

Elements of Value for Gene Therapy: A Systematic Review

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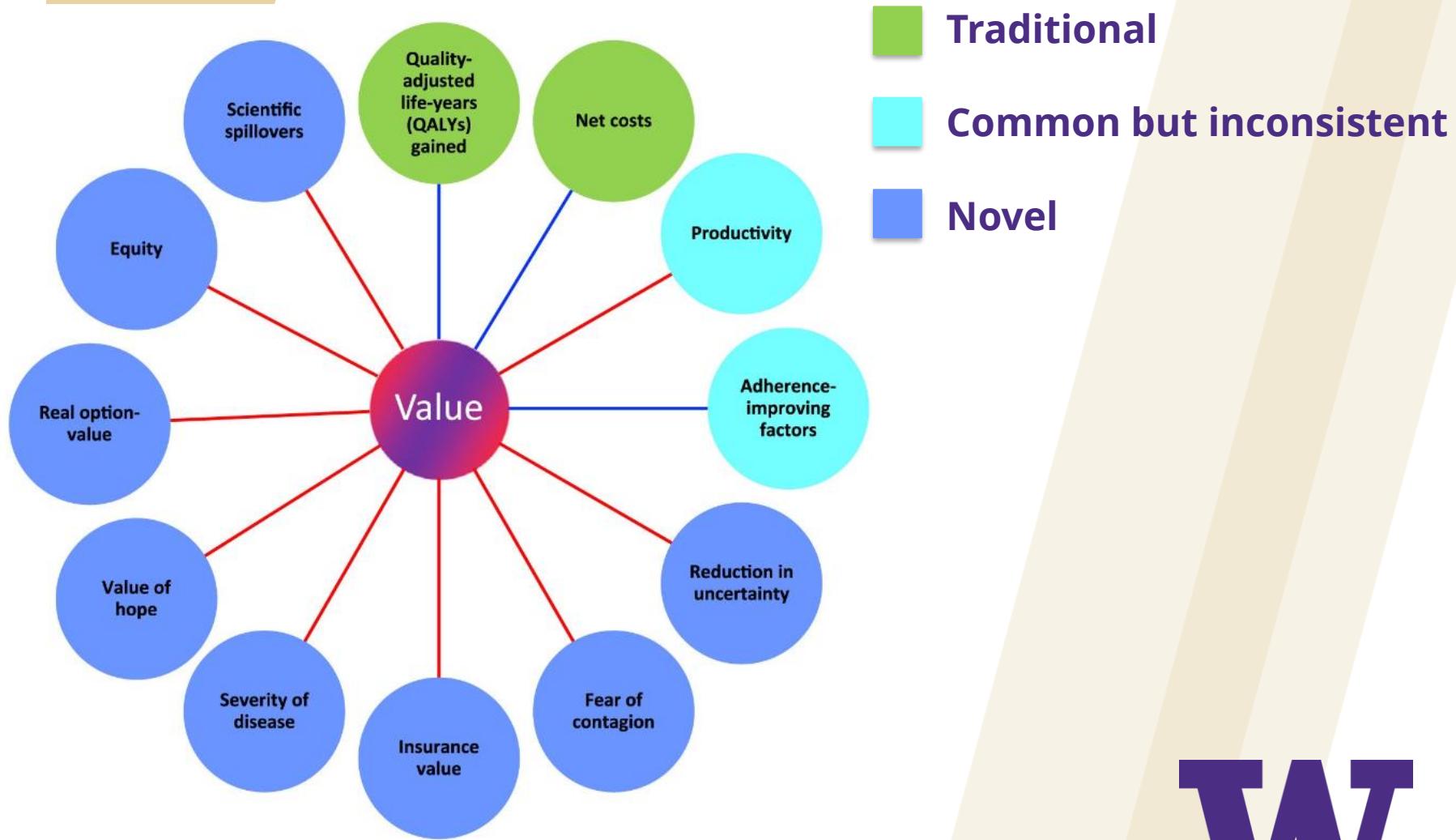
Disclosures

- > No funding received for this research

Author	Disclosure
EK	Postdoctoral fellow supported by Genentech, Inc.
KR	Employee of Genentech, Inc.
ZM	None
DV	Served as consultant



ISPOR – Elements of Value¹



1. Lakdawalla, Darius N., et al. "Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]." *Value in Health* 21.2 (2018): 131-139.

Systematic Review

Objective: To identify non-traditional elements of value relevant to gene therapies

Gene Therapies (9)

Provenge
Imlygic
Kymriah
Yescarta
Luxturna
Zolgensma
Zynteglo
Strimvelis
Valrox

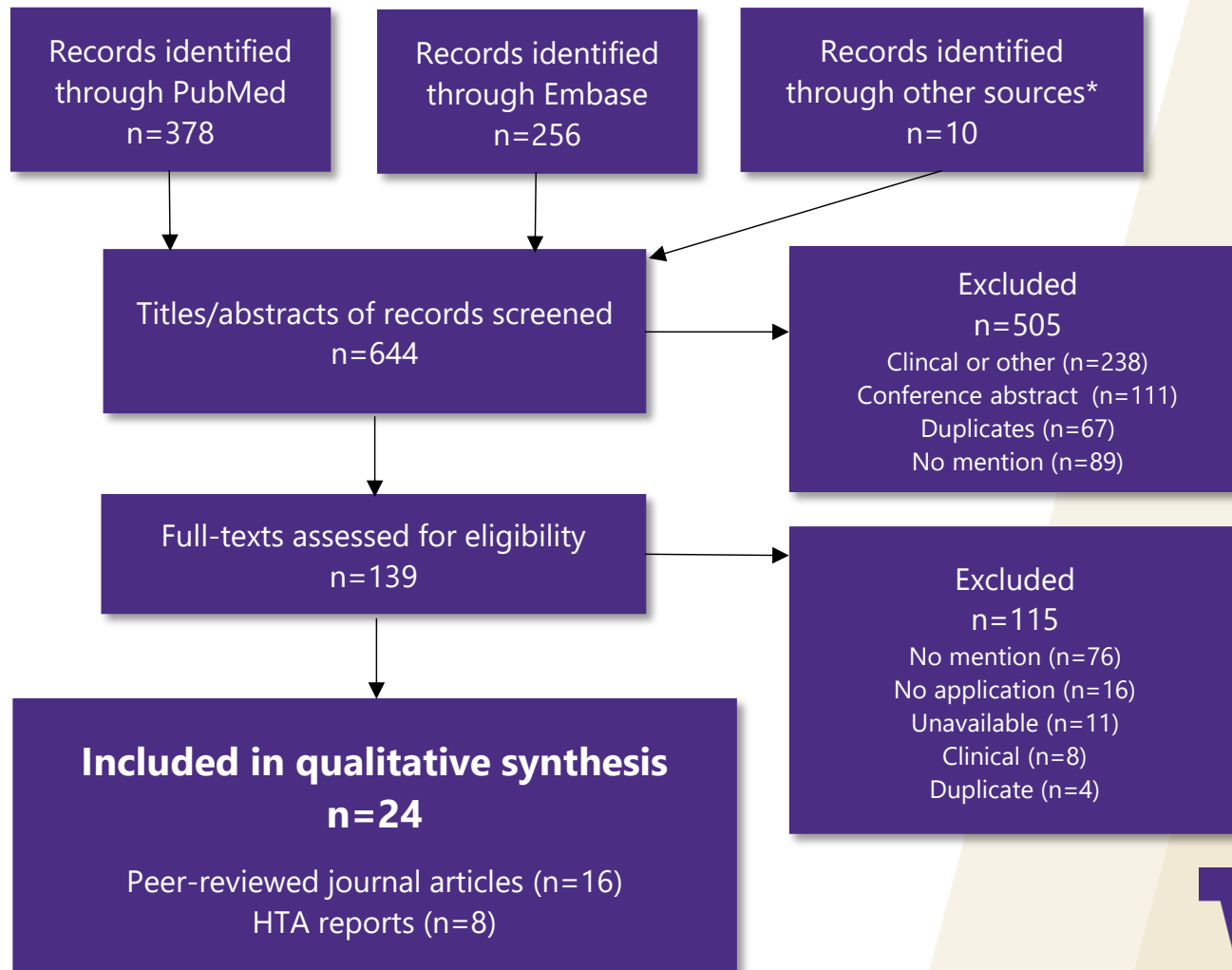
PubMed & Embase

Gene therapies
AND
Elements of value
AND
2015-2020

HTA Reports

ICER
NICE

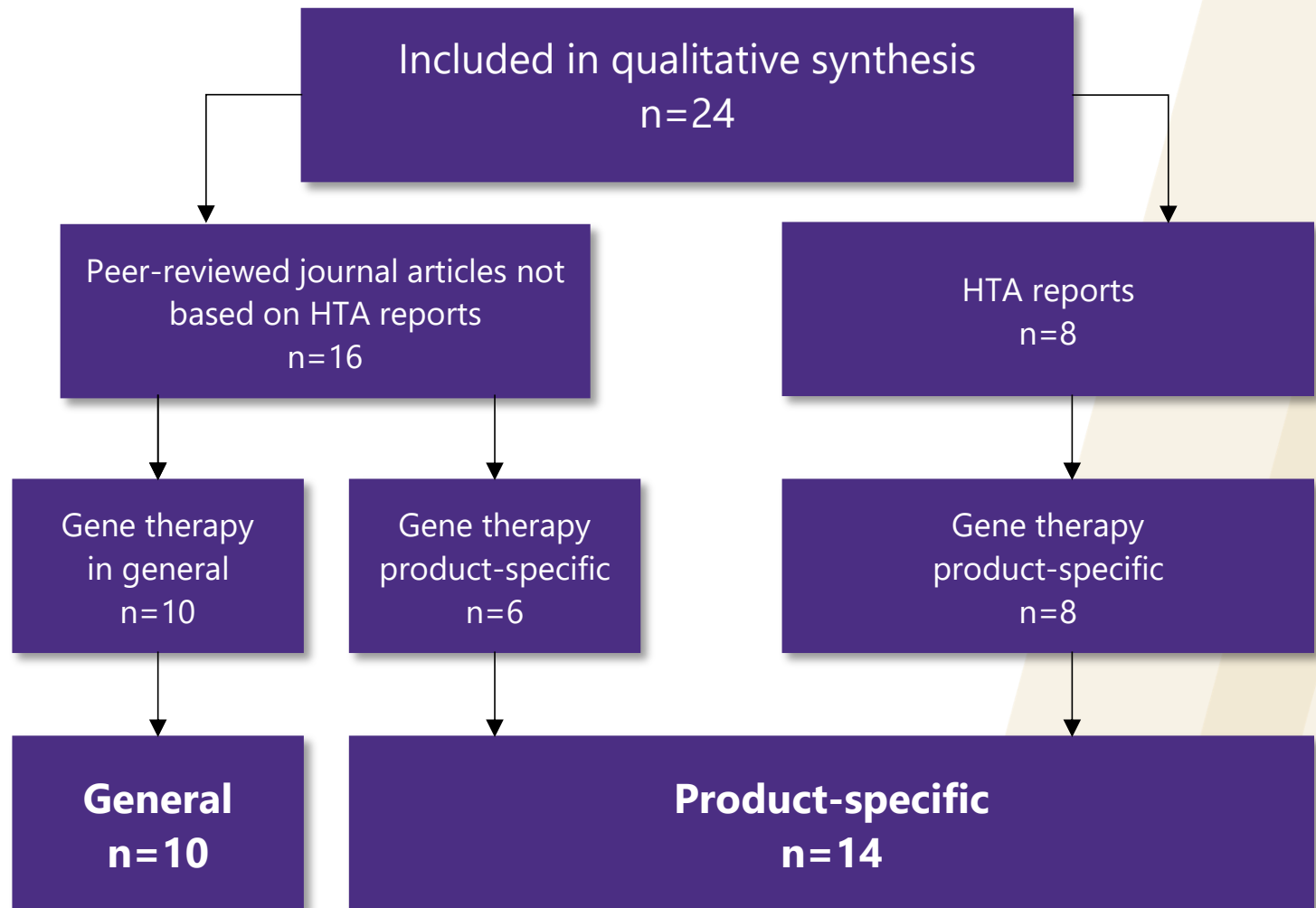
Results



*Other sources: 1) HTA reports from ICER and NICE, 2) Eligible references manually searched for in identified articles



Included Articles



Results

Source	Productivity	Novel Value Element(s)	How to Incorporate into Decision-Making
Angelis 2020	✓		MCDA
Jommi 2020		Scientific spillover	Immediate market access
AMCP Forum 2019	✓		MCDA
Drummond 2019	✓	- Severity of disease - Insurance value - Scientific spillover	- MCDA - Proportional QALY shortfall
Garrison 2019		- Severity of disease - Insurance value - Real option value - Value of hope	Increase CEA threshold
Pearson 2019		- Equity - Severity of disease - Real option value - Value of hope - Insurance value	- Vary CEA threshold - Disallow full credit for cost offsets - QALY cap
Iskrov 2019		- Equity - Severity of disease	Increase CEA threshold
Jonsson 2019		Severity of disease	Vary CEA threshold
Gardner 2017		Scientific spillover	Accelerated access pathway
Hettle 2017		- Real option value - Severity of disease	- QALY weighting - Increase CEA threshold

Included Diseases

Disease Area	No. of Articles/Reports
Inherited eye disease	6
Cancer	4
Beta thalassemia	1
Hemophilia	1
Spinal muscular atrophy	1
Severe immunodeficiency	1



Results

Gene Therapy (No. Articles)	Indication	Productivity	Novel Value Element(s)	Type(s) of Article (No. Articles)
Luxturna (n=6)	Inherited retinal disease	✓	• Equity	CEA (n=4) HTA report (n=2)
Yescarta, Kymriah (n=4)	B-cell malignancy	✓	• Scientific spillover	HTA report (n=3) Opinion (n=1)
Strimvelis (n=1)	ADA-SCID		• Equity	HTA report (n=1)
Valrox (n=1)	Hemophilia A	✓	• Equity • Severity of disease	HTA report (n=1)
Zolgensma (n=1)	Spinal muscular atrophy	✓		HTA report (n=1)
Zynteglo (n=1)	Beta thalassemia	✓		CEA (n=1)

Non-traditional Value Elements

Value Element (No. Articles)	Method of Incorporation into CEA or Real-World Decision Making
Productivity (n=12)	• Indirect cost in CEAs
Severity of disease (n=10)	• Conditional market access • Higher CEA thresholds • Lower discount rates • QALY weighting
Equity (n=4)	• Higher CEA thresholds • QALY weighting
Scientific spillover (n=4)	• Accelerated market access

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QALY Weighting – Luxturna

NICE National Institute for
Health and Care Excellence

- > **“Highly Specialized Technology”** pathway
 - Very small patient population
 - Chronic & severely disabling condition
 - Significant need
 - Very high cost
 - Potential for life-long use
 - Used exclusively in the context of a highly specialized service
 - Clinically distinct



Severity of Disease & Equity¹

Severity of Disease	Equity
“Treatments for individuals near end of life (or proximity to death) may be more valuable, either because the individuals themselves place higher value on the health gain or because they feel that society should give priority to treating those with severe disease.”	“Wish for more equal outcomes across rich and poor groups, or across healthy and sick groups... patients unlucky enough to suffer from rare, untreated illness are being treated inequitably, compared with their peers, who happen to suffer from treatable conditions.”

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QALY Weighting – Luxturna

Weighting of QALYs in HST

Incremental QALYs gained (per patient, using lifetime horizon)	Weight
Less than or equal to 10	1
11 – 29	Between 1 and 3 (using equal increments)
Greater than or equal to 30	3

- > Treatment offers significant QALY gains (12.1-17.7)
 - Applied QALY weight of 1.2

Special Access Pathway – CAR-T



> **“Innovative”**

- Automatically included on the regional formularies & funded through the national innovation fund

> **Scientific spillover**

- “Impact of a new technology on future generations of patient” (i.e., externality on future innovation); **“scientific novelty”**



Limitations

- > Reports from only two HTA bodies included
- > Novel value elements not explicitly stated but implied in articles/reports were interpreted at authors' discretion
- > Definition of “gene therapy” may have differed among articles



Summary

Non-traditional value elements commonly discussed:
productivity, equity, scientific spillover, and severity of disease

Methods of **incorporation of novel value elements**:
MCDA, QALY weighting, varying CEA thresholds, discount rates, market access

Paucity in literature indicates **current discussion but little application**, which has mostly occurred in policy decision-making by HTA bodies.

Implications for Future Research

- > **Prioritize & quantify novel value elements**
 - Discrete choice experiments
 - Stakeholder surveys
- > **Quantify disease-specific productivity loss**
 - To better inform economic evaluations



Thank You



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