Addendum for the creation of senior-proof guidelines

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Accountability

This addendum originated at the initiative of the Netherlands Association of Internal Medicine (Dutch abbreviation: NIV) and the Dutch Association of Clinical Geriatrics (Dutch abbreviation: NVKG). Its creation was made financially possible by the Foundation for Quality Funds for Medical Specialists (Dutch abbreviation: SKMS).

The working method was as follows: a core group consisting of a geriatric medicine internist / a clinical specialist in geriatric medicine, a clinical specialist in geriatric medicine and two guideline methodologists wrote an initial draft text. This draft text, which was created in 2014, was submitted to a working group of subject-matter specialists and a guideline methodologist for comments in several meetings. In the spring of 2015, the version of the addendum that was approved by the working group was submitted to a sounding board group of subject-matter experts in the field of geriatric medicine, other diagnostic medical specialties or surgical specialties, and/or experts in the field of guideline development, which was assembled by the core group. The suggestions and comments of the members of the sounding board group were processed by the core group, after which the revised version was submitted to the working group for approval. The present version is the result of this. Appendix 4 includes the composition of the core group, the working group and the sounding board group.
1. Objective of this addendum

This addendum aims to increase attention for elderly people in the broadest sense of the word (see 2.) in the development of new guidelines, or in the updating of existing ones. Up to now, guidelines have focused too little on this clinically often heterogeneous group, and certainly not systematically, i.e. in all stages of the development process. One of the consequences of this is that it is often not clear whether recommendations in condition-specific guidelines also apply to the elderly, or only to relatively healthy, middle-aged adults. Whether the subject of the guideline concerns a condition (for example COPD), a problem or a complaint (for example chronic pain in elderly people), or a specific intervention (for example combined endoscopic and laparoscopic removal of colon polyps), in all cases this addendum aims to offer support in the treatment of the elderly patient who is often faced with comorbidity and multimorbidity. This addendum is intended for use with both general guidelines and guidelines specifically aimed at the elderly as a target group.¹

The use of this addendum does not presuppose that one or more clinical geriatricians / geriatric medicine internists standardly sit in the guideline working group. Formulated differently, a guideline working group without these medical specialists can also use this addendum. This addendum stands alone, or rather does not take into account existing tools, such as the HARING-tools.²

This addendum was developed as an appendix to Medical Specialist Guidelines 2.0 (version of October 2011); it follows the organisation of the development process presented here as far as possible, and will be integrated in the procedure book for guideline development. Three stages are distinguished in Medical Specialist Guidelines 2.0: the preparation stage, the development stage and the completion stage (Medical Specialist Guidelines 2.0, p.p. 17-19). The preparation stage runs from the time at which the development of guidelines is discussed. This includes the selection of a subject, and determining which organisations are involved. The preparation stage runs up to and including the assembly of the working group. The development stage starts as and when the working group is complete. The development stage also includes a comprehensive analysis of problem areas, where a broad range of stakeholders are heard. The development stage ends when the working group has a draft guideline ready. Each of these stages features a number of main points that were adopted from Guideline for Guidelines (2010 version) of the former Management Council for the Quality of Care. In each stage of guideline development, this addendum offers tools for asking for attention to important matters, specifically for the elderly.

2. Introduction

In current medical practice, evidence-based medicine featuring evidence-based guidelines constitutes an important foundation for medical decision-making. Evidence-based treatment of and care for the elderly is a veritable challenge because this category is very much

¹ This version was mainly written from the perspective of a general guideline. It may be that for some sections there was too little focus on the starting point that this addendum also needs to be useful for guidelines written specifically for the elderly.

² The “Manual and toolbox for guideline development in Dutch healthcare” (Dutch acronym: HARING) consists of 13 support instruments for drafting, revising, implementing and evaluating guidelines.
underrepresented in scientific research. An important cause of this underrepresentation is that both biomedical research and healthcare are largely organised around a single disease or disorder.\(^3\) With the elderly, in particular vulnerable elderly people, there are often multi-organ problems that require a more integrated approach (Clegg et al., 2013). One of the results of the underrepresentation of the elderly in biomedical research is that, for this group specifically, medication that is frequently used by them is not evaluated (Watts, 2012). When elderly people do participate in trials, they are, for the most part, relatively healthy, have relatively little or no comorbidity, and are often not vulnerable (McMurdo et al., 2011).

It has already become apparent in healthy elderly people that outcomes of treatment may differ from those of young adults with the same condition; it is expected for vulnerable elderly people or elderly people with multimorbidity that there will be further divergence here (Van de Glind et al., 2014).\(^4\) In addition, elderly people are often interested in different outcome measures, such as remaining independent, quality of life and the prevention of serious side effects. For them, too, a more limited life expectancy plays a role in the considerations, and shared decision-making on whether or not to treat is not always possible (Scott and Guyatt, 2010). In short, elderly people form a clinically heterogeneous group for which the results of clinical-scientific research into young adults cannot automatically be used.

3. Preparation stage

3.1 Subject, target and target group

Identification and demarcation of the subject by the initiator occurs in the first stage of the development of a guideline.

This addendum distinguishes four groups of elderly people – persons aged 65 and older. It is noted that category four partly overlaps with categories two and three:

1. **Relatively healthy elderly people**;
2. **Elderly people with one additional specific (interfering) comorbid condition** (disease, disorder). Interfering comorbidity refers to co-existing conditions that impact upon the disease or disorder which is the subject of the guideline, namely via ‘drug-condition, drug-drug, and food-drug interactions’ (Boyd & Fortin, 2010). An example of interfering comorbidity is osteoporosis in elderly people with COPD (Gibson et al., 2010). Medication with corticosteroids in connection with COPD negatively impacts bone density and increases the risk of fractures;
3. **Elderly people with multimorbidity** (several co-existing chronic conditions), where it does not concern a single, specific comorbid condition;
4. **Vulnerable elderly people**. Vulnerability in elderly people is understood to mean ‘the decrease of reserves and capacity through an accumulation of deficiencies in several

\(^3\) Based on a systematic review, Townsley, Selby and Siu (2005) conclude that only a quarter to a third of elderly patients with cancer that would be eligible for participation in a clinical trial are actually included. Important reasons for excluding elderly patients are the perceptions of physicians, exclusion criteria in relation to comorbid conditions and an adequate functional status for optimising the tolerance of the treatment.

\(^4\) Radiotherapy for carcinoma in situ, for example, is more effective in elderly women with breast cancer than in younger women with this condition.
domains’ (Guideline for Comprehensive Geriatric Assessment (CGA), 2010) and Lutomski et al. (2014). Vulnerable elderly people have an increased risk of negative health outcomes, such as falls, delirium or functional limitations, non-specific symptoms such as extreme fatigue or unexplained weight loss, frequently occurring infections (Clegg et al., 2013), post-operative complications and mortality (HR 3.19, 95% CI 1.68 - 6.04 respectively HR 2.67, 95% CI 1.08 - 6.62) (Handforth et al., 2014). Sometimes a distinction is made between vulnerability (those with a threatening loss of self-reliance) and dependence (those with a significant functional dependence). For the purposes of this addendum, we consider both groups as belonging to the latter group, for the same considerations apply in the context of guideline development.

The extent to which a specific focus on elderly people is required or desirable within a guideline may be determined by applying the criteria for subject selection as established by the Management Council for the Quality of Care to the target group of elderly people. These criteria include:

- the prevalence of the disease or condition;
- the level of suffering;
- the social relevance; and
- the expectation that a guideline may improve the quality of care.

Whether there should be a focus on a specific group of elderly people as defined above, depends on whether or not prevalent interfering comorbidity or multimorbidity occurs in the target population of the guideline. For vulnerable elderly people, what will mainly be important is whether the prognosis, care organisation or outcome measures justify attention for this specific target group.

In order to verify whether one of the groups of elderly people requires more or less focus than another, a ‘quick search’ of the literature may be performed where elderly-specific evidence in the form of systematic reviews of landmark studies may be examined. It is also possible to look at the availability of adjacent guidelines (that are currently being developed), and at the expertise of subject-matter specialists, in particular that of a clinical geriatrician/geriatric medicine internist, and whether this is used.

Should the initiator of the guidelines decide not to focus specifically on elderly people, then they state this in the introduction to the guideline, where other considerations for the demarcation of the subject of the guideline are usually mentioned as well.

If the initiator – if necessary after consultation with the professional organisations primarily involved, and possibly the (umbrella) organisations for elderly people and informal carers – decides to focus specifically on elderly people, then the following is stated in the introduction to the guideline:

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5 The guideline for guidelines of the Management Council for the Quality of Care (2012; p. 7) states: ‘The selection of the subject is determined, among others, by the prevalence of the disease or condition, the level of suffering, the social relevance and the expectation that a guideline may improve the quality of care’.

6 The lack of scientific literature does not, in itself, constitute a reason not to focus on one of the groups mentioned in the guideline.
• the specific target group it involves: elderly people, elderly people with one additional specific (interfering) comorbid condition, elderly people with multimorbidity or vulnerable elderly people, and
• the starting questions that take this into account.

3.2 Considerations for participation by a clinical geriatrician/ geriatric medicine internist and organisations for elderly people in guideline working groups

The composition of a working group for a guideline is initially determined by the subject. Based on the subject, the primarily involved professional groups are approached by the initiator. When a decision has been made to focus on elderly people, then this is not to say that a clinical geriatrician/ geriatric medicine internist should sit in the working group. There are various ways in which a clinical geriatrician/ geriatric medicine internist may be involved in a working group:

• participation (where the NVKG/ NIV authorises this as well);
• provision of feedback on draft documents during the development stage or on a consultation basis for a single module;
• involvement in the analysis of problem areas and peer review.

A clinical geriatrician/ geriatric medicine internist is involved in the inventory and analysis of problem areas when a decision has been made to focus on elderly people due to the nature of the guideline subject.

When (overall) starting questions in relation to relatively healthy elderly people or elderly people with an interfering comorbid condition that is (medically) treated are included in the guideline project, deployment may be limited to the provision of feedback within the framework of peer review. In the event of an interfering comorbid condition it is also possible to consider a medical specialist in the field of this specific comorbid condition.

When it concerns (overall) starting questions in relation to elderly people with multimorbidity, a choice between participation during the development stage and providing feedback during the development stage depends on the nature of the multimorbidity.

When (overall) starting questions with regard to vulnerable elderly people are included in the guideline project, then participation or the provision of feedback during the development stage by a clinical geriatrician/ geriatric medicine internist is an obvious choice.

The beliefs, values or preferences of elderly patients are of importance for the preparation of the appropriate recommendations, in particular during the weighing of the pros and cons of treatment options. Involvement of an organisation for elderly people is therefore desirable (see also 4.4.2).
4. Development stage

4.1. Inventory and analysis of problem areas
An inventory and analysis of problem areas aims to align a guideline with the needs of daily practice in the best possible way. An analysis of problem areas may provide information on, among others, what starting questions are the most relevant, and on promoting and impeding factors for the implementation of recommendations. In the inventory of problem areas, the patient perspective must be explicitly involved. Some of the key issues here focus on:

- how care provision and care organisation are experienced
- what limitations in self-management are experienced
- the important treatment objectives or outcomes of care
- how patients weigh the pros and cons of various interventions.

When attention is paid to elderly people, then the suggested guideline with regard to the patient perspective is to involve organisations for elderly people and organisations of informal carers in the inventory of problem areas, and additionally to perform literature research, preferably in MEDLINE and the Cochrane Library. ‘Patient preferences’, ‘patient satisfaction’, ‘patient experiences’, ‘patient participation’, ‘physician-patient relations’ and ‘shared decision-making’ may be used as (controlled) keywords, in combination with the subject, and possibly limited to systematic reviews and/or elderly [tiab] or AGED[Mesh].

Care providers/informal carers may also contribute problem areas for the benefit of guidelines. When a decision has been made to pay attention to (vulnerable) elderly people, it is important to include this fact in the methods to be used. When, for example, a questionnaire survey is carried out among the supporters of working group members, it is sensible to include specific questions with regard to the target group of elderly people. In addition, it is possible, for example, to use panels from the networks of the National Programme for Care of the Elderly.

4.2. Preparing starting questions and determining the relative importance of outcome measures
For the preparation of tangible, specific starting questions, the ‘PICO’ methodology is generally recommended:

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7 Besides care providers, care users may also be approached for the provision of problem areas. Methods that may be used include: literature research, questionnaire surveys, focus groups, invitational conferences, interviews with key figures and web surveys (digital consultation). If a guideline explicitly focuses on elderly people, at least one of these methods should be used.

8 One of the aspects of a recommendation is its acceptability. Patient preferences are involved in determining the acceptability of an intervention (see 4.4.2). It cannot be ruled out in advance that patient preferences are based on outdated patient data. The guideline working group should be alert to this.
P = patients or population (e.g. patients with atrial fibrillation)

I = intervention (e.g. acenocoumarol)

C = comparison (e.g. placebo)

O = outcome (e.g. survival, severe haemorrhaging, CVA).

When a decision has been made to focus on elderly people in the guideline, then it is sensible to formulate sub-questions. The patient group may be narrowed down, for example. In the selected example, the ‘P’ could be narrowed down to:

1. elderly people (65+) with atrial fibrillation (P1);
2. elderly people (65+) with atrial fibrillation and peptic ulcer disease (P2); or
3. elderly people (65+) with atrial fibrillation and multimorbidity (P3);
4. vulnerable elderly people (with an increased risk of falling) with atrial fibrillation (P4).

The previously mentioned outcome measures (mortality, severe haemorrhaging and CVA) may perhaps be complemented by quality of life, hospitalisation, cognitive functioning, functional status or treatment burden (Guiding Principles, 2012; p. E7). In addition, consideration should be given to the required follow-up duration with regard to the outcome measures as this may be of importance in relation to the diagnosis (think of the time-to-benefit).

Determining the relative importance of the outcome measures may pan out differently for various (sub-)groups of patients. Tackling the symptoms and decreasing the treatment burden may become all the more important the older and more vulnerable a person is. Somebody with multimorbidity who has a high risk of incurring myocardial infarction or a cerebrovascular accident may consider the outcome of a problem, such as a fracture with osteoporosis, to be less important. In other words: identifying the relative importance of outcome measures needs to occur for each individual (sub-)group.

Three categories may be used for deciding the relative importance of an outcome measure (Guyatt et al., 2011):

- **crucial outcome measure**: an outcome measure that is vital for decision-making. For example: mortality, myocardial infarction and fractures in patients with kidney insufficiency and hyperphosphatemia, who are treated with phosphate-lowering medication;
- **important outcome measure**: for example: pain as a result of calcification of soft tissue in patients with kidney insufficiency and hyperphosphatemia, who are treated with phosphate-lowering medication;
- **less important outcome measure**: for example: flatulence in patients with kidney insufficiency and hyperphosphatemia, who are treated with phosphate-lowering medication.

Information on values and preferences of (elderly) people with the relevant condition (and comorbidity), or of elderly people with multimorbidity, or of vulnerable elderly people, is required in order to determine the importance of outcome measures and the extent of variation herein. This information can be obtained from various sources:
review of the literature. A good example of such a review is the study by MacLean et al. (2012) which checked what is known about the values, preferences and experiences of patients with regard to anti-thrombotic therapy and prophylaxis;

• focus group meetings or in-depth interviews; or
• direct input of patient representatives in the guideline working group.

If the guideline focuses on elderly people, then the relative importance of the various outcome measures for this target group needs to be explicitly stated.

4.3. Systematic review of the evidence

4.3.1. Search strategies
Search strategies will be set up based on the established PICOs. These search strategies will differ for the various target groups of elderly people that have been identified. Advice will be given below for the various target groups regarding the set-up of a search strategy, insofar as PubMed is used. These search strategies are suggested for general guidelines. For geriatric guidelines, a “geriatrics” search filter is recommended, for which a sensitive and a specific strategy was developed (appendix: geriatrics search filter).

Category 1. (Healthy) elderly people

Example 1.

P = adults (including elderly people) with atrial fibrillation

I = anticoagulants from the group of coumarins

In principle, it will suffice to use the same search strategy as that for younger adults, and in a later stage it is possible to limit the search results to articles featuring a high average age or articles in which a subgroup analysis is included. Depending on the number of search results and if desired, it is possible to narrow down to systematic reviews (see also 3.5.2) and/or narrow down with the help of keywords for the relevant outcome measures. The retrieved studies subsequently check for whether specific information on elderly people is reported.

If desired, it is possible to use an additional search strategy to examine whether there are studies that specifically report on ‘age factors’⁹. For example 1, a search strategy is developed below.

Search strategy 1 (PubMed):

P = atrial fibrillation AND

I = (Acenocoumarol OR Dicumarol OR Ethyl Biscoumacetate OR Phenprocoumon OR Warfarin) AND

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⁹ With the term ‘age factors’ it is possible to trace studies in which age is used or identified as a prognostic variable or risk factor.
Study type = systematic review (systematic*[sb] OR "review literature as topic"[MeSH] OR subgroup analysis [tw] OR individual patient data[tw]) AND Age factor*[tw]

**Category 2. Elderly people with one additional specific (interfering) comorbid condition**

Example 2.

P = adults (including elderly people) with atrial fibrillation and peptic ulcer disease

I = anticoagulants from the group of coumarins

For this category of elderly people, the relevant comorbid condition needs to be included in the search query. Depending on the number of search results and if desired, it is possible to narrow down to systematic reviews and/or narrow down with the help of keywords for the relevant outcome measures. The retrieved studies subsequently check whether specific information on elderly people is reported.

If desired, it is possible to use an additional search strategy to verify whether there are studies that specifically report on 'age factors'. For example 2, a search strategy is developed below.

Search strategy 2 (PubMed):

P = (peptic ulcer OR duodenal ulcer) AND atrial fibrillation AND

I = (Acenocoumarol OR Dicumarol OR Ethyl Biscoumacetate OR Phenprocoumon OR Warfarin) AND

Study type = systematic review (systematic*[sb] OR "review literature as topic"[MeSH] OR subgroup analysis [tw] OR individual patient data[tw]) AND Age factor*[tw]

**Category 3. Elderly people with multimorbidity (several co-existing chronic conditions)**

Example 3.

P = elderly people (65+) with atrial fibrillation and multimorbidity

I = anticoagulants from the group of coumarins

The American Geriatric Society (2012) developed the following search strategy for this category (shown in italics below). Applied to example 3, it looks as follows:

Search strategy 3 (PubMed):

P = (Chronic disease [MeSH Major Topic] OR Comorbidity [MeSH Major Topic] OR "Multiple chronic conditions" OR "Multiple chronic illnesses" OR "Multiple chronic diseases" OR "Multiple morbidity" OR "Multiple comorbidity" OR "Chronic condition" OR "Chronic illness" OR "Multiple conditions" OR "Multiple illnesses" OR "Multiple diseases" OR "Multimorbidity" OR "Multi morbidity" OR "Multimorbiditiy" OR "Comorbid disease") AND atrial fibrillation AND Aged: 65+ years

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10 See ‘Guiding principles for the care of older adults with multimorbidity: an approach for clinicians’. No information is provided on the sensitivity or specificity of the search strategy.
I = (Acenocoumarol OR Dicumarol OR Ethyl Biscoumacetate OR Phenprocoumon OR Warfarin)

**Category 4. Vulnerable elderly people**

<table>
<thead>
<tr>
<th>Example 4.</th>
</tr>
</thead>
<tbody>
<tr>
<td>P = vulnerable elderly people with atrial fibrillation</td>
</tr>
<tr>
<td>I = anticoagulants from the group of coumarins</td>
</tr>
</tbody>
</table>

In a recent systematic review (Bibas et al., 2014) the following search strategy (shown in italics below) is used.\(^\text{11}\) Applied to example, 4 it looks as follows.

**Search strategy 4 (PubMed):**


I= (Acenocoumarol OR Dicumarol OR Ethyl Biscoumacetate OR Phenprocoumon OR Warfarin)

It should be considered that some overlap may exist, in particular between elderly people belonging to category 3 or category 4. The results of both search strategies should therefore be considered.

Advice on search strategies for tracing literature on values and preferences of patients, and for determining the background risk in relation to assessing absolute risk reductions or increases is listed in 4.4.2. and 4.4.3. respectively.

It is possible that no scientific studies are found for any of the specified groups of elderly people, in which effects for relevant outcome measures are reported. In this case, extrapolation will need to occur, among others, on the basis of biomedical literature that relates to younger adults. See also 4.4.3.

**4.3.2. Subjects of study**

It may be rewarding to search for studies in which meta-analyses (of individual patient data), subgroup analyses or results of meta-regression are reported with regard to treatment effect and interactions between treatment effect and co-morbidity and/or age categories of elderly people (Trikalinos, Segal and Boyd, 2014; Van de Glind et al., 2014). In the event of a lack of subgroup analyses or results of meta-regressions, which will often occur, it may be examined whether effects for a certain outcome measure in studies that present general results vary depending on the average age of the study population, or the percentage of patients with the relevant comorbidity in each study.

In the event of questions about interventions (to evaluate therapies or diagnostic strategies\(^\text{12}\) for example), the advice is to limit oneself to searching (systematic reviews of) randomised clinical

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\(^{11}\) No information on the sensitivity or specificity of the search strategy is listed.

\(^{12}\) A diagnostic strategy does not only involve the results of a test, but also the outcomes of treatment that follows a test result that are relevant for the patient (Schünemann et al., 2008). Evaluation of a diagnostic strategy may therefore best take place with the help of an RCT.
trials. In principle, this study design offers the major advantage of proper internal validity.\(^\text{13}\) After inspection of the characteristics of the patients or population in the RCTs found, however, it may turn out that the study groups included do not (sufficiently) correspond with the patients or population defined in the starting question. In this case, there is (highly) indirect evidence due to the limited applicability. In such a situation, it is advisable to also search for (systematic reviews) of observational studies, for it is to be expected that these will produce more direct evidence. In addition, prospective cohort studies are preferred, as they basically have a greater internal validity than retrospective studies.

In the event of starting questions with regard to diagnostics, at least insofar as it pertains to diagnostic accuracy studies, the advice is to exclude case control studies in any event, because this type of study provides a distorted picture of the accuracy outcomes in any case (Whiting et al., 2011). Depending on the number of studies found, it is possible to narrow down to systematic reviews, or to studies in which subgroup analyses and “age factors” are reported.

**Studies on interventions**
Combining well-performed (systematic reviews of) RCTs and observational studies, preferably prospective cohort research, may have added value with a view to internal validity and applicability of studies with regard to various categories of elderly people, and depends on the importance of the starting question as established by the working group at the preparation stage.

**Studies on diagnostic accuracy**
Preferably focus on systematic reviews on diagnostic test accuracy, or on studies with sub-group analyses and “age factors”.

**4.3.3. Summarising study characteristics (“evidence table”)**
Guideline 2.0 advises drawing up evidence tables in English, so that knowledge may be shared. No specific format is advised. Within the framework of the creation of senior-proof guidelines, several sections of an evidence table warrant further explanation.

**Characteristics of patients**
Besides the inclusion and exclusion criteria, the setting/country and characteristics of the entire study group (among others, age, gender, ethnicity, disease status, comorbidity, living at home or staying in the hospital), provide the characteristics for each subgroup where possible (age, type of comorbidity or multimorbidity or vulnerability). There should be an indication of whether or not elderly people participated in the study and if so, what category of elderly people they represented. Describe why / why not.

\(^{13}\) Internal validity concerns the extent to which the results of a clinical study (do not) display distortion. Characteristics of a study that impact the internal validity are, among others, the degree of similarity between the control group and the experimental group in terms of important variables that may influence the outcomes, or the extent of accuracy of the measuring methods used.
Outcome measures and effect sizes
List all the reported effect sizes, including those for sub-groups. Clarify whether the outcome measures of elderly people in studies (effectiveness, side effects) were reported separately, and list them if this is the case.

Specify the background risk in the control group, the absolute risk reduction and the relative risk reduction with the accompanying reliability intervals, including those for sub-groups, and time-to-benefit.

Additional comments
Specify, among others, the number (percentage) of dropouts here for the experimental group and the control group, as well as the characteristics of the dropouts. Special attention should be given to the question of whether there was more than average representation of dropouts originating from the sub-groups (elderly people, comorbidity etc.).

It should be verified for clinical studies that focus on treatment of diseases which frequently occur in elderly people whether these studies produce the required evidence for elderly people by checking:

- whether elderly people are well-represented in the studies;
- whether it concerned a representative population of elderly people;
- whether the results (effectiveness and toxicity) of interventions in elderly people are listed separately.

4.3.4. Determining the quality of evidence for each outcome measure
In the GRADE approach, the quality of evidence is defined as *the degree of certainty that the assessments of the size of an effect are correct*. It is categorised in four levels:

<table>
<thead>
<tr>
<th>Quality Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High quality</td>
<td>the actual effect is close to the assessed effect;</td>
</tr>
<tr>
<td>Poor quality</td>
<td>the actual effect is probably close to the assessed effect, but there is a</td>
</tr>
<tr>
<td></td>
<td>possibility that it differs substantially from it;</td>
</tr>
<tr>
<td>Low quality</td>
<td>the actual effect possibly differs substantially from the assessed effect;</td>
</tr>
<tr>
<td>Very low quality</td>
<td>the actual effect probably differs substantially from the assessed effect.</td>
</tr>
</tbody>
</table>

There are eight factors that impact the quality of evidence: limitations in set-up and implementation of studies, degree of consistency of the effects found in the studies, the degree of applicability of the study results, the degree of accuracy of the effects found in the studies, the presence of publication bias, the size of the effects found, the presence of dose-effect relationships, and the extent to which plausible, disruptive variables would indeed underestimate an effect (Schünemann et al., 2008).

When determining the quality of evidence in relation to various categories of elderly people, one of the most important themes is the applicability of evidence.

The extent of the applicability of evidence may be different for each of the groups of elderly people, and also for the various outcome measures that are considered. The fact that a certain
category of elderly people was included in one or more studies does not mean that the results of these studies are automatically applicable to this group. This will depend, among others, on the included number of persons from a category of elderly people, and on whether a proper sub-group analysis was performed.

It is not only the extent of applicability but also limitations in the performance of studies that may require special attention in relation to elderly people. In clinical trials, older patients will probably be among the study dropouts more often than younger adults, among others due to cognitive decline, the occurrence of other symptomatic conditions, or because of logistical limitations preventing continued participation in the trial (Scott and Guyatt, 2010).

### 4.3.5. Determining the overall quality of evidence

The background to the notion of the overall quality of evidence is that the GRADE approach determines the quality of evidence for each outcome measure (e.g. mortality, fractures, quality of life). The quality of evidence may therefore differ for each outcome measure. The GRADE approach assumes that the overall quality of evidence cannot exceed the lowest level of quality of evidence for an outcome measure that is considered to be crucial (Guyatt et al., 2013).

The overall quality of evidence may differ for the various categories of elderly people because:
- various outcome measures may be used;
- the relative importance of an outcome measure may differ; and
- the quality of evidence may differ for each outcome measure, among others due to indirect evidence.

### 4.4. Formulating recommendations

#### 4.4.1. Determining the strength of recommendations

In the GRADE approach, the strength of a recommendation is defined as the extent to which we trust, for the patients for whom the recommendations are intended, that the desired effects of a diagnostic strategy or therapy are greater than the undesired effects or vice versa (Andrews et al., 2013). Four factors are used to determine the strength (strong/weak) and the direction (pro/contra) of a recommendation. These are the quality of evidence, the balance of desired and undesired effects, values and preferences of patients and costs or means. Generally speaking, a strong recommendation is more probable when:

- there is poor or high overall quality of evidence (see 4.2),
- the difference between the desired effects and the undesired effects is greater and more certain,
- there is demonstrably no or hardly any variation in the values and preferences of patients, and
- relatively few expenses are required for the net benefits (Andrews et al., 2013).

It may be expected that no strong recommendations can be formulated for the most part for the categories of elderly people with (interfering) comorbidity or with multimorbidity or for vulnerable elderly people. A strong recommendation is most logical when, for a certain option,
the difference between desired and undesired effects is great, the overall quality of evidence is poor or high, and when there is hardly any variability in the values and preferences of patients. Conditional recommendations in which the choice of one or other option is mainly determined by values and preferences will frequently be formulated.

4.4.2. Values and preferences

Values and preferences are an umbrella term that covers the perspectives of patients, and their views, expectations and objectives with regard to health and life. These values, as well as these preferences, therefore refer to the processes that individuals follow when weighing up the potential advantages, disadvantages, costs and inconveniences, such as treatment burden, of various (diagnostic or therapeutic) interventions (Andrews et al., 2013).

It is often difficult to assess how much significance should be assigned to various outcomes when weighing them up, and people will often use differing values. Those who assess on behalf of others, such as guideline working groups, have a stronger position when they have evidence with regard to the values of those who undergo a diagnostic procedure or therapeutic intervention. According to MacLean et al. (2012), the creation of guidelines should be standardly accompanied by a systematic review of the values and preferences of patients regarding a specific subject.

It is certainly possible to find information in the literature about the values and preferences of elderly people that relate to the weighing up of the benefits and drawbacks of treatment options. Research by Fried et al. (2011), for example, shows that the willingness of elderly people to use medication for primary prevention of cardiovascular incidents is relatively insensitive to the benefits, but more sensitive to the negative effects of therapy and that, in this respect, there is a great deal of variation among elderly people. 48% to 69% were reluctant or hesitant to take medication, if this were accompanied by fatigue, nausea or confused thinking.14

Search terms in PubMed for tracing literature on values and preferences (Guiding principles, 2012) may include:


4.4.3. Balance of desired and undesired effects

When no scientific studies whatsoever are found for one of the categories, the only remaining option is extrapolation on the basis of the biomedical literature on younger adults; this should, however, be explicitly stated in the guideline. Clinical expertise, biological plausibility, prognosis, and values and preferences of patients play a role here. Two essential questions that need to be asked in relation to extrapolation are:

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14 This research was conducted in the US in three centres for seniors. A research into the values and preferences is possibly country and culture-sensitive and cannot always be extrapolated to the Dutch context.
• is there a reason to expect that in younger adults proven *clinically relevant* benefits of an intervention differ from those in older adults (whether or not with comorbidity, multimorbidity or fragility)?

• Are the disadvantages of such an intervention comparable between younger and older adults (whether or not with co-morbidity, multimorbidity or fragility)?

A guiding principle in the weighing up of potential benefits and drawbacks of an intervention may be to attach a great deal of importance to potential damage and treatment burden in the considerations. Relatively great uncertainty about the size of adverse effects of an intervention, reflected in low or very low quality of evidence, makes a weak, *negatively formulated* recommendation more probable then. The rationale behind this is that the risk of damage is potentially greater in older patients due to the more frequent presence of multimorbidity and its treatment, or of fragility. In addition, the disadvantages of an intervention may also be accompanied sooner by a greater treatment burden and impairment of the capacity of older patients.

When examining the balance of desired and undesired effects, benefits and risks of interventions, medicine interactions, drug-disease interactions, treatment burden, patient capacity, the prognosis (remaining life expectancy, functional status, years spent with limitations, quality of life) and values and preferences (see 4.4.) are considered.

*Medicine interactions and drug-disease interactions*

These interactions are particularly important in the light of interfering comorbidity. Treatment of the index disease may have an effect on comorbidity and vice versa. Consultation of Dutch guidelines in which comorbidity is treated as an index condition is necessary to assess whether a medicament for treatment of the comorbidity exacerbates the symptoms, is contra-indicated, can only be applied with greater caution, or may be qualified as safe. The same categorisation applies to the effect of the treatment of the index disease on the comorbidity.

*Benefits and risks of interventions: absolute effects*

When examining the balance of desired and undesired effects, absolute effects should be taken into consideration. When only relative effects (relative risk reductions or increases) are presented, an assessment will have to be made of the background risk for one or more of the various categories of elderly people. The usual assumption is made here that the relative risk reduction is constant, regardless of the background risk. Incidentally, this assumption does not apply to undesired effects. When determining the background risk in elderly people, prediction rules are preferably used. In the deployment of an intervention with anticoagulants in elderly people, for example, a CHADS2 score may be calculated. A HAS-BLED score may be calculated for the risk of haemorrhages as a result of the use of anticoagulants.

15 Relative risk reductions multiplied by the background risk provide absolute risk reductions.

16 The percentage of events in RCTs is usually used by guideline working groups as an assessment of the background risk. The problem, however, is that these RCTs often do not include elderly people with comorbidity / multimorbidity and therefore may provide a distorted picture of the background risk. Population-based studies may provide a more realistic picture of the background risk with elderly people, providing they are performed with a low risk of bias (Spencer et al., 2012).

17 When searching for prediction rules, the following search strategy is recommended for PubMed: Predict*[tiab] OR Predictive value of tests[mh] OR Scor*[tiab] OR Observer*[tiab] OR Observer variation[mh]). This is a sensitive search filter. It is possible to narrow down by using the term [Majr]
Treatment burden and capacity
The current strategies for the management of several co-existing chronic diseases create an increasing treatment burden for patients. This treatment burden gives rise to insufficient compliance, waste of (financial) resources and poor outcomes. It is therefore important to establish the relative treatment burden of alternative interventions, and furthermore that in particular the priorities (what conditions improve to what extent with what anticipated outcome) of the elderly patient with (interfering) comorbidity, multimorbidity or vulnerability give direction to the balance of desired and undesired effects (May et al., 2009).

Life expectancy versus time-to-benefit
When considering life expectancy, it is important to note that the ‘time-to-benefit’ of an intervention may exceed life expectancy. In the case of diabetes mellitus, for example, many years of strict glycaemic control are required to reap its rewards. This is offset by greater risks of hypoglycaemia and polypharmacy. The same applies to screening procedures such as tests for PSA, hypoglycaemia and polypharmacy: these do not necessarily produce benefits, and are potentially damaging when the ‘time-to-benefit’ exceeds the remaining life expectancy, the more so as the risk of damage and the impact on the patient increase in tandem with age and the presence of comorbidity/multimorbidity.

‘Preference-sensitive’ considerations
When drawing up the balance, the values and preferences of patients play an important role, among others where it concerns ‘preference-sensitive’ considerations. This concerns scenarios in which a therapy that can improve one condition has a negative effect on another (for example: corticosteroids for the treatment of COPD may aggravate osteoporosis), or in which a therapy may offer long-term advantages, but at the price of short-term disadvantages (for example: medicaments for primary or secondary disease prevention with evident side effects, such as statins, which decrease the cardiovascular risk but may cause muscle weakness and therefore falls).

In the case of elderly people with (interfering) comorbidity or multimorbidity, or in the case of vulnerable elderly people, ‘preference-sensitive considerations’ are often required, and this helps to present the effects and side effects in number and measure as far as possible.

4.4.4. Costs
Issues related to costs play a systematic part in guideline development. For every starting question, existing literature on cost-effectiveness is consulted. In principle, the alternative with the most advantageous cost-effectiveness is to be preferred. The most frequently used techniques for economic evaluation in healthcare are cost-effectiveness and cost utility analyses. For areas in which no cost-effectiveness studies are available, an overview of costs

(major topic) for the conditions that are sought. For example: atrial fibrillation [Majr] or stroke [Majr] (Geersing et al., 2012).

18 According to current health-economic parlance, in the calculation of a cost-effectiveness ratio, the rewards of care provision can be expressed in widely varying effectiveness measures: life years gained, complaint-free days, millimetres Hg of blood pressure reduction etc. In the calculation of a cost utility ratio, specific demands are imposed on the outcome measure: it needs to be applicable to the entire domain of healthcare and represent the value that is assigned to the total of all health effects of a provision. A frequently used outcome measure is the Quality Adjusted Life Year (QALY). (Source: JND de Neeling. Kostenutiliteitsanalyse [Cost utility analysis]. The Hague: Health Council, 2003)
and benefits is presented with the recommendation, based on the available data. These considerations may be used in trade-offs within the framework of macro-budgeting and/or in the potential performance of a budget impact analysis (BIA). A BIA is advised for recommendations with a major financial or organisational impact and makes budget shifts transparent, which is important within the framework of implementation.

Recent experiences with the use of cost-effectiveness studies demonstrate that cost effectiveness data is often not available or that the quality of the studies is very limited (REF Advisory report in respect of the frontrunner project [Dutch: Koploperproject]). This will certainly also apply to elderly people. In these cases, a good alternative seems to be the description of cost considerations at a general level. When the data in the field of cost(–effectiveness) has been mapped out, it should subsequently be considered what alternative will be recommended. In the case of elderly people with (interfering) comorbidity or multimorbidity, or in the case of vulnerable people, several specific considerations need to be made here:

**Patient population**
The cost-effectiveness of a medical intervention frequently depends on the characteristics of the patient (age, health situation, consumption pattern and other diseases). The cost-effectiveness models are therefore often based on a very specific patient population. This may render statements on the cost-effectiveness of a medical intervention impossible for specific patient groups, such as (vulnerable) elderly people.

It is of significance, for example, that treatment of elderly people, for whom aspects such as a decreased cognitive function, decreased mobility and decreased functionality play a role, often takes more time than for younger patients. In the case of a single intervention, more complications and more side effects will generally occur in elderly people, as a result of which cost data cannot be easily extrapolated. When mapping out the costs, all these aspects need to be taken into account, and how they were dealt with in the relevant module should be explained.

In the case of elderly people, it is also important to factor in other aspects that greatly impact costs. Considerations that will not always play a role in other patient groups include: care aspects such as institutionalisation, forms of home care and informal care by informal carers. Participation in the workforce barely plays a part, but it does for informal care providers.

**Social appreciation of QALY**
Better use of cost-effectiveness information in decisions on new medical technology first of all requires policy-related choices regarding the threshold values to be used for the socially acceptable costs per QALY. It is unclear what a socially acceptable price for a QALY is. Moreover, there are strong indications that the social willingness to pay for a QALY depends on the seriousness of the condition and on the characteristics of the patient. With an acute life-threatening disease, for example, the willingness to pay for an extra QALY is much greater than with preventive care, and is also much greater for younger patients than for the elderly patient. The shorter 'payback period' for elderly people is also of importance. With many medical interventions, it is probable that the costs per QALY will increase with age because the period in which the benefits (health gains) occur, is shorter than with younger patients. This pleads in favour of political choices regarding the social appreciation of QALYs.
Future choices and benefits

A methodological problem area with both cost-effectiveness analyses and BIAs is whether or not to include future costs and benefits. In health economy, it is common to involve relevant costs and benefits in the analysis, but the dividing line between relevant and irrelevant costs and benefits often proves difficult to distinguish with elderly people. It is precisely the indirect costs and effects, however, that may have a considerable budget impact in practice, but which are often based on uncertain assumptions (out of necessity). It is therefore advisable to deal with this in a careful manner. By way of illustration, see an example below of the BIA for the guideline for dementia.

Neuropsychiatric symptoms regularly occur in patients with dementia. Antipsychotics may help to lessen these symptoms. However, research shows that antipsychotics increase the risk of CVAs and mortality. In the guideline ‘Dementia’, it is therefore recommended to exercise caution in the prescription of antipsychotics for patients with dementia.

It is expected that compliance with this recommendation from the guideline ‘Dementia’ will result in the prevention of a number of CVAs. This is why less CVA care is required, and this will lead to cost savings. Compliance with the recommendation will additionally also result in the prevention of a number of deaths. Care for patients suffering from dementia is expensive. The longer life expectancy of the patients that would otherwise have died prematurely, will therefore lead to a cost increase.

It is thus perceived that avoided mortality may actually have a negative effect on the budget. In this case, the guideline working group has decided that the indirect costs of avoided mortality should not play a role in the BIA. The question is whether the guideline working group would have come to the same decision if the avoided mortality would indeed have yielded a cost reduction.

4.4.5. Making recommendations more specific for the elderly

An important question is how recommendations for adults in a general guideline may be made more specific. Indeed, more specific with a view to the various categories of elderly people. The first aspect that needs to be examined concerns the strength of a recommendation.

For patients, the implication of a strong, positive recommendation is: nearly everybody wants the recommended therapy, and few people do not want it. The implication of a weak or conditional, positive recommendation is: the majority wants the recommended therapy, but

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19 It involves indirect costs within healthcare here. These concern the medical costs that may be incurred in life years gained.
many do not want it. For the clinician, a weak or conditional recommendation means they need to be willing to assist the patient in making a decision in accordance with the values and preferences of the patient, preferably using decision aids here (Andrews et al., 2013).

The second aspect is that weak or conditional recommendations clearly indicate the benefits and drawbacks of the various options and their respective treatment burden, as well as the values and preferences that play a role in the various options. If decision aids are available that are suitable for the older target group, they should preferably be mentioned. An example of a decision aid for whether or not to use medication (bisphosphonates) in relation to osteoporosis is included in the appendix ‘decision aid’.

We will use an example to illustrate how a recommendation may be made more specific, and which deliberations and considerations play a role here. Besides the desired and undesired effects, treatment burden, what a patient can withstand in terms of treatment burden, prognosis and values and preferences, these deliberations and considerations also concern possible medicine interactions.

<table>
<thead>
<tr>
<th>Hypothetical example</th>
</tr>
</thead>
<tbody>
<tr>
<td>The starting point is a strong recommendation for postmenopausal women younger than 65 years of age and suffering from osteoporosis to use a bisphosphonate. It is assumed that this recommendation is based on the high overall quality of evidence for the prevention of significant osteoporotic fractures.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Starting question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Should a vulnerably elderly person with postmenopausal osteoporosis use a bisphosphonate?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor, in connection with devaluation due to indirect evidence.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Balance of desired and undesired effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment burden</td>
</tr>
<tr>
<td>In many vulnerable elderly people polypharmacy will occur. In the prescription of medication in relation to osteoporosis, there is a considerable risk of poor compliance and lack of effectiveness of the medication.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant interactions are those of orally ingested bisphosphonates with oral acid inhibitors and with anticoagulants.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medicines with an adverse impact on bone metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Various diuretics and antidepressants (TCAs and SSRIs) have a negative effect on bone density and increase the risk of fractures.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Size of the desired effect (reduced risk of fractures)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates such as alendronate reduce the relative risk of fractures of the hip and spinal column by approximately 50% in 2 years’ time (table).</td>
</tr>
</tbody>
</table>
When, for a high risk group, the risk of a serious osteoporotic spinal fracture is 3% in a period of 2 years, an absolute risk reduction of 1.4% may be realised with the use of alendronate. This corresponds with a number ‘needed to treat’ (NNT) of 72.

The FRAX score may moreover be used for the assessment of the 10-year risk of a fracture.

Size of undesired effects

The combined assessment of the relative risk of ceasing the medication in relation to gastrointestinal complaints when using at least 5 mg of alendronate daily is 1.03 (95% BI: 0.81–1.30), and the combined assessment of the relative risk of gastrointestinal complaints when continuing the medication is 1.03 (95% BI: 0.98 – 1.07). These results may perhaps not be directly applicable to elderly people with comorbidity, multimorbidity or vulnerability because participants in trials are usually healthier and have less comorbidity.

Prognosis

Depending on the scores calculated with the aid of a measuring instrument that combines age, gender, body weight, degree of comorbidity and functional status, life expectancy may be forecast (see the example in the appendix of a prognostic index for 4-year mortality; see also: www.eprognosis.com). For a woman aged 75, with a BMI < 25 kg/m², diabetes mellitus type 2, heart failure and limitations such as not being able to walk more than a few hundred metres, the risk of mortality within 4 years is 28%. If there were additionally also limitations for washing or bathing, this risk would increase to 44%.

In the case of a mortality rate of 44% within 4 years’ time, the realisation of a relevant reduction of fractures cannot or can barely be expected.

Values and preferences

Research aided by a discrete selection model among persons with osteoporosis (n=257; average age 67; 83% female) into patient preferences for medication due to osteoporosis concluded that patients with osteoporosis have a preference for six-monthly subcutaneous injections and a monthly tablet, and dislike gastrointestinal side effects. At the same time, it appeared that, apart...
from the method of administration, there was variation in preferences for virtually all attributes (degree of effectiveness, possible side effects, administration frequency and costs) (Hiligsmann et al., 2014).

A good decision aid exists, although it was not specifically created for the target group of elderly people: http://osteoporosisdecisionaid.mayoclinic.org/index.php/site/index.

**Costs**

A cost-effectiveness analysis of alendronate in osteoporotic women with an average age of 70 with a T-score of -2.4 carried out in nine European countries, concludes that cost-effectiveness depends on the setting (country) threshold value for acceptable costs per Qaly (Ström et al., 2007). The Netherlands did not belong to the nine European countries. With a discount rate of 3, the costs per QALY vary from “cost-effective” (Norway/Sweden) to €15,489 (France) for women with a previous spinal fracture. For women without a previous spinal fracture, the costs per QALY varied from “cost-effective” (Norway/Sweden) to €39,712 (Italy). The applicability of these outcomes for the Dutch setting & for vulnerable elderly people is unclear.

**Recommendations**

Given the low absolute risk reduction when using alendronate in the first years, a bisphosphonate is not recommended for a vulnerable elderly person with osteoporosis and a life expectancy of less than two to four years. Support in the continuation of supplementation with calcium and vitamin D is recommended; dietary advice may be of importance here.

Bisphosphonates may be considered for vulnerable elderly people with osteoporosis and a life expectancy of 4 years or more when values such as remaining independent / self-reliant for as long as possible are essential, and side effects are considered to be of less importance. When avoiding side effects is a significant value, it is recommended to continue supplementation with calcium and vitamin D. Dietary advice may be of importance here.

**4.5. Implementation of recommendations**

During the entire process of guideline development, implementation needs to be reflected on. Besides mapping out barriers as far as possible, this also means involving the right organisations in the development of the guideline, and formulating the recommendations in such a way that implementation is facilitated. The organisations that need to be involved are the organisations that have to provide care. Care providers that specifically focus on elderly care are involved, as well as care providers that provide more general care, as well as care for the elderly. Furthermore, organisations need to be involved that fund and facilitate care. All these organisations may adopt a proactive approach to problem areas, possible solutions in the form a recommendation and in terms of what is required to actually implement this recommendation. Patient organisations may similarly contribute ideas from the perspective of patients.

When identifying barriers, it concerns barriers in the various echelons of care: the care provider, the organisation in which care is provided, and the healthcare system, as well as barriers at the level of the patient. With regard to the latter, think, for example of insufficient ‘health literacy’ due to an insufficient command of the language (Twickler et al.; Dutch Journal of Medicine. 2009; 153: A250) or insufficient number sense. Furthermore, different valuation of health may play a
role. Recommendations that insufficiently take this into account will be almost impossible to implement.

When formulating a recommendation that is specifically geared towards elderly people, there needs to be a constant focus on the question as to what specific barriers there may be, and how they may be overcome. This is possible, for example, under the header 'implementation considerations' before or after a specific recommendation, or in a separate chapter if necessary.

The table below offers a general framework for the inventory of possible barriers.

| Table. Examples of problem areas at the professional, organisational and system level |
|---------------------------------|-----------------------------------------------------------------------------------|
| **Level of the problem area**   | **Problem area**                                                                  |
| **Care provider**               | Not enough motivation to follow up the recommendation, because specific care for elderly people is considered to be unnecessary |
|                                 | Not enough knowledge of elderly people to follow up the recommendation             |
|                                 | Time duration too long to follow up the recommendation                            |
| **Organisation**                | Not enough knowledge of the content of the new guideline to adjust the organisation in the desired way |
|                                 | Not enough facilities, funds or staff to follow up the guideline                   |
|                                 | Insufficient co-operation between disciplines                                     |
|                                 | Accountability problem                                                            |
|                                 | Logistical organisation                                                           |
|                                 | Task re-allocation/task-shifting                                                   |
| **System**                      | Financial                                                                         |
|                                 | Insufficient training in the field of geriatric medicine                           |
|                                 | No tariffs for co-treatment, no treatment                                          |
|                                 | Peer group barriers                                                               |
| **Patient**                     | Physical limitations                                                              |
Cognitive limitations

Mobility disorders

Different health perception

The application of this general framework may be illustrated with a hypothetical example. In this example, the starting point is a recommendation in which various options for treatment are advised, a situation that will frequently occur with elderly people, among others due to variability in the values and preferences of the various categories of elderly patients.

**Example:** lessening of depressive complaints in elderly people with type 2 diabetes may be brought about with medication but also with specific exercise programmes. For patients who wish to limit the risks of medication, for example because polypharmacy already occurs with them, the non-medicament option may be attractive.

Barriers may manifest themselves at various levels when applying the recommendation to follow an exercise programme:

- **Level of the care provider:** presuppositions with regard to experiences of a few elderly people, which are extrapolated to other patients, as a result of which the choice is already made for the elderly person.
- **Level of the organisation:** due to a lack of time on the part of the care provider, there is too little space to discuss the pros and cons of both options.
- **Level of the healthcare system:** the absence of centres that organise exercise programmes for elderly people in the immediate living environment of the patient, or the absence of specifically trained physiotherapists, may form a barrier for the application of the non-medicament option.
- **Level of the patient:** hearing loss in elderly patients limits the options in group therapy.

Possible interventions to overcome the identified barriers or to limit them in any event:

**Level of care providers:**
Distributing recommendations from relevant guidelines to partnerships and professional groups as well as organising ‘clinical lessons’, to be taught by medical specialists that were involved in a guideline working group, in which recommendations were drawn up specifically for elderly people may perhaps help to reduce knowledge gaps and limit bias.

**Level of the organisation:**
It may help to involve a geriatrician/geriatric medicine internist in the treatment for the purpose of discussing the most suitable option for this elderly patient.

**Level of the system:**
More time for and reimbursement of consultations for elderly people by healthcare insurers may possibly limit this barrier.

The development of (local) initiatives by organisations for elderly people and/or professional organisations to create facilities for exercise programmes may possibly help here.

**Level of the patient:**
Individual therapy instead of group therapy may possibly offer a solution.
5. Identifying possible knowledge gaps

A knowledge gap will probably be detected for many a starting question that pertains to the various categories of elderly people. Not only because elderly people are underrepresented in clinical trials, but also because these trials often do not evaluate the end points that actually important to elderly people (Hurria et al., 2014. The Guideline for Guidelines drawn up by the Management Council for the Quality of Care recommends prioritising the identified knowledge gap with the aim of supplying information for ‘the’ research agenda.

The HARING tool ‘Knowledge gaps in guidelines’ (IQ Healthcare, 2013) recommends the following criteria for the identification of ‘good’ knowledge gaps:

- The gap concerns an important clinical question (disease burden, absenteeism, costs and burdening of family members). Yes/no;
- Filling the gap has consequence for the guideline. The recommendations in the guideline may change internally or a weak recommendation may become strong recommendation (or vice versa). Yes/no;
- Answering the question potentially improves the quality of care and/or patient outcomes (for example the quality of life). Yes/no;
- The gap may be researched and the intended research is feasible, that is to say that it has a reasonable chance of success in the current research practice and infrastructure. Do not only think of the costs here but also of ethical aspects. Yes/no.

The fourth criterion is too strict for scientific (biomedical) research into (vulnerable) elderly people, as the costs are higher due to the heterogeneity and limited mobility of elderly people. In addition, ethical aspects accompanying the inclusion of elderly people with cognitive problems may impede the inclusion. A “Multidisciplinary guideline regarding elderly people in scientific research” aims to provide tools to make research more feasible in this population, too.

The advice regarding knowledge gaps in relation to younger adults and (vulnerable) elderly people is to list and prioritise them separately in the guideline.
Literature


IKNL. Richtlijn Colorectaal Carcinoom 2014 [Guideline regarding the Colorectal Carcinoma 2014].


May C, Montori VM, Mair FS. We need minimally disruptive medicine. BMJ. 2009 Aug 11;339:b2803.

Medical Specialist Guidelines 2.0.


Appendix 1. Geriatrics search filter


No. 1: The most sensitive search filter (Se=94.8%, Sp= 88.7%)


No. 2: The most specific search filter (Se=69.1%, Sp=96.6%)
## Appendix 2. Example of a prognostic index for 4-year mortality

### Box. Four-Year Mortality Index for Older Adults

1. Age ____________________________

2. Sex (Male/Female)
   - Male: 2 points
   - Female: 2 points

3. a. Weight: ____________________________
   b. Height: ____________________________
   
   \[ 703 \times \text{(weight in pounds/ height in inches}^2) \]
   \[ \text{BMI} = \frac{\text{Weight}}{\text{Height}^2} \]

4. Has a doctor ever told you that you have diabetes or high blood sugar? (Y/N)
   - Diabetes: 1 point

5. Has a doctor told you that you have cancer or a malignant tumor, excluding minor skin cancers? (Y/N)
   - Cancer: 2 points

6. Do you have a chronic lung disease that limits your usual activities or makes you need oxygen at home? (Y/N)
   - Lung Disease: 2 points

7. Has a doctor told you that you have congestive heart failure? (Y/N)
   - Heart Failure: 2 points

8. Have you smoked cigarettes in the past week? (Y/N)
   - Smoke: 2 points

9. Because of a health or memory problem do you have any difficulty with bathing or showering? (Y/N)
   - Bathing: 2 points

10. Because of a health or memory problem, do you have any difficulty with managing your money—such as paying your bills and keeping track of expenses? (Y/N)
    - Finances: 2 points

11. Because of a health problem do you have any difficulty with walking several blocks? (Y/N)
    - Walking: 2 points

12. Because of a health problem do you have any difficulty with pulling or pushing large objects like a living room chair? (Y/N)
    - Push or Pull: 1 point

**Total Points: ________________**

Appendix 3. Example of a decision aid for medication (bisphosphonates) in connection with osteoporosis

Benefits

Without Medication
Roughly 40 in 100
have a fracture
within the next 10
years. 60 will not.

With Medication
Roughly 24 in 100
have a fracture
within the next 10
years. 76 will not.
10 have avoided
a fracture because
of the medication.

Downsides

Directions
This medication must be taken
• Once a week
• On an empty stomach in the morning
• With 8 oz of water
• While upright (sitting or standing for 30 min)
• 30 minutes before eating

Possible Harms
Abdominal Problems
About 1 in 4 people will have heartburn, nausea, or
belly pain. However, it may not be from the medication. If
the medication is the cause, the problem will go away if you
stop taking it.

Osteonecrosis of the Jaw
Fewer than 1 in 10,000 (over the next 10 years) will have
bone sores of the jaw that may need surgery.

Out of Pocket Cost
with insurance $30 | without insurance $70-90

What would you like to do?

Source: http://shareddecisions.mayoclinic.org/files/2012/06/Osteo_DA_high.pdf (assessed risk of a bone fracture over the next 10 years: ≥30%)
Appendix 4. Composition of the core group, the working group and the sounding board group

Work group and core group

Dr B.C. van Munster, geriatric medicine internist and clinical geriatrician (chairman; core group), NIV

5 A.J. Arends, clinical geriatrician (vice-chairman; core group), NVKG

Dr Ir. J.J.A. de Beer, guideline methodologist (CBO until 1 May 2014; as of 1 May 2014 Guide2Guidance; core group)

T.A. van Barneveld MSc, epidemiologist (Knowledge Institute of Medical Specialists; core group)

Prof A.B. Maier, geriatric medicine internist, NIV

Dr J.E.A. Portielje, internist oncologist, NIV

10 Ms G.S. Spronk, clinical geriatrician, NVKG

A.Y. Steutel MSc, guideline advisor, IKNL