

Osteoporosis

Clinical Practice Guideline on the Role of Vitamin D, Calcium and Exercise in Fracture Prevention in Elderly

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Dr. Youssef Saleh has received honoraria for giving presentations in workshops for MSD Pharmaceuticals, Servier Laboratories, Amgen, and Eli Lilly within the past 4 years (no presentations in 2013).

Dr. Basmah Wahhabi has received travel payments (Eli Lilly, MSD Pharmaceuticals, Novartis, Servier Laboratories) to attend meetings on osteoporosis, honoraria for giving lectures about osteoporosis in meetings organized by the pharmaceutical companies to orthopaedics and family medicine departments, and a one-time payment for serving as a member of an advisory board on osteoporosis management from Eli Lilly (participation has ceased).

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Executive summary

Introduction

The prevention of fractures in the elderly has been identified as a priority problem in the Kingdom of Saudi Arabia (KSA). With an estimated population of 1.4 million males and females over the age of 50 in Saudi Arabia, and a baseline risk of 6 proximal femoral fractures per 1000, it has been estimated in a 2007 study that the cost of management of these patients with femoral fractures in the KSA extrapolated to a national basis is US\$1.14 billion annually.¹ With an aging population, an increase in fractures in the elderly living in the community will further amplify the impact on the KSA healthcare system.

Given the importance of this topic, the Ministry of Health (MoH) of Saudi Arabia with the methodological support of the McMaster University working group produced clinical practice guidelines to assist health care providers in evidence-based clinical decision-making. This guideline evaluates the role of vitamin D and calcium supplementation, and exercise as interventions for fracture prevention in this population.

Methodology

This clinical practice guideline is a part of the larger initiative of the Ministry of Health of the Kingdom of Saudi Arabia (KSA) to establish a program of rigorous adaptation and de novo development of guidelines. The ultimate goals are to provide guidance for clinicians and reduce variability in clinical practice across the Kingdom.

The KSA guideline panel selected the topic of this guideline and all clinical questions addressed herein using a formal prioritization process. For all selected questions we updated existing systematic reviews that were used

for the 2014 Osteoporosis Canada Clinical practice guidelines for management of osteoporosis and fracture prevention for the frail elderly in long-term care, and considered data applicable to the elderly living in the community in Saudi Arabia.² We also conducted systematic searches for information that was required to develop full guidelines for the KSA, including searches for information about patients' values and preferences and cost (resource use) specific to the Saudi context. Based on the updated systematic reviews we prepared summaries of available evidence supporting each recommendation following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach.³ We used this information to prepare the *evidence to recommendation tables* used by the guideline panel to follow a structured consensus process and transparently document all decisions made during the meeting (see **Appendix 1**). The guideline panel met in Riyadh on December 4, 2013 and formulated all recommendations during this meeting. Potential conflicts of interests of all panel members were managed according to the World Health Organization (WHO) rules.⁴

How to use these guidelines

The guideline working group developed and graded the recommendations and assessed the quality of the supporting evidence according to the GRADE approach.⁵ Quality of evidence (confidence in the available estimates of treatment effects) is categorized as: high, moderate, low, or very low based on consideration of risk of bias, directness, consistency and precision of the estimates. High quality evidence indicates that we are very confident that the *true* effect lies close to that of the estimate of the effect. Moderate quality evidence indicates moderate confidence, and that the *true* effect is likely close to the estimate of the effect, but there is a possibility that it is substantially

different. Low quality evidence indicates that our confidence in the effect estimate is limited, and that the *true* effect may be substantially different. Finally, very low quality evidence indicates that the estimate of effect of interventions is very uncertain, the *true* effect is likely to be substantially different from the effect estimate and further research is likely to have important potential for reducing the uncertainty.

The strength of recommendations is expressed as either strong ('guideline panel recommends...') or conditional ('guideline panel suggests...') and has explicit implications (see **Table 1**). Understanding the interpretation of these two grades is essential for sagacious clinical decision making.

Table 1: Interpretation of strong and conditional (weak) recommendations

Implications	Strong recommendation	Conditional (weak) recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations	Policy making will require substantial debate and involvement of various stakeholders.

Key questions

1. Should vitamin D supplementation alone be recommended for prevention of fractures in the elderly living in the community?
2. Should vitamin D and calcium supplementation be recommended for prevention of fractures in the elderly living in the community?
3. Should calcium supplementation alone be recommended for prevention of fractures in the elderly living in the community?
4. Should exercise be recommended for prevention of fractures in the elderly living in the community?

Recommendations

Recommendation 1:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests not offering Vitamin D supplementation alone. (conditional recommendation; low quality evidence)

Remark:

This recommendation does not apply to patients who are diagnosed as vitamin D deficient.

Recommendation 2:

For fracture and/or fall prevention in elderly living in the community, the KSA MoH guideline panel suggests Vitamin D and Calcium for patients at high risk fractures and low risk of cardiovascular disease. (conditional recommendation; low quality evidence)

Recommendation 3:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel recommends not offering Calcium supplementation alone. (strong recommendation; low quality evidence)

Remark:

- This recommendation does not apply to patients with hypocalcaemia states.

Recommendation 4:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests individual exercise performed at home. (conditional recommendation; low quality evidence)

Scope and Purpose

The purpose of this document is to provide guidance about the role of vitamin D and calcium supplementation, and exercise in the prevention of fractures in elderly living in the community in Saudi Arabia. The target audience of these guidelines includes primary care physicians, internists and specialists (e.g. rheumatology, orthopaedics, endocrinology), and pharmacists in the Kingdom of Saudi Arabia. Other health care professionals and policy makers may also benefit from these guidelines.

Given the importance of this topic, the Ministry of Health (MoH) of Saudi Arabia with the methodological support of the McMaster University working group produced clinical practice guidelines to assist health care providers in evidence-based clinical decision-making. This clinical practice guideline is a part of the larger initiative of the Ministry of Health of Saudi Arabia to establish a program of rigorous adaptation and de novo development of guidelines in the Kingdom; the ultimate goal being to provide guidance for clinicians and reduce variability in clinical practice across the Kingdom.

Introduction

The prevention of fractures in the elderly has been identified as a priority problem in the Kingdom of Saudi Arabia (KSA). With an estimated population of 1.4 million males and females over the age of 50 in Saudi Arabia, and a baseline risk of 6 proximal femoral fractures per 1000, it has been estimated in a 2007 study that the cost of management of these patients with femoral fractures in the KSA extrapolated to a national basis is US\$1.14 billion annually.¹ With an aging population, an increase in fractures in the elderly living in the community will further amplify the impact on the KSA healthcare system.

Elderly, typically considered as those 60 years of age or more, living in the community in

Saudi Arabia may be at an increased risk of fractures. The absolute risk of fractures can be assessed using validated tools based on established risk factors, such as the Fracture Risk Assessment (FRAX) developed by a group of international experts through a World Health Organization (WHO) research project.⁶ However, the FRAX tool is currently only validated for Jordan, Lebanon, Tunisia and Turkey in the Middle East and Africa Region, and has not been validated with national data for Saudi Arabia.⁷ Using established risk factors to identify high risk populations is important for early intervention and management of patients. Vitamin D and calcium supplementation, as well as exercise, are commonly proposed interventions for prevention of fractures. This guideline evaluates the role of vitamin D and calcium supplementation, and exercise as interventions for fracture prevention in this population.

Methodology

To facilitate the interpretation of these guidelines; we briefly describe the methodology we used to develop and grade recommendations and quality of the supporting evidence. We present the detailed methodology in a separate publication.⁸

The KSA guideline panel selected the topic of this guideline and all clinical questions addressed herein using a formal prioritization process. For all selected questions we updated existing systematic reviews that were used for the 2014 Osteoporosis Canada Clinical practice guidelines for management of osteoporosis and fracture prevention for the frail elderly in long-term care, and considered data applicable to the elderly living in the community in Saudi Arabia (see **Appendix 2**).² We also conducted systematic searches for information that was required to develop full guidelines for the KSA, including searches for information about patients' values and preferences and cost (resource use) specific to the Saudi context. Based on the updated systematic reviews we prepared summaries of available evidence supporting each recommenda-

tion following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach.³ We obtained local baseline risk data for patient-important outcomes where available,^{1,9} and considered best estimates from data from other large population-based studies and trials where local data were not available (see **Appendix 3**). For decision-making, the panel also considered the effects of interventions across a range of baseline risks (see Summary of Findings Tables in **Appendix 1**).

We assessed the quality of evidence using the system described by the GRADE working group.⁵

Quality of evidence is classified as “high”, “moderate”, “low”, or “very low” based on decisions about methodological characteristics of the available evidence for a specific health care problem. The definition of each category is as follows:

- *High*: We are very confident that the true effect lies close to that of the estimate of the effect.
- *Moderate*: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- *Low*: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- *Very low*: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

According to the GRADE approach, the strength of a recommendation is either strong or conditional (weak) and has explicit implications (see **Table 1**). Understanding the interpretation of these two grades – either strong or conditional – of the strength of recommendations is essential for sagacious clinical decision-making.

We used this information and the input of KSA MoH panel members to prepared the *evi-*

dence-to-recommendation tables that served the guideline panel to follow a structured consensus process and transparently document all decisions made during the meeting (see **Appendix 1**). The guideline panel met in Riyadh on December 4, 2013 and formulated all recommendations during this meeting. Potential conflicts of interests of all panel members were managed according to the World Health Organization (WHO) rules.⁴

How to use these Guidelines

The MoH of KSA and McMaster University Clinical Practice Guidelines provide clinicians and their patients with a basis for rational decisions in the management of elderly patients at risk of fractures. Clinicians, patients, third-party payers, institutional review committees, other stakeholders, or the courts should never view these recommendations as dictates. No guidelines and recommendations can take into account all of the often-compelling unique features of individual clinical circumstances. Therefore, no one charged with evaluating clinicians’ actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion.

Statements about the underlying values and preferences as well as qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate an accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines.

Key questions

The following is a list of the clinical questions selected by the KSA guideline panel and addressed in this guideline. For details on the process by which the questions were selected for this guideline please refer to the separate methodology publication.

1. Should vitamin D supplementation alone be recommended for prevention of fractures in the elderly living in the community?
2. Should vitamin D and calcium supplementation be recommended for prevention of fractures in the elderly living in the community?
3. Should calcium supplementation alone be recommended for prevention of fractures in the elderly living in the community?
4. Should exercise be recommended for prevention of fractures in the elderly living in the community?

Recommendations

I. Vitamin D and/or Calcium Supplementation

Summary and Quality of the Evidence:

We identified in our search 7 systematic reviews and meta-analyses¹⁰⁻¹⁶ and 2 trials^{17,18} about the benefits and harms of vitamin D and/or calcium supplementation in the elderly living in the community (see Summary of Findings table in **Appendix 1**). The evidence for the majority of the patient-important outcomes was rated as moderate quality, most often due to risk of bias in the trials included in the systematic reviews. The overall quality of the evidence was then downgraded by one level to low due to indirectness of the data for the Saudi Arabia healthcare setting. When considering the rating of evidence, we considered systematically the issue of indirectness (e.g. Vitamin D deficiency being prevalent in the KSA)¹⁹⁻²¹ and lack of local data about baseline risk and downgraded the overall quality of evidence from moderate to low. The judgment of indirectness would be ideally accompanied by a judgment of how the effect (direction and potential size of the effect) in the population of interest would be different (e.g. in population with vitamin D deficiency would we expect a higher reduction in fracture incidence).

The populations included in the studies were primarily over the age of 60, consisting of a majority of women (>70%). The majority of cases were from the community, with one or more risk factors, and with or without vitamin D deficiency (without subgroup analyses). The studies evaluated the effect of Vitamin D (D2 and D3, not analogues) most commonly at a dosage of 800IU and Calcium at a dosage of 1000mg for prevention of fractures, and most in comparison to a placebo (see Summary of study characteristics in **Appendix 4**).

Values and Preferences:

There are no published data on patients' values and preferences specifically with respect to vitamin D and/or calcium supplementation and fracture prevention in the context of the KSA. The KSA guideline panel considered that patients in general would accept taking a supplement pill. The panel also noted that patients assign a high value on preventing fractures. *Acceptability:*

Based on current prescribing practices in the KSA, Vitamin D and calcium supplementation was viewed by the panel as acceptable to key stakeholders, including healthcare providers and policymakers.

Feasibility:

Vitamin D and calcium supplementation was viewed as feasible by the guideline panel as it is available in the healthcare system and is currently prescribed to certain patients.

Resource Use:

Based on data from the Saudi Food and Drug Authority²² and the Saudi Drug Database²³ the cost of vitamin D and calcium supplement packages ranges from approximately 10 to 30 SAR (for various dosages and package sizes). The panel considered that the resources required for vitamin D and/or calcium supplementation would be small. However, due to lack of local resource use data related to the intervention and outcomes, as well as cost-effectiveness studies and assessments of volume costs, the KSA guideline panel was uncertain about whether the incremental cost would be small relative to the net benefits.

Implementation Considerations and Monitoring:

Given the current prescribing trends for vitamin D and calcium supplementation in the KSA, the panel noted that implementing the options of vitamin D and/or calcium supplementation would not pose challenges in the KSA healthcare system.

The KSA guideline panel suggests monitoring and evaluation of implementation of the recommendation at the healthcare system level. Periodic and formal evaluations of adherence to the recommendations of this guideline should be according to their strength:

- Strong recommendations should be applied to the large majority of patients. Therefore, the adherence to the course of action proposed by strong recommendations could be used as a quality criterion or performance indicator.
- For conditional (weak) recommendations, however, it is important to recognize that different choices could be appropriate for different patients. Therefore, measuring the adherence to the course of action proposed by weak recommendations is not appropriate for quality criteria or performance indicators.

Research Priorities:

The KSA MoH panel was faced with a lack of local data for decision-making. It was therefore suggested that urgent research is needed on the incidence of fractures and associated morbidity and mortality among elderly people living in the community in Saudi Arabia. A national registry is suggested to track local data on fracture rates. Validation of the FRAX tool in the Saudi Arabia population is also required. Additionally, due to the resulting uncertainty about the estimates of effect based on the current evidence it is suggested that high-quality studies are needed to assess the effects of vitamin D and/or calcium supplementation on fracture rates.

Question 1: Should vitamin D supplementation alone be recommended for prevention of fractures in the elderly living in the community?

Benefits of the Option:

For vitamin D supplementation alone, absolute effects across the range of baseline risks were not found by the guideline panel to differ significantly for hip fractures between elderly at high risk of fractures and those not at high risk. The meta-analysis showed that vitamin D supplementation alone does not seem to reduce or has no effect on hip fractures (Odds Ratio (OR) 1.13, 95% Confidence Interval (CI): 0.94 to 1.34), with 1 fewer hip fracture per 1000 people (95% CI: from 1 fewer to 4 more) at a baseline risk of 11 hip fractures per 1000.¹⁶ It also showed likely little to no effect on vertebral fractures (OR 0.96, 95% CI: 0.59 to 1.58), with 0 fewer fractures per 1000 people (95% CI: from 4 fewer to 6 more), and non-vertebral fractures (OR 1.01, 95% CI: 0.85 to 1.20), with 0 fewer fractures per 1000 (95% CI: from 4 fewer to 6 more),¹⁶ quality of life (QoL),¹⁷ and mortality.¹⁰ There was some uncertainty around the effect on falls since vitamin D supplementation alone showed an apparent increase in the rate of falls, with 140 more falls per 1000 people (95% CI: from 30 fewer to 270 more), and also likely no effect on the number of people who fall (Risk Ratio (RR) 1.08, 95% CI: 0.93 to 1.26), with 24 more people falling at least once per year per 1000 people (95% CI: from 21 fewer to 78 more).¹⁵ (see Summary of Findings table in **Appendix 1**)

Harms of the Option:

The meta-analysis showed that vitamin D supplementation may result in an increase in gastrointestinal events (mild or serious) (OR 1.04, 95% CI: 1.00 to 1.08), with 7 more events per 1000 people (95% CI from 0 to 14 more).¹⁰

Balance between desirable and undesirable consequences:

The KSA MoH panel considered that vitamin D alone was shown to have probably small to no effect on reduction in hip fractures, vertebral

fractures, and non-vertebral fractures in those through a range of fracture risks. It was also shown to likely not have substantial undesirable consequences. The panel, therefore, noted that the balance between desirable and undesirable consequences is closely balanced or uncertain.

Recommendation 1:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests not offering Vitamin D supplementation alone. (conditional recommendation; low quality evidence)

Remarks:

- This recommendation does not apply to patients who are diagnosed as vitamin D deficient.

Question 2: Should vitamin D and calcium supplementation be recommended for prevention of fractures in the elderly living in the community?

Benefits of the Option:

For vitamin D and calcium supplementation, a small significant difference in absolute effect was shown only for hip fractures mainly in elderly at high risk of fractures (baseline risk of 30 hip fractures per 1000), with 6 fewer fractures per 1000 people (95% CI: from 1 to 9 fewer). In the lower risk group (baseline risk of 11 hip fractures per 1000), vitamin D and calcium supplementation was shown to reduce hip fractures, with 2 fewer fractures per 1000 people (95% CI: from 0 fewer to 3 fewer). Vitamin D with calcium versus no vitamin D or calcium, therefore, probably reduces hip fractures more when compared with the effect shown for vitamin D or calcium alone (OR 0.81, 95% CI: 0.68 to 0.96).¹⁶ Vitamin D and calcium supplementation also suggests a possible reduction in overall mortality (RR 0.94, 95% CI: 0.88 to 1.00), with 7 fewer deaths per 1000 (95% CI: from 14 fewer to 0) in the high risk population. Vitamin D with calcium probably has little or no effect on vertebral fractures (0 fewer per 1000 in the lower risk population, 95% CI: from 3 fewer to 4 more),

nonvertebral fractures (2 fewer per 1000 in the lower risk population, 95% CI: from 5 fewer to 1 more),¹⁶ quality of life,¹⁷ number of falls, and number of fallers.¹⁵

Harms of the Option:

Vitamin D and calcium supplementation together was shown to result in an increase in myocardial infarction (RR 1.21, 95% CI: 1.01 to 1.44), with 23 more MIs per 1000 people (95% CI: from 1 to 48 more) at a baseline risk of 110 MIs per 1000.¹² Vitamin D and calcium supplementation also showed a slight increase in renal disease (calculi or insufficiency) (OR 1.16, 95% CI: 1.02 to 1.33), and in gastrointestinal events (OR 1.04, 95% CI: 1.00 to 1.08).¹⁰

Balance between desirable and undesirable consequences:

The KSA MoH panel considered that vitamin D and calcium supplementation was shown to reduce hip fractures in those at higher risk, but was also shown to have an undesirable consequence of increase in myocardial infarction. The benefits of vitamin D and calcium supplementation may therefore outweigh the potential harms only for those at high risk of fractures and low risk of cardiovascular disease.

Research Priorities:

The KSA MoH panel suggests studies to determine whether there are sustained benefits and a reduction in adverse effects with calcium dosages lower than 1000mg.

Recommendation 2:

For fracture and or fall prevention in elderly living in the community, the KSA MoH guideline panel suggests Vitamin D and Calcium for patients at high risk fractures and low risk of cardiovascular disease. (conditional recommendation; low quality evidence)

Question 3: Should calcium supplementation alone be recommended for prevention of fractures in the elderly living in the community?

Benefits of the Option:

For calcium supplementation alone, the meta-analysis showed that there is probably little or no effect on hip fractures (OR 1.14, 95% CI: 0.82 to 1.59), on vertebral fractures (OR 0.71, 95% CI: 0.45 to 1.12), with 3 fewer vertebral fractures per 1000 people (95% CI: from 5 fewer to 1 more) at a baseline risk of 10 vertebral fractures per 1000, and on non-vertebral fractures (OR 1.00, 95% CI 0.83 to 1.22), with 0 fewer non-vertebral fractures per 1000 people (95% CI: from 5 fewer to 6 more).¹⁶ Calcium supplementation alone also probably has little or no effect on overall mortality (OR 1.07, 95% CI: 0.95 to 1.19) , with 5 more deaths per 1000 (95% CI: from 4 fewer to 13 more).¹²

Harms of the Option:

Calcium supplementation alone showed an increase in myocardial infarction (RR 1.27, 95% CI: 1.01 to 1.59), with 30 more MIs per 1000 people (95% CI from 1 to 65 more).¹² Calcium supplementation alone also showed little or no effect on renal disease, hypercalcaemia and gastrointestinal events, based on low or very low quality evidence.

Balance between desirable an undesirable consequences:

The KSA MoH panel considered that calcium supplementation alone was shown to have probably little to no benefit on fracture reduction, and was shown to have an undesirable consequence of increase in myocardial infarction. The panel, therefore, noted that the undesirable consequences probably outweigh desirable consequences in most settings.

Recommendation 3:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel recommends not offering Calcium supplementation alone. (strong recommendation; low quality evidence)

Remarks:

- This recommendation does not apply to patients with hypocalcaemia states.

II. Exercise

Question 4: Should exercise be recommended for prevention of fractures in the elderly living in the community?

Summary and Quality of the Evidence:

There was overall low quality evidence for exercise in preventing fractures in the elderly living in the community. The quality of evidence was downgraded to low primarily due to risk of bias of the studies included in both systematic reviews.^{15,24} The 2013 review by Kemmler and colleagues reported patient-important outcomes such as fractures.²⁴ The 2012 review by Gillespie and colleagues reported the effectiveness of exercise on the prevention of falls, and did not report on other outcomes such as quality of life, mobility or pain.¹⁵ Home-based exercise interventions assessed in the systematic reviews included balance, strength, endurance and resistance training exercises, walking; simple exercises that would not require trainer guidance or facilitation as would typically be used for exercise interventions provided in institutions (see **Appendix 4**).

Benefits of the Option:

Home and centre-based exercises which focused on endurance, resistance training, balance, flexibility, jumping and general coordination training assessed in the systematic reviews were shown to decrease vertebral fracture rates (RR 0.56, 95% CI: 0.30 to 1.04), with 88 fewer fractures per 1000 people (95% CI: from 140 fewer to 8 more), but the results were not precise and do not exclude no effect.²⁴ Exercise was also shown to decrease the number of overall fractures (RR 0.49, 95% CI: 0.31 to 0.76), with 56 fewer fractures per 1000 people (95% CI: from 26 to 75 fewer). Gillespie et al. provided subgroup analyses based on different types of exercises, carried out both in group sessions and at home. Programs containing multiple categories of exercise (mainly a combination of balance and functional training with muscle strengthening and resistance training as well as flexibility exercises) performed individually at home were effective in reducing both the rate of

falls (RR 0.68, 95% CI: 0.58 to 0.80), with 320 fewer falls per 1000 people per year (95% CI: from 200 to 420 fewer) and risk of falling at least once (RR 0.78, 95% CI: 0.64 to 0.94), with 66 fewer falling per 1000 people (95% CI: from 18 to 108 fewer). Low quality evidence, due to risk of bias and imprecision, showed that programs based on a single category of exercise likely do not reduce the risk of falls. (see Summary of Findings table in **Appendix 1**)

Harms of the Option:

The harms of home-based exercise were not assessed.

Values and Preferences:

There are no published data on patients' values and preferences with respect to home-based exercise in the KSA. The panel considered that patients value and understand the importance of exercise, but with possible variability geographically in Saudi Arabia with respect to how exercise is viewed by the elderly at risk of fractures. The panel also considered that patients assign a high value on preventing fractures.

Resource Use:

There were no cost data available for home-based exercise, and costs of providing exercise interventions were not reported in the systematic reviews. The panel considered that exercises done individually at home would not require significant resources.

Acceptability:

The panel considered the option acceptable to healthcare providers and policy makers, and that most carers and family members would accept exercise for elderly and provide support.

Feasibility:

The panel considered that recommending exercise was feasible to implement from a policy-making perspective.

Implementation Considerations and Monitoring:

Implementation of the recommendation should include creation of public spaces for observed exercise as well as creation of safe walking spaces for elderly living in the community. Exercise as an intervention to reduce the risk of fractures should receive promotion by the Ministry of Health as an intervention to improve bone health.

Research Priorities:

The KSA MoH panel suggests research about the acceptability of exercise by the elderly living in the community in Saudi Arabia.

Recommendation 4:

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests individual exercise performed at home. (conditional recommendation; low quality evidence)

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19. Al-Othman A, Al-Musharaf S, Al-Daghri NM, et al. Effect of physical activity and sun exposure on vitamin D status of Saudi children and adolescents. *BMC pediatrics*. 2012;12:92.
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22. Middle East Medicine Prices Database. 2011; <https://medprice.sfda.gov.sa/>.
23. Saudi Drug Database. 2013; <http://nassersite.com/drugdb/>.
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Appendices

1. Evidence-to-Recommendation and Summary of Findings Tables
2. Search Strategies and Results
3. Table of Baseline Risks
4. Summary of Characteristics of Included Studies

Appendix 1: Evidence-to-Recommendation and Summary of Findings Tables

Evidence to recommendation framework 1

Question 1: Should vitamin D supplementation alone be recommended for prevention of fractures in the elderly living in the community?

Panelists in attendance: Drs. Hanan Al Rayes, Mona Fouda, Salwa Al Aidarous, Safia Sherbeeni, Mir Sadat, Riad Sulimani

Additional COI declared at the beginning of the meeting: None declared

Problem: Elderly in the community
Option: Vitamin D to prevent fractures
Comparison: No vitamin D
Setting: Community
Perspective: Health care system

Background: The question addressed in the systematic reviews used for the 2014 Osteoporosis Canada guideline addressed Vitamin D supplementation for prevention of fractures in the elderly living in long term care facilities. This guideline addresses this question in the elderly living in the community in Saudi Arabia.

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS
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PROBLEM Is the problem a priority?	No Probably No Uncertain Probably Yes Yes <i>Varies</i>					<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
	Outcome	Assumed Baseline Risks						
		Overall risk in the community	High risk in the community	Elderly living in the community in Saudi Arabia				
	Hip fractures /femoral fractures	11 per 1000	30 per 1000	6 per 1000 ¹				
	Vertebral fractures	10 per 1000	200 per 1000	203 per 1000 ⁹				
	Non-vertebral fractures / osteoporotic fractures	30 per 1000	80 per 1000	n/a				
	Number of falls (per year)	1000 per 1000	3000 per 1000	n/a				
	Number of people who fell at least once per year	300 per 1000	500 per 1000	n/a				
	Mortality	70 per 1000	120 per 1000	n/a				
	Quality of life (EQ-5D)	0.7	n/a	n/a				
	Myocardial infarct	110 per 1000	n/a	n/a				
	Gastrointestinal events (any)	200 per 1000	n/a	n/a				
	Hypercalcaemia	6 per 1000	n/a	n/a				
Renal disease (calculi or insufficiency)	4 per 1000	4 per 1000	n/a					

The KSA guideline panel identified fractures in elderly living in the community as a priority problem. However there is an absence of current local data about the incidence of fractures and the associated morbidity and mortality in the elderly population in Saudi Arabia. The panel also noted inconsistency in practice in prescribing vitamin D supplementation.

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No	Probably No	Uncertain	Probably Yes	Yes	Varies											
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RESOURCE USE	Are the resources required small?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<p>Summary of the evidence for resource use:</p> <p>Based on data from the Saudi Food and Drug Authority²² and the Saudi Drug Database²³ the cost of vitamin D and calcium supplement packages ranges from approximately 10 to 30 SAR (for various dosages and package sizes). Therefore, given the unit costs the panel considered that the resources required for supplementation would be small.</p>	<p>The KSA guideline panel considered that the resources required for Vitamin D supplementation would be small. However, due to lack of local resource use data related to the intervention and outcomes, the KSA guideline panel was uncertain about whether the incremental cost would be small relative to the net benefits.</p> <p>D. Bubshait and M. Sadat-Ali 2007:</p> <ul style="list-style-type: none"> Estimated cost for total hospital stay for femoral fracture in men was SR 46,456.61 ± 29,700.23, and in women SR 53,581.05 ± 26,988.95. With risk of 6 fractures per 1000 (984 proximal femoral fractures in 164,121), cost of management of these patients with femoral fractures estimated at SR 48 million (US\$12.78 million) annually, extrapolated to
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Balance of consequences

Undesirable consequences *clearly outweigh* desirable consequences in most settings

Undesirable consequences *probably outweigh* desirable consequences in most settings

The balance between desirable and undesirable consequences *is closely balanced or uncertain*

Desirable consequences *probably outweigh* undesirable consequences in most settings

Desirable consequences *clearly outweigh* undesirable consequences in most settings

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS
				national basis (1,461,401 males and females >50, 8,768 fractures), cost estimated at SR 4.27 billion (US\$1.14 billion) annually.
EQUITY	What would be the impact on health inequities?	<p>Increased <input type="checkbox"/> Probably increased <input type="checkbox"/> Uncertain <input checked="" type="checkbox"/> Probably reduced <input type="checkbox"/> Reduced <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	The panel was uncertain whether recommending Vitamin D supplementation would reduce or increase inequity in the healthcare system due to the dearth of data on resource use.
ACCEPTABILITY	Is the option acceptable to key stakeholders?	<p>No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	Vitamin D supplementation was viewed by the panel as acceptable to key stakeholders, including healthcare providers and policymakers.
FEASIBILITY	Is the option feasible to implement?	<p>No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	Vitamin D supplementation was viewed as feasible as it is available in the healthcare system and is currently prescribed to certain patients.



Type of recommendation

We recommend against offering this option

We suggest not offering this option

We suggest offering this option

We recommend offering this option



Recommendation (text)

For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests not offering Vitamin D supplementation alone. (conditional recommendation; low quality evidence)

Remarks:

- This recommendation does not apply to patients who are diagnosed as vitamin D deficient.

Note: The recommendation was achieved through panel vote: 5 in favor, 1 against the recommendation.

Justification

This recommendation is conditional due to low quality evidence and close balance between the desirable and undesirable consequences for Vitamin D supplementation alone.

Subgroup considerations

-

Implementation considerations

-

Monitoring and evaluation

Monitor and evaluate implementation of the recommendation at the healthcare system level.

Research priorities

Research on incidence of fractures and associated morbidity and mortality among elderly people living in the community in Saudi Arabia.
Setting up a national registry to track local data on fracture rates.
Urgent high-quality research to assess the effects of vitamin D supplementation on fracture rates.

Evidence to recommendation framework 2

Question 2: Should vitamin D and calcium supplementation be recommended for prevention of fractures in the elderly living in the community?

Panelists in attendance: Drs. Hanan Al Rayes, Mona Fouda, Salwa Al Aidarous, Safia Sherbeeni, Mir Sadat, Riad Sulimani, Mohammad Al Shaker

Additional COI declared at the beginning of the meeting: None declared

Problem: Elderly in the community

Option: Vitamin D and calcium to prevent fractures

Comparison: No vitamin D or calcium

Setting: Community

Perspective: Health care system

Background: The question addressed in the systematic reviews used for the 2014 Osteoporosis Canada guideline addressed Vitamin D and Calcium supplementation for prevention of fractures in the elderly living in long term care facilities. This guideline addresses this question in the elderly living in the community in Saudi Arabia.

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Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings
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EQUITY	What would be the impact on health inequities?	<table border="0"> <tr> <td>Increased</td> <td>Probably increased</td> <td>Uncertain</td> <td>Probably reduced</td> <td>Reduced</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Increased	Probably increased	Uncertain	Probably reduced	Reduced	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	No evidence identified	The panel was uncertain whether recommending Vitamin D and Calcium supplementation would reduce or increase inequity in the healthcare system due to the dearth of data on resource use.
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Type of recommendation

We recommend against offering this option

We suggest not offering this option

We suggest offering this option

We recommend offering this option



Recommendation (text)

For fracture and or fall prevention in elderly living in the community, the KSA MoH guideline panel suggests Vitamin and Calcium for patients at high risk fractures and low risk of cardiovascular disease. (conditional recommendation; low quality evidence)

Justification

This recommendation is conditional due to low quality evidence demonstrating an apparent small benefit in terms of reduction in hip, vertebral and non-vertebral fractures, with an increase in myocardial infarction for Vitamin D and Calcium supplementation.

Subgroup considerations

-

Implementation considerations

Available validated tools should be used for proper assessment of fracture risk (e.g. FRAX tool) and cardiovascular risk (e.g. Framingham score).

Monitoring and evaluation

Monitor and evaluate implementation of the recommendation at the healthcare system level.

Research priorities

Local research to evaluate the benefits and harms of Vitamin D and Calcium in the Saudi Arabia healthcare setting.
Validation of the FRAX tool in the Saudi Arabia population.
Determine whether there are sustained benefits and a reduction in side effects with Calcium dosages lower than 1000mg.

Evidence to recommendation framework 3

Question 3: Should calcium supplementation alone be recommended for prevention of fractures in the elderly living in the community?

Panelists in attendance: Drs. Hanan Al Rayes, Mona Fouda, Salwa Al Aidarous, Safia Sherbeeni, Mir Sadat, Riad Sulimani, Mohammad Al Shaker

Additional COI declared at the beginning of the meeting: None declared

Problem: Elderly in the community

Option: Calcium to prevent fractures

Comparison: No calcium

Setting: Community

Perspective: Health care system

Background: The question addressed in the systematic reviews used for the 2014 Osteoporosis Canada guideline addressed Calcium supplementation for prevention of fractures in the elderly living in long term care facilities. This guideline addresses this question in the elderly living in the community in Saudi Arabia.

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS																																																			
<p style="writing-mode: vertical-rl; transform: rotate(180deg);">PROBLEM</p> <p>Is the problem a priority?</p>	<p>No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/></p>	<table border="1"> <thead> <tr> <th rowspan="2">Outcome</th> <th colspan="3">Assumed Baseline Risks</th> </tr> <tr> <th>Overall risk in the community</th> <th>High risk in the community</th> <th>Elderly living in the community in Saudi Arabia</th> </tr> </thead> <tbody> <tr> <td>Hip fractures /femoral fractures</td> <td>11 per 1000</td> <td>30 per 1000</td> <td>6 per 1000</td> </tr> <tr> <td>Vertebral fractures</td> <td>10 per 1000</td> <td>200 per 1000</td> <td>203 per 1000</td> </tr> <tr> <td>Non-vertebral fractures / osteoporotic fractures</td> <td>30 per 1000</td> <td>80 per 1000</td> <td>n/a</td> </tr> <tr> <td>Number of falls (per year)</td> <td>1000 per 1000</td> <td>3000 per 1000</td> <td>n/a</td> </tr> <tr> <td>Number of people who fell at least once per year</td> <td>300 per 1000</td> <td>500 per 1000</td> <td>n/a</td> </tr> <tr> <td>Mortality</td> <td>70 per 1000</td> <td>120 per 1000</td> <td>n/a</td> </tr> <tr> <td>Quality of life (EQ-5D)</td> <td>0.7</td> <td>n/a</td> <td>n/a</td> </tr> <tr> <td>Myocardial infarct</td> <td>110 per 1000</td> <td>n/a</td> <td>n/a</td> </tr> <tr> <td>Gastrointestinal events (any)</td> <td>200 per 1000</td> <td>n/a</td> <td>n/a</td> </tr> <tr> <td>Hypercalcaemia</td> <td>6 per 1000</td> <td>n/a</td> <td>n/a</td> </tr> <tr> <td>Renal disease (calculi or insufficiency)</td> <td>4 per 1000</td> <td>4 per 1000</td> <td>n/a</td> </tr> </tbody> </table>	Outcome	Assumed Baseline Risks			Overall risk in the community	High risk in the community	Elderly living in the community in Saudi Arabia	Hip fractures /femoral fractures	11 per 1000	30 per 1000	6 per 1000	Vertebral fractures	10 per 1000	200 per 1000	203 per 1000	Non-vertebral fractures / osteoporotic fractures	30 per 1000	80 per 1000	n/a	Number of falls (per year)	1000 per 1000	3000 per 1000	n/a	Number of people who fell at least once per year	300 per 1000	500 per 1000	n/a	Mortality	70 per 1000	120 per 1000	n/a	Quality of life (EQ-5D)	0.7	n/a	n/a	Myocardial infarct	110 per 1000	n/a	n/a	Gastrointestinal events (any)	200 per 1000	n/a	n/a	Hypercalcaemia	6 per 1000	n/a	n/a	Renal disease (calculi or insufficiency)	4 per 1000	4 per 1000	n/a	<p>The KSA guideline panel identified fractures in elderly living in the community as a priority problem. However there is an absence of current local data about the incidence of fractures and the associated morbidity and mortality in the elderly population in Saudi Arabia. The panel also noted inconsistency in practice in prescribing.</p>
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Is the incremental cost small relative to the net benefits?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											

Balance of consequences

Undesirable consequences *clearly outweigh* desirable consequences in most settings

Undesirable consequences *probably outweigh* desirable consequences in most settings

The balance between desirable and undesirable consequences *is closely balanced or uncertain*

Desirable consequences *probably outweigh* undesirable consequences in most settings

Desirable consequences *clearly outweigh* undesirable consequences in most settings

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS
				fractures estimated at SR 48 million (US\$12.78 million) annually, extrapolated to national basis (1,461,401 males and females >50, 8,768 fractures), cost estimated at SR 4.27 billion (US\$1.14 billion) annually.
EQUITY	What would be the impact on health inequities?	<p>Increased <input type="checkbox"/> Probably increased <input type="checkbox"/> Uncertain <input checked="" type="checkbox"/> Probably reduced <input type="checkbox"/> Reduced <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	The panel was uncertain whether recommending Calcium supplementation would reduce or increase inequity in the healthcare system due to the dearth of data on resource use.
ACCEPTABILITY	Is the option acceptable to key stakeholders?	<p>No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	Calcium supplementation was viewed by the panel as acceptable to key stakeholders, including healthcare providers and policymakers.
FEASIBILITY	Is the option feasible to implement?	<p>No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input type="checkbox"/> Yes <input checked="" type="checkbox"/> <i>Varies</i> <input type="checkbox"/></p>	No evidence identified	Calcium supplementation was viewed as feasible as it is available in the healthcare system and is currently prescribed to certain patients.

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Recommendation (text)	For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel recommends not offering Calcium supplementation alone. (strong recommendation; low quality evidence)			
	Remarks: <ul style="list-style-type: none"> This recommendation does not apply to patients with hypocalcaemia states. 			
Justification	This recommendation is strong due to undesirable consequences (i.e. increase in mortality and myocardial infarction) outweighing the desirable consequences for Calcium supplementation alone.			
Subgroup considerations	-			
Implementation considerations	-			
Monitoring and evaluation	Monitor and evaluate implementation of the recommendation at the healthcare system level.			
Research priorities	-			



Summary of Findings Table: Vitamin D and/or Calcium Supplementation

Author(s): Itziar Etxeandia & Wojtek Wiercioch

Date: 2013-11-28

Bibliography: Murad 2012, Avenell 2009; Bischoff-Ferrari 2012, Gillespie 2012, Bolland 2011, Bolland 2010, Elamin 2011, Grant 2005, Reid 2006

Outcomes	Effects and Quality of the Evidence			
	Vitamin D alone	Vitamin D with calcium	Calcium alone	Placebo/no treatment
Hip fractures	<p>Overall risk 1 more per 1000 (1 fewer to 4 more)</p>	<p>Overall risk 2 fewer per 1000 (0 to 3 fewer)</p>	<p>Overall risk 2 more per 1000 (2 fewer to 6 more)</p>	<p>Overall risk 11 hip fractures per 1000</p>
	<p>OR 1.13 (0.94 to 1.34)</p> <p>High risk 4 more per 1000 (2 fewer to 10 more)</p>	<p>OR 0.81 (0.68 to 0.96)</p> <p>High risk 6 fewer per 1000 (1 to 9 fewer)</p>	<p>OR 1.14 (0.82 to 1.59)</p> <p>High risk 4 more per 1000 (5 fewer to 17 more)</p>	<p>High risk 30 hip fractures per 1000</p>
	<p>Murad includes 139,647 participants with 2567 hip fractures, 40 trials, for all interventions assessed. ⊕⊕⊕⊖ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community. Estimate similar in Avenell 2009 (only community; 16,524 participants with 351 hip fractures in 9 studies) RR 1.2 (0.98 to 1.48), and Bischoff-Ferrari 2012 (Vit D with and without Ca vs. placebo or Ca) RR 0.90 (0.80 to 1.01).</p>	<p>Murad includes 139,647 participants with 2567 hip fractures, 40 trials, for all interventions assessed. ⊕⊕⊕⊖ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community. Estimate similar to Avenell 2009 (only community; 42,805 participants with 491 hip fractures in 6 studies) RR 0.91 (0.76 to 1.08), and Bischoff-Ferrari 2012 (Vit D with and without Ca vs. placebo with/without Ca) RR 0.90 (0.80 to 1.01).</p>	<p>Murad includes 139,647 participants with 2567 hip fractures, 40 trials, for all interventions assessed. ⊕⊕⊕⊖ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community.</p>	

Outcomes	Effects and Quality of the Evidence			
	Vitamin D alone	Vitamin D with calcium	Calcium alone	Placebo/no treatment
Vertebral fractures	<p>Overall risk 0 fewer per 1000 (4 fewer to 6 more)</p> <p>OR 0.96 (0.59 to 1.58)</p> <hr/> <p>High risk 6 fewer per 1000 (71 fewer to 83 more)</p>	<p>Overall risk 0 fewer per 1000 (3 fewer to 4 more)</p> <p>OR 0.99 (0.74 to 1.41)</p> <hr/> <p>High risk 2 fewer per 1000 (44 fewer to 61 more)</p>	<p>Overall risk 3 fewer per 1000 (5 fewer to 1 more)</p> <p>OR 0.71 (0.45 to 1.12)</p> <hr/> <p>High risk 49 fewer per 1000 (99 fewer to 19 more)</p>	<p>Overall risk 10 vertebral fractures per 1000</p> <hr/> <p>High risk 200 vertebral fractures per 1000</p>
	<p>Murad includes 126,423 participants with 2929 vertebral fractures, 67 trials, for all interventions assessed. ⊕⊕⊕⊕ low From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community. Estimate similar to Avenell 2009 (community; 5698 participants with 83 vertebral fractures in 3 studies) RR 1.13 (0.5 to 2.55) with inconsistency in estimate of effect between studies.</p>	<p>Murad includes 126,423 participants with 2929 vertebral fractures, 67 trials, for all interventions assessed. ⊕⊕⊕⊕ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community. Estimate similar to Avenell 2009 (only community; 38,980 participants with 379 vertebral fractures in 2 trials) RR 0.91 (0.75 to 1.11).</p>	<p>Murad includes 126,423 participants with 2929 vertebral fractures, 67 trials, for all interventions assessed. ⊕⊕⊕⊕ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community.</p>	
Nonvertebral fractures	<p>Overall risk 0 more per 1000 (4 fewer to 6 more)</p> <p>OR 1.01 (0.85 to 1.20)</p> <hr/> <p>High risk 1 more per 1000 (11 fewer to 14 more)</p>	<p>Overall risk 2 fewer per 1000 (5 fewer to 1 more)</p> <p>OR 0.94 (0.84 to 1.02)</p> <hr/> <p>High risk 5 fewer per 1000 (13 fewer to 2 more)</p>	<p>Overall risk 0 fewer per 1000 (5 fewer to 6 more)</p> <p>OR 1.00 (0.83 to 1.22)</p> <hr/> <p>High risk 0 fewer per 1000 (13 fewer to 16 more)</p>	<p>Overall risk 30 non-vertebral fractures per 1000</p> <hr/> <p>High risk 200 non-vertebral fractures per 1000</p>
	<p>Based on 136 557 participants with 12041 non-vertebral fractures, 66 trials ⊕⊕⊕⊕ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community. Similar to Avenell 2009 (institution) RR 0.96 (0.80 to 1.15) and higher than in Bischoff-Ferrari 2012 (Vit D with and without Ca vs. placebo with and without Ca) RR 0.93 (0.87 to 0.99).</p>	<p>Based on 136 557 participants with 12041 non-vertebral fractures, 66 trials ⊕⊕⊕⊕ moderate From Murad 2012 trials with risk of bias; population primarily community Consistent with Avenell 2009, 42,928 participants with 4434 nonvertebral fractures in 7 studies, only in community. RR 0.97 (0.91 to 1.02) and including the estimation in Bischoff-Ferrari 2012 (Vit D with and without Ca vs. place with and without Ca) RR 0.93 (0.87 to 0.99).</p>	<p>Based on 136 557 participants with 12041 non-vertebral fractures, 66 trials ⊕⊕⊕⊕ moderate From Murad 2012 network meta-analysis with trials with risk of bias; population primarily community</p>	

Outcomes	Effects and Quality of the Evidence			
	Vitamin D alone	Vitamin D with calcium	Calcium alone	Placebo/no treatment
Number of falls per person time	<p>Overall risk 140 more per 1000 (30 more to 270 more)</p> <p>Rate Ratio 1.14 (1.03 to 1.27)</p> <p>High risk 420 more falls per 1000 (90 more to 810 more)</p>	<p>Rate Ratio 0.96 (0.89 to 1.04)</p> <p>High risk 120 fewer falls per 1000 (330 fewer to 120 more)</p>	n/a	<p>Overall risk 1000 falls per 1000 people per year</p> <p>High risk 3000 falls per 1000 people year</p>
	<p>Based on 2478 participants with, 2 trials ⊕⊕⊕⊖ Moderate From Gillespie 2012 (community only), imprecision.</p>	<p>Based on 6586 participants, 3 trials ⊕⊕⊕⊖ low From Gillespie 2012, only in community, risk of bias limitation and some inconsistency and also some imprecision (including benefit in high risk population, and harm)</p>		<p>Overall risk 1000 falls per 1000 people per year</p> <p>High risk 3000 falls per 1000 people year</p>
Number of people who fell at least once per year	<p>Overall risk 24 more per 1000 (21 fewer to 78 more)</p> <p>RR 1.08 (0.93 to 1.26)</p> <p>High risk 40 more per 1000 (35 fewer to 130 more)</p>	<p>RR 0.98 (0.92 to 1.03)</p> <p>High risk 10 fewer per 1000 (40 fewer to 15 more)</p>	n/a	<p>Overall risk 300 people per 1000</p> <p>High risk 500 people per 1000</p>
	<p>Based on 4516 participants 1356 people with >=1 fall, 3 trials ⊕⊕⊕⊖ moderate From Gillespie 2012, only in community some inconsistency and also some imprecision (including benefit, no effect and harm)</p>	<p>Based on 6576 participants 2233 people with >=1 fall, 3 trials ⊕⊕⊕⊖ moderate From Gillespie 2012, only in community, risk of bias limitation.</p>		<p>Overall risk 300 people per 1000</p> <p>High risk 500 people per 1000</p>

Outcomes	Effects and Quality of the Evidence					
	Vitamin D without calcium		Vitamin D with calcium		Calcium	Placebo/no treatment
Quality of life EQ-5D (Scale: 0 to 1, optimal health) or SF12 2 years	No differences in quality of life.		No differences in quality of life.		No differences in quality of life.	
	Based on 5292 participants, 1 trial ⊕⊕⊕⊖ Moderate Risk of bias due to unclear reporting. From Grant 2005, Community only		Based on 5292 participants, 1 trial ⊕⊕⊕⊖ Moderate Risk of bias in data reporting. From Grant 2005 Community only		Based on 5292 participants, 1 trial ⊕⊕⊕⊖ Moderate Risk of bias in data reporting. From Grant 2005Community only	
Mortality	OR 0.90 (0.77 to 1.07)	Overall risk 7 fewer per 1000 (16 fewer to 5 more)	RR 0.94 (0.88 to 1.00)	Overall risk 4 fewer per 1000 (8 fewer to 0 more)	OR 1.07 (0.95 to 1.19)	Overall risk 5 more per 1000 (4 fewer to 13 more)
		High risk 12 fewer per 1000 (28 fewer to 8 more)		High risk 7 fewer per 1000 (14 fewer to 0 more)		High risk 8 more per 1000 (6 fewer to 23 more)
	Based on 2686 participants with 471 deaths, 1 trial ⊕⊕⊕⊖ moderate From Avenell 2009 (community) some imprecision few events (including benefit and no effect)		Based on 48284 participants with 3086 deaths, 8 trials ⊕⊕⊕⊖ moderate From Avenell 2009 (community) some risk of bias, and some imprecision (including benefit and no effect) consistent with Bolland 2011 community only (RR 1.01, 0.90 to 1.12)		Based on 10410 participants with 1076 deaths, 8 trials ⊕⊕⊕⊖ moderate From Bolland 2010 community only imprecise Benefits and Harm	
Myocardial infarction	RR 1.02 (0.93 to 1.13)	2 more per 1000 (8 fewer to 14 more)	RR 1.21 (1.01 to 1.44)	23 more per 1000 (1 to 48 more)	RR 1.27 (1.01 to 1.59)	30 more per 1000 (1 to 65 more)
	Based on 39 879 participants, 6 trials ⊕⊕⊕⊖ moderate Risk of bias, community only in Elamin 2011—some include calcium in both groups; inconsistent with mortality; dosages at 1000 mg calcium or more		Based on 20 090 participants, 3 trials ⊕⊕⊕⊖ moderate Risk of bias; community only in Bolland 2011—most not taking calcium before; inconsistent with mortality; dosages at 1000 mg calcium or more		10210 participants, 6 trials ⊕⊕⊕⊖ moderate Risk of bias; and some imprecision (including no effect and harms)community only in Bolland 2010—some studies with vitamin D; inconsistent with mortality; dosages at 1000 mg calcium or more	
Renal disease (calculi or insufficiency)	OR 0.66 (0.03 to 16.20)	Overall risk 1 fewer per 1000 (4 fewer to 60 more)	OR 1.16 (1.02 to 1.33)	Overall risk 1 more per 1000 (0 to 1 more)	No difference	0 more per 1000
		High risk 7 fewer per 1000 (19 fewer to 300 more)		High risk 3 more per 1000 (0 to 7 more)		High risk 20 renal diseases per 1000

<p>Based on 393 participants, 1 trial ⊕⊕⊖⊖ low From Avenell 2009 Risk of bias, community; Imprecise – very few events</p>	<p>Based on 41574 participants, 3 trials ⊕⊕⊕⊖ moderate From Avenell 2009, community only in analysis;</p>	<p>Based on 2643 and 1471 participants, 2 trials ⊕⊕⊖⊖ low Imprecise; community (Grant 2005 and Reid 2006)</p>
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Outcomes	Effects and Quality of the Evidence				Placebo/no treatment
	Vitamin D without calcium		Vitamin D with calcium		
Gastrointestinal events (mild or serious)	OR 1.04 (1.00 to 1.08)	7 more per 1000 (0 to 14 more)	OR 1.04 (1.00 to 1.08)	7 more per 1000 (0 to 14 more)	Participants reported more with calcium carbonate (1 g; includes Vitamin D) vs placebo; more constipation with calcium citrate (1 g) vs placebo 179 GI events per 1000
	Based on 42010 participants, 4 trials ⊕⊕⊖⊖ low From Avenell 2009, community, indirect data for VitD with Calcium		Based on 42010 participants with 7654 events, 4 trials ⊕⊕⊕⊕ high From Avenell 2009 Risk of bias, community;		
Hypercalcaemia	OR 0.39 (0.02 to 8.15)	5 fewer per 1000 (8 fewer to 55 more)	OR 1.7 (0.73 to 3.96)	2 more per 1000 (1 fewer to 8 more)	No difference 0 more per 1000 6 hypercalcaemia per 1000
	Based on 393 participants with 2 events, 1 trials ⊕⊖⊖⊖ Very low From Avenell 2009, community. Risk of bias; community Imprecise – very few events		Based on 5878 participants with 22 events, 4 trials ⊕⊖⊖⊖ Very low From Avenell 2009 community, Risk of bias;; Imprecise – very few events		

Evidence to recommendation framework 4

Question 4: Should exercise be recommended for prevention of fractures in the elderly living in the community?

Panelists in attendance: Drs. Hanan Al Rayes, Mona Fouda, Salwa Al Aidarous, Safia Sherbeeni, Mir Sadat, Riad Sulimani, Mohammad Al Shaker

Additional COI declared at the beginning of the meeting: None declared

Problem: Elderly in the community
Option: Exercise to prevent fractures
Comparison: No exercise
Setting: Community
Perspective: Health care system

Background: The question addressed in the systematic reviews used for the 2014 Osteoporosis Canada guideline addressed exercise for prevention of fractures in the elderly living in long term care facilities. The adapted guideline addresses this question in the elderly living in the community in Saudi Arabia.

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS																							
<p>PROBLEM</p> <p>Is the problem a priority?</p>	<p>No Probably No Uncertain Probably Yes Yes <i>Varies</i></p> <p><input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/></p>	<table border="1"> <thead> <tr> <th rowspan="2">Outcome</th> <th colspan="3">Assumed Baseline Risks</th> </tr> <tr> <th>Overall risk in the community</th> <th>High risk in the community</th> <th>Elderly living in the community in Saudi Arabia</th> </tr> </thead> <tbody> <tr> <td>Vertebral fractures</td> <td>10 per 1000</td> <td>200 per 1000</td> <td>203 per 1000</td> </tr> <tr> <td>Overall fractures</td> <td>109 per 1000</td> <td>310 per 1000</td> <td>n/a</td> </tr> <tr> <td>Number of falls (per year)</td> <td>1000 per 1000</td> <td>3000 per 1000</td> <td>n/a</td> </tr> <tr> <td>Number of people who fell at least once per year</td> <td>300 per 1000</td> <td>500 per 1000</td> <td>n/a</td> </tr> </tbody> </table>	Outcome	Assumed Baseline Risks			Overall risk in the community	High risk in the community	Elderly living in the community in Saudi Arabia	Vertebral fractures	10 per 1000	200 per 1000	203 per 1000	Overall fractures	109 per 1000	310 per 1000	n/a	Number of falls (per year)	1000 per 1000	3000 per 1000	n/a	Number of people who fell at least once per year	300 per 1000	500 per 1000	n/a	<p>The KSA guideline panel identified the problem as a priority. However there is an absence of current local data about the incidence of fractures and the associated morbidity and mortality in the elderly population in Saudi Arabia.</p>
Outcome	Assumed Baseline Risks																									
	Overall risk in the community	High risk in the community	Elderly living in the community in Saudi Arabia																							
Vertebral fractures	10 per 1000	200 per 1000	203 per 1000																							
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	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS																									
BENEFITS & HARMS OF THE OPTIONS	What is the overall certainty of this evidence?	<table border="0"> <tr> <td>No included studies</td> <td>Very low</td> <td>Low</td> <td>Moderate</td> <td>High</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No included studies	Very low	Low	Moderate	High	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>The relative importance or value of the main outcomes of interest:</p> <table border="1"> <thead> <tr> <th>Outcome</th> <th>Relative importance</th> <th>Certainty of the evidence</th> </tr> </thead> <tbody> <tr> <td>Vertebral fractures</td> <td>Critical</td> <td>Low</td> </tr> <tr> <td>Overall fractures</td> <td>Critical</td> <td>Low</td> </tr> <tr> <td>Number of falls per person per year</td> <td>Important</td> <td>Moderate</td> </tr> <tr> <td>Number of person who fall at least once in one year</td> <td>Important</td> <td>Moderate</td> </tr> </tbody> </table> <p>Summary of the evidence for patients' values and preferences: The panel considered that:</p> <ul style="list-style-type: none"> High value is placed on avoiding hip fractures and falls which may result in serious injury, as well as fear of falling. <p>Summary of findings: Please see Summary of Findings table.</p>	Outcome	Relative importance	Certainty of the evidence	Vertebral fractures	Critical	Low	Overall fractures	Critical	Low	Number of falls per person per year	Important	Moderate	Number of person who fall at least once in one year	Important	Moderate	<p>The KSA guideline panel considered that patients value and understand the importance of exercise, but with possible variability geographically in Saudi Arabia with respect to how exercise is viewed by the elderly at risk of fractures. Patients also assign a high value on preventing fractures.</p> <p>There was no data available about undesirable effects of exercise for the elderly, and the panel considered that there are no perceived significant harms of exercise for this population.</p>
	No included studies	Very low	Low	Moderate	High																								
	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																								
	Outcome	Relative importance	Certainty of the evidence																										
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Number of person who fall at least once in one year	Important	Moderate																											
Is there important uncertainty about how much people value the main outcomes?	<table border="0"> <tr> <td>Important uncertainty or variability</td> <td>Possibly important uncertainty or variability</td> <td>Probably no important uncertainty or variability</td> <td>No important uncertainty or variability</td> <td>No known undesirable outcomes</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability	No known undesirable outcomes	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																		
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Are the desirable anticipated effects large?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																
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CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS
effects?			

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS
RESOURCE USE	Are the resources required small?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input checked="" type="checkbox"/> Yes <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/>	No evidence identified	The panel considered that exercises done individually at home would not require many resources, but noted that a substantive percentage of women who would not be able to afford exercise programs that required high use of resources.
	Is the incremental cost small relative to the net benefits?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input checked="" type="checkbox"/> Yes <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/>	No evidence identified	
EQUITY	What would be the impact on health inequities?	Increased <input type="checkbox"/> Probably increased <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably reduced <input checked="" type="checkbox"/> Reduced <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/>	No evidence identified	The panel considered that offering an effective and low-cost intervention that would benefit those who are disadvantaged would probably reduce health inequities.

Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings <input type="checkbox"/>	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings <input type="checkbox"/>	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> <input type="checkbox"/>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings <input checked="" type="checkbox"/>	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings <input type="checkbox"/>
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	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	KSA GUIDELINE PANEL CONSIDERATIONS												
ACCEPTABILITY	Is the option acceptable to key stakeholders?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	No evidence identified	The panel considered the option acceptable to healthcare providers and policy makers, and that most carers and family members would accept exercise for elderly and provide support.
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
FEASIBILITY	Is the option feasible to implement?	<table border="0"> <tr> <td>No</td> <td>Probably No</td> <td>Uncertain</td> <td>Probably Yes</td> <td>Yes</td> <td>Varies</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	No evidence identified	The panel considered that recommending exercise was feasible to implement from a policy-making perspective.
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											

Type of recommendation	We recommend against offering this option <input type="checkbox"/>	We suggest not offering this option <input type="checkbox"/>	We suggest offering this option <input checked="" type="checkbox"/>	We recommend offering this option <input type="checkbox"/>
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Recommendation (text) For fracture and/or fall prevention in the elderly living in the community, the KSA MoH guideline panel suggests individual exercise performed at home. (conditional recommendation; low quality evidence)

Justification The recommendation is conditional due to low quality evidence.

Subgroup considerations -

Implementation considerations

Creation of public spaces for observed exercise.
Creation of safe walking spaces
Promotion from the Ministry of Health for exercise as an intervention to improve bone health.

Monitoring and evaluation

Monitor and evaluate uptake of the recommendation.

Research priorities

Research about the acceptability of exercise by the elderly living in the community in Saudi Arabia.



Summary of Findings Table: Exercise

Author(s): Itziar Etxeandia & Wojtek Wiercioch

Date: 2013-11-28

Bibliography: Gillespie LD, 2012; Kemmler W, 2013

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference Exercise versus control or placebo (95% CI)
Vertebral Fractures	205 (3 studies)	⊕⊕⊖⊖ LOW due to risk of bias, inconsistency and imprecision with low sample size From Kemmler 2013	RR 0.56 (0.30 to 1.04)	Study population (High Risk)	
				200 per 1000	88 fewer per 1000 (from 140 fewer to 8 more)
				Overall Risk	
				10 per 1000	4 fewer per 1000 (from 7 fewer to 0 more)
Overall Fractures	1424 (10 studies)	⊕⊕⊖⊖ LOW some inconsistency and imprecision for few events and risk of bias From Kemmler 2013. Slightly greater effect in Gillespie 2012 [RR 0.34 (0.18 to 0.63), 810 participants 6 studies)	RR 0.49 (0.31 to 0.76)	Study population	
				109 per 1000	56 fewer per 1000 (from 26 to 75 fewer)
				High Risk	
				310 per 1000	158 fewer per 1000 (from 74 to 214 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference Exercise versus control or placebo (95% CI)
Rate of falls Number of falls per person per year	951 (7)	⊕⊕⊕⊖ MODERATE due to risk of bias From Gillespie 2013	Rate Ratio 0.68 (0.58 to 0.8)	Individual exercise at home: Multiple categories of exercise vs control	
				Overall Risk 1000 falls per 1000 people per year	320 fewer per 1000 (from 200 fewer to 420 fewer)
				High Risk 3000 per 1000 people per year	960 fewer per 1000 (from 600 fewer to 1000 fewer)
				Individual exercise: LiFE program (balance and strength training in daily life activities) vs control	
	34 (1)	⊕⊖⊖⊖ VERY LOW due to risk of bias and imprecision From Gillespie 2013	Rate Ratio 0.21 (0.06 to 0.71)	1000 per 1000	790 fewer per 1000 (from 290 fewer to 940 fewer)
	128 (1)	⊕⊖⊖⊖ VERY LOW imprecision low sample size From Gillespie 2013	Rate Ratio 1.19 (0.77 to 1.82)	Individual exercise: Balance training vs control	
				1000 per 1000	19 more per 1000 (from 23 fewer to 82 more)
	222 (1)	⊕⊖⊖⊖ VERY LOW due to risk of bias, imprecision From Gillespie 2013	Rate Ratio 0.95 (0.77 to 1.18)	Individual exercise at home: Resistance training vs control	
				1000 per 1000	50 fewer per 1000 (from 230 fewer to 180 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference Exercise versus control or placebo (95% CI)
At least one fall per year	714 (6)	⊕⊕⊕⊖ MODERATE due to risk of bias From Gillespie 2013	RR 0.78 (0.64 to 0.94)	Individual exercise at home: Multiple categories of exercise vs control	
				Overall Risk 300 per 1000	66 fewer per 1000 (from 18 fewer to 108 fewer)
				High Risk 500 per 1000	110 fewer per 1000 (from 30 fewer to 180 fewer)
				Individual exercise: LiFE program (balance and strength training in daily life activities) vs control	
	31 (1)	⊕⊖⊖⊖ VERY LOW due to risk of bias and imprecision From Gillespie 2013	RR 0.73 (0.39 to 1.37)	300 per 1000	81 fewer per 1000 (from 183 fewer to 111 more)
	222 (1)	⊕⊖⊖⊖ VERY LOW due to risk of bias and imprecision From Gillespie 2013	RR 0.97 (0.68 to 1.38)	Individual exercise at home: Resistance training vs control	
				300 per 1000	9 fewer per 1000 (from 96 fewer to 114 more)
	196 (1)	⊕⊖⊖⊖ VERY LOW due to risk of bias and imprecision From Gillespie 2013	RR 0.82 (0.53 to 1.26)	Individual exercise: General physical activity (e.g. walking) vs control	
				300 per 1000	54 fewer per 1000 (from 141 fewer to 78 more)

Appendix 2: Search Strategies and Results

Questions 1-3: Should vitamin D and/or calcium supplementation be recommended for prevention of fractures in the elderly living in the community?

Database: Cochrane Library - Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Technology Assessments, Economic Evaluations and Cochrane Groups	
Search strategy:	Date of search: 30/10/2013
<ol style="list-style-type: none"> 1. MeSH descriptor: [Vitamin D] explode all trees 2. (vitamin?d) or dihydrotachysterol or calcitriol or cholecalciferol or alfacalcidol or alphacalcidol or colecalciferol or ergocalciferol or hydroxyvitamin 3. MeSH descriptor: [Calcium] explode all trees 4. Calcium or Calciu* 5. #1 or #2 or #3 or #4 6. MeSH descriptor: [Fractures, Bone] explode all trees 7. fracture or "bone fractur*" or fractu* or "Fragility" 8. #6 or #7 9. #5 and #8 from 2012 to 2013, in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials and Technology Assessments <p>Date limit: 01/2012 - 12/2013</p> <p>Study Types: Systematic Reviews and Meta-Analyses</p>	
Records Retrieved	104 (73 Cochrane Reviews, 4 Other Reviews, 25 Trials, 2 Technology Assessments)

Data base: Medline	
Search strategy:	Date of search: 04/11/2013
<ol style="list-style-type: none"> 1. Vitamin D/ or Calcium/ or Vitamin D Deficiency/ 2. (Vitamin D or Calcium or Vitamin D Deficiency).mp 3. (vitamin?d or dihydrotachysterol or calcitriol or cholecalciferol or alfacalcidol or alphacalcidol or colecalciferol or ergocalciferol or hydroxyvitamin).mp 4. (Calcium or Calciu\$).mp 5. 1 or 2 or 3 or 4 6. limit 5 to yr="2012 -Current" 7. limit 12 to "reviews (maximizes sensitivity)" <p>Date limit: 01/2012 - 11/2013</p> <p>Study Types: Systematic Reviews and Meta-Analyses</p>	
Records Retrieved	156

Data base: Embase	
Search strategy:	Date of search: 04/11/2013
<ol style="list-style-type: none"> 1. colecalciferol/ or vitamin D/ 2. (colecalciferol or vitamin D).mp 3. (vitamin?d or dihydrotachysterol or calcitriol or cholecalciferol or alfacalcidol or alphacalcidol or colecalciferol or ergocalciferol or hydroxyvitamin).mp 4. 1 or 2 or 3 5. calcium/ 6. 1 or 2 or 3 or 4 or 5 or 6 	

7. fracture/
8. Fractures, Bone.mp
9. (fracture or fractur\$ or "bone fractur\$" or fractu* or Fragility or fragi\$).mp
10. 8 or 9 or 10
11. 7 and 11
12. limit 12 to (embase and "reviews (maximizes sensitivity)" and yr="2012 -Current")
13. limit 13 to (embase and "reviews (maximizes specificity)" and yr="2012 -Current")
Date limit: 01/2012 - 11/2013
Study Types: Systematic Reviews and Meta-Analyses
Records Retrieved 50

Summary of Searches

Total No. Retrieved:	310
Cochrane Library:	104
Medline:	156
Embase:	50
Duplicates:	0
No. Total without duplicates:	310
Screening (Title and Abstract Review)	
No. Excluded:	301
Included for Full Text review:	9
Selection (Full Text Review)	
No. Excluded:	8
Reasons for exclusions:	
1. Included in original guideline (4)	
2. Full-text not available (2)	
3. Conference abstract (1)	
4. Narrative review (1)	

Question 4: Should exercise be recommended for prevention of fractures in the elderly living in the community?

Database: Cochrane Library - Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Technology Assessments, Economic Evaluations and Cochrane Groups	
Search strategy:	Date of search: 30/10/2013
<ol style="list-style-type: none"> 1. MeSH descriptor: [Exercise] explode all trees 2. Exercis* or exercise 3. MeSH descriptor: [Environment Design] explode all trees 4. "Environment Design" or "Environm* Desig*" 5. MeSH descriptor: [Patient Education as Topic] explode all trees 6. "Patient Education" or "Patient* Educati*" or Educatio* 7. MeSH descriptor: [Combined Modality Therapy] explode all trees 8. "multimodal intervention*" or "multifactorial interventio*" or "multifa* treatment" or "multifa*" 	

<p>interventio*"</p> <ol style="list-style-type: none"> 9. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 10. MeSH descriptor: [Fractures, Bone] explode all trees 11. fracture or "bone fractur*" or fractu* or "Fragility" 12. MeSH descriptor: [Accidental Falls] explode all trees 13. fall* 14. #10 or #11 or #12 15. #9 and #14 from 2012 to 2013, in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Technology Assessments, Economic Evaluations and Cochrane Groups <p>Date limit: 01/2012 - 11/2013</p> <p>Study Types: Systematic Reviews and Meta-Analyses</p>	
Records Retrieved	218 (148 Cochrane Reviews, 19 Other Reviews, 45 Trials, 6 Economic Evaluations)

Database: Pubmed	
Search strategy:	Date of search: 30/10/2013
<ol style="list-style-type: none"> 1. "Search (((("exercise"[MeSH Terms]) OR Exercis*) OR "patient education as topic/education") OR ("Patient Education" or "Patient* Educati*" or Educatio*))" 2. "Search (((("fractures, bone") OR (fracture or "bone fractur*" or fractu* or "Fragility" or "Fragil*")) OR ("accidental falls/prevention and control" OR "accidental falls prevention and control")))" 3. "Search (#1 and #2)" 4. "Search (#3) AND ("2012"[Date - Publication] : "2013"[Date - Publication])" 5. "Search ("Cochrane Database Syst Rev" or search* or meta-analysis or "systematic review")" 6. "Search (#4 and #5)" <p>Date limit: 01/2012 - 11/2013</p> <p>Study Types: Systematic Reviews and Meta-Analyses</p>	
Records Retrieved	92

Database: Embase	
Search strategy:	Date of search: 30/10/2013
<ol style="list-style-type: none"> 1. exercise/ 2. patient education/ 3. (Exercis* or "patient education " or "Patien* adj Educati*" or "Patient* Educati*" or Educatio*).mp 4. 1 or 2 or 3 5. fracture/ 6. falling/ 7. ("fractures, bone" or fracture or "bone fractur*" or fractu* or "Fragility" or "Fragil*" or ("accidental falls/prevention and control" or "accidental falls prevention and control")).mp 8. 5 or 6 or 7 9. ("Cochrane Database Syst Rev" or search* or meta-analysis or "systematic review").mp 10. 8 and 9 11. limit 10 to yr="2012 -Current" 12. exercise/ or Exercis*.mp 13. 8 and 9 and 11 and 12 <p>Date limit: 01/2012 - 11/2013</p> <p>Study Types: Systematic Reviews and Meta-Analyses</p>	
Records Retrieved	91

Summary of Searches

Total No. Retrieved:	401
Cochrane Library:	218
Pubmed:	92
Embase:	91
Duplicates:	23
No. Total without duplicates:	378
Screening (Title and Abstract Review)	
No. Excluded:	369
Included for Full Text review:	10
Selection (Full Text Review)	
No. Excluded:	9
Reasons for exclusions:	
<ol style="list-style-type: none"> 1. Included in original guideline (7) 2. Studies specific to interventions in long-term care facilities and hospitals (2) 	

Appendix 3: Table of Baseline Risks

Outcome	Baseline risk	References and Notes
Overall risk of hip fracture	11/1000	<u>Avenell 2009</u> studies in community only: - Vit-D group: *low risk: (without previous fracture): 1.6% *medium risk: (with or without previous fracture): 1.8% * high risk: (with previous fracture): 3% - Vit-D & Ca group: *low risk: (without previous fracture): 1.1% *medium risk: (with or without previous fracture): 1.2% *high risk: (with previous fracture): 1.8%
High risk of hip fracture	30/1000	<u>Pap 2005</u> : mainly non vertebral fractures: 163/5143/3y*1000= 10.56/1000 <u>Crilly 2010</u> : The risk of hip fracture is 1.8 times greater in LTC than in the community for people of similar age and gender.
Risk of hip fracture in elderly living in the community in Saudi Arabia	6/1000	Bubshait D, Sadat-Ali M. Economic implications of osteoporosis-related femoral fractures in Saudi Arabian society. Calcif Tissue Int. 2007;81:455–458.
Overall risk of vertebral fracture	10/1000	<u>Kanis 2004</u> (80+ years, community setting, clinical and morphometric vertebral fractures)
High risk of vertebral fracture	200/1000	<u>Avenell 2009</u> studies in community only: - Vit-D group: *low risk: (without previous fracture): 0.07% *medium risk: (with or without previous fracture): 1.5% * high risk: (with previous fracture): 2.7% - Vit-D & Ca group: *low risk: (without previous fracture): 0.07% *medium risk: (with or without previous fracture): 1.0% *high risk: (with previous fracture): 1.08% <u>Lindsay 2001</u> (mean age 74 years, with fracture in previous year): 200/1000
Risk of vertebral fracture in elderly living in the community in Saudi Arabia	203/1000	Sadat-Ali M et al. (2009) Osteoporosis-related vertebral fractures in postmenopausal women: prevalence in a Saudi Arabian sample. EMHJ 15: 1420-1425: Saudi women over the age of 50 years visiting the emergency room at King Fahd Hospital of the University
Overall risk of non-vertebral fracture (not including hip)	30/1000	<u>Ioannidis 2013</u> Non-spine, non-hip fractures (n=1,654) 1,654 / 51,491= 32/1000
High risk of non-vertebral fracture (not including hip)	80/1000	<u>Chen 2009</u> : 200/5 years= 40 per year 40-10 hip fractures= 30/1000 <u>Avenell 2009</u> studies in community only: -Vit-D group: n/a - Vit-D & Ca group: *low risk: (without previous fracture): 8.2% *medium risk: (with or without previous fracture):10.4% *high risk: (with previous fracture): 10.8% 108- 30 hip fractures= 80/1000
Overall risk of falls per person per year	1000 falls per 1000 people year	<u>Gillespie 2012</u> Latham 2003 study (hospital): placebo fall rate 0.99 per person-year

High risk of falls per person per year	3000 falls per 1000 people year	Sanders 2010 study (community women): placebo fall rate 0.727 per person-year Bischoff-Ferrari 2006 (community): reported "at least 1 fall" per person Karkkainen 2010 (community): annualized rate not reported; 1944 falls in 1573 women during study period Porthouse 2005 (community): n/a Dhesi 2004 (community): 24 falls in 14 patients (no annualized data) <u>Kerse 2004</u> : 2.6 falls [0.7 SD] <u>Rapp 2012</u> : 2.8 falls in men and 1.49 falls in women
Overall risk of at least 1 fall per year	300 /1000	<u>Gillespie 2012</u> - Vit D group: 286 people per 1000
High risk of at least 1 fall per year	500/1000	- Vit D & Ca group: 320 people per 1000 <u>Muir 2012</u> review and <u>Beauchet 2011</u> review of prospective/retrospective studies show rates at 12 months of 29%, 52%, 52%, 64% and 36%, 47%, 60%, 41%, 45%, 29%, respectively. Note: includes injurious and non-injurious falls
Overall risk of mortality	70 deaths per 1000	<u>Avenell 2009</u> : - Vit D & Ca group: 68 deaths per 1000 - Ca group: 102 deaths per 1000 - Vit D group: 184 deaths per 1000
High risk of mortality	120/1000 deaths per 1000	<u>Nikitovic 2012</u> (80+ years): range from 7 to 18%; community index 6% <u>Nikitovic 2012</u> (80+ years), range from 7 to 18%; Long term care index 23%
Gastrointestinal events: mild or serious	200/1000	<u>Avenell 2009</u> (community)
Hypercalcaemia	6/1000	<u>Avenell 2009</u> (community)
Overall risk of renal disease (calculi or insufficiency)	4/1000	<u>Avenell 2009</u> (community) Vit D group: 3.8 with renal disease per 1000 Vit D & Ca group: 19 with renal disease per 1000
High risk of renal disease (calculi or insufficiency)	20/1000	
Quality of life	0.7 EQ-5D	Grant 2005 (community)
Myocardial infarction	110/1000	Aronow 2002 (long term care residents)

Appendix 4: Summary of Characteristics of Included Studies

Summary of systematic reviews and studies assessing vitamin D and calcium supplementation:

STUDY	SETTING	PATIENTS	INTERVENTION	COMPARATOR	OUTCOMES
Murad 2012 SR-Network-MA	Mostly community	Trials that enrolled patients with established or at risk for osteoporosis; 139,647 patients with a median age of 64 yr; 86% were females and 88% Caucasians. The median length of follow-up was 24 months.	All doses Pharmacological and VitD and Ca		fragility fractures (vertebral, hip, and nonvertebral fractures)
Gillespie 2012 SR-MA	Community 21 countries (mostly occidental Europe-America)	>= 60 years Overall, women 70% of included participants. All participants were women in 37 trials, and men in two trials. 83 included studies specified a history of falling or evidence of one or more risk factors for falling. Lower serum vitaminD (i.e. vitaminD insufficiency or deficiency) was an inclusion criterion in four trials of vitamin D supplementation. Seven trials recruited older people who had recently sustained a hip fracture or fall-related fracture. Fourteen other trials recruited on the basis of a specific condition.	Preventive interventions: Exercise, multifactorial, Vitamin D with or without Calcium	Placebo, control or Calcium	- rate of falls - risk of falling (number of fallers) - fall-related fractures (hip, wrist, humerus, etc)
Bishop 2012 SR-MA	Mostly Community -dwelling	42279 individuals with a mean age of 78 years, and 89% were women. Treatment duration varied from 12 to 84 months	Vitamin D with/without Calcium Received dose of vitamin D was 400 IU/d or less in 3 trials, whereas the other 9 RCTs had mean intake of 482 to 770 IU/d.	Placebo or Calcium A total of 500 to 1200 mg/d of calcium supplementation	- first or repeated nonvertebral fracture - hip fracture
Avenell 2009 SR-MA	Community and residential units and home for older people (subgroup analysis)	Men over 65 year and postmenopausal women	Vitamin D and analogues with or without Calcium	Placebo or calcium	- hip fracture - nonvertebral fracture - vertebral fracture - adverse effects

Summary of systematic reviews assessing exercise:

STUDY	SETTING	PATIENTS	INTERVENTION	COMPARATOR	OUTCOMES
Gillespie 2012 SR-MA	Community 21 countries (mostly Europe, America)	>= 60 years Overall, women 70% of included participants. All participants were women in 37 trials, and men in two trials. 83 included studies specified a history of falling or evidence of one or more risk factors for falling. Lower serum vitaminD (i.e. vitaminD insufficiency or deficiency) was an inclusion criterion in four trials of vitamin D supplementation. Seven trials recruited older people who had recently sustained a hip fracture or fall-related fracture. Fourteen other trials recruited on the basis of a specific condition.	Home: multiple categories of exercise balance and strength training in daily life activities resistance training general physical activity (walking)	Usual care No intervention	- rate of falls - risk of falling (number of fallers) - fall-related fractures (hip, wrist, humerus, etc)
Kemmler W, 2013 SR-MA	Community in 9/10 RCT	Mainly postmenopausal women but also 2 studies with men, half of studies with >65 years, the others >45. Mainly Caucasian and one Chinese study.	Home based in half of studies and centre-based in other half. Endurance, resistance training: Balance Flexibility Jumping General coordination Range of 6 months to 10 years	Usual care No intervention to improve bone strength and decrease falls	-vertebral fractures -overall fractures

From Kemmler et al., 2013:

Table 1 Study characteristics with special regard to the exercise protocol

Author, year	Focus of the intervention	Exercise type in the EG/supplementation	Study length	Setting of the intervention	Exercise frequency (attendance rate)	Intervention score	Intervention CG
Ashburn, 2007	Fall Reduction	E, RT, B, F	6 months	Home-based	Daily (length?) (n.g.)	Low	"Usual care" (mainly contact with nurse)
Chan, 2004	Bone Strength	Tai Chi (Yang-Style)	12 months	Center-based	5×45 min/w. (84 %)	Low	No intervention
Ebrahim, 1997	Bone Strength and Fall Reduction	Walking	24 months	Home-based	3×40 min/w. (100 %)	Moderate	Exercises for the upper limb; study nurse-visits
Karinkanta, 2007	Bone Strength and Physical Functioning	RT vs. B, J vs. R,B,J.	12 months	Center-based	3×40-50 min/w. (67 %)	High	No physical intervention
Kemmler, 2010	Bone Strength and Fall Reduction	E, RT, B, GC Calcium/Vit-D	18 months	Center-based/ home-based	2×60 min/w. (76 %) ¹ 2×25 min/w. (42 %) ²	High	No physical intervention, Ca/ Vit-D supplementation
Kemmler, 2012	Bone Strength	E, RT, J. Calcium/Vit-D	12 years	Center-based/ home-based	2×60 min/w. (72 %) ¹ 2×25 min/w. (35 %) ²	High	Exercising "Wellness-CG"; Ca/Vit-D supplementation
Korpelainen, 2006	Bone Strength	E, B, RT, J	30 months	Predominantly home-based	1×60 min/w. for 6 months/year (75 %) ¹ 7×20 min/w. (43 %) ²	Moderate	No physical intervention Social interaction
McMunlo, 1997	Bone Strength and Fall Reduction	E, RT Calcium	24 months	Center-based	3×45 min/w. for 3×10 w./year (76 %)	Low	No physical intervention Calcium supplementation
Preisinger, 1996 ³	Bone Strength and Back Pain	RT, B, F, GC	48 months	Predominantly home-based	≥3×20 min/w. (100 %)	Moderate	No intervention
Robertson, 2001	Fall Reduction	E, RT, B, GC	12 months	Home-based	≥3×30 min/w. (n.g) ⁴ ≥2× walking/w. (71 %)	High	"Usual care" (study nurse visits)
Simaki, 2002	Bone Strength	RT (BE)	10 years	Home-based (first 2 years)	5×10 reps/w. (n.g.)	High	No intervention

E endurance, RT resistance training, B balance, F flexibility, J jumping, GC general coordination, n.g. not given, min/w: minutes per week

¹ Joint exercise session

² Home exercise program

³ A corresponding study of the authors [47] with the same cohort and comparable results was not given here

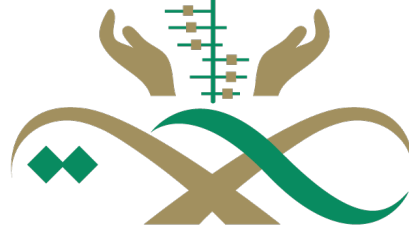
⁴ Forty-three percent of the participants underwent three and more sessions per week, 72 % carried out at least two sessions per week

From Gillespie et al., 2012:

Appendix 6. Categories of exercise (ProFaNE) in interventions containing exercise alone

Study ID	Gait/balance/ functional training	Strength/ resistance training	Flexibility	3D (Tai Chi, dance etc)	Gen- eral physical activity	Endurance	Other
Bischoff- Ferrari 2010	***** extended physiotherapy groups ^b	***** extended physiotherapy groups					
Campbell 1997	*****	*****	*****		*****		
Campbell 1999	*****	*****	*****		*****		
Clemson 2010	***** embedded in daily activities	***** embedded in daily activities					
Haines 2009	*****	*****		***** (dynamic slow movement similar to Tai Chi)			

Kamide 2009	*****	*****	*****				
Kemmler 2010	***** high-intensity group low-intensity group	***** high-intensity group low-intensity group	***** high-intensity group low-intensity group	***** high-intensity group (dance) low-intensity group (dance)		***** high-intensity group low-intensity group	
Korpelainen 2006	*****			***** (dance)			***** (stamping)
Latham 2003		*****					
Lin 2007	*****	*****	*****				
Liu-Ambrose 2008	*****	*****	*****		*****		
McMurdo 1997	*****						
Pereira 1998					***** (walking)		
Robertson 2001a	*****	*****	*****		*****		
Smulders 2010	*****				***** (walking)	*****	***** (training in fall techniques, lifting techniques)
Wolf 1996	***** balance platform training group			***** Tai Chi group			



وزارة الصحة
Ministry of Health