Title: Correlation between clinical and radiological outcome following matrix-induced autologous chondrocyte implantation in the femoral condyles.

Running Title: Correlation of clinical and radiological outcome following MACI.

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TITLE

Correlation of clinical and radiological outcome following matrix-induced autologous chondrocyte implantation in the tibiofemoral joint.

ABSTRACT

Background: Matrix-induced autologous chondrocyte implantation (MACI) is an established technique for the repair of knee chondral defects, though the correlation between clinical and radiological outcome following surgery is poorly understood.

Purpose: The aim of this study was to determine the correlation between clinical and radiological outcomes throughout the post-operative time line to five years following MACI.

Study Design: Retrospective study.

Methods: This retrospective study was undertaken in 83 patients (53 males, 30 females) with complete clinical and radiological follow up at 1, 2 and 5 years following MACI. The mean age of patients was 38.9 years (range, 13-62 years), with a mean body mass index (BMI) of 26.6 (range, 16.8-34.8), defect size of 3.3cm^2 (range, 1-9) and pre-operative duration of symptoms of 9.2 years (range, 1-46). Patients indicated for MACI in this follow-up were 13-65 years of age, though excluded if they had a BMI > 35, had undergone a prior extensive meniscectomy or had ongoing progressive inflammatory arthritis. Patients were assessed clinically using the Knee Injury and Osteoarthritis Outcome Score (KOOS). Magnetic resonance imaging (MRI) was used to evaluate graft assessment using a 1.5 T or 3 T clinical scanner. MRI assessment included eight parameters of graft repair (infill, signal intensity, border integration, surface contour, structure, subchondral lamina, subchondral bone and effusion) based on the magnetic resonance observation of cartilage repair tissue (MOCART), as well as an MRI composite score. Spearman's correlation coefficient (SCC) assessed the

degree of association between the MRI parameters KOOS subscales at each post-operative time point, and significance was determined at $p < 0.05$. Ethics approval was obtained from the appropriate hospital and university Human Research Ethics Committees, and informed consent was gathered from all patients.

Results: The only MRI parameter displaying consistent evidence of association with KOOS subscales was effusion, with a pattern of increasing strength of correlations over time, and statistically significant associations at 5 years with Pain (SCC 0.25, p=0.020), Activities of Daily Living (SCC 0.26, p=0.018) and Sport (SCC 0.32, p=0.003). Apart from a significant correlation between subchondral lamina and KOOS Sport at 1 year (SCC 0.27, p=0.016), no further significant findings were observed.

Conclusion: Apart from some consistent evidence of association between the KOOS and effusion, this analysis demonstrated limited correlative capacity between clinical and radiological outcomes up to 5 years post-surgery.

Keywords: matrix-induced autologous chondrocyte implantation, post-operative assessment, clinical outcome, radiological outcome, magnetic resonance imaging, correlation.

What is known about this subject: Matrix-induced autologous chondrocyte implantation (MACI) has demonstrated good clinical efficacy for the repair of full thickness articular cartilage defects in the knee. However, the correlation between clinical and radiological outcome following MACI surgery is poorly understood. This is an area that requires investigation, and may provide further insight into which MRI-based parameters are most associated with certain clinical outcomes. In time, this may provide further insight into which MRI-based parameters of evaluating graft repair are most important after MACI (as well as other types of cartilage repair), and how MRI may be used to predict longer-term maintenance of the repair, as well as the future progression/reoccurrence of pain/symptoms.

What this study adds to existing knowledge: While understanding the association between clinical and MRI-based outcomes after cartilage repair is important in treating these patients, there is a paucity of evidence currently available. There is currently no study of this size, specifically evaluating the correlation of a commonly used patient-reported outcome (PRO) measure (i.e. KOOS), with the most commonly employed MRI scoring system (MOCART) for evaluating cartilage repair, in patients following MACI.

INTRODUCTION

Matrix-induced autologous chondrocyte implantation (MACI) has become an established technique for the repair of full thickness chondral defects in the knee,[6, 8, 23] and involves isolating and culturing a patient's own chondrocytes *in vitro*, and then re-implanting those cells into the cartilage defect. In order to evaluate patient outcome after MACI, there has been an increasing need to develop accurate, yet non-invasive ways to assess patient-reported pain and function, as well as the quality of tissue repair after surgery.

Several commonly used patient-reported outcome (PRO) measures have been employed to evaluate outcome after MACI, including: the Knee Injury and Osteoarthritis Outcome Score (KOOS)[19, 23, 33, 45];[50] the Lysholm score;[6, 8, 31, 33, 45] the Tegner activity scale;[6, 8, 31, 32, 45] the Visual Analogue Pain Scale (VAS);[19, 27, 63] the International Knee Documentation Committee (IKDC) Subjective Knee Form;[27, 33] the Cincinnati Knee Rating System[5, 45] and; the Short Form Health Survey (SF-36).[4, 19, 31] Furthermore, magnetic resonance imaging (MRI) has also demonstrated efficacy in the evaluation of tissue repair[1, 16, 39, 40, 47, 59] and, while a number of MRI scoring systems have been reported,[29, 40, 47, 59] the magnetic resonance observation of cartilage repair tissue (MOCART)[39, 40] classification has been the most common system utilized for cartilage repair.[10]

While clinical and radiological improvement has been well documented after MACI, the correlation between clinical and MRI-based outcome is poorly understood. Better understanding of this link may provide further insight into which MRI-based parameters are most associated with clinical outcomes and which are most important after MACI, and how MRI may be used to predict longer-term maintenance of the MACI graft repair, as well as the future reoccurrence of pain and/or symptoms. Two recent systematic reviews have

highlighted the paucity and heterogeneity of studies currently available,[10, 15] as well as the need for more robust studies with longitudinal clinical and MRI follow-up after various cartilage repair techniques,[10] in order to better define the correlation between these outcomes. The aim of this study was to determine the correlation between clinical and radiological outcome throughout the post-operative time line to five years following MACI.

MATERIALS AND METHODS

Patients

This retrospective analysis consisted of 83 patients (53 males, 30 females) that underwent MACI to address femoral condylar defects (62 medial, 21 lateral), between June 2002 and June 2007. All patients had complete clinical and radiological follow up at 1, 2 and 5 years post-surgery. Prior to MACI, none of the patients had undergone prior extensive meniscectomy or had ongoing progressive inflammatory arthritis. Patients indicated for MACI in this follow-up were 13-65 years of age and all suffered from persistent pain associated with grade III or IV chondral lesions, assessed with the International Cartilage Repair Society (ICRS) chondral defect classification system.[12] Patients with ligamentous instability or varus/valgus abnormalities (> 3° tibiofemoral anatomic angle) underwent MACI, provided these were addressed prior to or at the time of MACI grafting. Patients were further excluded if they had a body mass index (BMI) > 35, had undergone a prior extensive meniscectomy or had ongoing progressive inflammatory arthritis.

The mean age of patients in this retrospective analysis was 38.9 years (range, 13-62 years), the mean body mass index (BMI) was 26.6 (range, 16.8-34.8) and the mean defect size at implantation was 3.3cm^2 (range, 1-9). The pre-operative duration of symptoms was 9.2 years (range, 1-46) and, on average, patients had undergone 1.4 prior procedures (range, 0-4). At the time of surgery, 7 of the 83 patients had concomitant documented procedures at the time of MACI grafting, including high tibial osteotomy (n, 1), partial meniscectomy (n, 2), anterior cruciate ligament (ACL) reconstruction (n, 3) and posterior cruciate ligament (PCL) reconstruction (n, 1). Ethical approval was obtained from the appropriate hospital and

university Human Research Ethics Committees, and all patients had provided signed informed consent to allow their clinical data to be de-identified and used for research programmes.

The MACI Surgical Technique

The MACI technique has been previously described.[19, 23] MACI is a 2-stage technique, where arthroscopic surgery was initially performed to harvest a sample of normal articular cartilage from a non weight-bearing area of the knee. After harvest, chondrocytes were isolated, cultured and seeded onto a type I/III collagen membrane (ACI-Maix, Matricel GmbH, Herzogenrath, Germany) ex vivo over a 6- to 8-week period. At the time of second-stage implantation, the chondral defect was prepared via an open mini-arthrotomy by removing all damaged cartilage down to, but not through, the subchondral bone plate. The defect was measured and used to shape the membrane, which was secured to the bone using fibrin glue. The wound was closed after assessment of graft stability.

Outcome Measures

Clinical Assessment

All patients in this cohort completed the Knee Injury and Osteoarthritis Outcome Score (KOOS) at 1, 2 and 5 years after MACI. The KOOS is a knee specific questionnaire which includes 42 questions in five individual subscales: Pain, Symptoms, Activities of Daily Living (ADL), Sport and Recreation (Sport/Rec) and Knee Related Quality of Life (QOL).[50] Each of these five subscales is scored from 0 (worst) to 100 (best). The KOOS has been recommended for use with cartilage repair patients[49] and, more recently, has demonstrated validity and reliability in patients after the surgical treatment of focal cartilage lesions.[9] It has been used extensively in patients following ACI. [7, 17, 19, 23, 33, 43, 45, 48, 51, 65, 66]

Radiological Assessment

All patients underwent MRI scans on their operated knee at 1, 2 and 5 years after MACI, performed using 1.5 T or 3 T clinical scanners (Siemens, Erlangen, Germany; Philips, Best, the Netherlands; General Electric, Milwaukee, WI, USA). All examinations were performed using a dedicated knee coil with 4, 8 or 16 receiver channels, depending on the particular scanner. Standardized proton density and T2-weighted fat-saturated images were obtained in coronal and sagittal planes (slice thickness 3 mm, field of view 14-15 cm, 512 matrix in at least one axis for proton density images with a minimum 256 matrix in one axis for T2-weighted images). Additional axial proton density fat-saturated images were obtained (slice thickness 3-4 mm, field of view 14-15 cm, minimum 224 matrix in at least one axis).

Radiological assessment of the post-operative MACI grafts in this study was assessed in two ways. Firstly, we employed the magnetic resonance observation of cartilage repair tissue (MOCART) scoring system,[39, 40] whereby eight pertinent parameters of graft repair (signal intensity, graft infill, border integration, surface contour, structure, subchondral lamina, subchondral bone and effusion) were selected to best describe the morphology and signal intensity of the repair tissue, each scored individually from 1-4 (1=poor; 2=fair; 3=good; 4=excellent) in comparison to the native cartilage (Figure 1). An additional score of 3.5 for 'graft infill' was awarded for a fifth level (very good) corresponding with 'graft hypertrophy' (Figure 2).[40, 61] Secondly, an MRI composite score was calculated by multiplying each of the eight individual scores by a weighting factor,[48] and summing the weighted scores.[18, 48] This composite score also ranged from 1-4 (1=poor; 2=fair; 3=good; 4=excellent). MRI evaluation was performed by an independent, experienced musculo-skeletal radiologist, with almost 10 years of experience with the MOCART scoring system for cartilage repair since its initial publication in 2004.

Statistical Analysis

Firstly, the kappa coefficient was used to assess intra-observer reliability for the eight pertinent morphological MRI scores, while the intra-class correlation coefficient was used for the continuous MRI composite score. This was achieved by re-scoring 20 randomly selected MRI images filtered through a second time to the radiologist. Due to the ordinal nature of the MRI scoring system subscales, Spearman's correlation coefficient (SCC) with associated 95% confidence interval (CI), was used to assess the degree of association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with each of the five KOOS subscales at 1, 2 and 5 years after MACI. Analysis was performed using Stata/IC 13.1 for Windows (StataCorp LP, College Station, TX, USA).

RESULTS

Evaluation of intra-observer reliability for the MRI scoring system indicated perfect agreement for six of the eight individual MRI parameters (graft infill = 1.00; signal intensity = 1.00; border integration = 0.93; surface contour = 1.00; structure = 0.92; subchondral lamina = 1.00; subchondral bone = 1.00 and; effusion = 1.00), and an intra-class correlation coefficient for the MRI composite score of 0.996 (95%CI: 0.991 – 0.999), for the 20 randomly selected image pairs.

Figures 1 to 5 present the Spearman correlation coefficients with 95% confidence intervals and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with the KOOS subscales of Pain (Figure 3), Symptoms (Figure 4), ADL (Figure 5), Sport/Rec (Figure 6) and QOL (Figure 7), at each post-operative assessment time point (1, 2 and 5 years post-surgery). The only MRI parameter displaying consistent evidence of association with KOOS subscales was ‘effusion’, with a pattern of increasing strength of correlations over time, and statistically significant associations at 5 years with KOOS Pain (SCC 0.25, CI 0.04 to 0.45, p=0.020) (Figure 3), ADL (SCC 0.26, CI 0.05 to 0.45, p=0.018) (Figure 5) and Sport/Rec (SCC 0.32, CI 0.12 to 0.50, p=0.003) (Figure 6). Additionally, a significant correlation was observed between subchondral lamina with KOOS Sport-Rec at 1 year (SCC 0.27, CI 0.05 to 0.46, p=0.016) (Figure 6), though no further significant findings were observed.

Insert Figures 1-5.

DISCUSSION

In this study, limited correlative capacity was demonstrated between clinical and radiological outcomes up to 5 years post-surgery. The only morphological MRI scoring variable that was consistently associated with the KOOS was effusion, with the strength of the association between the two becoming stronger with time. Previous research has demonstrated significant associations between clinical scores and effusion (assessed via MRI) for osteochondral autologous transplantation[38, 56] and microfracture,[35] with only one study to the best of our knowledge in ACI[34] patients and all studies using the IKDC as the clinical measure. However, the clinical relevance of effusion to the graft must be evaluated with caution, given that the MOCART system (and all reported MRI-based scoring systems) specifically aims to score the graft repair, rather than the knee in general. Effusion may not be associated with the graft itself, rather a further unrelated knee condition, or ongoing knee degeneration. This may also reflect the increasing strength of the association throughout the post-operative time line.

Conflicting outcomes exist with respect to the correlation between clinical and MRI-based outcome after cartilage repair, at least in the limited and poorly reported literature specifically on correlative outcomes. This is highlighted by the findings of two recent systematic reviews on the topic;[10, 15] one of which concluded that graft hypertrophy and signal intensity were the strongest MRI-based correlates with clinical outcome after ACI,[10] the other found that the overall MRI score and graft infill were found to correlate most often with clinical outcome,[15] albeit after a range of cartilage repair procedures. We observed no correlations between graft infill, signal intensity or the composite score with KOOS domains, as outlined by these systematic reviews. Furthermore, we did not specifically evaluate graft hypertrophy as a parameter on its own, rather it was incorporated into the overall MRI composite score. Several studies specifically using the MOCART scoring system to evaluate ACI have

252 reported no correlation between clinical and radiological outcomes, using varied PRO clinical
253 measures and across varied post-operative time points.[18, 20, 23, 26, 46, 52, 54, 65, 67]
254
255 While the MOCART classification has been the most common system utilized for cartilage
256 repair,[10] there are a number of issues in using these morphological scoring systems for the
257 purposes in this study. Firstly, clearly the post-operative timeline will play an important role
258 in graft maturity and integration, with Blackman et al.[10] reporting that the most consistent
259 correlations between clinical and MRI-based assessments occur between 6-36 months. They
260 suggested the earliest time point with clinical utility is six months, given the MRI findings
261 that are considered abnormal before this time though are a normal part of the repair/healing
262 process. They also suggested the poor longer term correlations observed in their review may
263 reflect the potential for degenerative changes in the knee or a new (though unrelated) knee
264 injury. Second, given the most clinically relevant MRI parameters appear to differ between
265 different cartilage repair methods,[10] it is possible that they also differ between different
266 generations of ACI (periosteal, collagen-covered and matrix-induced ACI, as well as
267 arthroscopic methods of performing the technique). Therefore, the association between
268 clinical and MRI-based outcome may differ from one ACI patient to the next, depending on
269 the surgical and implantation method. Thirdly, using a composite score to evaluate MRI-
270 based outcome may disturb its use in predicting clinical outcome, given the large number of
271 variables that combine to make such a score.[14] Fourthly, the clinical significance of many of
272 these individual MRI-based variables is not completely understood, with particular reference
273 to subchondral bone and lamina.[32, 41] Furthermore, other factors not included in these
274 combined MRI-based scores, or even visible on MRI, such as inflammation, increased
275 vascular penetration and nerve growth, may also influence clinical outcome.[2, 3, 14] Finally, any
276 predictive value of MRI may prove difficult given the wide array of variables that may
277 influence patient outcome, including age,[13, 18, 19, 31, 36] BMI,[18, 30] chondral defect size,[18, 20, 24]

location[11, 42, 44] and aetiology,[46] joint degeneration[53] at the time of surgery, pre-operative duration of symptoms,[24, 36, 46, 51] number of prior knee surgeries[36] and post-operative rehabilitation.[19, 21, 22, 24]

A number of limitations existed within this retrospective study. Firstly, we employed the KOOS as our method of clinical assessment, though a number of other clinically important PROs have been employed to assess the effectiveness of ACI.[62] At present, there is currently no agreement on a 'gold standard' PRO measure for the evaluation of cartilage repair surgery,[28] let alone ACI. Tanner et al.[55] have reported that the KOOS and IKDC contain the most items important to post-operative knee patients, including ACL reconstruction, meniscal tears and osteoarthrtitis. However, all five KOOS subscales have previously demonstrated large effect sizes,[25, 49] while certain aspects of the KOOS such as the Sport/Rec and QOL subscales have scored higher in mean importance to patients, when compared with the IKDC.[28] Furthermore, the KOOS (in particular the Sport/Rec and QOL subscales) has shown to be very responsive to improvement after MACI surgery.[25]

Secondly, for the assessment of radiological outcome we employed a morphological scoring system,[39, 48, 61, 64] whereby morphological parameters may be less consistent and contingent on graft maturity.[14, 53, 58] While the MOCART classification has been the most common system utilized for cartilage repair,[10] new methods of assessing the biochemical characteristics of repair tissue are emerging.[37, 57, 60] This may assist in evaluating the 'ultra-structure' of the repair tissue[16] and, in time, may reflect a more accurate assessment of MRI-based outcome, thereby altering the correlation between MRI-based and patient-reported clinical outcomes. Thirdly, the outcomes of this retrospective analysis are limited to patients undergoing MACI to the femoral condyles. It has been shown that the most clinically relevant MRI parameters

differ between different cartilage repair methods[10] and, therefore, they may also differ between different generations of ACI and specific graft locations.

To the best of our knowledge, this is the first study to specifically determine the correlation of a commonly used PRO measure (i.e. KOOS), with the most commonly employed MRI scoring system (MOCART) for evaluating cartilage repair, in MACI patients to five years post-surgery. Apart from consistent evidence of association between KOOS subscales and effusion, with a pattern of increasing strength of correlations over time, this analysis demonstrated limited correlative capacity between clinical and radiological outcomes. Further research through larger prospective trials is required to better evaluate these associations in patients following varied generations of ACI, as well as different cartilage repair methods.

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FIGURE LEGENDS

FIGURE 1. Proton density fast spin echo magnetic resonance image of a MACI graft (between white arrows) to the medial femoral condyle at 5 years post-surgery, demonstrating equivalent signal and infill characteristics, as well as good integration with the adjacent native cartilage and underlying bone.

FIGURE 2. Proton density fast spin echo magnetic resonance image of a hypertrophic MACI graft (between white arrows) to the medial femoral condyle at 5 years post-surgery.

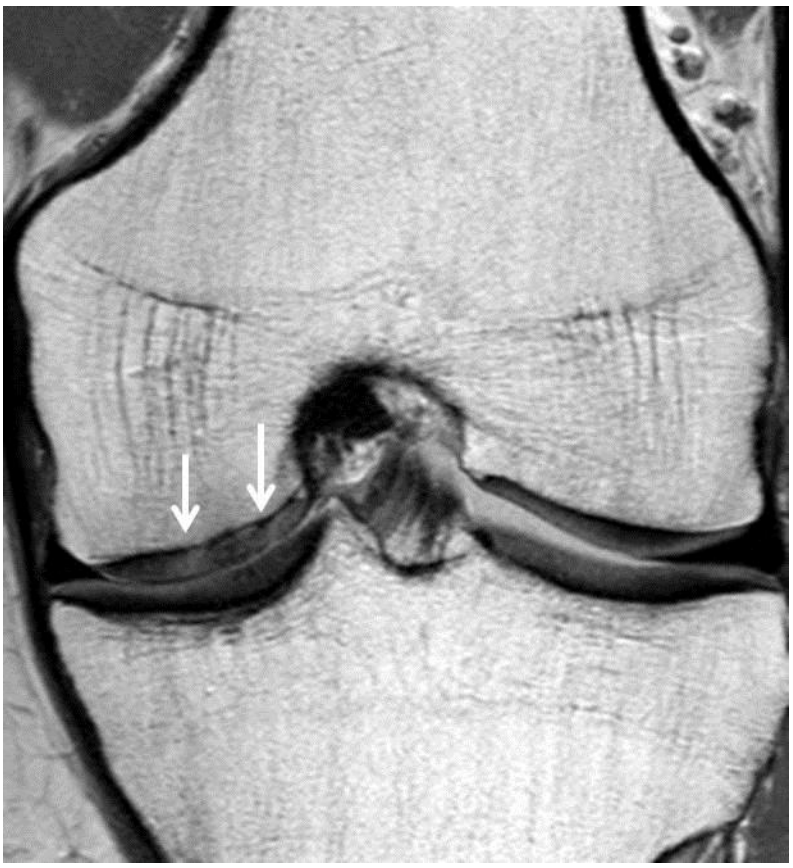
FIGURE 3. Spearman correlation coefficients with 95% confidence intervals (CI) and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with KOOS Pain at 1 year (1y), 2 years (2y) and 5 years (5y) after MACI.

FIGURE 4. Spearman correlation coefficients with 95% confidence intervals (CI) and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with KOOS Symptoms at 1 year (1y), 2 years (2y) and 5 years (5y) after MACI.

FIGURE 5. Spearman correlation coefficients with 95% confidence intervals (CI) and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with KOOS ADL at 1 year (1y), 2 years (2y) and 5 years (5y) after MACI.

FIGURE 6. Spearman correlation coefficients with 95% confidence intervals (CI) and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with KOOS Sport/Rec at 1 year (1y), 2 years (2y) and 5 years (5y) after MACI.

FIGURE 7. Spearman correlation coefficients with 95% confidence intervals (CI) and p-values for the association between each of the eight individual morphological MRI parameters, as well as the MRI composite score, with KOOS QOL at 1 year (1y), 2 years (2y) and 5 years (5y) after MACI.



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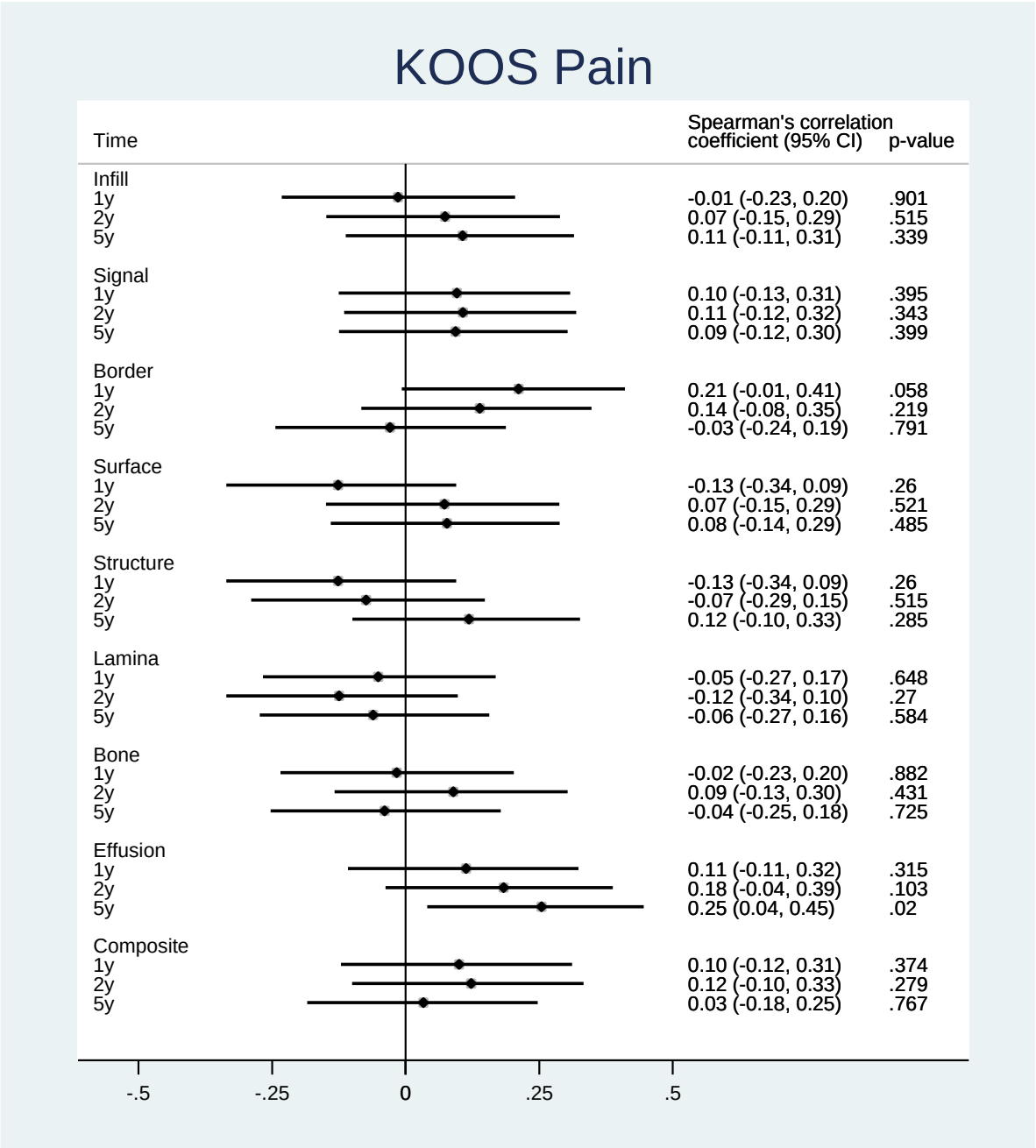
KOOS Pain
Time
Spearman's correlation coefficient (95% CI)
p-value
Infill
1y -0.01 (-0.23, 0.20) .901
2y 0.07 (-0.15, 0.29) .515
5y 0.11 (-0.11, 0.31) .339
Signal
1y 0.10 (-0.13, 0.31) .395
2y 0.11 (-0.12, 0.32) .343
5y 0.09 (-0.12, 0.30) .399
Border
1y 0.21 (-0.01, 0.41) .058
2y 0.14 (-0.08, 0.35) .219
5y -0.03 (-0.24, 0.19) .791
Surface
1y -0.13 (-0.34, 0.09) .26
2y 0.07 (-0.15, 0.29) .521
5y 0.08 (-0.14, 0.29) .485
Structure
1y -0.13 (-0.34, 0.09) .26
2y -0.07 (-0.29, 0.15) .515
5y 0.12 (-0.10, 0.33) .285
Lamina
1y -0.05 (-0.27, 0.17) .648
2y -0.12 (-0.34, 0.10) .27
5y -0.06 (-0.27, 0.16) .584
Bone
1y -0.02 (-0.23, 0.20) .882
2y 0.09 (-0.13, 0.30) .431
5y -0.04 (-0.25, 0.18) .725
Effusion
1y 0.11 (-0.11, 0.32) .315
2y 0.18 (-0.04, 0.39) .103
5y 0.25 (0.04, 0.45) .02
Composite
1y 0.10 (-0.12, 0.31) .374
2y 0.12 (-0.10, 0.33) .279
5y 0.03 (-0.18, 0.25) .767
-.5
-.25
0
.25
.5

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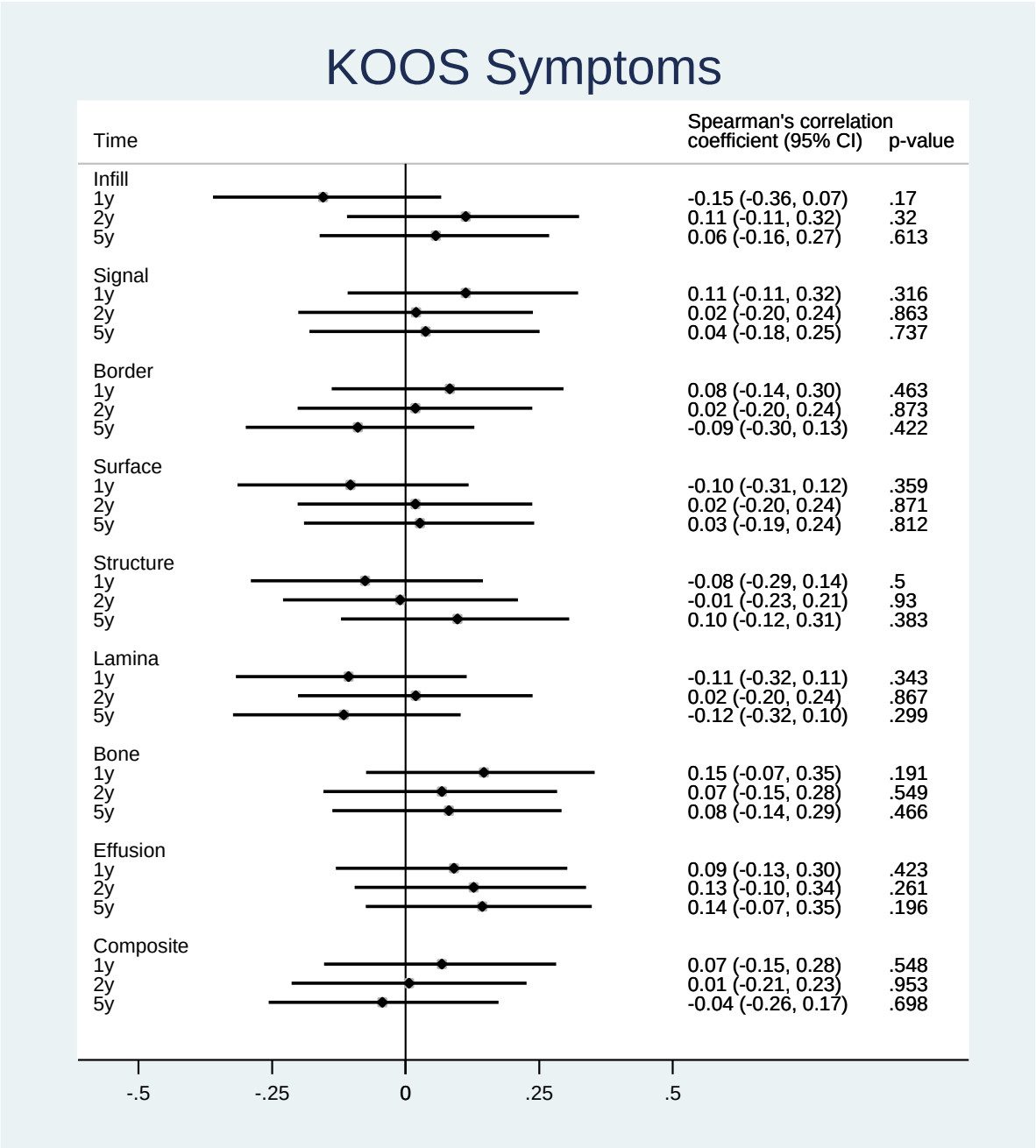
KOOS Symptoms
Time
Spearman's correlation coefficient (95% CI)
p-value
Infill
1y -0.15 (-0.36, 0.07) .17
2y 0.11 (-0.11, 0.32) .32
5y 0.06 (-0.16, 0.27) .613
Signal
1y 0.11 (-0.11, 0.32) .316
2y 0.02 (-0.20, 0.24) .863
5y 0.04 (-0.18, 0.25) .737
Border
1y 0.08 (-0.14, 0.30) .463
2y 0.02 (-0.20, 0.24) .873
5y -0.09 (-0.30, 0.13) .422
Surface
1y -0.10 (-0.31, 0.12) .359
2y 0.02 (-0.20, 0.24) .871
5y 0.03 (-0.19, 0.24) .812
Structure
1y -0.08 (-0.29, 0.14) .5
2y -0.01 (-0.23, 0.21) .93
5y 0.10 (-0.12, 0.31) .383
Lamina
1y -0.11 (-0.32, 0.11) .343
2y 0.02 (-0.20, 0.24) .867
5y -0.12 (-0.32, 0.10) .299
Bone
1y 0.15 (-0.07, 0.35) .191
2y 0.07 (-0.15, 0.28) .549
5y 0.08 (-0.14, 0.29) .466
Effusion
1y 0.09 (-0.13, 0.30) .423
2y 0.13 (-0.10, 0.34) .261
5y 0.14 (-0.07, 0.35) .196
Composite
1y 0.07 (-0.15, 0.28) .548
2y 0.01 (-0.21, 0.23) .953
5y -0.04 (-0.26, 0.17) .698
-.5
-.25
0
.25
.5

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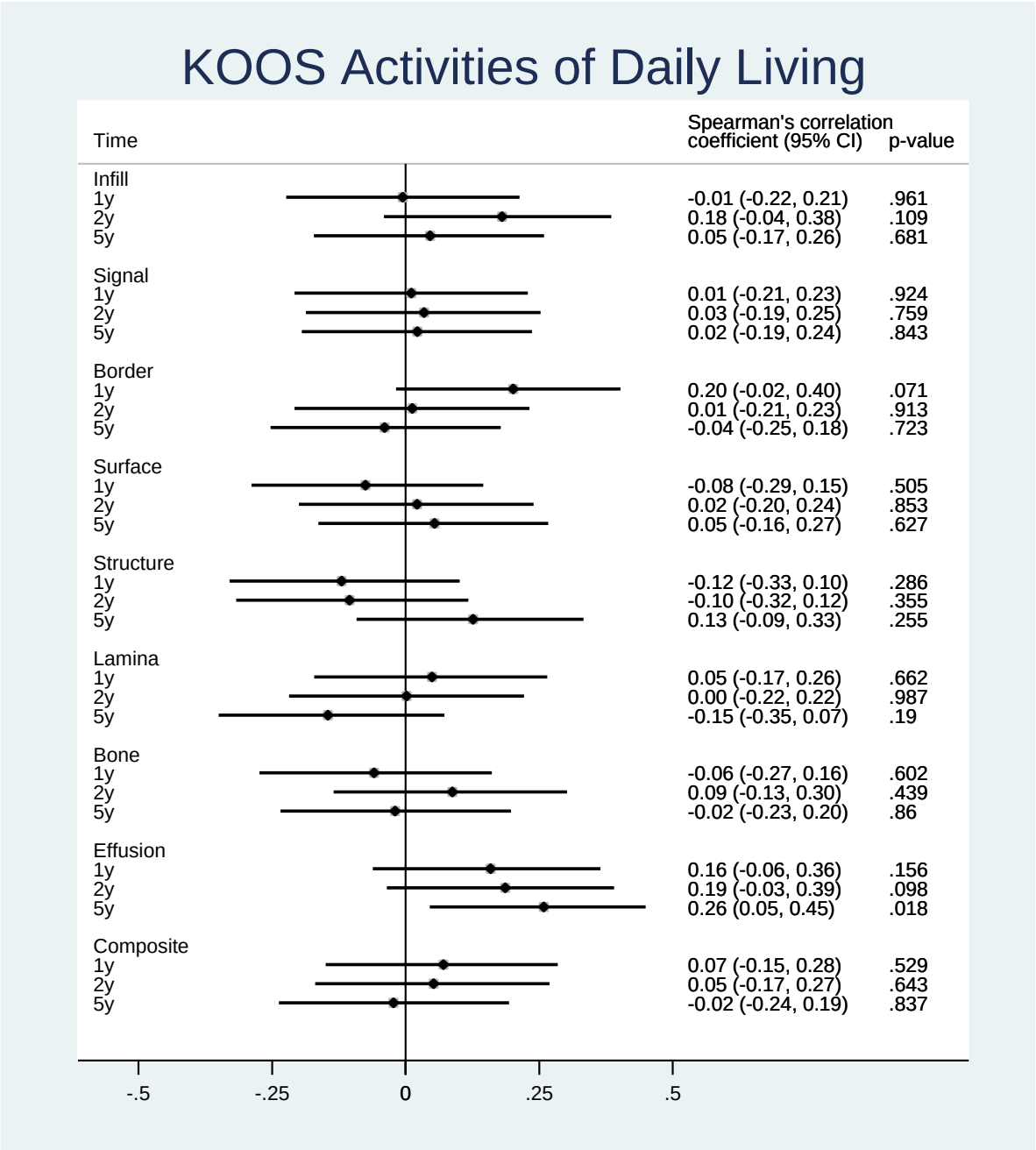
KOOS Activities of Daily Living
Time
Spearman's correlation coefficient (95% CI)
p-value
Infill
1y -0.01 (-0.22, 0.21) .961
2y 0.18 (-0.04, 0.38) .109
5y 0.05 (-0.17, 0.26) .681
Signal
1y 0.01 (-0.21, 0.23) .924
2y 0.03 (-0.19, 0.25) .759
5y 0.02 (-0.19, 0.24) .843
Border
1y 0.20 (-0.02, 0.40) .071
2y 0.01 (-0.21, 0.23) .913
5y -0.04 (-0.25, 0.18) .723
Surface
1y -0.08 (-0.29, 0.15) .505
2y 0.02 (-0.20, 0.24) .853
5y 0.05 (-0.16, 0.27) .627
Structure
1y -0.12 (-0.33, 0.10) .286
2y -0.10 (-0.32, 0.12) .355
5y 0.13 (-0.09, 0.33) .255
Lamina
1y 0.05 (-0.17, 0.26) .662
2y 0.00 (-0.22, 0.22) .987
5y -0.15 (-0.35, 0.07) .19
Bone
1y -0.06 (-0.27, 0.16) .602
2y 0.09 (-0.13, 0.30) .439
5y -0.02 (-0.23, 0.20) .86
Effusion
1y 0.16 (-0.06, 0.36) .156
2y 0.19 (-0.03, 0.39) .098
5y 0.26 (0.05, 0.45) .018
Composite
1y 0.07 (-0.15, 0.28) .529
2y 0.05 (-0.17, 0.27) .643
5y -0.02 (-0.24, 0.19) .837
-.5
-.25
0
.25
.5

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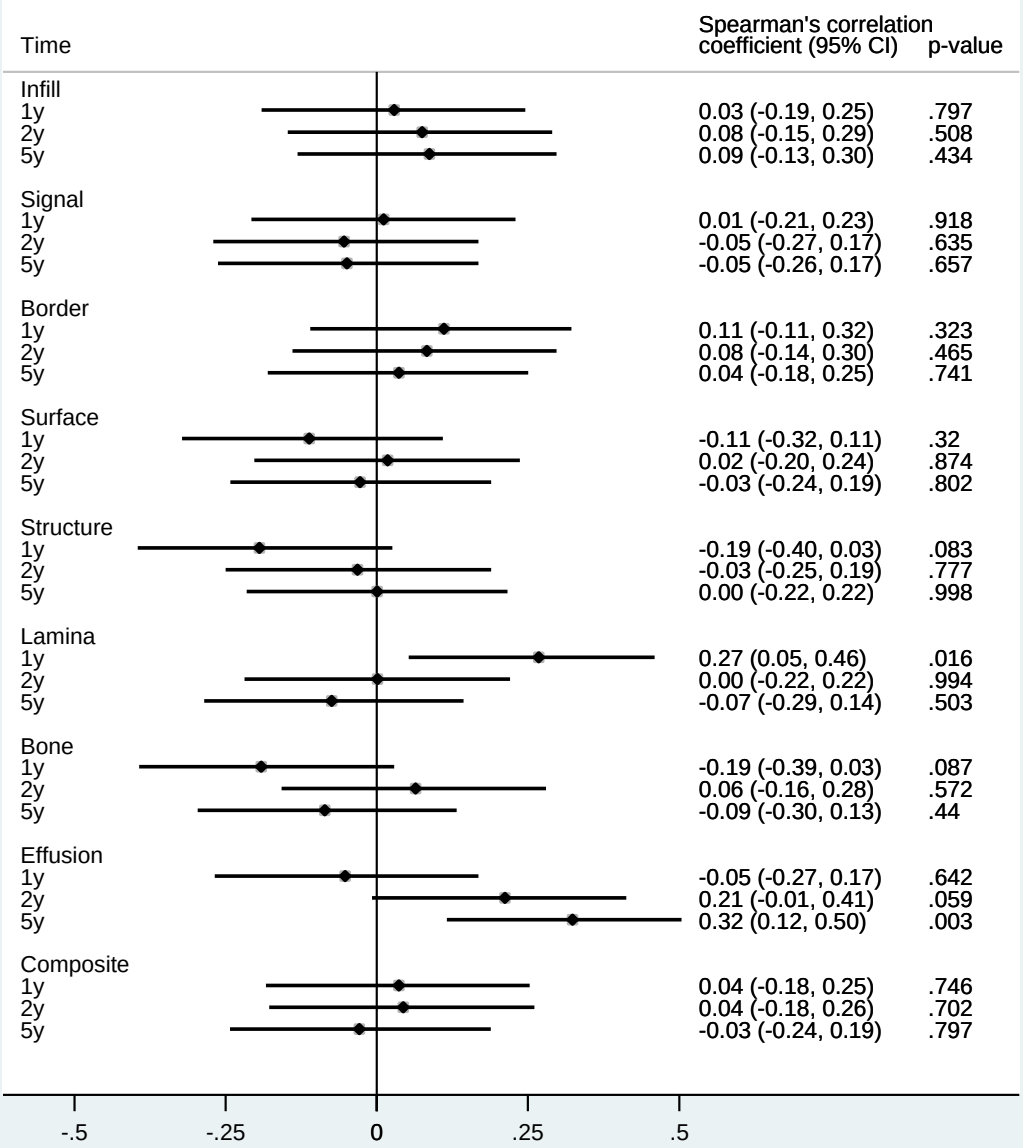
KOOS Sport & Recreation



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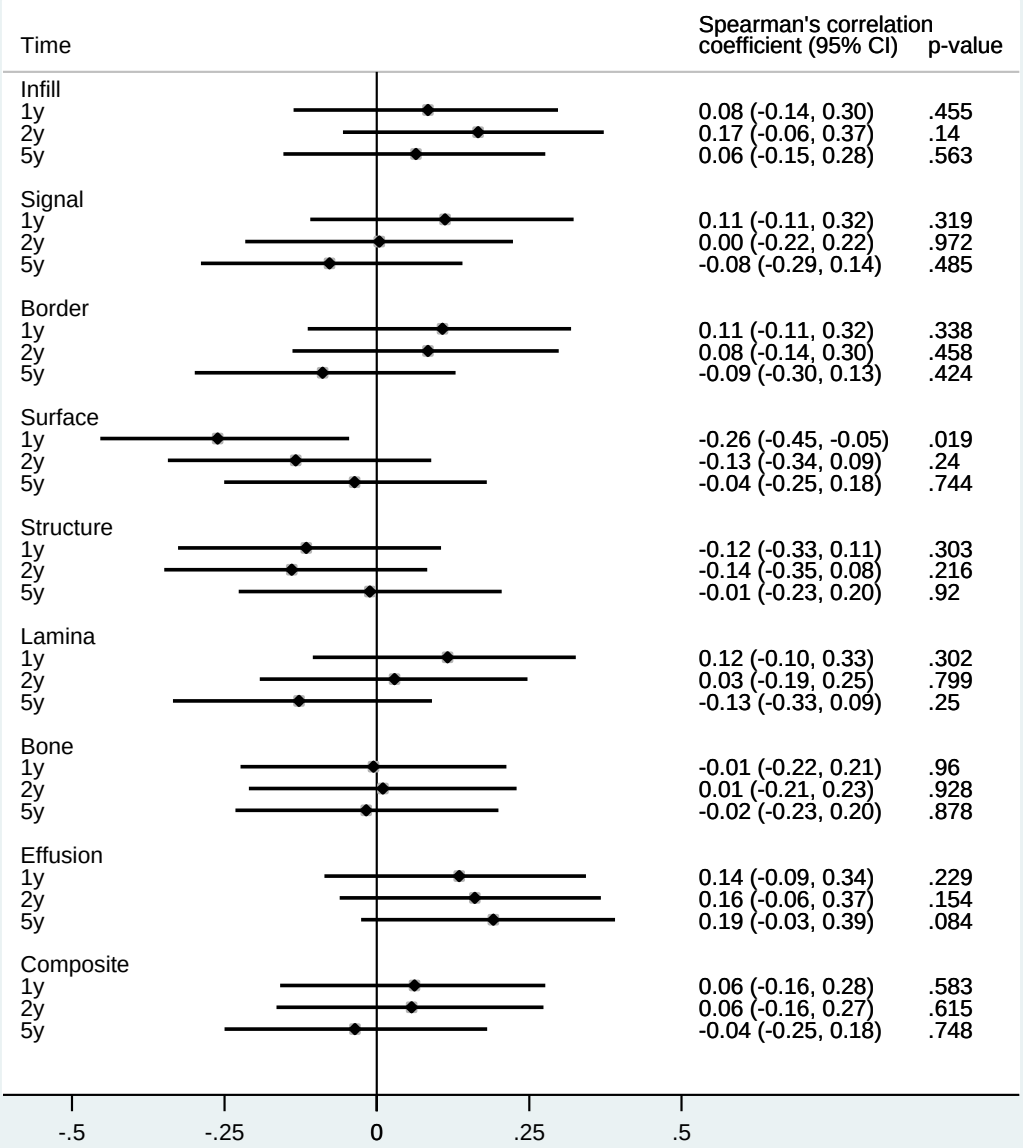
KOOS Quality of Life



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