Improving quality of care for patients with ovarian and endometrial cancer

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CHAPTER 3

The impact of centralization of services on treatment delay in ovarian cancer: a study on process quality

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ABSTRACT

Objectives

Emphasis on improving health care quality has led to centralization of services for patients suspected of ovarian cancer. As centralization of services may induce treatment delays, we aimed to assess health system interval guidelines in patients suspected of ovarian cancer within our managed clinical network.

Methods

Compliance with national guidelines regarding health system intervals of patients treated for ovarian cancer in the University Medical Center Groningen in 2013 and 2014 was evaluated. Health system intervals were compared between 2013 and 2014, and between patients that were referred to the gynecology department in the UMCG directly and indirectly.

Results

Between 2013 and 2014 a clinically relevant improvement in compliance with guidelines was demonstrated. Within this period, median treatment intervals decreased from 34 days to 29 days, and the percentage of patients in whom treatment interval guidelines were met increased from 63.5% to 72.2%. New regulations and increased awareness of health system intervals inspired changes in local practice leading to improved compliance with guidelines. Compliance was highest in patients that were directly referred to our academic hospital.

Conclusion

Evaluation of health system intervals in patients suspected of ovarian cancer was feasible and may be applicable to other managed clinical networks. Though compliance with guidelines improved within the study period, there is potential for improvement. Establishing uniformity of electronic patient files in a managed clinical network is deemed essential to facilitate real-time evaluation of compliance with national guidelines in the future.

INTRODUCTION

Within the past decade health care expenses have escalated. The increase may be attributed to factors such as an ageing population and development of expensive new treatment strategies. As expenditures place an increasing strain on health care budgets, a transition from volume-based payment models to value-based payment models has been suggested(1). Though many of the specific quality indicators to be used in value-based payment models still need to be defined, it is evident that standardization of services is essential.

To direct standardization of services for oncological patients, the development of guidelines based on specific, accurate and measurable quality indicators is important. It has previously been suggested that such guidelines should cover three elements: structure, process and outcome(2). In the case of ovarian cancer care, quality indicators have been identified in all three areas. For example, it has been demonstrated that complete cytoreduction is strongly associated with improved survival(3–6) and that patients treated in high volume hospitals by specialized gynecologic oncologists have better surgical outcomes(7–12). Implementation of national guidelines has led to centralization of services for patients with ovarian cancer in the Netherlands(13). In Europe, similar efforts have led to the development of Quality Indicators by the European Society of Gynecologic Oncology(14).

Within the Netherlands general practitioners act as gatekeepers and refer patients to hospital when, and if, needed. Traditionally, patients suspected of ovarian cancer were staged and treated in the hospital of their choice. However, as of January 2013, guidelines were implemented requiring centralization of cytoreductive surgery to high-volume hospitals with specialized gynecological oncologists on staff. Other important aspects of these guidelines include mandatory discussion of all patients within a multidisciplinary setting, regional cooperation and the presence of an intensive care unit with sufficient experience in patients that have undergone large gynecologic surgeries.

To monitor quality of care for patients suspected of gynecological cancer within the north-eastern region of the Netherlands, a Managed Clinical Network (MCN) was created. The network raises awareness for quality indicators in oncological health care and aims to improve the quality and uniformity of care for patients with ovarian cancer within the north-eastern region of the Netherlands. The University Medical Center Groningen (UMCG) is part of this MCN and receives patients from a total of 10 regional hospitals.

One of the drawbacks of a centralized care system is the possibility of inducing delay(15). While the effect of longer waiting times on survival in ovarian cancer patients is debatable(16–18), delays in therapy have been linked to anxiety, reduced patient satisfaction and quality of life(17,19). Furthermore, delay may be a reflection of inefficiently organized care. It has recently been demonstrated that early initiation of therapy in women suspected of epithelial ovarian cancer leads to additional

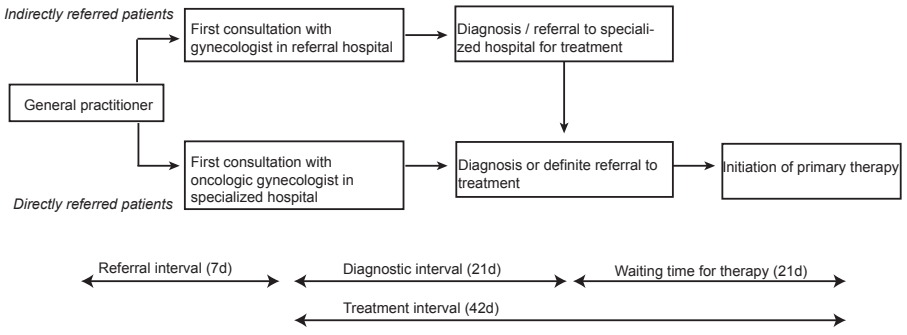
quality-adjusted life years and is cost-effective in the Netherlands (20).

To prevent occurrence of delay, national guidelines were implemented regarding time intervals between first medical consultation, diagnosis and the start of primary therapy(13). The time intervals in the national guidelines are defined as follows:

- *referral interval,* defined as the time between first medical consultation with general practitioner and first consultation with a gynecologist,
- *treatment interval*, defined as time from first consultation with a gynecologist to start of primary therapy,
- *diagnostic interval*, defined as time from first consultation with gynecologist to date of diagnosis or definite referral to treatment.

Additionally, our MCN locally implements the guideline *waiting time for therapy* (primary surgery or chemotherapy) after diagnosis or definite referral to treatment. Due to centralization of services for patients suspected of ovarian cancer, primary surgery is currently performed in specialized high volume hospitals, whereas neo-adjuvant chemotherapy may also be administered in local low volume hospitals. A graphic representation of these four time intervals, including the maximal number of days that were set for each interval according to the guidelines, is shown in figure 1.

Figure 1. Overview of time intervals used in the current study



To assess compliance with these guidelines, regular measurement of specific health care intervals is essential. Within our region, these intervals have not been investigated systematically in patients suspected of ovarian cancer. Therefore, a pattern of care study was conducted to measure health care intervals for patients referred to the UMCG with a suspicion of ovarian cancer in the years 2013 and 2014. Within the current study, compliance with national health system interval guidelines was defined as primary outcome. Assessment of statistical process control within our managed clinical network (MCN) and identification and elimination of special causes of delay were defined as secondary outcomes.

METHODS

Study design

A retrospective cohort study was performed concerning women referred to the UMCG with a suspicion of ovarian cancer. We measured health system intervals within the first two years following the implementation of centralized services for ovarian cancer. All patients billed with the specific hospital consultation code for ovarian cancer in the UMCG between January 1st 2013 and December 31st 2014 were included in the study. Patients with missing health system interval data were excluded, as were patients that were referred for a second opinion from outside the region. Electronic patient files were used to measure time intervals as defined in the national guidelines.

Outcome measures

Compliance with national guidelines was defined as primary outcome. Assessment of statistical process control within our managed clinical network (MCN) and identification and elimination of special causes of delay were defined as secondary outcomes.
Definitions of the time intervals used in the current study are the same as those used in the national guidelines and those used in previously published studies. All time intervals were measured in days.

Data analysis

Health system intervals of directly referred patients (referred from general practitioner to the UMCG) and indirectly referred patients (referred from general practitioner to a regional hospital before referral to the UMCG) were analyzed separately to enable comparison of these two groups. Furthermore, a comparison was made between health system intervals of patients referred to our hospital in 2013 and 2014.

To improve quality of care, identification of exceptional reasons for treatment delay is essential. This is termed 'special cause variation'. Statistical process control, a key approach to quality improvement, was used to discriminate between expected ('common cause') variation and exceptional ('special cause') variation of the measured health system intervals, (21–23). Control charts were used to visualize and assess statistical process control within the MCN. Health system intervals from individual patients were plotted in chronological time order. Within the control charts, the dotted horizontal line represents the maximal time interval according to national guidelines. Treatment intervals marked with a red square and a 1 were located >3 standard deviations above the mean and were defined as outliers. These treatment intervals were investigated further to assess any reasons for special cause variation. Median health system intervals were compared to the national guidelines to assess compliance.

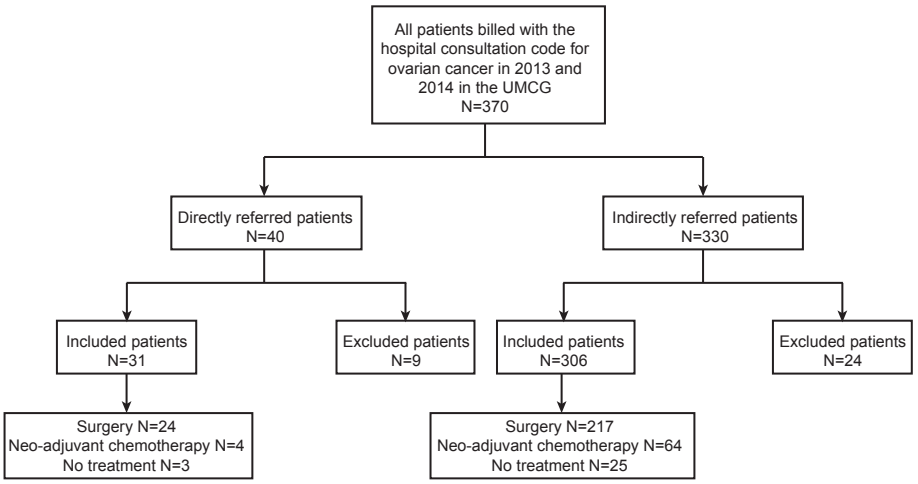
The Kruskall Wallis test for independent groups was used to investigate differences in intervals among patients diagnosed in 2013 and 2014. Differences were considered statistically significant at $p<0.05$. Statistical analyses were carried out using Minitab 17, Minitab Inc, Pennsylvania, United States of America.

RESULTS

Patients

Medical records from 370 patients that were referred to the UMCG with a suspicion of ovarian cancer between January 1st 2013 and December 31st 2014 were retrieved. In total, 306 of the indirectly referred patients and 31 patients of the directly referred patients were included in the analyses (figure 2). An overview of the waiting times for indirectly referred patients is shown in table 1.

Figure 2. Flowchart of patients included in analyses



Treatment interval

The most important interval defined in the national guidelines is the treatment interval. The maximal time for this interval is 42 days. In total, 281 indirectly referred patients that were suspected of ovarian cancer underwent treatment in the MCN in 2013 and 2014. The median treatment interval was 34.0 days (interquartile range (IQR) 22.0-51.0 days) in 2013, and 29.0 days (IQR 22.0-43.5days) in 2014.

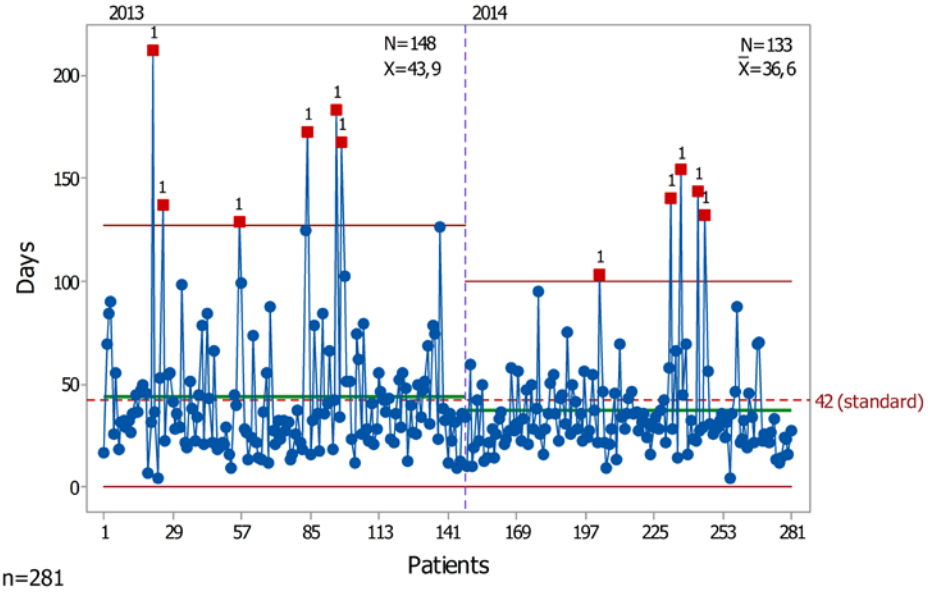
Though not statistically significant, the median treatment intervals improved between 2013 (median of 34.0, IQR of 22.0-51.0 days) and 2014 (median of 29.0, IQR of 22.0-43.5 days), (p=0.118). The proportion of patients that were compliant with the national guideline increased over time (63.5% in 2013 compared to 72.2% in 2014) (figure 3).

Table 1. Overview of waiting times of the indirectly referred patients

	N	Standard (days)	Waiting time 2013 (days) Median, IQR	Waiting time 2014 (days) Median, IQR	Difference in waiting time 2013 vs 2014	% of patients compliant with national guideline
Referral interval	2013: 116 2014: 102	7	7.0, 5.0-9.0	5.0, 3.0-6.3	P = 0.299	2013: 80.7% 2014: 81.4%
Diagnostic interval	2013: 158 2014: 145	21	19.0, 13.0-29.0	18.0, 12.0-26.0	P = 0.044	2013: 60.5% 2014: 67.6%
Waiting time surgery	2013: 107 2014: 110	21	17.0, 9.0-24.0	13.0, 6.0-17.0	P = 0.000	2013: 63.1% 2014: 83.9%
Waiting time chemotherapy	2013: 41 2014: 23	21	6.0, 2.5-20.5	14.0, 7.0-17.0	*	2013: 78.0% 2014: 82.6%
Treatment interval	2013: 148 2014: 133	42	34.0, 22.0-51.0	29.0, 22.0-43.5	P = 0.118	2013: 63.5% 2014: 72.2%

*All statistical analyses were performed using Kruskal-Wallis. *no statistical analysis was performed for waiting time to chemotherapy due to small sample size. IQR: interquartile range*

Figure 3. Control chart demonstrating treatment intervals of all patients.



The red dotted horizontal line represents the maximal interval as set by the national guidelines, the green horizontal line represents the average treatment interval of patients in 2013 (left) and 2014 (right). The upper red line represents the upper control limit, and the lower red line represents the lower control limit. Treatment intervals marked with a red square and a 1 were identified as outliers.

Further investigation of the outliers depicted in figure 3 uncovered a number of reasons for the exceptionally long treatment intervals of these patients. First of all, in some patients treatment for suspected ovarian cancer was only initiated after a second opinion. Furthermore, in a few patients treatment was postponed (due to patient's own wishes or medical reasons), and other patients had long referral intervals due to difficulties in obtaining additional diagnostic information. A number of factors were identified which may have contributed to the reduction in treatment intervals between 2013 and 2014. For example, in 2013 there were technical problems concerning retrieval of CT-scans from external sources, and there was a relatively long waiting list for surgery. In 2014 these problems were solved, which may have contributed to the reduction in treatment intervals.

Referral interval

The maximal referral interval is 7 days. The data that was needed to calculate the referral interval was available for 218 indirectly referred patients. No change was determined in median referral intervals between 2013 and 2014; they measured 7.0 days (IQR 5.0-9.0 days) in 2013 and 5.0 days (IQR 3.0-6.3 days) in 2014. Although the median referral intervals described were compliant with the national guideline, the maximal referral time was exceeded in 19.3% of patients in 2013 and 18.6% of patients in 2014. The relatively large range in referral intervals can partially be explained by a number of outliers. Within this group of outliers, a majority of patients were suspected of ovarian cancer after a coincidental finding on ultrasound imaging during the first consultation with a gynecologist.

Diagnostic interval

The maximal diagnostic interval is 21 days. Diagnostic intervals were calculated for 303 indirectly referred patients. In 2013 the guideline was met in 60.5% of patients, and this increased to 67.6% of patients in 2014 ($p=0.044$). The median diagnostic interval was 19.0days (IQR 13.0-29.0 days) in 2013 and18.0 days (12.0-26.0 days) in 2014.

Waiting time for therapy

The maximal waiting time for therapy is 21 days. Waiting time for therapy for patients undergoing surgery was evaluated for 217 indirectly referred patients. An improvement was seen in the surgical treatment intervals between 2013 and 2014 ($p<0.001$). In 2013 the median surgical treatment interval was 17.0 days (IQR 9.0-24.0 days) and the guideline was met in 63.1% of patients. In comparison, in the following year, the median surgical treatment interval was 13.0 days (IQR 6.0-17.0 days) and the guideline was met in 83.9% of the patients.

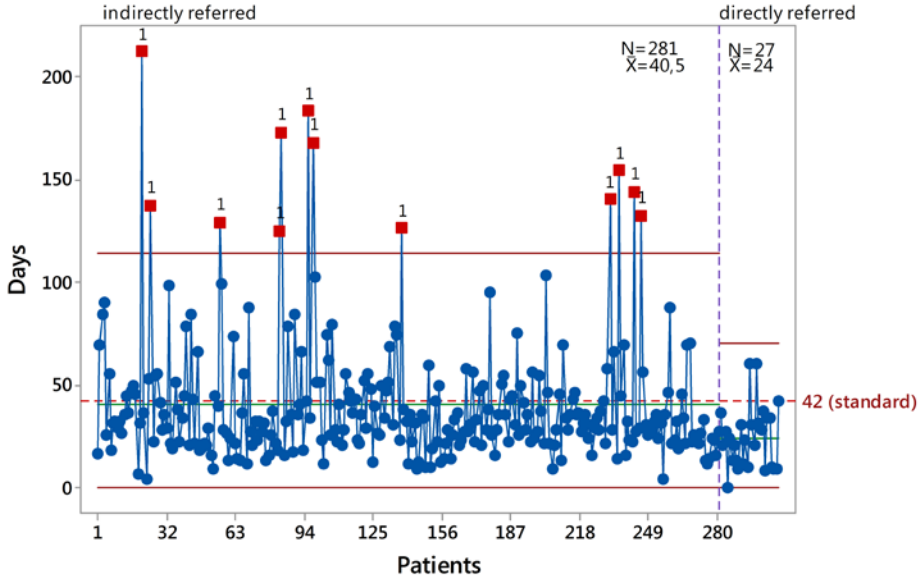
Waiting time for patients undergoing neo-adjuvant chemotherapy was evaluated for 64 patients. An increase in the median chemotherapy treatment interval was seen between 2013 and 2014, however the number of patients involved was too small to calculate whether this was statistically significant. In 2013, the median chemotherapy treatment interval was 6.0 days (IQR 2.5-20.5 days) and the guideline was met in 78% of patients. In 2014, the median chemotherapy treatment interval was 14.0 days (IQR

7.0-17.0 days) and the guideline was met in 82.6% of patients.

Directly referred vs indirectly referred patients

In total, 31 patients suspected of ovarian cancer were directly referred from general practitioner to the UMCG. Twenty-eight of them received treatment (figure 2). We compared treatment intervals in 27 directly referred patients with 281 indirectly referred patients that received treatment (figure 4). The median treatment interval for directly referred patients in 2013 was 34.0 days (IQR 22.0-51.0 days) with 88.9% of all patients meeting the national guideline, in 2014 the median treatment interval was 29.0 days (IQR 22.0-43.5 days) with 100% of all patients meeting the national guideline. In 2014, patients referred to the UMCG directly had a shorter median treatment interval compared to indirectly referred patients; the median treatment interval for indirectly referred patients was 28.0 days (IQR 9.0-35.5 days).

Figure 4. Control chart demonstrating treatment intervals of patients that were indirectly and directly referred to our academic hospital.



The red dotted horizontal line represents the maximal interval as set by the national guidelines, the green horizontal line represents the average treatment interval of patients that were indirectly (left) and directly (right) referred. The upper red line represents the upper control limit, and the lower red line represents the lower control limit. Treatment intervals marked with a red square and a 1 were identified as outliers.

The median diagnostic interval for directly referred patients was 6.0 days (IQR 4.5-12.5 days) in 2013, with 83.4% of all patients meeting the national guideline. In 2014 the median diagnostic interval was 6.5 days (IQR 0.0-19.0 days) with 90.0% of all patients meeting the national guideline.

Table 2. Health system intervals of indirectly referred patients and directly referred patients in 2013 and 2014

	Indirectly referred patients		
	N	**Waiting time in days (median, IQR)**	**% of patients compliant with national guideline**
Referral interval	2013: 116 2014: 102	2013: 7.0, 5.0-9.0 2014: 5.0, 3.0-6.3	80.7 81.4
Diagnostic interval	2013: 158 2014: 145	2013: 19.0, 13.0-29.0 2014: 18.0, 12.0-26.0	60.5 67.6
Treatment interval	2013: 148 2014: 133	2013: 34.0, 22.0-51.0 2014: 29.0, 22.0-43.5	63.5 72.2

IQR: interquartile range

The median referral interval of directly referred patients in 2013 was 12.0 days (IQR 2.3-22.8 days) and 40% of all patients were compliant with the national guideline. In 2014 the referral interval was 4.5 days (IQR 0.0-8.5 days) and 80.0% of all patients were compliant with the national guideline.

A comparison of the health system intervals of patients that were directly and indirectly referred can be found in table 2.

DISCUSSION

Within the current study, health care intervals in patients suspected of ovarian cancer were measured to evaluate compliance with national guidelines. Identification of patients using hospital consultation codes for ovarian cancer and calculation of health system intervals from electronic patient files was feasible. However, the lack of shared electronic patient files and comprehensive privacy regulations impeded efficient data collection. Special causes of delay were identified and eliminated, and improvements in compliance with national guidelines were demonstrated between 2013 and 2014.

Within the study period, new national regulations and improved awareness of health system intervals led to changes in local practice, resulting in improved compliance with guidelines. For example, a standardized one-weekly consultation between regional general gynecologists and gynecologic oncologists was initiated within our referral region and access to external CT-scans was arranged. Continuous implementation of changes in local practice may explain the absence of statistically significant improvements between 2013 and 2014. Importantly, the improvements in health system intervals that were demonstrated within this period are viewed to be clinically relevant.

Directly referred patients		
N	**Waiting time in days (median, IQR)**	**% of patients compliant with national guideline**
2013: 20	2013: 12.0, 2.3-22.8	40.0
2014: 10	2014: 4.5, 0.0-8.5	80.0
2013: 17	2013: 6.0, 4.5-12.5	83.4
2014: 10	2014: 6.5, 0.0-19.0	90.0
2013: 18	2013: 21.5, 12.5-30.3	88.9
2014: 10	2014: 28.0, 9.0-35.5	100.0

Though the improvements that were achieved in compliance with health system interval guidelines were present in directly and indirectly referred patients, compliance with diagnostic and treatment interval guidelines was strikingly lower in indirectly referred patients. The reasons for this difference are currently unclear. We therefore suggest that further investigation is required, especially as the majority of patients are referred to the UMCG in an indirect manner. Another noteworthy finding was the unexpectedly low compliance with referral interval guidelines for directly referred patients in 2013 (40%). Reasons for this low compliance rate, and the increase in compliance to 80% in 2014 are also unclear.

While compliance with guidelines improved within the study period, the compliance rates themselves demonstrate the potential for improvement. Within the United Kingdom, the National Institute for Health and Care Excellence (NICE) referral guidelines for suspected cancer were implemented in 2005. In a study by Neal and colleagues, 15 cancer types were selected and diagnostic intervals were evaluated before and after implementation of these guidelines. The authors conclude that implementation of the NICE guidelines contributed to a reduction of diagnostic intervals in the United Kingdom between 2001-2002 and 2007-2008(24). Further implementation of national guidelines regarding health system intervals in the Netherlands is therefore deemed essential.

Whether a further reduction in health system intervals will improve survival of patients with ovarian cancer is subject of debate(14,16,17). Indeed, the time between decision regarding treatment and start of treatment was not included in the newly published European Society of Gynecologic Oncology Quality Indicators due to a lack of evidence. Nevertheless, it has been suggested that shorter waiting times may improve patient satisfaction and quality of life (16,17,19). Furthermore, Hoyer and colleagues used a discrete event simulation model to demonstrate that a reduction in treatment

intervals leads to additional QALY's (20). The model estimated an incremental cost effectiveness ratio (ICER) of €2592 per QALY, which is far below the informal ceiling ratio that has been set at €80,000 in the Netherlands. Therefore, a reduction of health system intervals is deemed cost effective. As health expenditures are quickly accumulating, implementation of cost effective measures is of the utmost importance.

One of the challenging aspects of the current study was the involvement of 10 referral hospitals, and consequently a number of different electronic information systems. No readily accessible database containing medical information of all patients within the MCN exists, preventing real-time monitoring of health system intervals. The presence of digital borders between health care institutes was previously noted by Porter and colleagues, who stated that the current organization of healthcare and information systems impede the measurement of health care quality(19). Development of an integrated information system covering all regional hospitals (and perhaps even all national hospitals) may aid the identification of factors that prolong health system intervals and facilitate rapid intervention where needed. Importantly, patient privacy must be ensured at all times according to European privacy and data protection laws, making this a difficult (but seemingly not impossible) challenge.

One of the main strengths of this study is the application of statistical process control in the context of quality improvement. As control charts are relatively easy to interpret for (clinical) staff without prior experience in statistical process control, they can provide important information needed to reduce health system intervals(22,25). Within the current study, the use of control charts indeed facilitated distinction between common cause variation and special cause variation, allowing us to focus on special causes of delay within the MCN. Furthermore, these analyses demonstrated a difference in health system intervals between directly and indirectly referred patients. While median health system intervals for both directly and indirectly referred patients were within the set guidelines in 2014, differences between these two pathways should be monitored closely as uniform quality of clinical care and service for patients within the region is one of the aims of the MCN. Moreover, regular evaluation of health system intervals using control charts will ensure rapid identification of potential new special causes of delay.

Another perceived strength of this study was the use of internationally accepted time intervals, allowing comparison with other studies. However, we are aware of only two other studies describing health system intervals specific for patients suspected of ovarian cancer(26,27). The large variations in health system intervals described in these three studies suggest differences in organization of care between the three hospitals/regions. These differences hinder any valuable comparison between the three studies. A comparison with other hospitals within the Netherlands may have provided useful information, however these data were not available.

There are a number of limitations to this study. First of all, no data was gathered from the period before the implementation of the national guidelines. Moreover, the study design did not include markers of patient outcome such as survival, patient satisfaction or quality of life. Though not part of our primary objective, the absence of these data limit analyses on the impact of reducing health system intervals within this group of patients. It would be of interest to include markers of patient outcome in future studies regarding health system intervals for patients with ovarian cancer. Importantly, all quality measures require frequent re-evaluation and patient perspectives of care should be incorporated into evaluation of hospital quality, as previously emphasized by Dy and colleagues(28).

In conclusion, we have described a method to measure health system intervals in patients suspected of ovarian cancer using hospital consultation codes and electronic patient files. This method may be applicable to other departments wishing to raise awareness of health system intervals and improve quality of care. Within the study period awareness of health system intervals inspired changes in local practice leading to improved compliance with guidelines, though there is clearly still room for improvement. Regular monitoring and evaluation of statistical process control are essential to enable further improvement of process quality within the MCN. However, establishing uniformity of electronic patient files in the MCN is deemed essential to aid real-time measurements of health system intervals.

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REFERENCES

1. Liang MI, ElNaggar AC, Nekkanti S, O'Malley DM, Hade EM, Copeland LJ, et al. Setting the bar: compliance with ovarian cancer quality indicators at a National Cancer Institute-designated Comprehensive Cancer Center. Gynecol Oncol [Internet]. Elsevier Inc.; 2015;138(3):689–93. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0090825815300810
2. Donabedian A. Quality assurance. Structure, process and outcome. Nurs Stand [Internet]. Jan [cited 2016 May 4];7(11 Suppl QA):4–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1489693
3. Griffiths CT. Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma. Natl Cancer Inst Monogr. UNITED STATES; 1975;42:101–4.
4. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol. Kelly Gynecologic Oncology Service, Department of Gynecology and Obstetrics, Johns Hopkins Medical Institutions, Baltimore, MD 21287-1248, USA. rbristo@jhmi.edu; 2002;20(5):1248–59.
5. Chang SJ, Hodeib M, Chang J, Bristow RE. Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. Gynecol Oncol. Department of Obstetrics and Gynecology, Ajou University School of Medicine, Suwon, Republic of Korea.: Elsevier Inc; 2013 Sep;130(3):493–8.
6. du Bois A, Reuss A, Pujade-Lauraine E, Harter P, Ray-Coquard I, Pfisterer J. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzin. Cancer. Department of Gynecology & Gynecologic Oncology, Dr. Horst Schmidt Klinik, HSK Wiesbaden, Germany (AGO-OVAR). prof.dubois@googlemail.com: American Cancer Society; 2009;115(6):1234–44.
7. Vernooij F, Heintz AP, Coebergh JW, Massuger LF, Witteveen PO, van der Graaf Y. Specialized and high-volume care leads to better outcomes of ovarian cancer treatment in the Netherlands. Gynecol Oncol. Department of Gynecological Surgery and Oncology, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands. f.vernooij@umcutrecht.nl; 2009;112(3):455–61.
8. Harter P, Muallem ZM, Buhrmann C, Lorenz D, Kaub C, Hils R, et al. Impact of a structured quality management program on surgical outcome in primary advanced ovarian cancer. Gynecol Oncol [Internet]. Elsevier Inc.; 2011;121(3):615–9. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0090825811001260
9. Horowitz NS, Miller a., Rungruang B, Richard SD, Rodriguez N, Bookman M a., et al. Does Aggressive Surgery Improve Outcomes? Interaction Between Preoperative Disease Burden and Complex Surgery in Patients With Advanced-Stage Ovarian Cancer: An Analysis of GOG 182. J Clin Oncol [Internet]. 2015;33(8). Available from: http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2014.56.3106
10. van Altena AM, van den Akker PA, de Hullu JA, Ottevanger PB, Aalders AL, Gerritse R, et al. Efficacy of a regional network for ovarian cancer care. Obstet Gynecol. Department of Obstetrics and Gynecology, Radboud University Medical Centre, Nijmegen, the Netherlands. A.vanAltena@obgyn.umcn.nl; 2013 Sep;122(3):668–75.
11. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med. Department of Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, USA. john.birkmeyer@hitchcock.org: Massachusetts Medical Society; 2003 Nov 27;349(22):2117–27.
12. Bristow RE, Zahurak ML, Diaz-Montes TP, Giuntoli RL, Armstrong DK. Impact of surgeon and hospital ovarian cancer surgical case volume on in-hospital mortality and related short-term outcomes. Gynecol Oncol. The Kelly Gynecologic Oncology Service, Departments of Gynecology and Obstetrics and Oncology, The Sidney Kimmel Comprehensive Cancer Center, The Johns Hopkins Medical Institutions, 600 North Wolfe Street, Phipps #281, Baltimore, MD 21287, USA. (TRUNCATED; 2009 Dec;115(3):334–8.
13. Stichting Oncologische Samenwerking. Multidisciplinaire normering oncologische zorg in Nederland [Inter-

net]. 2014. Available from: http://www.iknl.nl/docs/default-source/Palliatieve-zorg-in-de-ziekenhuizen/soncos.pdf?sfvrsn=0

14. Querleu D, Planchamp F, Chiva L, Fotopoulou C, Barton D, Cibula D, et al. European Society of Gynaecologic Oncology Quality Indicators for Advanced Ovarian Cancer Surgery. Int J Gynecol Cancer. 2016;26(7):1354–63.
15. Yun YH, Kim Y a., Min YH, Park S, Won YJ, Kim DY, et al. The influence of hospital volume and surgical treatment delay on long-term survival after cancer surgery. Ann Oncol. 2012;23(May):2731–7.
16. Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer [Internet]. 2015;112 Suppl:S92-107. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4385982&tool=pmcentrez&rendertype=abstract
17. Robinson KM, Christensen KB, Ottesen B, Krasnik A. Diagnostic delay, quality of life and patient satisfaction among women diagnosed with endometrial or ovarian cancer: a nationwide Danish study. Qual Life Res [Internet]. 2012;21:1519–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22138966
18. Feng Z, Wen H, Bi R, Yang W, Wu X. Prognostic impact of the time interval from primary surgery to intravenous chemotherapy in high grade serous ovarian cancer. Gynecol Oncol [Internet]. Elsevier Inc.; 2016;141(3):466–70. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0090825816301482
19. Porter M. What is the value in health care. N Engl J Med [Internet]. 2010;363:2477–81. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:New+engla+nd+journal#0
20. Hoyer T, Bekkers R, Gooszen H, Massuger L, Rovers M, Grutters JPC. Cost-Effectiveness of Early-Initiated Treatment for Advanced-Stage Epithelial Ovarian Cancer Patients. Int J Gynecol Cancer [Internet]. 2014;24(1):75–84. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00009577-201401000-00013
21. Thor J, Lundberg J, Ask J, Olsson J, Carli C, Härenstam KP, et al. Application of statistical process control in healthcare improvement: systematic review. Qual Saf Health Care [Internet]. 2007 Oct [cited 2016 Mar 1];16(5):387–99. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2464970&tool=pmcentrez&rendertype=abstract
22. Fretheim A, Tomic O. Statistical process control and interrupted time series: a golden opportunity for impact evaluation in quality improvement. BMJ Qual Saf [Internet]. 2015 Dec [cited 2016 May 6];24(12):748–52. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4680165&tool=pmcentrez&rendertype=abstract
23. Perla RJ, Provost LP, Murray SK. The run chart: a simple analytical tool for learning from variation in healthcare processes. BMJ Qual Saf [Internet]. 2011 Jan [cited 2016 May 6];20(1):46–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21228075
24. Neal RD, Din NU, Hamilton W, Ukoumunne OC, Carter B, Stapley S, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: analysis of data from the UK General Practice Research Database. Br J Cancer [Internet]. Nature Publishing Group; 2014;110(3):584–92. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3915139&tool=pmcentrez&rendertype=abstract
25. Mohammed MA, Cheng KK, Rouse A, Marshall T. Bristol, shipman, and clinical governance: Shewhart's forgotten lessons. Lancet. 2001;357(9254):463–7.
26. Vandborg MP, Christensen RD, Kragstrup J, Edwards K, Vedsted P, Hansen DG, et al. Reasons for diagnostic delay in gynecological malignancies. Int J Gynecol Cancer. 2011;21(6):967–74.
27. Hansen RP, Vedsted P, Sokolowski I, Søndergaard J, Olesen F. Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. BMC Health Serv Res [Internet]. 2011;11:284. Available from: http://www.biomedcentral.com/1472-6963/11/284
28. Dy SM, Chan KS, Chang HY, Zhang A, Zhu J, Mylod D. Patient perspectives of care and process and outcome quality measures for heart failure admissions in US hospitals: How are they related in the era of public reporting? Int J Qual Heal Care. 2016;28(4):522–8.