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Title: Capturing Patient Value in an Economic Evaluation

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Abstract

Objective: Economic evaluations predominantly use generic outcomes, such as EuroQol-5 Dimension (EQ-5D), to assess the health status. However, because of the generic nature, they are less suitable to capture the quality of life of patients with specific conditions. Given the transition to patient-centered (remote) care delivery, this study aims to evaluate the possibility to use disease-specific measures in a cost-effectiveness analysis (CEA).

Methods: A real-life cohort from Maasstad Hospital (2020-2021) in the Netherlands, with 772 Rheumatoid Arthritis (RA) patients, was used to assess the cost-effectiveness of electronic consultations (e-consultations) compared with face-to-face consultations. The Incremental Cost-Effectiveness Ratio (ICER) based on the generic EQ-5D was compared with ICER's based on RA specific measures; Rheumatoid Arthritis Impact of Disease (RAID) and Health Assessment Questionnaire-Disability Index (HAQ-DI). To compare the cost-effectiveness of these different measures, HAQ-DI and RAID were expressed in QALYs via estimated conversion equations.

Conclusions: The conventional ICER (e.g. EQ-5D) indicates that e-consultations are cost-effective with cost savings of - €161k per QALY gained for a prevalent RA cohort treated in a secondary trainee hospital. RA specific measures show similar results, with ICER's of - €163k per HAQ-DI(QALY) and - €223k per RAID(QALY) gained. RA specific measures capture patient-relevant domains and offer the opportunity to improve the assessment and treatment of the disease impact.

Discussion: Disease-specific patient-reported outcome measures (PROMs) offer a promising alternative for traditional measures in economic evaluations, capturing patient-relevant domains more comprehensively. As PROMs are increasingly applied in clinical practice, the

next step entails modelling of a RA patient-wide conversion equation to implement PROMs in economic evaluations.

Key words: Economic evaluation, Electronic consultations, Patient-reported outcome measures, Value-based healthcare, Rheumatoid Arthritis

Significance and Innovations:

- By including the patient perspective in an economic evaluation, domains of patient value can be incorporated in the assessment of health technologies.

- Disease-specific patient-reported outcomes are a valuable instrument to evaluate health care for patients with a chronic condition.

- Disease-specific outcome measures (RAID and HAQ-DI) can yield similar results with respect to the Incremental Cost-Effectiveness Ratio (ICER) as the generic measure EQ-5D.

- The ICER of RAID, HAQ-DI and EQ-5D indicate that e-consultations are cost-effective.

Introduction

Due to the adoption of technological innovations, conventional healthcare provision is shifting from hospitals and other facilities to the day-to-day life of patients. Results of earlier studies have shown the (cost) efficacy of e-health and telemonitoring solutions [1] [2] [3]. Patients with chronic conditions visit the hospital for check-ups regularly; Rheumatoid Arthritis (RA) sufferers approximately every three to four months. RA patients experience challenges in managing check-up appointments, transportation to outpatient clinics and their employability, due to relapses of the disease [4]. Although accelerated by COVID-19, the adoption of e-health and telemonitoring is perceived as a structural component of a broader transformation to patient-centered healthcare [1]. E-health and telemonitoring are considered to be promising methods to monitor RA patients remotely, thereby easing the burden for patients and promoting a shift toward a more patient-centered healthcare system [1] [5] [6]. A recent study by Bos et al. (2021) demonstrated that patients with rheumatic and musculoskeletal diseases (RMDs) were satisfied with telemedicine, i.e. telephone and video consultations, provided in the Netherlands [1]. However, quantitative results on patient-reported outcomes are lacking and therefore the added value in terms of healthcare effects and costs is still unclear.

In conventional economic evaluations within rheumatology and other diseases, the focus with respect to the assessment of the health-related quality of life as experienced by patients is predominantly on generic measures, such as the Euro Quality of Life- 5 Dimension (EQ-5D) or the Short Form Health Survey 36-Item (SF-36). However, utilities such as Quality Adjusted Life Years (QALYs), derived from the EQ-5D and SF-36, limit the patient perspective on health outcomes in economic evaluations as they are calculated on a more generic population basis and not specific to one health condition [7]. With the desired

transition to more personalized and patient-centered care delivery, these instruments are less suitable to capture the full spectrum of patient relevant domains, as covered by for example the International Consortium of Health Outcome Measures (ICHOM) sets [8]. Patient relevant outcome domains are the cornerstone of the transition to a more value-based healthcare (VBHC) system, as embraced in several countries including the Netherlands [9] [10].

Although the EQ-5D is the preferred tool in cost-utility analysis, evidence concerning the applicability of the questionnaire in non-commercial, clinical practice is lacking [11]. The usability of the EQ-5D in clinical practice is limited due to the so-called ceiling effect, i.e. health scores clustering at the positive end of the scale [12]. Moreover, the EQ-5D was initially developed as a supplemental tool, in addition to more disease-specific patient-reported outcome measures (PROMs) [12]. As a result, the EQ-5D is used less often in clinical daily practice, which might influence the economic evaluation purposes of this questionnaire. However, patient relevant outcomes can be applied to broaden the current elements of value, e.g. QALYs and net costs, in health technology assessment (HTA) [13].

To incorporate the full spectrum of patient relevant domains as captured through PROMs and the transition to patient-centered (remote) care delivery in an economic evaluation, this study examines the impact on costs and perceived healthcare effects by RA patients engaging in electronic consultations (e-consultations). For this purpose, a comparison is made between the conventional economic methodology of valuing health by assessing the QALYs as obtained via the traditional measure EQ-5D versus the RA specific measures Rheumatoid Arthritis Impact of Disease (RAID) and Health Assessment Questionnaire-Disability Index (HAQ-DI).

Materials and methods

Study design and population

The real-life retrospective cohort of over 3,000 patients receiving RA care in the first quarter of 2020 (with a one-year follow-up) at the rheumatology department of the Maasstad Hospital in Rotterdam, the Netherlands, served as the base population for this study. Patients aged 18 years and over were included if RA was diagnosed by a rheumatologist at least one year earlier, and the patient's PROM and disease activity were available within 6 to 12 months after the consultation date [14]. Patients were excluded from the study if their PROMs were unavailable and/or their disease activity score (DAS) was lacking. This resulted in a study population of 772 patients (see supplementary file 1). As part of the study protocol (T2016-76) institutional permission is given to evaluate retrospective data.

Real-life (intervention) groups

The study population was split into two groups: RA patients using face-to-face consultations (control group) versus those with e-consultations (intervention group). E-consultations were defined as consultations performed via telephone and/or internet, the latter through a software service ("BeterDichtbij©"), made available by Maasstad Hospital as a secured (web-based) application [15]. Face-to-face consultations were defined as the patient visiting the healthcare provider at the hospital site. To minimize the difference in patients concerning their underlying disease characteristics (e.g. disease activity) between the two groups, the first consultation in the year 2020 was selected as the baseline measure point. If only one type of consultation, i.e., either an e-consultation or face-to-face consultation, occurred in 2020, the patient was assigned to that specific group. Since most of the patients received both a face-to-face and an e-consultation in 2020, for these patients a computerized random sample was derived from the study population by using Stata SE (version 15.0). According to Dutch guidelines, patients visit the rheumatologist every 3 to 4 months.

Data collection

Data were extracted from the Business Intelligence data warehouse of Maasstad Hospital, that holds financial data concerning all healthcare activities and procedures performed at Maasstad Hospital (i.e. in the rheumatology department and all other departments). Electronic health records were consulted to examine the number of patients receiving e-consultations and/or face-to-face consultations. Health costs were retrieved from the electronic medical dossiers of the patients, that provide information on the healthcare procedures performed and the related cost prices.

(Clinical) assessments

The patients' age, gender, disease duration, disease activity scores (DAS28CRP) and number of (multi-)morbidities were used to assess whether there was potential bias between the intervention and control group in terms of baseline characteristics. Disease duration is defined as the time (in years) between the diagnosis date and January 1st 2020. The number of multi-morbidities is stated as the occurrence of at least one other diagnosis besides RA. The DAS28CRP is a measure for the disease activity in RA patients by assessing the 28-joint count and the C-reactive protein (CRP) levels in the blood, the scores ranging from 0 to 9.4. A DAS28CRP-score below 2.6 indicates remission of RA [16].

Patient-reported outcomes

Outcomes, i.e. utilities, are obtained from PROM questionnaires which are filled out at home approximately two weeks before a consultation. At the rheumatology department of the Maasstad Hospital, the ICHOM standard set for Inflammatory Arthritis is implemented to assess the PROMs every 6 to 12 months as advised by ICHOM [14]. This standard set comprises five questionnaires of which, for the purpose of this study, the Work Productivity and Activity Impairment (WPAI), the Health Assessment Questionnaire - Disability Index

(HAQ-DI), Rheumatoid Arthritis Impact of Disease (RAID) and the generic EQ-5D were assessed. The HAQ-DI is a score ranging from 0 to 3 and the scale of the RAID questionnaire runs from 0 to 10, with higher scores indicating worse health outcomes [17] [18]. These specific questionnaires were selected since they are most commonly applied in research and in clinical practice concerning RA [19] [20]. Moreover, the HAQ-DI and RAID are included as these questionnaires cover a broader and more RA specific range of patient-relevant domains, frequently used in healthcare cost studies [17] [18]. The difference between the RAID and HAQ-DI is that the HAQ-DI is specifically geared toward the physical functioning of patients, whereas the RAID comprises RA specific domains that are considered relevant to be patient. In comparison with the EQ-5D questionnaire, the RAID questionnaire encompasses the additional RA relevant patient domains of fatigue, sleeping problems and generally dealing with RA.

Costs

Healthcare costs as well as non-medical expenses were incorporated in the study. Healthcare costs include all expenditures incurred by the hospital, such as consultations, laboratory, inpatient, emergency and medication costs (see Supplementary Table 2) within one year from the baseline measure (first quarter of 2020). Regarding the non-medical costs, travel costs (direct) and productivity losses (indirect) were considered. The travel costs were only calculated for the conventional outpatient visit group, assuming that the intervention group (e-consultations) had no travel costs. Zip codes of participants were used to determine the distance from the patients' home addresses to the outpatient clinic at Maasstad Hospital in Rotterdam. The distance in kilometers for the required return trip was calculated per patient. Subsequently, the kilometers were multiplied by the assumed cost of €0.19 per kilometer and €3.00 per hospital visit was added with respect to the parking costs [21]. The productivity loss

or lost wages applies to the study population under 67 years of age, as patients above this threshold are formally retired citizens who should not experience productivity losses. The loss of productivity regarding the visit to the hospital was estimated using the Human Capital method. The productivity losses were examined through the earlier mentioned WPAI questionnaire. Since the recall period concerning the WPAI questionnaire is one week, the potential productivity costs were only calculated for the week the consultation took place. To value the total productivity loss as a result of RA, the working hours lost were multiplied by the mean average wage per hour. The Dutch mean hourly wage is €36.40 according to Statistics Netherlands [22]. Costs were not discounted since the time horizon of the study was limited to one year and all costs calculations were based on 2019 prices.

Cost-effectiveness analysis

Decision tree

To examine the cost-effectiveness (utility) of telemonitoring concerning a societal perspective, a decision tree was constructed that consisted of two primary pathways. A decision analytical tree method was selected given that two alternative forms of consultation, i.e. face-to-face and e-consultations, were evaluated. The results of the decision tree were used to evaluate the quality of life by assessing the HAQ-DI, RAID and EQ-5D questionnaires. The results of the health effects from the patient perspective were compared with the quality of life as expressed in QALYs. Depending on the random assignment, patients with both face-to-face and e-consultations in 2020 followed either the e-consultation branch or the face-to-face consultation branch. Patients can move to different health states depending on their DAS28CRP scores. The DAS28CRP scores were applied as cut-off values regarding the health states in the decision tree. A score of 2.6 or lower indicates RA remission and higher values correspond with an inflammatory (active) state of disease [23].

Different input parameters are required for the decision tree analysis. The utilities in the different health states are obtained from the RAID, HAQ-DI and EQ-5D questionnaires. The transition probabilities were calculated based on the real-world cohort, i.e., the number of patients moving to the specific health states. To estimate the cost-effectiveness of e-consultations, an Incremental Cost Effectiveness Ratio (ICER) was calculated by subtracting the expenditures in the face-to-face consultation group from the expenditures in the e-consultation group and dividing the costs by the score of the EQ-5D, HAQ-DI and RAID respectively, for the intervention group versus the control group. A cost-effectiveness threshold of €50k per QALY was considered, which is in line with the relevant Dutch guidelines [21].

Statistical analysis

Descriptive statistics were used to summarize the baseline characteristics of the two patient groups. Depending on the data distribution, continuous variables are presented by their mean and standard deviation (unless stated otherwise) and categorical variables as percentages. Although most patients were randomly allocated between the two groups, the characteristics of the intervention group and control group were tested for potential bias since the consultation type was assessed retrospectively. The unpaired sample t-test and the Mann Whitney U test were applied to examine the statistical difference between the mean costs and health outcomes of both groups. Additionally, a sensitivity analysis with t-tests and Mann Whitney U tests were performed to assess the difference between patients who solely had e-consultations and face-to-face consultations. With respect to the HAQ-DI and RAID, the scores were converted into an EQ-5D equivalent scale to increase the comparability of the disease specific (RA) versus the generic health perspective. Following the approach applied in a previous study with respect to the HAQ-DI, conversion equations were estimated [24]. Basically, the HAQ-DI and RAID scores were converted to a comparable EQ-5D score

through linear regressions with EQ-5D scores as explanatory variable and the HAQ-DI or RAID as outcome variable. To test the generalizability of the outcomes for a RA population, the entire Maasstad Hospital patient population filling out PROMs in 2020 (N=890), instead of the applied study sample, was used as validation cohort.

Sensitivity analysis

To examine the robustness of the model results and to identify the key cost drivers, univariate and probabilistic sensitivity analyses were conducted. As part of the univariate sensitivity analysis, the healthcare perspective, i.e., excluding productivity losses, was selected to assess the switch of perspective on the ICER. A Monte Carlo simulation was conducted to perform the probabilistic sensitivity analysis, resulting in a cost-effectiveness plane. A gamma distribution was applied regarding the costs, as costs are generally skewed to the right, i.e., outliers with high expenditures, and a beta distribution was considered regarding the outcomes [25]. All data analyses were conducted using StateSE 15 for Windows, whereby a p-value of 5% was considered to be statistically significant.

Results

Patient population

A total of 772 patients were included from the 1231 patients who participated in the PROM inquiry, of which 148 patients solely had e-consultations and 41 patients only face-to-face consultations (Table 1, Supplementary Figure 1, Supplementary Table 2). Approximately 60% of the included patients had available PROMs within the time frame of six months after the consultation date. The patients in the e-consultation group were on average slightly younger (59.5; SD = 13.0) in comparison with the face-to-face consultation group (60.5; SD = 11.9). Females were overrepresented in the face-to-face consultation group (71.8%). Multi-morbidities were slightly more prevalent in patients of the face-to-face consultation group and the mean disease activity (i.e. DAS28CRP) was lower in the e-consultation group. The observed differences between the face-to-face and e-consultation group were not statistically significant on a 5% alpha level. The sensitivity analysis concerning the patients with solely e-consultations and face-to-face consultations also showed no significant differences.

Decision tree analysis (outcomes and costs)

The probabilities of patients moving from one health state to the other, are depicted in table 2. For the patients in the face-to-face consultation group, the probability of inflammation is 41%. Hence, the probability of being in a state of remission is 59%. Regarding the e-consultation group, patients' chance of being in a state of remission is slightly lower than in the control group (55% versus 59%).

Outcomes

The average HAQ-DI, RAID and EQ-5D scores are displayed in table 2. A lower score on the HAQ-DI and RAID scale indicates a better patient-reported health outcome, whereas for the EQ-5D the contrary applies. In the e-consultation group, patients in remission scored 0.56,

2.64 and 0.79 (mean, SD) on the HAQ-DI, RAID and EQ-5D respectively and for inflammatory patients this was 1.03, 4.62 and 0.66. Patients in remission in the control group had an average score of 0.60 (HAQ-DI), 3.13 (RAID) and 0.77 (EQ-5D), compared with inflammatory patients mean scores of 1.10, 4.32 and 0.66. Comparing the scores between the remission and inflammation patients by means of the Mann-Whitney test, showed that the inflammatory patients in the face-to-face consultation group had significant better outcomes on the RAID and EQ-5D scores (*p<0.01*), however patients scored worse on the HAQ-DI scores (*p<0.01*). The patients in remission within the e-consultation group scored significantly better on the RAID questionnaire in comparison with the control group (*p=0.03*), but not on the HAQ-DI (*p=0.870*) and EQ-5D scores (*p=0.229*).

Costs

Figure 1 illustrates the total costs incurred for RA patients, both by consultation type and health state. Overall, patients in the face-to-face consultation group induced higher costs, with cost savings for the e-consultation group of €1,066 per patient. Differences in costs were predominantly because of direct healthcare expenses, consultations and medication costs and as a result of travel costs. However, the unpaired t-tests shows no significant difference in costs between the face-to-face and electronic group (*p=0.225*). The same was found for the patients in remission in the two groups (*p=0.592*). Inflammatory patients in the face-to-face group caused significantly higher expenditures than in the e-consultation group (*p=0.041*). In the latter group, 60% of patients had at least one face-to-face consultation in the 6 months following the e-consultation; for the face-to-face group that percentage was 96%.

Cost-effectiveness analysis

To compare the cost effectiveness of e-consultations versus face-to-face consultations, the patient-reported outcomes based on the RA specific measures HAQ-DI and RAID were

converted into comparable generic measure EQ-5D scores. The equations to convert the HAQ-DI and RAID scores in EQ-5D values are displayed in equation 1 and 2 below. The transformed HAQ-DI values range from 0.889 in an optimal health state to 0.304 in the worst health state. Regarding the RAID score, 0.933 is the maximum EQ-5D equivalent value (perfect health) and the minimum value 0.383. The R^2 value of both equation estimates was 0.42, indicating that the RAID and HAQ-DI score explain 42% of the variability in EQ-5D measure (*p<0.001*). Regarding the robustness of the estimates, the complete PROM sample (N=890) generated similar estimates for both the HAQ-DI and RAID: 0.891 – (0.213 * HAQ-DI) with a R^2 value of 42% and 0.955 – (0.062 * RAID) also with a R^2 of 0.42.

Equation 1. Equation to convert HAQ-DI scores into EQ-5D scores
$$EQ - 5D = 0.889 - (0.195 * HAQ - DI)$$

Equation 2. Equation to convert RAID scores into EQ-5D scores
$$EQ - 5D = 0.933 - (0.055 * RAID)$$

The results of the cost-effectiveness analysis (CEA) are depicted in table 3. The e-consultation group scored 13 points more favorable on the conventional, i.e., unconverted, HAQ-DI questionnaire and 34 points better on the unconverted RAID questionnaire, the difference was 2.5 and 1.8 in terms of transformed QALYs respectively. Although the favorable difference per patient in the e-consultation group is small in terms of HAQ-DI and RAID scores (i.e. health outcomes), implementation of e-consultations is a cost-effective strategy; - €163,159 based on the HAQ-DI(QALY) and - €223,002 for RAID(QALY). Regarding HAQ-DI and RAID scores, e-consultations are cost-effective given the Dutch QALY threshold of €50K. The same conclusion can be drawn when considering the conventional cost-utility analysis based on EQ-5D scores, as the implementation generates a cost saving of - €161,491 per QALY gained.

Sensitivity analysis

A change from a societal to a healthcare perspective, affected the expenditures. The switch of perspective unaltered the health outcomes, however the difference in expenditures resulted in slightly lower cost savings, €949 instead of €1,066 from the societal perspective. This resulted in less negatives ICERs compared to the societal perspective. ICERs decreased from −€161,491 to −€143,750 for the EQ-5D, −€223,002 to −€198,504 for the RAID(QALY) and −€163,159 to −€145,235 with respect to the HAQ-DI(QALY) scores.

Results from the probabilistic sensitivity analysis indicate that in 37.8% (HAQ-DI), 27.3% (RAID) and 21.7% (EQ-5D) of the 1000 Monte Carlo iterations, e-consultations were less effective from a societal perspective, although they were cost saving (figure 2). In the majority of the probabilistic sensitivity analysis cases, the expenses of the e-consultations were lower and resulted in better health outcomes than face-to-face consultations.

Discussion

Integrating the disease specific RA patient perspective in an economic evaluation by means of the HAQ-DI and RAID is a promising alternative for the traditional generic measure EQ-5D. The implementation of e-consultations for RA patients is a dominant strategy according to economic evaluation considering both the EQ-5D and RA specific outcome measures. The ICER of the generic outcome measure, i.e. − €161,491 per QALY(EQ-5D) gained, corresponds to the ICERs encompassing the RA specific perspective, namely − €163,159 per HAQ-DI(QALY) gained and − €223,002 per RAID(QALY) gained in a RA cohort, treated in a secondary trainee center. Although the ICERs of the generic and RA specific measures are comparable, incorporation of disease specific patient-reported outcomes in economic evaluations have been proposed as method to better capture the patient-relevant domains of the disease impact than the generic measure EQ-5D. Hence, the use RA specific measures in cost-effectiveness analysis of healthcare technologies offers the opportunity to improve the assessment and treatment RA patients.

Although ICERs of both the RA specific reported outcome and generic outcome measures indicate that e-consultations are cost-effective, that effect is predominantly achieved through cost savings. A likely explanation for the cost savings is the lower probability of at least one (face-to-face) follow-up consultation for patients within the e-consultation group. Probably patients that are in remission and have a stable disease process and/or milder symptoms are less likely to opt for a face-to-face consultation. For those patients an e-consultation suffices.

The differences in outcomes of the cost-effectives analysis, based on (transformed) QALYs, are minor between the e-consultation and face-to-face group. These results are in line with other articles investigating the impact of telemonitoring on the cost-effectiveness [3] [26]. Because the HAQ-DI and RAID scores are converted to EQ-5D scores by performing linear regressions on a relatively small study population, the robustness of the results is potentially

affected. However, similar approaches are conducted in the literature [24] [27]. A possible explanation for the difference in the ICERs of the HAQ-DI and EQ-5D versus the RAID, is the broader range of the RAID, capturing more RA patient-relevant domains. Furthermore, the EQ-5D and HAQ-DI questionnaires are both prone to ceiling effects, negatively affecting the sensitivity to quality of life changes in the higher spectrum [12] [28]. The RAID is also less sensitive to changes in scores caused by increasing age and disease duration [29]. Hence, the RAID can be exploited as key PROM for RA patients with respect to the assessment of the disease specific relevant outcomes [30].

As healthcare systems are under increasing pressure regarding budgets, the evaluation of new technologies but also of the current healthcare delivery is of importance [31]. However, although the current Dutch guideline advises to apply EQ-5D and alternative questionnaires may only be used in addition to the reference case (i.e. EQ-5D) [21], the need to move beyond the classical viewpoint concerning the evaluation of healthcare interventions is increasing. As a result, several initiatives have been introduced, such as the ISPOR value flower [13]. The goal of the ISPOR value flower is to enhance a cost-effectiveness analysis in terms of the relevant aspects considered [13]. An example is the incorporation of the value of hope, referring to patients' risk tolerance, i.e. the value patients place on the variability in outcomes [13]. The concept of the ISPOR value flower is however geared toward evaluations from a more process and societal viewpoint instead of a patient centered approach. Therefore, examining PROMs can complement the ISPOR value flower, as data are assessed at patient level (i.e. micro level) in the shift toward more personalized care delivery.

The findings of this study should be interpreted considering certain potential limitations. First, the cohort of RA patients was followed during the COVID-19 pandemic, since in the preceding years, the utilization of e-consultations was too low to allow for a reliable cost-effectiveness analysis. However, the exceptional circumstances of the pandemic could bias

the results, as for example the more severe or complex RA patients opted for face-to-face consultations. To address that bias, a random sample was created by placing patients in either the e-consultation or face-to-face consultation group. Based on the performed statistical tests regarding the baseline characteristics of the two groups, a (weak) statistically insignificant difference was determined in terms of disease activity. The DAS28CRP scores were on average 0.2 points higher in the face-to-face consultation group compared with the e-consultation group, which can explain the higher expenditures and lower health outcomes in that group. A second limitation is related to the questionnaires, as nearly 40% of the patients filled out the questionnaires outside the recommended timeframe of 6 months. Therefore, the patient reported as well as generic outcomes will be less representative concerning the actual health outcomes at the time of the consultation. A third limitation arises in terms of the productivity costs, because the WPAI questionnaire is limited to the productivity losses in one week, a comprehensive view on the productivity losses over a longer time period is lacking. To minimize the impact on the research findings, productivity costs were exclusively calculated for the week in which the consultation took place. Due to the limited time frame concerning the WPAI questionnaire, the productivity losses are likely to be underestimated. Lastly, primary care costs were not considered in the ICER due to privacy laws impeding the data exchange of patients in the Netherlands. However as diagnosing, treatment and monitoring of RA takes place in the hospital, primary care costs are expected to be low.

Strengths of the study comprise the use of real-world data to examine the impact of e-consultations on both costs and health outcomes, instead of obtaining utilities and transition probabilities from the literature. To our knowledge, this is the first time a comparison of the disease specific perspective with the generic perspective in a cost-effectiveness analysis for e-consultations by RA patients is made. The fact that a societal perspective is considered, is important for patient empowerment. A third strength concerns the robustness of the outcomes:

the univariate and multivariate probabilistic sensitivity analysis of the results of the performed ICERs yielded comparable results. Furthermore, an internal validation was conducted to ensure that the obtained values from the conversion equations of the PROMs into the patient valued QALYs, were robust in a larger study sample.

To further enhance the inclusion of patient reported outcomes in economic evaluations, future research should focus on the creation of general conversion equations for disease specific outcomes by conducting the research on a broader patient population. In addition, the follow-up should be extended to examine the effects of electronic consultations in the long-term and inclusion of patient experience indicators as an outcome parameter could provide insights with respect to the delivered care.

Conclusions

In conclusion, to foster the incorporation of disease specific patient-reported outcomes in CEAs, this study provided evidence on the implementation of PROMs in an economic evaluation of RA consultations within a prevalent RA cohort, treated in a secondary single-hospital. Electronic consultations showed to be a cost-effective strategy in terms of scores on the RA specific measures RAID and HAQ-DI, comparable to the score based on the more generic EQ-5D. As PROMs are increasingly adapted in clinical practice, providing patient-relevant perspectives not reflected in generic measures, these tailor-made PROMs will better reflect the patient domains in CEAs than generic outcome measures. Hence, as disease specific PROMs provide more information regarding the effects of treatment decisions, they are recommended for application in economic evaluations over generic measures.
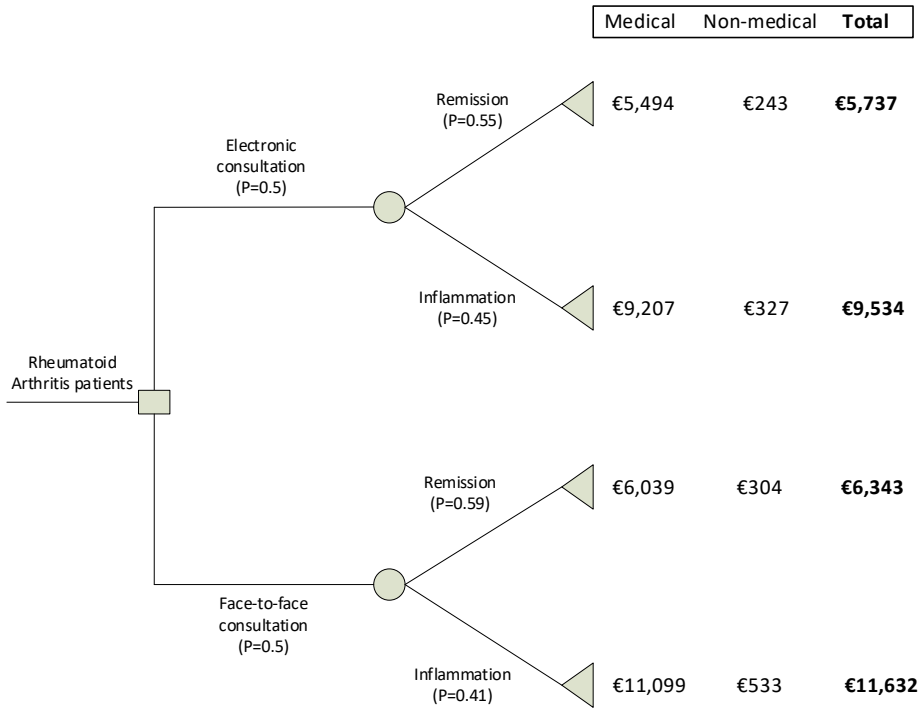
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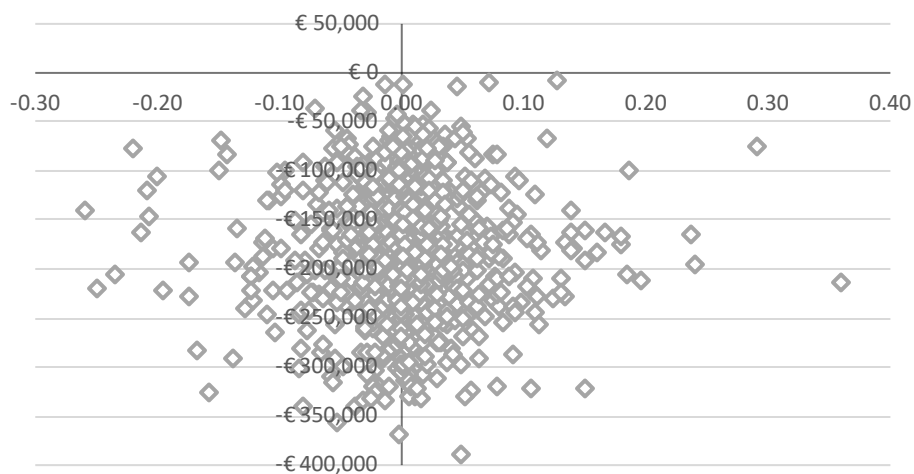[31] Ministerie van Volksgezondheid, Welzijn en Sport, "Integraal Zorgakkoord," Rijksoverheid, Den Haag, 2022.

Figure 1. Model outputs: costs (per patient)

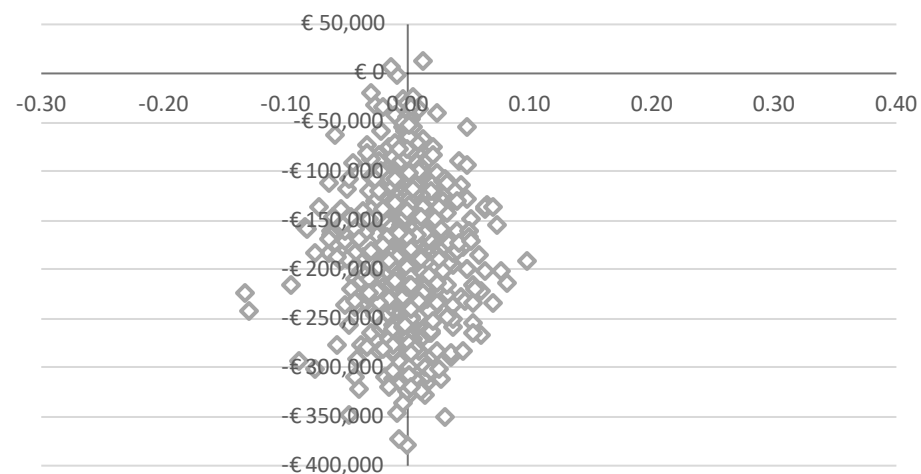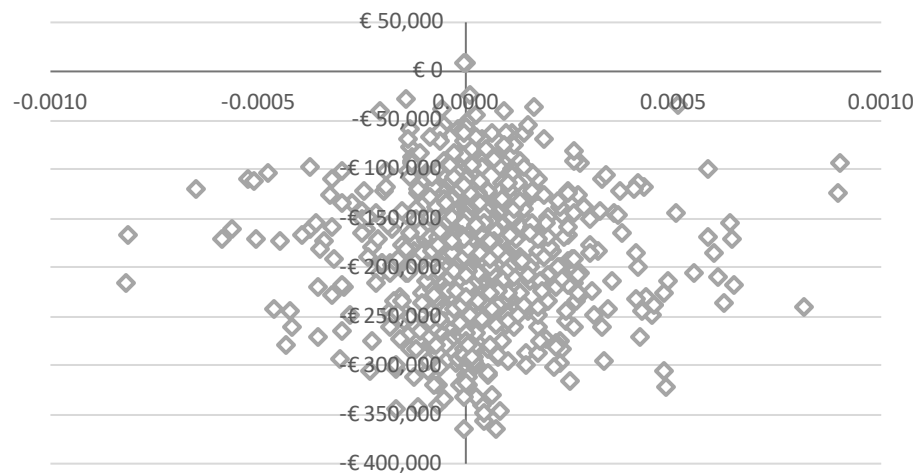Figure 2. Cost-effectiveness planes (probabilistic sensitivity analysis)

	Medical	Non-medical	Total
Remission (P=0.55)	€5,494	€243	**€5,737**
Inflammation (P=0.45)	€9,207	€327	**€9,534**
Remission (P=0.59)	€6,039	€304	**€6,343**
Inflammation (P=0.41)	€11,099	€533	**€11,632**

Electronic consultation (P=0.5)

Face-to-face consultation (P=0.5)

Rheumatoid Arthritis patients

a) HAQ-DI (QALY)

b) RAID (QALY)

c) EQ-5D

Table 1. Patient characteristics

Characteristics	Face-to-face consultation (N=386)	E-consultation (N=386)
Female (N, %)	277 (71.8)	262 (67.9)
Age (years)	60.5 (11.9)	59.5 (13.0)
Disease duration (years)	9.2 (4.6)	8.8 (4.6)
Disease activity score (range 0-9.4)	2.6 (1.0)	2.4 (1.0)
% Inflammation	41	45
Presence of multi-morbidities (N, %)		
0	92 (23.8)	105 (27.2)
1-5	219 (56.8)	219 (56.7)
6-10	61 (15.8)	52 (13.7)
>10	14 (3.6)	10 (2.6)

Note. Data presented as mean and standard deviation unless stated otherwise

Table 2. Model outputs: health effects (patient-reported outcomes)

Consultation type	Disease activity status	HAQ-DI* (mean, SD)	RAID* (mean, SD)	EQ-5D¶ (mean, SD)
Face-to-face	Remission	0.60 (0.6)	3.13 (2.3)	0.77 (0.19)
	Inflammation	1.10 (0.7)	4.32 (2.2)	0.66 (0.26)
Electronic	Remission	0.56 (0.6)	2.64 (2.2)	0.79 (0.18)
	Inflammation	1.03 (0.7)	4.62 (2.1)	0.66 (0.24)

Note. HAQ-DI: Health Assessment Questionnaire - Disability Index, RAID: Rheumatoid Arthritis Impact of Disease. Disease activity status (DAS28CRP): remission < 2.6, inflammation ≥ 2.6; higher scores on RAID and HAQ-DI indicate worse outcomes. *p<0.05 in face-to-face group. ¶p<0.05 in electronic group

Table 3. Cost-utility analysis

	Costs	HAQ-DI (QALYs)	RAID (QALYs)	QALYs*
E-consultations	€2,874,021	298 (285)	1363 (285)	285
Face-to-face consultations	€3,285,435	311 (282)	1397 (272)	283
Increment	- €411,414	- 13 (2.5)	- 34 (1.8)	2.6
ICER		- €31,816 (- €163,159)	- €12,265 (- €223,002)	- €161,491

Note. A higher score on the questionnaires is worse; therefore the effect is reversed; *obtained from the EQ-5D