Cost-effectiveness of quantitative ultrasound as a technique for screening of osteoporotic fracture risk: report on a health technology assessment conducted in 2001

Kosten-Effektivität der quantitativen Ultraschalluntersuchung im Rahmen der Osteoporoseversorgung (Früherkennung des Frakturrisikos): Bericht über einen 2001 durchgeführten ökonomischen HTA

Abstract

Aim: On behalf of the German Agency for Health Technology Assessment (DAHTA@DIMDI) a rapid economic HTA was conducted. Aim of the HTA was to evaluate the cost-effectiveness of quantitative ultrasound (QUS) for screening of osteoporotic fracture risk. Study population was formed by postmenopausal women. QUS was compared to the dual X-ray absorptiometry (DXA) as the most frequently used method of measurement.

Methods: According to the recommendations for rapid economic HTA a comprehensive literature search was conducted. Data of identified and relevant publications have been extracted in form of a qualitative and quantitative information synthesis. The authors calculated incremental cost-effectiveness ratios for different screening procedures: (1) one-step proceeding comparing QUS with DXA, (2) two-step proceeding starting with QUS followed by DXA in pathologic cases.

Results: An additional case diagnosed by DXA in a one-step proceeding rises additional costs of about 1,000 EURO. A two-step proceeding with QUS is cost-effective as long as the costs of one QUS examination are lower than 31%-51% of the costs of one DXA examination.

Discussion: All considered studies showed methodological limitations. None of them included long term effects like avoided bone fractures. Considering long-term effects probably would change the results. Due to the weakness of data no concluding judgement about the cost-effectiveness of QUS can be given.

Zusammenfassung

Zielsetzung: Im Auftrag des DAHTA@DIMDI wurde ein ökonomischer Kurz-HTA mit dem Ziel durchgeführt, die Kosten-Effektivität der quantitativen Ultraschalluntersuchung (QUS) für die Einschätzung des Frakturrisikos aufgrund von Osteoporose und konsekutiv zur Vermeidung von Frakturen zu bestimmen. Studienpopulation waren Frauen im postmenopausalen Alter, als Vergleichstechnologie wurde die duale X-ray Absorptiometrie (DXA) als am häufigsten angewandte Messmethode herangezogen.

Methoden: Nach den Vorgaben zur Durchführung ökonomischer Kurz-HTAs wurde eine ausführliche Literaturrecherche durchgeführt. Die Daten aus den identifizierten und als relevant befundenen Studien wurden in einer qualitativen und quantitativen Informationssynthese zusammengeführt. Aus den gewonnenen Daten konnten von den Autoren inkrementelle Kosten-Effektivitäts-Relationen für verschiedene Screening-Strategien berechnet werden: (1) Einsatz des QUS als alleinige Untersuchung im Vergleich zur DXA als alleinige Untersuchung (einstufiges Vorgehen), (2) zweistufiges Vorgehen mit QUS als erster Untersuchung und DXA bei pathologischen Befunden im QUS.
**Objective**

The German Agency for Health Technology Assessment (DAHTA) at the German Institute for Medical Documentation and Information (DIMDI) commissions research projects for Health Technology Assessment (HTA) based on the legal order to build up an information system for the evaluation of medical technology. The authors were engaged to conduct a rapid economic HTA to assess the cost-effectiveness of Quantitative Ultrasound (QUS) as a technique for screening the fracture risk due to osteoporosis and consecutive preventing fractures [1]. The rapid economic HTA was conducted according to the German methodological recommendations for health economic short HTA [2]. Information synthesis is based on a systematic literature search and subsequently on extracting cost data out of the identified literature. Osteoporosis is a disease that mainly concerns postmenopausal women and may increase fracture risk [3]. The risk for osteoporosis and fractures is age dependent. Nearly 50% of women in the age over 70 years show osteoporotic alterations [4]. Fractures due to osteoporosis cause costs, reduce quality of life and may lead to death. Main fracture localisations are found at the distal forearm, spine and femoral neck. The annual incidence rate of fractures of the femoral neck for women is about 291 per 100,000 inhabitants [5]. Factors associated with a increased risk for osteoporosis are age, postmenopause, smoking, lack of physical exercise, nutrition, low body weight, positive family history, alcohol abuse, and medication. The causal interdependence of the mentioned risk factors with the development of osteoporosis are partially not validated.

Osteoporosis can be treated (among others) by calcium and Vitamin D in combination with bisphosphonates and therapy with raloxifen [6], [7].

The diagnosis of osteoporosis covers clinical parameters and the measurement of bone mineral density (BMD). Several techniques for the determination of bone mineral density are described in the literature. The dual x-ray absorptiometry (further DXA) is at present the most frequently used method of measurement. Furthermore the peripheral quantitative computed tomography (pQCT) and the quantitative computed tomography (QCT) are of relevance. Increasingly the Quantitative Ultrasound (further QUS) is becoming important as it is an easily and quickly feasible technique [8], [9].

In Germany QUS examinations are not covered by the statutory health insurance fund and have to be financed out of pocket by the patients. Three main proceedings do exist: (1) DXA might be used as a screening technology alone, (2) QUS might be used as a screening technology alone, (3) two step strategy with QUS as a first step followed by DXA as a second step for women with a pathological QUS examination.

**Study Question**

Aim of the rapid health economic HTA was to evaluate the cost-effectiveness of different proceedings for the application of QUS compared to DXA as a technique for screening of osteoporotic fracture risk and subsequently for the prevention of osteoporotic fractures in postmenopausal women.

**Methods**

To assess the cost-effectiveness of QUS as a technique for screening of fracture risk due to osteoporosis a comprehensive literature search was performed in the medical and economical literature databases Medline, Embase and Econlit. Table 1 presents the used search strategy.

The HTA databases DARE (Database of Abstracts of Reviews of Effectiveness), NHS (Economic Evaluation Database), HTA (Health Technology Assessment) as well as the Cochrane library were searched for relevant HTA reports and reviews. Internet pages of 17 international HTA-institutions were visited and searched for references to relevant HTA-reports. No restrictions were made in respect to publication language and publication date. The literature search was performed in November 2001.

Following a data extraction, qualitative and quantitative information was consolidated in form of tables. Relevant qualitative characteristics have been author, year, country, type of evaluation and study population, quantitative characteristics have been the main medical effects and economic parameters.

In addition the authors calculated the incremental cost-effectiveness for the different proceedings: of a two-step proceeding compared to a one-step proceeding (DXA...
Table 1: Search strategy used for the literature search in Medline, Embase and Econlit

| step | search strategy |
|------|----------------|
| #1   | cost-allocation OR cost-savings OR cost-benefit-analysis OR cost-control OR cost-of-illness OR costs- and-cost-analysis |
| #2   | economics-hospital OR economics-medical OR economics-nursing OR economics-pharmaceutical OR economics- OR health-care-economics-and-organizations |
| #3   | #1 OR #2 |
| #4   | cost-of-illness OR cost- OR drug-cost OR health-care-cost OR hospital-cost OR cost-benefit-analysis OR cost-control OR cost-effectiveness-analysis OR cost-minimization-analysis OR cost-utility-analysis OR hospital-running-cost |
| #5   | economic-evaluation OR health-economics OR economics- pharmacoeconomics |
| #6   | #4 OR #5 OR #6 |
| #7   | cost* OR economic* |
| #8   | #3 OR #7 OR #8 |
| #9   | (QUS OR (quantitat* ultraso*)) AND (osteopo* OR (bone adj density)) |
| #10  | #9 AND #10 |

alone) as well as a comparison of the one step proceedings QUS alone vs. DXA alone.

The considered studies reported the costs of bone mineral density measurements in different currencies. A currency conversion to EURO was done according to the recommendations for german HTA reports [10] by the purchasing-power parities of the OECD.

Results

67 references of publications and projects were identified. 62 references were excluded, because of being a duplicat (number: 22), they did not deal with the costs of QUS or osteoporosis as a target diagnosis (number: 38), the results of the studies have not been available at the time of the literature search.

Four of the remaining five publications dealt with the question of the cost-effectiveness of QUS as a screening instrument in a two-step proceeding [11], [12], [13], [14].

One publication was the summary of a HTA report concerning the effectiveness of osteodensitometry and gave some information about costs of DXA and QUS. Costs have not been set in relation to the medical effects [15]. For this reason this study was not considered in the further calculations.

All five publications had limitations in regard to methods, especially in the consideration of relevant cost parameters. Just Langton et al. (1997 [12] and 1999 [13]) gave information about cost types included, namely obsolescence of device, personnel costs and costs due to transport. Due to methodological weaknesses of the studies the results can not be used without limitation.

Table 2 presents the main quantitative parameters of the four relevant studies.

One study was conducted in Switzerland [11], the remaining three in Great Britain. Study population of the study of Langton et al. (1997) have been women in the age of 60 to 69 years [12], of the study of Langton et al. (1999) women between the age of 50 to 54 years [13]. The remaining two studies had an age range from 50 to 80 years [14] and 44 to 80 years [11]. None of the studies reported the cost-effectiveness of a one-step proceeding with QUS compared to one-step DXA. However, data of the studies of Langton et al. (1997 [12] and 1999 [13]) and Sim et al. (2000) [14] allowed to calculate the cost-effectiveness of the two techniques in a one step proceeding. Results of this calculation are presented in Table 3. According to the studies of Langton et al. (1997) [12] and Sim et al. (2000) [14], approximately additional 1,000 EURO are necessary per additional identified case of osteoporosis diagnosed by one-step DXA compared to one-step QUS. The high costs resulting of the data of Langton et al. (1999) [13] are due to the low prevalence in younger women. It also has to be considered that QUS will rise more false positive cases that subsequently will get a costly treatment. These false positive cases will potentially be identified in a two-step proceeding with DXA as a second test.

The cost-effectiveness of a two-step proceeding compared to a one-step proceeding depends on the relation of costs of QUS to the costs of DXA. In all four studies a cut-off-point could be calculated, that tells under what level an examination with QUS in a two-step screening procedure is more cost-effective compared to a one-step proceeding with DXA. Depending on the considered study a two-step proceeding is cost-effective as long as the costs of one QUS examination lies between 31% and 51% of an examination with DXA.

Table 4 shows the calculations of a monetary cut-off point in a two-step proceeding.
Table 2: Quantitative parameters of the four relevant studies

|                        | Langton et al. (1997) [12] | Langton et al. (1999) [13] | Sim et al. (2000) [14] | Lippuner et al. (2000) [11] |
|------------------------|-----------------------------|-----------------------------|------------------------|-----------------------------|
| costs/DXA exam         | EUR 71                      | EUR 68                      | EUR 68                 | not stated                  |
| costs/QUS exam         | EUR 8                       | EUR 7                       | EUR 23                 | not stated                  |
| Sensitivity of QUS     | 73%                         | 73%                         | 93%                    | 90%                         |
| Specificity of QUS     | 81%                         | 73%                         | 84%                    | 64%                         |
| Positive predictive value of QUS | 56% \(^1\)     | 18.8%                      | 89% \(^1\)           | 52% \(^1\)               |
| Negative predictive value of QUS | 90% \(^1\)     | 97% \(^1\)                 | 89%                   | 94% \(^1\)               |

\(^1\) own calculations

Table 3: Calculation of the incremental cost-effectiveness ratio of one-step proceedings

|                                                      | Langton et al. (1997) [12] GB | Langton et al. (1999) [13] GB | Sim et al. (2000) [14] GB |
|------------------------------------------------------|-------------------------------|-------------------------------|--------------------------|
| costs/DXA exam                                       | EUR 71                        | EUR 68                        | EUR 68                   |
| costs/QUS exam                                       | EUR 8                         | EUR 7                         | EUR 23                   |
| Cost-effectiveness ratio one-step proceeding with QUS (per diagnosed case) | EUR 43                        | EUR 128                       | EUR 42                   |
| Cost-effectiveness ratio one-step proceeding with DXA (per diagnosed case) | EUR 292                       | EUR 867                       | EUR 116                  |
| Incremental cost-effectiveness ratio one-step proceeding QUS versus DXA (per additional diagnosed case) | EUR 969                       | EUR 2,868                     | EUR 1,043                |

GB = Great Britain

Table 4: Calculation of a monetary cut-off point in a two-step proceeding

|                                                      | Langton et al. (1997) [12] GB | Langton et al. (1999) [13] GB | Sim et al. (2000) [14] GB |
|------------------------------------------------------|-------------------------------|-------------------------------|--------------------------|
| Cost-effectiveness ratio two-step proceeding (QUS+DXA) per diagnosed case | EUR 169                       | EUR 491                       | EUR 118                  |
| Cost-effectiveness ratio DXA per diagnosed case      | EUR 292                       | EUR 867                       | EUR 116                  |
| Incremental cost-effectiveness ratio one-step versus two-step proceeding | EUR 623 Per additional diagnosed case of one-step proceeding | EUR 1,884 Per additional diagnosed case of one-step proceeding | EUR 91 Per additional diagnosed case of one-step proceeding |
| Cost-effectiveness per QUS examination for a price below a value of | EUR 30 \(^1\)                | EUR 29                        | EUR 21 \(^1\)           |
| Cut-off point in percentage                           | <42% \(^1\) of cost of one DXA examination | <42% \(^1\) of cost of one DXA examination | <31% \(^1\) of cost of one DXA examination | <51% of cost of one DXA examination |

GB = Great Britain, CH = Switzerland

\(^1\) own calculations
Discussion

A main limitation of the results is seen in the lack of explanatory power of the obtained study results in the context of the German health care system. So far screening for osteoporosis is not conducted in Germany by default of a valid screening instrument. It is to mention that the results of DXA and QUS examinations are hardly comparable. DXA measures bone density, but it is not proved which entity of bone is measured with QUS. Costs due to a QUS examination are not reimbursed by the statutory health insurance fund and have to be financed out of pocket by the patients. As no valid information was found in the literature concerning costs of a QUS or DXA examination in Germany we recommend to assess German cost data and perform adjusted calculations.

As pointed out above due to the methodological limitations the evidence of the studies is restricted decisively. Limitations are seen in the insufficiently performed description of quantities and prices for the calculation of costs. No study sufficiently discussed the own study results or potential limitations of the study. No study performed a sufficient sensitivity analysis.

The time horizon of considered studies was limited to the end point of diagnosis of osteoporosis. False positive results will lead to the application of an unnecessary and costly treatment, false negative will not reduce the fracture risk and associated costs. For this reason the long-term outcomes of a diagnosed case of osteoporosis in regard to fracture risk, avoided death and improvement of quality of life as much as the costs of a treatment of osteoporosis and treatment of fractures are of special interest. Because of the short time horizon none of the studies included these long time outcomes. Therefore the scientific evidence of the results of all considered studies is strongly limited. Decision analytic models that analyse long-term outcomes do exist in the literature [e.g. [16], [17]]. We strongly recommend to adopt decision analytic models to calculate the cost-effectiveness of QUS considering long-term effects.

Conclusions

Due to the weakness of data and the limited time horizon of all considered studies no concluding judgement about the cost-effectiveness of QUS as a first step of a two-step proceeding (QUS followed by DXA in case of a pathological result) or as a one-step proceeding (QUS alone) can be given.

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