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Consideration of Bereavement Effects in HTA

Dr Chris Skedgel

DIRECTOR | OHE

Outline for today’s Issue Panel

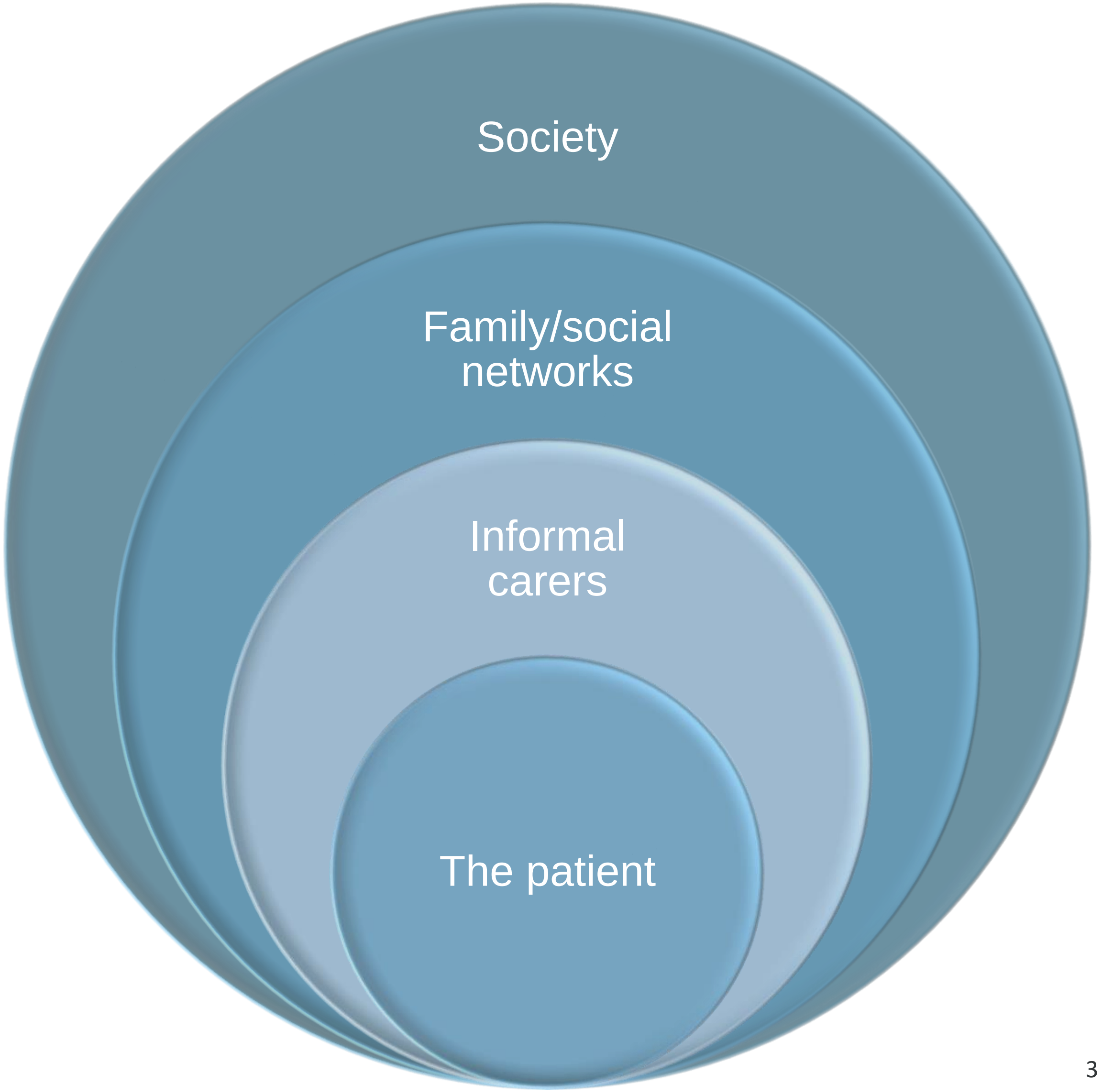
1. Introducing Bereavement Effects
2. Audience poll #1
3. Our speakers
4. Panel discussion and audience Q&A
5. Audience poll #2

Bereavement Effect is a form of Spillover Effect.

Ill-health affects the patient but also a range of individuals and networks beyond the patient.

Bereavement Effects describe the negative health or wellbeing impacts of a patient's death on those individuals and networks.

As with any spillover effect, there is value in minimising the impact of these effects.

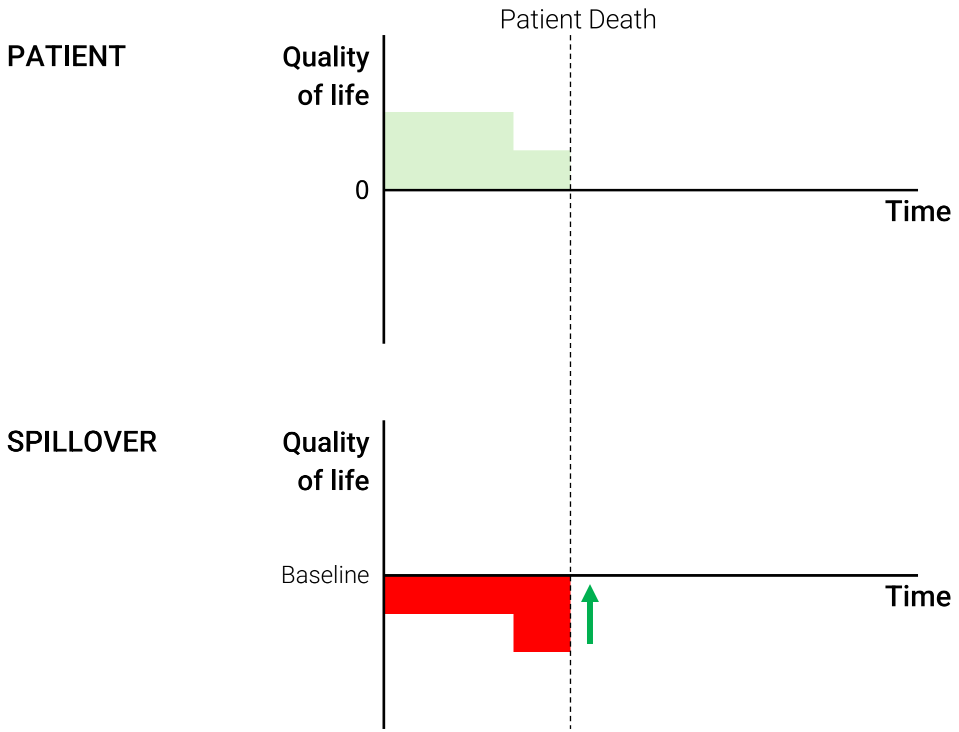

Society

Family/social networks

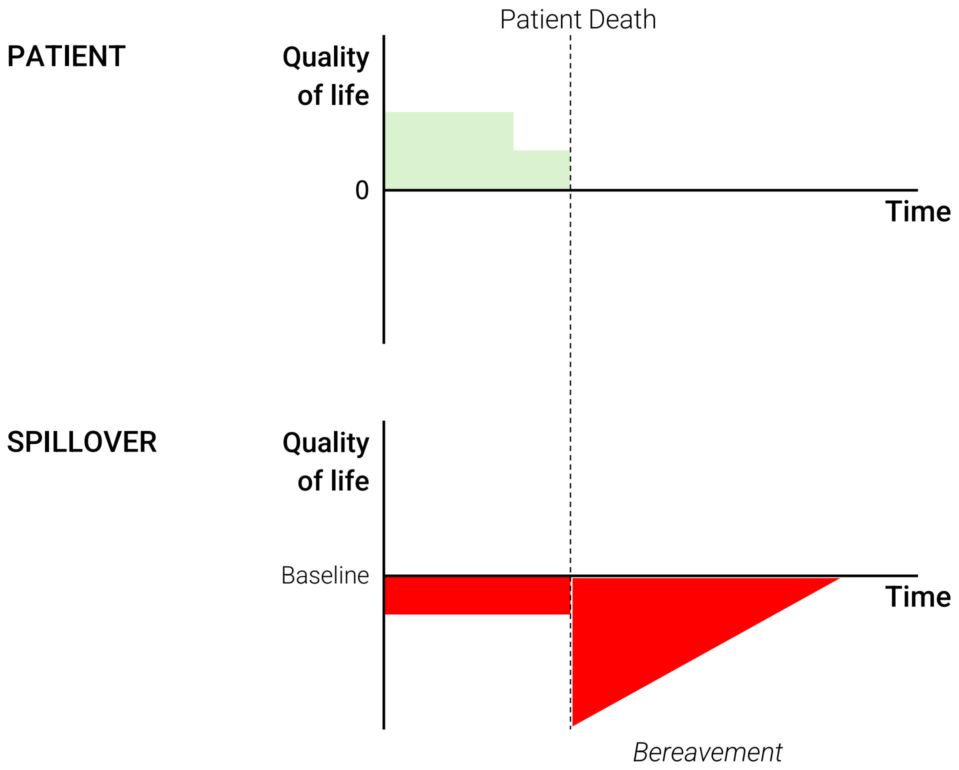
Informal carers

The patient

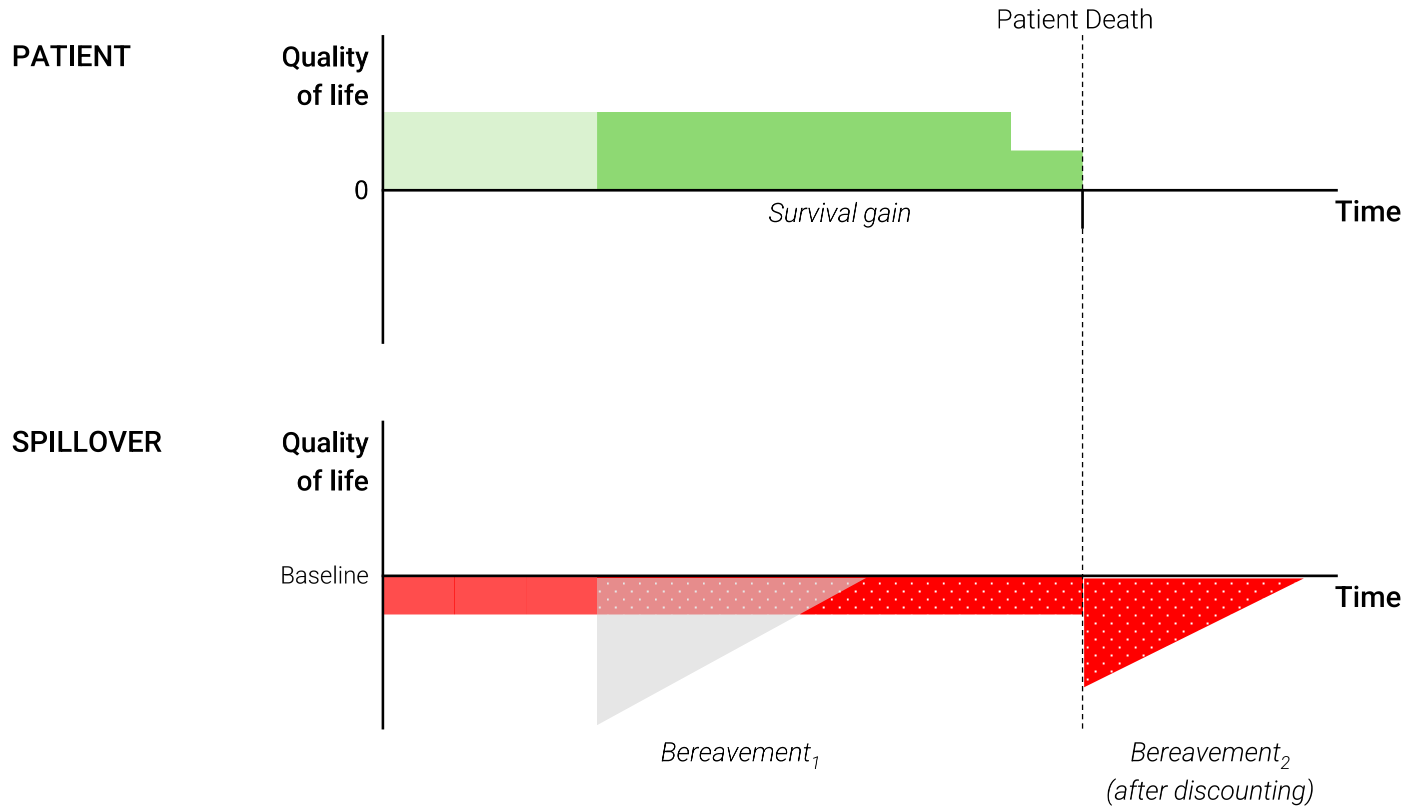
HTA allows for spillover effects related to caring but normally assumes *immediate return to baseline* upon death of the patient.



Bereavement Effect is the (theoretical) loss of QOL to carers, family, and wider networks *following* the death of the patient.



Extending survival benefits the patient but it can also delay – *and potentially reduce* – bereavement effects.



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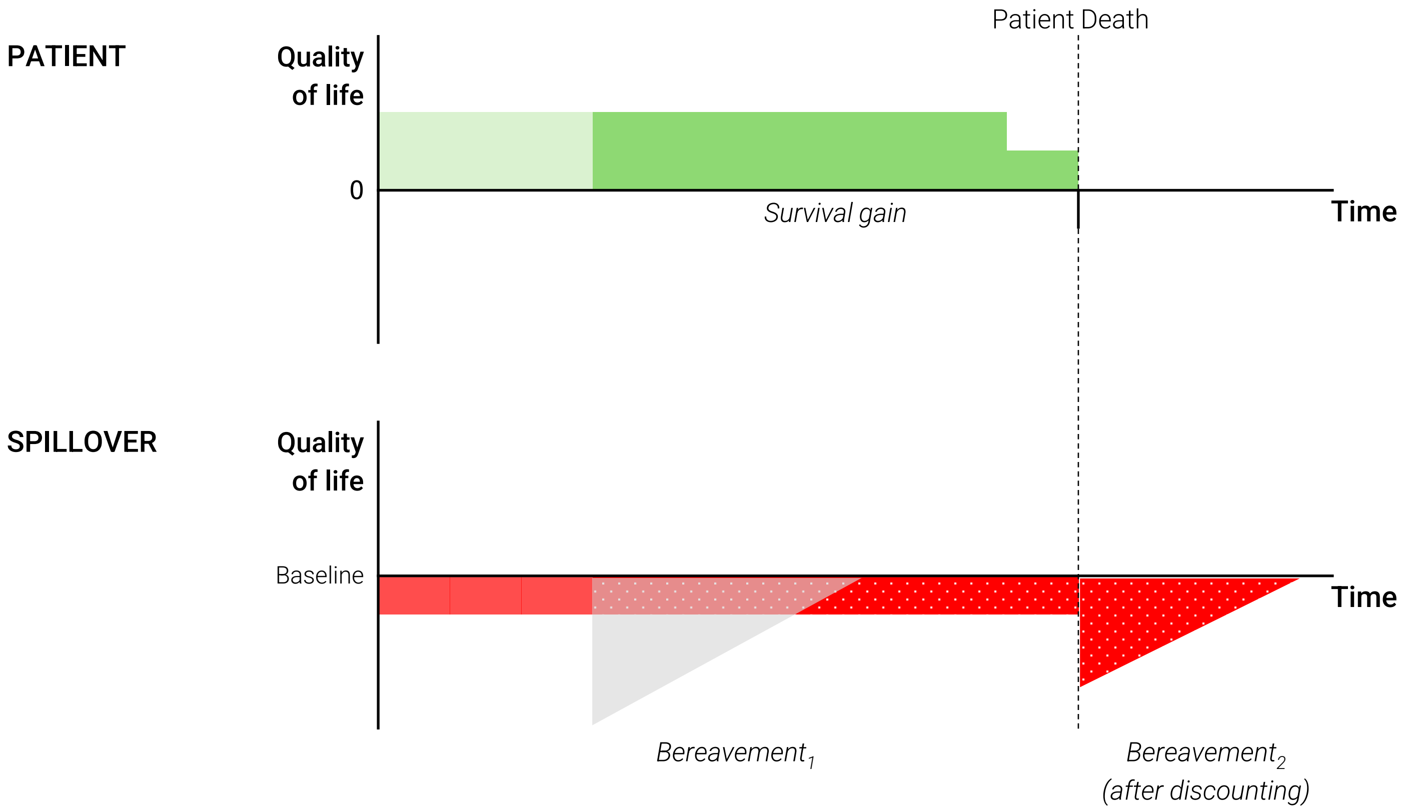

1. **Discounting reduces PV of QALYs lost due to bereavement.**
2. **Bereavement as a function of age or ‘life milestones’ of the patient?**

QALY gains associated with ‘discounted’ bereavement likely to be small, but could offer some escape from the *“Carer QALY Trap”*.

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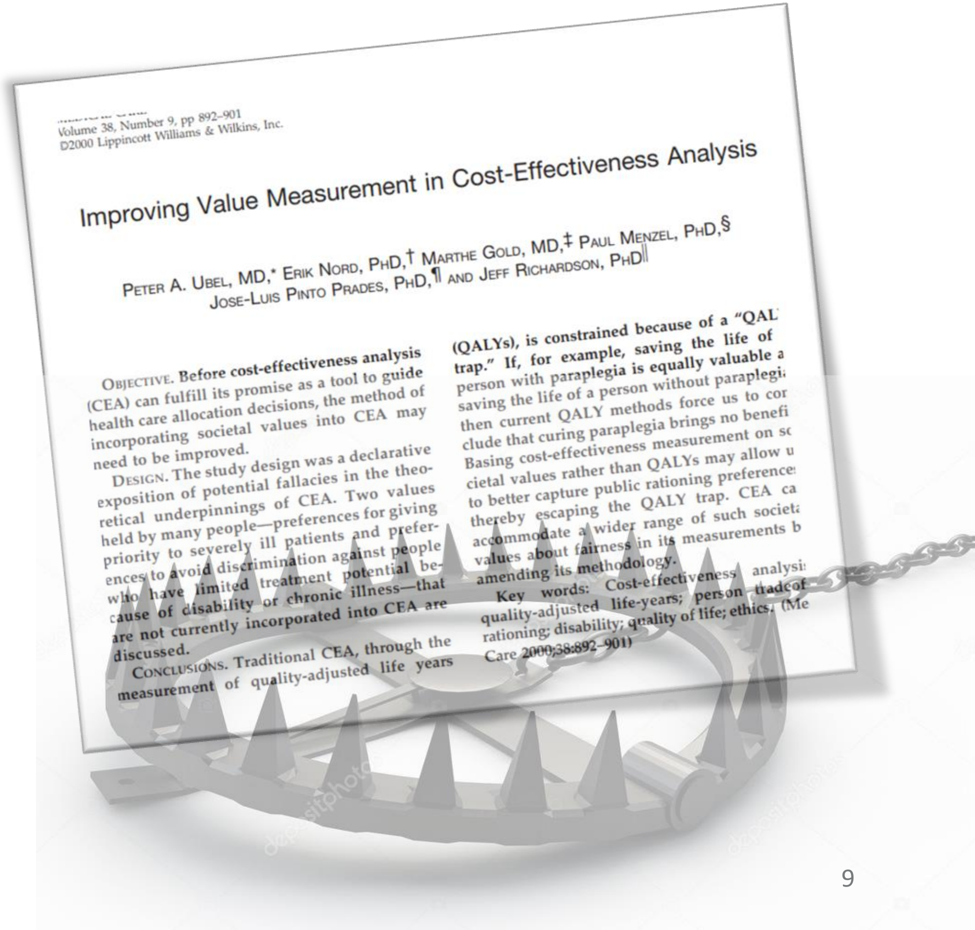
Under the **‘classic’ QALY Trap**, described by Ubel *et al*. (2000)

- Extending the life of **a person with a chronic illness** is less valuable in QALY terms than extending the life of a person in full health, all else equal.
- If society chooses to disregard HRQOL in valuing a life extension, and assign equal value to all lives, it implies that **curing the chronic illness has no value**.



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Improving Value Measurement in Cost-Effectiveness Analysis

Peter A. Ubel, MD,[*] Erik Nord, PhD,[†] Marthe Gold, MD,[‡] Paul Menzel, PhD,[§]
Jose-Luis Pinto Prades, PhD,[¶] and Jeff Richardson, PhD[||]

Objective. **Before cost-effectiveness analysis (CEA) can fulfill its promise as a tool to guide health care allocation decisions, the method of incorporating societal values into CEA may need to be improved.**

Design. **The study design was a declarative exposition of potential fallacies in the theoretical underpinnings of CEA. Two values held by many people—preferences for giving priority to severely ill patients and preferences to avoid discrimination against people who have limited treatment potential because of disability or chronic illness—that are not currently incorporated into CEA are discussed.**

Conclusions. **Traditional CEA, through the measurement of quality-adjusted life years (QALYs), is constrained because of a “QAL
trap.” If, for example, saving the life of
person with paraplegia is equally valuable a
saving the life of a person without paraplegi
then current QALY methods force us to cor
clude that curing paraplegia brings no benefi
Basing cost-effectiveness measurement on sc
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to better capture public rationing preference
thereby escaping the QALY trap. CEA ca
accommodate a wider range of such societ
values about fairness in its measurements b
amending its methodology.**

Key words: Cost-effectiveness analysi
quality-adjusted life-years; person tradeof
rationing; disability; quality of life; ethics. (Me
Care 2000;38:892–901)

Ubel PA, Nord E, Gold M, Menzel P, Prades JL, Richardson J. Improving value measurement in cost-effectiveness analysis. Med Care. 2000 Sep;38(9):892-901.

QALY gains associated with ‘discounted’ bereavement likely to be small, but could offer some escape from the *“Carer QALY Trap”*.

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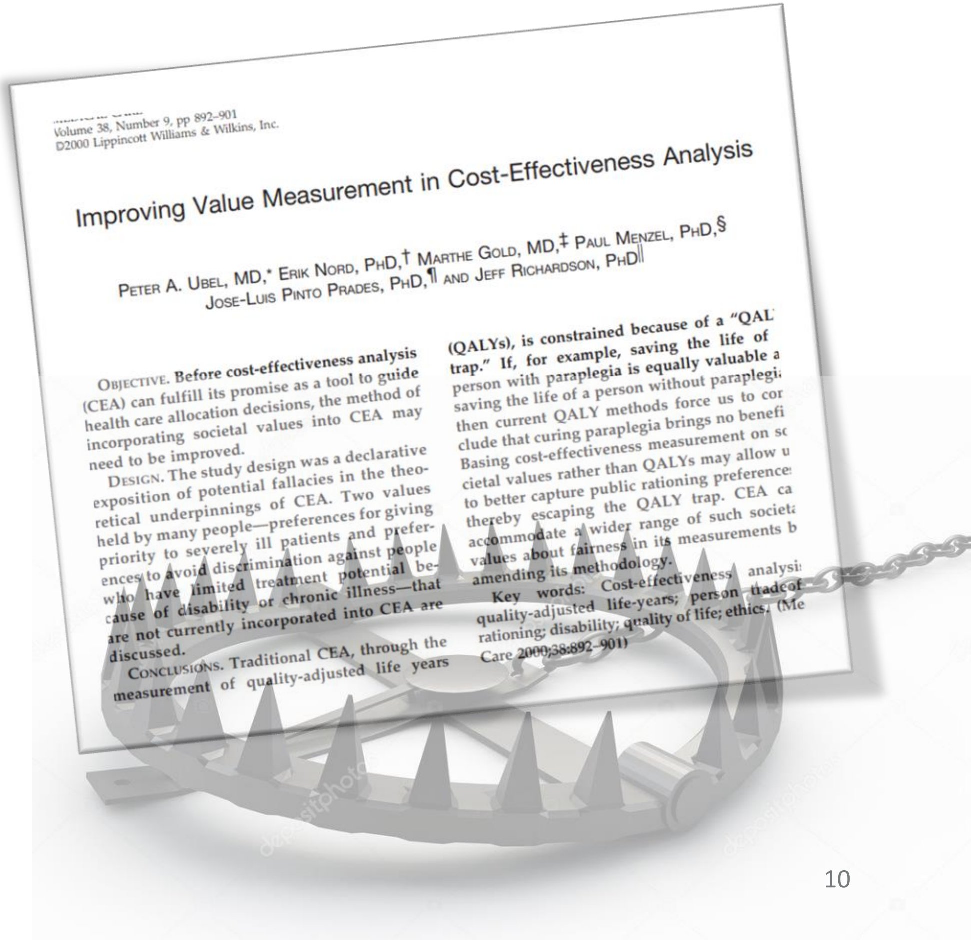
Under the **Carer QALY Trap** described by Mott *et al*. (2023),

- Extending the life of **a person with an informal carer** is less valuable in QALY terms than extending the life of a person without a carer, all else equal.
- If society chooses to disregard the HRQOL of carers in valuing a life extension, it implies that **reducing the burden on the carer has no value**.



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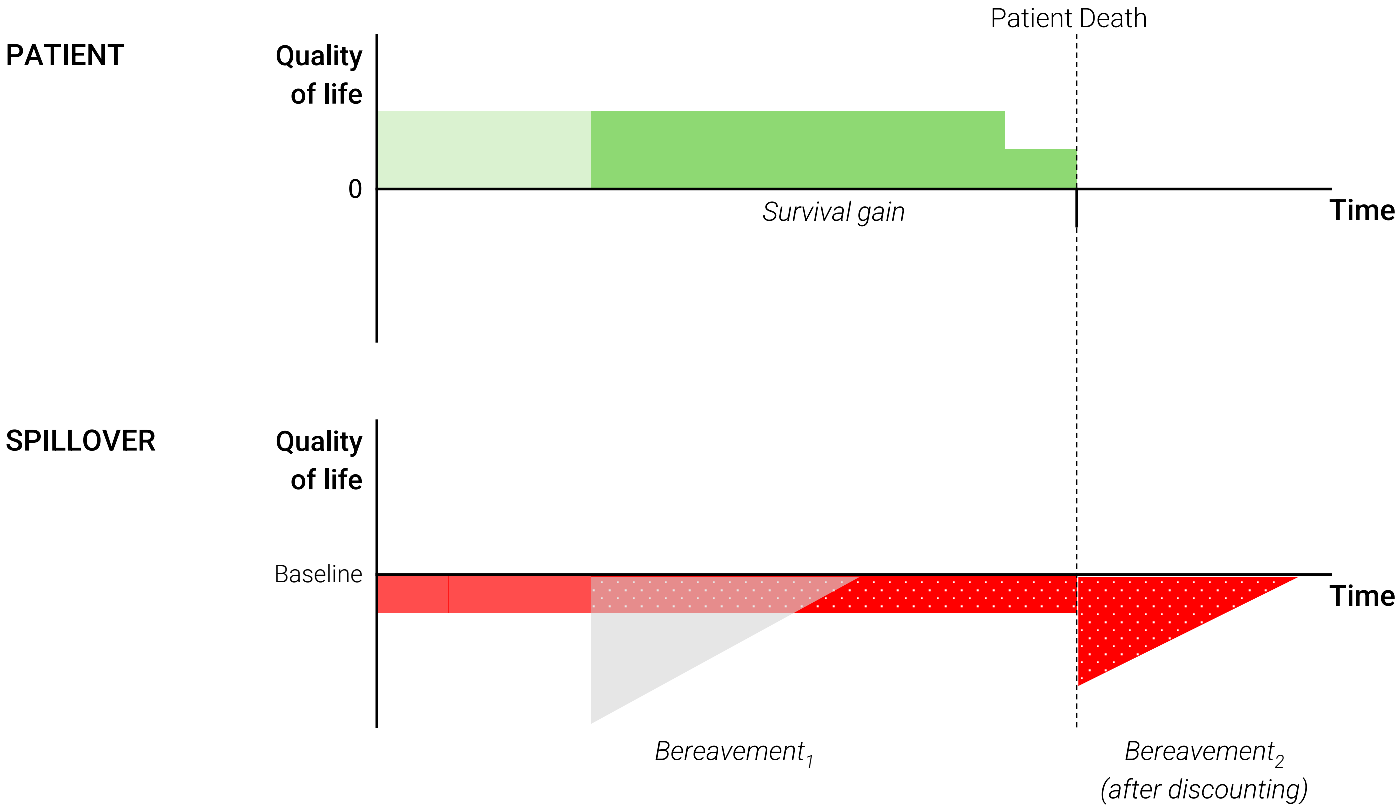
Mott DJ, Schirrmacher H, Al-Janabi H, Guest S, Pennington B, Scheuer N, Shah KK, Skedgel C. Modelling Spillover Effects on Informal Carers: The Carer QALY Trap. Pharmacoeconomics. 2023 Dec;41(12):1557-1561.

Accounting for delay in bereavement can *offset* the extended carer burden associated with greater patient survival.



Net QALY gain =

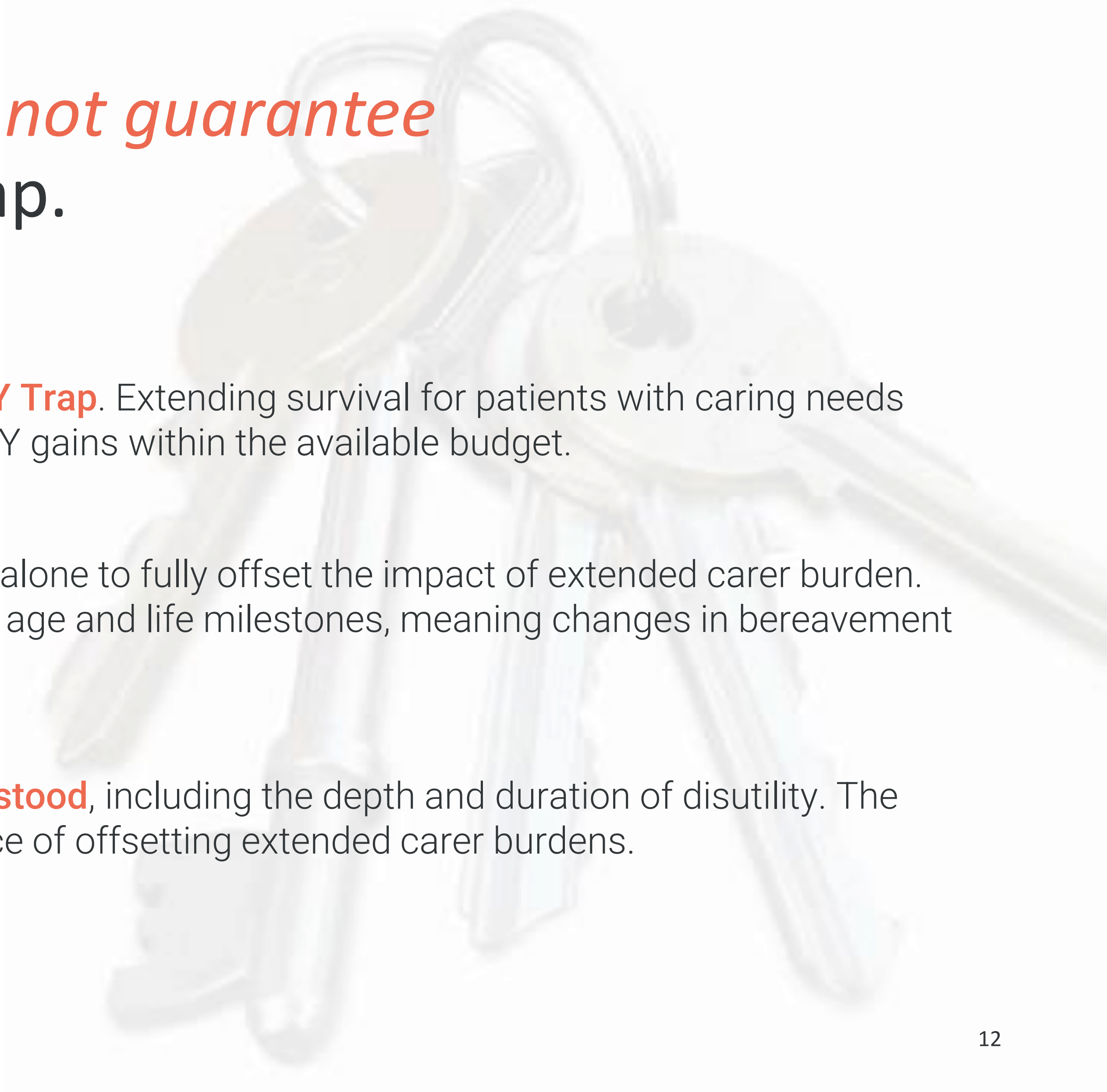
+ Extended patient survival

– Extended carer burden

+ [Bereavement$_2$ – Bereavement$_1$]

If [Bereavement$_2$ – Bereavement$_1$] is greater than the extended carer burden, we have escaped the Carer QALY Trap.

Accounting for bereavement *does not guarantee* an escape from the Carer QALY Trap.



1. **There is nothing fundamentally incorrect in the Carer QALY Trap**. Extending survival for patients with caring needs extends the burden on carers and can lead to fewer net QALY gains within the available budget.

2. **Survival gains will need to be considerable** for discounting alone to fully offset the impact of extended carer burden. However, bereavement effects may also be affected patient age and life milestones, meaning changes in bereavement effects may not be strictly proportional to survival.

3. **The ‘shape’ of any bereavement effects are not well understood**, including the depth and duration of disutility. The deeper and longer any bereavement effects, the more chance of offsetting extended carer burdens.

Today's issues for discussion

1. Are bereavement effects *'real'*? If so, what are their characteristics?
2. Are bereavement effects *meaningful enough* to be relevant for HTA?

Our panellists

Tara Lavelle

Tufts University School of Medicine and Tufts Medical Center

Boston, USA

Becky Pennington

University of Sheffield

Sheffield, United Kingdom

Saskia Knies

Zorginstituut Nederland

Diemen, Netherlands

Audience poll #1

A two-part question: do you believe that **bereavement effects are meaningful**, and that **they should be included in HTA**?

- Bereavement effects **are not meaningful** and **should not be included in HTA**
- Bereavement effects **are meaningful** but **are not relevant** to HTA
- Bereavement effects **are meaningful** and **are relevant** to HTA

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TuftsMedicine

Quality of Life and Work Functioning of Parents of Children Who Have Died from Spinal Muscular Atrophy

Tara Lavelle, PhD
Assistant Professor
Center for the Evaluation of Value and Risk in Health
Tufts Medical Center
Boston, MA USA

Spinal muscular atrophy (SMA)

zolgensma®
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion

SPINRAZA®
(nusinersen) injection
12 mg/5 mL

Evrysdi®
risdiplam
60 mg
powder for oral solution

How does grief affect parent quality of life and work productivity?

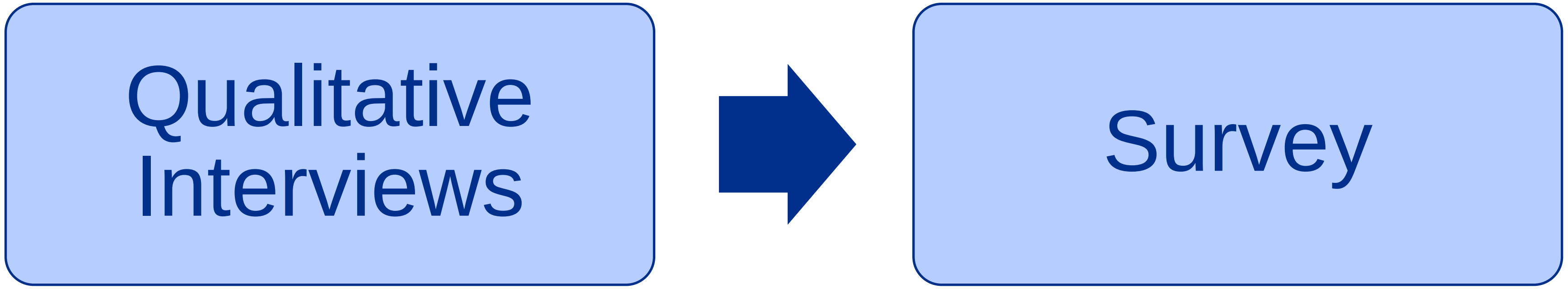
What are the implications for economic evaluations?

Objective:

Measure the impact of parental grief

Study population:

Parents bereaved following the death of a child with SMA



Qualitative Interviews

Survey

Interviewed 16 bereaved parents about:

- Care experience
- Context of their child’s death
- Impact of grief on quality of life, work, and social connections

Survey components

- Grief
- Quality of Life
- Physical Health
- Mental Health
- Work Productivity
- Changes in Interests

Sent survey to 880 bereaved parents

cure SMA

72 responses

Respondent characteristics

Gender/relationship	n (%)
Female/biological mother	56 (77.8%)
Male/biological father	16 (22.2%)

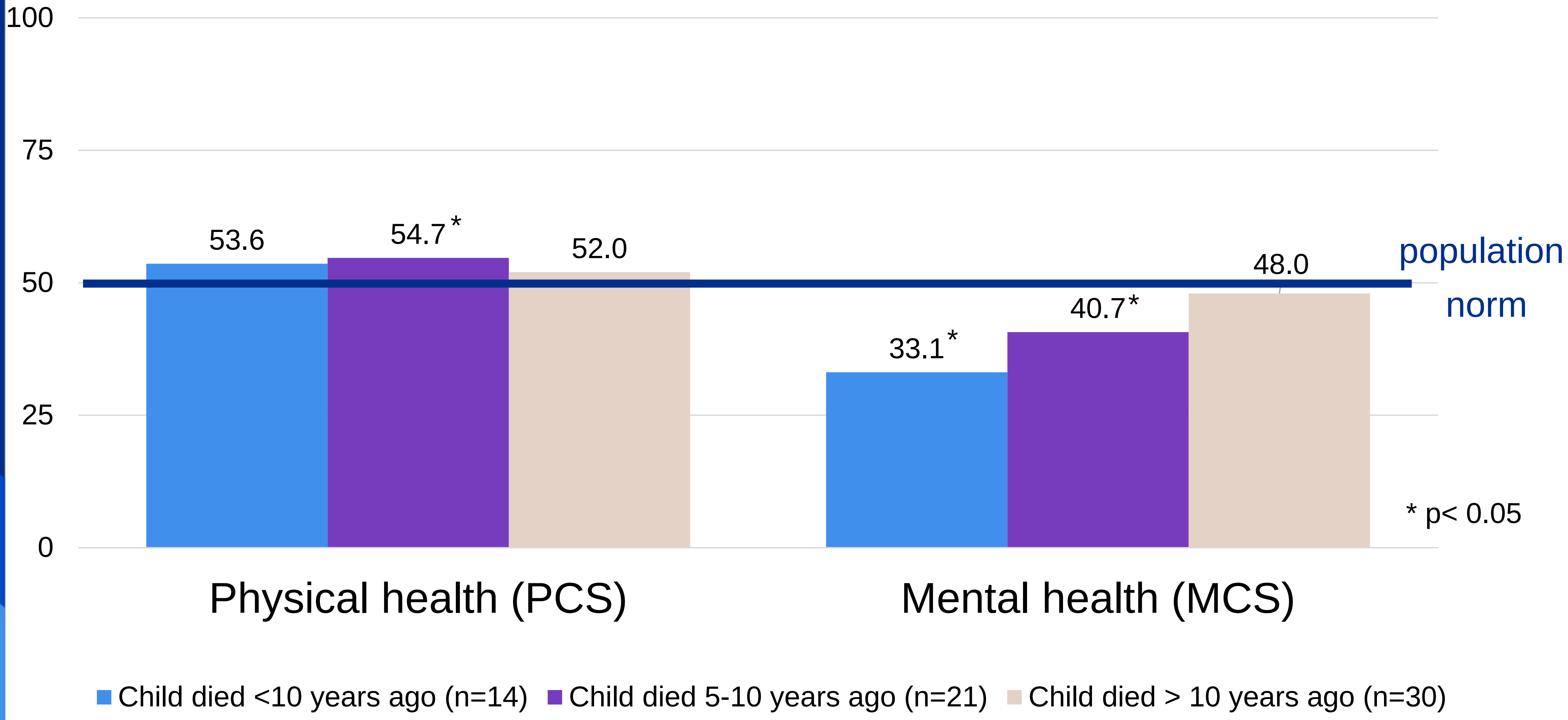
Respondent characteristics

Race	n (%)
White or Euro-American	61 (84.7%)
Asian American	5 (6.9%)
Black or African American	3 (4.2%)
Other	2 (2.8%)
Not reported	1 (1.4%)

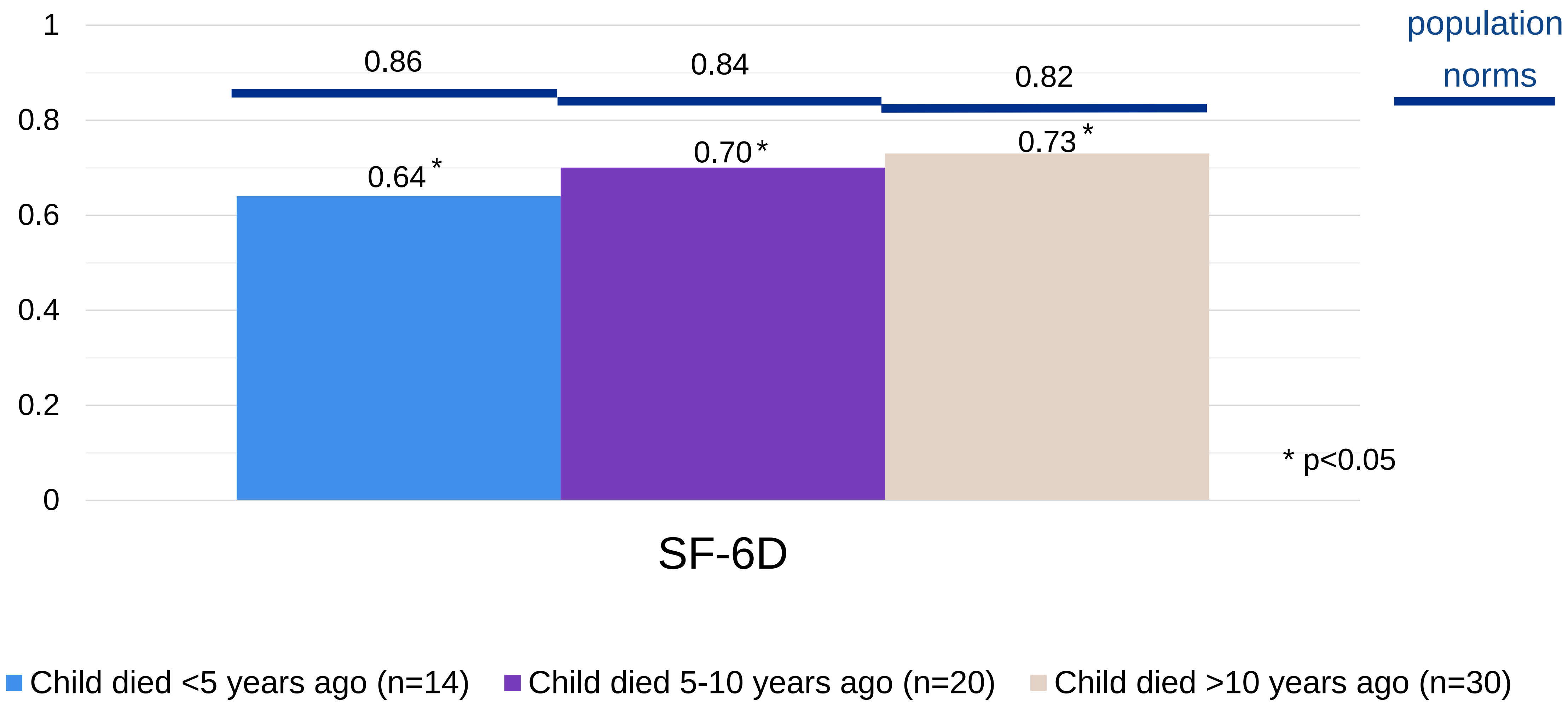
Child characteristics

Age of child at death	n (%)
<12 months	44 (61.1%)
12-24 months	9 (12.5%)
>24 months	17 (23.6%)
Not reported	2 (2.8%)

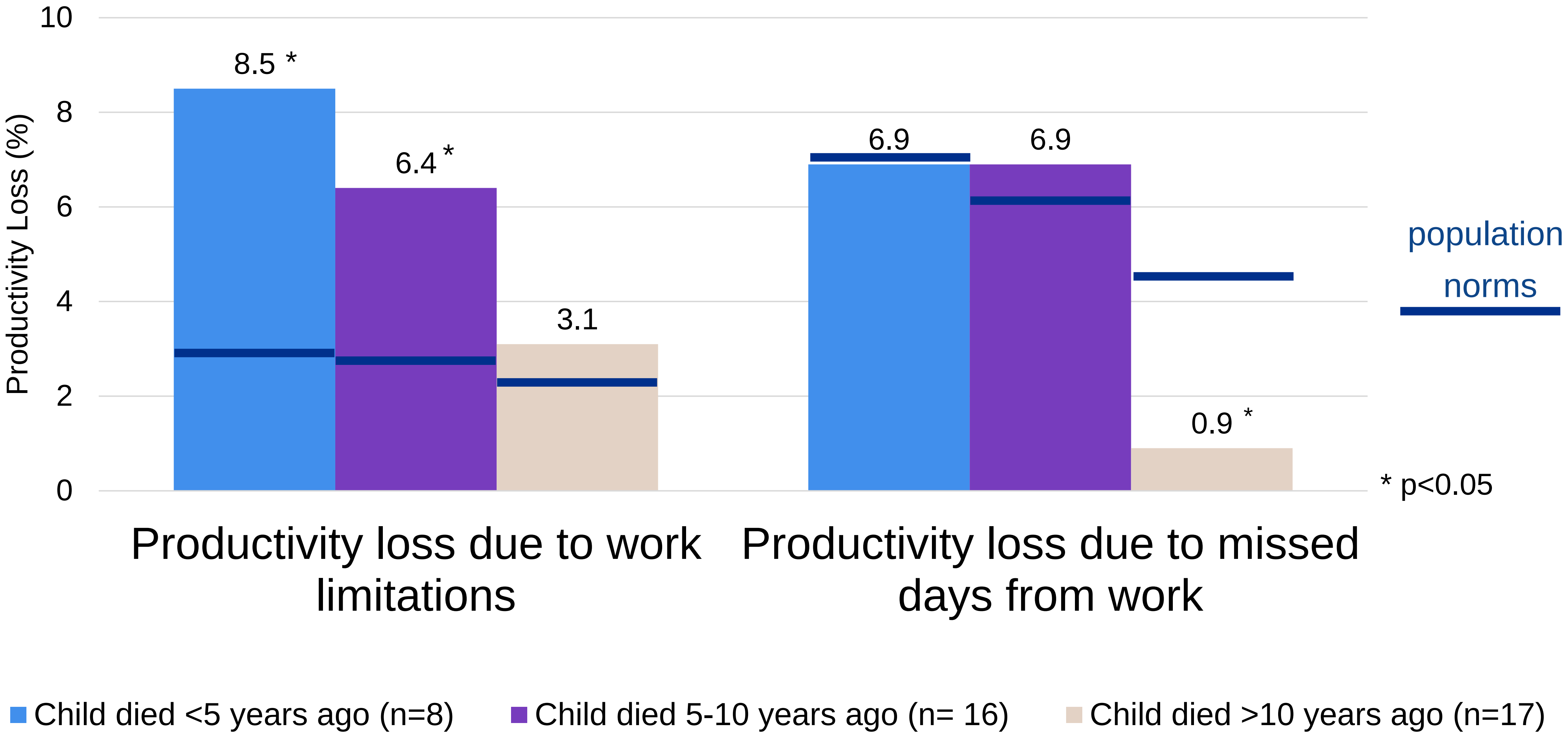
HRQoL (SF-12)


100
75
50
25
0
53.6
54.7*
52.0
48.0
33.1*
40.7*
population norm
* p< 0.05
Physical health (PCS)
Mental health (MCS)
Child died <10 years ago (n=14)
Child died 5-10 years ago (n=21)
Child died > 10 years ago (n=30)

Health Utility Values



Work Limitations – Presenteeism and Absenteeism



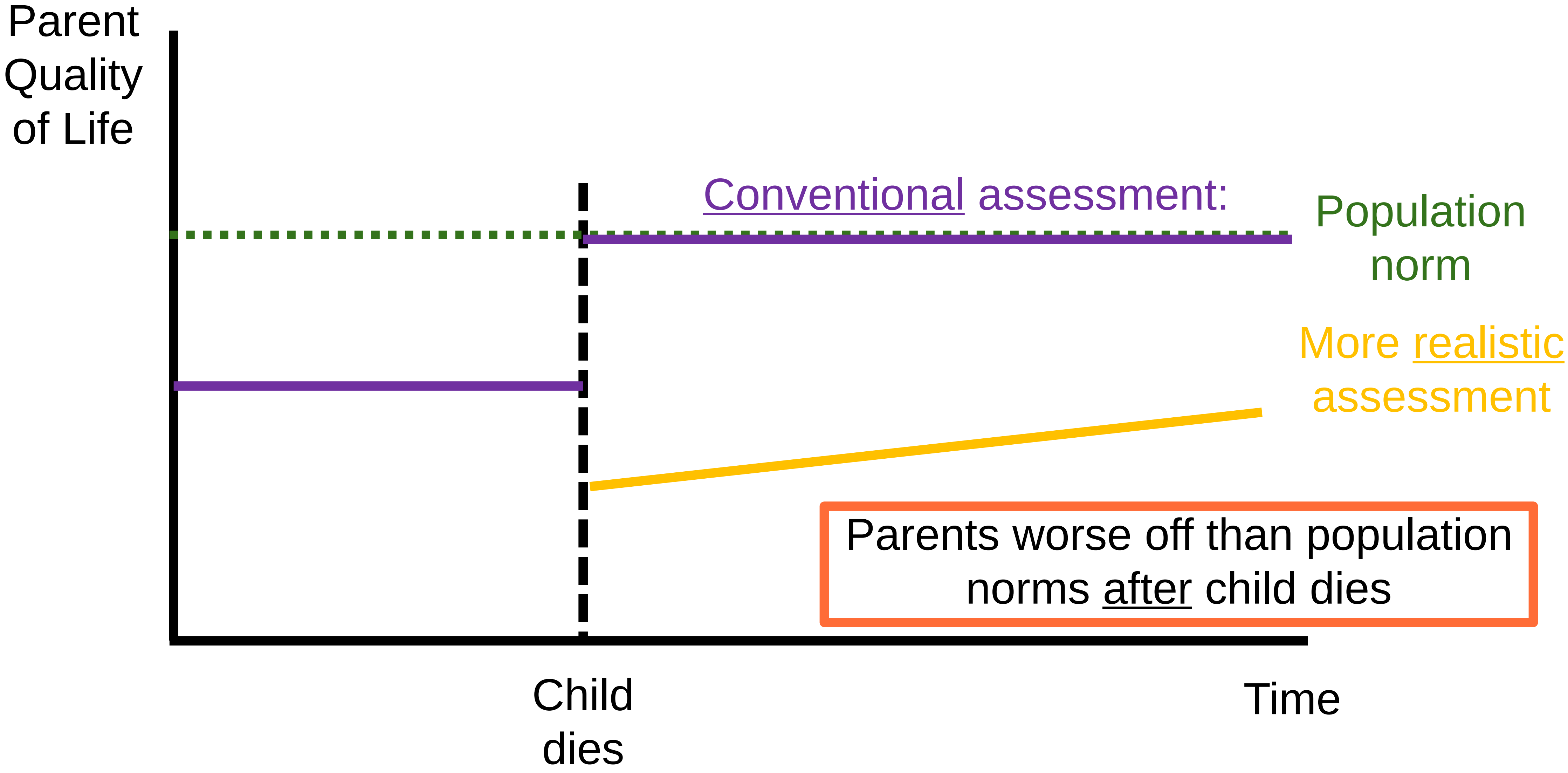
Key findings

- The death of a child negatively impacts parent health-related quality of life and work productivity
- Some impacts are substantial and long-lasting

How does grief affect parent quality of life and work productivity?

What are the implications for economic evaluations?

Conventional assessment (hypothetical)



Parents worse off than population norms after child dies

Why does it matter?

- Conventional assessment makes comparator (base case) look better than it is in reality
- Diminishes the incremental benefit of a new treatment
- Ignores that new treatment not only prolongs life expectancy of child, but delays the impacts of grief in the family
- Diminishes estimated value of new intervention

Will including bereavement change results of HTA?

- Depends not only on magnitude of bereavement effect, but on the impact of treatment on functioning and survival
- Context specific
- Important area for future research

Acknowledgements

- Abigail Riley
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- David Fox
- Cure SMA
- Scientific Advisory Committee
- Study participants

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Thank you

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CEVR
Center for the Evaluation of Value and Risk in Health

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Bereavement, caring and health-related quality of life (HRQoL)

Analysis of UKHLS data

Becky Pennington
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ISPOR Europe 2024

Disclaimers

This work was funded through my National Institute for Health and Care Research doctoral research fellowship (NIHR300160)

This work was supervised by Mónica Hernández Alava and Mark Strong

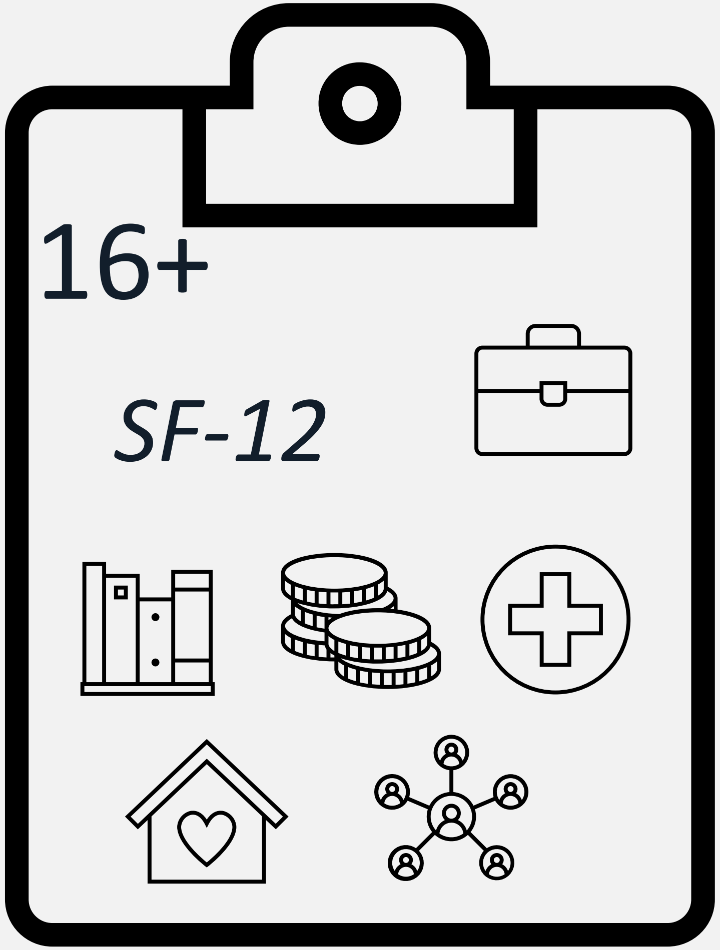
I am a member of the National Institute for Health and Care Excellence (NICE) Technology Appraisal Committee A

All views expressed are my own and not necessarily reflective of those of NIHR, NICE or the University of Sheffield

Observational data from UKHLS

UK Household Longitudinal Survey (Understanding Society):

- 40,000 households
- 13 waves (years)



UKHLS households…and bereavement…and carers

Households asked in each wave:

- Who lives here?
- What is their relationship to each other?

- Are they still living together at the next wave?
- If not, why not? Has one of them died before the next wave?

Individuals are asked in each wave:

- Is there anyone living with you who is sick, disabled or elderly whom you look after or give special help to (for example, a sick, disabled or elderly relative, husband, wife or friend etc)? (And who)

We have longitudinal (multiple time points) data for:

1. People who cared for a household member who died (Bereaved carers n=1,447)
2. People who cared for a household member who didn't die (Non-bereaved carers n=8,846)
3. People whose household member died, but they weren't caring for them (Bereaved non-carers n=721)
4. People who weren't caring for any household members, and whose other household members did not die (Non-bereaved non-carers n=44,731)

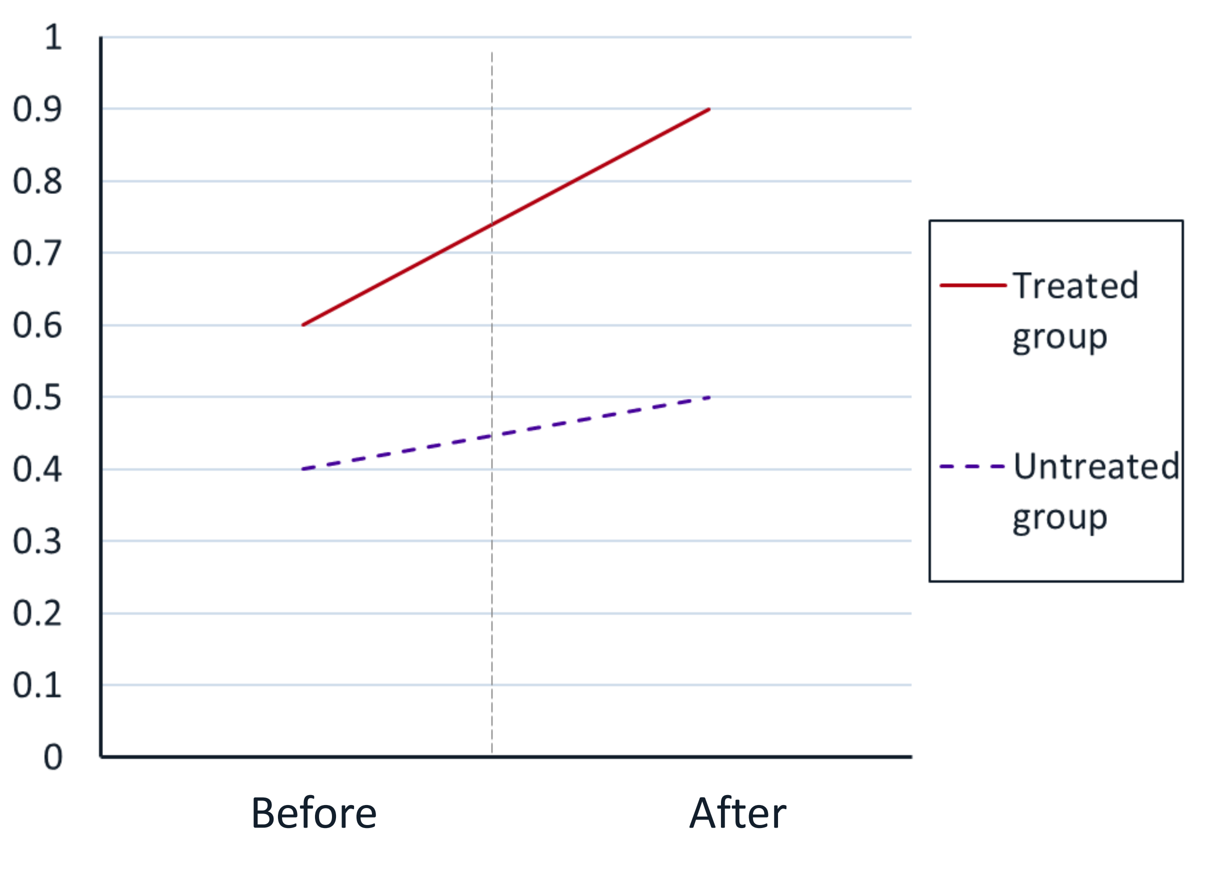
- Data before and after (potential) bereavement for carers and non-carers
- Health-related quality of life (SF-6D in this case)
- Data on other variables which may affect health-related quality of life changes (age, sex, socioeconomic status)

Our research questions

- How does carers' health-related quality of life change when the person they care for dies?
- How does the health-related quality of life of people who *aren't* carers change when a close person dies?
- If there is a bereavement effect, does it differ for carers and non-carers?
  - Three hypotheses (Schulz 2008):
    1. Cumulative stress: carers have worse bereavement outcomes than non-carers
    2. Stress reduction perspective: carers have better bereavement outcomes than non-carers
    3. Anticipatory grief: carers have worse outcomes before bereavement and better outcomes after bereavement

Difference-in-Differences

Statistical technique to attempt to mimic an experimental research design using observational data



One group is treated
One group is untreated
Outcomes changes for both groups
We want the *differential* effect

Difference in outcomes for treated group
= 0.9 – 0.6 = 0.3

Difference in outcomes for untreated group
= 0.5 – 0.4 = 0.1

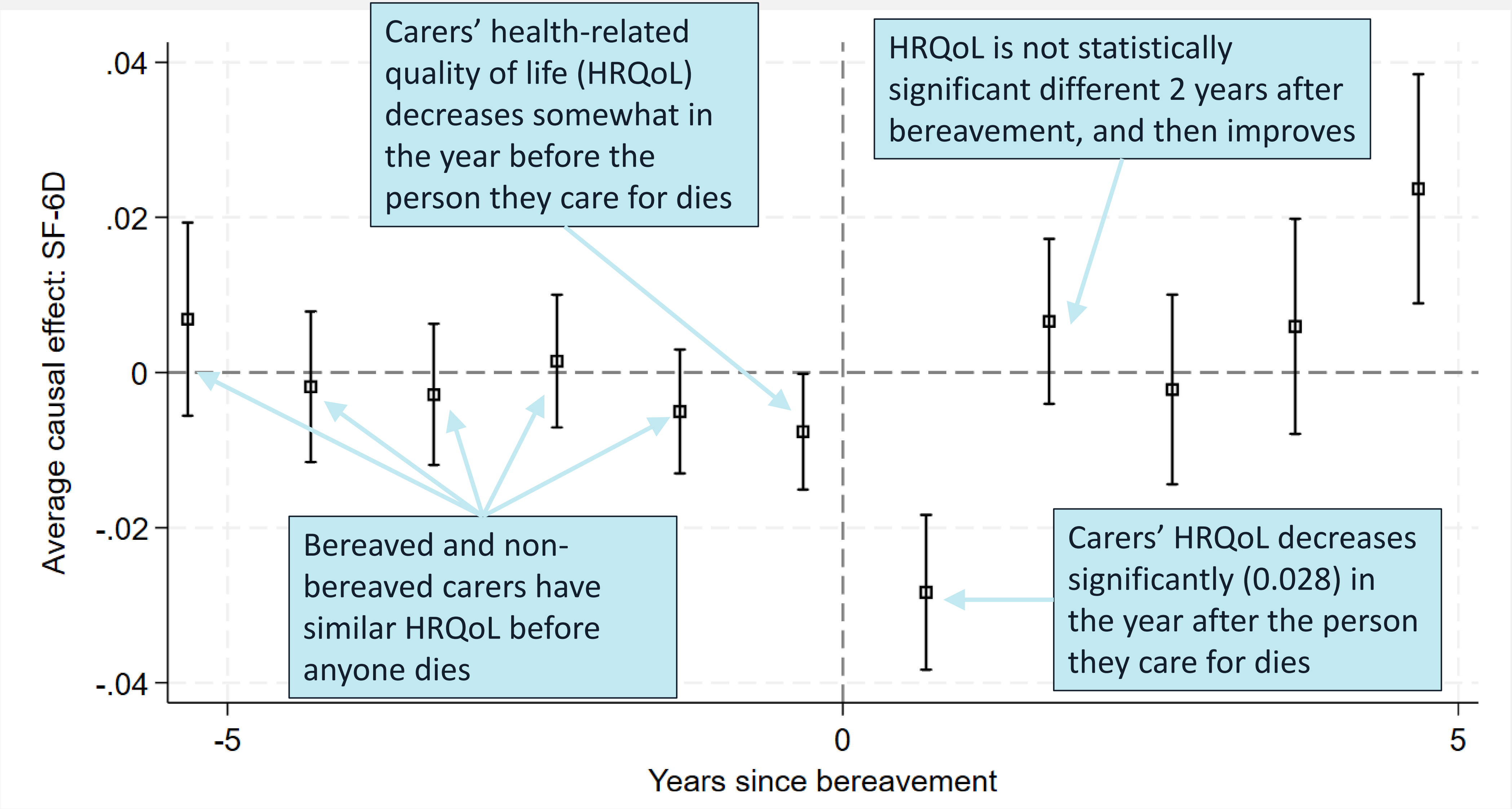
Difference-in-Differences
= 0.3 – 0.1 = 0.2

Method: Difference-in-Differences

- Studies the differential effect of bereavement on the bereaved group versus the non-bereaved group
- We calculate the effect of bereavement on health-related quality of life by comparing:
    - Change over time in health-related quality of life for the bereaved group to the
    - Change over time in health-related quality of life for the non-bereaved group

- Separately for carers and non-carers:
    - 1. bereaved carers versus 2. non-bereaved carers
    - 3. bereaved non-carers versus 4. non-bereaved non-carers

Results: bereaved carers compared to non-bereaved carers



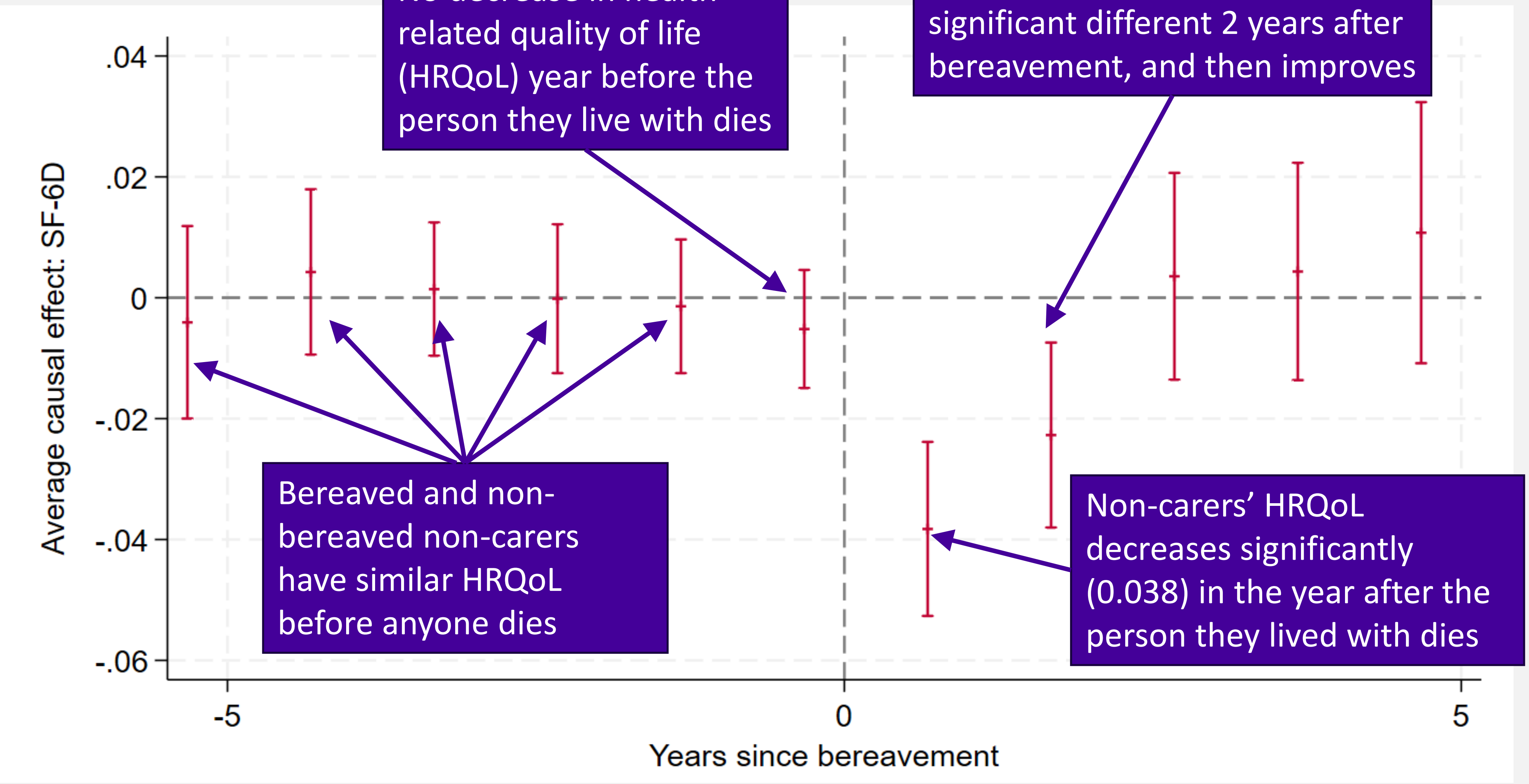
Carers' health-related quality of life (HRQoL) decreases somewhat in the year before the person they care for dies

HRQoL is not statistically significant different 2 years after bereavement, and then improves

Bereaved and non-bereaved carers have similar HRQoL before anyone dies

Carers' HRQoL decreases significantly (0.028) in the year after the person they care for dies

Results: bereaved non-carers compared to non-bereaved non-carers



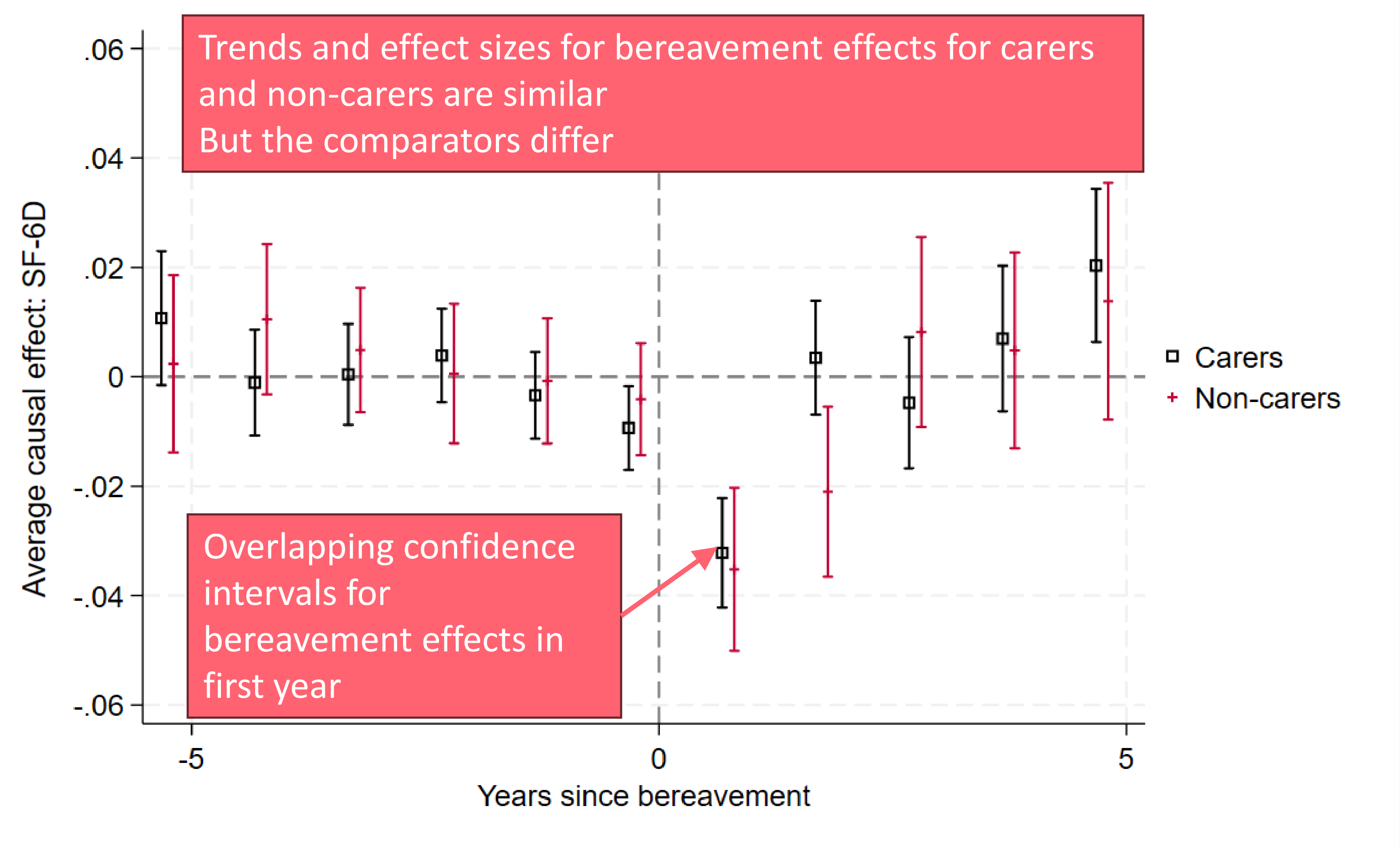
No decrease in health-related quality of life (HRQoL) year before the person they live with dies

HRQoL is still statistically significant different 2 years after bereavement, and then improves

Bereaved and non-bereaved non-carers have similar HRQoL before anyone dies

Non-carers' HRQoL decreases significantly (0.038) in the year after the person they lived with dies

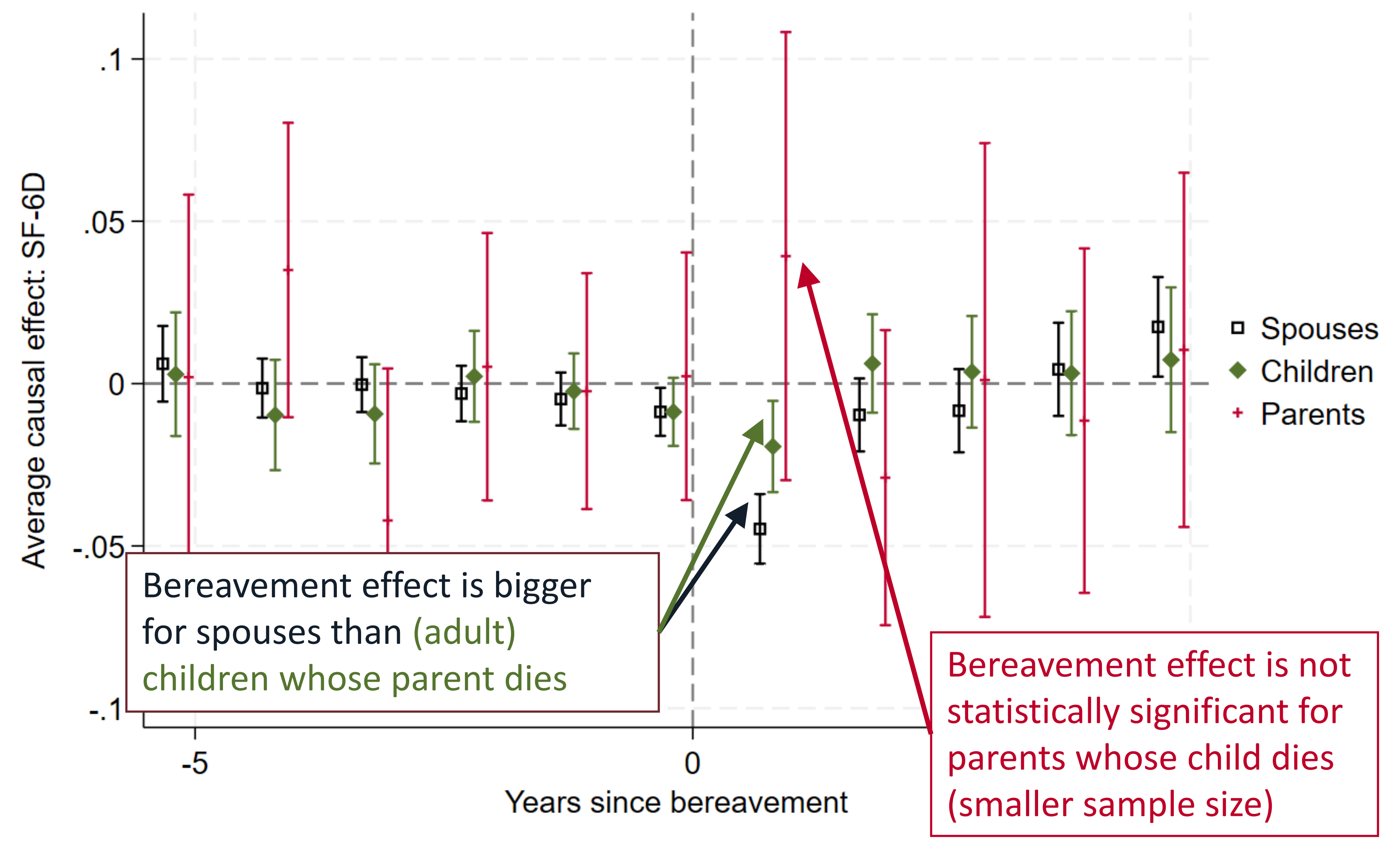
Results: bereavement effect for carers and non-carers



Trends and effect sizes for bereavement effects for carers and non-carers are similar
But the comparators differ

Overlapping confidence intervals for bereavement effects in first year

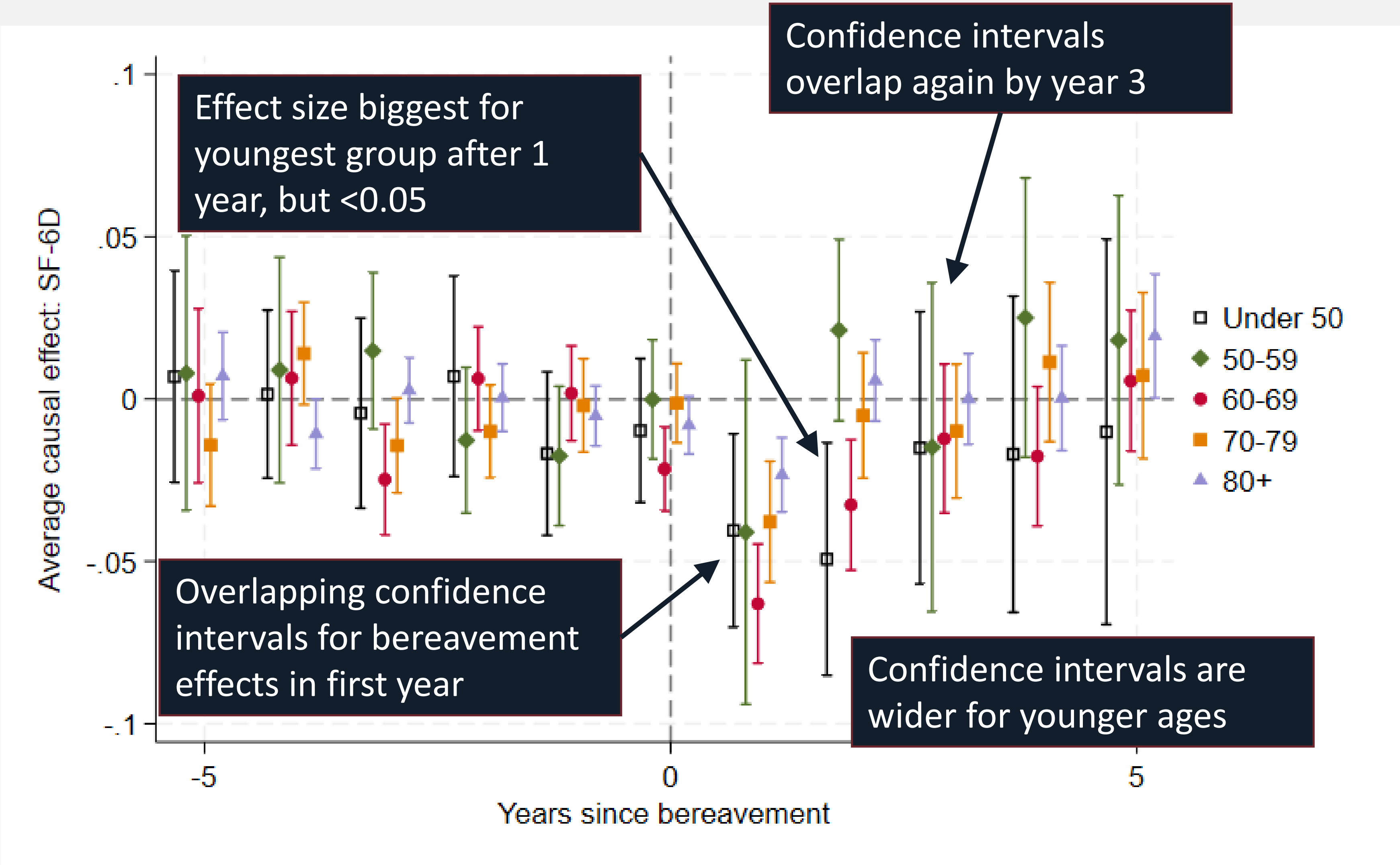
Results: bereavement effect by relationship



Bereavement effect is bigger for spouses than (adult) children whose parent dies

Bereavement effect is not statistically significant for parents whose child dies (smaller sample size)

Results: bereavement effect by age of deceased at death



Effect size biggest for youngest group after 1 year, but <0.05

Confidence intervals overlap again by year 3

Overlapping confidence intervals for bereavement effects in first year

Confidence intervals are wider for younger ages

Findings

- Evidence for a small, short-term negative bereavement effect (health-related quality of life loss) for carers and non-carers
- No evidence to suggest that the bereavement effect is greater for carers than for non-carers
- Carers’ and non-carers’ health-related quality of life returns to non-bereaved level within 2 years after bereavement
- Short-term bereavement effect is greater for bereaved spouses than bereaved children
- Bereavement effect for bereaved parents highly uncertain
- Small differences in short-term bereavement effect by age at death, but no long-term differences

Thank you

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| Van goede zorg verzekerd |

Should HTA include the bereavement effect on HRQoL?

Perspective from an HTA agency

Saskia Knies PhD

National Health Care Institute

ISPOR Europe 2024

Monday 18 November

Disclaimer

The views expressed in this presentation are from myself as the presenter and not necessarily from my employer Zorginstituut Nederland (ZIN; National Health Care Institute)

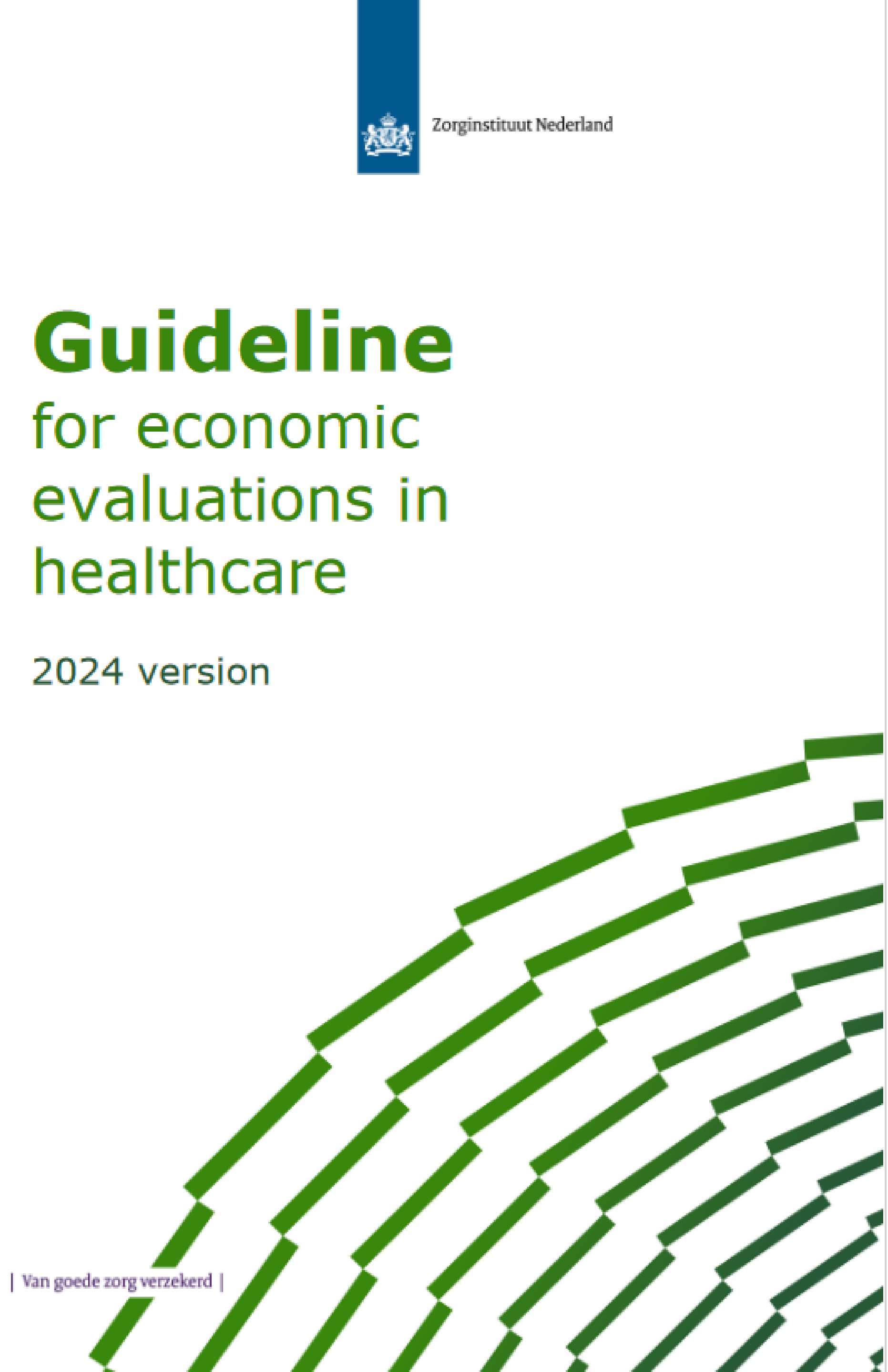
Dutch Health economic guideline

New version published in January 2024 (4th edition)

Mandatory for new reimbursement dossiers from October 2024 onwards

Developed with input from:

- Experiences health economists ZIN
- Expert committee
- Survey
- External consultation



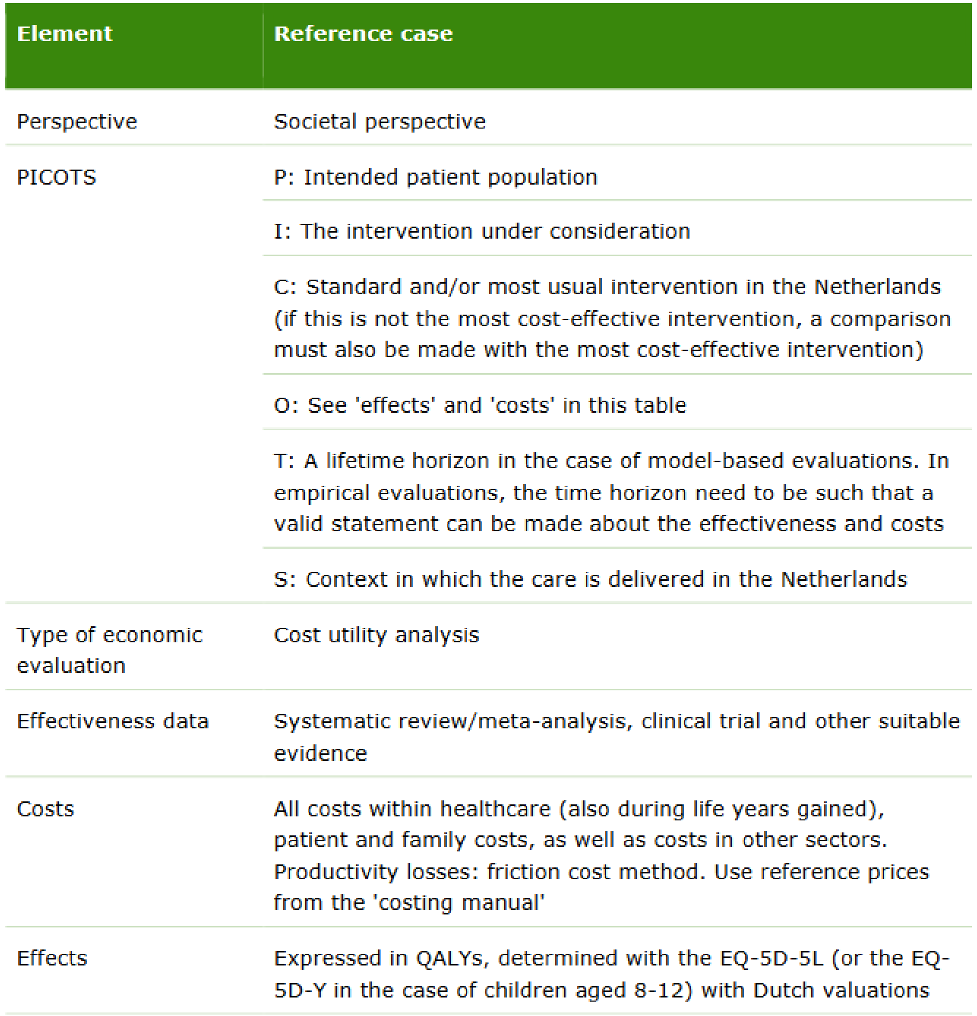
Zorginstituut Nederland

Guideline
for economic evaluations in healthcare

2024 version

| Van goede zorg verzekerd |

Reference case



Element	Reference case
Perspective	Societal perspective
PICOTS	P: Intended patient population
	I: The intervention under consideration
	C: Standard and/or most usual intervention in the Netherlands (if this is not the most cost-effective intervention, a comparison must also be made with the most cost-effective intervention)
	O: See 'effects' and 'costs' in this table
	T: A lifetime horizon in the case of model-based evaluations. In empirical evaluations, the time horizon need to be such that a valid statement can be made about the effectiveness and costs
	S: Context in which the care is delivered in the Netherlands
Type of economic evaluation	Cost utility analysis
Effectiveness data	Systematic review/meta-analysis, clinical trial and other suitable evidence
Costs	All costs within healthcare (also during life years gained), patient and family costs, as well as costs in other sectors. Productivity losses: friction cost method. Use reference prices from the 'costing manual'
Effects	Expressed in QALYs, determined with the EQ-5D-5L (or the EQ-5D-Y in the case of children aged 8-12) with Dutch valuations

From first version (1999) onwards: societal perspective

Operationalization:

- Costs: patient and family costs (including informal care)
- Tariff for informal care: €18.8 per hour
- Effects: patient

Questions to consider when including new QoL effects

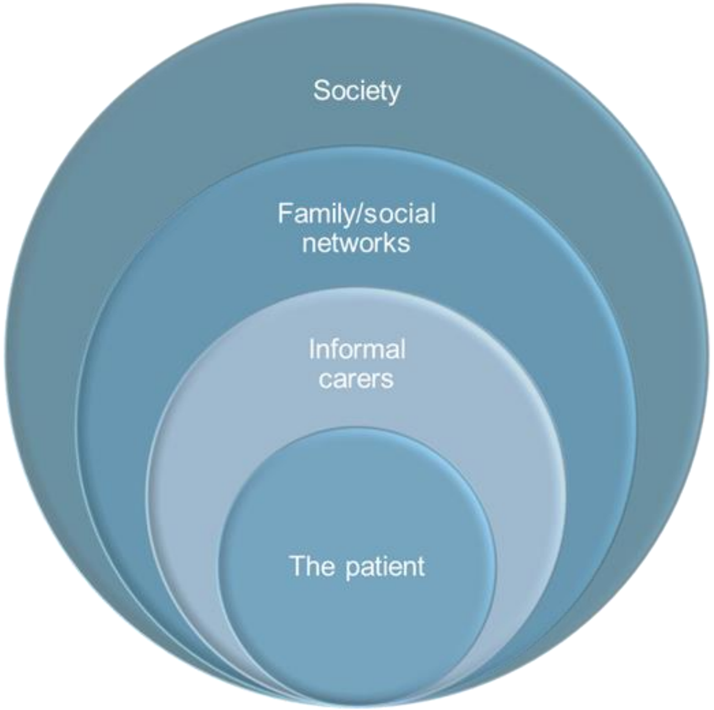
Whose effects should be taken into account? Any maximum number of people?

How to measure effects? Which questionnaire to use?

How to include in analysis? Disutility or additive

Time horizon of analysis

- Now lifelong until death of patient, how much longer?
- When does the beraevement period start and end?



What about including effects on informal caregivers?

What kind of effects?

- Caregiver burden?
- Bereavement?

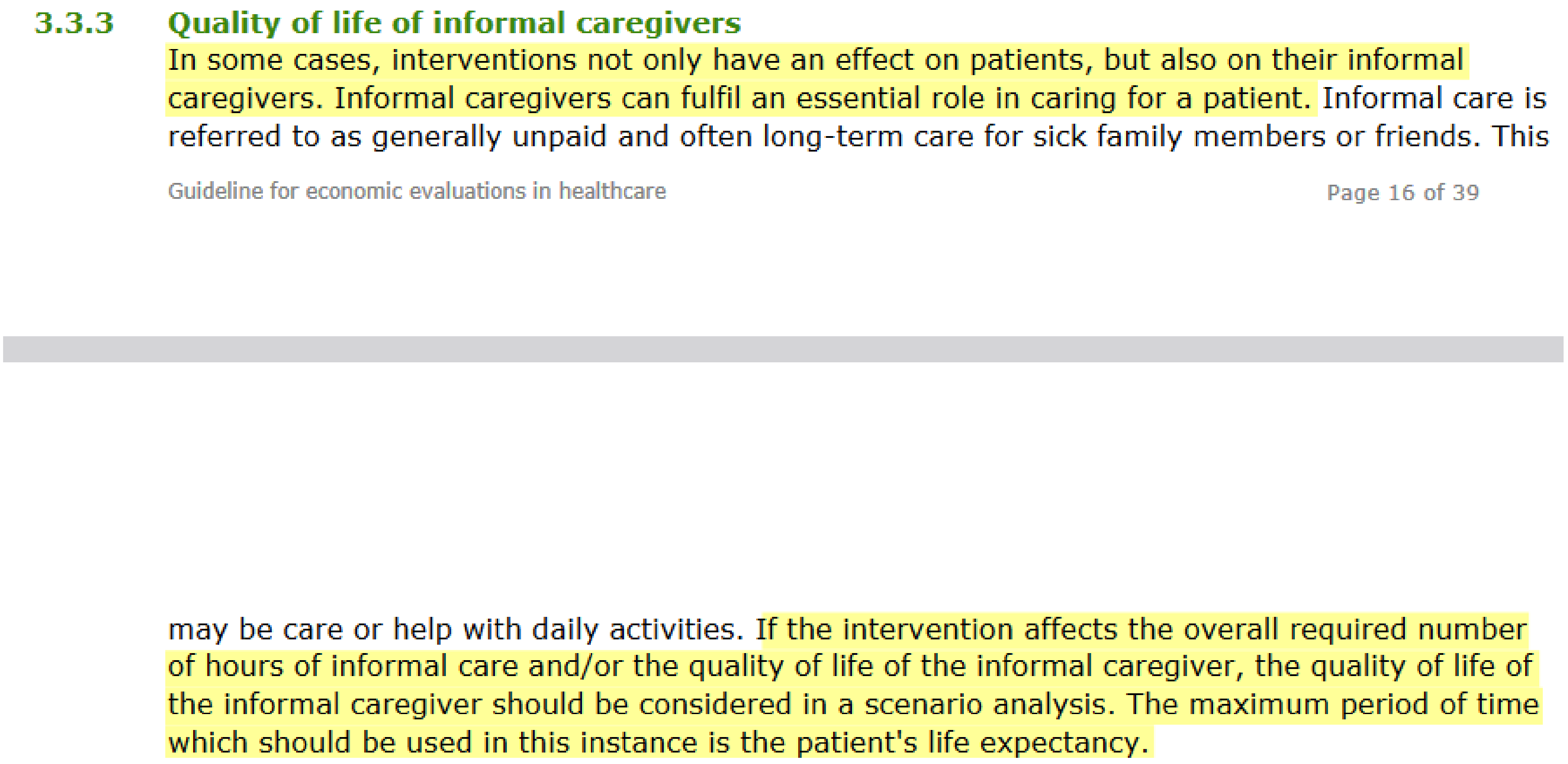
Why? Societal Perspective

  - The costs were already taken into account, so why not include the effects...
- Some care is partly initiated to relieve the burden on the informal caregiver
    - This means that the informal caregiver is indeed the target for care

Why not? Is it an issue?

  - Is informal care not a 'fact of life', like caring for children...
  - Add effect on informal caregiver to patient effect?

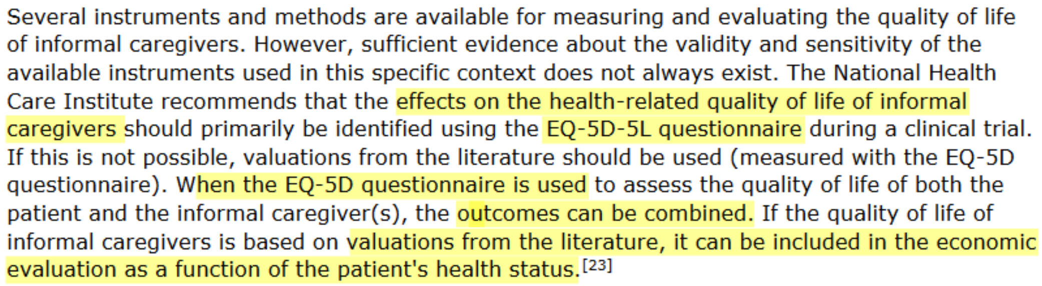
Recommendation: quality of life caregivers



3.3.3 Quality of life of informal caregivers

In some cases, interventions not only have an effect on patients, but also on their informal caregivers. Informal caregivers can fulfil an essential role in caring for a patient. Informal care is referred to as generally unpaid and often long-term care for sick family members or friends. This may be care or help with daily activities. If the intervention affects the overall required number of hours of informal care and/or the quality of life of the informal caregiver, the quality of life of the informal caregiver should be considered in a scenario analysis. The maximum period of time which should be used in this instance is the patient's life expectancy.

Measuring QoL caregivers



Several instruments and methods are available for measuring and evaluating the quality of life of informal caregivers. However, sufficient evidence about the validity and sensitivity of the available instruments used in this specific context does not always exist. The National Health Care Institute recommends that the effects on the health-related quality of life of informal caregivers should primarily be identified using the EQ-5D-5L questionnaire during a clinical trial. If this is not possible, valuations from the literature should be used (measured with the EQ-5D questionnaire). When the EQ-5D questionnaire is used to assess the quality of life of both the patient and the informal caregiver(s), the outcomes can be combined. If the quality of life of informal caregivers is based on valuations from the literature, it can be included in the economic evaluation as a function of the patient's health status.[23]

Using EQ-5D-5L

Effect mostly likely on:

- Daily activities
- Pain/discomfort
- Anxiety/depression

There does not have to be any effect...

- Not always a caregiver burden present

Other considerations measuring QoL caregivers

No effect (assumed) on EQ-5D-5L

- Emphasis on low physical health

Other general questionnaires

- Such as the AQoL, ASCOT, SF-6D, EQ-HWB
- More emphasis on well-being, mental aspects of health

In addition, 'caregiver specific' questionnaires (broader aspects than only health)

- CES, ASCOT caregiver, CareQoL-7D

Problem: difficulties with linking to patient QALYs….

Why this recommendation for caregiver QoL?

Whose effects should be taken into account? Any maximum number of people?

- Quality of life of 1 caregiver in scenario analysis

How to measure effects? Which questionnaire to use?

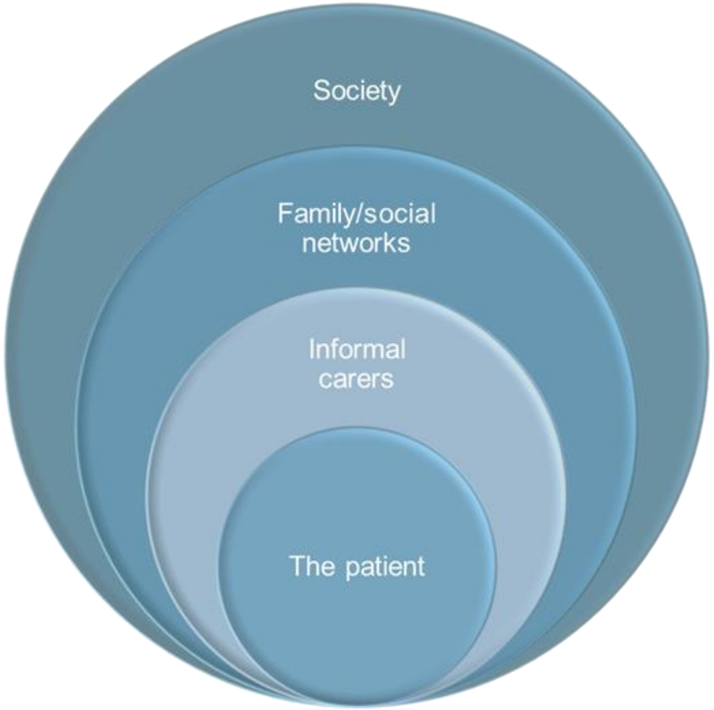
- Preference for EQ-5D-5L

How to include in analysis?

- Combine with QoL of patient

Time horizon of analysis

- Life long until death of patient



Zorginstituut Nederland

Thank you for your attention

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| Van goede zorg verzekerd |

Audience poll #2

Based on what you’ve heard, have you changed your opinion?

- Bereavement effects **are not meaningful** and **should not be included in HTA**
- Bereavement effects **are meaningful** but **are not relevant** to HTA
- Bereavement effects **are meaningful** and **are relevant** to HTA