# Value of outcomes research in colorectal cancer care

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Chapter 3

# THE INFLUENCE OF HOSPITAL VOLUME ON CIRCUMFERENTIAL RESECTION MARGIN INVOLVEMENT: RESULTS OF THE DUTCH SURGICAL COLORECTAL AUDIT (DSCA).

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## ABSTRACT

**Objective:** To evaluate the association between hospital volume and CRM involvement in rectal cancer surgery.

**Summary Background Data:** To guarantee the quality of surgical treatment of rectal cancer, the Association of Surgeons of the Netherlands (ASN) has stated a minimal annual volume standard of 20 procedures per hospital. The influence of hospital volume has been examined for different outcome variables in rectal cancer surgery. Its influence on the pathological outcome (CRM) however remains unclear. As long-term outcomes are best predicted by the CRM status, this parameter is of essential importance in the debate on the justification of minimal volume standards in rectal cancer surgery.

**Methods:** Data from the Dutch Surgical Colorectal Audit (2012) was used. Hospital volume was divided into three groups and baseline characteristics were described. The influence of hospital volume on CRM involvement was analysed, in a multivariate model, between low and high volume hospitals, according to the minimal volume standards.

**Results:** This study included 5161 patients. CRM was recorded in 86 percent of patients. CRM involvement was 11 percent in low volume group versus 7,7 and 7,9 percent in the medium and high volume group (p=<0.001). After adjustment for relevant confounders, the influence of hospital volume on CRM involvement was still significant (OR 1.54; 95% CI 1,12-2,11).

**Conclusions:** The outcomes of this pooled analysis support minimal volume standards in rectal cancer surgery. Low hospital volume was independently associated with a higher risk of CRM involvement (OR 1.54; 95% CI 1,12-2,11).

## INTRODUCTION

Improving the outcomes of oncologic surgery has been widely discussed over the last decades.[1] In this context, hospital differences regarding quality of care have received much attention in recent years.[2]

In rectal cancer surgery, implementation and standardization of the technique of total mesorectal excision (TME) using surgical training programmes, as well as the introduction of preoperative (chemo) radiotherapy has led to major improvements in local disease control and survival rates.[3-5] Despite this evolution, a lower though significant proportion of these patients will develop local recurrences.[6, 7] The status of the circumferential resection margin (CRM) is a significant prognostic factor for local recurrence and distant metastasis and the most accurate predictor of survival after rectal cancer surgery.[7-10]

Several patient, tumor and treatment related factors have been associated with a higher risk of CRM involvement, such as tumor stage, response to neo-adjuvant radiotherapy and abdominoperineal excision (APR).[7, 11] Consequently, hospital variation in outcomes may be influenced by differences in patient- and tumor related factors.[2] Hospital characteristics, like procedural volume, have also proven to be important factors influencing outcomes in oncologic surgery, including rectal cancer treatment.[12-14] Hospital volume seems to be a proxy for the experience of the multidisciplinary team (MDT) and more specifically the surgical quality with respect to a specific procedure.

In the Netherlands a standard was set at 20 resections for rectal cancer per hospital per year. The relation between hospital volume and specific pathological outcome measures, such as CRM involvement, is less well defined with contradictory findings in literature.[15-18] Therefore, the objective of this study was to evaluate the effect of hospital volume on CRM involvement in rectal cancer surgery in the Netherlands, based on data from a national clinical registry.

## METHODS

Data were derived from the Dutch Surgical Colorectal Audit (DSCA), a disease specific national audit.[19] This audit collects information on patient, tumor, treatment and outcome characteristics and contains approximately 97 percent of all patients with a resection for primary colorectal carcinoma in the Netherlands in 2012. The dataset is based on evidence-based guidelines and compared on a yearly basis with the data registered in the Netherlands Cancer Registry (NCR).[20] The registered CRM rate in the DSCA was 80 percent in 2011 and 92 percent in 2012 with a high level of concordance with the NCR. Details of this dataset regarding data collection and methodology have been published previously.[2, 19]

### Patients

For this study, no ethical approval or informed consent was required under Dutch law. All patients (n=5552) undergoing surgical resection for primary rectal cancer between January 1st 2011 and December 31th, 2012, and registered in the DSCA before March 15, 2013, were evaluated. Minimal data requirements to consider a patient eligible for analyses were information on tumor location, date of surgery and 30-day mortality (n=5534). All these patients, except those treated with a transanal resection (n=140), were included for the calculation of annual hospital volume. However, to create a homogenous cohort, patients with multiple synchronous colorectal tumors (n=233) were excluded from the analysis.

### CRM involvement

CRM was considered positive if tumor cells were in a distance of ≤1mm from the inked margin according to the definition of the Royal college of Pathologists. CRM involvement was only calculated for patients with a recorded CRM. The percentage of CRM involvement per hospital was presented in a funnel plot, showing the overall average CRM involvement with its 95% confidence limits, based on a Poisson distribution, varying in relation to the population size. The plot allowed for identification of hospitals with a CRM involvement rate that was significantly higher or lower than average.

### Hospital volume

The mean annual operative caseload was calculated for each hospital based on their respective numbers of rectal cancer cases, including patients with multiple synchronous colorectal tumors. Volume was stratified in two groups (< 20 and ≥ 20 cases/year), based on the mandatory annual volume of rectal cancer surgery per hospital in the Netherlands and three groups (< 20, 20-40, ≥ 40 cases/year) to evaluate the influence of a higher hospital volume than is currently required. Patients with an unknown CRM status were not excluded from this calculation.

Potential patient- and tumor specific risk factors (casemix) for CRM involvement were selected from the dataset and, together with treatment characteristics, compared between the three volume groups using the chi-square test. Subsequently, a univariable analysis was performed to determine the effect of hospital volume on CRM involvement. The significance level was set at a two-tailed p-value of 0.05. Factors were entered in the multivariable analysis at a p-value of 0.10 using an ENTER model. No process or treatment characteristics were included in the multivariable analysis for adjustment.

Statistical analyses were performed in PASW Statistics, version 20 (SPSS inc., Chicago, IL).

## RESULTS

### Patient characteristics

A total of 5,161 patients, registered by 91 hospitals, met the inclusion criteria. Hospitals were categorized into three volume groups; low volume (n=25), medium volume (n=47) and high volume hospitals (n=19). Patient, tumor, treatment and outcome characteristics were displayed by hospital volume category in table 1. In medium and high volume hospitals, there was a higher proportions of advanced tumors (cT3-4: 68 and 66 versus 59%, p=< 0.001) and elective surgery (1,8 and 1,1 versus 3,7%). There was an uneven distribution in preoperative pelvic imaging; high volume hospitals showed a significantly higher percentage of patients with no recorded type of imaging. (7.0 versus 3.1 and 2.1%, p=< 0.001). Significant differences in type of neo-adjuvant treatment were observed between hospital categories with increasing use of chemoradiotherapy and decreasing use of short course radiotherapy (SCRT) with increasing volume. As for the type of surgical procedure, there was no

difference in APR rate, but medium volume hospitals treated more patients by laparoscopy than the other volume categories did (58 versus 50 and 40%, p=<0.001). Medium and high volume hospitals showed a higher percentage of patients with more than 10 examined lymph nodes. There was no significant difference between these groups for sex, age, ASA classification, Body Mass Index, distance from the tumor to the anal verge, registered CRM and postoperative morbidity and mortality.

**CRM involvement**

CRM was recorded in 86 percent of all included patients, with no marked differences between the volume categories. Univariable analysis showed 8 factors with a significant influence on CRM involvement (table 2). The significance level was set at a two-tailed p-value of 0.10. Sex, non-elective surgery, distance between tumor and the anal verge, a preoperative MRI, clinical T classification, preoperative (chemo) radiotherapy, laparoscopic surgery and the APR procedure were of significant influence.

Hospital volume significantly influenced the rate of CRM involvement. A positive CRM was more frequently encountered in low volume hospitals compared to medium and high volume hospitals (p=0.026). However, no difference was seen between medium and high volume hospitals (OR 0.69 and 0.71). When CRM rate was analysed using a cut-off level of 20 procedures per year, hospitals with high volume had significantly lower rates of CRM involvement than hospitals treating <20 patients annually (OR 0.70, CI 0.52 - 0.94).

**Forrest plot**

The influence of hospital volume (low volume vs medium/high volume) on CRM involvement in specific subgroups was plotted in a forest plot (figure 1). This figure shows that there is a marked influence of hospital volume in certain subgroups of patients. Low hospital volume has, like was already apparent in the whole group, in most groups a negative effect on CRM involvement, as is shown by the different odds ratio's.

**Multivariable analysis**

With adjustment for sex, clinical T classification and the distance from the tumor to the anal verge, hospital volume was still of significant

influence on CRM involvement (table 3). The risk of CRM involvement was 1.5 times as high in patients operated in a low volume setting (OR 1.54, CI 1.12-2.11). Furthermore, clinical T classification was an independent predictor for CRM involvement (cT3; OR 1.31, CI 1.00-1.72, cT4; OR 2.99, 2.08-4.31 when compared to cT1-2).

**Funnelplot**

Figure 2 shows the CRM involvement rate, after adjustment for casemix, of 91 hospitals varying between 0 and 50 percent. All hospitals, except for 3, were within the upper 95 percent confidence limit of the average. Nine hospitals showed significantly lower rates than average.

## DISCUSSION

This population-based study is the first to analyse and demonstrate a casemix adjusted association between hospital volume and CRM involvement in rectal cancer resections. The relation remained significant after adjustment for clinical T classification, distance from the tumor to the anal verge and whether or not the resection took place in an elective setting. Patients treated in low-volume hospitals had a 1.5-fold higher risk of CRM involvement than patients operated in high-volume hospitals. Treatment strategy related factors that were both inherently related to hospital preferences or experience as well as to outcome (e.g. preoperative (chemo) radiotherapy, preoperative MRI, surgical procedure and approach) were not adjusted for.

Many studies have evaluated the influence of procedural volume on clinical outcomes like morbidity, mortality and survival.[12-14] Only few studies evaluated the influence of this factor on oncological outcome parameters like CRM.[15-18] Supportive evidence for the influence of hospital volume on CRM involvement has been scarce. Harling et al. included over 5,000 patients and found no influence in univariable analysis of hospital volume on pathological outcome.[17] Another smaller (n=302) more recently published study by Kennely et al. showed no relationship either by analysing the influence of unit APR volume (≤5, >5 per year) on CRM involvement.[18] Cornish et al. included over 7,000 patients and did find a significant relationship in univariable analysis.

High volume trusts (annual volume ≥190 colorectal procedures, rectal procedures were not mentioned) were more likely to have a negative CRM than trusts with a lower volume of cases. They did not investigate this relationship in a multivariable analysis. A higher volume per surgeon was not associated with improved CRM rates.[16] Borowski et al analysed the influence of both hospital and surgeon volume on CRM involvement; high volume surgeons had better outcomes, though hospital volume was not associated with this outcome.[15]

The definition of a high volume hospital differs between countries; minimal volume standards seem to be introduced on a rather arbitrary basis.[15] Numbers required to qualify a hospital as 'high volume' varied widely between studies. Cut off points for low volume hospitals ranged between 5 and 20 and for high volume hospitals between 10 and 40 cases a year.[21] National audits like the DSCA make continuous verification of these volume standards possible, which is important as it has substantial implications for healthcare delivery. Extensive population based audit registrations with feedback adjusted for casemix would be the ideal alternative and could make rigid minimal volume standards obsolete. However, until this is fully realised, minimal volume standards can result in better care for patients with colorectal cancer.[14, 22]

Our study has some limitations. As it is known from other national audits, the status of the CRM is not registered for every patient.[23] The proportion of reported CRM, however, did not differ significantly between the hospital volume groups. Eighty percent of the patients had a registered CRM in 2011, which increased to 92 percent in 2012. This is a high percentage compared to the audits in our neighbouring countries like the UK (60%) and Belgium (88%).[23, 24] The rate of MRI documented threatened CRM (distance to the mesorectal fascia < 1 mm) was not registred for 71 percent of all patients. Therefore, this variable was excluded from analysis. The available data revealed that high volume hospitals treated more patients with a threatened CRM (8.2% versus 7.3%) and achieved higher percentages of a negative CRM in these patients (92% versus 78 %). This suggests that MRI documented threatened CRM would not significantly have changed outcomes.

Furthermore, as the level of expertise in high volume hospitals could lead to better patient selection, diagnostic procedures and therapeutic strategies, translating into better outcomes for patients, we did not

adjust for treatment strategy related factors such as a preoperative MRI and neoadjuvant treatment. Nevertheless, we explored the potential impact of the use of 'pre-treatment MRI' and 'neoadjuvant treatment' on CRM positivity. Inclusion of these two additional variables in the multivariable model resulted in a persisting, significant and independent effect of hospital volume on CRM positivity (OR 1,58; 95% CI 1,15 – 2,17).

As the DSCA provides no results on long-term outcomes, we were only able to analyse CRM involvement as a surrogate endpoint. Nonetheless, it seems reasonable to extrapolate these outcomes to the overall quality of care for rectal cancer patient as the status of the CRM gives an accurate estimation of long-term oncological outcomes.[25]

The influence of volume on the outcomes of rectal cancer surgery has been analysed for procedural volume per surgeon and per hospital.[12, 15] The working mechanism has been described in great detail.[26] A large volume per surgeon results in greater experience but on top of that it is generally believed that volume is to be seen as a 'proxy' for other important structural and process factors in the chain of multidisciplinary treatment.[13, 22] This study underlines the importance of a high quality care process, extending beyond the surgical part of the treatment. The quality of these factors is more likely to be realised and sustained in high volume hospitals.[27, 28] By this means, the Association of Surgeons of the Netherlands decided to dictate minimal volume standards per hospital instead of minimal annual volume standards per surgeon. It is important however to conclude that individual small volume hospitals can provide the same standard of care compared to high volume hospitals as shown in figure 2. In this way, hospital volume does not guarantee quality.

In conclusion, this article supports the minimal annual volume standard of 20 rectal cancer resections a year, implemented by the Association of Surgeons of the Netherlands, by showing an independent and significant relationship between volume and CRM involvement. The question is whether there is a need for further centralisation of rectal cancer surgery in the Netherlands, since there were no marked differences in CRM involvement rates between medium and high volume hospitals and CRM status alone may not be the only outcome measure to determine optimal volume.

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## TABLES AND FIGURES

**Table 1:** Patient, tumor, treatment and outcome characteristics categorised per hospital volume. Complicated postoperative course: a complication leading to a surgical, endoscopic or radiological re-intervention, to an in-hospital stay of more than 14 days, or to death. MDT=Multidisciplinary team meeting; SCRT=Short course radiotherapy; CRT=Chemoradiotherapy; LAR=Low anterior resection; APR=Abdominoperineal resection.

| | **< 20 / year** | | **20-40 / year** | | **> 40 / year** | | $\chi^2$ |
|---|---|---|---|---|---|---|---|
| **No. of patients** | 618 | 12% | 2607 | 50% | 1936 | 38% | |
| **No. of hospitals** | 25 | | 47 | | 19 | | |
| **Patient** | | | | | | | |
| **Sex** | | | | | | | 0.780 |
| male | 390 | 63% | 1609 | 62% | 1192 | 62% | |
| female | 228 | 37% | 998 | 38% | 744 | 38% | |
| **Age** | | | | | | | 0.751 |
| <75 yrs | 232 | 72% | 993 | 73% | 729 | 74% | |
| >75 yrs | 91 | 28% | 364 | 27% | 257 | 26% | |
| **ASA classification** | | | | | | | 0.500 |
| I - II | 519 | 84% | 2141 | 82% | 1603 | 83% | |
| III | 90 | 15% | 445 | 17% | 320 | 17% | |
| IV - V | 6 | 1.0% | 15 | 0.6% | 12 | 0.6% | |
| **Body mass index** | | | | | | | 0.509 |
| <20 | 8 | 1.7% | 53 | 2.7% | 44 | 3.2% | |
| 20-25 | 155 | 34% | 620 | 32% | 427 | 31% | |
| 25-29 | 207 | 45% | 879 | 45% | 655 | 47% | |
| >30 | 89 | 19% | 393 | 20% | 260 | 19% | |
| **Tumor** | | | | | | | |
| **Clinical T classification** | | | | | | | <0.001 |
| cT 1-2 | 237 | 41% | 810 | 32% | 617 | 35% | |
| cT3 | 309 | 53% | 1531 | 60% | 965 | 54% | |
| cT4 | 35 | 6.0% | 210 | 8.2% | 205 | 12% | |

**Continuation of Table 1**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Distance tumor to anal verge** | | | | | | | 0.112 |
| <=5 cm | 229 | 40% | 900 | 36% | 697 | 40% | |
| 6-10 cm | 230 | 40% | 1035 | 42% | 677 | 39% | |
| >10 cm | 116 | 20% | 558 | 22% | 382 | 22% | |
| **Diagnostics** | | | | | | | |
| **Preoperative MRI pelvis** | | | | | | | <0.001 |
| No | 41 | 6.6% | 197 | 7.6% | 127 | 6.6% | |
| Yes | 558 | 90% | 2356 | 90% | 1674 | 87% | |
| Unknown | 19 | 3.1% | 54 | 2.1% | 135 | 7.0% | |
| **Preoperative MDT meeting** | 592 | 96% | 2524 | 97% | 1896 | 98% | 0.009 |
| **Treatment** | | | | | | | |
| **Preoperative (chemo) radiotherapy** | | | | | | | <0.001 |
| None | 88 | 14% | 409 | 16% | 412 | 21% | |
| SCRT | 306 | 50% | 1205 | 46% | 743 | 38% | |
| CRT | 224 | 36% | 993 | 38% | 781 | 40% | |
| **Procedure** | | | | | | | 0.356 |
| LAR | 420 | 70% | 1782 | 70% | 1245 | 68% | |
| APR | 182 | 30% | 766 | 30% | 587 | 32% | |
| Laparoscopic surgery | 310 | 50% | 1522 | 58% | 763 | 40% | <0.001 |
| Non-elective surgery | 23 | 3.7% | 46 | 1.8% | 22 | 1.1% | <0.001 |
| **Pathology** | | | | | | | |
| More than 10 harvested lymph nodes | 412 | 67% | 1885 | 72% | 1394 | 72% | 0.017 |
| Registred circumferential resection margin | 527 | 85% | 2241 | 86% | 1662 | 86% | 0.907 |
| **Postoperative course** | | | | | | | |
| Complicated postoperative course | 167 | 27% | 621 | 24% | 436 | 23% | 0.071 |
| 30-day mortality | 19 | 3.1% | 53 | 2.0% | 43 | 2.2% | 0.288 |

**Table 2:** Prevalence of CRM involvement in various casemix factors and univariate analysis of the influence of these casemix factors on CRM involvement. CRM+ = CRM involvement, MDT = Multidisciplinary team, SCRT=Short course radiotherapy, CRT=Chemoradiotherapy, LAR=Low anterior resection; APR=Abdominoperineal resection.

| | CRM + | OR | 95% CI | 95% CI |
|---|---|---|---|---|
| **Patient** | | | | |
| **Sex** | | | | |
| male | 8.7% | ref | | |
| female | 7.2% | 0.81 | 0.65 | 1.02 |
| **Age** | | | | |
| < 75 yrs | 8.1% | ref | | |
| > 75 yrs | 7.4% | 0.92 | 0.65 | 1.29 |
| **ASA classification** | | | | |
| I - II | 7.8% | ref | | |
| III | 9.7% | 1.26 | 0.95 | 1.66 |
| IV - V | 12% | 1.60 | 0.48 | 5.39 |
| **Body mass index** | | | | |
| <20 | 11% | 1.21 | 0.61 | 2.42 |
| 20-25 | 9.3% | ref | | |
| 25-29 | 8.0% | 0.85 | 0.64 | 1.12 |
| ≥30 | 7.6% | 0.80 | 0.56 | 1.14 |
| **Tumor** | | | | |
| **Clinical T-classification** | | | | |
| cT 1 and 2 | 6.4% | ref | | |
| cT3 | 7.8% | 1.23 | 0.95 | 1.60 |
| cT4 | 17% | 2.91 | 2.06 | 4.11 |
| **Distance tumor to anal verge** | | | | |
| ≤ 5 cm | 9.6% | 1.17 | 0.87 | 1.56 |
| 6-10 cm | 6.7% | 0.80 | 0.59 | 1.09 |
| > 10 cm | 8.3% | ref | | |

**Continuation of Table 2**

| | | | | |
|---|---|---|---|---|
| **Diagnostics** | | | | |
| **Preoperative MRI pelvis** | | | | |
| no | 14% | 1.84 | 1.29 | 2.62 |
| yes | 7.9% | ref | | |
| unknown | 4.2% | 0.51 | 0.22 | 1.16 |
| **Preoperative MDT meeting** | | | | |
| yes | 10% | 1.26 | 0.67 | 2.37 |
| no | 8.1% | ref | | |
| **Treatment Preoperative (chemo) radiotherapy** | | | | |
| None | 12% | ref | | |
| SCRT | 5.7% | 0.45 | 0.33 | 0.61 |
| CRT | 9.6% | 0.80 | 0.60 | 1.06 |
| **Procedure** | | | | |
| LAR | 7.1% | ref | | |
| APR | 10% | 1.49 | 1.19 | 1.86 |
| **Approach** | | | | |
| Open | 9.8% | ref | | |
| Laparoscopic | 6.5% | 0.64 | 0.51 | 0.79 |
| **Setting** | | | | |
| Elective | 7.9% | ref | | |
| Urgent | 24% | 3.63 | 2.01 | 6.54 |
| **Hospital volume** | | | | |
| **Volume in 2 groups** | | | | |
| low volume | 11% | ref | | |
| high volume | 7.8% | 0.697 | 0.517 | 0.939 |
| **Volume in 3 groups** | | | | |
| low volume | 11% | ref | | |
| medium volume | 7.7% | 0.69 | 0.50 | 0.94 |
| high volume | 7.9% | 0.71 | 0.51 | 0.99 |

**Table 3:** Assessment of the influence of hospital volume on CRM involvement in a multivariate analysis. CI=Confidence interval; OR=Odds ratio.

| | Sig. | OR | 95% CI | 95% CI |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | | | | ref |
| Female | .112 | 0.82 | 0.65 | 1.05 |
| **Clinical T classification** | | | | |
| cT 1 and 2 | | | | ref |
| cT3 | .050 | 1.31 | 1.00 | 1.72 |
| cT4 | .000 | 2.99 | 2.08 | 4.31 |
| **Distance tumor - anal verge** | | | | |
| ≤ 5 cm | .654 | 1.07 | 0.79 | 1.45 |
| 6-10 cm | .230 | 0.83 | 0.60 | 1.13 |
| > 10 cm | | | | ref |
| **Hospital volume** | | | | |
| low volume | .008 | 1.54 | 1.12 | 2.11 |
| high volume | | | | ref |

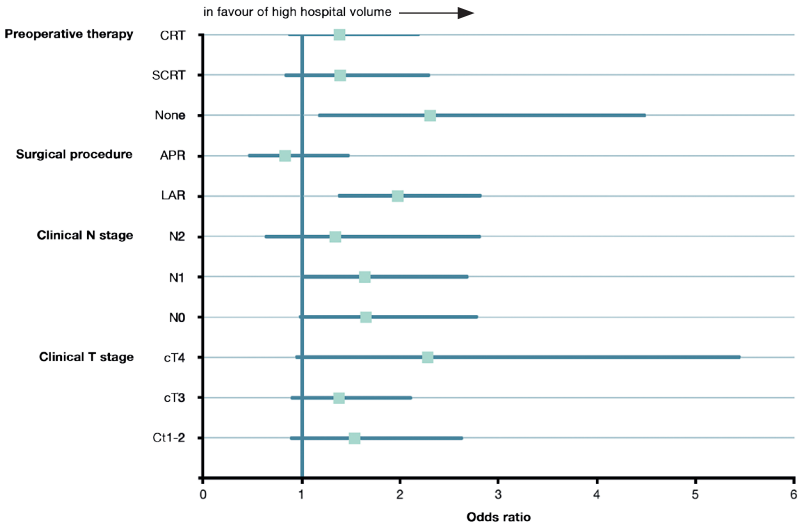


**Figure 1:** Forest plot representing the OR and CI of the influence of low hospital volume versus high hospital volume on CRM involvement, seperately presented for different subgroups (hier subgroepen beschrijven?) cT=clinical T classification, cN=clinical N classification, LAR=Low anterior resection, APR=Abdominoperineal resection, SCRT=Short course radiotherapy, CRT=Chemoradiotherapy).

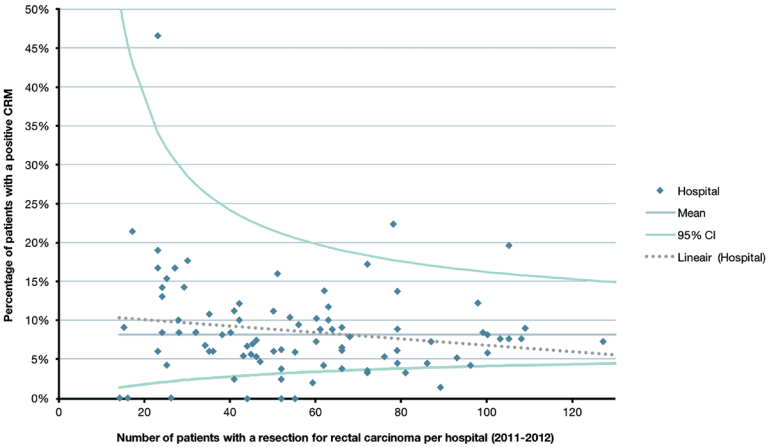


**Figure 2:** Funnel plot showing differences in risk-adjusted CRM involvement rates between hospitals (2011-2012). Casemix adjustments were made for sex, clinical T classification and the distance from tumor to the anal verge.