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Design and rationale of a routine clinical care pathway and prospective cohort study in older patients needing intensive treatment

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Abstract

Background: Treatment decisions concerning older patients can be very challenging and individualised treatment plans are often required in this very heterogeneous group. In 2015 we have implemented a routine clinical care pathway for older patients in need of intensive treatment, including a comprehensive geriatric assessment (CGA) that was used to support clinical decision making. An ongoing prospective cohort study, the Triaging Elderly Needing Treatment (TENT) study, has also been initiated in 2016 for participants in this clinical care pathway, to study associations between geriatric characteristics and outcomes of treatment that are relevant to older patients. The aim of this paper is to describe the implementation and rationale of the routine clinical care pathway and design of the TENT study.

Methods: A routine clinical care pathway has been designed and implemented in multiple hospitals in the Netherlands. Patients aged ≥70 years who are candidates for intensive treatments, such as chemotherapy, (chemo-)radiation therapy or major surgery, undergo frailty screening based on the Geriatric 8 (G-8) questionnaire and the Six-Item Cognitive Impairment Test (6CIT). If screening reveals potential frailty, a CGA is performed. All patients are invited to participate in the TENT study. Clinical data and blood samples for biomarker studies are collected at baseline. During follow-up, information about treatment complications, hospitalisations, functional decline, quality of life and mortality is collected. The primary outcome is the composite endpoint of functional decline or mortality at 1 year.

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Discussion: Implementation of a routine clinical care pathway for older patients in need of intensive treatment provides the opportunity to study associations between determinants of frailty and outcomes of treatment. Results of the TENT study will support individualised treatment for future patients.

Trial registration: The study is retrospectively registered at the Netherlands Trial Register (NTR), trial number NL8107. Date of registration: 22-10-2019.

Keywords: Older patients, Comprehensive geriatric assessment, Frailty, Geriatric oncology, Aortic valve replacement, Oesophageal cancer, Head and neck cancer, Colon cancer, Study protocol

Background

Clinical decision making in relation to older patients with an indication for intensive treatment can be very challenging. The rate of ageing differs between individuals, resulting in heterogeneity in physiological and functional characteristics, life expectancy and treatment tolerance [1, 2]. Older patients are underrepresented in clinical trials [3, 4] and due to strict inclusion criteria and the selective inclusion practiced by physicians, the majority of older trial participants is generally in relatively good health and has a good performance status [5, 6]. As a result, treatment decisions in older patients with poorer health status are not supported by scientific evidence. In addition, most endpoints of clinical trials are related to mortality and treatment toxicity [7], whereas older patients might prioritize functional and cognitive outcomes and quality of life over prolonged survival [8, 9]. Therefore, studying alternative adverse events such as early treatment discontinuation or unplanned hospitalisation may help to better weigh treatment risks and benefits and support the treatment decision process. Currently, however, detailed information on the determinants of relevant outcomes is often lacking.

A comprehensive geriatric assessment, performed by a geriatrician, is a multidisciplinary evaluation to assess the multiple problems of older patients and develop an integrated care plan for treatment and follow-up [10]. With an assessment of the four geriatric domains (somatic status, psychological status, functional status and social status) an overall view of the patients' level of frailty is provided. Geriatric screening tests can be used to identify patients who might benefit from CGA [11]. A shorter geriatric assessment that focuses on identifying health issues can alternatively be performed by other physicians or nurses [12]. Although geriatric assessment is currently not part of routine clinical practice, it is known to predict treatment-related outcomes including survival, treatment toxicity [13, 14] and postoperative complications [15], and can support treatment choices and intensity [13, 16–18]. Several biomarkers may characterize the biological age of an older patient and predict outcomes, but have not yet been studied in a clinical context.

We have designed and implemented a routine clinical care pathway, which integrates geriatric assessment, to improve clinical decision making for older patients. The first aim of this paper is to describe the implementation and rationale of this pathway initiated in 2015. The second aim is to describe the rationale and design of the Triaging Elderly Needing Treatment (TENT) study, an ongoing prospective cohort study of participants in the clinical pathway.

Methods

Routine clinical care pathway

Starting in 2015, we have designed and implemented a routine clinical care pathway at Leiden University Medical Center (LUMC, Leiden), Haga Hospital (the Hague), Haaglanden Medical Center (HMC, the Hague), and the Reinier de Graaf Hospital (RdG, Delft). In this clinical pathway patients aged ≥70 years who are candidates for intensive treatment (e.g. surgery, chemotherapy, (chemo-)radiation therapy, immunotherapy or other cancer therapies) and are potentially frail are identified by geriatric screening and then undergo standardized CGA in the outpatient clinics at participating hospitals. CGA results are explained to the patient and discussed during a multidisciplinary team meeting to support individualised treatment decisions. Below we describe the elements of the care pathway and explain the rationale of the tests we chose. Table 1 provides a detailed description of the different tests, score ranges and cut-off scores used.

- Patients
  Patients aged ≥70 years who are candidate for intensive treatment in cardiovascular, thoracic, orthopaedic and oncology outpatient clinics undergo geriatric screening.
- Geriatric screening
  A trained nurse uses geriatric screening to identify patients with potential frailty who may be in need of further evaluation by comprehensive geriatric assessment [11]. Geriatric screening consists of the Geriatric 8 (G-8) screening questionnaire [19] and the Six-Item Cognitive Impairment Test (6CIT) [20] and takes about 5 minutes to complete. The G-8 is

Table 1 Description of different tests

Test	Explanation	Scores
	Geriatric screening	
G-8 [19]	8-item screening test. Assesses domains of nutritional status, mobility, neuropsychological problems, medication use, self-rated health status and age	Score ranges from 0 to 17, lower score indicates more impairment, cut-off score ≤ 14
6CIT [20, 21]	6-item cognitive screening test. One memory, two attention and three orientation questions	Score ranges from 0 to 28, higher score indicates more significant cognitive impairment, cut-off score > 7
	Comprehensive geriatric assessment	
Somatic status		
Medical history	Polypharmacy, multi-morbidity using CCI [22]: 16 medical condition of which 3 are stratified according to severity	Score ranges from 0 to 33, higher score indicates more comorbidities
Physical measurement	Weight, height, BMI, blood pressure, heart rate, orthostatic hypotension, complete physical examination on indication	N/A
MNA-SF® [23]	6-item screening test. Assesses loss of appetite, weight loss, BMI, mobility, the occurrence of stress or an acute disease and neuropsychological problems	Score ranges from 0 to 14, lower score indicates greater risk of malnutrition, cut-off score ≤ 11
Psychological status		
PHQ-2 [24]	2-item screening test for depression	Score ranges from 0 to 6, higher score indicates more depressive symptoms, cut-off score ≥ 3
GDS-15 [25]	15-item questionnaire. Assesses depressive symptoms	Score ranges from 0 to 15, higher score indicates more depressive symptoms, cut-off score ≥ 5
Optimism questionnaire [26]	3-item questionnaire. Assesses optimism on a 5-point Likert scale: 0 corresponds to "strongly disagree" and 4 to "strongly agree"	Score ranges from 0 to 12, higher score indicates greater optimism
VAT [27]	Learning task that assesses visual associative memory	Score ranges from 0 to 12, lower score indicates more cognitive impairment
Clock drawing [28]	Cognitive test that assesses visuospatial and executive functioning	Score ranges from 0 to 14, lower score indicates more executive impairment, cut-off score < 10
Functional status		
Katz ADL [29]	6-item questionnaire. Assesses bathing, dressing, toileting, transfers, continence and feeding	Score ranges from 0 to 6, higher score indicates greater dependency
Lawton IADL [30]	8-item questionnaire. Assesses more complex independent living skills: ability to use a phone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for personal medications, ability to handle finances	Score ranges from 0 to 8, lower score indicates greater dependency
Gait speed [31, 32]	Timed 4-m walking test	Lower score represents slow gait speed, cut-off speed ≤0.8 m/s
Handgrip strength [33, 34]	Handgrip strength measurement, using a Jamar Handheld Dynamometer. Best of 3 measurements using the dominant hand	Reference values depend on age and gender
Social status	Living arrangement (independent, institutionalised, hospitalised), the availability of a caregiver, hours of (home)care	N/A
Quality of life		
EQ-5D-3L [35, 36]	5-item questionnaire. Assesses health-related quality of life exploring five dimensions: mobility, self-care, daily activities, pain/complaints, mood. Three possible levels of answers: no problems, some problems, extreme problems	An index score is calculated, score ranges from − 0.33 to 1.0. Score < 0 represents worse than dead and 1 represents full health
EQ-VAS [35, 36]	Verbal description of an overall health state visual analogue scale, registered on a numerical rating scale	Score ranges from 0 to 100, higher score indicates higher health-related quality of life

Abbreviations: *6CIT* 6 Item Cognitive Impairment Test, *ADL* Activities of Daily Living, *BMI* Body mass index, *CCI* Charlson Comorbidity Index, *EQ-5D-3L* EuroQol five dimensions three levels questionnaire, *EQ-VAS* EuroQol Visual Analogue Scale, *G-8* Geriatric eight, *GDS-15* Geriatric Depression Scale-15, *IADL* Instrumental Activities of Daily Living, *MNA-SF®* Mini Nutritional Assessment Short Form, *N/A* Not applicable, *PHQ-2* Patient Health Questionnaire, *VAT* Visual Association Test

an eight-item questionnaire developed for older cancer patients but also used in other populations. It covers multiple domains and places significant weight on nutritional status (47% of the total score). In a review by Decoster et al. the reported sensitivity to detect a need for further evaluation by geriatric assessment was over 80% in six studies [11]. The G-8 does not actually test cognition. Cognitive impairment is generally associated with adverse health outcomes such as delirium [37], a prolonged length of hospital stay [38] and subsequent mortality [38].
The 6CIT is a brief and simple cognitive test and correlates well with the Mini-Mental State Examination (MMSE) [21]. The original cut-off score of the 6CIT is ≥11 (i.e. MMSE 24), an alternative cut-off score is > 7 [20, 21]. When using the cut-off score of > 7, the reported sensitivity is 78.6% and the specificity is 100% [21]. We chose to use the alternative cut-off score > 7 to enhance sensitivity and identify more patients with potential cognitive impairment.
Patients are referred for CGA when their G-8 score is ≤14 and/or the 6CIT is > 7, or if the patient has a history of delirium or dementia (Fig. 1).

- Comprehensive geriatric assessment
In those patients with an abnormal geriatric screening a CGA is subsequently performed in the geriatric outpatient clinic. Time scheduled for this consultation is 60–90 min. Content:
  - Somatic status
  The somatic status includes information about the current diagnosis and symptoms, medical history and medication use. Weight, height, body mass index (BMI), blood pressure, heart rate and orthostatic hypotension are measured and a complete physical examination is performed when indicated. Malnutrition is associated with mortality and functional dependency in different patient populations [39]. Nutritional status is assessed using the Mini Nutritional Assessment Short Form (MNA-SF®) [23]. The MNA-SF® is the test preferred by the Inspectorate of Public Health in the Netherlands [40].
  - Psychological status
  Depressive symptoms are associated with outcomes such as mortality [41, 42] and functional decline [43]. The two-item Patient Health Questionnaire (PHQ-2) [24] is a short instrument used to screen for depression. This screening instrument is suitable since a score ≥ 3 shows a sensitivity of 83% and specificity of 92% for detecting major depression [24]. When further evaluation is needed, the Geriatric Depression Scale-15 (GDS-15) [25] is administered.
  Previous studies have shown an association between a higher level of optimism and a lower risk of cardiovascular events and all-cause mortality [44]. To measure optimism a three-item questionnaire is used that contains the three positively worded questions of the Life Orientation Test-Revised (LOT-R) [26].
  In the event of an abnormal 6CIT on geriatric screening, the Visual Association Test (VAT) [27] and the Clock Drawing Test [28] are performed to assess cognition. The VAT tests visual associative memory and the Clock Drawing Test assesses visuospatial and executive functioning. When indicated, a neurocognitive assessment including a full neuropsychological battery of tests is performed.
  - Functional status

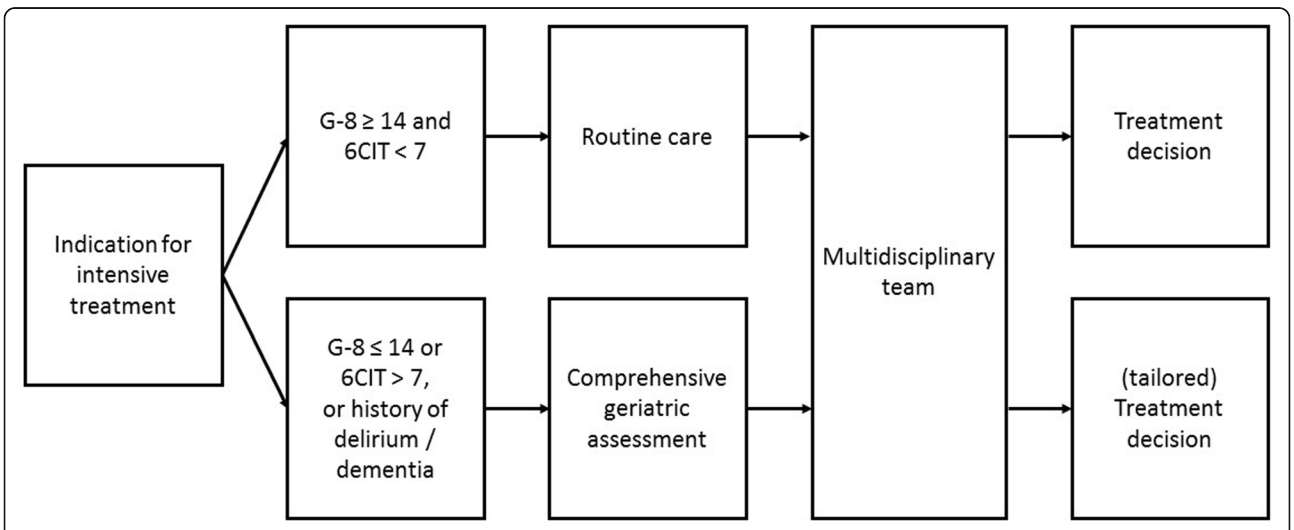

Fig. 1 Overview of the routine clinical care pathway

Functional dependency is associated with mortality in both the general population and in hospitalised patients [45]. To explore patients' functional status, the Activities of Daily Living score (Katz ADL) [29] and Instrumental Activities of Daily Living (Lawton IADL) [30] are assessed. The 6-item Katz ADL was chosen because it is already administered to all hospitalised patients aged ≥70 years as part of a mandatory national Dutch Safety Management System (Veiligheid Management Systeem Kwetsbare ouderen, VMS) and is suitable for extended follow-up. Furthermore, we previously successfully used the Katz ADL to follow over 2600 older patients who visited the Emergency Department [46, 47]. The 8-item Lawton IADL focuses on more complex activities of daily living. The aim of these questionnaires is to assess the overall (representative) functional status and is not based on (sub)acute functional decline prior to clinical evaluation. Furthermore, a 4-m gait speed measurement and handgrip strength are performed to assess physical capacity. Slow gait speed [31, 48] and poor handgrip strength [49, 50] are associated with outcomes such as mortality, disability and cognitive decline.

  - Social status

    The patients' social status is explored by asking about living arrangements (independent, institutionalized, hospitalised), the availability of a formal caregiver and level of support (number of days with home care).

  - Quality of life

    Health-related quality of life is associated with mortality and functional decline in older hospitalised patients [51] and is measured using the EuroQol five dimensions questionnaire (EQ-5D-3L), including the visual analogue scale (EQ-VAS) [35]. Since the EQ-VAS is part of the outcome measures of the TENT study and is collected by telephone at follow-up, we chose to use a verbal description of the EQ-VAS and register the patients' verbal answer on a numerical rating scale. Previous studies have shown comparable results between telephone administration of the EQ-5D and EQ-VAS and face-to-face administration [52] and patient-completed forms [53].

- Clinical decision making

  During a multidisciplinary team meeting different treatment options are considered, including standard care, less intensive treatment options and best supportive care. Information obtained from the comprehensive geriatric assessment, the remaining life expectancy, expected effect of different forms of treatment on relevant outcomes for older patients and patient preferences are taken into account. Patient preferences are assessed by asking the patients' perspective on possible treatment goals, e.g. prolonged survival, maintaining independence, reducing symptoms or other personal goals. Less intensive treatment is proposed when the CGA indicates frailty and hence an increased risk of functional decline. Treatment recommendations that are formulated during multidisciplinary team meetings are again discussed with the patient during the final treatment decision consult, emphasizing patient perspective and the predictive value of existing geriatric impairments on relevant outcomes. This entire process results in individualised treatment decisions.

TENT study

The TENT study is embedded in the routine clinical care pathway, with the aim of developing prediction models to predict the outcome of various intensive treatments. The primary outcome is the composite endpoint of functional decline or mortality at 1 year. We hypothesize that elements of comprehensive geriatric assessment predict outcomes of intensive treatment in older patients and support treatment decisions.

We defined the following objectives:

1. To study the prevalence of geriatric impairments in older patients needing various intensive treatments.
2. To study the incidence of adverse health outcomes (mortality, functional decline, reduced quality of life) at 6 and 12 months.
3. To study associations between geriatric impairments and adverse health outcomes.
4. To study associations between biomarkers and determinants of frailty and adverse health outcomes.
5. To develop models to predict outcomes, containing geriatric determinants and biomarkers.

Below we describe the study design, participants, data collection and outcomes of interest and the statistical analyses that will be carried out.

- Study design

  The TENT study is a prospective cohort study that commenced on 1st February 2016 in the aforementioned hospitals. Inclusion is still ongoing. Patients in the care pathway are asked to participate in the present study, in which we collect clinical data and additional blood samples at baseline. Participants are followed for 1 year.

- Participants
  In order to assemble a representative cohort it is important that all patients in the clinical care pathway actually participate, including those patients without signs of frailty during geriatric screening. Consequently, all patients are invited to participate in the TENT study and are subsequently assessed for eligibility based on the criteria aged ≥70 years and candidate for intensive treatment, including surgery, chemotherapy, (chemo-)radiation therapy, immunotherapy or other cancer therapies. Participants who are not able to understand the Dutch language, or are not able to provide informed consent and have no proxy available, are excluded. When geriatric screening indicates potential frailty, the patient is referred to the geriatric outpatient clinic for comprehensive geriatric assessment and invited to participate. Patients without signs of frailty during geriatric screening are contacted by telephone for inclusion. The Medical Ethics Committee of the LUMC issued a 'certificate of no objection' for retrospective data collection of patients with the same diagnosis not included in the TENT study. This means we will be able to determine whether included patients are representative of the overall patient population in terms of baseline characteristics, treatment administered, and selected outcomes (mortality, treatment complications).
- Data collection
  - Baseline
    The following data are collected from the digital patient files: medical history, medication use, smoking and alcohol status and history, level of education, multi-morbidity using the Charlson Comorbidity Index (CCI) [22], diagnosis that indicated intensive treatment, treatment choice, laboratory tests, geriatric screening, comprehensive geriatric assessment and in case of a malignancy, WHO performance status, tumour characteristics and stage. When a participant is not referred to the geriatric outpatient clinic, a short geriatric assessment is administered by telephone by a research nurse or researcher. This geriatric assessment includes psychological status (PHQ-2, optimism questionnaire), functional status (Katz ADL, Lawton IADL), social status and quality of life (EQ-5D-3L and EQ-VAS). Physical capacity tests are not performed.
  - Follow-up
    Participants are contacted by telephone for follow-up at 6 and 12 months after the start of treatment. The following data are collected: Katz ADL, Lawton IADL, EQ-5D-3L and EQ-VAS, and social status. In case a participant is not able to answer the questions, a proxy is allowed to answer all questions except the EQ-VAS. The proxy is registered as contact in the digital patient file, or another caregiver involved in daily care is asked.
  - Biomaterial
    At baseline blood samples are collected to study biomarkers of ageing. These samples consist of two gel tubes (8.5 cc), one tube of EDTA plasma (10 cc), and one sodium citrate tube (4.5 ml). We plan to use several methods to measure biological ageing, including algorithms that are based on routinely collected blood chemistry data, measurement of metabolomics, and epigenetics [54].
  - Data management
    Data are recorded on Case Record Forms, encrypted and stored in an electronic data management system (Castor EDC [55]), in accordance to General Data Protection Regulations (GDPR).
- Outcomes
  The primary outcome is the composite endpoint of functional decline or mortality at 1 year. Data on the following endpoints are currently being collected:
  - All-cause mortality, by consulting municipal registries (in Dutch: Basisregistratie Personen).
  - Functional status at 6 and 12 months after treatment initiation. Functional improvement is defined as an at least one-point decrease in Katz ADL compared to baseline. Functional decline is defined as at least one-point increase in Katz ADL compared to baseline or a new institutionalization.
  - Change in quality of life between baseline and 6 and 12 months follow-up based on the EQ-5D-3L index score and EQ-VAS.
  - Complications during hospital admission or treatment, such as infections, delirium, re-operation, grade 3–5 toxicity of chemotherapy, radiation therapy or other cancer therapy, early treatment discontinuation, or adjustment of treatment intensity. This information is obtained from digital patient files.
  - Total length of hospital stay, defined as the number of days between hospital admission for intensive treatment (surgery) and discharge. This information is obtained from digital patient files.
  - Unplanned admission to an intensive care unit. This information is obtained from digital patient files.
  - Unplanned hospital admission. This information is obtained from digital patient files.

- Statistical analysis
  Statistical analysis will be performed using SPSS software version 25 or STATA version 14. Determinants and endpoints will be tabulated to gain insight into data and regression models (Cox regression, linear regression and linear mixed models, binary logistic regression) used to study associations between determinants of endpoints, taking into account potential confounding. Excessive testing can be avoided by formulating hypotheses before the data analysis, reducing false-positive findings. When necessary, correction for multiple testing will be applied. Moreover, to illustrate the clinical significance of associations, results will be compared to the minimal clinically important difference. Table 2 shows the minimal clinically important differences (MCID) of the Katz ADL [56], Lawton IADL [56], EQ-5D-3L [57] and EQ-VAS [57] as reported in previous studies that most closely resemble our study population.
  We will also transform predictive values from the multivariate models into individual risk scores, predicting the selected endpoint using Receiver Operating Curves (ROC) and their area under the curve (AUC, also called c-statistic). Sensitivity, specificity, positive and negative predictive power will also be assessed. Several techniques are available to evaluate models. We intend to use bootstrapping methods for internal validation.
- Sample size calculation
  The number of participants differs per disease, but we aim to have sufficient power to predict adverse health outcomes in the various groups. We will carry out a formal power calculation per research question depending on the disease, determinant and outcome studied. An example of a sample size calculation is provided for a prediction model with the composite outcome of functional decline or 1-year mortality. Functional decline is defined as an at least one point increase in Katz ADL score or new institutionalization at 1-year follow-up. To reduce the risk of false positive findings (predictors) the so-called 'EPV (events per variable) 1 to 10 rule of thumb' is often applied. This rule suggests that at least 10 events per candidate predictor are needed for reliable prediction modelling [58, 59]. As we expect the model to include 8 predictors, at least 80 patients with the event of interest will be needed. When the incidence of the composite outcome in a certain patient population is 30% and the drop-out rate is 10%, the target sample size for the prediction model would be 294 patients.
- Ethics approval and consent to participate
  The TENT study protocol was approved by the Medical Ethics Committee (METC) at Leiden University Medical Center. All participants or a proxy provided written informed consent.

Table 2 Minimal clinically important difference (MCID) of follow-up tests

Test	Scale	Minimal important difference
Katz ADL	0–6	0.18–0.47 [56]
Lawton IADL	0–8	0.31–0.77 [56]
EQ-5D-3L	−0.33 – 1.0	0.06–0.08 [57]
EQ-VAS	0–100	7 [57]

Abbreviations ADL Activities of Daily Living, *EQ-5D-3L* EuroQol five dimensions three levels questionnaire, *EQ-VAS* EuroQol Visual Analogue Scale, *IADL* Instrumental Activities of Daily Living

Discussion

This paper describes the implementation and rationale of a routine clinical care pathway and design of the TENT study.

Implementation of a routine clinical care pathway provides the opportunity to prospectively study associations between determinants of frailty and outcomes of treatment. These results are continuously evaluated to improve care. Figure 2 illustrates the interplay between the care pathway and TENT study using a Plan-Do-Study-Act (PDSA) cycle. As one example of this interplay, van Deudekom et al. showed that nutritional status and mobility were determinants of 1-year mortality in older patients with head and neck cancer at the LUMC [60].

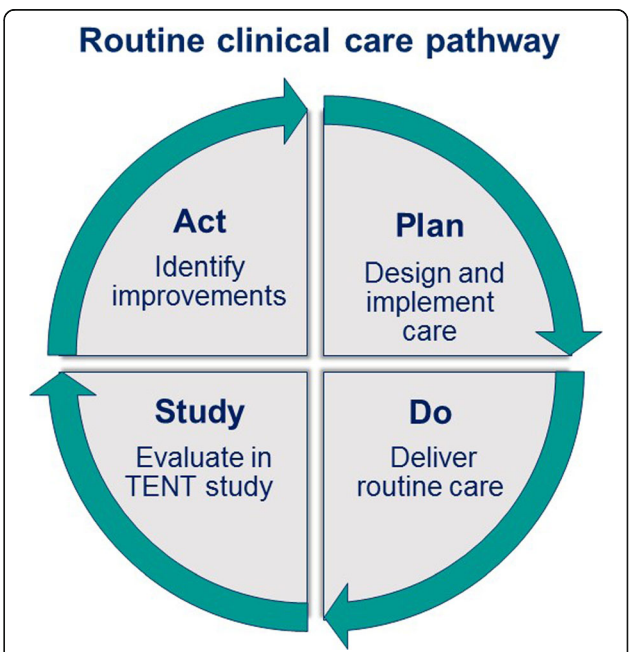

Fig. 2 Interplay between routine clinical care pathway and TENT study in a Plan-Do-Study-Act (PDSA) cycle

These results are now integrated into treatment advice in current daily practice.

Due to heterogeneity in the older patient population, design of an individualised treatment plan will require better approaches to patient characterization. Despite good evidence supporting its important role in formulating treatment decisions and improving communication regarding age related concerns [61], CGA is not yet part of routine clinical care and in the majority of clinical trials it is either not performed or not reported [62]. In addition, biomarkers (of ageing) might also help to individualise treatment. An example of incorporating routinely measured biomarkers into a prediction tool is the Cancer and Aging Research Group's (CARG) Chemo-Toxicity Calculator [14], which combines serum creatinine and haemoglobin, clinical data and geriatric parameters to predict risk of chemotherapy toxicity. Recent studies have shown promising results in measuring biological age and predicting adverse health outcomes in population-based cohorts [63–65]. However, their added value to a comprehensive geriatric assessment in clinical practice is still uncertain.

Randomised clinical trials are considered the highest level of evidence. However, only a small proportion of current randomised clinical trials focus on older patients [66, 67]. As one example of a randomised clinical trial, Hall et al. showed that a lower dose of chemotherapy in frail patients with advanced gastroesophageal cancer is non-inferior in terms of progression-free survival and resulted in less toxicity [68]. In the absence of sufficient clinical trials, observational studies can contribute to fill the evidence gap in older patients [69]. Prospective cohort studies that include geriatric assessment at baseline together with relevant outcomes will provide valuable real-life based data, an example of which is the 'Carolina Senior' registry (NCT01137825). The TENT study will also contribute to filling the evidence gap by including representative older patients, phenotyping their psychological, social and physical status and studying relevant endpoints that have rarely been addressed in previous studies. This will help to determine which patients may benefit from intensive treatment and reveal the impact of intensive treatment on alternative study endpoints, such as functional decline, quality of life and early treatment discontinuation. The TENT study will also contribute to knowledge on the pathophysiological mechanisms that drive ageing and disease by studying the association between geriatric parameters and biomarkers of ageing. We aim to combine geriatric assessment variables and biomarkers to develop models to predict treatment outcomes that are feasible to implement in clinical practice, and thereby support treatment decisions for future patients. Ultimately, the scientific evidence showing that this approach leads to improvement in relevant study endpoints should be derived from a randomised clinical trial, for example a step-wedge design.

Finally, collaboration of multiple hospitals in the study ensures a uniform approach to older patients, based on use of the same geriatric screening tests and instruments for geriatric assessment. This will improve communication between clinicians in different hospitals and with general practitioners. Moreover, it promotes inclusion of sufficient numbers of older patients in observational studies and provides opportunities for data sharing and the validation of tests and prediction tools [70].

Conclusion

Implementation of a routine clinical care pathway for older patients in need of intensive treatments provides the opportunity to study associations between determinants of frailty and outcomes of treatment. Results of the TENT study will support individualised treatment for future patients.

Abbreviations

6CIT: Six Item Cognitive Impairment Test; ADL: Activities of Daily Living; AUC: Area under the curve; BMI: Body mass index; CARG: Cancer and Aging Research Group; CCI: Charlson Comorbidity Index; EPV: Events per variable; EQ-5D: EuroQol five dimensions questionnaire; EQ-5D-3L: EuroQol five dimensions three levels questionnaire; EQ-VAS: EuroQol Visual Analogue Scale; G-8: Geriatric eight; GDPR: General Data Protection Regulation; GDS-15: Geriatric Depression Scale-15; HMC: Haaglanden Medical Center; IADL: Instrumental Activities of Daily Living; IEMO: Institute for Evidence-based Medicine in Old Age; LOT-R: Life Orientation Test-Revised; LUMC: Leiden University Medical Center; MCID: Minimal Clinically Important Difference; METC: Medical Ethics Committee; MMSE: Mini-Mental State Examination; MNA-SF®: Mini Nutritional Assessment Short Form; NTR: Netherlands Trial Register; PDSA: Plan-Do-Study-Act; PHQ-2: Patient Health Questionnaire; ROC: Receiver Operating Curve; RdG: Reinier de Graaf hospital; TENT: Triage of Elderly Needing Treatment; VAT: Visual Association Test; VMS: Veiligheid Management Systeem (Dutch for Safety Management System); VOILA: Vitality Oriented Innovations for the Lifecourse of the Ageing Society

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Authors' contributions

FJvD, AUdB, MS, GJL, FvdB, JMvdB, GJB, JEAP and SPM designed the care pathway. YvH, FJvD, ST, IP, AUdB, MJTvdE, NAdG, DvH, GL, MA, MS, GJL, FvdB, JMvdB, GJB, JEAP and SPM designed and implemented the study. SPM is the principal investigator. YvH, FJvD, ST, AUdB, MJTvdE, NAdG, DvH, GL, MA, MS, GJL, FvdB, JMvdB, GJB, JEAP and SPM participate in patient inclusion and outcome assessment. YvH and FJvD drafted the current paper. All authors critically revised the manuscript for important intellectual content and approved the final paper.

Authors' information

YvH and FJvd contributed equally to this paper.

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Availability of data and materials
Not applicable.

Ethics approval and consent to participate
The TENT study protocol was approved by the Medical Ethics Committee (METC) of Leiden University Medical Center (ID number NL53575.058.15) and by representatives of all participating centers. All participants or a proxy provided written informed consent.

Consent for publication
Not applicable.

Competing interests
ZonMw has no role in the design of the study, collection, analysis and interpretation of data and writing of the manuscript. The authors declare that they have no competing interests.

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