Dyadic coping and its association with emotional functioning in couples confronted with advanced cancer: Results of the multicenter observational eQuiPe study

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Abstract

Objective: How patients and their partners cope with advanced cancer as a couple, may impact their emotional functioning (EF). The aim of this study was to assess dyadic coping (DC) of couples confronted with advanced cancer and its association with EF.

Methods: Actor-partner interdependence models were used to analyze baseline data of 566 couples facing advanced cancer participating in an observational study on quality of care and life. Measures included the DC Inventory and the European Organization for Research and Treatment of Cancer quality of life questionnaire (EQLQ-C30).

Results: Negative DC (mean 86–88) was most often used and common DC (both mean 66) was least often used. We found small to moderate interdependence ($r = 0.27-0.56$) between patients’ and partners’ DC perceptions. Compared to partners, patients were more satisfied with their DC ($p < 0.001$). Partners’ satisfaction with DC was positively associated with their own ($B = 0.40, p < 0.001$) and patients’ ($B = 0.23, p = 0.04$) EF. We found positive actor (patients $B = 0.37, B = 0.13, p = 0.04$) and partner (both $B = 0.17, p < 0.05$) associations for negative DC in patients and partners. Partners’ supportive DC was negatively associated with patients ($B = -0.31, p = 0.03$) and partners’ EF ($B = -0.34, p = 0.003$).

Conclusions: This study highlight the importance of DC (especially from the partners’ perspective) for EF in advanced cancer but also identifies differences in the experience of patients and their partners. Future research is needed to understand the mechanisms of such relations and the common and unique support options that may facilitate adjustment in patients with advanced cancer and their partners.

Trial registration: The eQuiPe study is registered as NTR6584 in the Netherlands Trial Register.
1 | BACKGROUND

A diagnosis of advanced cancer is a shared interpersonal experience that impacts both patients and their partners.1-3 The emotional impact of advanced cancer on patients and their partners is intertwined4,5 and evidence suggests that death anxiety, dysfunctional attitudes and their quality of life are linked.6 This suggest that how couples cope with an advanced cancer diagnosis is also likely to affect their emotional functioning (EF).

When confronted with a stressful life event such as an advanced cancer diagnosis, couples tend to communicate their stress to each other and to cope together with it, which is called dyadic coping (DC).7 DC includes the coping efforts of both partners of a dyad and its reciprocal nature (i.e., the coping of one person may affect the other person and vice versa). Just like individual coping, DC efforts can be categorized into different coping styles, including negative DC (i.e., hostile, ambivalent, superficial responses) or common DC (i.e., working together to handle stress).7 When both partners cope adequately together, they are able to communicate their stress to each other and provide and receive support in a manner that is constructive to their situation and relationship. However, coping styles are not mutually exclusive and one coping style does not necessarily prevail.

Some studies on the effect of coping on quality of life of couples confronted with advanced cancer have been conducted, showing that acceptance coping (i.e., letting go of any resistance towards the stressor) in patients with advanced cancer is associated with less depression in their partners, while seeking emotional support by patients is associated with more depressive symptoms in their partners.8 Another study found that the use of avoidance (i.e., denial or minimization of the stressor), emotion-focused coping (i.e., regulation of the emotional response to stress), and problem-focused coping (i.e., targeting the cause of stress) in partners are associated with poorer physical functioning and higher symptom burden in patients with advanced cancer.9 Two studies showed that more common DC is related to less severe depressive symptoms but to more cancer-related distress in patients with metastatic breast cancer. In their partners, more common DC was related to less cancer-related distress but to more severe depressive symptoms.10-12 However, to the best of our knowledge, only one study also included the dyadic effects of DC efforts among couples coping with advanced cancer.13 This study showed that supportive DC of the partner was positively associated with better mental functioning of patients. Also, satisfaction with DC according to partners was negatively associated with physical functioning of patients.13

It is of great importance to gain a better understanding on DC and dyadic effects in couples coping with advanced cancer together, as their DC may impact each other’s EF. Therefore, the aim of this study is to describe DC in couples coping with advanced cancer, including their interdependence. We also aim to assess the association between DC and EF in patients and partners. We hypothesize that there is moderate to high interdependence between patients and their partners regarding their DC perceptions. Because DC in couples coping with cancer is positively associated with EF,15 we also hypothesize that DC of both patients and their partners would be positively associated with the EF of the other party.

2 | METHODS

2.1 | Study design

We used baseline data of patients and their partners who participated in a prospective, longitudinal, multicentre, observational study on the experienced quality of care and quality of life of patients with advanced cancer and their relatives that was conducted in the Netherlands. Patients and their relatives were invited to participate by their treating physician from one of the 40 participating hospitals or were self-enrolled between November 2017 and January 2020. Patients were contacted by phone by the research team to discuss participation and were asked if a relative was interested in participating in the study. After giving written informed consent, patients and relatives completed questionnaires every 3 months until the patient’s death. Questionnaires were completed on paper or online via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry.14 Clinical data of the patient were obtained by linking the information to the Netherlands Cancer Registry (NCR). The study was exempted from medical ethical review according to the Dutch Medical Research Involving Human Subjects Act (WMO; Wet Medisch-wetenschappelijk Onderzoek), reviewed declared by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491). The study is registered as NTR6584 in the Netherlands Trial Register. Details of the study protocol are reported elsewhere.15

2.2 | Study population

Patients with advanced cancer (metastatic solid cancer stage IV) and their relatives were eligible. Additional criteria for patients with breast or prostate cancer were present, respectively metastases in multiple organ systems and castration-resistant disease. Participants had to be ≥ 18 years and able to complete a Dutch questionnaire. In total, 1695 patients were eligible and invited to participate (Figure 1). Of these patients, 255 (15%) did not want to participate. Via participating patients we were able to enroll 1171 relatives in the
study. Another 337 (20%) patients and 340 (29%) relatives dropped out, resulting in 1103 patients and 831 relatives who completed the baseline questionnaire. For this study, baseline data of unique patient-partner couples (n = 566) were used.

2.3 | Measurements

2.3.1 | Emotional functioning

Emotional functioning was assessed with the European Organization for Research and Treatment of Cancer Quality of life-C30 Questionnaire (EORTC QLQ-C30). The EF subscale consists of four items measuring feeling tense, worried, irritable or down using a four-point Likert scale from 1 "Not at all" to 4 "Very much". A higher score indicates better EF. While the EORTC QLQ-C30 is developed to measure quality of life of patients with cancer, it has also previously been used to assess quality of life in partners of patients with cancer.

2.3.2 | Dyadic coping

Dyadic coping was assessed with the Dyadic Coping Inventory (DCI). This 37-item questionnaire assesses DC as perceived by (i) each partner about their own coping ("what I do when I am stressed and what I do when my partner is stressed"), (ii) each partner's perception of the other's coping ("what my partner does when he or she is stressed, and what my partner does when I am stressed"), and (iii)
each partner’s view of how they cope as a couple (“what we do when we are stressed as a couple”). The DCI includes four coping scales: common coping (working together to handle stress), delegated coping (taking over responsibilities), negative coping (hostile, ambivalent or superficial responses), and supportive coping (problem- and/or emotion-focused support). The DCI also has an evaluation of DC scale (satisfied with your coping as a couple) and a stress communication scale (letting your partner know how you feel). Item scores range from one “very rarely” to five “very often” and were transformed to a 0–100 scale. The total DCI score is a sum of all items excluding two items regarding evaluation of DC scale. A total score calculated for patients and partners. Interdependence between patients and partners was in the normal range (74.4 and 72.3 respectively, of 0.20 is considered small, a correlation of 0.50 is medium, and a correlation of 0.80 is large.26)

We used the actor-partner interdependence model (APIIM).27 The APIIM is developed to analyze dyadic processes and shows the association between own DC and (1) own EF score (actor effect), and (2) EF of the partner (partner effect). Data of patients and partners are likely to be dependent of each other. Multilevel modeling with a pairwise dataset accounts for this inter-dependence within couples and is considered one of the best methods to examine effects in the APIIM.27,28 The univariate Pearson correlations between patients and partners indicated that the APIIM was appropriate to use and there was no presence of multicollinearity. We controlled for gender, age, education (low, medium, high), being a caregiver (partners only). We also controlled for a priori defined factors associated with DC based on previous studies among couples coping with cancer,13,29–31 including relationship satisfaction and the patients’ physical functioning. As only 1% of respondents reported a relationship duration of 0–5 years, this variable was not suitable for the APIIM.

Illness perception is known to be predictive of coping22 and therefore the patient’s illness perception was also included. Multiple imputation was applied to handle missing data (missing data ranged between 0.5% and 11.1% for patients and 0.4%–8.7% for partners) because missings were not at completely at random. A sensitivity analysis showed that results of the regression analyses did not change after imputation of data. A p-value <0.05 was considered significant. Effect sizes for each significant continuous variable were calculated. In accord with the APIIM model, these are partial correlations following the formula: \( r = \sqrt{\frac{t^2}{t^2 + df}} \).27 All statistical analyses were conducted in STATA version 16.0.

## RESULTS

Of the 566 couples, most couples were together for more than five year (99%) and 14 were same-sex couples. About half of the patients and partners were male (56% and 45% respectively) and the mean age of both groups was 65 years (Table 1). Most patients and partners had a medium level of education (40% and 45% respectively). Most patients were diagnosed with lung cancer (28%) or colorectal cancer (19%) and the majority of patients (82%) was diagnosed with their primary cancer tumor in the past 5 years. The mean score of EF was 77.3 (SD 21.3) for patients and 69.4 (SD 21.7) for partners. The mean score on happiness in the partnered relationship was 4.1 (SD 1.2) for patients and 4.0 (SD 1.2) for partners. The mean score of patients on illness perceptions was 33.1 (SD 13.8) and their physical functioning score was 70.7 (SD 22.3).

### 3.1 Dyadic coping

Most patients (81%) and partners (75%) rated their total DC efforts as normal or above average, total DC effort scores in patients and partners were in the normal range (74.4 and 72.3 respectively,
Table 2). Negative DC (i.e., hostile, ambivalent or superficial responses) was most often used by both patients and partners, respectively 88 and 86. Common DC was rated (i.e., working together to handle stress) the lowest (both 66). Correlations showed small to moderate interdependence between patients and partners, ranging between 0.27 for delegated DC and 0.56 for total DC score. Patients were more satisfied with DC compared to their partners, respectively 86 and 79 ($p < 0.001$).

### Table 1

Sociodemographic and clinical characteristics of patients with advanced cancer ($n = 566$) and their partners ($n = 566$)

|                         | Patients with advanced cancer | Partners        |
|-------------------------|------------------------------|-----------------|
|                         | $n$ (%)                       | $n$ (%)         |
| **Gender**              |                              |                 |
| Male                    | 318 (56)                     | 256 (45)        |
| Female                  | 248 (44)                     | 310 (55)        |
| **Age**                 |                              |                 |
| Mean (SD), range        | 65 (9.1), 29–88              | 65 (9.6), 18–87 |
| **Education**           |                              |                 |
| Low                     | 161 (28)                     | 160 (28)        |
| Medium                  | 227 (40)                     | 254 (45)        |
| High                    | 172 (30)                     | 147 (26)        |
| **Duration of relationship** |                           |                 |
| 0–5 years               | 8 (1)                        | 8 (1)           |
| >5 years                | 558 (99)                     | 558 (99)        |
| **Primary tumor**       |                              |                 |
| Lung                    | 155 (28)                     |                 |
| Colorectal              | 107 (19)                     |                 |
| Breast                  | 72 (13)                      |                 |
| Prostate                | 77 (14)                      |                 |
| Other                   | 155 (28)                     |                 |
| **Time since primary diagnosis** |                       |                 |
| <1 year                 | 184 (33)                     |                 |
| 1–3 years               | 274 (49)                     |                 |
| >3 years                | 101 (18)                     |                 |
| **Treatments in the prior 3 months** |                  |                 |
| None                    | 34 (6)                       |                 |
| Chemotherapy            | 343 (61)                     |                 |
| Radiotherapy            | 81 (14)                      |                 |
| Surgery                 | 18 (3)                       |                 |
| Immunotherapy           | 156 (28)                     |                 |
| Other                   | 105 (19)                     |                 |
| **Number of comorbidities** |                        |                 |
| None                    | 240 (42)                     |                 |
| 1                       | 199 (35)                     |                 |
| >1                      | 127 (22)                     |                 |

Note: Missing data was <5%. Responses of the other person was used to handle missings regarding relationship duration.

*Educational levels are categorized according to International Standard Classification of Education guidelines.

*Comorbidities defined as physical conditions from the Self-administered Comorbidities Questionnaire.  

*Treatments were self-reported. Patients could receive more than one treatment modality, the percentages do not sum up to 100%.
Results of the multivariable linear regression analysis showed that the positive association between satisfaction with DC and EF was stronger for partners compared to patients (\(B = 0.40\) and \(B = 0.03\) respectively, \(p < 0.001\)) (Table 3). The positive association between satisfaction with DC of the other person was more strongly associated with EF in patients compared to partners (\(B = 0.23\) and \(B = 0.02\), \(p = 0.04\)). The perception on negative DC was positively associated with EF and this relationship was stronger for patients compared to partners (\(B = 0.37\) and \(B = 0.13\), \(p = 0.04\)). The perception of the other person on negative DC was positively associated with EF in both patients and partners (\(B = 0.17\), \(p < 0.05\)). The perception on supportive DC was negatively associated with EF in partners, but not in patients (\(B = -0.34\) and \(B = 0.06\), \(p = 0.003\)). The perception of the other person on supportive DC was negatively associated with EF in patients, but not in partners (\(B = -0.31\) and \(B = 0.07\), \(p = 0.03\)).

### 4 | DISCUSSION

Our study shows that the vast majority of patients with advanced cancer and their partners have a normal to above average level of DC efforts. Negative DC (i.e., hostile, ambivalent or superficial responses) was most common in both groups, while common DC (i.e., working together to handle stress) was least often used by both. There was a small to moderate interdependence between patients and partners regarding their DC efforts. Compared to partners, patients were more satisfied with DC, but their satisfaction with DC was not as strongly associated with EF (e.g., feeling tense, worried, irritable or down). Satisfaction with DC of the other person was more strongly associated with the EF of patients compared to partners. We also found positive actor and partner associations for negative DC in both patients and partners. Supportive DC as perceived by the partner was negatively associated with the EF of both.

Some findings deserve particular attention. First, most patients and partners in our study had a normal to above average level of DC.
| Variables                              | Mean difference (b) | SE   | CI95%          | p-value | t     | Effect size |
|----------------------------------------|---------------------|------|----------------|---------|-------|-------------|
| **Satisfaction with DC**               |                     |      |                |         |       |             |
| Satisfaction with DC (actor effect)    | 0.40                | 0.07 | 0.26 to 0.54   | <0.001**| 5.71  | 0.17        |
| Satisfaction with DC (actor effect)*role | −0.37              | 0.11 | −0.58 to −0.16 | <0.001**| −3.36 | 0.10        |
| Satisfaction with DC (partner effect)  | 0.02                | 0.07 | −0.13 to 0.16  | 0.83    | 0.29  | 0.01        |
| Satisfaction with DC (partner effect)*role | 0.21               | 0.10 | 0.01 to 0.41   | 0.04*   | 2.10  | 0.06        |
| **Supportive DC**                      |                     |      |                |         |       |             |
| Supportive DC (actor effect)           | −0.34               | 0.11 | −0.57 to −0.12 | 0.003*  | −3.09 | 0.09        |
| Supportive DC (actor effect)*role      | 0.40                | 0.17 | 0.07 to 0.74   | 0.02*   | 2.35  | 0.07        |
| Supportive DC (partner effect)         | 0.07                | 0.13 | −0.18 to 0.32  | 0.58    | 0.54  | 0.02        |
| Supportive DC (partner effect)*role    | −0.38               | 0.17 | −0.71 to −0.04 | 0.03*   | −2.36 | 0.07        |
| **Negative DC**                        |                     |      |                |         |       |             |
| Negative DC (actor effect)             | 0.13                | 0.08 | −0.03 to 0.29  | 0.12    | 1.63  | 0.05        |
| Negative DC (actor effect)*role        | 0.24                | 0.12 | 0.01 to 0.48   | 0.04*   | 2.00  | 0.06        |
| Negative DC (partner effect)           | 0.17                | 0.08 | 0.00 to 0.33   | 0.05*   | 2.13  | 0.06        |
| **Delegated DC**                       |                     |      |                |         |       |             |
| Delegated DC (partner effect)          | 0.15                | 0.09 | −0.02 to 0.33  | 0.07    | 1.67  | 0.05        |
| **Stress communication**               |                     |      |                |         |       |             |
| Stress communication (actor effect)     | 0.18                | 0.10 | −0.01 to 0.37  | 0.06    | 1.80  | 0.05        |
| **Between dyads covariates**           |                     |      |                |         |       |             |
| Patient illness perception (actor effect)| −0.19              | 0.06 | −0.32 to −0.07 | 0.002*  | −3.17 | 0.09        |
| Patient illness perception (partner effect)*role | −0.21              | 0.08 | −0.38 to −0.05 | 0.01*   | −2.63 | 0.08        |
| Physical functioning of patient (actor effect) | 0.09               | 0.04 | 0.01 to 0.17   | 0.03*   | 2.25  | 0.07        |
| Physical functioning of patient (partner effect)*role | 0.18               | 0.05 | 0.07 to 0.28   | 0.001*  | 3.60  | 0.11        |
| Being a caregiver (partner variable)   | −5.10               | 1.72 | −8.46 to −1.73 | 0.003*  | −2.97 | 0.09        |
| Being a caregiver (partner variable) (partner effect)*role | 5.27               | 2.32 | 0.73 to 9.81   | 0.02*   | 2.27  | 0.07        |
| **Other covariates (actor effects)**   |                     |      |                |         |       |             |
| Happiness in the relationship          | −0.27               | 0.84 | −1.91 to 1.38  | 0.75    | −0.32 | 0.01        |
| Happiness in the relationship*role     | 2.67                | 1.16 | 0.39 to 4.95   | 0.02*   | 2.30  | 0.07        |
| Age                                    | 0.38                | 0.09 | 0.21 to 0.55   | <0.001**| 4.22  | 0.13        |
| Age*role                               | −0.22               | 0.12 | −0.46 to 0.02  | 0.07    | −1.8   | 0.05        |
| Education                              |                      | 0.58 |                |         |       |             |
| Low                                    | 1                   |      |                |         |       |             |
| Medium                                 | −1.70               | 1.88 | −5.38 to 1.98  | 0.37    | 0.90  | 0.03        |
| High                                   | −2.07               | 2.21 | −6.40 to 2.25  | 0.35    | 0.94  | 0.03        |
| Education*role                         |                      | 0.05*|                 |         |       |             |
| Low                                    | 1                   |      |                |         |       |             |
| Medium                                 | 5.98                | 2.69 | 0.71 to 11.25  | 0.03*   | 2.22  | 0.07        |
| High                                   | 6.43                | 3.04 | 0.48 to 12.39  | 0.03*   | 2.12  | 0.06        |

(Continues)
efforts. This is in line with a previous study among couples with breast cancer showing similar scores on the total DCI. However, that study also showed lower scores for negative DC: raw scores were 26 and 24 for respectively patients and partners compared to 35 and 34 in our study. The greater frequency of perceived negative DC in our study compared to this group might be due to the larger sample size, older age and more advanced cancer in our study. Metastatic cancer comes with a great threat to life, higher symptom burden, and the requirement of advance care planning and end-of-life care. These challenges in advanced cancer may be associated with greater feelings of uncertainty and helplessness, which may lead to more negative DC, as observed in our study. However, the previous study was consistent with our finding that patients and partners rate their DC efforts equally high.

Negative DC was the most common coping style used by patients with advanced cancer and their partners in our study. A previous study of DC among patients with metastatic breast cancer showed that patients used more positive common DC than negative common DC. However, this study used a modified version of the Dyadic Coping Questionnaire (FDCT: Fragebogen zur Erfassung des Dyadischen Coping als Tendenz) to measure common negative DC ("When we are both stressed, we withdraw and avoid each other") and three items accounted for positive common DC. The approach to measure negative DC in this study differs from the individual approach on negative coping in the DCI (e.g., "I blame my partner for not coping well enough with stress"), which limits the comparability of the findings. Common DC seems more beneficial for couples, as it appears to strengthen the feelings of "we-ness" in the relationship. However, common DC was least often used by the couples in our study. In addition to distress related to the advanced cancer diagnosis, couples may experience distress related to the relative lack of "we-ness" in the relationship and adequate DC. Such coping strategies may be amenable to psychological treatment, such as cognitive behavioral therapy.

Our results also show that satisfaction with DC in partners was positively related to their own and to the patients’ EF. Sparla et al (2016) showed, with their qualitative research on couples facing advanced cancer, that partners can experience feelings of helplessness regarding the patients’ deterioration which adversely affect their EF. Satisfaction from coping together as a unit may reduce feelings of helplessness in partners and improve their EF by fostering the sense of "we-ness”. This positive effect may affect the EF of patients because caregiver mastery (i.e. the feeling of being in control and not helpless) has been associated with better patient outcomes. Remarkably, patients’ satisfaction with DC and their perception on DC styles were not related to their own or their partners’ EF. Most likely, in patients with advanced cancer, other factors are more strongly related to their EF, such as their physical functioning and symptoms or cancer treatment.

### 4.1 Limitations

To our knowledge, this is the first study of DC in advanced cancer based on a large sample of patients and their partner. However, there are some limitations to the findings of this study. The validated questionnaire for DC (DCI) was developed to measure DC in case of stress in general, not stress specifically related to health or cancer, although it has been widely used in healthcare settings. We did not control for the duration of the dyadic relationship, which was measured categorically and most couples were together for more than 5 years. However, based on our results and previous studies, the quality of the relationship may be more important than the duration in assessing DC. The effect sizes of our results were rather small, indicating that the magnitude of the association between DC and EF may not be clinically relevant. Finally, this cross-sectional analysis could not determine causality of effects. It remains unclear, therefore, whether satisfaction with DC has a causal effect on the EF of patients and their partners. Longitudinal follow-up of the couples in our study is expected to provide more insight into the directionality of these effects.

### 4.2 Clinical implications and future research

This study highlights the important relationship between DC in couples confronted with advanced cancer and their EF. The findings suggest that the EF and DC of patients and partners are interrelated. Health care professionals should be aware of the social context of patients and address how couples cope as a unit. They should also pay attention to the perspective of partners on DC and perceive them as a source of support for patients as well as individuals in need.

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**Table 3 (Continued)**

| Variables | Mean difference (b) | SE | CI95%     | p-value | t   | Effect-size |
|-----------|---------------------|----|-----------|---------|-----|-------------|
| Role      |                     |    |           |         |     |             |
| Patient   | 14.12               | 15.59 | −16.43 to 44.67 | 0.37    | 0.91 | 0.03        |

Note: The regression model included all scales of the Dyadic Coping Inventory. Interaction terms were added between those items and role and between role and covariates. Only significant associations are shown. Multiple imputations were applied to handle missing data. Variance inflation factor (VIF) values were <5, confirming the absence of multicollinearity. Only significant associations are presented.

*p < 0.05, **p < 0.01.
of support for themselves. Future research should explore factors that contribute to DC in couples confronted with advanced cancer and how this may evolve over time and at what point in the trajectory individual and/or couple-based support may be most needed and most effective. Also, future research should utilize a shortened version of the DCI, as the length of this questionnaire may become too burdensome for patients nearing death.

4.3 Conclusions

The present study demonstrates an association of DC with the EF of patients with advanced cancer and their partners. The partners' perspective on DC appears to be particularly related to their own EF and that of the patient. These findings highlight the potential importance of dyadic functioning for the wellbeing of patients with advanced cancer and their partners but also identifies differences in these domains between patients and their partners. Future research is needed to understand these relationships and the potential benefit of interventions directed to improve DC in couples with advanced cancer.

AUTHORS’ CONTRIBUTIONS

JvR, NR, and LvdP were involved in the study design. JvR, NR, LvdP, JK, EK, TS, LvdV were involved in the data collection. JvR conducted the analysis and drafted the manuscript. All authors were involved in interpretation of the results, reviewed the manuscript and gave final approval of the manuscript.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

DATA AVAILABILITY STATEMENT

Since 2011, PROFILES registry data is freely available according to the FAIR (Findable, Accessible, Interoperable, Reusable) data principles for non-commercial (international) scientific research, subject only to privacy and confidentiality restrictions. The datasets analyzed during the current study are available through Questacy (DDI 3.x XML) and can be accessed by our website (www.profilesregistry.nl). In order to arrange optimal long-term data warehousing and dissemination, we follow the quality guidelines that are formulated in the ‘Data Seal of Approval’ (www.datasealofapproval.org) document, developed by Data Archiving and Networked Services. The data reported in this manuscript will be made available when the eQuiPe study is completed.

ETHICS APPROVAL

This study was performed in line with the principles of the Declaration of Helsinki. The study was reviewed by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital in the Netherlands (METC17.1491). Written informed consent was obtained from all individual participants included in the study.

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