MR imaging of the knee in primary care

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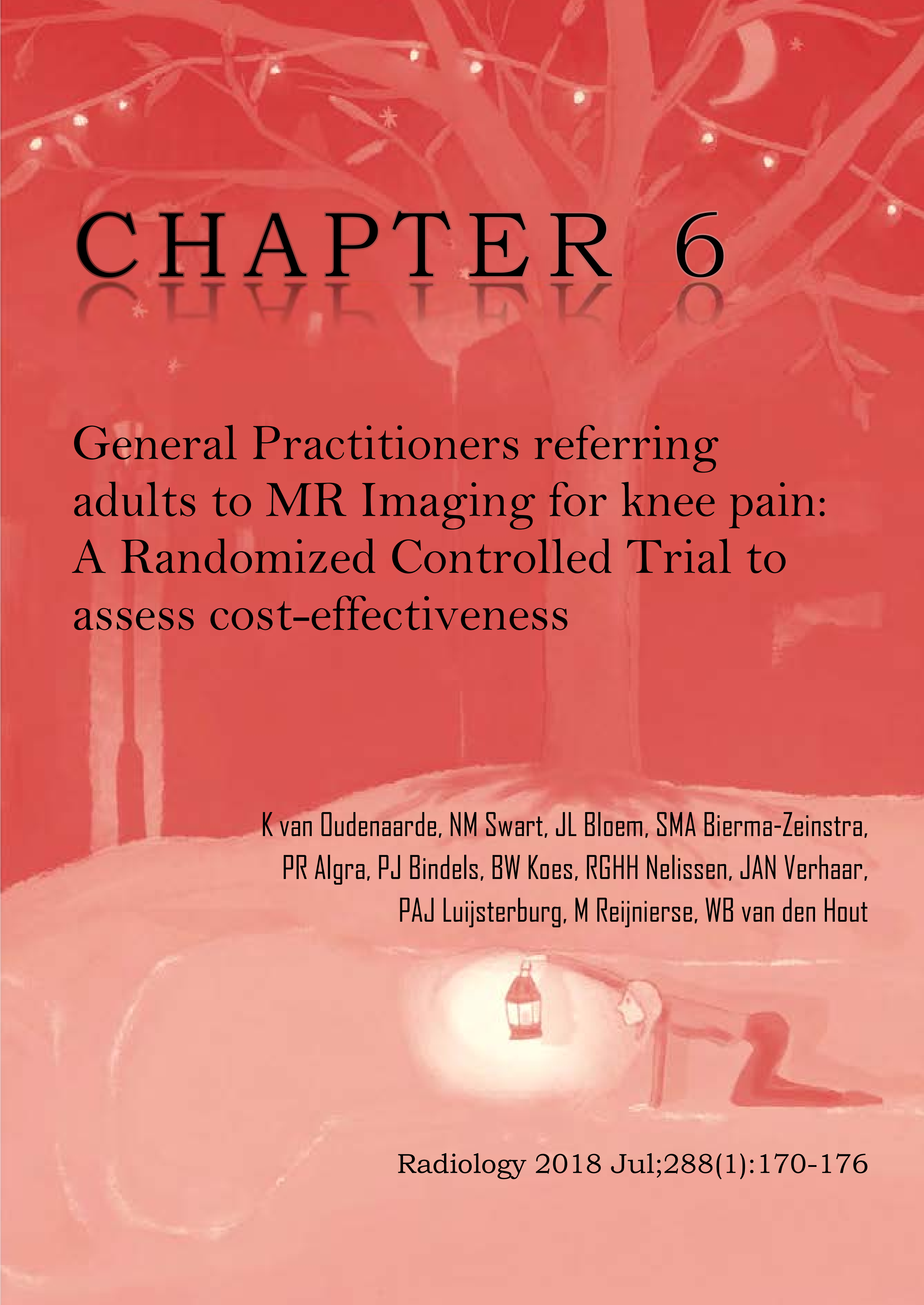
Title: MR imaging of the knee in primary care
Issue Date: 2018-11-22



CHAPTER 6

General Practitioners referring adults to MR Imaging for knee pain: A Randomized Controlled Trial to assess cost-effectiveness

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Radiology 2018 Jul;288(1):170-176

Abstract

Purpose

To determine the cost-effectiveness of early referral by the general practitioner for magnetic resonance (MR) imaging compared with usual care alone in patients aged 18–45 years with traumatic knee symptoms.

Materials and Methods

Cost-utility analysis was performed parallel to a prospective multicenter randomized controlled trial in Dutch general practice. A total of 356 patients with traumatic knee symptoms were included from November 2012 to December 2015 (mean age, 33 years ±8 [standard deviation]; 222 men [62%]). Patients were randomly assigned to usual care (n = 177; MR imaging was not performed, but patients were referred to an orthopedic surgeon when conservative treatment was unsatisfactory) or MR imaging (n = 179) within 2 weeks after injury. Main outcome measures were quality-adjusted life years (QALYs) and costs from a healthcare and societal perspective. Multiple imputation was used for missing data. The Student t test was used to assess differences in mean QALYs, costs, and net benefits.

Results

Mean QALYs were 0.888 in the MR imaging group and 0.899 in the usual care group (P = .255). Healthcare costs per patient were higher in the MR imaging group (€1109) than in the usual care group (€837) (P = .050), mainly due to higher costs for MR imaging, with no reduction in the number of referrals to an orthopedic surgeon in the MR imaging group.

Conclusion

MR imaging referral by the general practitioner was not cost-effective in patients with traumatic knee symptoms; in fact, MR imaging led to more healthcare costs, without an improvement in health outcomes.

Introduction

After lower back pain, knee pain is the most commonly reported musculoskeletal reason for patients to visit their general practitioner (GP).[1,2] Among these patients are those with knee pain due to trauma, which has a substantial effect on quality of life, especially in younger patients.[3] The estimated incidence of new knee injuries ranges from one to two cases per 1000 patients per year, with a peak incidence of four to six cases per 1000 patients per year in patients aged 15–25 years.[2,4]

Magnetic resonance (MR) imaging is the modality of choice in the diagnosis of a soft-tissue lesion, with a sensitivity of 87% and a specificity of 93% in the overall detection of meniscus and anterior cruciate ligament tears.[5,6] The high diagnostic accuracy of MR imaging made diagnostic arthroscopy obsolete and justified the use of MR imaging to make a diagnosis after knee trauma.[5]

Although the majority of knee MR examinations are still requested by orthopedic surgeons (with well-established added value), in the past decade, a shift toward earlier MR imaging in primary care has been seen.[7,8] The suggested potential beneficial effects of MR imaging in primary care are as follows: In case of negative findings, patients can be reassured and might be able to avoid unnecessary referrals to secondary care. In case of positive findings, an earlier diagnosis can be made, potentially resulting in earlier recovery.[8–14]

However, due to the lack of evidence regarding the added value of MR imaging in primary care, the Dutch College of General Practitioners guidelines[15] recommend not to request MR imaging in these patients. Other countries have developed similar guidelines that provide conflicting or unclear advice regarding when to perform MR imaging in primary care or when to refer to a patient to an orthopedic surgeon.[5,16–18]

The aim of this study was to determine the cost-effectiveness of early referral by the GP for MR imaging compared with usual care alone in patients with traumatic knee symptoms over a 1-year period.

Materials and Methods

All patients approved and signed the informed consent form before entering this study. The study was approved by the medical ethics committee of the Erasmus Medical Center and by the Dutch National Central Committee on Research Involving Human Subjects (Dutch trial registration, NTR3689).

Study Design and Patients

We conducted an economic evaluation parallel to a prospective pragmatic multicenter open-labeled noninferiority randomized controlled trial with 12 months of follow-up. Details of the research protocol already have been published.[9] We chose a noninferiority design, since MR imaging was regarded as a newly introduced diagnostic tool in general practice. The study was powered to detect this noninferiority.[9] From October 2012 to December 2015, patients aged 18–45 years who consulted or reconsulted their GP with knee symptoms due to a traumatic injury or a sudden onset of pain, function loss, or both in the preceding 6 months were included. The age criterion (≤45 years) was chosen to exclude subjects with a relatively higher prevalence of degenerative findings for which no clear treatment options are currently available, meaning the MR findings would have had little influence on subsequent treatment. Exclusion criteria were indications for direct referral (eg, a fracture or a locked knee), patients already in secondary care for their current knee symptoms, previous surgery in the affected knee, knee osteoarthritis diagnosed earlier by a physician, other nontraumatic arthropathy (eg, isolated patellofemoral pain or patella luxation), a previous MR examination for current knee symptoms, and contraindications to MR imaging. When a patient again consulted the GP with persistent knee symptoms and was not invited to participate during the first visit, the patient was only eligible for inclusion when the performed diagnostics and treatment adhered to Dutch guidelines after the first consultation, without MR imaging or an orthopedic referral. These patients still experienced symptoms of traumatic knee injury but usually had a longer history of symptoms. A total of 150 GPs located in the western part of the Netherlands invited all the patients included in this trial directly during consultation or afterward by sending invitation letters to eligible patients who were missed during the first consultation.

Randomization and Subject Group

After the patients signed the informed consent form and completed the first questionnaire, the researchers (KvO, NMS) performed the randomization. An independent person produced a randomization list with a computer by using random blocks of four and six without stratifying for patient characteristics. The researchers had no access to the randomization list, resulting in a concealed allocation that could not be predicted or influenced. A total of 356 patients (mean age, 33 years 6 8 [standard deviation]; age range, 18–45 years) were included and randomly assigned to one of the groups. Of these patients, 222 (62%) were male, with a mean age of 32 years ± 8 (range, 18–45 years), and 134 were female (38%; mean age, 33 years ± 8; range, 18–45 years). Mean duration of symptoms was 52 days ± 44.

Patients were evenly allocated to undergo either usual care or MR imaging, and no patient or caregiver was blinded to group assignment (Fig 1). Patients in the usual care group were treated by the GP according to Dutch clinical guidelines[15] which provide advice on (a) whether rest or specific exercises are necessary, (b) pain medication, and (c) physiotherapy. All GPs in this study were instructed not to request an MR examination in this trial arm when the former treatment did not have satisfactory results but to refer the patient to an orthopedic surgeon. Patients in the MR group underwent MR imaging within 2 weeks after completing the first questionnaire in addition to usual care based on the aforementioned guidelines.[15]

Intervention: MR Imaging

MR imaging was performed with a 1.5-T MR imager by using a dedicated knee coil at six different centers (one university hospital, four peripheral hospitals, and a private MR center with several locations in the Netherlands). Prior to the start of the study, three radiologists evaluated and approved all “acute knee” MR protocols used at each center. These protocols were optimized for each MR imager, were familiar to the radiologists in that particular center, and provided a good reflection of the factual diagnostics, as used in the Netherlands. All protocols included sequences in the sagittal, coronal, and transverse planes, with at least one sequence with fat suppression and one gradient echo sequence targeted on cartilage damage.

Prior to the start of this study, two orthopedic surgeons defined positive MR findings that might need further assessment by an orthopedic surgeon (ie, trabecular fracture, complete rupture of a collateral ligament, meniscus tear, cruciate ligament rupture, fullthickness cartilage defect). In the present study, we specifically instructed and trained 12 musculoskeletal radiologists, each with at least 10 year of experience. Referral advice was based on the presence of positive MR findings and was automatically derived from an encrypted Web-based standardized MR imaging knee report.[19] The referring GP received a speech-based free-text report, as usual. In addition, radiologists were asked to conclude their MR report with the referral advice derived from the structured online MR report. These patients returned to their GP for the MR result and continued in primary care with treatment as described in the Dutch clinical guidelines[15], unless they were referred to an orthopedic surgeon, who would subsequently take over their care and treatment.

Primary Outcome Measures: QALYs and Costs

We performed a cost-utility analysis from a healthcare and societal perspective with a 1-year time horizon, according to the Consolidated Health Economic Evaluation Reporting Standards (or CHEERS).[20] We used the three-level EQ-5D questionnaire (Euroqol, Rotterdam, the Netherlands) to calculate quality-adjusted life years (QALYs) as the area under the curve of the utility scores measured over 12 months, according to the Dutch tariff.[21,22] Scores were measured at baseline, 6 weeks, and 3, 6, 9, and 12 months. Costs were evaluated by using self-reported questionnaires at 3, 6, 9, and 12 months, reflecting on the previous 3 months. Healthcare costs included costs for GP visits, physiotherapy sessions, orthopedic surgeon visits, MR imaging, conventional imaging, arthroscopy, hospital admission, and medication. Nonhealthcare costs included costs for work absenteeism, work presenteeism (reduced quality of work), unpaid work (groceries, housekeeping, children; calculated only over the differences between the two groups), housekeeping, caregiving by the family, traveling, and medical aids, such as knee braces or crutches. Unit costs sources are presented in the Table and were mostly derived from the Dutch guideline for economic evaluation with standard reference prices in Euros at the 2015 price level, without discounting.[23,24]

Statistical Analyses

All analyses were performed according to the intention-to-treat principle. Missing data were corrected for possible selective nonresponse by using multiple imputations with fully conditional specification and predictive mean matching.[25] We imputed 100 data sets with four iterations by using the following predictors: randomization group, age, sex, body mass index, loss to follow-up, clinical scores (eg, Lysholm scores), and utilities. The Student t test was used to assess differences in mean QALYs, costs, and net benefits between the MR group and the usual care group. $P<.05$ indicated a significant difference. We expressed cost-effectiveness by using cost-effectiveness acceptability curves from both a healthcare perspective and a societal perspective. Depending on the willingness to pay (WTP) per QALY, the acceptability curves show the probability that MR imaging has a more favorable net benefit (NB = WTP * QALYs - Costs), than does usual care. Additionally, we plotted 400 bootstrap replicates of the average difference in costs and effects in the incremental cost-effectiveness plane to express the uncertainty of our cost-effectiveness analysis. All analyses were performed by using statistical software (IBM SPSS, version 22.0; SPSS, Chicago, Ill).

Ancillary Analyses

Three secondary analyses were performed, two of which were purely in specific subgroups of patients. The first subgroup consisted of patients with a duration of knee symptoms of 4 weeks or longer, since referral to an orthopedic surgeon in the 1st weeks after knee trauma should have no effect on the treatment course, as stated in the Dutch clinical guidelines.[15] On the basis of these guidelines and with consensus in the project research group (GPs, radiologists, and orthopedic surgeons), we intended to include only those patients with persistent knee symptoms lasting 4 weeks or longer. However, during the start of the study, the participating GPs preferred to also include patients with a shorter duration of symptoms, since this was more in keeping with daily practice. The second subgroup of patients also had knee symptoms for more than 4 weeks, and they were directly included during the first consultation by the GP. In the third and final ancillary analysis, which included all patients, we measured QALYs with the transformed Visual Analog Scale (VAS) of the EQ-5D questionnaire ranging from 0 (worst imaginable health) to 100 (perfect health) by using the power transformation $1 - (1 - VAS/100)^{1.61}$.

Results

Patients

The GPs invited 836 patients to participate in this study, 356 of whom could be included and randomized (Fig 1). Of the 179 patients allocated to the MR imaging group, 174 underwent MR imaging. Three patients did not attend their MR imaging appointment, one patient was pregnant, and one did not undergo MR imaging because of personal circumstances. Of the 177 patients allocated to the usual care group, at least 10 underwent MR imaging requested by the GP (responders' data).

QALYs and Costs

No significant differences were found in mean QALYs over the 12-month follow-up period between the MR group and the usual care group (0.888 vs 0.899, P = .225) (Fig 2). There were significantly higher healthcare costs per patient in the MR group (€1109) than in the usual care group (€837) (mean difference, €273; 95% confidence interval: 0, 545) (Table). This difference was mainly based on higher costs of MR imaging and on insignificantly higher costs of physiotherapy and arthroscopy in the MR group. In the MR group, 22% of patients underwent arthroscopy compared with 16% of patients in the usual care group (P = .150). Furthermore, insignificant higher nonhealthcare costs were observed in the MR group (mean difference, €302; 95% confidence interval: -2659, 3262). These higher nonhealthcare costs were mainly based on higher costs for work absenteeism in the MR group, with a mean of 10.3 absent workdays in the MR group compared with 7.8 absent workdays in the usual care group (P = .188).

Figure 1: Flowchart shows patient allocation in this randomized controlled trial. *GP* = general practitioner, *IQR* = interquartile range.

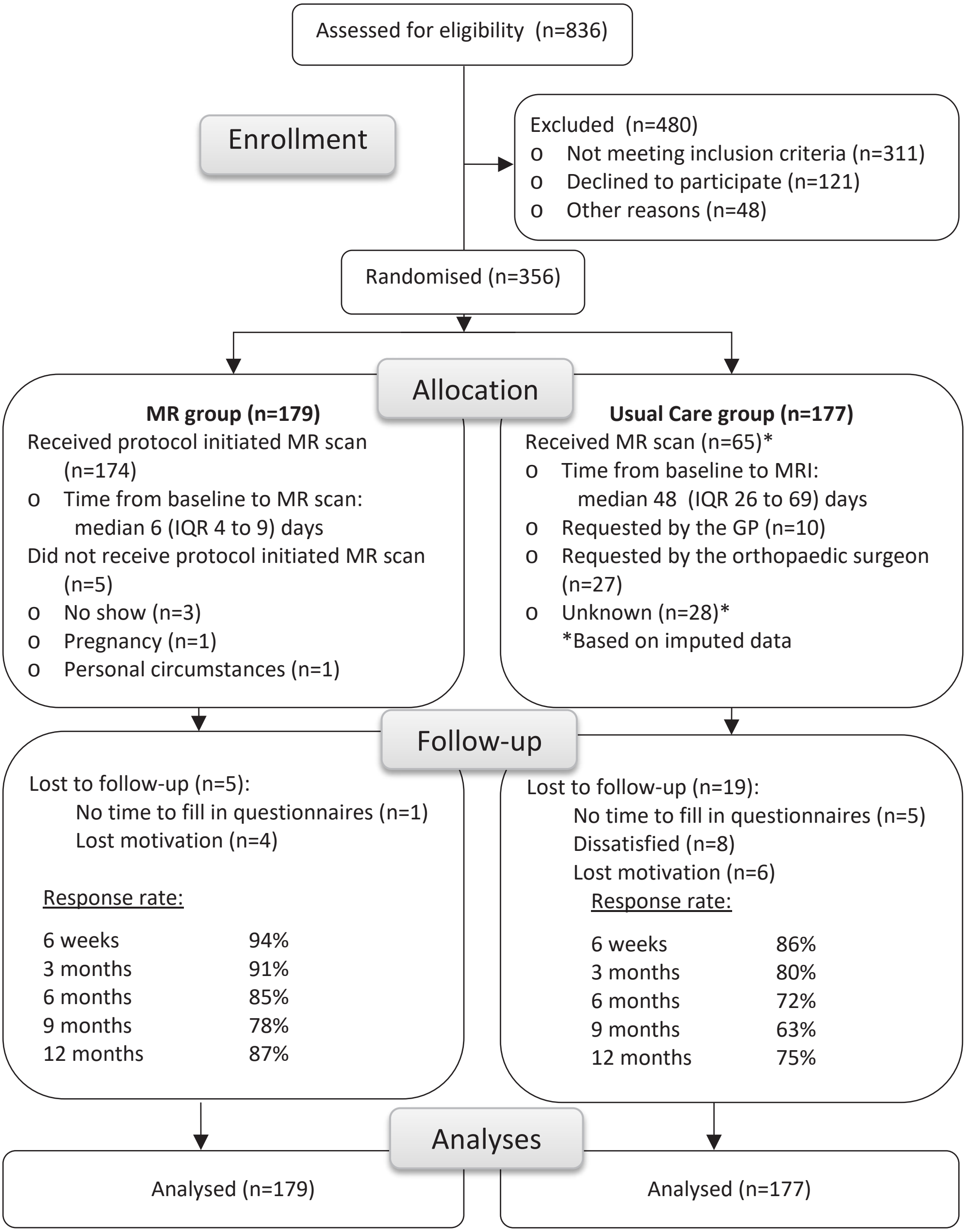
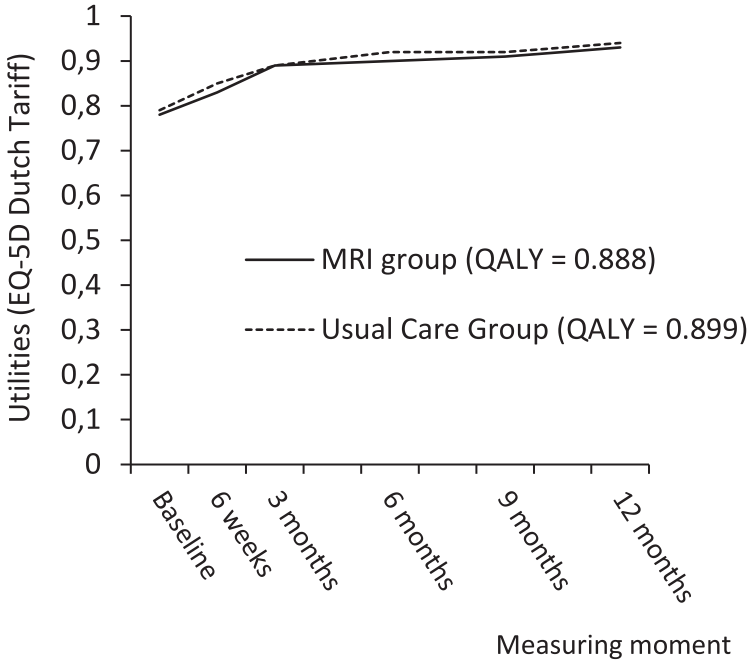


Table 1 Healthcare and non-healthcare costs per patient over the 12-months follow-up (n=356)

			MRI group n=179			Usual Care group n=177			
	Unit costs in €	Costs Source	Overall (%)	Mean volume	Costs in €	Overall (%)	Mean volume	Costs in €	Mean difference in costs in € (95%CI)
GP visit	33	A	41	0.84	28	47	1.13	37	-9 (-20 to 1)
Physical therapy sessions	33	A	60	10.58	349	55	8.52	281	68 (-56 to 192)
Orthopaedic surgeon visit	91	A	44	1.20	109	41	1.20	109	0 (-37 to 37)
Other medical specialists visit[a]	91	A	9	0.19	17	8	0.17	16	2 (-15 to 18)
Company doctor visit	100	B	12	0.26	26	12	0.30	30	-4 (-26 to 19)
Nursing help, hours	73/hr	A	0	0	0	0	0.22	16	16 (-48 to 15)
Conventional imaging	42	B	32	0.34	14	35	0.38	16	-2 (-7 to 3)
MRI scan	215	A	100	1.09	235	37	0.44	94	140 (115 to 166)
Arthroscopy	950	B	22	0.25	235	16	0.18	166	69 (-31 to 168)
Hospital admission (daycare), days	276	A	23	0.30	82	15	0.18	50	31 (-2 to 65)
Hospital admission (clinical), nights	476	A	2	0.02	12	3	0.04	18	-6 (-26 to 14)
Intra-articular injections	4	C	4	0.04	0	8	0.11	0	0 (-1 to 0)
Medication		C	34	NA	2	34	NA	3	-1 (-4 to 2)
Total healthcare costs					**1,109**			**837**	**273 (0 to 545)**
Absenteeism, days[b]	35/hr	A, D	54	10.3	2,520	49	7.8	2,046	474 (-498 to 1,446)
Presenteeism, reduced quantity[c]	35/hr	A, D	38	4%	1,872	37	4%	1,856	17 (-907 to 940)
Unpaid self-produced labour[d], hours	-14/hr	A	100	1269	-90	100	1256	93	-184 (-2,756 to 2,389)
Housekeeping help, hours	20/hr	A	4	55	55	2	12	12	43 (-14 to 100)
Help by family, hours	14/hr	A	9	7.3	103	14	10.5	148	-45 (-170 to 79)
Travel costs		A	100	NA	25	75	NA	19	6 (0 to 12)
Costs medical aids[e]		D	56	NA	41	58	NA	50	-9 (-24 to 6)
Total non-healthcare costs					**4,526**			**4,224**	**302 (-2,659 to 3,262)**
TOTAL COSTS					**5,635**			**5,061**	**574 (-2,462 to 3,611)**

95%CI: 95% confidence interval, A: guideline for economic evaluations (The Dutch National Healthcare Institute), updated September 2015. B: own data. C: www.medicijnkosten.nl, D: self-reported patient data [a]Other medical specialists, including surgeons, rheumatologists, revalidation specialists, neurologists. [b]Friction method: maximum of 85 absence days for a job with 5 workdays a week, i.e. maximum of 12 weeks absence, self-reported job hours and days per week, €34.75 per working hour (A), 90% of the patients had a paid job with a mean of 4.4 days and 33 hours per week. [c]Reduced quantity ranging from 0%: normal production quantity to 100%: produced nothing. Expressed as the mean percentage reduced quantity over 12 months. [d]Unpaid labour includes hours spent on housekeeping, groceries, odd jobs, volunteering, kids and education. Only the difference between groups calculated. [e]Medical aids includes costs for braces, compresses, inlays, crutches and salves.

Figure 2 Graph shows patients' utility scores and mean quality-adjusted life years (QALY) over the 12 months of follow up



QALY was measured as the area under the curve over 12 months with the EuroQol 5 dimensions (EQ-5D) utility score (Dutch tariff) ranging from -0.329 (worst health status) to 1.000 (best health status).

Cost-effectiveness

From a healthcare perspective, the probability that MR imaging is a cost-effective alternative to usual care ranged from 3% for €0 WTP per QALY (ie, when only costs count) to 8% for €80 000 WTP/QALY (ie, the unofficial upper bound threshold for cost-effectiveness in the Netherlands) (Fig 3). From a societal perspective, because of the larger uncertainty of the cost difference, the probability starts higher at 36% for €0 WTP/ QALY and then decreases to 21% for €80 000 WTP/QALY. The accompanying scatter plot (Fig 4) shows the majority of the bootstrap replicates in the northwest quadrant (91% for the healthcare perspective, 61% for the societal perspective), meaning overall higher costs for lower QALYs.

Figure 3 Probability that MR imaging in primary care is cost-effective compared to usual care in patients with traumatic knee complaints.

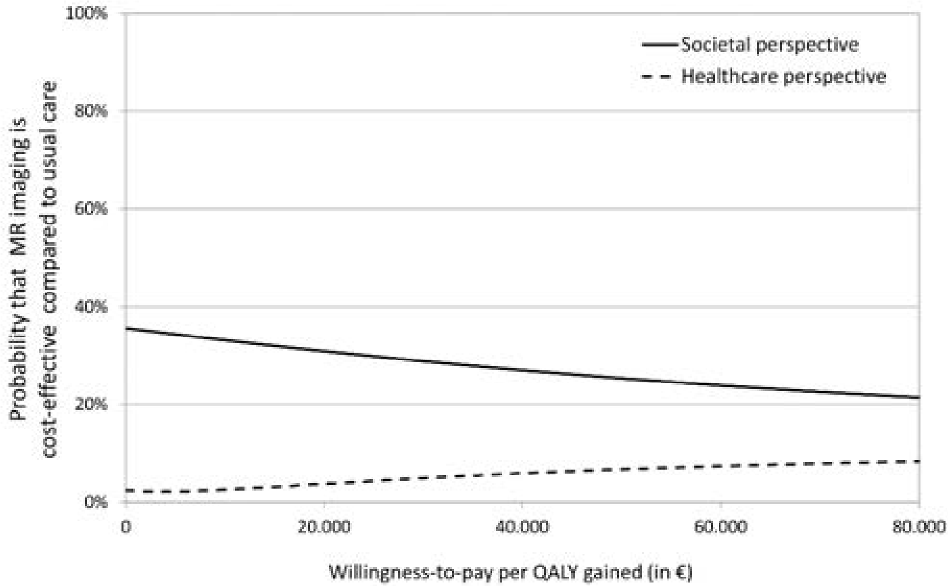
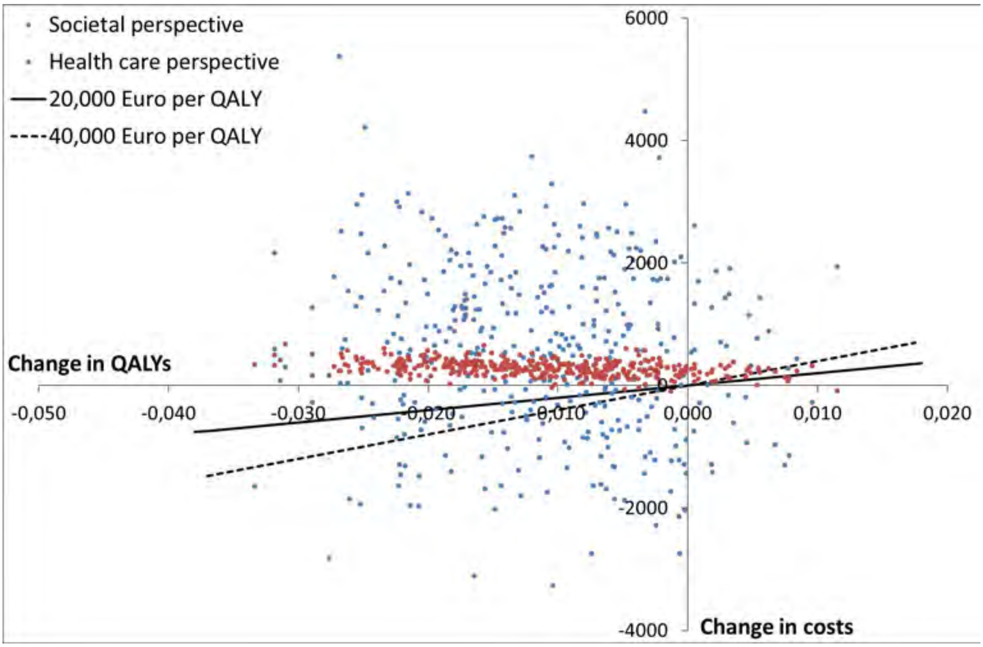


Figure 4 Incremental cost-effectiveness plane from a societal and healthcare perspective using 400 bootstrap replicates for each



Ancillary Analyses

In the Appendix we present the figures and tables for ancillary analyses. Most analyses enabled us to confirm the economic preference for usual care. Only the second exploratory analysis in the subgroup of patients directly included by the GP and with a duration of symptoms of 4 weeks or more (n = 94) showed a probability of MR imaging being cost-effective compared with usual care ranging from 75% for €0 WTP/ QALY to 83% for €20 000 WTP/QALY from a healthcare perspective. From a societal perspective, this was 58% and 62%, respectively. However, caution is required when interpreting these findings, as there were only 94 patients in this subgroup, implying considerable uncertainty.

Discussion

In patients aged 18–45 years with a traumatic knee symptoms seeking medical attention in a primary care setting, no differences in mean QALYS over the 12-month follow-up period were found between the MR group and the usual care group. The MR group had significantly higher healthcare costs, mainly because of more physiotherapy sessions and more arthroscopies, in addition to the study-initiated MR examinations. Furthermore, in the MR group, there was no reduction in the referral rate to an orthopedic surgeon. Total costs unrelated to healthcare were also slightly higher (this difference was not significant) in the MR group based on more work absenteeism. From the cost-utility analyses, we concluded that referral for early MR imaging by the GP is unlikely to be cost-effective compared with usual care in patients aged 18–45 years with traumatic knee symptoms.

In the United Kingdom, a randomized controlled trial was performed on the cost-effectiveness of MR imaging in a subgroup of patients suspected of having an internal derangement who were referred to an orthopedic surgeon.[10] Patients were randomly assigned to (a) imaging with a provisional orthopedic appointment or (b) orthopedic referral without prior MR imaging. The authors included 553 patients and analyzed 386 complete cases; no significant differences were found in mean QALYs over 24 months between these two groups.[26] The accompanying efficiency study showed that patients in the MR group also reported no significant improvement over time measured with the Short Form 36-item physical functioning scale in contrast to the patients in the direct orthopedic referral

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group.[27] In the cost-effectiveness study, only healthcare costs were considered and were higher in the MR group. In the MR group, 40% underwent arthroscopy compared with 28% in the orthopedic group, with more subsequent work absenteeism in the MR group; our results are in line with these findings.[10] On the basis of an insignificant increase in QALYs in the MR group of 1.444 compared with 1.393 in the orthopedic referral group, the authors concluded that MR imaging in primary care was 80% likely to be cost-effective in patients presenting with knee symptoms, with an incremental cost-effectiveness ratio of £5000 to £6,000 per QALY. However, the authors recommend caution when interpreting their findings because private costs and productivity losses were not considered, 30% of the cases were excluded because of missing data, and there was a potential recall bias with the last questionnaire reflecting on the past 12 months.

Another randomized controlled trial with cost-effectiveness analysis included 120 patients who presented to the emergency department with knee pain and who were referred to an orthopedic surgeon.[28] All patients underwent MR imaging; however, prior to the MR examination, patients were randomized and only half of the cohort was informed about the MR result. The other half, including the involved orthopedic surgeon, was blinded to the MR result (ie, the no MR imaging group). Overall, higher utilities with significantly lower costs were observed in the no MR imaging group (arthroscopy rate was 24% in this group and 30% in the MR imaging group), and these findings were in line with our results. Also, in patients with lower back pain, routine diagnostic imaging led to worse or, at best, unimproved self-reported outcomes, supporting the robustness of our findings.[29]

To our knowledge, this study is the first to thoroughly assess the cost-effectiveness of MR imaging in primary care. With a multicenter design involving 150 GPs and six different MR centers, we compiled a sample of patients aged 18–45 years with traumatic knee symptoms, reflecting (to a large extent) daily MR imaging practice. We evaluated a wide range of associated costs, including the costs for productivity losses. Furthermore, we analyzed all cases according to the intention-to-treat principle, without excluding cases for missing data. Possible attrition bias was handled with multiple imputations.

Unfortunately, difficulties were encountered in including a sufficient number of patients, despite our efforts to regularly remind GPs via telephone calls, office visits, and newsletters.

The sample size calculation in this study was based on the primary endpoint, which was to show noninferiority of knee-related daily function as measured with the Lysholm Knee Scoring Scale. The current study was developed to address secondary objectives of QALYs and costs; any observed null findings could be attributed to a lack of power. Eventually, the sample size was decreased from 520 to 356 patients, and invitation letters were sent to eligible patients who were not directly invited during the first consultation. The effect of this intervention was reviewed in the ancillary explorative analyses by using specific subgroups. These analyses were not predefined and have a low statistical power, with a small number of patients in each subgroup. Data on quality of life and costs were collected every 3 months, minimizing recall bias. Bias could have been introduced by the unblinded randomization. For patients who were satisfied with the randomization to MR imaging, this could hypothetically result in a higher quality of life in the MR imaging group that was not detected. We believe the unblinded randomization had no influence on the reported costs.

Furthermore, no data were collected on surgery for anterior cruciate ligament reconstruction, and we evaluated only the performed arthroscopies. However, this may not have affected our main results, because this probably concerns only a few patients evenly distributed over both groups, since most patients with an anterior cruciate ligament rupture do not undergo reconstructive surgery.[30]

On the basis of the present results, referral by the GP for MR imaging was not cost-effective in patients aged 18–45 years with traumatic knee symptoms. MR imaging led to more healthcare costs, without improving health outcomes. Although our exploratory analyses indicated that a subgroup of patients might exist in whom MR imaging could be cost-effective, the characteristics of this subgroup need to be evaluated in a future study. For the moment, usual care as described in the Dutch general practice guidelines (15) without referral for MR imaging and with referral to an orthopedic surgeon in patients with persistent knee symptoms should be the guideline of choice. Our results can also be applied to other healthcare systems in which healthcare providers other than orthopedic surgeons are involved in the primary care and diagnostic work-up of patients with symptoms after a traumatic knee injury. Not to request an MR examination might be challenging in the current climate of defensive medicine, in which patients are demanding and healthcare providers have a limited amount of time. With the presented results, we hope to support both patients and healthcare providers in the primary evidence-based care of patients with traumatic knee symptoms.

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Ancillary analysis 1

Subgroup of patients with a duration of knee complaints for 4 weeks or longer, n=218

Appendix Table 1 Baseline characteristics of a subgroup of patients with less than 4 weeks complaints (n=218)

Baseline characteristics	MR group n=102	Usual care group n=116
Age, mean (SD) years	34 (8)	33 (8)
Male gender, n (%)	66 (65)	66 (57)
Body Mass Index, mean (SD)	25 (4)	26 (4)
Duration of complaints at inclusion, mean (SD) days	73 (36)	79 (40)
Quality of Life, EQ-5D mean (SD)	0.820 (0.158)	0.822 (0.139)

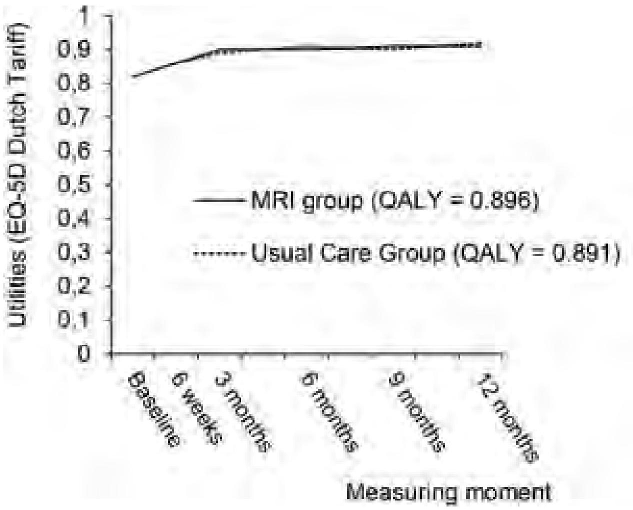
SD: standard deviation, EQ-5D: EuroQol 5 dimensions utility score with the Dutch tariff ranging from -0.329 (worst health status) to 1.000 (best health status)

Appendix Table 2 Healthcare and non-healthcare costs per patient over the 12-months follow-up in a subgroup of patients with traumatic knee complaints for 4 weeks or longer (n=218)

			MRI group n=102			**Usual Care group n=116**			
	Unit costs in €	Costs Source	Overall (%)	Mean volume	Costs in €	Overall (%)	Mean volume	Costs in €	Mean difference in costs in € (95%CI)
GP visit	33	A	40	0.81	27	42	0.94	31	-4 (-18 to 9)
Physical therapy sessions	33	A	54	7.74	256	46	6.46	213	42 (-84 to 169)
Orthopaedic surgeon visit	91	A	34	0.94	85	38	0.98	89	-4 (-46 to 38)
Other medical specialists visit[a]	91	A	10	0.23	21	9	0.21	19	2 (-22 to 25)
Company doctor visit	100	B	5	0.06	6	13	0.31	31	-24 (-49 to 0)
Nursing help, hours	73/hr	A	0	0	0	0	0	0	NA
Conventional imaging	42	B	24	0.27	11	30	0.35	14	3 (-10 to 3)
MRI scan	215	A	100	1.09	234	32	0.38	82	152 (121 to 182)
Arthroscopy	950	B	20	0.23	215	12	0.14	133	83 (-40 to 206)
Hospital admission (daycare), days	276	A	22	0.28	78	10	0.12	33	45 (3 to 86)
Hospital admission (clinical), nights	476	A	2	0.02	9	2	0.02	9	1 (-17 to 19)
Intra-articular injections	4	C	4	0.04	0	10	0.14	1	0 (-1 to 0)
Medication		C	33		2	34		1	1 (-1 to 2)
Total healthcare costs					**944**			**657**	**288 (-16 to 591)**
Absenteeism, days[b]	35/hr	A, D	46	7	1,664	49	8	2,012	-348 (-1,393 to 697)
Presenteeism, reduced quantity[c]	35/hr	A, D	38	5%	2,370	41	5%	2,261	109 (-1,325 to 1,544)
Unpaid self-produced labour[d], hours	-14/hr	A	100	1290	-87	100	1279	67	-154 (-3,348 to 3,039)
Housekeeping help, hours	20/hr	A	1	2	38	1	1	12	26 (-50 to 102)
Help by family, hours	14/hr	A	12	6	80	18	11	159	-78 (-207 to 51)
Travel costs		A	100		21	70		16	6 (-1 to 12)
Costs medical aids[e]		D	52		35	56		53	-17 (-37 to 2)
Total non-healthcare costs					**4,123**			**4,579**	**-457 (-4,160 to 3,246)**
TOTAL COSTS					**5,067**			**5,236**	**-169 (-3,937 to 3,599)**

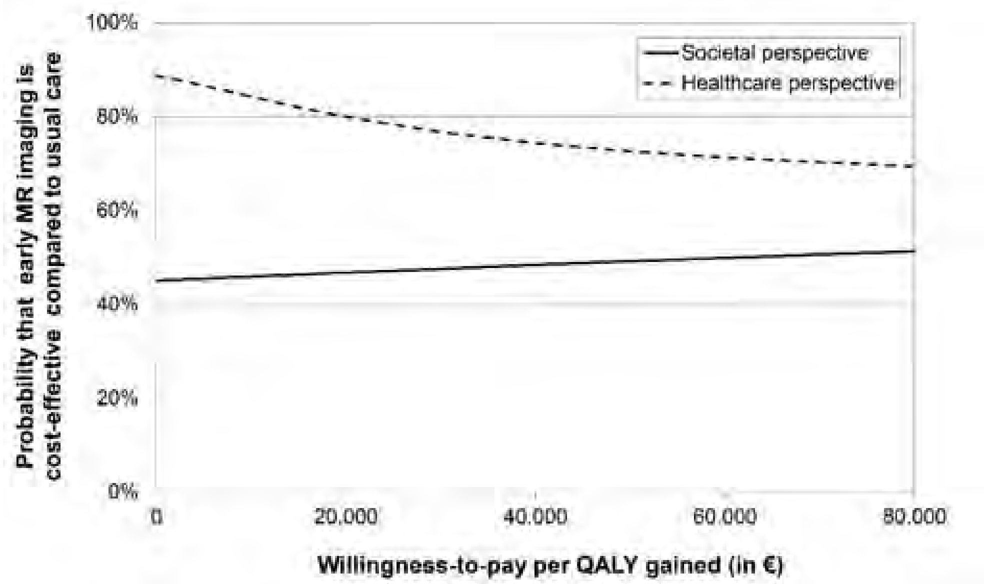
95%CI: 95% confidence interval, A: guideline for economic evaluations (The Dutch National Healthcare Institute), updated September 2015. B: own data. C: www.medicijnkosten.nl, D: self-reported patient data [a]Other medical specialists, including surgeons, rheumatologists, revalidation specialists, neurologists. [b]Friction method: maximum of 85 absence days for a job with 5 workdays a week, i.e. maximum of 12 weeks absence, self-reported job hours and days per week, €34.75 per working hour (A), 90% of the patients had a paid job with a mean of 4.4 days and 33 hours per week. [c]Reduced quantity ranging from 0%: normal production quantity to 100%: produced nothing. Expressed as the mean percentage reduced quantity over 12 months. [d]Unpaid labour includes hours spent on housekeeping, groceries, odd jobs, volunteering, kids and education. Only the difference between groups calculated. [e]Medical aids includes costs for braces, compresses, inlays, crutches and salves.

Appendix Figure 1 Patients' utility scores and mean QALY over the 12-months follow-up in a subgroup of patients with traumatic knee complaints for 4 weeks or longer (n=218)



QALY: Quality Adjusted Life Year measured as the area under the curve over 12 months with the EuroQol 5 dimensions utility score (Dutch tariff) ranging from -0.329 (worst health status) to 1.000 (best health status)

Appendix Figure 2 Probability that MR imaging in primary care is cost-effective compared to usual care in a subgroup of patients with knee complaints for 4 weeks or longer (n=218)



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Ancillary analysis 2

Subgroup of patients with more than 4 weeks of complaints and directly included by the general practitioner, n=94

Appendix Table 1 Baseline characteristics of a subgroup of patients with less than 4 weeks complaints (n=218)

Baseline characteristics	MR group n=43	Usual care group n=51
Age, mean (SD) years	32 (9)	33 (8)
Male gender, n (%)	26 (60)	29 (57)
Body Mass Index, mean (SD)	24 (4)	25 (3)
Duration of complaints at inclusion, mean (SD) days	64 (37)	69 (37)
Quality of Life, EQ-5D mean (SD)	0.812 (0.137)	0.806 (0.107)

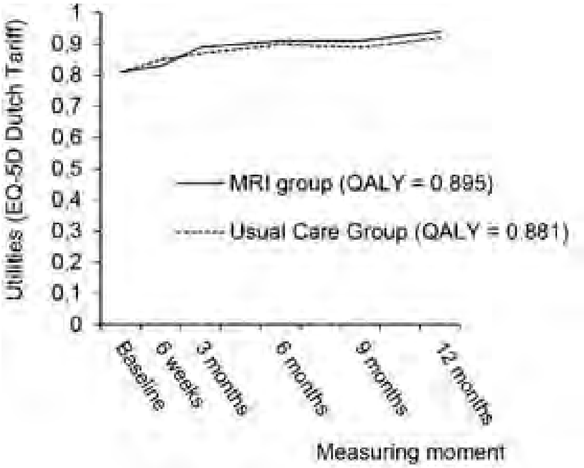
SD: standard deviation, EQ-5D: EuroQol 5 dimensions utility score with the Dutch tariff ranging from -0.329 (worst health status) to 1.000 (best health status

Appendix Table 4 | Healthcare and non-healthcare costs per patient over the 12-months follow-up in a subgroup of patients with ≥4 weeks complaints and directly included by the general practitioner (n=94)

			MRI group n=43			**Usual Care group n=51**			
	Unit costs in €	Costs Source	Overall (%)	Mean volume	Costs in €	Overall (%)	Mean volume	Costs in €	Mean difference in costs in € (95%CI)
GP visit	33	A	53	0.93	31	68	1.23	40	-10 (-29 to 9)
Physical therapy sessions	33	A	75	7.47	246	73	9.02	298	-51 (-227 to 125)
Orthopaedic surgeon visit	91	A	50	1.03	94	65	1.35	123	-29 (-88 to 30)
Other medical specialists visit[a]	91	A	24	0.23	21	43	0.52	47	-26 (-61 to 8)
Company doctor visit	100	B	24	0.17	17	43	0.50	50	-32 (-70 to 5)
Nursing help, hours	73/hr	A	0	0	0	0	0	0	NA
Conventional imaging	42	B	43	0.37	15	60	0.59	25	-9 (-20 to 1)
MRI scan	215	A	100	1.08	232	57	0.59	127	106 (60 to 151)
Arthroscopy	950	B	34	0.26	243	45	0.33	316	-74 (-276 to 130)
Hospital admission (daycare), days	276	A	26	0.22	60	32	0.23	62	-2 (-55 to 50)
Hospital admission (clinical), nights	476	A	17	0.08	36	33	0.14	69	-33 (-90 to 25)
Intra-articular injections	4	C	23	0.11	0	44	0.30	1	-1 (-1 to 0)
Medication		C	50		2	65		2	0 (-1 to 1)
Total healthcare costs					**999**			**1,160**	**-161 (-630 to 308)**
Absenteeism, days[b]	35/hr	A, D	48	4	1,026	66	7	1,783	-757 (-1,735 to 221)
Presenteeism, reduced quantity[c]	35/hr	A, D	54	4%	2,421	72	5%	2,463	-42 (-1,713 to 1,629)
Unpaid self-produced labour[d], hours	-14/hr	A	100	1280	335	100	1324	-285	620 (-3,179 to 4,419)
Housekeeping help, hours	20/hr	A	8	5	100	14	2	39	62 (-114 to 237)
Help by family, hours	14/hr	A	27	7	103	49	20	286	122 (-422 to 56)
Travel costs		A	100		22	88		24	-3 (-12 to 7)
Costs medical aids[e]		D	63		45	76		77	-32 (-61 to -3)
Total non-healthcare costs					**4,052**			**4,387**	**-335 (-4,870 to 4,200)**
TOTAL COSTS					**5,050**			**5,546**	**-496 (-5,150 to 4,158)**

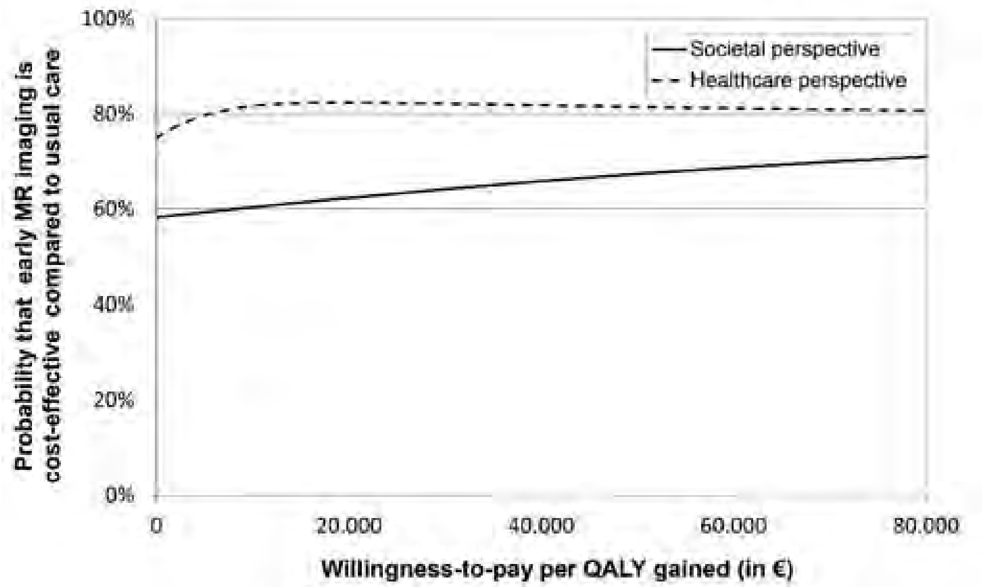
95%CI: 95% confidence interval, A: guideline for economic evaluations (The Dutch National Healthcare Institute), updated September 2015. B: own data. C: www.medicijnkosten.nl, D: self-reported patient data [a]Other medical specialists, including surgeons, rheumatologists, revalidation specialists, neurologists. [b]Friction method: maximum of 85 absence days for a job with 5 workdays a week, i.e. maximum of 12 weeks absence, self-reported job hours and days per week, €34.75 per working hour (A), 90% of the patients had a paid job with a mean of 4.4 days and 33 hours per week. [c]Reduced quantity ranging from 0%: normal production quantity to 100%: produced nothing. Expressed as the mean percentage reduced quantity over 12 months. [d]Unpaid labour includes hours spent on housekeeping, groceries, odd jobs, volunteering, kids and education. Only the difference between groups calculated. [e]Medical aids includes costs for braces, compresses, inlays, crutches and salves.

Appendix Figure 3 Patient utilitiy scores and mean QALY over the 12-months follow-up in a subgroup of patients with more than 4 weeks complaints and directly included by the GP (n=94)



QALY: Quality Adjusted Life Year measured as the area under the curve over 12 months with the EuroQol 5 dimensions utility score (Dutch tariff) ranging from -0.329 (worst health status) to 1.000 (best health status)

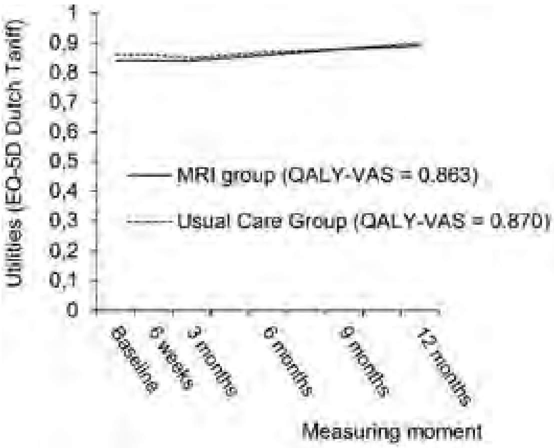
Appendix Figure 4 Probability that MR imaging in primary care is cost-effective compared to usual care in a subgroup of patients with more than 4 weeks complaints and directly included by the GP (n=94)



Ancillary analysis 3

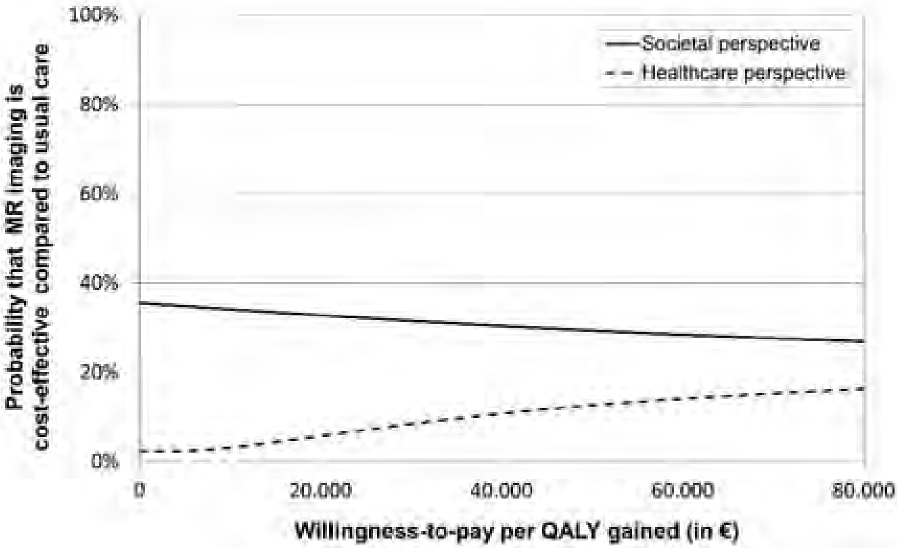
Cost-effectiveness using the Visual Analogue Scale (VAS) of the Euroqol, n=356

Appendix Figure 5 Patients' utility scores measured with a Visual Analogue Scale (VAS) over the 12-months follow-up (n=356)



QALY-VAS: Quality Adjusted Life Year – Visual Analogue Scale, measured with the Euroqol VAS as the area under the curve over 12 months using the power transformation 1-(1-VAS/100)^1.61. Ranging from 0 (worst health status) to 1 (best health status)

Appendix Figure 6 Probability that MR imaging in primary care is cost-effective compared to usual care in patients with traumatic knee complaints using a Visual Analogue Scale (n=356)



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