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Cost-Effectiveness of Type 2 Diabetes Screening: Results from Recently Published Studies

*Kosten-Nutzen-Analyse des Screenings zum Typ-2-Diabetes:
Ergebnisse neuerer Studien*

Übersicht

Zusammenfassung

Typ-2-Diabetes-Screening wird von verschiedenen internationalen Diabetes-Fachgesellschaften empfohlen. Eine Literaturrecherche wurde durchgeführt, um publizierte Kosten-Nutzen-Analysen (CEA) zum Typ-2-Diabetes-Screening systematisch zu identifizieren und zu beschreiben. Drei Analysen wurden einbezogen. Eine Studie kommt aus Deutschland, basierend auf den Daten des KORA-Surveys S4 (1999/2001). Zwei Studien stammen aus den USA. Die deutsche und eine amerikanische Studie evaluierten Kosten pro entdecktem Fall als Hauptzielvariable. Im Gegensatz zu der amerikanischen Studie nahm die deutsche Studie in der Basisanalyse eine unvollständige Teilnahme an den Screeningprogrammen an. HbA1c-Test in Kombination mit dem oralen Glukose-Toleranztest (OGTT) war teurer als der OGTT oder die Nüchternblutbestimmung (fasting glucose testing), aber aufgrund einer hohen Teilnahme der Patienten an diesem Test auch am effektivsten in der Entdeckung von Fällen. Die zweite amerikanische Studie untersuchte die Lebenszeit-Cost-Effectiveness des Typ-2-Diabetes-Screenings basierend auf einem Markov-Modell und berechnete Kosten pro QALY. Daten zur Effektivität von Interventionen wurden zwei großen Interventionsstudien bei klinisch diagnostizierten (d.h. nicht mittels Screening identifizierten) Diabetespatienten entnommen. Die Autoren schlussfolgern, dass Typ-2-Diabetes-Screening kosteneffektiv ist, insbesondere ein gezieltes Screening bei älteren

Abstract

Type 2 diabetes screening is recommended by various international diabetes associations. We conducted a literature research to identify and describe systematically recently published cost effectiveness analyses (CEA) for type 2 diabetes screening. Three analyses were included. One of them was conducted in Germany, based on the data of the KORA survey S4 (1999/2001). Two studies came from the US. The German as well as one of the US studies evaluated cost per detected diabetic case as main outcome. In contrast to the US study, the German study considered incomplete participation in the screening programs as baseline case. HbA1c testing combined with the oral glucose tolerance test (OGTT) was more expensive than OGTT or fasting glucose testing, but also most effective in detecting cases, due to high participation in this screening strategy. The second US study investigated the lifetime cost effectiveness of type 2 diabetes screening, based on a Markov model to calculate cost per quality-adjusted life year (QALY). Effectiveness data were derived from two large intervention studies in clinically diagnosed (not identified by screening) diabetic subjects. The authors conclude that type 2 diabetes screening is cost effective, in particular targeted screening in elderly hypertensive subjects. Diabetes screening may be cost effective. However, the effectiveness of early detection and treatment of type 2 diabetes has not yet been shown, and data regarding the course of early detected diabetes are lacking so

note

The KORA study group consists of H.-E. Wichmann (speaker), H. Löwel, C. Meisinger, T. Illig, R. Holle, J. John and co-workers who are responsible for the design and conduct of the KORA studies.

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hypertensiven Personen. Diabetes-Screening ist potenziell kosteneffektiv. Jedoch wurde die Effektivität einer frühen Entdeckung und Behandlung des Typ-2-Diabetes bisher nicht nachgewiesen. Auch fehlen Daten zum Verlauf eines früh entdeckten Diabetes. Die wichtigste Frage für die Zukunft ist, ob Typ-2-Diabetes-Screening und die frühe Behandlung effektiv im Hinblick auf klinische Outcomes sind.

Schlüsselwörter

Cost-Effectiveness-Analyse · Strategien des Typ-2-Diabetes-mellitus-Screenings

far. In the future, the most important question is whether type 2 diabetes screening and early treatment is effective with respect to clinical outcomes.

Key words

Cost effectiveness analyses · screening strategies for undetected type 2 diabetes mellitus

Background

Undetected diabetes may be as prevalent as diagnosed type 2 diabetes [1, 2]. In a population-based study in Germany, the prevalence of known diabetes was 8.4% among 55 to 74 year old subjects, and 8.2% had previously undiagnosed diabetes mellitus [3].

There is a lack of data on the efficacy and effectiveness of type 2 diabetes screening with respect to reduced morbidity or mortality [4]. Nevertheless, the topic is widely discussed, in particular with reference to subjects aged 45 years or older [5–7]. Several screening strategies have been suggested, including fasting glucose, the oral glucose tolerance test (OGTT), or HbA1c testing, and preceding risk factor assessment to perform targeted screening [8–10].

Although there is a variety of recommendations that screening for type 2 diabetes should be implemented, there has been limited consideration of the economic aspects involved. A review, published in 2003 [11], identified only one cost effectiveness analysis for type 2 diabetes screening [12], which was based on type 1 diabetes data and therefore considered not to give valid estimates [13]. Aim of this article was to identify and describe recently published cost effectiveness analyses for type 2 diabetes screening by a Medline literature research.

Literature research for recently published studies

We undertook a Medline research reaching back to 1999. We chose this period since in a recent review [11], the only cost effectiveness analysis which was reported stems from 1998 [12]. According to the above mentioned review, search terms included “diabetes”, “economic”, “economic evaluation”, “cost effectiveness”, and “cost benefit”, further “cost utility”. We included cost effectiveness analyses for type 2 diabetes screening only (e. g. no cost of screening analyses or cost effectiveness of screening for late complications).

We identified six analyses. From these, two cost effectiveness analyses [14, 15] were based on type 1 diabetes data as the study identified by the previous review, which were considered not to give valid estimates [13]. Another paper [16] was a methodological work and not included.

The three remaining articles can be classified into two categories: two analyses evaluated cost per detected case [17, 18], and one

took a lifetime horizon and evaluated cost per quality adjusted life year (QALY) [13]. According to the previous review, we used a general format recommended by the UK National Health Service Economic Evaluation Database [19] to extract information from the identified studies. This format is well adapted to recommendations made in the “Methods for economic evaluations of health care programs” [20] and the checklist for health economic papers of the British medical journal [21] (Table 1).

Cost effectiveness analyses evaluating cost per detected diabetic case

Cost effectiveness analysis by Zhang et al. [17]

Primary aim of this analysis was to evaluate cost effectiveness of screening for impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) in the US population aged 45–74 years. The detection of undiagnosed diabetes was included as a “by-product” and not reported in detail. Zhang et al. analyzed cost, effectiveness, and cost per detected case. The time horizon was one year. Five detection strategies were assumed: 1.) oral glucose tolerance test alone (OGTT), 2.) fasting glucose test, 3.) HbA1c measurement (HbA1c), 4.) capillary blood glucose testing (CBG), and 5.) a risk assessment questionnaire, with a diagnostic fasting glucose or OGTT testing in cases when the tests 2.) to 5.) were above a defined threshold. Outcome measures were identified cases, cost, and cost per case identified (each strategy compared to no screening). Data was derived from the 2000 NHANES, census data, Medicare, and published literature. The analysis took into consideration the perspectives of a single-payer and of society.

Overall OGTT testing was the most effective strategy, but the CBG test and risk assessment questionnaire had lower cost per detected case. From the sensitivity analysis the authors conclude that the fasting glucose strategy would be the most effective if people were less willing to participate in the OGTT than in the fasting glucose testing (50% and 75% assumed). Using the fasting glucose testing combined with OGTT, 758 \$ per detected undiagnosed type 2 diabetic case from societal perspective was calculated. Further results of the separate type 2 diabetes screening were not presented.

Cost effectiveness study in Germany, based on the KORA S4 (S2000) survey data [18]

The aim of this study was to evaluate the cost-effectiveness of type 2 diabetes screening for several recommended strategies in

the age group 55–74 years. A decision analytic model was performed, covering a one year time horizon. The following screening strategies were analyzed: 1.) fasting glucose testing alone, 2.) oral glucose tolerance test (OGTT) following fasting glucose testing in subjects with impaired fasting glucose, 3.) OGTT alone, and 4.) HbA1c measurement with following OGTT, if HbA1c was >5.6%. These four strategies were considered as universal screening (screening all subjects) or as targeted screening. For the latter, a first-step pre-selection was assumed, identifying subjects with hypertension, elevated triglycerides, obesity, or a diabetes family history. The pre-selection was considered to be associated with cost. Main outcome measures were cost, type 2 diabetes cases, and cost per detected case (incremental cost effectiveness ratios). The analysis took both third party payers' and a societal perspective. Prevalences of impaired glucose metabolism were derived from the KORA S4 (S2000) survey performed from 1999 to 2001 in Augsburg. The participation (assumptions: OGTT 30%, fasting glucose testing 35%) was derived from a population practice study in the U.K. [22]. Cost data were taken from routine statistics.

Targeted screening strategies were all less effective and more costly than the universal screening strategies (they were "dominated") and thus could be excluded. OGTT (4.90€ per patient) yielded lowest cost from the perspective of the statutory health insurance, and fasting glucose testing combined with OGTT (10.85€) from societal perspective. HbA1c test combined with OGTT was most expensive (21.44€ and 31.77€), but also most effective (54% detected cases). The incremental cost effectiveness ratios (additional cost per additionally detected cases) for the HbA1c combined with OGTT strategy compared to the less costly and less effective strategies were 771€ and 831€ from the perspective of the statutory health insurance and from society, respectively. In Monte Carlo analysis, the hierarchy of the strategies with respect to their cost and effectiveness remained unchanged in 100 and 68% (statutory health insurance' and societal perspective) of simulated populations. However, when a participation level of 60% or higher for fasting glucose testing and 55% or higher for the OGTT test was achieved, OGTT testing alone would be the most effective strategy, so that the more expensive strategy "HbA1c testing combined with OGTT" would be excluded.

Cost effectiveness analysis evaluating a life time horizon

Cost effectiveness analysis by Hoerger et al. [17]

Aim of this very detailed analysis was to estimate the cost effectiveness of two screening strategies compared to no screening in the US population: universal screening and targeted screening to people with hypertension. The type 2 diabetes screening was based on capillary blood glucose testing (CBG) and following fasting glucose testing in case of elevated CBG. For the selection of hypertensive subjects, no cost were considered. The analysis used an elaborated Markov model and a lifetime horizon. Outcomes were cost, life years gained and QALY's¹, and cost per life year gained or per QALY. All analyses were conducted age-group specific. Data sources were census data, two large intervention

studies (United Kingdom Prospective Diabetes Study [UKPDS], and Hypertension Optimal Treatment trial [HOT trial]), and recent cost data. The participation in the screening programs was assumed to be complete. The analysis took the perspective of a third party payer.

At all age groups, cost effectiveness ratios (screening compared to no screening) were reported to be more favourable for screening targeted to people with hypertension than for universal screening (cost per year of life saved in universal screening: more than 300,000 \$), although using universal screening would identify more cases (data not given). Screening was observed to be more cost-effective for ages 55 to 75 years than for younger ages (e.g. cost per year of life saved in a 55-year-old person with hypertension: 34,375 \$). The results were stable for a variety of input data within the sensitivity analysis. The authors conclude that the cost effectiveness of screening elderly persons with hypertension is well within the range that American society is typically willing to pay for health care treatments.

Discussion

In the German KORA-based cost effectiveness analysis, HbA1c measurement combined with OGTT was the most effective screening strategy. This observation can be explained by high participation in this strategy. However, cost were lower when screening with fasting glucose testing combined with OGTT or OGTT alone. Because identifying subjects with risk factors (e.g. hypertension) was considered to be associated with cost, targeted screening among these subjects at risk was found to be less effective and more costly than universal screening.

Zhang et al. evaluated the cost effectiveness of screening for IGT, IFG, and undiagnosed type 2 diabetes. In contrast to the KORA-based study, they considered complete participation as baseline condition. From the sensitivity analysis, they reported that fasting glucose testing combined with OGTT would be the most effective strategy for screening for undetected diabetes, IFG, and IGT, if people were much less willing to participate in the OGTT than in the fasting glucose testing. However, they did not report results from a sensitivity analysis for the screening of type 2 diabetes alone.

A major limitation of the KORA-based CEA and the study of Zhang is that it used an intermediate outcome, the cost per detected case. Including information on potential cost following the screening procedure and benefits of treatment would provide a more complete picture of the cost-effectiveness of screening for diabetes. However, no population-based data regarding the natural disease process of early detected diabetes or results describing the effectiveness of early intervention after diabetes screening are available so far [4, 5].

Hoerger et al. found targeted screening (people with hypertension) to be more cost effective in the lifetime horizon than universal screening, however, the authors assumed that selecting hypertensive subjects would not incur cost. The study of Hoerger did not take incomplete participation into account. However, complete participation in screening programs cannot be as-

¹ QALY = quality-adjusted life years

Tab. 1 Description of cost effectiveness analyses (CEA) for type 2 diabetes screening (according to recommended general format [19–21])

author	Icks et al.	Zhang et al.	Hoeger et al.
Year of publication	2004	2003	2004
Year used for cost calculation	2000	2000	1997
Country of analysis	Germany	US	US
Currency used for cost valuation	€	US\$	US\$
Methodology (model)	Decision analytic model	Analysis of cost, effectiveness, cost per detected case	Markov model
Alternative considered for evaluation	Four screening strategies for type 2 diabetes, each universal and targeted, versus no screening	Five screening strategies for IFG, IGT, and type 2 diabetes versus no screening	Universal and targeted screening for type 2 diabetes versus no screening, intensive anti-hyperglycemic and antihypertensive therapy versus standard therapy
Cost-effectiveness measure	Cost per case detected	Cost per case detected	Cost per QALY
Population	German population, 55–74 years of age KORA Survey, Region of Augsburg	US population, 45–74 years of age	US population
Effectiveness data sources	KORA Survey, population practice study	Census data	NHANES, census data, intervention trials (UKPDS, HOT trial)
Cost elements	Screening cost, cost for selecting subjects at high risk	Screening cost	Screening and treatment cost
Cost data sources	Routine statistics	Medicare	Routine statistics
Time horizon	One year	One year	Lifetime
Discount rate	No discounting required	No discounting required	3 %
Variables included in the sensitivity analysis	Prevalence of IFG, IGT, and diabetes, participation, indirect cost	Participation, prevalence of IFG, IGT and diabetes, addition of a confirmatory OGTT	Various input variables
Baseline results	<ul style="list-style-type: none"> – Targeted screening was less effective and more costly than universal screening and therefore excluded – Lowest cost: OGTT (perspective of statutory health insurance: 4.90 € per patient), fasting glucose testing combined with OGTT (societal perspective: € 10.85 per patient) – HbA1c combined with OGTT most expensive, but also most effective (54 % detected cases) 	<ul style="list-style-type: none"> – OGTT testing most effective strategy – Capillary blood glucose test and risk assessment questionnaire (both combined with OGTT) had lower cost per detected case – Using the fasting glucose testing combined with OGTT, cost per detected case 758 \$ from societal perspective 	Targeted screening to people with hypertension more cost-effective Screening more cost-effective for ages 55 to 75 years than for younger ages E.g. cost per year of life saved more than 300,000 \$ in universal screening, and 34,375 \$ in targeted screening in the age group 55–74 years
Results from sensitivity analysis	<ul style="list-style-type: none"> – Hierarchy of the strategies with respect to their cost and effectiveness unchanged in the majority of Monte Carlo simulated populations – If a participation level of near 60 % for fasting glucose or OGTT testing was achieved, OGTT would be the most effective strategy 	Fasting glucose testing combined with OGTT would be the most effective strategy if people were much less willing to participate in the OGTT than in the fasting glucose testing	Results stable for a variety of input data
Authors' conclusions	The most favourable strategy depends on if the goal of the screening program is to identify more cases or pursue lower cost at reasonable effectiveness. Participation level in screening programs has to be taken into account	Tradeoff between effectiveness and cost-effectiveness in choosing a strategy. The expected percentage of the population willing to take an OGTT is also a consideration	The cost effectiveness of type 2 diabetes screening among subjects aged 55–74 years with hypertension seems to be well within the range that American society is typically willing to pay for health care treatment

OGTT: oral glucose tolerance test; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; CER: cost effectiveness ratio; QALY: quality adjusted life year

sumed, and the participation level can be considered to influence the decision about favourable strategies to a large extent. Results of cost effectiveness analyses may be misleading if real conditions such as an incomplete participation in screening programs are not considered.

As described above, population-based data regarding the natural disease process of early detected diabetes or results describing the effectiveness of early intervention after diabetes screening are lacking so far [4, 5]. Thus, as also discussed by the authors, a

major limitation of the study is that clinical data is derived from subjects with clinically diagnosed diabetes.

Conclusions and perspective

In general, a cost effectiveness analysis cannot determine which strategies should be implemented. The choice depends on the goal of the screening program. It may be to identify the most possible cases of previously undiagnosed diabetes or to pursue low-

er cost per case identified. Cost-effectiveness analyses can indicate which strategies can be ruled out since they are less effective and more costly than others. Further they can show the strategy with the lowest effectiveness and the lowest cost, and can provide information about additional cost per additionally detected cases, when more effective strategies are used. A decision maker can use this information to choose the most suitable screening procedure for a program by taking into account the maximum limit to be spent per additional case detected.

With respect to the screening for undiagnosed type 2 diabetes, further studies are warranted in order to answer the question as to which screening procedure is most appropriate. To achieve better and less costly screening, participation in screening tests needs to become more accepted by the target population.

Type 2 diabetes screening, in particular targeted screening of elderly hypertensive subjects, may be cost effective, that means that is well within the range that societies are willing to pay for health care treatment. However, the evidence is limited, since valid data is lacking. Although type 2 diabetes screening is recommended, the effectiveness of early detection and treatment of type 2 diabetes has not yet been shown. In the future, the most important question is whether type 2 diabetes screening and early treatment is effective with respect to clinical outcomes.

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