Palliative Cancer Care: Meta-Analysis

Slides & Graphics

Hoerger, M., Wayser, G. R., Schwing, G., Suzuki, A., & Perry, L. M. (2019). Impact of interdisciplinary outpatient specialty palliative care on survival and quality of life in adults with advanced cancer: A meta-analysis of randomized controlled trials. Annals of Behavioral Medicine.

Why was this study conducted?

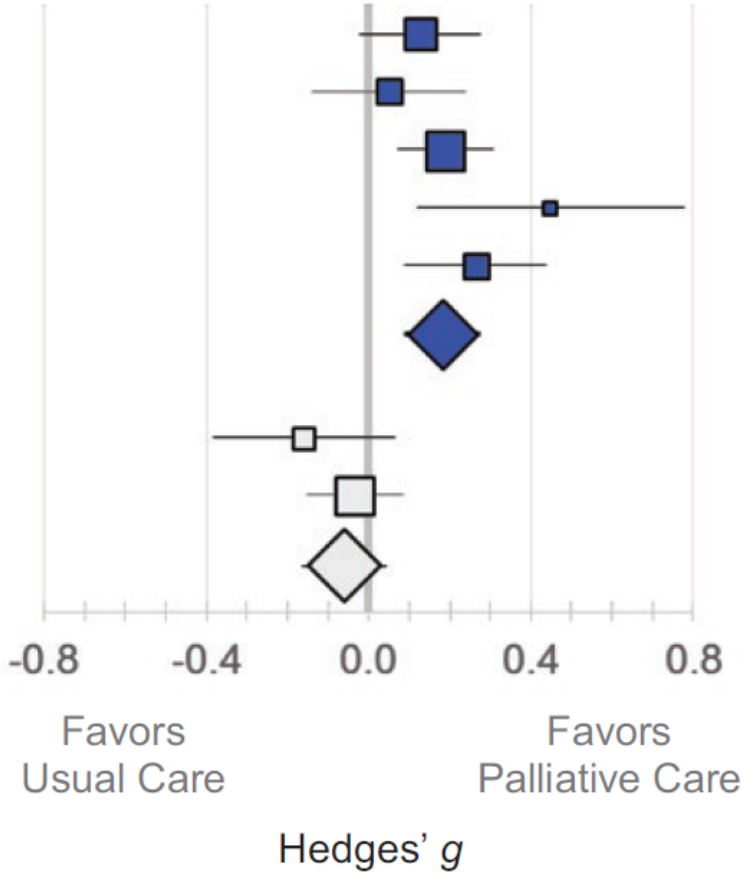
- Goal of the research was to improve care for patients with advanced cancer by statistically summarizing the medical evidence for outpatient palliative cancer care
- Strong medical evidence is the foundation for good medical decision making
- When patients, families, clinicians, payers, administrators, and policy makers know what works, they can ensure patients get that care

What did the researchers do?

- Reviewed and statistically summarized all RCTs of outpatient models of interdisciplinary palliative care for patients with advanced cancer
- 9 RCTs identified, 8 with outcomes for statistical analysis, and 5 classified as high quality
- Primary outcomes: Patient quality of life and 1-year survival
- Secondary outcomes: Physical/psychological quality of life, quarterly and median survival
- Quality criteria & outcomes defined/registered *a priori*

Quality-of-life advantage in RCTs of outpatient palliative cancer care

Study	*N*	*g*	95% CI	*p*
High-Quality RCTs				
Temel et al. (2017)	300	.13	[-.02, .28]	.10
Bakitas et al. (2015)	207	.05	[-.14 .24]	.61
Zimmerman et al. (2014)	461	.19	[.07, .31]	.002
Temel et al. (2010)	151	.45	[.12, .78]	.008
Bakitas et al. (2009)	279	.27	[.09, .44]	.003
Pooled estimate	1,398	.18	[.09, .28]	<.001
Preliminary RCTs				
McCorkle et al. (2015)	122	-.16	[-.39, .07]	.16
Jordhøy et al. (2001)	434	-.03	[-.15, .08]	.58
Pooled estimate	556	-.06	[-.16, .04]	.26



Hoerger et al. (2019). Annals of Behavioral Medicine. [Fig 4]

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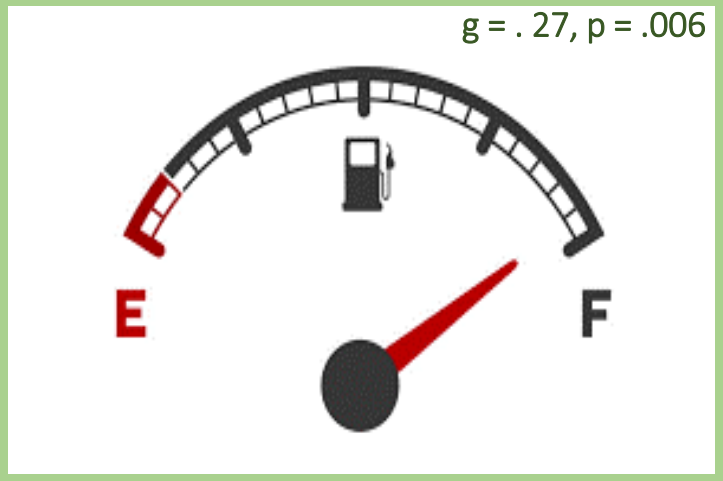
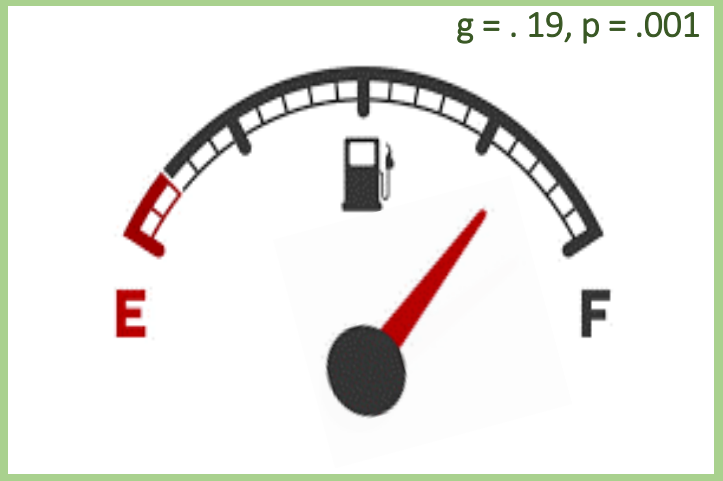
Physical vs. Psychological QOL

- Quality-of-life benefit was consistent when separately examining physical vs. psychological measures of quality of life
- Physical QOL (physical symptoms, physical well-being, functional well-being)
  - g = .27, p = .006 (n = 358)
- Psychological QOL (depression, anxiety, emotional well-being, social well-being)
  - g = .19, p = .001 (n = 1,340)

Meta-analysis of RCTs of Outpatient Palliative Cancer Care Shows….



Physical well-being



Psychological well-being

Palliative Care Improves Quality of Life, Both Physically and Psychologically

Hoerger et al. (2019). Annals of Behavioral Medicine.

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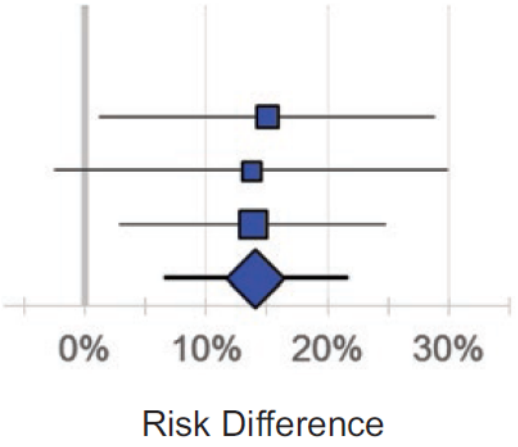
Do Palliative Care Studies Underestimate QOL Benefit?

- RCTs reviewed may underestimate quality-of-life advantage of outpatient palliative cancer care
- Why? (see Discussion and Supp Fig A1)
  - Broad eligibility criteria = heterogeneity of presenting symptoms
  - Broad outcome measures
  - Each outcome measure only relevant to subsets of patients (e.g., anxiety measures only relevant to anxious patients, social functioning measures to those with interpersonal strain, etc.)
- Real effects may by 2-4 times greater than observed effects

Survival advantage, RCTs of outpatient palliative cancer care, 1-yr endpoint

Study	*N*	1-Year Survival PC	Control	Risk Diff.	95% CI	*p*
High-Quality RCTs						
Bakitas et al. (2015)	194	63.0%	48.0%	15.0%	[1.2%, 28.8%]	.03
Temel et al. (2010)	141	49.1%	35.4%	13.7%	[-2.4%, 29.8%]	.10
Bakitas et al. (2009)	311	55.3%	41.5%	13.8%	[2.8%, 24.8%]	.01
Pooled estimate	646	56.2%	42.1%	14.1%	[6.5%, 21.7%]	<.001



Hoerger et al. (2019). Annals of Behavioral Medicine. [Fig 2]

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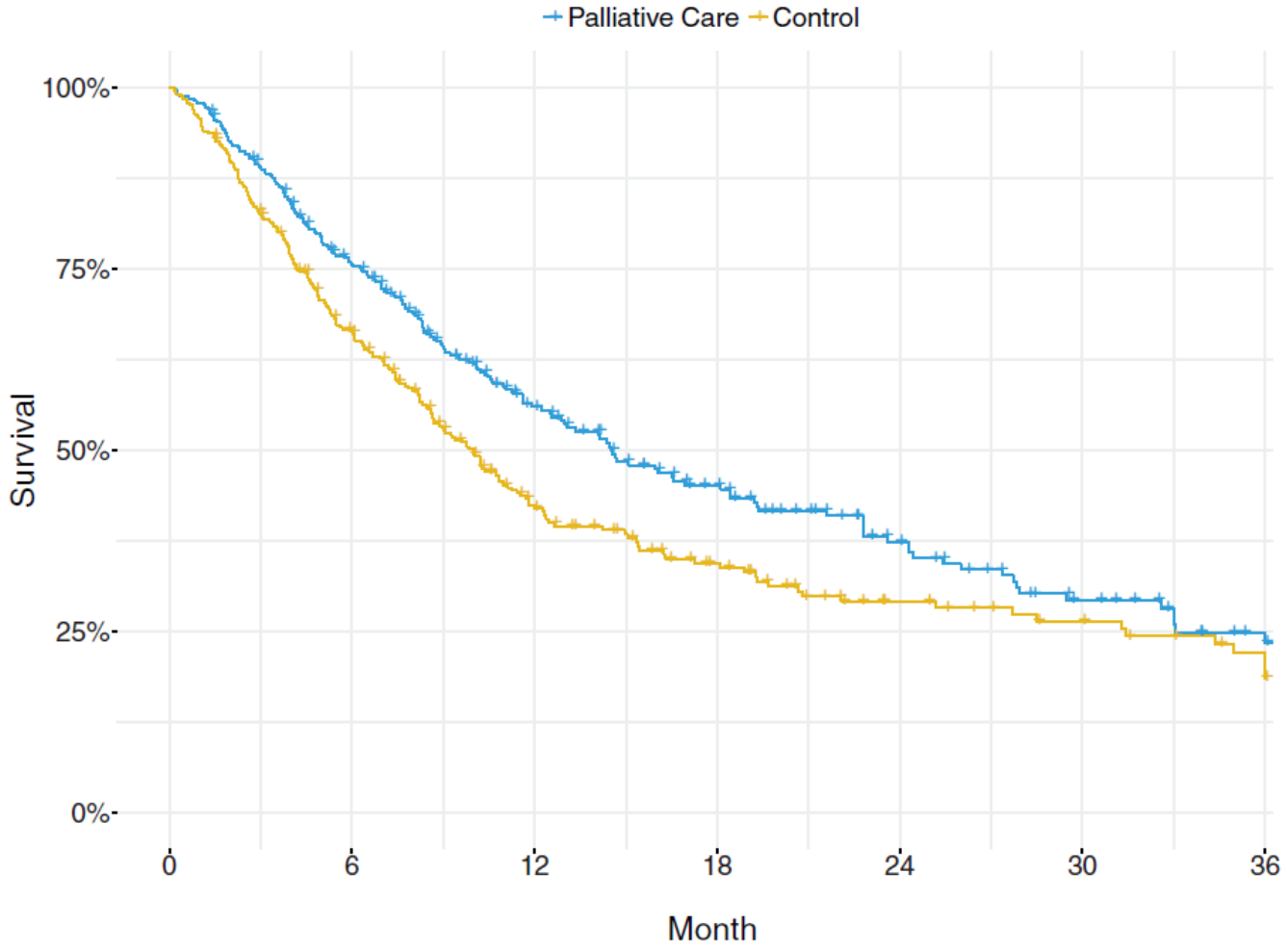
Survival advantage, RCTs of outpatient palliative cancer care (pooled n = 680)



Hoerger et al. (2019). Annals of Behavioral Medicine. [Fig 3]

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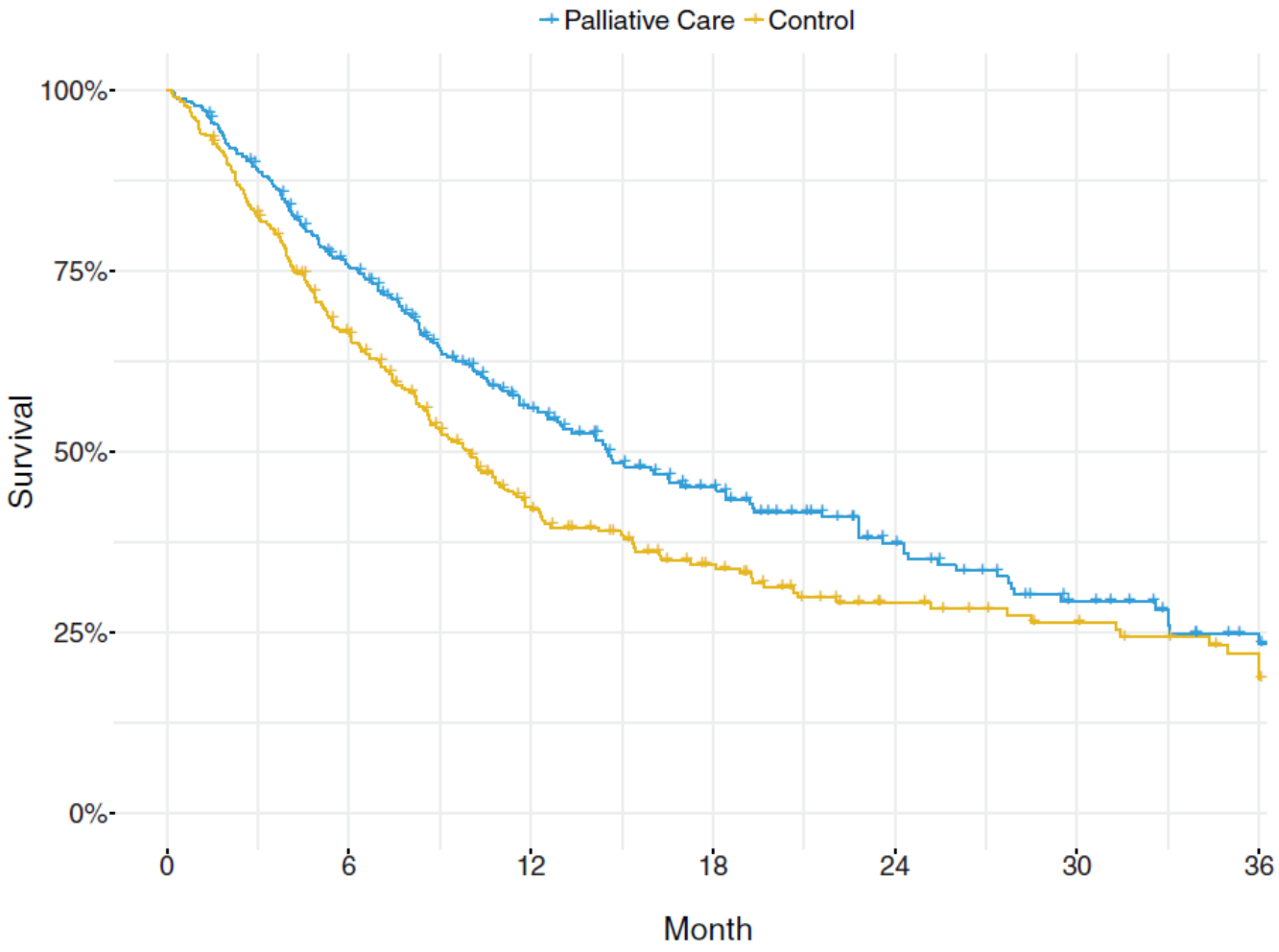
Outpatient palliative care extends survival duration in high-quality studies

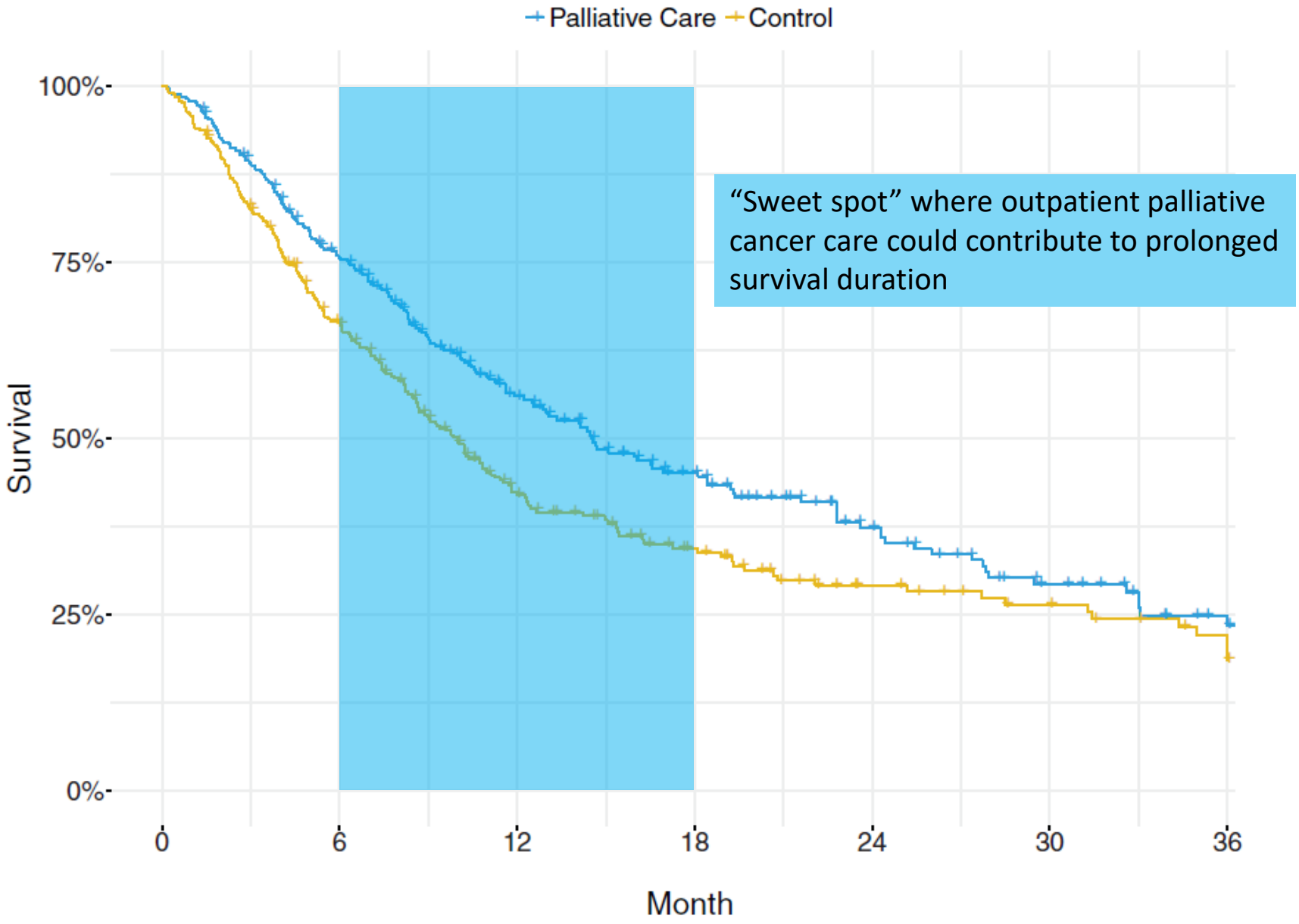


Meta-analysis of n=680 patients in high-quality RCTs

4.5 month survival advantage

Hoerger et al. (2019). Annals of Behavioral Medicine. [Fig 3]

Survival advantage, RCTs of outpatient palliative cancer care (pooled n = 680)



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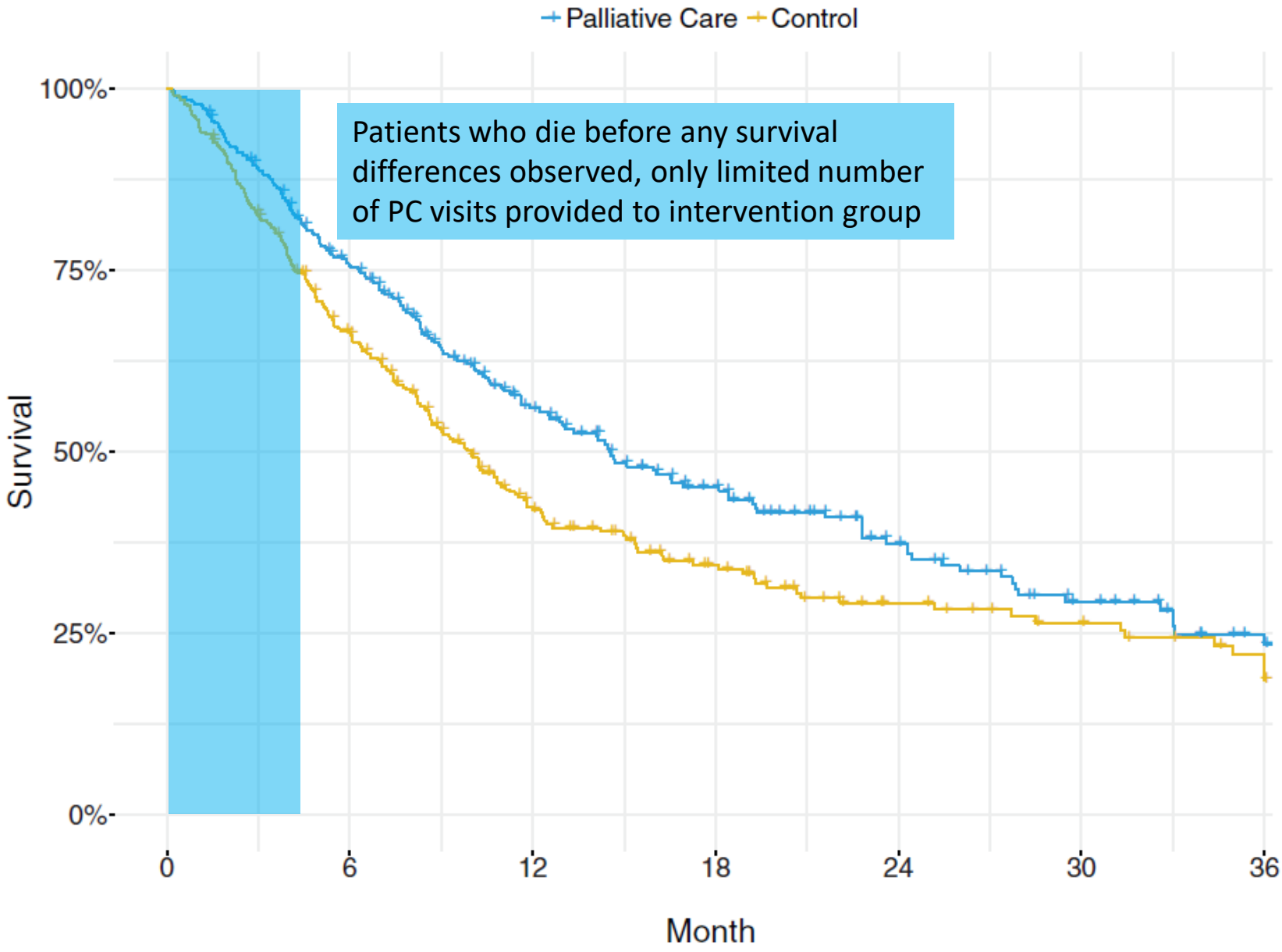

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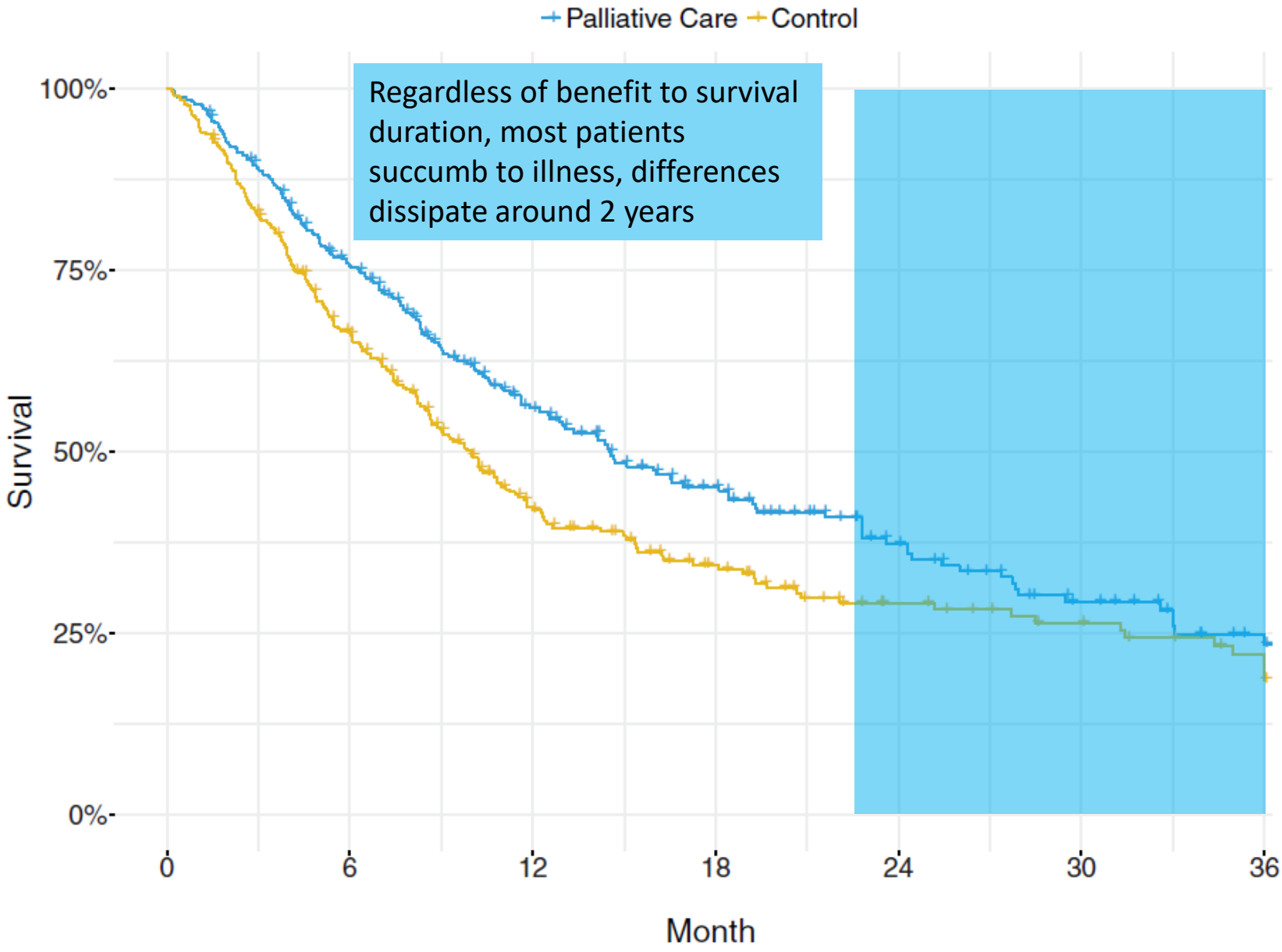

Hoerger et al. (2019). Annals of Behavioral Medicine. [Fig 3]

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Survival advantage in RCTs of outpatient palliative cancer care, quarterly endpoints

Survival Endpoint	*N* Participants	*K* Studies	PC Survival Advantage	*P*
3-mo[1]	1,993	8	0.7%	.76
6-mo[2]	1,009	4	6.2%	.02
9-mo	659	3	11.1%	.003
12-mo*	646	3	14.1%	<.001
15-mo	436	2	10.0%	.03
18-mo	421	2	12.7%	.04
21-mo	407	2	14.9%	.06
24-mo[3]	818	3	6.4%	.39

**Pre-specified, registered primary survival endpoint*

[1]Includes 5 high-quality and 3 low-quality studies, no heterogeneity present

[2]Study quality accounted for heterogeneity, only value for high-quality studies noted here

[3]Includes 2 high-quality studies and 1 low-quality study (that didn't report most endpoints), no heterogeneity present

Note. Survival data at all remaining endpoints were only available from high-quality studies, as low-quality studies typically had shorter-term follow-up

Hoerger et al. (2019). Annals of Behavioral Medicine. [see Fig 2 & Table A5] pallonc.com

Meta-analysis: Outpatient palliative care has no impact on long-term survival in advanced cancer

Palliative Care

4 in 7 alive
at 1 year

Usual Care

3 in 7 alive
at 1 year

but may boost chances of living 1 year

Hoerger et al. (2019). Annals of Behavioral Medicine.

How do reasonable people interpret these findings on PC and survival?

Objective Optimists	Passionate Promoters

In our experience, painting with broad strokes, 1 in 4 ways

Pessimistic Politicians	Biomedical Bulwarks

Objective Optimists (our view)

- Optimistic: View findings favorably
  - Effect size is sizeable, precision due to large sample size ($p<.0001$), 1-yr benefit is consistent across studies and generalizes reasonably to other time points from 6-18 months
- Objective: Want follow-up studies identifying mechanisms, more replication
  - Not like drug trials where early phases (preclinical, phase I) identify mechanisms, so need to work backwards toward identifying them (common in psychosocial research)

Objective Optimists

- Need to fund large palliative care RCTs, focused on potential mechanisms of prolonged survival
- Examples:
  - Reductions in grade 5 toxicities
  - Increased tolerability of chemotherapy early in treatment
  - Reduced chemotherapy and other intensive interventions near end of life
  - Reduced unnecessary polypharmacy
  - Reduced alcohol use
  - Reduced tobacco use
  - Increased exercise
  - Fewer suicides
- Mechanisms must emerge in first few months of PC (to have an effect by 6 months)
- Mechanisms must be dramatic (capable of prolonging survival duration by several months) within subsets of patients

Objective Optimists

- Objective optimists primarily…
  - Balance optimism with caution in describing these and any positive findings
  - Encourage pragmatic decision making based on present evidence
  - Want to see high-quality mechanistic follow-up studies
  - Use data to refute lay beliefs that PC may shorten life

Passionate Promoters

- Passionate promoters lead by describing palliative care as having astonishing survival benefits (over-optimistic)
- May lack understanding of scientific method (need to balance caution/ humility with optimism)
- May have a zeal for growing palliative care, or financial interest

Pessimistic Politicians

- Also passionate about palliative care but think talking about survival is “off message”
- Want to focus on palliative care’s important benefits for quality of life
- Politically, fear that null or negative findings for survival could foster backlash against palliative care
  - View the state of palliative care as fragile
  - Worry the biomedical bulwarks will stomp out the passionate promoters

Biomedical Bulwarks

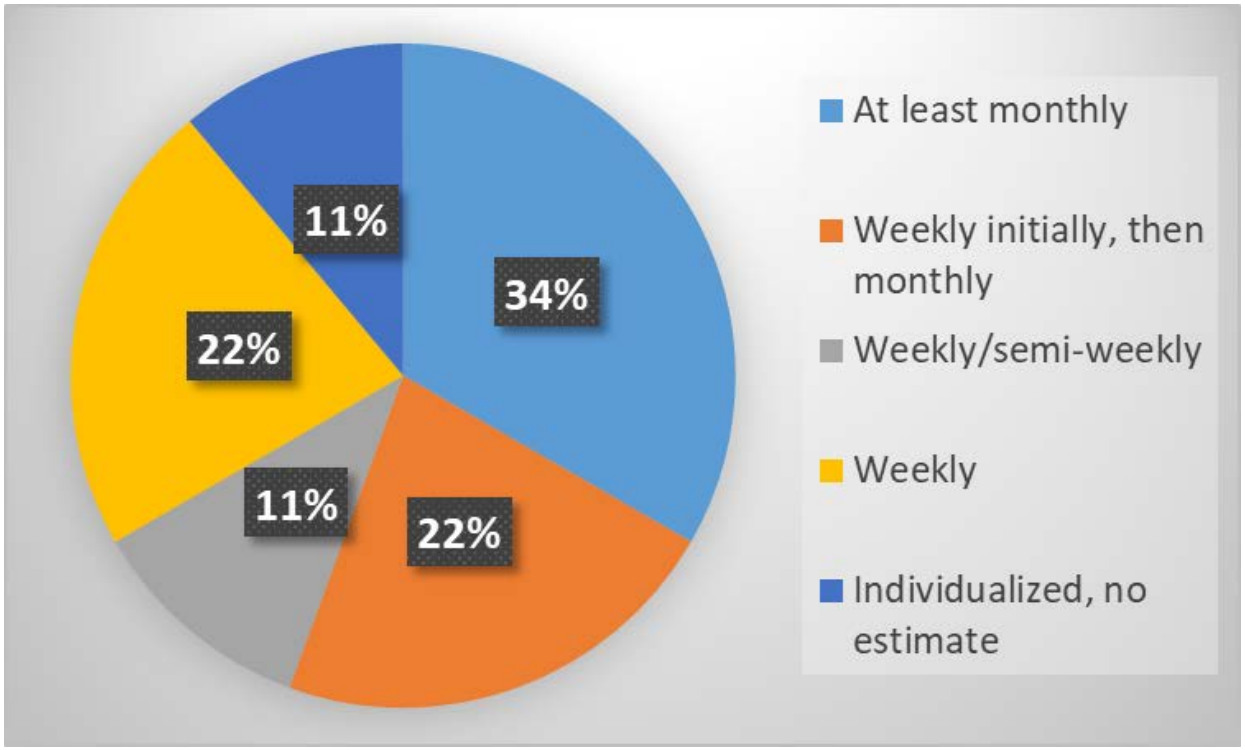
- Biased to favor biomedical over bio-psycho-social interventions
- View bio-psycho-social research as soft science
- Dismiss important of palliative care, perhaps regardless of evidence
- If (non-PC) clinicians, believe they are already doing palliative care

Additional, Rich, Descriptive Findings: Outpatient Palliative Care "Dose"

- How frequently?
- How long were visits?
- How many total visits?

Palliative care, how frequently?

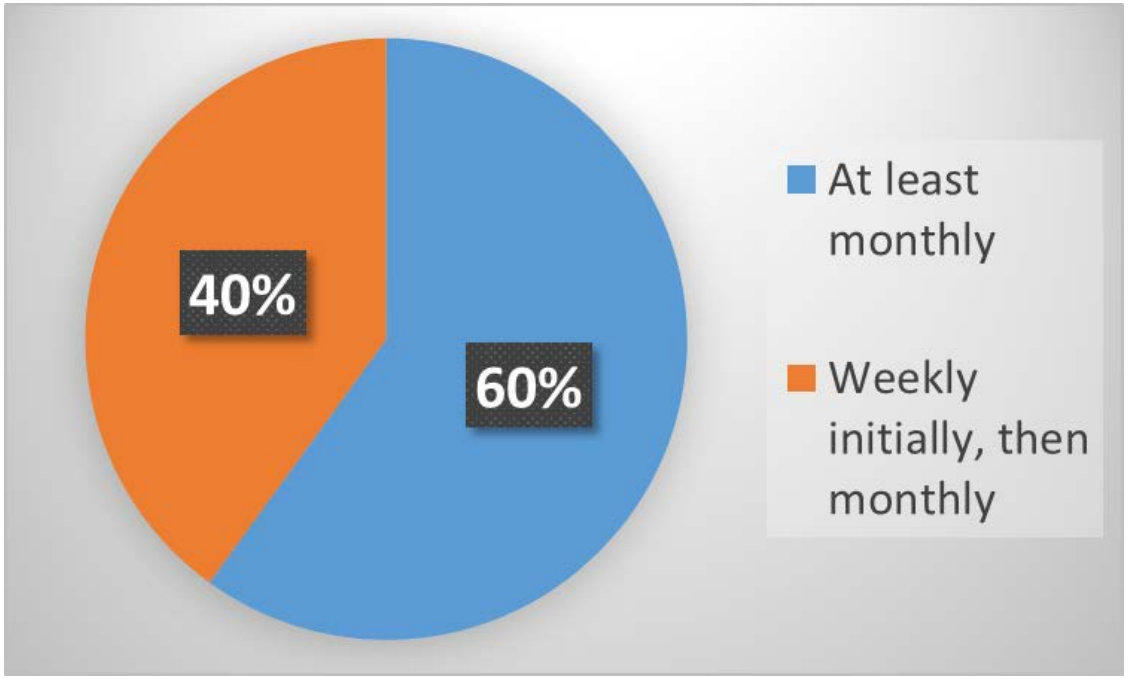
- In 9 RCTs in the systematic review, patients typically had outpatient PC visits…



Hoerger et al. (2019). Annals of Behavioral Medicine.

Palliative care, how frequently?

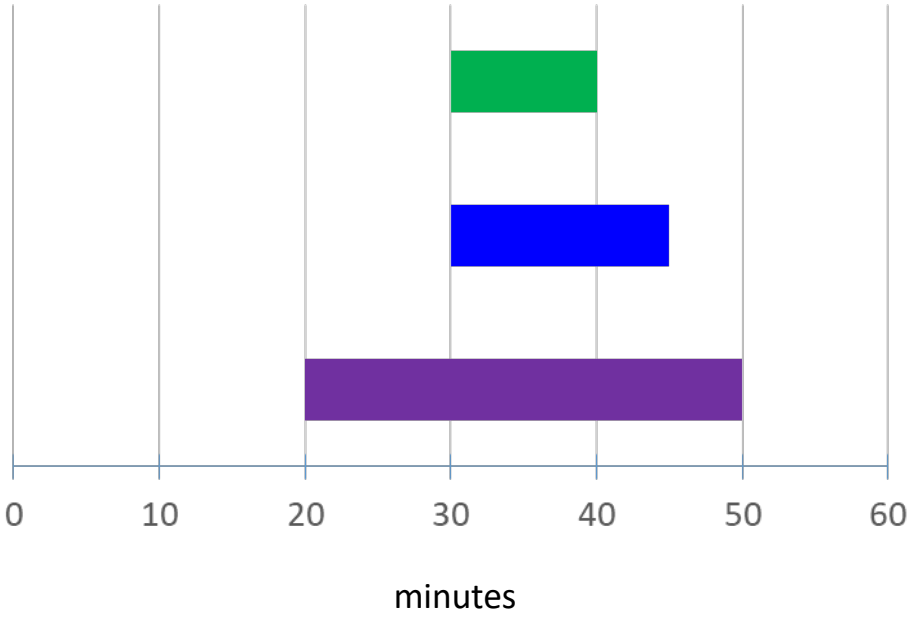
- In 5 high-quality RCTs in the systematic review & meta-analysis, patients typically had outpatient PC visits…



Hoerger et al. (2019). Annals of Behavioral Medicine.

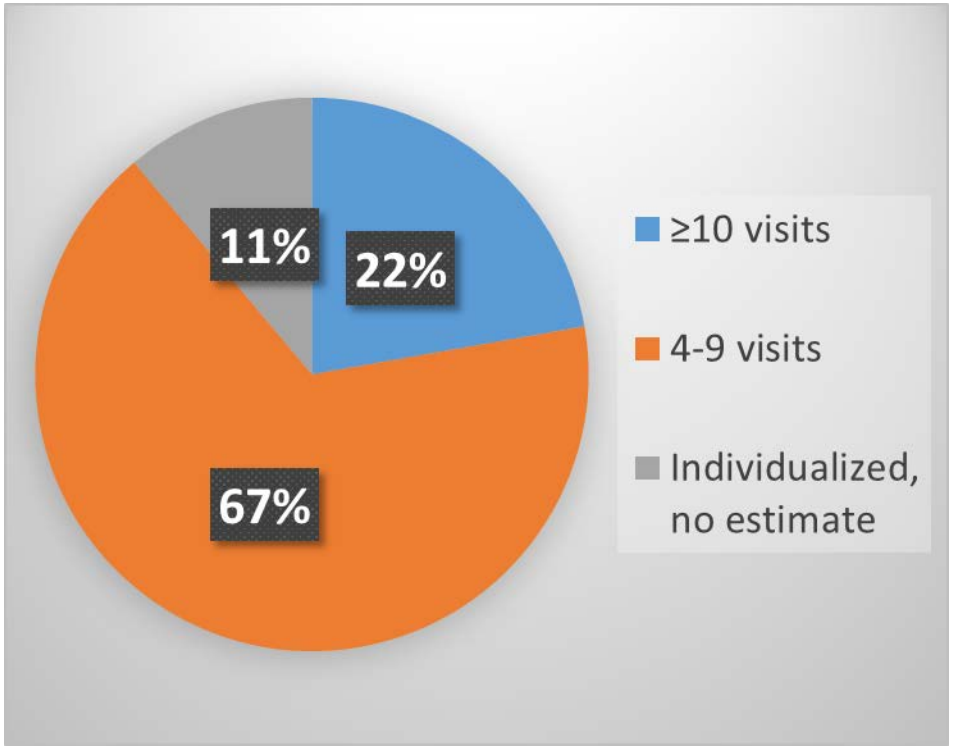
Palliative care, how long were visits?

- In 9 RCTs in the systematic review, only 3 studies (all high-quality) reported the typical visit duration
- Mdn of 35 mins for a "typical" visit
- Similar to what we found elsewhere (Mean of 34 min, SD of 15 min; Hoerger et al., *JCO*, 2018)



Palliative care, how many total visits?

- In 9 RCTs in the systematic review, all estimated the typical number of outpatient PC visits…



Hoerger et al. (2019). Annals of Behavioral Medicine.

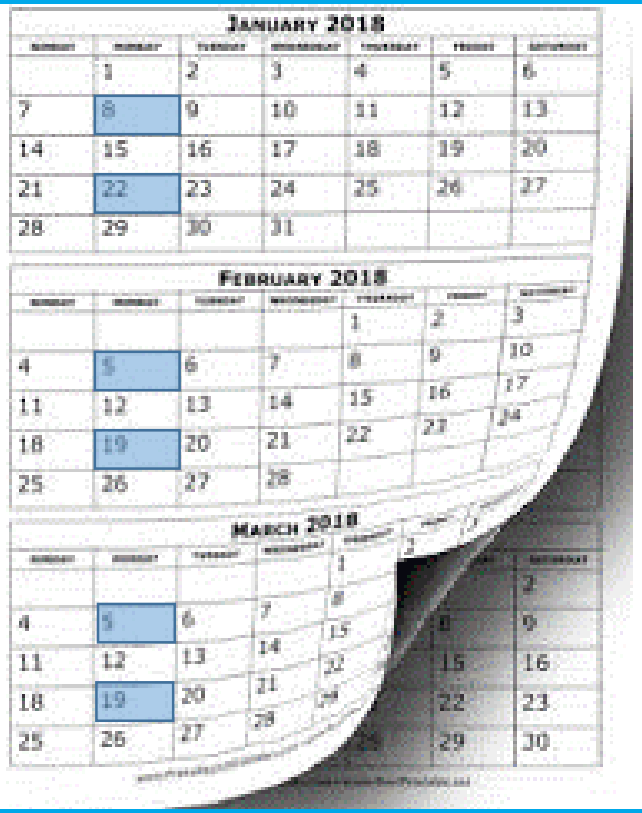
Outpatient Palliative Care "Dose"

In sum, outpatient palliative care is typically weekly to monthly, about 35 minutes each visit, 4-9 visits total

The frequency, duration, and total number of visits is individually-tailored to provide optimal family-centered care

Outpatient Palliative Cancer Care

Most patients go for 35 minutes, weekly to monthly, 4-9 times total



…for better quality of life.

Hoerger et al. (2019). Annals of Behavioral Medicine.

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Outpatient Palliative Care Content

- What are the key ingredients?

  or…

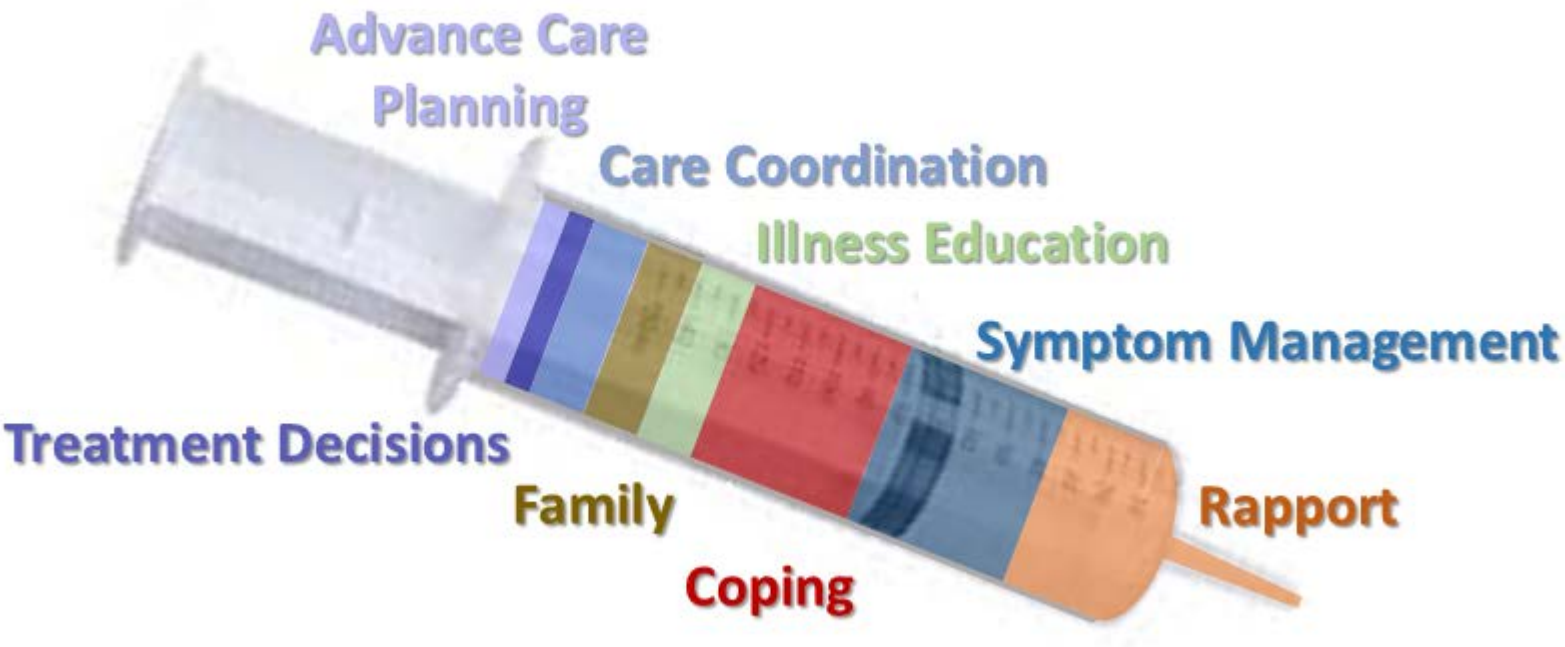
- What's in the palliative care "syringe"?

Key Elements of Palliative Care

Across the 9 studies reviewed, most models of outpatient palliative care emphasized….

- Two key hallmarks
  - Symptom assessment and management
  - Coping support
- Other important ingredient
  - Rapport
  - Treatment decision making
  - Advance care planning
  - Illness education
  - Care coordination
  - Family support

What's in the Palliative Care "syringe"?



Hoerger et al. (2019). Annals of Behavioral Medicine.

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What's in the Palliative Care "syringe"?

Palliative care is a complex **bio-psycho-social** intervention

It involves developing a warm therapeutic **relationship**, **symptom** assessment and management, **coping** support, illness **education**, treatment **decision** support, care **coordination**, support for **families**, and advance care **planning**

These skills cannot fit in a syringe.

Who's on the Outpatient Palliative Cancer Care Team?

All 9 Studies Reviewed

- Physicians (89%)
- Nurses (89%)
- Social Workers (44%)
- Clergy (22%)
- Nutritionists (22%)
- Physiotherapists (22%)
- Psychologists (11%)
- Pharmacists (11%)

5 High-quality studies

- Physicians (100%)
- Nurses (100%)
- Social Workers (0%)
- Clergy (0%)
- Nutritionists (0%)
- Physiotherapists (0%)
- Psychologists (0%)
- Pharmacists (0%)

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Note: Only the studies of lower quality methodologically explicitly included diverse disciplines on the care team. There is plenty to learn from those studies' models of palliative care, even if methodologic limitations preclude strong inferences about study outcomes

Physicians and Nurses

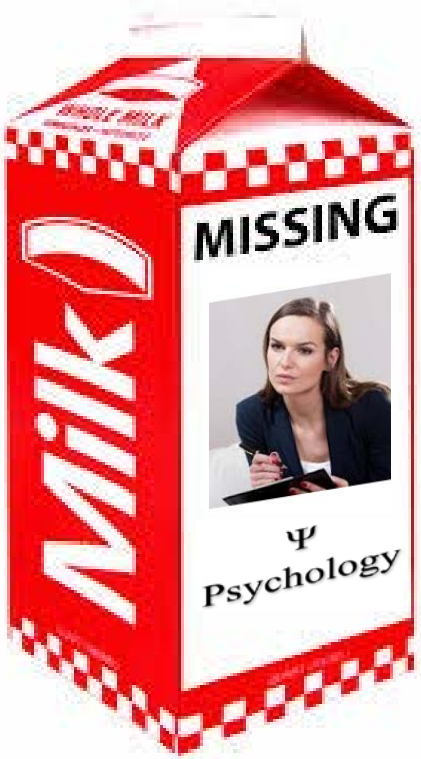
Involved in 89% of outpatient palliative care teams in RCTs in the systematic review

And all 5 of the high-quality studies

Champions of outpatient palliative cancer care

If coping is a key element of palliative care….

Coping is the 2nd biggest focus of palliative care[1]



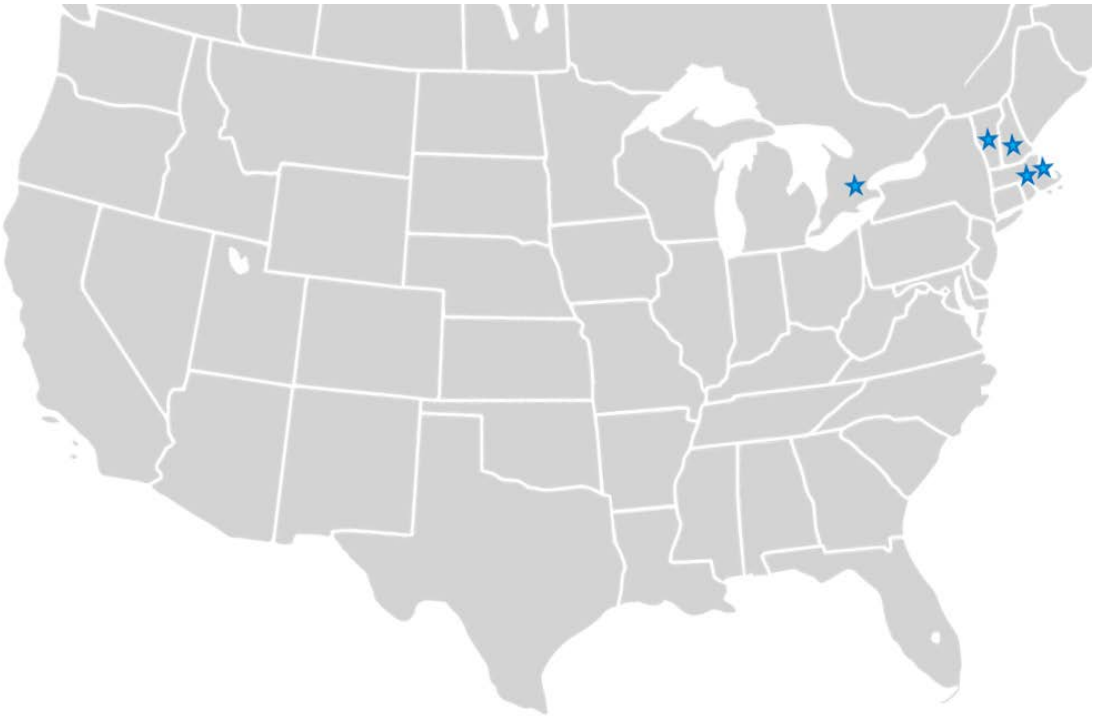
Meta-analysis finds **psychologists on 0% of palliative care teams** in high-quality RCTs[2]

Where are the palliative care psychologists?

1. Hoerger et al. (2018). Journal of Clinical Oncology.
2. Hoerger et al. (2019). Annals of Behavioral Medicine.

Geographic Limitations

- All 5 high-quality RCTs conducted within <500 mile region in north-eastern U.S. and Canada
- Need high-quality RCTs in Deep South, western U.S., internationally across the globe



Hoerger et al. (2019). Annals of Behavioral Medicine.

Racial and Ethnic Limitations

- All 5 high-quality RCTs had limited racial and ethnic diversity
  - 1 study reported no race/ethnicity data
  - In 4 remaining studies, white participants represented 92%, 97%, 97%, and 99% of the samples
- Need for inclusion of racially and ethnically diverse patients

Hoerger et al. (2019). Annals of Behavioral Medicine. [see Table 1]