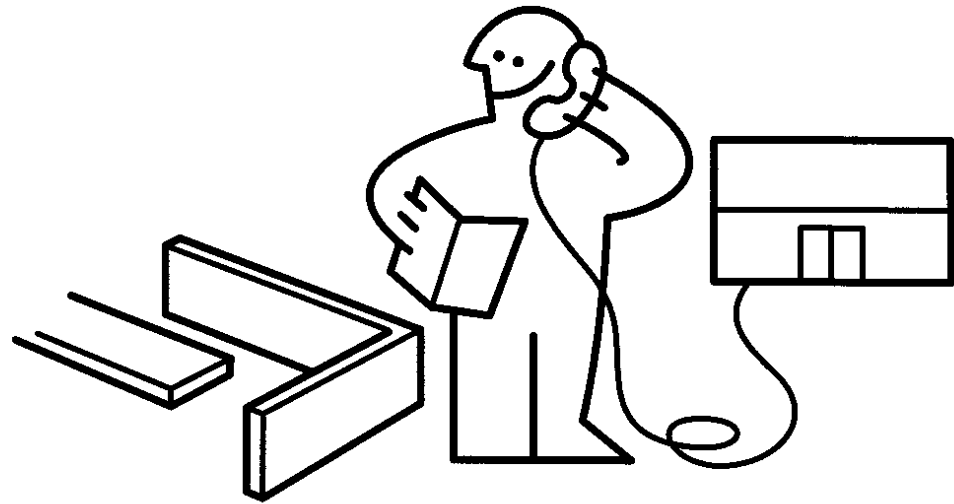
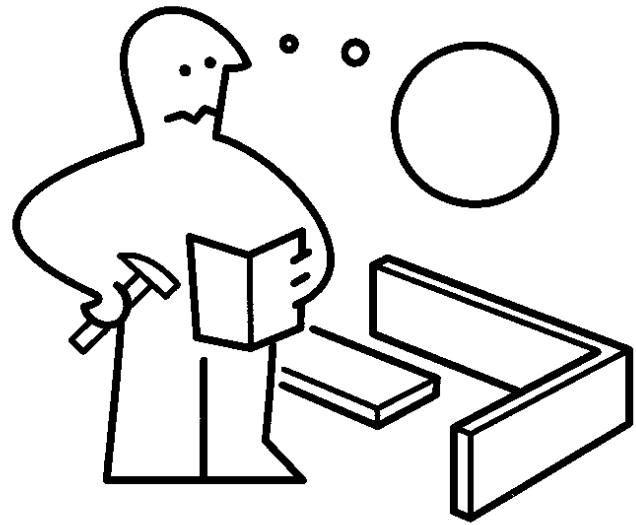
$$\int_{-\pi/2}^{\pi/2} \sin^4 x \cdot \cos^3 x dx \quad \lim_{x \rightarrow 0} \frac{e^{2x} - 1}{5x} = \frac{2}{5} \quad \iiint_M z dx dy dz = \int_0^{2\pi} \left(\int_0^2 \left(\int_{\frac{1}{2}}^1 r^2 dr \right) d\varphi \right) d\varphi$$

Choosing a pharmacy?



Screening for Glaucoma





Reflections as a patient.....





Maggie's Aberdeen.

**Offering practical,
emotional, psychological
and social support...**



**Value the patient
experience...**

It's important.