ANTICOAGULATION THERAPY IN THE LAST PHASE OF LIFE

Eric Geijteman
Medical oncologist, clinical pharmacologist
Senior researcher ‘end-of-life care’

Erasmus MC
Universitair Medisch Centrum Rotterdam
Kanker Instituut


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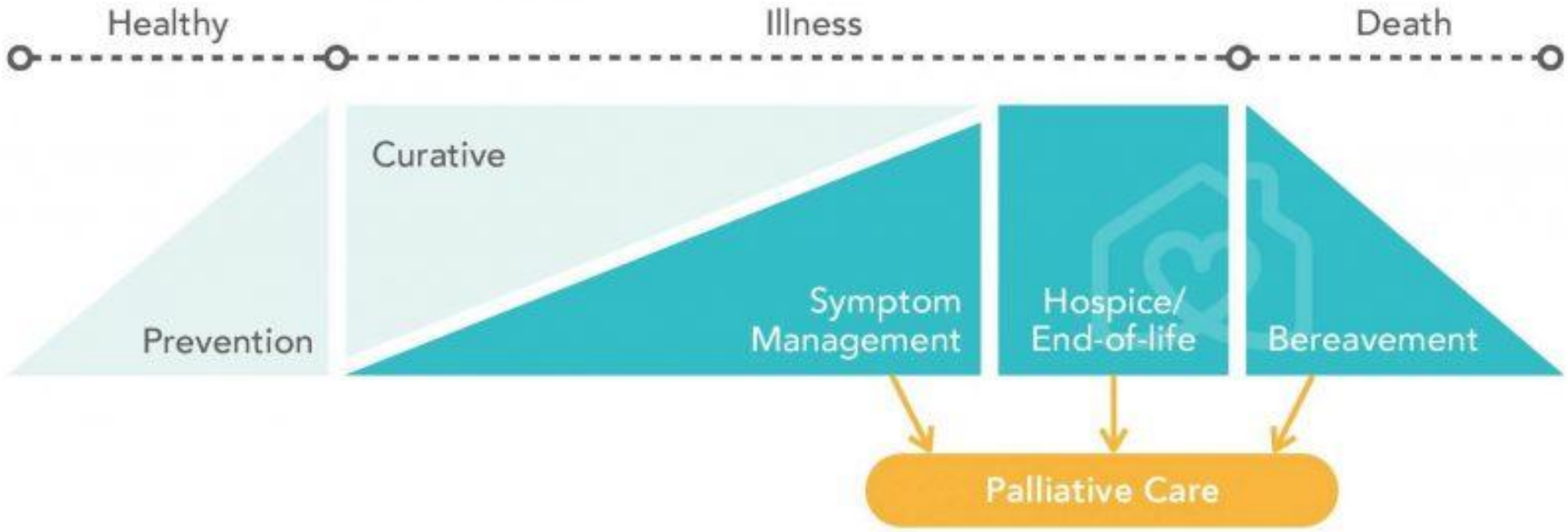
MØLLER WOLFE

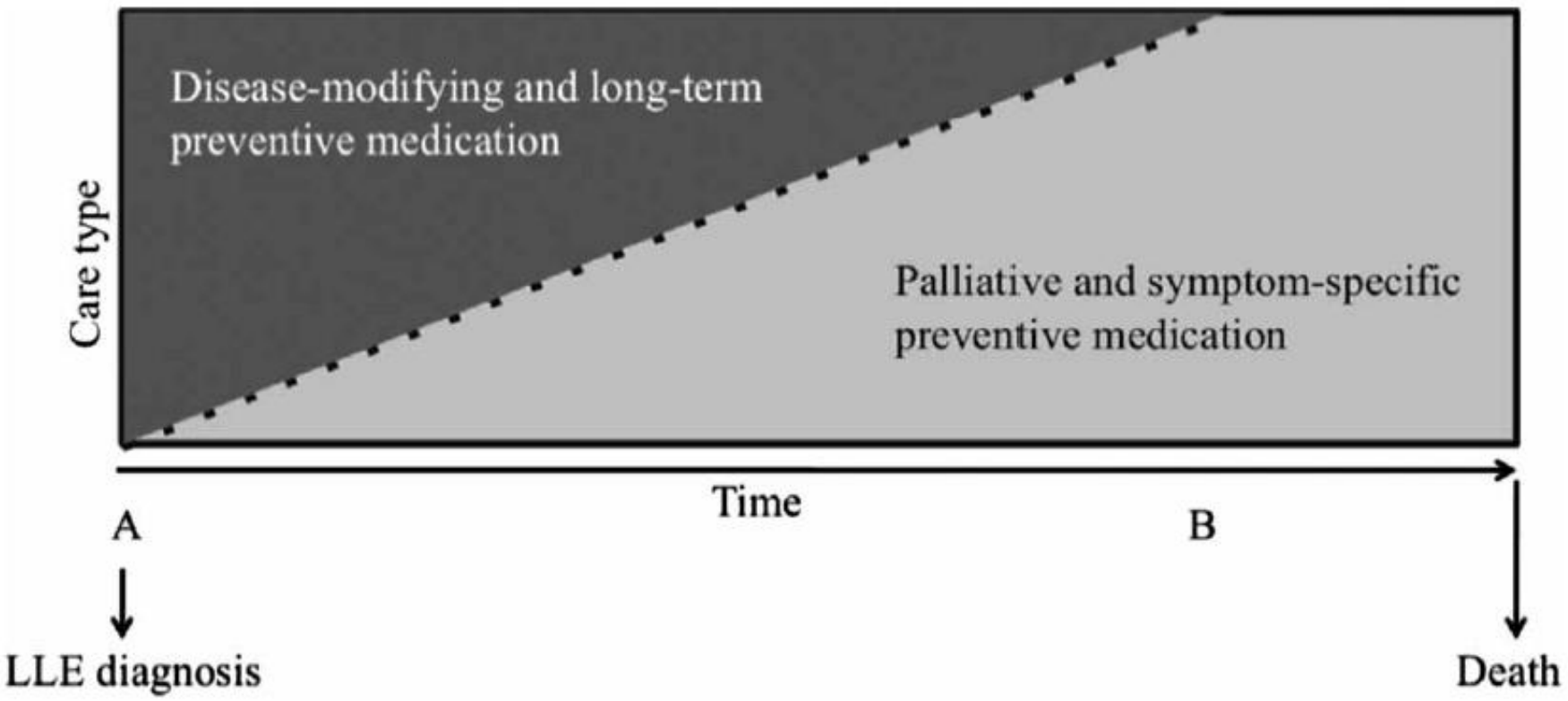
Disclosure belangen spreker – Eric Geijteman	
Nederlands Trombose Congres – 16 mei 2025	
(potentiële) Belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relaties met bedrijven	
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk:	Several research grants (ZonMw, H2020, NWO, NIV, Erasmus MC)

Care at the end of life



Pharmacotherapy at the end of life

(Maddison et al, Progr Palliat Care, 2011)



Discontinuation of drugs: practice

- Many so-called inappropriate medications are continued up until the very end of life
  - Mean number of medications is nine during day 7 before death and six on the day of death (Arevalo et al, J Pall Med, 2018)
  - More than a quarter of all patients used a preventive medication on the day of death

- Use of medication increases as death approach (Currow, JAGS, 2007; Ma, Am J Hosp Palliat Care, 2014)
  - increase of symptom treatment drugs;
  - continuation of drugs for co-morbid diseases

Discontinuation of medications: why?

- Side effects
- Time until benefit
  - *No benefit of tight glucose control can be expected for at least a decade (Lancet, 1998)*
  - *It takes at least two years for statins to be effective (Cruz, Drugs&Aging, 2012)*
- Changes in body functions
- Difficulty taking medications (Cruz, Drugs&Aging, 2012)
- Costs
  - *Discontinuing statin therapy alone could save the US health care system $603 million annually (Kutner, JAMA internal medicine, 2015)*

Three groups of medication

- Appropriate medications (such as symptom relievers)
- **Potentially inappropriate medications (e.g. anticoagulants)**
- Inappropriate medications

Use of anticoagulants

- 7-47% of frail older patients and patients with advanced cancer use an anticoagulant in the last weeks of life (Holmes, Cancer, 2010; Gartner, Support Care Cancer, 2012)

- Anticoagulant therapy is usually continued until the last days before death (Arevalo, J Pall Med, 2018; Van Nordennen, JAMDA, 2016)

- Decision-making is reactive (triggers are: active bleeding, inability to swallow, start of the dying phase) (Van Hylckama Vlieg, in preparation)

Positive effects of using anticoagulants

Preventing or treating venous thrombosis

Thrombosis occurs in more than 30% of patients in hospice (White et al, Lancet Haematol, 2019)

Prevention of infarction

Side effects of using anticoagulants

Minor and major bleedings

10%-20% of patients in the last phase of life develop a clinically relevant bleeding
(Tardy et al, J Thromb Haemost, 2017, Mahé et al, NEJM, 2025)

INR fluctuation in the final weeks of life (Visser et al, accepted for publication)

Low molecular heparin injections

- Until now, there is little evidence on benefits and risks of (dis)continuation of anticoagulation therapy in the last phase of life
- Evidence-based guidelines to support decision-making regarding anticoagulation therapy for patients in the last phase of life are lacking

Towards optimizing anticoagulation therapy in the last phase of life

a) What are the opinions of patients, their informal caregivers, and physicians regarding anticoagulation therapy at the end of life?

b) What are the advantages and disadvantages of anticoagulation therapy at the end of life?

Interview study

- Objective: to gain an in-depth understanding of the experiences, perspectives, and preferences of healthcare professionals regarding decision-making about anticoagulation therapy in the last phase of life

- A multicentre qualitative study among 32 healthcare professionals

Interview study – results

- Healthcare professionals experience decision-making regarding anticoagulation therapy in the last phase of life as difficult and multifactorial, due to:

- A lack of knowledge on the incidence of occurrence of events after (dis)continuing anticoagulation therapy
- The variety of patient groups and characteristics
- Prognostic uncertainty

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Lack of knowledge

“Stopping is not necessarily wrong, continuing is not necessarily wrong.... No one knows what wisdom is. …. Right now, it seems that we simply don't know, which is why everyone is approaching it [decision- making] differently ” *(Participant 30, Neurologist)*

“Regarding patients in the palliative phase taking an anticoagulant, I am at a loss. Because I have no idea what to do with the anticoagulant. ... I often think, am I doing this [decision-making] right” *(Participant 17, GP)*

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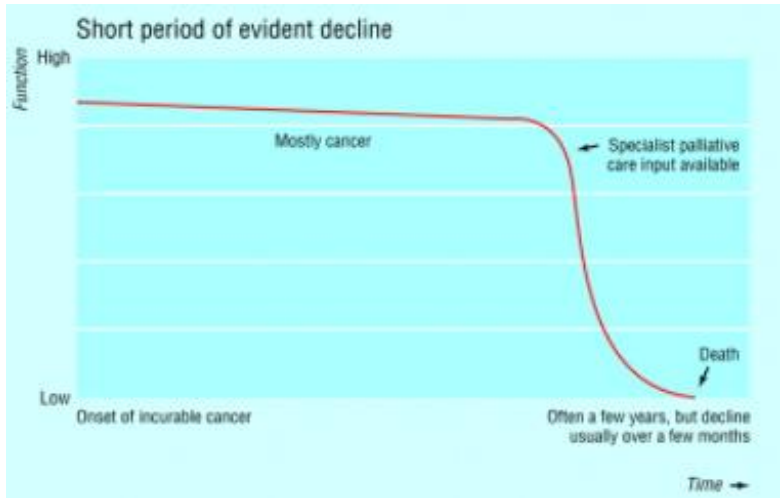
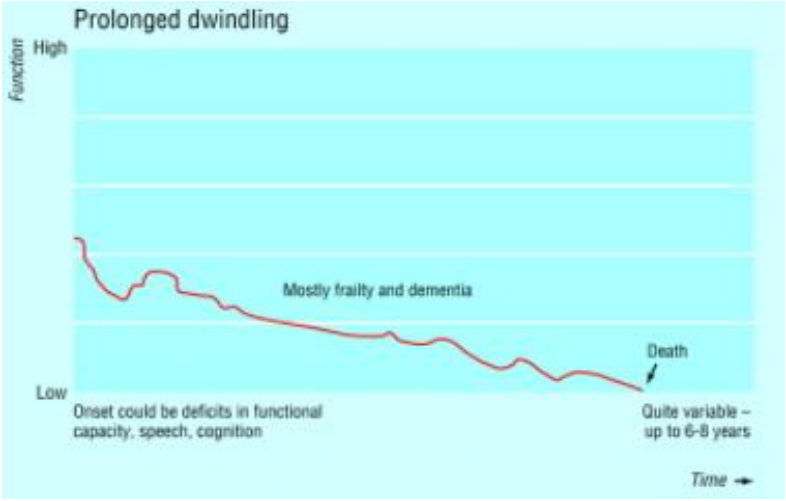
Predicting prognosis

“Well, it [decision-making] starts with the question ‘can you predict that [properly estimating life expectancy]?’ I wish I could.” (Participant 29, Cardiologist)

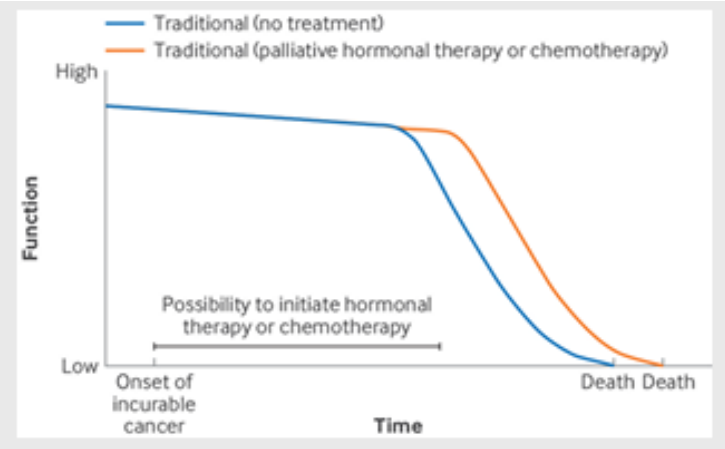
“When patients are in their final week or two of life, I generally discontinue anticoagulation therapy at that point.” (Participant 22, Specialist in elderly care)

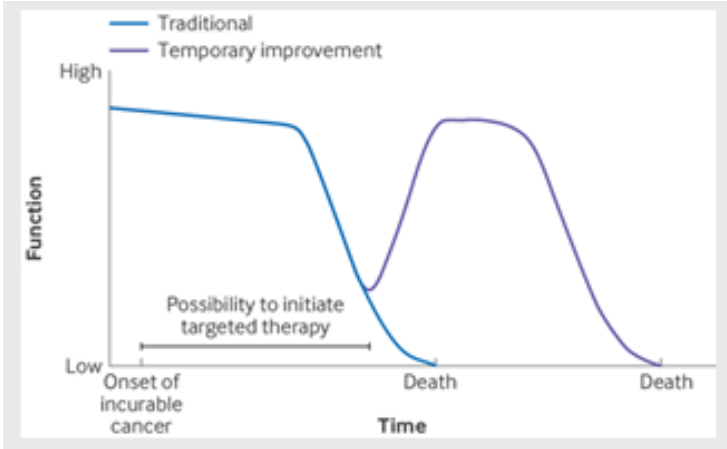
Illness trajectories of patients with advanced illnesses (Murray et al, BMJ, 2005)

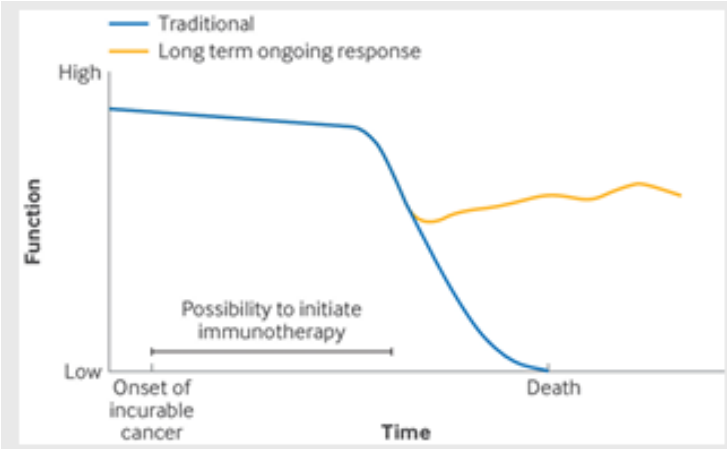




Illness trajectories of patients with advanced cancer (Gejteman et al, BMJ, 2024)







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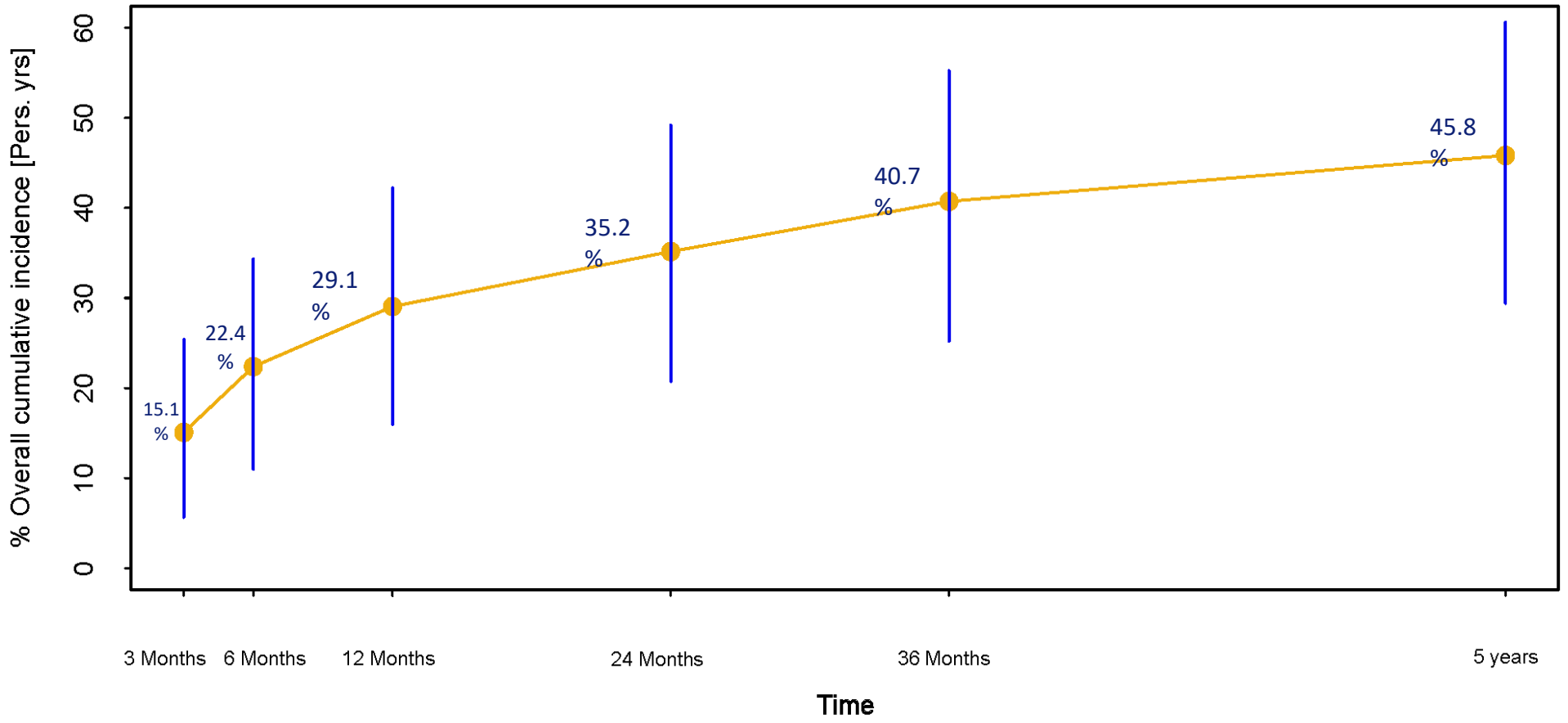
Recurrent thromboembolism

- The optimal duration of anticoagulant therapy for cancer-associated VTE is unknown
- Guidelines: *“Anticoagulant therapy for at least 6 months and to continue anticoagulant therapy for as long as the cancer is active”*
- Rate of recurrent VTE after discontinuation of anticoagulant therapy in patients with cancer-associated VTE
- Primary outcome: rate of recurrent VTE after discontinuation of anticoagulant therapy at different time intervals

Events / 100 person-years

Van Hylckama Vlieg et al. The risk of recurrent venous thromboembolism after discontinuation of anticoagulant therapy in patients with cancer-associated thrombosis: a systematic review and meta-analysis. eClinicalMedicine, 2023

Cumulative VTE recurrence rates



Horizon 2020 project (SERENITY), led by Professor Erik Klok (LUMC), and Professor Simon Noble (Cardiff University)

- Review the positive and negative impacts of the use of antithrombotic therapy in patients with advanced cancer in their final stage of life

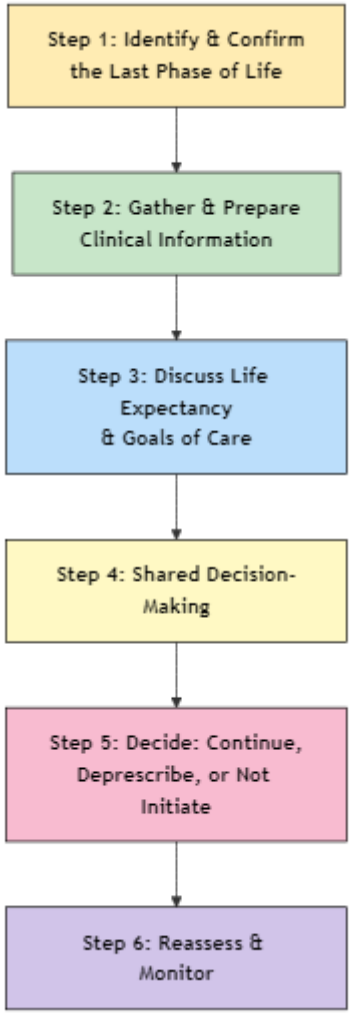
- Patient and physician preferences and trade-offs

- RCT to study the impact of implementation of a shared decision support tool on bleeding events and symptoms related to thrombosis (CoClarity trial)

Advices for daily practice

Review medication list as death approaches (Hassan et al, submitted) taking into account:

- Original indication
- Risk of continuing and stopping medication
- Patient preferences



Thank you

e.geijteman@erasmusmc.nl

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