Surgical and non-surgical complications after colorectal cancer surgery in older patients: time-trends and age-specific differences

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Surgical and non-surgical complications after colorectal cancer surgery in older patients; time-trends and age-specific differences

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ABSTRACT

Background: Trends of surgical and non-surgical complications among the old, older and oldest patients after colorectal cancer (CRC) surgery could help to identify the best target outcome to further improve postoperative outcome.

Materials and methods: All consecutive patients ≥70 years receiving curative elective CRC resection between 2011 and 2019 in The Netherlands were included. Baseline variables and postoperative complications were prospectively collected by the Dutch ColoRectal audit (DCRA). We assessed surgical and non-surgical complications over time and within age categories (70–74, 75–79 and ≥ 80 years) and determined the impact of age on the risk of both types of complications by using multivariate logistic regression analyses.

Results: Overall, 38648 patients with a median age of 76 years were included. Between 2011 and 2019 the proportion of ASA score ≥3 and laparoscopic surgery increased. Non-surgical complications significantly improved between 2011 (21.8%) and 2019 (17.1%) and surgical complications remained constant (from 17.6% to 16.8%). Surgical complications were stable over time for each age group. Non-surgical complications improved in the oldest two age groups. Increasing age was only associated with non-surgical complications (75–79 years; OR 1.17 (95% CI 1.10–1.25), ≥80 years; OR 1.46 (95% CI 1.37–1.55) compared to 70–74 years), not with surgical complications.

Conclusion: The reduction of postoperative complications in the older CRC population was predominantly driven by a decrease in non-surgical complications. Moreover, increasing age was only associated with non-surgical complications and not with surgical complications. Future care developments should focus on non-surgical complications, especially in patients ≥75 years.

1. Introduction

Postoperative complications after colorectal cancer (CRC) surgery are common [1] and are accountable for short-term consequences (prolonged length of stay, readmission and mortality) and long-term outcomes (lower five-years survival [2] and quality of life [3]). To improve postoperative complications after CRC surgery, special attention should be paid to the older population. In this group of older patients, postoperative complications occur more often [4–7] and result in higher morbidity than in younger patients [8].

The impact of postoperative complications is not only age-specific (young vs old), but it also depends on the type of complication as well. Warps et al. [9] showed that non-surgical complications (like cardiopulmonary events) had a stronger impact on long-term survival for CRC patients than surgical complications (like anastomotic leakage or bleeding). Furthermore, our research

Abbreviations: CRC, Colorectal Cancer; CCI, Charlson comorbidity index; CGA, comprehensive geriatric assessment; DCRA, Dutch ColoRectal Audit; ERAS, enhanced recovery after surgery.

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group found that prehabilitation in older CRC patients predominantly affects non-surgical complications [10]. These results suggest that surgical and non-surgical complications should be evaluated separately, especially in the older population.

Considering several care developments that have been (partly) implemented in clinical practice, such as minimally invasive surgery, enhanced recovery after surgery (ERAS), geriatric co-management and prehabilitation programs, it would be interesting to have information about recent trends of both postoperative surgical and non-surgical complications in older (≥70 years) CRC patients. As these developments have already been shown to gradually close the gap in postoperative mortality between younger and older CRC patients [11,12], it is unknown whether there is still a gap in postoperative complications between the old, older and oldest patients.

The studies that have investigated the risk for postoperative complications in several age-groups within the older CRC population (≥70 years) showed inconsistent results. Some found an increased risk of overall postoperative complications with increasing age [6,13–15], others found no difference [16] or only an increased risk of infectious complications [17]. However, these studies did not differentiate clearly between surgical and non-surgical complications.

This study aims to describe both types of postoperative complications, i.e. surgical and non-surgical, with respect to both time-trends as well as age-specific (70–74 years, 75–79 years and ≥80 years) results in older patients with colorectal cancer on a population level.

2. Material and methods

2.1. Study population and design

For this nationwide population-based cohort study, patients were identified through the Dutch Colorectal Audit (DCRA). The DCRA is an obligatory audit, which registered all newly diagnosed colorectal malignancies in the Netherlands to monitor, evaluate and improve Dutch colorectal cancer care [18]. The DCRA prospectively collects patients' demographics, tumor- and treatment characteristics and postoperative outcome parameters. As the DCRA is an obligatory audit and all DCRA data is de-identified, medical ethics committee approval or informed consent was not required [18]. This observational cohort study included all consecutive patients of 70 years and older who received elective surgery for stage I-III colon or rectal cancer between 2011 and 2019 in the Netherlands. Patients were excluded in case of local excision or elective surgery after stenting or after an ileostomy procedure.

2.2. Data collection and outcome parameters

The following baseline information was extracted from the DCRA: age at diagnosis, sex, American Society Anesthesiology (ASA) score, Charlson Comorbidity Index (CCI) [19], clinical and pathologic tumor (T) and nodal (N) stage, neo-adjuvant therapy and surgical approach (open, laparoscopic, robot-assisted and other). Open surgery did not include converted laparoscopic surgeries. The ASA score was subdivided in ASA I/II and ≥III and the CCI in 0, 1, 2 and ≥ 3 (according to an earlier DCRA study [1])The DCRA registered several outcome measurements including postoperative mortality, postoperative surgical and non-surgical complications, length of stay and readmission. The primary outcome is the proportion of surgical and non-surgical complications. A surgical complication is defined as the occurrence of at least one surgical complication (anastomotic leakage, abscess, bleeding, ileus, fascia dehiscence, bowel perforation, leakage from bladder or ureter or surgical wound infection) and a non-surgical complication is defined as the occurrence of at least one non-surgical complication (pulmonary, cardiac, thromboembolic or neurologic event, infection (other than pulmonary or wound infection) or other). Between 2011 and 2017, the DCRA registered all outcome measurements till 30 days after surgery and from 2018 till 90 days after surgery. Due to this change in registration, we need to keep in mind that the postoperative complication rate for 2018 and 2019 will be a slight overestimation in comparison to the complication rate in 2011–2017.

2.3. Statistical analysis

Continuous baseline variables were expressed as mean (normally distributed) with standard deviation (SD) and median (non-normally distributed) with interquartile range (IQR) and categorical variables as frequencies with percentages. To give an understandable overview of the trend in baseline characteristics, we compared the complete nine years by cohorts of three years; 2011–2013, 2014–2016 and 2017–2019. The postoperative complication rates (any, surgical and non-surgical) were depicted for each year separately. We performed multivariate logistic regression analysis to assess whether postoperative complications remained similar ($p > 0.05$), decreased (OR <1.0 and $p < 0.05$) or increased (OR >1.0 and $p < 0.05$) over the complete time period (2011–2019). Year of surgery was included as continuous variable. For multivariate analysis we considered age, sex, ASA-class, tumor localization, tumor stage and neo-adjuvant radiotherapy as clinically relevant. Only for tumor stage, the 'unknown' (missing and not judgeable) cases were categorized. The missing values of all other independent variables were excluded from the logistic regression analysis, as they hardly occurred (<0.002%) and were considered at random. As we assumed collinearity (based on epidemiological grounds) between 1.'year of surgery' and 'surgical approach and 2.'CCI score' and 'ASA score' combined with a significant interaction ($p < 0.05$), both 'surgical approach' and 'CCI score' were excluded from the multivariate model. Subsequently we have stratified our cohort by three age categories: 70–74 years, 75–79 years and ≥80 years (as these groups had comparable number of patients) and performed the same analyses. Finally, we determined the impact of age on surgical or non-surgical complications during the complete study period using a multivariate logistic regression analysis including age as categorical variable. P-values below 0.05 were considered as statistically significant and all statistical analysis were performed with SPSS 25.0.

3. Results

3.1. Study population

Overall, 39788 patients ≥70 years underwent stage I-III CRC resection between 2011 and 2019 in the Netherlands. Of these, 1140 patients were excluded as 862 received a local excision and 278 patients had elective surgery after stenting or after a temporary decompressing stoma. Eventually, the study included 38648 patients (Fig. 1).

3.2. Baseline characteristics

Table 1 shows the patient-, tumor- and treatment characteristics of the years 2011–2013, 2014–2016 and 2017–2019. The median age was comparable between the three year cohorts and ranged between 76 and 77 years. The proportion of patients undergoing CRC resection with an ASA score ≥ III increased from 30.2% (2011–2013) and 30.4% (2014–2016) to 38.4% in 2017–2019. We

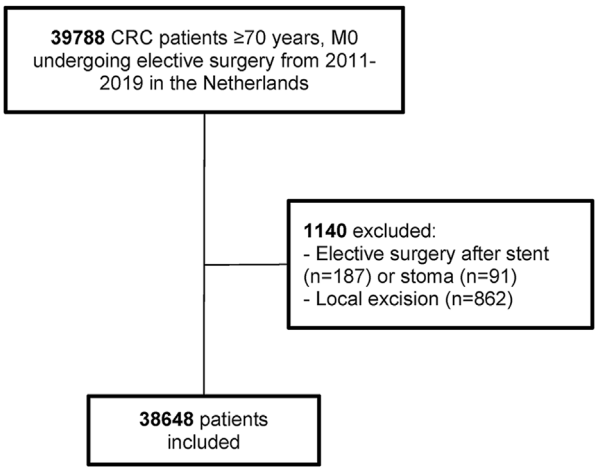

Fig. 1. Flow diagram of patient inclusion.

Table 1
Baseline characteristics of the study cohort in proportions (%).

	2011–2013	2014–2016	2017–2019
	N = 11678	N = 13911	N = 13059
Median Age (IQR)	77 (73–82)	76 (73–81)	76 (73–81)
Sex			
Male	6220 (53.3)	7684 (55.2)	6994 (53.6)
Female	5458 (46.7)	6223 (44.7)	6063 (46.4)
ASA score			
ASA I/II	8126 (69.6)	9685 (69.6)	8047 (61.6)
ASA III+	3532 (30.2)	4224 (30.4)	5012 (38.4)
Charlson comorbidity index			
0	4709 (40.3)	5376 (38.6)	5105 (39.1)
1	3044 (26.1)	3446 (24.8)	3312 (25.4)
2	2129 (18.2)	2702 (19.4)	2344 (17.9)
≥3	1796 (15.4)	2387 (17.2)	2298 (17.6)
Tumor localization			
Colon	8505 (72.8)	10316 (74.2)	9761 (74.7)
Rectum	3168 (27.1)	3593 (25.8)	3297 (25.2)
TNM stage			
Stage 0	193 (1.7)	205 (1.5)	208 (1.6)
Stage 1	3024 (25.9)	4051 (29.1)	3734 (28.6)
Stage 2	4523 (38.7)	5228 (37.6)	4754 (36.4)
Stage 3	3671 (31.4)	4344 (31.2)	4066 (31.1)
Unknown*	267 (2.3)	83 (0.6)	297 (2.3)
Surgical approach			
Open	5264 (45.1)	2832 (10.4)	1182 (9.1)
Laparoscopic	6403 (54.8)	10952 (78.7)	10569 (80.9)
Robot assisted	0	0	688 (5.3)
Other**	0	84 (0.6)	277 (2.1)
Unknown	11 (0.1)	43 (0.3)	343 (2.6)
Neo adjuvant radiotherapy[α]			
None	599 (18.9)	1566 (43.6)	1740 (52.8)
Not specified	2569 (81.1)	1946 (54.2)	510 (15.5)
5 × 5 Gy	0	30 (0.8)	534 (16.2)
Chemoradiation	0	51 (1.4)	504 (15.3)
Neo adjuvant chemotherapy[α]			
None	1916 (60.5)	1742 (48.5)	2203 (66.8)
Yes	356 (11.2)	366 (10.2)	532 (16.1)
Unknown	896 (28.3)	1485 (41.3)	562 (17.0)

Abbreviations: ASA *American Society of Anesthesiologists*.
Additional missing data: sex (6 patients), ASA score (22 patients), localization (8 patients).
* missing or not judgeable.
** other: transanal and transabdominal endoscopic TME (TaTME of TAMIS TME).
[α] Exclusively the patients with rectal cancer.

found a clear decrease in open CRC resections (45.1% in 2011–2013 to 10.4% in 2014–2016) and increase in laparoscopic surgery (54.8% in 2011–2013 to 78.8% in 2014–2016) and robot-assisted surgery (0% in 2014–2016 to 5.3% in 2017–2019). Regarding patients with rectal cancer, neo-adjuvant radiotherapy played an increasingly minor role in standard care. Between 2011 and 2013, 19.8% of the older patients were not treated with neo-adjuvant radiotherapy, in contrary to 43.6% in 2014–2016 and 52.8% in 2017–2019.

3.3. Time-trends of postoperative complications

In the complete study cohort (n = 38648), 12324 (31.9%) patients experienced any complications, 7166 (18.5%) experienced one or more surgical complications, 8143 (21.1%) experienced one or more non-surgical complications and 3220 (8.3%) experienced both. Fig. 2 shows the trend of any complications, surgical and non-surgical complications. In 2011, 33.4% of the patients experienced any complications, 17.6% surgical complications and 21.8% non-surgical complications compared to respectively 27.6%, 16.8% and 17.1% in 2019. Both any, surgical and non-surgical complications peaked in 2015 to respectively 34.2%, 20.2% and 24.0%. The multivariate time-trend analyses showed a significant reduction in any (OR 0.97 (95% CI 0.96–0.98, p < 0.001) and non-surgical complications (OR 0.97 (95% CI 0.96–0.98, p < 0.001). The rate of surgical complications (OR 1.00 (95% CI 0.99–1.01, p = 0.524) was constant over time.

3.4. Age-specific time-trends in postoperative complications

Overall, surgical complications occurred in 18.3% of the patients aged 70–74 years, in 18.3% of the patients aged 75–79 years and in 19.0% of the patients aged ≥80 years. Increasing age was not associated with surgical complications; the OR for patients aged 75–79 year was 1.00 (95% CI 0.94–1.06) and 1.03 (95% CI 0.97–1.10) for patients aged ≥80 compared to patients aged 70–74 years. Non-surgical complications occurred in 17.8%, 20.4% and 25.1% in patients aged 70–74 years, 75–79 years and ≥80 years respectively. Increasing age significantly increased the risk for non-surgical complications, as the OR for age 75–79 years was 1.17 (95% CI 1.10–1.25) and for ≥80 years1.46 (95% CI 1.37–1.55) compared to patients aged 70–74 years.

The trends of surgical (A) and non-surgical (B) complications per age group are shown in Fig. 3. Within the age groups 70–74 years, 75–79 years and ≥80 years, 17.7%, 17.0% and 18.1% experienced surgical complications in 2011 compared to 16.9%,14.9% and 18.1%

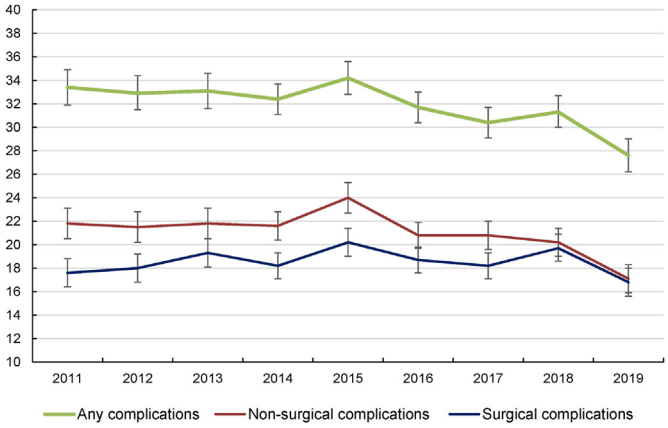

Fig. 2. The time-trend (in proportions) of postoperative complications between 2011 and 2019 in the Netherlands.
NB. "Any complication" does not represent the sum of surgical and non-surgical complications, as one patient may experience both a surgical and a non-surgical complication.

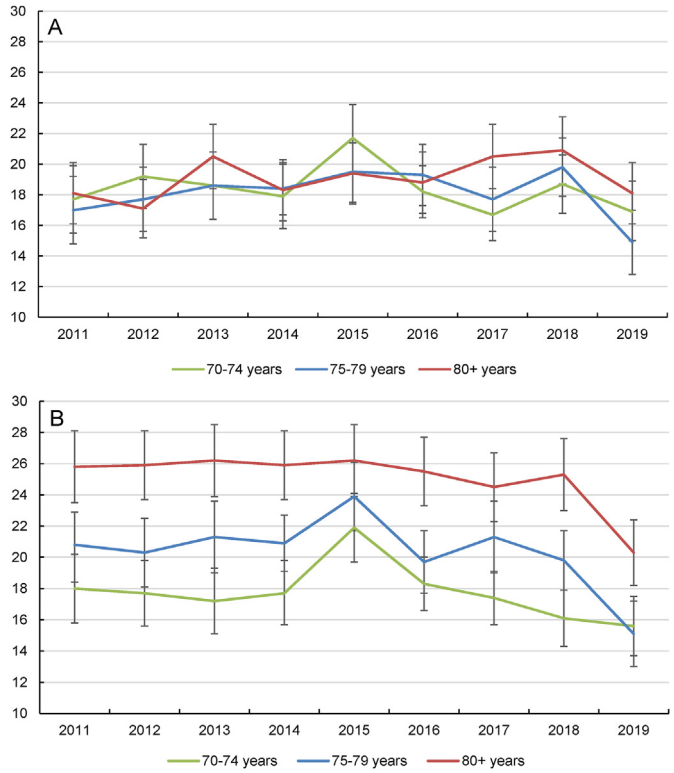

Fig. 3. The time-trend (in proportions) of surgical (A) and non-surgical (B) complications between 2011 and 2019 in the Netherlands.

in 2019. None of these improvements were significant ($p > 0.05$). The rate of non-surgical complications was 18.0%, 20.8% and 25.8% in 2011 compared to 15.6%, 15.1% and 20.3% in 2019. The improvement was only significant for patients aged 75–79 years and ≥80 years. (70–74 years: $p = 0.061$, 75–79 years; $p = 0.009$, ≥80 years; $p < 0.001$).

4. Discussion

This study provides insight in the time-trends and age-specific risk differences of postoperative complications in patients of 70 years and older receiving elective non-metastatic CRC surgery by differentiating between surgical and non-surgical complications. Between 2011 and 2019, the rate of complications declined. This improvement must be completely attributed to the reduction of non-surgical complications, since the surgical complication rate did not significantly improve. The same trends were observed after stratifying by age category. Increasing age was only associated with non-surgical complications and not with surgical complications.

To our knowledge, this is the only study describing such recent and nationwide time-trends of postoperative complications in older CRC patients. Our findings are in line with the study from de Neree tot Babberich et al., that consisted of patients receiving elective CRC surgery of all ages in the Netherlands from 2009 to 2016. They described a slight increase in surgical an non-surgical complications in 2015/2016 (in line with Fig. 2) and suggested that complications may have been registered and identified more thoroughly [1]. Furthermore, changes in baseline characteristics (Table 1) could positively or negatively affect the a priori risk of postoperative complications, such as the increased proportion of comorbidity (ASA and CCI score ≥ III), a higher percentage of early CRC cancer (the Dutch colorectal cancer screening program was initiated in 2014) or a less frequent use of neo-adjuvant radiotherapy [20].

Since we corrected for these baseline characteristics, our findings suggest that several care developments (such as minimally invasive surgery, enhanced recovery after surgery (ERAS), comprehensive geriatric assessments (CGA)and prehabilitation programs) have a larger effect on non-surgical complications than on surgical complications. Minimally invasive surgery, the ERAS protocol and geriatric screening followed by a CGA have been increasingly implemented throughout the Netherlands over the last decade [21]. Prehabilitation has been taken up by several hospitals in the context of research or quality-improvement programs, but is not widely implemented yet [22–25]. Earlier studies showed that minimally invasive surgery and the ERAS protocol mainly improve postoperative medical morbidity [26–30]. Evidence for geriatric-specific care pathways – such as preoperative comprehensive geriatric assessment (CGA) and in-hospital geriatric co-management – to reduce (non)-surgical complications, is still inconsistent. Although Ommundsen et al. described a significant decrease in Grade I–V complications after CGA [31], Hempenius et al. [32] found no effect on postoperative delirium or overall complications. Geriatric co-management improves 90-days mortality [33] and reduces delirium and other geriatric syndromes (e.g. falls, pressure ulcers) [34]. However, a positive effect on postoperative complications was only found in (two out of seven) studies which are not performed in older CRC patients [35]. Furthermore, a recent study from our group suggested that prehabilitation in older patients has more value for reducing non-surgical complications than surgical complications [10]. Two randomized trials demonstrated that prehabilitation reduces the overall postoperative complication rate [24,36] Interestingly, in the Barbaran-Garcia-study this reduction was also driven by a decrease in non-surgical complications and no reduction was observed for surgical complications [36].

The present study demonstrated that the risk for non-surgical complications increased with increasing age and the risk for surgical complications was similar among the old, older and oldest CRC patients. Several studies support the fact that – within the older population – increasing age is associated with any complication [6,13,14,17]. However, none of these studies initially differentiate between surgical and non-surgical complication. Some studies indicate a potential higher impact of age on non-surgical complications than surgical complications. For example, Kvasnovsky et al., in a retrospective cohort of elderly patients receiving laparoscopic CRC surgery, described an increase of infectious complications (especially chest infections), from 14.8% (in patients <65 years) to 22.7% (in patients 65–80 years) and to 44.4% in patients >80 years ($P = 0.01$) [17]. Barina et al., including a retrospective cohort of 47704 older patients (≥65 years) undergoing laparoscopic CRC surgery, showed an increase in overall postoperative complications with increasing age, however there was no association among patients aged 65–74 years, 75–84 years and ≥85+ years regarding anastomotic leakage or surgical site infections [14].

Approximately 40% of the older CRC population is frail [37], characterized by an high vulnerability state that increased the risk for adverse health outcomes [38] like postoperative complications [4,6,7,39–42]. It is suggested that non-surgical complications, such as cardiopulmonary complications, are related to a poor preoperative condition or reduced postoperative activity during hospital admission [43]. Frailty may have a limited interaction with surgical complications, as perioperative factors (e.g., surgical approach, surgeon expertise) and tumor characteristics (tumor size, lymph node invasion) may outweigh frailty. The increasing prevalence of frailty with increasing age [44] might explain why the age-specific differences are predominantly found in non-surgical complications and not in surgical complications.

The decrease in non-surgical complications was only seen in the oldest two age groups (Fig. 3) and suggests that the oldest patients may be more prone to improvement of the non-surgical complications or that clinical practice already has shifted attention in pre- and perioperative care towards the oldest patients. This supports the hypothesis that future care developments – like prehabilitation – should target non-surgical complications in the geriatric population.

Our study has a few limitations. Our cohort only included patients that were considered fit enough for surgical treatment. This selection may have influenced complications rates. The lower complication rates in recent years may have been due to an improved selection prior to surgery. Furthermore, this pre-selection could have been more dominant in the oldest age groups as older patients are less likely to undergo surgery, especially for rectal cancer [45,46].

Although colon and rectal cancer are usually combined in the literature, both diseases have different patient characteristics and postoperative outcome [47]. We have checked whether results were different for colon and rectal cancer in our study. The stratified analysis showed comparable results. However, for rectal cancer surgery results were less straightforward for two reasons. First, surgical complications increased in 2018–2019. This could have been because from 2018 the registration-period in DCRA changed from 30- to 90-days post-surgery and because of a significantly lower number of defunctioning stomas over recent years. Second, in recent years the differences in non-surgical complication rates between the old, older, and oldest patients were smaller. As rectal cancer patients tend to be somewhat younger than colon cancer patients, the results for older rectal cancer patients could be slightly skewed. Especially because in rectal cancer there are more alternatives to surgical treatment (chemotherapy, radiotherapy, watch and wait), surgery is offered less frequent to older patients [45]. This could explain the smaller gap between the old, older and oldest patients, as in the oldest group only the most fit would undergo surgery we had no data on the severity of complications, and we were unable to rank complications using the Clavien-Dindo Classification. Likewise, we had no information about the potential long-term impact of complications. Furthermore, we had no detailed information about frailty characteristics that could have been helpful to further interpret our findings. However, the main strength of this study is its large sample size representing 'real life' data on a national level. The completeness of the DCRA data has been reported to be over 95% [18].

5. Conclusions

Over the years, the overall improvement in postoperative complications after CRC resection in the older population was predominantly driven by a decrease in non-surgical complications. Moreover, increasing age was only associated with non-surgical complications and not with surgical complications. Therefore, future care developments should preferably focus on non-surgical complications, especially in the oldest patients (≥75 years).

CRediT authorship contribution statement

Heleen C. van der Hulst: Conceptualization, Methodology, Validation, Formal analysis, Data curation, Writing – original draft. **Jessica M. van der Bol:** Conceptualization, Writing – review & editing, Supervision. **Esther Bastiaannet:** Conceptualization, Methodology, Validation, Formal analysis, Writing – review & editing. **Johanna E.A. Portielje:** Conceptualization, Writing – review & editing, Supervision. **Jan Willem T. Dekker:** Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision.

Declaration of competing interest

None.

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