Assuring quality in cancer care: A challenging multidisciplinary responsibility

Beck, N.

ASSURING QUALITY IN CANCER CARE

A CHALLENGING MULTIDISCIPLINARY RESPONSIBILITY

NAOMI BECK

Assuring Quality in Cancer Care

a challenging multidisciplinary responsibility

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Assuring Quality in Cancer Care
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in dierbare herinnering

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CHAPTER 1

General introduction and thesis outline

GENERAL INTRODUCTION

Worldwide cancer currently is one of the leading causes of morbidity and mortality. Its' global burden is expected to increase even more, with a predicted 24 million new cancer cases in 2035, compared to the 18 million in 2018 and 14 million in 2012.[1–3] With the rising life expectancy, the prevalence of cancer – being a disease mainly of the aging – will increase. Also, prevalence will increase due to more accurate detection and the expansion of treatment possibilities leading to an often more favourable prognosis. Cancer will influence more lives for a longer time and therefore will increasingly be a global health challenge.

In 2018 breast, lung, colorectal, prostate, and stomach cancer represented 55% of the global cancer incidence and about 25% of the cancer related deaths was caused by lung or stomach cancer.[3] In the Netherlands, in 2017, also around 25% of all cancer related deaths were caused by lung or stomach cancer.[4]

Multidisciplinary cancer care

In most solid cancers, surgery has an important role in curative treatment. There is a growing evidence for the added value of (neo)adjuvant therapy with chemotherapy, radiotherapy, hormone therapy, targeted therapy or combinations of these therapies. In some cases surgery is even replaced as the main curative treatment.[5,6]

Gastric cancer and non-small cell lung cancer (NSCLC) are two types of cancer eminently treated with combined (multimodal) therapy. In gastric cancer perioperative chemotherapy is recommended for all patients with non-metastasised resectable gastric cancer (excluding stage I) provided that the patient is in good condition.[7,8] In lung cancer there is a range of treatment options depending on tumour stage. Stage I NSCLC is preferably treated surgically, though in patients

unfit for surgery stereotactic radiotherapy is considered as a good alternative.[9,10] Surgically treated patients with NSCLC stage II-IIIA benefit from adjuvant chemotherapy.[9] For patients with locally advanced (stage III) NSCLC the optimal treatment consists of combined chemoradiotherapy. Selected patients may benefit from chemoradiotherapy followed by surgery, so called trimodality therapy.

With the growing possibilities and rising complexity in oncologic care, multidisciplinary teams (MDTs) are widely incorporated in the standard of oncologic care. MDTs are considered to improve communication, patient coordination, clinical decision-making, practice of evidence-based medicine and thereby overall quality of care.[11]

Quality evaluation and variation in cancer care

An increase in possibilities also arises the chances on variation. Considerable variation in the treatment and outcomes of various types of cancer in the Netherlands was demonstrated for the first time on a national level in the "quality of cancer care" report by the Dutch Cancer Society.[12] However, from the available data, reasons for these differences could hardly be defined.

In order to gain insight in the observed variation and to provide medical teams with performance information, nationwide clinical audits were introduced. Clinical auditing is defined as the systematic analysis of processes and outcomes with the ultimate aim of improvement and typically follows the plan-do-check-act (PDCA) cycle.[13] Within this cycle, data are compared with pre-defined quality indicators and continuously fed back to participating centres.

Against this background, the objective of this thesis was to provide insight in the development and implementation of clinical audits for the evaluation of multidisciplinary care and to investigate treatment variation of two eminently multimodal treated cancer types; lung cancer and gastric cancer.

OUTLINE OF THESIS

Part I. Quality assurance in multidisciplinary cancer care

In 2010, the "quality of cancer care" report by a signalling committee of the Dutch Cancer Society concluded that the overall quality of care for patients with cancer was high, though could be further improved by the reduction of regional and between-hospital variation. One of the pillars to improve quality and equality of oncologic care was the development of quality standards. Since the report was published, professional societies like the Association of Surgeons in the Netherlands have started to define quality standards for the surgical treatment of various tumours. Subsequently, the Dutch federation of oncological societies (SONCOS) started to develop multidisciplinary general oncologic and tumour specific standardisation reports with requirements to assure high quality multidisciplinary cancer care in every hospital in our country.[14]
The second pillar to improve quality of care is the participation in a national clinical audit.

The fundamental thoughts for auditing in medical practices already exist longer with ideas described by doctor Thomas Percival (1803), nurse Florence Nightingale (1820) and doctor Ernest Codman (1869). The latter stated that "every hospital should follow every patient it treats, long enough to determine whether or not the treatment has been successful, and then to inquire 'if not, why not' with a view to preventing similar failures in the future". This so-called 'end-result theory' is considered as the foundation for modern clinical audits.

One of the leading organisations providing clinical auditing in the Netherlands is the Dutch Institute of Clinical Auditing (DICA, founded in 2011). **Chapter II** provides

insight into how Codman's clinical auditing concept has been implemented on a nationwide scale in the Dutch healthcare system. It describes the development of DICA and demonstrates its effects on care processes and outcomes for patients.

Initially, DICA audits were mono-disciplinary and treatment-specific, mainly focusing on the surgical treatment of cancer. Following the increasing importance of multidisciplinary care, audits expand to include non-surgical treatments such as radiotherapy and medical oncology. The ultimate intend is to integrally evaluate the entire multidisciplinary care pathway. One of the first national audits to multidisciplinary evaluate cancer care is the Dutch Lung Cancer Audit. Its core principles, initiation and development, first results and what lessons can be learned from its development are described in **Chapter III**.

Quality information is of primary importance to clinicians and medical teams. However, amongst other stakeholders in healthcare there is a rising interest in hospital-specific performance information. The demand to use so called 'quality indicators' as public information for policy makers, insurers and patients is growing. To accommodate to this more wide use of data, its presentation must meet a number of conditions, such as relevance, usability, reliability and validity.[15]

When using outcome indicators to benchmark hospitals, differences might not only reflect the differences in quality, but also differences in patient population per hospital. This so-called 'casemix' is a combination of patient- and disease characteristics. In **Chapter IV** we examined the need for casemix adjustment evaluating hospital outcomes specifically for lung cancer surgery and a casemix adjustment model useful in practice is proposed.

Part II. Variation in multidisciplinary cancer treatment

In all DICA audits variation on structural, procedural and outcome indicators is monitored. Between-hospital variation on indicator scores is typically displayed with funnel-plots as graphical aids. In these figures all hospitals are represented by a dot. The benchmark to which the hospitals can be compared can be set at the national average or any defined norm. The confidence intervals around this norm demonstrate to which extent hospitals deviate from the set value. Hospitals outside the confidence intervals could be identified as outliers and can subjected to in-depth investigations. When relevant, casemix adjustment is applied.

Variations in outcome measures such as mortality, fortunately, seem low. However, the potential of using variation for outcome improvement is influenced by the number of events and the patient volume per hospital. For diseases or outcomes with a low incidence it is more challenging to identify improvement potential based on variation. Several studies focused on this issue by investigating alternative statistical approaches or composite measures.[16–18]

At the start of most DICA audits there was a considerable between-hospital variation, mainly in process indicators (e.g. discussion in MDTs, pre-operatively recorded TNM stage and completeness of pathology records). After providing caregivers with this information, variation notably declined and improvement on the national mean was observed. Providing caregivers with feedback information on procedural measures, such as the use of certain diagnostic tools, therapies or for instance risk-increasing modalities like neoadjuvant treatment can also influence final outcomes.[19,20]

In lung cancer surgery, such a high-risk procedure is pneumonectomy, the removal of an entire lung. The postoperative mortality of this procedure is about 3 times higher compared to less extensive resections.[21] The proportion of pneumonectomies

was therefore suggested as a quality indicator by Jakobsen et al.[22] To apply such a quality indicator, between-hospital variation and possibilities for proper casemix adjustment first need to be studied. **Chapter V** focuses on this subject.

Variation between hospitals or regions is assessed to identify either opportunities for quality improvement, e.g. by learning from best practices, or potential controversies guiding new research or guideline improvement. While current guidelines in curatively treated gastric cancer recommend perioperative chemotherapy to improve survival, recent studies using audit data show substantial variation in its use.[23,24] In **Chapter VI** underlying (organisational and process) factors associated with the use of perioperative therapy were identified. The multidisciplinary aspect of care was a subject of interest in particular. For this in-depth investigation a composite database was developed, using pre-existing data from the Dutch Upper GI Cancer Audit (DUCA) combined with data derived from in-hospital medical records.

In addition to this, a qualitative approach with semi-structured interviews among surgical and medical oncologists was used in **Chapter VII** to evaluate 'physician supply-side factors' such as clinicians' preferences as a potential underlying factor for between-hospital variation. All variation studies aim to provide leads to minimise unwanted variation in the operative en perioperative treatment of cancer.

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PART I

ASSURING QUALITY IN MULTIDISCIPLINARY CANCER CARE

CHAPTER 2

The Dutch Institute for Clinical Auditing: achieving Codman's dream on a nationwide basis

N. Beck, A.C. van Bommel, E.H. Eddes, N.J. van Leersum, R.A.E.M. Tollenaar, M.W.J.M. Wouters. On behalf of the Dutch Clinical Auditing Group*

* Can be found under the heading 'Collaborators'

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BACKGROUND

For the medical community, information on care processes and outcomes of their daily clinical practice is often lacking. An important tool in gaining insight and improving healthcare quality is clinical auditing, defined as the systematic analysis of processes and outcomes of medical care with the ultimate aim of improvement. The concept was introduced over a century ago by Dr. Ernest Amory Codman.[1] His 'end-result theory' states: "that every hospital should follow every patient it treats, long enough to determine whether or not the treatment has been successful, (...) with a view to preventing similar failures in the future".

In the Netherlands, one of the leading organisations that facilitates clinical auditing is the Dutch Institute for Clinical Auditing (DICA). DICA was founded in 2010, at a time when the demand for transparent, hospital-specific performance information was growing. Simultaneously, professional organisations wanted to redirect the performance discussion from merely procedural volume to a broader outcome-based evaluation.[2] The main goal of DICA is to gain better outcomes for patients by measuring quality of care, giving benchmarked feedback to clinicians, stimulating short-cycled improvement initiatives, enabling external transparency and reducing healthcare costs.

This article provides insight into how Codman's clinical auditing concept has been implemented on a nationwide scale in the Dutch healthcare system.

DEVELOPMENT

Origins and organisation

In the Netherlands, the Dutch Colo-Rectal Audit (DCRA) was the first nationwide professional-driven initiative to provide medical teams with benchmarked, hospital-specific performance information, offering new opportunities to improve their care.[3] It was launched in 2009 as an initiative of the Association of Surgeons of the Netherlands. The DCRA served as a blueprint for subsequent DICA audits.

Figure 1 visualises DICA's governance structure. A key feature is the leading role of those "personally engaged in the activity concerned": the clinicians. The Scientific Committee (SC) determines audit objectives and dataset content, takes the lead in interpreting data and functions as a link with other clinicians in the professional associations. DICA's scientific bureau provides methodological and operational support and is backed by a methodological advisory committee and a privacy committee.

DICA is a non-profit organisation. Since 2016, audits are structurally financed by an umbrella organisation of healthcare insurance companies (ZN). They consider DICA audits as an important source of reliable, independent hospital specific information. Although ZN participates in the establishment of the transparent indicator sets, it does not influence or have access to audit content or data analyses.

Dataset development and quality measurement

The SC composes the dataset using (inter)national evidence-based guidelines, taking into account what is meaningful and actionable information for clinicians. Quality indicators meet the requirements of relevance, validity, reliability and feasibility. In accordance with the Donabedian model, indicator sets consist of structure, process and outcome indicators.[4] Indicators are primarily of use in quality assurance and improvement initiatives by participating hospitals (local quality cycle), though data

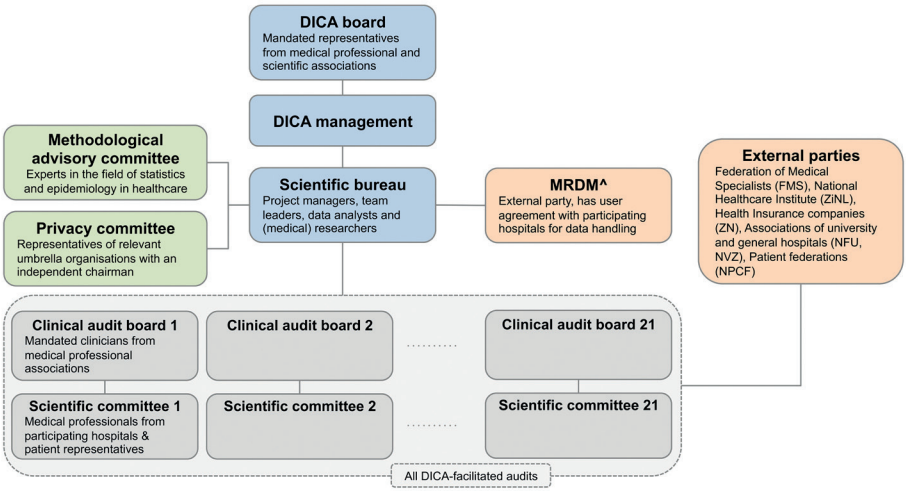

Figure 1. Organisational structure of the Dutch Institute for Clinical Auditing (DICA).
^ Medical Research Data Management.

are also used to evaluate performance at national level (national quality cycle). To ensure their continuing value, the audits' focuses and quality indicators are critically evaluated on a yearly basis.

Data entry, storage and quality assurance

Depending on the indicators defined, datasets contain information on hospital structure variables, care processes and patient outcomes. Baseline patient characteristics are included to enable risk adjustment.

For data collection, encryption, storage and processing there is close cooperation with a certified data processor: Medical Research Data Management (MRDM). Participating hospitals retain ownership of their data. All data is subjected to several validation processes: in the web-based registration system, by means of an electronic error report and by in-hospital verification of registered data by an independent third party.

Internal feedback and external transparency

Through a weekly updated, secure, online environment called '*My*DICA' participating physicians are provided with hospital-specific feedback, including information on patient, disease and treatment characteristics. Quality-indicator results are presented in funnel-plots with 95% confidence intervals around the national average or a defined norm, anonymous with regard to other hospitals.

If indicators are found relevant and valid, indicator scores can be used as public information, casemix adjusted when applicable. Hospital-specific information becomes externally available in a stepwise process agreed on by all stakeholders – patients, professionals, payers and government organisations, collaborating in a biannual meeting to define transparent indicator sets.

Hospitals authorise the sharing of their indicator scores through a DICA-facilitated web-portal, being unable to change these scores.

Quality improvement at national level

The SC plays a major role in evaluating and interpreting audit data. Between-hospital variation is assessed to identify opportunities for quality improvement, e.g. by learning from best practices, or potential controversies guiding new research or guideline improvement. The medical community is informed through an annual report, conferences and scientific articles. Professional organisations use audit results in their integrated quality policy, e.g. to verify adherence to guidelines and quality standards, and to catalyse quality improvement at national level.

Outcomes research

Detailed population-based audit data become available for research provided they are complete and verified. Research applications are assessed for relevance, methodology and availability of data. Types of research questions that have arisen thus far include: evaluation of clinical practice patterns for diagnostics and

treatments, reports on the introduction of new techniques, mechanisms behind hospital variation, identification of best practices and methodological research developing new (composite) measures or risk stratification models.

The next section highlights the most important accomplishments. All publications using DICA-data up to 2018 are included in **Supplemental Table 1**.

ACCOMPLISHMENTS

Expansion of the audits

DICA was founded in 2011. Up to December 2017, 21 nationwide audits have been initiated, resulting in the registration of over 700,000 patients (**Figure 2**). Initially, audits were mono-disciplinary and treatment-specific, mainly focusing on cancer surgery. Over time, this has expanded to include non-malignant diseases, non-surgical treatments and evaluation of the entire multidisciplinary care pathway. Audits with additional functionalities include the Dutch Melanoma Treatment Registry, used to study cost-effectiveness and real-world performance of newly developed treatments (immune and targeted therapies) at population level, and the Dutch Head and Neck Cancer Audit additionally evaluating paramedical care, like swallowing and speech therapy.

The number of medical associations involved increased from five (2011) to seventeen (2017). In parallel, the number of clinicians actively involved in the SCs and CABs rose from 32 to 243.

The number of transparent indicators calculated from DICA audits rose from six (2012) to 161 (2017). National improvements were observed together with a decline in between-hospital variance.

DICA data provided a reliable source to ascertain compliance with the volume standards and to study the volume-outcome relationship in several diseases.[5,6]

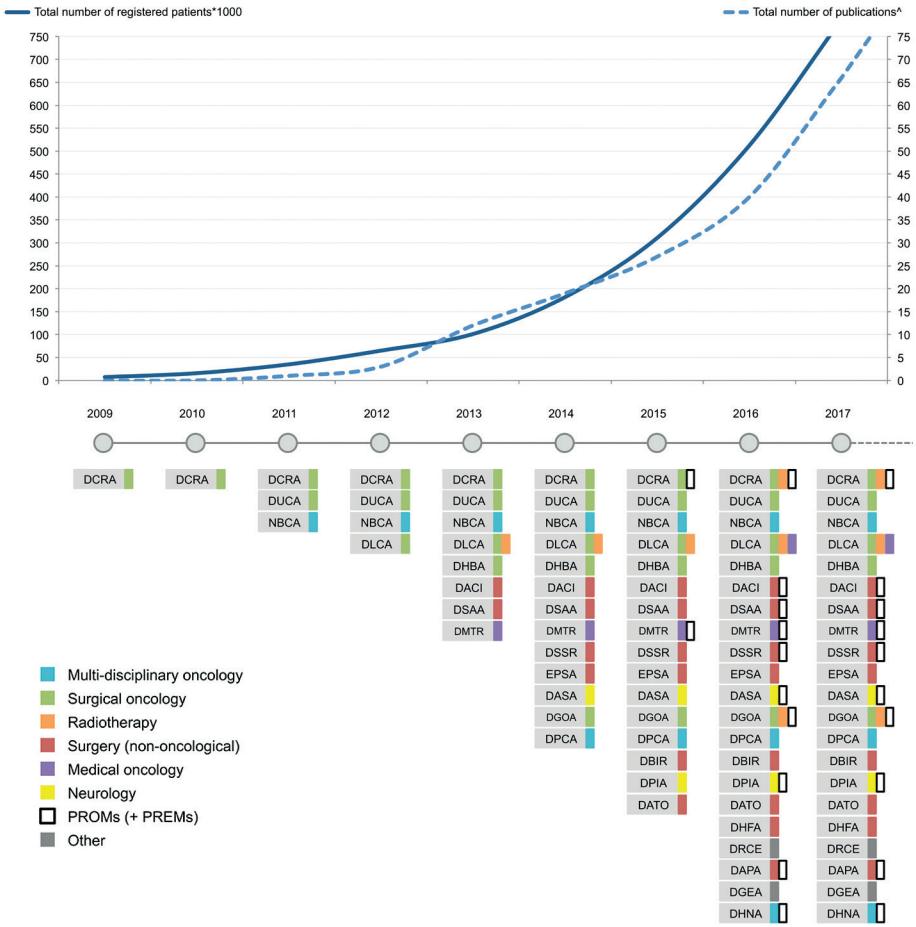

Figure 2. The evolution of DICA-facilitated audits: type of audits, number of registered patients and publications per year.
^ An overview of all publications can be seen in **Supplemental Table 1**, an abbreviation list of all DICA audits can be seen in **Supplemental Table 2**.

Developments in quality evaluation

Since single-measurement indicators can be less suitable for hospital comparison, new composite measures were developed, such as 'failure to rescue' and 'textbook outcome' for colorectal cancer, oesophagogastric cancer and elective aneurysm

surgery.[7] Risk adjustment models were developed to enable valid hospital comparisons.

Insights into national clinical practice

Variation observed between caregivers, hospitals or internationally is an important stimulus for in-depth investigation of underlying causes and improvement. For example, the relatively high use of neoadjuvant radiotherapy for rectal cancer in the Netherlands compared to other countries in 2011, led to guideline adjustment in 2014. Rapid implementation was observed, with a decrease in radiotherapy use from 84.2% to 64.4% in two years, without compromising oncologic outcomes.[8] Other findings include the increased use of minimally invasive surgery at national level.[9] Although learning curves were observed, minimally invasive procedures proved to be safely introduced and were considered to be important drivers for postoperative outcome improvement.[9]

Nationwide quality improvements

Figure 3 shows two examples of process indicator improvements for lung cancer and breast cancer, with an increased national average and a decreased between-hospital variation. For example, the national percentage of patients undergoing lung cancer surgery with a preoperatively recorded clinical TNM stage increased from 75.4% to 98.3% (2012-2016) (**Figure 3a-b**). Subsequently, variation decreased from 0-100% to 82-100%. Several process indicators regarding time to treatment also improved at national level with a decline in between-hospital variation. The number of patients treated within a certain time limit increased for the surgical treatment of carotid stenosis (63% to 79%) and lung cancer (41% to 71%), the radiotherapeutic treatment of lung cancer (60% to 71%) and any treatment of ovarian cancer (77% to 86%), rectal cancer (49% to 56%) and oesophageal cancer (31% to 47%).

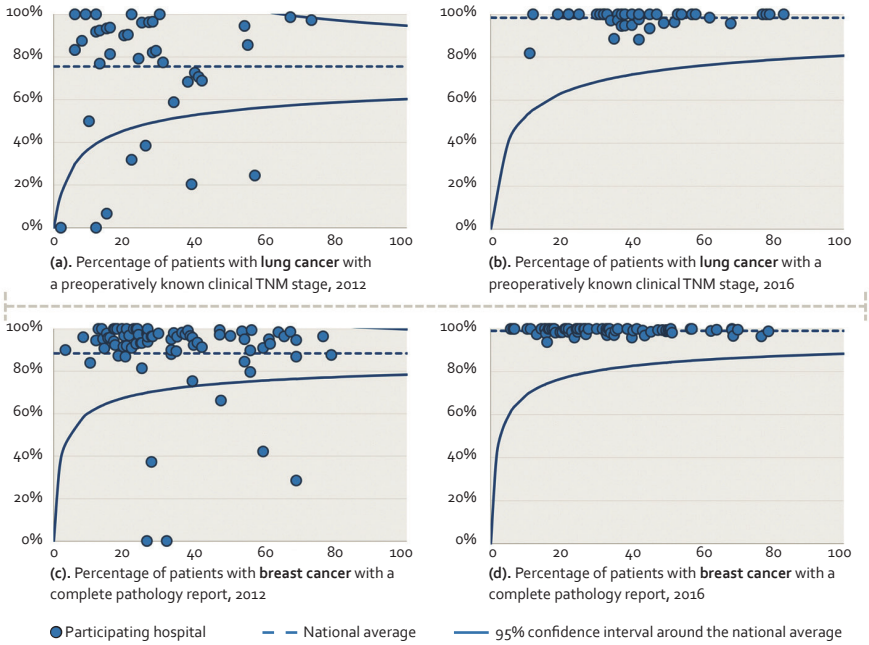

Figure 3. Decrease in variation in process indicators for lung cancer (a,b) and breast cancer (c,d).

Improvements on the outcome indicator 'postoperative 30-day or in-hospital mortality' were seen in various DICA audits. For example, between 2012 and 2015, postoperative mortality decreased from 4.2% to 2.5% after resection for colon cancer and from 2.5% to 1.7% for rectal cancer, resulting in a reduction of more than 200 care-related deaths per year in the Netherlands.[10] In surgical colorectal cancer treatment improvements were also seen in severe complication rates, 'failure to rescue' (the proportion of patients that die following severe complications) and oncologic resection quality. For carotid artery interventions, there was a decrease in 'complicated course' from 4.3% to 2.7% (2013-2016). A decrease in hospitalisation days was observed after resection for gastric cancer: from a median of ten days in 2012 to eight days in 2016.

In colorectal cancer surgery, improvements in mortality and complication rates reduced the mean cost per patient from €14,237 to €13,145 (-7.7%).[11] Extrapolating to national level, the potential additional savings could be over 20 million Euros per three years if all hospitals perform as best practices.

The observed improvements are likely to be multifactorial – with simultaneous centralisation, specialisation and introduction of new techniques – and not solely attributable to the audits. Nevertheless, the audits provided insights into performance of the national healthcare system and individual providers that were previously not available. Reliable, actionable data from the audits form the basis for improvement.

PERSPECTIVES

Worldwide many initiatives have been developed to monitor and improve healthcare quality by using data. What distinguishes DICA-facilitated audits is the central role of clinicians and their professional societies, close collaboration with other parties involved in healthcare provision, short-cycled benchmarked feedback, national coverage and data verification processes to secure data quality. The leading role of clinicians and cooperation with other parties is essential to produce meaningful quality information. DICA data is simultaneously used to provide internal feedback to medical teams at hospital level and to calculate externally transparent indicators. Instead of a merely volume-based discussion, DICA's hospital specific outcome information has led to a more solid quality of care discussion. Integrating audits into quality assurance policies, e.g. via mandatory 'participation indicators' and stepwise external transparency has stimulated nationwide participation, allowing better hospital comparisons and the provision of unbiased information, in contrast to registries of more voluntary nature.

Today, there are some limitations to the current audits, whether or not to be resolved by DICA. One limitation is the administrative burden associated with data collection. A solution already being worked on is partly automated data collection from Electronic Patient Records. To achieve this, in-hospital workflow redesign will be necessary and close cooperation between doctors and hospital IT providers is indispensable. Increasingly stringent privacy legislation could be a barrier in linking various data sources for audit purposes. Second, finding a balance with demands on transparency is challenging. In DICA's view, caregivers should retain the option of evaluating data internally, allowing medical teams to act on their results in a safe environment. Third, a current barrier to achieving maximum benefit from clinical auditing is the fixed format in which feedback information is offered. More dynamic, interactive systems could optimise information provision for clinicians and stimulate data use for quality improvement cycles and data-driven discussions by medical teams. For that reason DICA introduced exploratory 'Codman dashboards' in 2019, in which clinicians can select certain patient groups and compare their results in these groups with a national benchmark.

Generally, a potential flaw of transparent indicators is their potential influence on clinical decisions and risk-averse behaviour. There are no indications in the current audits for the latter.[12] A more 'disease-focused' rather than treatment-specific quality evaluation could contribute to insights into risk-averse behaviour. Future perspectives therefore focus on quality evaluation of the entire care spectrum per condition.

Recapitulating, the digital era has brought opportunities to realise Codman's dream, by implementing his clinical auditing model on a nationwide basis. This brings the insights and improvements in healthcare quality he intended one hundred years ago. Although there are challenges to be overcome, the DICA example shows important principles for a successful introduction of these audits: clinicians in

the lead, close collaboration with various stakeholders in healthcare, use of audit outcomes in improvement initiatives of professional associations and real-world data with timely actionable feedback information for clinicians. Clinical audits can catalyse internal quality improvement, ultimately leading to equal distribution of healthcare quality and accountability to all stakeholders.

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Collaborators

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Supplemental Table 1. Publications from DICA facilitated audits (last PubMed search:15 May 2018).

Disease	Subject	Finding	Year	Reference
Colorectal cancer	Audit implementation	It is feasible to accomplish a nationwide surgical audit program, with national coverage and high case ascertainment, in a relatively short period of time.	2013	Van Leersum et al.[1]
	National clinical practice	From an international perspective, the use of radiotherapy (RT) for rectal cancer in the Netherlands is currently very high. Considerable hospital variation was observed for RT in stage I and for the proportion of chemoradiotherapy among all RT schemes.	2013	Van Leersum et al.[2]
	National clinical practice	An increasing percentage of patients undergoing low anterior resection for rectal cancer receive a defunctioning stoma, 70% in current Dutch practice. Clinically relevant anastomotic leakage rates remained similar. Routine use of defunctioning stomas should be questioned.	2012	Snijders et al.[3]
	National clinical practice	In the treatment of a left-sided malignant colon obstruction, acute resection as first choice treatment seems justified. However, for frail, elderly patients, with mortality rates of over 30% after acute resection, the need for alternative treatment strategies was stressed.	2015	Tanis et al.[4]
	National clinical practice	After the introduction of the Dutch Surgical Colorectal Audit, a dramatic improvement in circumferential resection margin (CRM) reporting and a major decrease in CRM involvement after rectal cancer surgery occurred.	2015	Gietelink et al.[5]
	National clinical practice	After a colorectal cancer resection, there is excess mortality among patients aged ≥85 compared to patients aged <85 years, particularly in the first year after surgery. Excess mortality in patients aged ≥85 years in the first year after surgery (expected mortality based on national life tables) was 12.1%.	2016	Verweij et al.[6]
	National clinical practice	The revised national guideline on colorectal cancer was rapidly implemented with a substantial decrease in RT use for low-risk resectable rectal cancer, and increased specificity of MRI for N-staging.	2017	Gietelink et al.[7]
	National clinical practice	Since the introduction of the National Bowel Cancer Screening Program in the Netherlands, there has been a clear increase in the number of surgical resections, without affecting waiting times.	2017	De Neree tot Babberich et al.[8]

Colorectal cancer	National clinical practice	By benchmarking the results of a population-based study against results of landmark RCTs, it was demonstrated that rectal cancer care in the Netherlands has considerably improved over time. Fewer positive CRMs have been seen since the TME trial and after the COLOR II trial oncologically safe implementation of minimally invasive surgery was achieved.	2017	Dutch Snapshot Research Group[9]
	National clinical practice	In 2011, after low anterior resection for rectal cancer in the Netherlands (with high use of neoadjuvant RT) one third of anastomotic leakages (AL) were diagnosed beyond 30 days. Almost half of the ALs did not heal and developed into a chronic sinus.	2017	Borstlap et al.[10]
	National clinical practice	In the Netherlands, the use of laparoscopic colorectal cancer surgery increased to ≥ 80% at national level. Conversion rate decreased and was significantly related to laparoscopic hospital volume. Conversion has only minimal impact on short-term postoperative outcomes.	2017	De Neree tot Babberich et al.[11]
	Quality indicators	Guideline adherence in processes for patients with colorectal cancer is not associated with a better short-term outcome for the individual patient. However, hospitals with favorable scores on guideline adherence also have better postoperative outcome rates.	2012	Kolfschoten et al.[12]
	Quality indicators	Hospital variation with regard to anastomotic leakages (ALs) is relatively independent of differences in casemix. AL rates may therefore be suitable as an outcome indicator for measurement of surgical quality of care.	2012	Snijders et al.[13]
	Quality indicators	'Textbook outcome' (TO) gives a simple summary of hospital performance, while preventing indicator-driven practice. As a result TO is meaningful for patients, providers, health insurance companies and the healthcare inspectorate.	2013	Kolfschoten et al.[14]
	Quality indicators	Hospital type and annual hospital volume are not independently associated with failure to rescue (FTR) rates in colorectal cancer surgery.	2013	Henneman et al.[15]
	Quality indicators	In quality improvement projects, feedback to hospitals of failure to rescue (FTR) rates, along with complication rates, may illustrate shortcomings (prevention or management of complications) per hospital, which may be an important step in reducing mortality.	2013	Henneman et al.[16]

Supplemental Table 1. (continued).

Disease	Subject	Finding	Year	Reference
	Quality indicators	Individual quality indicators are not suitable as a surrogate measure for the complete evaluation of hospital performance on quality of colorectal cancer care.	2013	Gooiker et al.[17]
	Quality indicators	An 'unplanned reoperation after elective colorectal cancer surgery' quality indicator seems suitable as benchmark information to hospitals but less suitable for identifying poor performers.	2014	Henneman et al.[18]
	Quality indicators	A combined measure of volume and outcome can be used as an indicator to identify hospitals that provide adequate quality and is associated with better outcomes in the subsequent year.	2014	Kolfschoten et al.[19]
	Quality indicators	To compare outcomes between hospitals it is crucial to consider noise due to low hospital case volume with a random effects model.	2015	Fischer et al.[20]
	Risk prediction	The incidence of severe postoperative complications is lower after colon cancer than rectal cancer resection; however, the risk of dying from a severe complication (failure to rescue: FTR) is twice as high after colon cancer resection, even after casemix adjustment.	2014	Henneman et al.[21]
	Risk prediction	For elderly patients with two or more additional risk factors, a non-elective resection for colon cancer should be considered a high-risk procedure with a mortality risk of up to 41%.	2012	Kolfschoten et al.[22]
	Risk prediction	Elderly patients and those with co-morbidity have a higher mortality risk after anastomotic leakage (AL) following a resection for colon carcinoma. Mortality was significantly higher for patients with AL than those without.	2014	Bakker et al.[23]
	Risk prediction	Synchronous colorectal carcinomas (CRCs) require different surgical treatment than solitary CRCs. Postoperative outcomes for synchronous CRC are unfavorable, most likely because of the extent of the resection.	2014	Van Leersum et al.[24]
	Risk prediction	Non-elective colon cancer resection is associated with high mortality compared to elective resections. Particularly at risk are patients with tumour perforation or right-sided resections.	2014	Bakker et al.[25]
	Risk prediction	Anastomotic leakage (AL) after a low anterior resection (LAR) for rectal cancer is a frequently observed complication. Differences in clinical outcomes suggest that grade C (requiring reoperation) and B (requiring drainage) leakage should be considered as separate entities.	2017	Frouws et al.[26]

	Risk prediction	No significant impact of annual hospital volume on rectal cancer surgery outcomes could be demonstrated among 71 Dutch hospitals. The majority of patients were treated at medium-volume (20-50 rectal cancer resections) hospitals.	2017	Jonker et al.[27]
	Risk prediction	Based on nationwide data, a number of previously reported clinical predictors of pathologic complete response (pCR) after chemoradiotherapy for rectal cancer were confirmed: clinical tumour, nodal and metastasis stage, signs of obstruction, differentiation and histologic subtype.	2018	Van der Sluis et al.[28]
	Risk prediction	There is a significant association between the level of digitalisation in hospitals and the length of stay after colorectal cancer surgery, suggesting that advanced electronic medical records support healthcare providers in achieving desired quality outcomes.	2017	Van Poelgeest et al.[29]
	Hospital variation	There is no even distribution of high-risk patients among hospitals providing surgical treatment to patients with colorectal cancer in the Netherlands. This underlines the need for risk adjustment when comparing hospital performances.	2011	Kolfschoten et al.[30]
	Hospital variation	Caution is needed when interpreting hospital rankings on the basis of postoperative mortality, since hospital variation is largely due to chance.	2014	Henneman et al.[31]
	Hospital variation	There is large variation in the use of defunctioning stomas for patients with rectal cancer and a lack of uniformity of selection criteria for defunctioning stomas between surgeons.	2015	Snijders et al.[32]
	Hospital variation	Low hospital volume in rectal cancer surgery is independently associated with a higher risk of circumferential resection margin (CRM) involvement, even after adjustment for relevant confounders. This supports minimal volume standards in rectal cancer surgery.	2016	Gietelink et al.[33]
	Hospital variation	For cT4 rectal cancer, high-volume hospitals may offer better multimodality treatment while for cT1-3 rectal cancer, centralization appears to have no advantages.	2017	Jonker et al.[34]
	Hospital variation	In colon cancer surgery, it seems possible to deliver excellent care regardless of the hospital teaching status. Best performers are found in all hospital teaching types.	2018	Van Groningen et al.[35]
	Treatment evaluation	Use of laparoscopic techniques in colorectal cancer surgery in the Netherlands is safe and results are better in terms of short-term outcome than those for open surgery.	2013	Kolfschoten et al.[36]

Supplemental Table 1. (continued).

Disease	Subject	Finding	Year	Reference
	Treatment evaluation	Delaying surgery for rectal cancer until the 15th or 16th week after the start of neoadjuvant chemoradiotherapy (CRT) (10–11 weeks from the end of CRT) seems to result in the highest chance of a pathologic complete response.	2013	Sloothaak et al.[37]
	Treatment evaluation	Laparoscopic re-intervention following laparoscopic surgery for colorectal cancer is accompanied by lower mortality and faster recovery compared to open re-interventions. Though laparoscopic re-interventions seem feasible, future research is needed to define their exact benefits.	2014	Vennix et al.[38]
	Treatment evaluation	Although creation of a defunctioning stoma in patients undergoing an oncologic resection for mid or high rectal cancer results in lower anastomotic leakages, it is also associated with more postoperative complications, mortality and a longer hospital stay, even after p adjustment.	2014	Bakker et al.[39]
	Treatment evaluation	The technique of abdominoperineal excision (APE) for non-advanced rectal cancer is not inferior to the low anterior resection (LAR) with respect to resection margin involvement.	2014	Van Leersum et al.[40]
	Treatment evaluation	A pronounced tendency towards defunctioning stoma construction in rectal cancer surgery does not result in lower overall anastomotic leakage or mortality rates. It seems that hospitals with low stoma rates are better at selecting high-risk patients.	2015	Snijders et al.[41]
	Treatment evaluation	Laparoscopic resection reduces the risk of postoperative mortality compared with open resection in an elective setting in patients with non-locally advanced, non-metastasized colorectal cancer. Frail, elderly patients in particular seem to benefit.	2016	Gietelink et al.[42]
	Treatment evaluation	In patients undergoing a Hartmann procedure for rectal cancer, neoadjuvant radiotherapy (RT) is independently associated with an increased risk of postoperative intra-abdominal abscess requiring re-intervention. RT did not affect overall re-interventions and mortality.	2015	Jonker et al.[43]
	Treatment evaluation	In the surgical treatment of rectal cancer after RT, a low Hartmann's procedure (LHP) was found to be associated with a lower risk of complications and reoperation than LAR without a defunctioning ileostomy (DI) and was in this respect similar to a LAR with a DI.	2016	Jonker et al.[44]

	Treatment evaluation	In high-risk patients with a malignant obstruction of the proximal colon, a bridging strategy (stent or stoma) may be a valid alternative to an acute resection, since it is accompanied by significantly lower postoperative mortality.	2016	Amelung et al.[45]
	Treatment evaluation	In contrast to previous assumptions, omentoplasty after abdominoperineal resection with primary perineal closure for non-locally advanced rectal cancer appeared not to improve perineal wound healing and seemed to increase the occurrence of perineal hernia.	2018	Blok et al.[46]
	Treatment evaluation	Elective surgery for rectal cancer <4 days after preoperative short-course radiotherapy resulted in an increase in anastomotic leakages. Optimal intervals should be assessed.	2018	Sparreboom et al.[47]
	Treatment evaluation	In elective right-sided colectomy for cancer, an open approach seems to have a higher risk of complications and mortality compared to laparoscopic, even after adjusting for confounders.	2018	Bosker et al.[48]
	Health care costs	Complications after colorectal cancer surgery are associated with a substantial increase in costs. Although not all surgical complications can be prevented, reducing complications will result in considerable cost savings.	2015	Goveart et al.[49]
	Health care costs	Obesity in colorectal cancer surgery is associated with a significant increase in hospital costs, compared to normal-weight patients. This may be explained by the significantly higher severe complication rate in obese patients.	2016	Govaert et al.[50]
	Health care costs	There is evidence for simultaneous quality improvement and cost reduction in colorectal cancer surgery. Improving quality will potentially catalyse cost savings as well.	2016	Govaert et al.[51]
	Health care costs	In elective colon cancer surgery, laparoscopic resection was significantly less expensive than open resection. The largest cost reduction was seen in patients aged ≥ 75 years with ASA I-II. Elective rectal cancer surgery was significantly more expensive when performed laparoscopically.	2017	Govaert et al.[52]
Gastric / esophageal cancer	Audit implementation	Nationwide implementation of an audit of the surgical treatment of upper GI cancer in the Netherlands has been successful, showing improvements on various process and outcome indicators.	2016	Busweiler et al.[53]

Supplemental Table 1. (continued).

Disease	Subject	Finding	Year	Reference
	National clinical practice	In esophageal cancer surgery, the number of lymph nodes (LNs) retrieved increased between 2011 and 2016. Retrieval of ≥15 LNs was not associated with increased postoperative morbidity/mortality.	2018	Van der Werf et al.[54]
	Quality indicators	A composite measure defined as 'textbook outcome' (TO), to assess quality of care was defined. There was wide variation between hospitals in achieving textbook outcome.	2017	Busweiler et al.[55]
	Quality indicators	Patients with gastric cancer are more likely to die if a (major) postoperative complication occurs (failure to rescue – FTR). Next to morbidity and mortality, FTR should be considered as an important outcome measure after esophagogastric cancer resections.	2017	Busweiler et al.[56]
	Risk prediction	In gastrectomy for gastric cancer, ASA grade, neoadjuvant chemotherapy and type of resection are independent predictors of morbidity and death, irrespective of age.	2017	Nelen et al.[57]
	Treatment evaluation	Laparoscopic techniques in gastric cancer surgery have been safely introduced in the Netherlands with overall morbidity and mortality comparable to open surgery and with shorter hospitalization.	2017	Brenkman et al.[58]
	Treatment evaluation	In the Netherlands, there is an increasing trend towards minimally invasive esophagectomy (MIE) compared to open esophagectomy (OE) for cancer. There are no relevant differences in mortality and pulmonary complications between OE and MIE. Anastomotic leaks and re-interventions were more frequently observed in patients after MIE. MIE was associated with a shorter hospital stay.	2017	Seesing et al.[59]
	Treatment evaluation	An interval of ≥12 weeks between end of neoadjuvant chemoradiotherapy and esophagectomy for cancer is associated with higher pathologic complete response (pCR), but not with increased intra- or post-operative complications.	2018	Van der Werf et al.[60]
	Treatment evaluation	In esophagectomy for cancer, intrathoracic anastomosis (compared to cervical) was associated with lower anastomotic leak rate, lower rate of recurrent nerve paresis and a shorter hospital stay. Risk factors for anastomotic leak were co-morbidities and proximal tumours.	2018	Gooszen et al.[61]

	Hospital variation	Considerable hospital variation in the probability of receiving adjuvant chemo(radio)therapy after gastric cancer resection was observed. Its omission was strongly associated with postoperative complications, underlining the need to further reduce perioperative morbidity.	2018	Schouwenburg et al.[62]
	Hospital variation	There is considerable hospital variation in the use of perioperative therapy in patients with gastric cancer. Besides known casemix factors, use of perioperative therapy was associated with the level of involvement of multidisciplinary care.	2018	Beck et al.[63]
	Health care costs	Complications after esophagectomy for cancer are associated with a substantial increase in hospital costs. Anastomotic and chyle leakage resulted in the largest additional costs.	2017	Goense et al.[64]
Pancreatic cancer	Audit implementation	In the first few years after establishment, the Dutch Pancreatic Cancer Audit was implemented at national level, has high-quality data and reports good outcomes of pancreatic surgery at national level.	2017	Van Rijssen et al.[65]
	Hospital variation	In pancreatoduodenectomy, between-hospital variations in mortality were explained mainly by differences in failure to rescue (FTR), rather than the incidence of major complications.	2018	Van Rijssen et al.[66]
Breast cancer	National clinical practice	There is a trend towards less extensive axillary surgery in Dutch cT1-T4N0M0 breast cancer patients. Variations in patterns of care in axillary surgery are present.	2017	Poodt et al.[67]
	Hospital variation	Hospital organisational factors affect the use of immediate breast reconstruction (IBR) in the Netherlands. Optimization of these factors could lead to less variation in IBR rates.	2017	Schreuder et al.[68]
	Hospital variation	A large degree of hospital variation was found in post-mastectomy immediate breast reconstruction rates in the Netherlands for both invasive breast cancer and ductal carcinoma in situ, even after adjustment for patient and tumour factors.	2017	Van Bommel et al.[69]
	Hospital variation	In stage III breast cancer, nationwide use of neoadjuvant chemotherapy (NAC) was 79%. Considerable between-hospital variation in use of NAC was observed, even after adjustment for patient, tumour, clinical management and hospital factors.	2017	Spronk et al.[70]

Supplemental Table 1. (continued).

Disease	Subject	Finding	Year	Reference
	Outcome improvement	Nationwide implementation of an audit of breast cancer treatment in the Netherlands has been successful. Data show that overall quality of breast cancer care in all hospitals is high. Improvement on most quality indicators has been seen over time.	2017	Van Bommel et al.[71]
Lung cancer	Audit implementation	The Dutch Lung Surgery Audit provides reliable benchmarked information for caregivers and hospital management with potential to start local, regional or national improvement initiatives.	2018	Ten Berge et al.[72]
	Audit implementation	The Dutch Lung Cancer Audit (DLCA) is a unique registry to evaluate the quality of multidisciplinary lung cancer care. It has been accepted and implemented nationwide, enabling participating healthcare providers to obtain insight into their performance.	2018	Beck et al.[73]
	Audit implementation	Data quality in a nationwide audit can be promoted in various ways. Useful tools are: on-site data verification processes and a completeness indicator. Both methods are used in the DLCA.	2018	Hoeijmakers et al.[74]
	National clinical practice	Accuracy of NSCLC staging in the Netherlands is low. Accurate nodal staging remains particularly challenging.	2016	Heineman et al.[75]
	National clinical practice	Concordance between clinical and pathologic staging in the Netherlands is low. In patients with clinical stage I Non-Small Cell Lung Carcinoma (NSCLC), 22.6% are upstaged to pathologic stage II or higher. Improvement in accuracy of staging is needed.	2016	Heineman et al.[76]
	National clinical practice	In patients with a stage III NSCLC, a large treatment variation in the use of chemoradiotherapy (sequential vs. concurrent) was observed between and within the Netherlands and Belgium. Higher age and N-stage were significantly associated with choice of therapy.	2017	Walraven et al.[77]
	Risk prediction	The between-hospital variation in casemix of patients undergoing surgery for NSCLC emphasizes the importance of proper adjustment when comparing hospitals on outcome indicators.	2018	Beck et al.[78]
	Risk prediction	Operative mortality was significantly higher among octogenarians than among younger patients, whereas the incidence of complications was similar in all age groups.	2018	Detillion et al.[79]

Melanoma	National clinical practice	Nationwide implementation of a unique comprehensive population-based registry in advanced melanoma treatment in the Netherlands has been successful and has led to the safe introduction of new therapeutic options for advanced melanoma in the Netherlands.	2017	Jochems et al.[80]
	National clinical practice	This nation-wide study provides valuable insights into the healthcare costs of advanced cutaneous melanoma patients who were treated with ipilimumab in clinical practice. Most of the costs were attributable to ipilimumab, but the costs and its distribution varied considerably across subgroups.	2018	Franken et al.[81]
	National clinical practice	Real-world outcomes of ipilimumab in the Netherlands slightly differ from outcomes in phase III trials. Although phase III trials are crucial for establishing efficacy, real-world data are of great added value enhancing the generalizability of outcomes of ipilimumab in clinical practice.	2018	Jochems et al.[82]
	Risk prediction	The clinical outcomes of vemurafenib in BRAF-mutant metastatic melanoma patients with a favorable risk profile are comparable with the pivotal trials. However, as the majority of patients have a less favorable risk profile, trial results cannot be generalized to a more heterogeneous patient population in daily practice.	2018	Schouwenburg et al.[83]
Vascular disease	Quality indicators	Risk-adjusted mortality (in accordance with V(p)-POSSUM score) for elective abdominal aortic aneurysm (AAA) surgery has limited capability for hospital comparison quality assessment.	2017	Lijftogt et al.[84]
	Quality indicators	The composite measure 'textbook outcome' (TO) generates additional information to evaluate overall quality of care in elective aneurysm surgery.	2017	Karthaus et al.[85]
	Treatment evaluation	Based on nationwide Dutch registry data, the intervention threshold for elective endovascular AAA repair is 55 mm in men and 52mm in women. The almost doubled mortality risk for elective open repair in women argues for a conservative approach when considering open repair.	2017	Tomee et al.[86]
Obesity surgery	Audit implementation	The Dutch Audit for Treatment of Obesity has rapidly matured. Essential in this process were: a well-organised national structure, cooperation with DICA, government funding and most important, the support and dedication of the bariatric surgeons themselves.	2017	Poelemeijer et al.[87]

Supplemental Table 2. Abbreviation list of DICA audits.

DACI	Dutch Audit for Carotid Interventions
DAPA	Dutch Audit for Peripheral Artery Disease
DASA	Dutch Acute Stroke Audit
DATO	Dutch Audit for Treatment of Obesity
DBIR	Dutch Breast Implant Registry
DCRA	Dutch ColoRectal Audit
DGEA	Dutch Gastroinestinal Endoscopy Audit
DGOA	Dutch Gynaecological Oncology Audit
DHBA	Dutch Hepato Biliary Audit
DHFA	Dutch Hip Fracture Audit
DHNA	Dutch Head and Neck Audit
DLCA	Dutch Lung Cancer Audit
DMTR	Dutch Melanoma Treatment Registry
DPCA	Dutch Pancreatic Cancer Audit
DPIA	Dutch Parkinson's Insight Audit
DRCE	Dutch Registration of Complications in Endoscopy
DSAA	Dutch Surgical Aneurysm Audit
DSSR	Dutch Spine Surgery Registry
DUCA	Dutch Upper GI Cancer Audit
EPSA	European Pediatric Surgery Audit
NBCA	Nabon Breast Cancer Audit

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CHAPTER 3

Lessons learned from the Dutch Institute for Clinical Auditing: the Dutch model for quality assurance in lung cancer treatment

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ABSTRACT

Background | quality registries play an important role in the professional quality system for cancer treatment in the Netherlands. This article provides insight into the Dutch Lung Cancer Audit (DLCA); its core principles, initiation and development, first results and what lessons can be learned from the Dutch experience.

Methods | cornerstones of the DLCA are discussed in detail, including: audit aims; the leading role for clinicians; web-based registration and feedback; data handling; multidisciplinary evaluation of quality indicators; close collaborations with all stakeholders in healthcare and transparency of results.

Results | in 2012 the first Dutch lung cancer specific sub-registry, focusing on surgical treatment was started. Since 2016 all major treating specialisms (lung oncologists, radiation-oncologists, general- and cardiothoracic surgeons – represented in the DLCA-L, -R and -S sub-registries respectively) have joined. Over time, the number of participating hospitals and included patients has increased. In 2016, the numbers of included patients with a NSCLC were 3502 (DLCA-L), 2427 (DLCA-R) and 1979 (DLCA-S). Between sub-registries mean age varied from 66 to 70, occurrence of ECOG performance score 2+ varied from 3.3% to 20.8% and occurrence of clinical stage I-II from 27.6% to 81.3%. Of all patients receiving chemoradiotherapy 64.2% was delivered concurrently. Of the surgical procedures 71.2% was started with a minimal invasive technique, with a conversion rate of 18.7%. In 2016 there were 17 publicly available quality indicators – consisting of structure, process and outcome indicators- calculated from the DLCA.

Conclusions | the DLCA is a unique registry to evaluate the quality of multidisciplinary lung cancer care. It is accepted and implemented on a nationwide level, enabling participating healthcare providers to get insight in their performance, and providing other stakeholders with a transparent evaluation of this performance, all aiming for continuous healthcare improvement.

BACKGROUND

As in the rest of the world, in the Netherlands lung cancer is the leading cause of cancer related mortality.[1,2] On a population of almost 17 million inhabitants, in 2016 over 12,000 persons were diagnosed with primary lung cancer.[2,3] Of these, the vast majority is Non-Small Cell Lung Cancer (NSCLC).

In the Netherlands, there is a national multidisciplinary evidence-based guideline on the diagnoses and treatment of NSCLC, which is revised about every 5 years. Despite this, in 2010, a study using population-based data from the Dutch Cancer Registry showed significant regional differences and between-hospital variation in treatment patterns and outcomes for patients with NSCLC and other malignancies, though reasons for these differences could hardly be identified.[4] In order to improve the quality and equality of cancer care in the Netherlands, multidisciplinary quality standards were developed, by The Dutch Federation of Oncologic Societies.[5] In these standards general and cancer specific requirements for optimal cancer care are described, including organisation of care, the presence of certain facilities and minimum volume standards.

At the same time, nationwide clinical audits – facilitated by the Dutch Institute for Clinical Auditing (DICA) – were introduced in the Netherlands. Clinical auditing is a process of systematic analysis of quality of healthcare, with the aim to improve patient outcomes. With a clinical audit system, guideline adherence, patient outcomes and other quality indicator results can be accurately studied and compared.

The first Dutch lung cancer-specific audit started in 2012 and was focussed on surgical treatment. Since then more specialties involved in lung cancer care have joined and nowadays quality of lung cancer care is evaluated multidisciplinary in the nation-wide Dutch Lung Cancer Audit (DLCA).

This article provides insight into the DLCA; its core principles, initiation and development, first results and what lessons can be learned from the successful Dutch experience.

METHODS

Aim

The care for patients with lung cancer ideally takes place in a multidisciplinary setting, for both the diagnostic and treatment process. The DLCA therefore is a collaboration of multiple disciplines involved in the treatment of lung cancer. The aim of the DLCA is to evaluate the multidisciplinary care for lung cancer patients, with the potential to improve care processes and outcomes on a national level.

Development

The development of the DLCA was facilitated by DICA and design was in accordance with the DICA blueprint.[6] In 2012 the first national quality registry on lung cancer was initiated, focussing on surgical treatment: the Dutch Lung Surgery Audit. In the Netherlands, lung surgery is performed by cardiothoracic surgeons and by general surgeons with a specialisation in lung surgery. Initially, mainly the hospitals with general surgeons participated in the audit, but from 2015 on all cardiothoracic centres joined as well. In 2014 a quality registry was launched focussing on the radiotherapeutic treatment of lung cancer: the Dutch Lung Radiotherapy Audit. As of 2016, in addition to these two registries, pulmonologists joined the audit. Therefore, from 2016 on the audit was renamed as the DLCA, with sub-registries for lung oncologists (DLCA-L), surgeons (DLCA-S) and radiation-oncologists (DLCA-R), together encompassing the whole care path of lung cancer patients in Dutch hospitals.

The DLCA was developed in close collaboration with all relevant professional associations (the Dutch Society of Physicians for Lung Diseases and Tuberculosis

- NVALT, the Netherlands Association for Cardio-Thoracic Surgery - NvT, the Dutch Society for Lung Surgery - NVvL-NVvH and the Dutch Society for Radiotherapy and Oncology - NVRO).

Organisation

The organisational structure of the DLCA is visualised in **Figure 1**. Clinicians mandated by their professional association and a patient representative form a joint clinical audit board (CAB). The CAB is responsible for the development and progress of the complete audit. Overarching quality issues, interdisciplinary quality

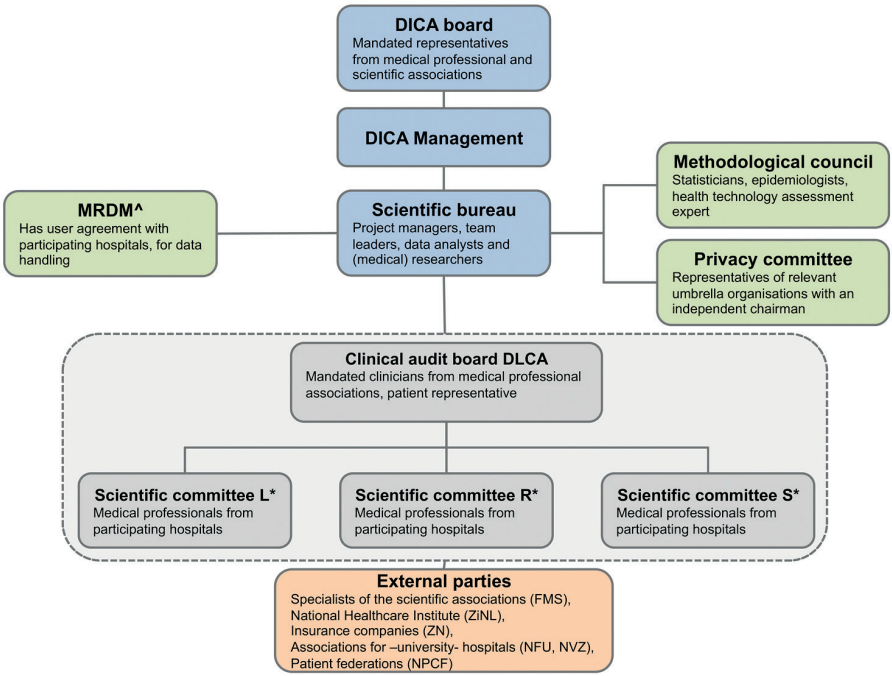

Figure 1. Organisational structure of DLCA.
* L = lung-oncologists, R = radiotherapeutic-oncologists, S = surgical-oncologists.
^ Medical Research Data Management.

indicators and joined meetings are the responsibility of the board. In addition, the three sub-registries have their own scientific committee (SC), responsible for the content of the audit and participation of their colleagues in the institutions providing lung cancer care. In the CAB each SC is represented by its chairman. The audit is supported by the DICA scientific bureau, which in turn is backed by a methodological council and a privacy committee. The SC's have approximately three separate meetings a year in which the datasets, results and future goals are discussed. The joint results and objectives are discussed in the CAB approximately twice a year.

Funding

The development and implementation of all DLCA sub-registries were project based. These projects were funded and executed via quality improvement grants from the federation of medical specialists (FMS – SKMS). Since 2017, the DLCA is completely financed by an umbrella organisation of ten healthcare insurance companies in the Netherlands (ZN). Apart from funding, these companies do not influence the DLCA organisation. Costs of data registration for participating hospitals are not centrally compensated.

Inclusion

The DLCA includes all patients with primary lung cancer of any stage. In addition, in the DLCA-S there are audit possibilities for patients undergoing surgery for other mediastinal diseases, lung metastasis or benign lung diseases. In the DLCA-L, besides primary lung cancer, there is also a minimal registration of patients with malignant mesothelioma and thymomas or thymic carcinoma. In the DLCA-R only patients with stage I-III disease, treated with curative intent, are included. In the DLCA-L and -S this selection does not apply.

Dataset

The collected data is primarily based on established or future quality indicators – reflecting quality of care on a hospital level – and potential casemix factors one should account for in between-hospital comparisons. The International Consortium of Health Outcome Measurement (ICHOM) standard dataset was adopted as much as possible.[7]

Registered information for casemix adjustment includes baseline patient (e.g. age, gender, performance score) and tumour characteristics (e.g. disease stage and histology). The development of a suitable casemix model is subject of a separate methodology that is described elsewhere.[8] Furthermore the registry includes items regarding processes of care (e.g. modalities used in the diagnostic process, time to treatment and evaluation of the patient in a Multi Disciplinary Team (MDT) meeting) and outcomes (e.g. short-term mortality, complications or toxicity, reinterventions and length-of-hospital-stay).

The content of the dataset is evaluated by the SC and can be adjusted on a yearly base.

Data collection and security

Data collection is preferably prospective and takes place through a secured web-based survey system or via batches of data uploaded by the hospital. Data can be supplemented or modified online when needed, for instance when follow-up information is available. An example of the web-interface of the DLCA-S data collection and feedback report is shown in **Figure 2**. Hospitals can decide themselves which method they prefer and who carries out data collection (for example: clinicians themselves or trained data-managers). For every hospital, the final responsibility for the completeness and correctness of collected data rests with a clinician. The ownership of the own data remains with the hospital. Current data dictionaries are freely available online.[9]

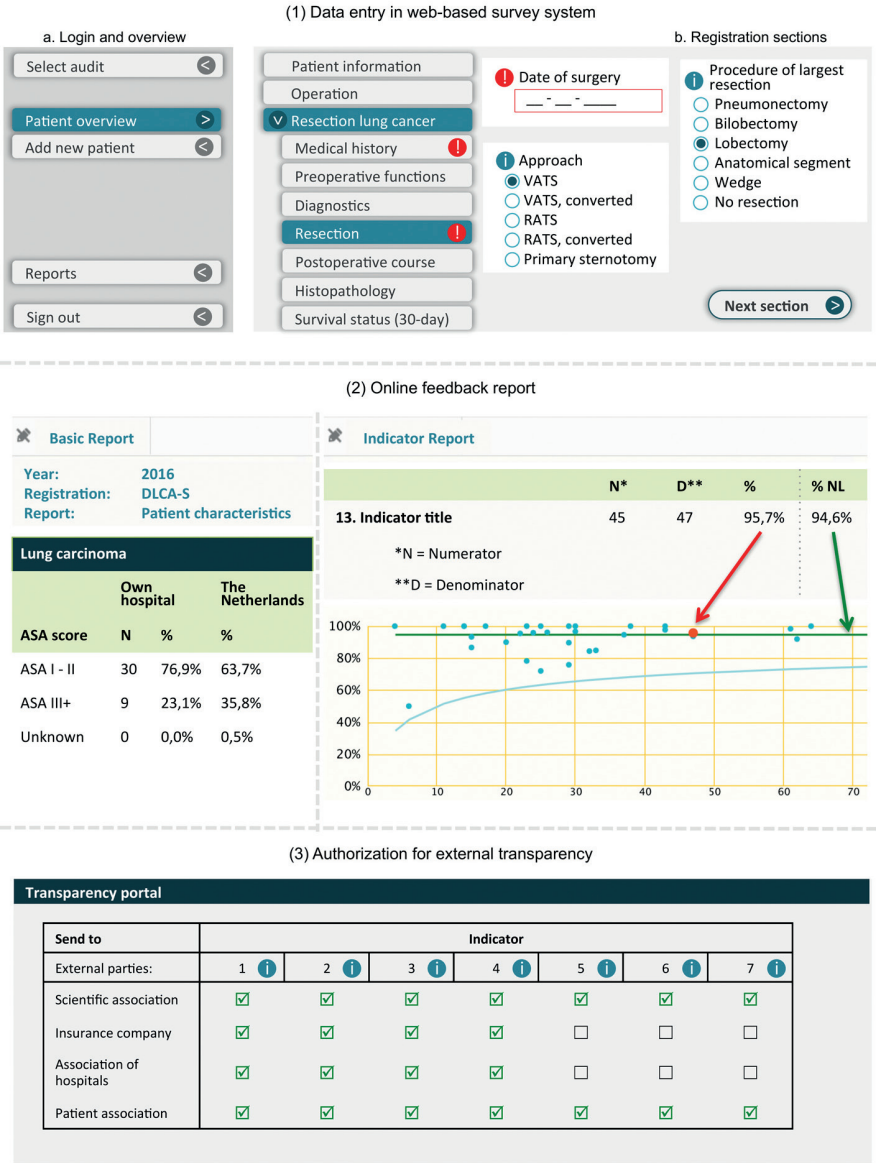

Figure 2. Illustration: 'What does the doctor see?
Example of the web interface of the DLCA data collection (1), feedback reports (2) and authorisation portal for external transparency (3).

There is a close cooperation with a data processor: Medical Research Data Management (MRDM) for data-collection, -encryption and safe storage. MRDM has a user agreement with all participating hospitals. A servicedesk is available by telephone or e-mail during working hours for all questions.

Data quality

Assurance of data quality takes place in multiple ways. One of these is the on-site verification of registered data in the (electronic) patient records of the hospital, by an independent third party. During the data verification, the completeness of patient inclusion by hospitals is checked, as well as the accuracy of the most important data on patient level. Verification takes place for the first time approximately 3 years after the start of the registry. Thus, a registry has to be more 'mature' for this data validity check. The data verification process and results of the DLCA-S verification in 2016, as well as other methods to assure data quality are described as a separate topic by Hoeijmakers et al.[10]

Auditing process

Feedback information is provided through weekly updated online reports, of which an example of the DLCA-S is shown in **Figure 2**. Participating hospitals can use these reports to continuously monitor their results compared to a national benchmark. DICA provides two types of online reports: 'the basic report' and 'the indicator report'. The more unprocessed information on the treated population is displayed in the basic report and divided into different sections. The indicator scores are displayed in the indicator report, typically in funnel plots with 95% confidence intervals around the national average or a defined norm and adjusted for casemix factors when relevant.

Quality indicators and transparency

To reflect quality of care on a hospital level, quality indicators were developed.

Quality indicators primarily serve as information for healthcare providers (internal use). Clinicians thus play a leading role in the development and determination of the DLCA indicator sets.

Since quality information is also of interest for other parties in the Dutch healthcare system (e.g. insurance companies, patient federations, government), a part of the set is agreed to be of use as transparent information (external use or 'transparency'). Indicators are tested on relevance, validity, reliability and feasibility.[11] The decision whether an indicator is suitable for external use is made tripartite with mandated representatives from the SC and the external parties in **Figure 1**. In accordance with the Donabedian concept, indicator sets consist of structure, process and outcome indicators.[12] Twice a year the content of indicator sets for public transparency is discussed between all relevant parties in a meeting facilitated by DICA's scientific bureau.

Public transparency of hospital specific indicator scores follows a stepwise model: participation and structure indicators are released in the first year of the audit, process indicators in the second and outcome indicators in the third. External indicator scores are calculated after a 'database-lock' three months after expiry of the registration year. Hospitals are obliged to provide external parties with their external indicator scores. Hospital boards are facilitated to share this information with different stakeholders after the annual database lock through a web based authorisation portal facilitated by DICA, shown in **Figure 2**.

Statistical analysis

Information of all patients registered in the DLCA for primary lung cancer between 1 January 2012 and 31 December 2016 (DLCA-R: 2014-2016, DLCA-L: 2016) was used for analysis. A minimum number of items per patient was required in order to consider a patient eligible for analysis. Descriptive statistics were used to assess patient, tumour and treatment characteristics for all analysable patients with a

NSCLC registered in the DLCA-L, -R or -S in 2016.

Statistical analyses were performed using SPSS (IBM SPSS Statistics for Macintosh, Version 23.0).

RESULTS

Growing participation in the DLCA

Figure 3 displays the development of the DLCA from 2012 on. The number of participating hospitals and included patients with a NSCLC increased over time. The participation of all cardiothoracic centres in the DLCA-S from 2015 on is also clearly visible in this figure.

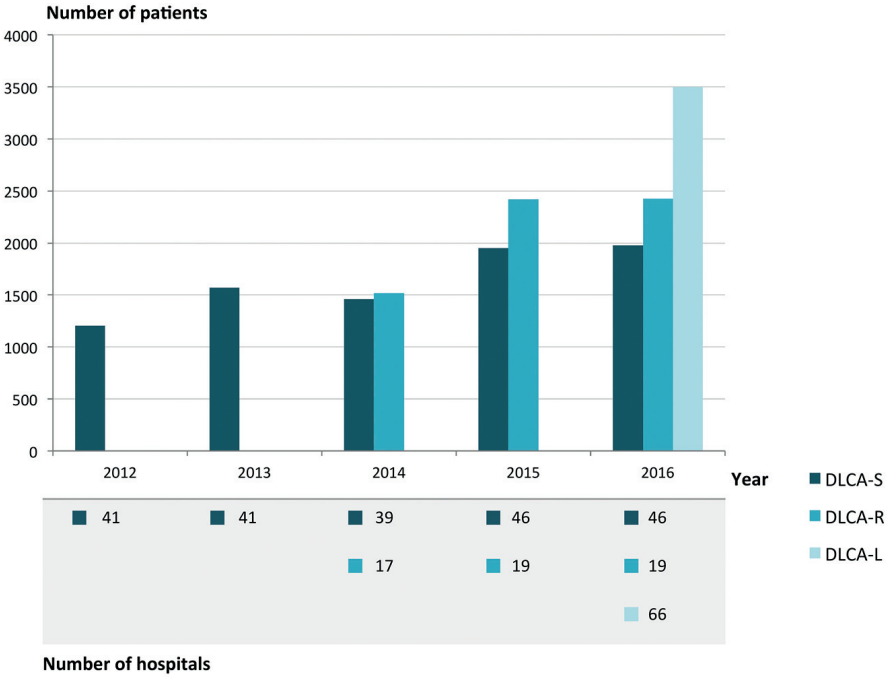

Figure 3. Evolution of the DLCA.
Number of participating hospitals and number of registered patients with NSCLC per sub-registry.
* L = lung-oncologists, R = radiotherapeutic-oncologists, S = surgical-oncologists.

With the more multidisciplinary character of the audit, the number of cooperating specialists in the DLCA CAB and SCs rose to 55 (representing five medical professional associations) and one patient representative.

Patient characteristics

In 2016, the total numbers of registered patients in DLCA-L, -R and -S were respectively 4544, 2883 and 2391. For the DLCA-L 4192 patients (92.3%) were considered eligible for analysis. For the DLCA-R and -S the number of analysable patients were 2767 (96.0%) and 2349 (98.2%) respectively.

Of these analysable patients, in DLCA-L 3502 (83.5%) were diagnosed with NSCLC. In the DLCA-R 2427 (87.7%) and in the DLCA-S 1979 (84.2%) NSCLC patients were included.

Patient and tumour characteristics of all patients with a NSCLC included in the DLCA in 2016 are shown in **Table 1.1**, stratified per DLCA sub-registry. As expected, there are differences in these characteristics between the sub-registries, with the surgically treated patients being younger, with better performance score and more frequently having a clinically stage I-II NSCLC.

Diagnostic characteristics

Of all analysable patients with NSCLC registered in the DLCA-L in 2016 (n = 3502), 2867 (81.9%) had pathologically proven disease. Of these the majority was proven histologically (1566, 54.6%) (**Table 1.2**). Of all analysable patients with a NSCLC registered in the DLCA-R (n = 2427), 1230 (50.7%) had pathologically proven disease, 703 (29.0%) did not and in 494 (20.4%) it was not recorded in the database (data not shown).

The most used invasive diagnostic, according to the DLCA-L, was endoscopic ultrasound, with 985 of 3502 (28.1%) undergoing an EUS and/or EBUS in the diagnostic work-up of a NSCLC (**Table 1.2**).

Table 1.1. Patient and tumour characteristics of patients with a NSCLC in the DLCA -L, -R and -S in 2016.

	[L] (Total N = 3502)		[R] (Total N = 2427)		[S] (Total N = 1979)	
	N	**%**	**N**	**%**	**N**	**%**
Age in years, mean (± SD) [median]	68.9 (10.1) [70]		70.0 (9.5) [70]		66.4 (8.8) [67]	
Age (years)						
<60	604	17.2%	355	14.6%	436	22.0%
60-74	1819	51.9%	1240	51.1%	1177	59.5%
75+	1079	30.8%	832	34.3%	366	18.5%
Gender						
Male	1998	57.1%	1392	57.4%	1079	54.5%
Female	1504	42.9%	1035	42.6%	900	45.5%
Performance score [a]						
ECOG 0-1	2378	67.9%	1494	61.6%	1604	81.1%
ECOG 2+	729	20.8%	423	17.4%	66	3.3%
Unknown	395	11.3%	510	21.0%	309	15.6%
ASA [b]						
I-II	NA		NA		1187	60.0%
III+	NA		NA		603	30.5%
Unknown	NA		NA		189	9.6%
Lung function						
FEV1 [c] and DLCO [d] ≥80%*	454	13.0%	228	9.4%	550	27.8%
FEV1 [c] or DLCO [d] <80%	1659	47.4%	1184	48.8%	1223	61.8%
FEV1 [c] and DLCO [d] unknown	1389	39.7%	1015	41.8%	206	10.4%
Clinical stage [e]						
Stage I	689	19.7%	1265	52.1%	1050	53.1%
Stage II	278	7.9%	223	9.2%	558	28.2%
Stage III	588	16.8%	701	28.9%	263	13.3%
Stage IV	1239	35.4%	NA		20	1.0%
Unknown	708	20.2%	238	9.8%	88	4.4%

[a] Performance score according to WHO or ECOG

[b] American Society of Anaesthesiologists score

[c] Forced Expiratory Volume in 1 second, percentage of expected

[d] Diffuse Lung Capacity for Oxygen, percentage of expected

[e] TNM7 staging

* FEV1 and DLCO ≥80% or one of the values missing

Table 1.2. Diagnostic and treatment characteristics of patients with a NSCLC in the DLCA-L in 2016 (N = 3502).

	N	%
Diagnostic		
Pathologic proven disease		
No	573	16.4%
Unknown	62	1.8%
Yes, with:	2867	81.9%
Histology	1566	54.6%
Cytology	899	31.4%
Unknown	402	14.0%
Invasive diagnostics^		
Transthoracic punction^	948	27.1%
EUS and/or EBUS^	985	28.1%
Mediastinoscopy^	228	6.5%
Molecular diagnostics		
No / unknown	2129	60.8%
Yes	1373	39.2%
Which successful	1310	95.4%
Treatment		
Treatment goal		
Curative	1449	41.4%
Palliative with active anti-tumour treatment	901	25.7%
Palliative without active anti-tumour treatment	886	25.3%
Unknown	266	7.6%
Initial treatment plan (n = 2350)		
Surgery (combined with other therapy)	615	26.2%
Radiotherapy (combined with other non-surgical therapy)	933	39.7%
Systematic treatment* only	618	26.3%
Different	145	6.2%
Unknown	39	1.7%

^ In case of the invasive diagnostic techniques, only the 'yes' option is shown, therefore the total does not add up to 100%. EUS: endoesophageal ultrasound, EBUS: endobronchial ultrasound.
* Includes: chemotherapy, immunotherapy, targeted therapy.

Treatment plan (DLCA-L)

Of all analysable patients with NSCLC registered in the DLCA-L in 2016 (n = 3502), the primary treatment goal was curative in 1449 patients (41.4%) and palliative in 1787 patients (51.0%). In 266 patients (7.6%) information on the treatment plan is missing.

An active anti-tumour treatment (n = 2350) comprised of combinations of surgery, radiotherapy, chemotherapy, immunotherapy and targeted therapy. Surgery, whether or not combined with another treatment, was planned for 615 patients (26.2%). Radiotherapy, whether or not combined with another non-surgical treatment, was applied in 933 patients (39.7%). And another 618 patients (26.3%) were planned for systemic therapy only (**Table 1.2**).

Radiotherapy (DLCA-R)

Of all analysable patients with a (stage I-III) NSCLC undergoing radiotherapeutic treatment and registered in the DLCA-R (n = 2427), most were treated with Stereotactic Body Radiation Therapy (SBRT, n = 1294, 53.3%). Other patients were treated with conventional radiotherapy (296, 12.2%) or chemoradiotherapy (837, 34.5%), of which 64.2% was delivered concurrently (**Table 1.3**).

Surgery (DLCA-S)

Of all analysable patients with NSCLC undergoing surgery and registered in the DLCA-S (n = 1979), 166 (8.4%) underwent a pneumonectomy, 1618 (81.8%) a (bi) lobectomy, 55 (2.8%) an anatomic segment resection, 127 (6.4%) a subparenchymal resection and 13 (0.7%) did not undergo a resection. Most operations were started with a minimal invasive technique, video or robotic assisted resection (VATS or RATS): 1409 (71.2%), with a conversion rate of 18.7% (n = 263) (**Table 1.4**).

Table 1.3. Treatment characteristics of patients with a NSCLC in the DLCA-R in 2016 (N = 2427).

	N	%
Type of radiotherapy		
Conventional	296	12.2%
SBRT*	1294	53.3%
Chemoradiotherapy	837	34.5%
Of which concurrent	537	64.2%

* SBRT = Stereotactic Body Radio Therapy

Table 1.4. Treatment characteristics of patients with a NSCLC in the DLCA-S in 2016 (N = 1979).

	N	%
Surgical approach		
VATS / RATS*	1409	71.2%
Converted to open	263	18.7%
Primary thoracotomy	479	24.2%
Different / unknown	91	4.6%
Resection type		
Pneumonectomy	166	8.4%
(Bi)lobectomy	1618	81.8%
Anatomic segment resection	55	2.8%
Wedge / different	127	6.4%
No resection (open-close)	13	0.7%

* VATS: Video Assisted Thoracoscopic Surgery, RATS: Robot Assisted Thoracoscopic Surgery

Quality indicators

In **Table 2** all quality indicators that are part of the externally transparent indicator sets in 2016, 2017 and 2018 are demonstrated. Also shown in **Table 2** are the results of national quality indicators of 2016, with for all indicators the number of patients included in the indicator calculation ('denominator') and the percentage meeting the indicator definition (numerator divided by denominator). For the two volume indicators only the numerators are displayed.

The structure indicator "completeness of data entry…" is scored 'yes' on patient level when all items required for calculating external indicators are registered and thereby gives an indication on the validity of other indicator results. In 2016, the average data completeness on patient level was 90.7% in the DLCA-S and 84.0% in the DLCA-R.

The percentage of patients with NSCLC discussed in a meeting prior to radiotherapeutic treatment was 95.1%. Of the surgically treated patients with a NSCLC, 97.1% was discussed in a postoperative MDT meeting, an increase of 15% compared to the 82.2% in 2012.

Outcome indicator results are calculated over a period of two consecutive years. The national average 30-day/in-hospital mortality of patients after a resection for primary lung cancer was 2.3% in 2015-2016. The national average 90-day mortality of all patients treated with combined chemoradiotherapy for a primary NSCLC was 6.4% in 2015-2016.

DISCUSSION

In the Netherlands, clinical audits are integrated as a part of the professional quality system. This report provides insight in the Dutch Lung Cancer Audit (DLCA), one of the first nationwide-implemented quality registries to evaluate the multidisciplinary care for patients with lung cancer worldwide. The DLCA was developed according to the blueprint of the Dutch Institute for Clinical Auditing, one of the leading organisations facilitating clinical auditing in the Netherlands. Although the audit in its current format is still 'immature' (with 2016 as the first registration year for lung oncologists), the core principles are clear. In this paper the first results were presented.

Several initiatives to monitor quality of (surgical) lung cancer care have been developed worldwide.[13–18] The design and intents of these initiatives differ in various ways.

Table 2. External indicator sets for lung carcinoma from 2016-2018 and national indicator scores in 2016.

Indicator type	DLCA subset*	Indicator description	Part of set in '18	'17	'16	Nationwide scores 2016** Patients in denominator (n)	Indicator score (%)
Structure							
	L	Registration of at least one patient in the DLCA-L per hospital.	☐	☐	☑	NA	
	L	Completeness of data entry^ in DLCA-L.	☑	☐	☐	NA	
	L	Volume of new patients registered in the DLCA-L per location.	☑	☑	☐	NA	
	R	Completeness of data entry^ in DLCA-R.	☑	☑	☑	2214	84.0%
	R	Volume of patients undergoing radical radiation treatment for NSCLC per location.	☑	☑	☑	2387	
	S	Completeness of data entry^ in DLCA-S.	☑	☑	☑	1979	90.7%
	S	Volume of anatomical parenchymal resections~ for malignant or benign pathology per hospital location.	☑	☑	☑	2359	
Process							
	L	Percentage of patients discussed in a MDT meeting prior to the start of treatment.	☑	☑	☐	NA	
	L	Percentage of patients -clinical stage III NSCLC and intentional curative treatment- in whom cerebral imaging was performed.	☑	☑	☐	NA	
	L	Percentage of patients with stage IV adenocarcinoma, not eligible for curative treatment, with molecular diagnostics.	☑	☐	☐	NA	
	R	Percentage of patients - with radiation treatment with radical intent - discussed in a MDT meeting prior to the start of treatment.	☐	☐	☑	2214	95.1%
	R	Percentage of patients - with SBRT with radical intent- with a waiting time (between day of referral and first day of radiation) of ≤21 days.	☐	☐	☑	1162	70.7%
	R	Percentage of stage III NSCLC patients - with radiation treatment with radical intent– undergoing concurrent chemoradiotherapy.	☐	☐	☑	686	55.5%

Table 2. (continued)

	S	Percentage of patients -having surgery for a NSCLC- discussed in a postoperative MDT meeting.	☐	☑	☑	1809	97.1%
	S	Percentage of patients -having surgery for a NSCLC- in which the clinical TNM stage is known during the preoperative MDT meeting.	☐	☑	☑	1790	98.3%
	S	Percentage of patients -having surgery for a NSCLC- in which the pathological TNM stage is known during the preoperative MDT meeting.	☐	☑	☑	1749	99.3%
	S	Percentage of patients -having surgery for a NSCLC- with a waiting time (between the last MDT meeting and day of surgery) of ≤21 days.	☐	☑	☑	1660	65.0%
Outcome**							
	R	Percentage of patients undergoing a combined chemoradiotherapy treatment that died within 90 days from the last radiation.	☐	☐	☑	1696	6.4%
	R	Percentage of patients with a grade IV or V toxicity within 90 days from the last radiation treatment with curative intent.	☑	☑	☑	4469	0.9%
	S	Percentage of patients died within 30 days after resection -for primary lung carcinoma- or during primary admission.	☑	☑	☑	3573	2.3%
	S	Percentage of patients with a complicated course after resection for primary lung carcinoma.	☑	☑	☑	3573	15.6%
	S	Percentage of patients with an irradical resection (R1 or R2) after resection for primary NSCLC.	☐	☐	☑	3573	6.2%

NSCLC = non-small cell lung carcinoma, MDT = multidisciplinary team, NA = not available for 2016.

* L: lung-oncologists, R: radiotherapeutic-oncologists, S: surgical-oncologists

** Outcome indicators scores are calculated over a two-year period, thus for 2016: 2015-2016.

^ Completeness means that all items required for calculating external indicators are registered per patient

~ Includes: pneumonectomy, (bi)lobectomy or anatomical segment resection (excludes: wedge excisions)

The DLCA distinguishes itself from other initiatives through; the central role of clinicians, weekly updated feedback information with national benchmark information, participation of all major treating specialisms, a centrally financed system and close collaboration with other parties in healthcare with tripartite agreements on data transparency. Furthermore, participation in the DLCA has been incorporated in the professional quality system, thereby stimulating nationwide implementation and unbiased information, in contrast with registries with a more voluntary nature. Implementation of evidence-based guidelines and quality standards is evaluated with the audit, on a local as well as a national level.

Design and implementation of the DLCA sub-registries has been a phased process. After independent data-verification of the surgical part of the audit, the data of the DLCA-S are considered mature and the data of the DLCA-R will follow soon. The pulmonologists joined the DLCA-L only recently and the number of analysable patients with NSCLC included in this sub-registry in 2016 is limited to 35-40 percent of the national incidence.[2] It is expected that case ascertainment will rapidly increase over time, especially from the moment hospitals are provided with benchmarked feedback.[6,19–21] The great incentive for clinicians to participate in the audit is the information they receive on the quality of their performance in clinical practice with indicator results benchmarked to the national average (intrinsic motivation). In addition, the Netherlands Healthcare Inspectorate demands participation in the audit, insurance companies use the audit information for reimbursement and the National Healthcare Institute demands indicator scores from the audit for public transparency, which makes participation more or less mandatory for hospitals (external stimulus).

In this first year of multidisciplinary collaboration in the DLCA, one of the biggest advantages experienced by all specialism was the opportunity to address overlapping

issues in the combined CAB and SC meetings and the quick implementation of new knowledge into national clinical practice. This has contributed to the implementation of TNM8 in the DLCA in 2017, only a few months after publication,[22] leading to a nationwide in-hospital adoption of TNM8.

Sub-registries in themselves also provided important information already. DLCA-S data showed that national use of minimally invasive techniques (VATS/RATS) is high, around 70%. Internationally this percentage varies between 22-63%.[23,24] Postoperative mortality after primary lung cancer resection in the Netherlands has been as low as between 2.0 and 2.5% from the start of the DLCA-S. This is comparable to international data.[23–26]

An important issue that arose from the DLCA-S is the unfavourable quality of staging compared to for example Denmark.[27,28] In the DLCA-S staging accuracy was assessed comparing clinical with pathological TNM stage, regardless of whether discrepancies influenced treatment strategy. This definition differs from Danish studies, which reported inaccuracy only if this had clinical consequences. Nevertheless, the DLCA studies demonstrated there is room for improvement in preoperative staging in the Netherlands. In the diagnostic path – leading to a clinical stage – pulmonologists play a major role. Hence, to improve pre-treatment staging, a multidisciplinary approach is essential.

The primary aim of clinical auditing is to improve outcomes for patients by providing meaningful, actable, benchmarked, short-cycled feedback information on daily clinical practice to the multidisciplinary teams in hospitals. Thereby stimulating improvement initiatives on both local and national level. Ultimately, quality assurance for the whole clinical care path of every lung cancer patient is intended. Therefore, the DLCA evolves from a procedure based mono-disciplinary audit to a condition based multidisciplinary audit, tracking patients from diagnosis until death.

Simultaneously, a shift of focus on structural and process indicators towards outcome indicators, clinical as well as patient reported, is intended. The standard set for lung cancer of the International Consortium of Health Outcome Measurement (ICHOM) was adopted, to be able to participate in international comparisons in the near future. On the other hand, the DLCA is also a platform for clinicians themselves to develop new meaningful quality indicators. DICA's well-respected agreement with external stakeholders on 'stepwise' transparency is imperative in this context, because it gives clinicians the opportunity to evaluate the validity of an indicator and its results, before hospital specific information is made public.

Initially, the idea was to set up the DLCA as a multidisciplinary audit in which multiple disciplines distributed over various hospitals could contribute to registration of one patient. Unfortunately, the construction of such a 'chain registry' has not been achieved yet. Largely, this is due to privacy legislation, causing difficulties in sharing patient data across different hospitals.[29] Additionally, such a 'chain registry' needs clear agreements on who registers what and how, since part of the feedback information (including externally transparent indicators) will be based on information provided by a clinician one might not know. Taking into account the aforementioned issue of low case ascertainment in the novice DLCA-L, completeness of data – that should be relied on – is not guaranteed. Therefore the current design was chosen: 3 DLCA sub-registries (DLCA -L, -R and -S). This has the disadvantage that some information is repeatedly registered unnecessarily.
In extension to this, a general limitation of quality registries is the administrative burden associated with data collection, which frequently rests on the shoulders of clinicians themselves. Still, to evaluate the quality of all essential points in the patients' care path a substantial amount of data is needed. In addition, proper casemix adjustments are imperative in between-hospital comparisons, for which a set of patient and disease characteristics has to be registered for each case. A

meaningful registration may be an administrative burden, though on the other hand reduces the obligations to provide less-meaningful – but externally imposed – indicators to other partners in healthcare (e.g. insurance companies).
One of the solutions to reduce administrative burden is (partly) automated data extraction from existing data sources (e.g. Electronic Patient Records (EPDs), structured reports of diagnostics, treatment or pathology). Being part of a larger platform, like DICA, can be an advantage in this, when close cooperation is sought between the registry platform, the data processor and hospital-IT-providers.

The main challenge of the DLCA in the (near) future is the integration of three separate sub-registries, the DLCA-L, -R and -S into one 'chain registry' system as described above. This integrated system facilitates registration of data by different disciplines and institutions in one patient record, thereby maximizing multidisciplinary quality evaluation possibilities and minimizing administrative burden of the registration.
In addition, there should be more focus on outcome indicators in the audit. Next to clinical outcomes, functional outcomes and quality of life are of great value for patients. Measuring such patient reported outcomes (PROMs) or patient reported experiences (PREMs) in daily practice can be challenging, especially low response rates can hamper valid comparisons between hospitals. Though, linkage of patient reported data to clinical data could provide clinicians with 'new' valuable information and can facilitate (shared) personalised treatment decisions.

In conclusion, with the start of the DLCA in 2016, there is a unique nationwide audit system to evaluate the quality of multidisciplinary lung cancer care. The DLCA is accepted and implemented on a nationwide level, enabling healthcare providers insight in their performance together with a national benchmark, and providing other stakeholders with a transparent evaluation of this performance. When

challenges of shared data input and access – mostly concerning privacy legalisation – are solved, the accomplishment of a completely integrated audit remains a main aspiration. The possibilities of multidisciplinary quality evaluation will be maximised further, with the highest aim of continuous healthcare improvement.

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CHAPTER 4

National comparison of hospital performances in lung cancer surgery: the role of casemix adjustment

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ABSTRACT

Background | When comparing hospitals on outcome indicators, proper adjustment for casemix (a combination of patient and disease characteristics) is indispensable. This study examines the need for casemix adjustment in evaluating hospital outcomes for non-small cell lung cancer surgery.

Methods | Data from the Dutch Lung Cancer Audit for Surgery were used to validate factors associated with postoperative 30-day mortality and complicated course with multivariable logistic regression models. Between-hospital variation in casemix was studied by calculating medians and interquartile ranges for separate factors on the hospital level and the 'expected' outcomes per hospital as a composite measure.

Results | A total of 8040 patients, distributed over 51 Dutch hospitals, were included for analysis. Mean observed postoperative mortality and complicated course were 2.2% and 13.6%, respectively. Age, American Society of Anesthesiologists classification, Eastern Cooperative Oncology Group performance score, lung function, extent of resection, tumour stage, and postoperative histopathologic findings were individual significant predictors for both outcomes of postoperative mortality and complicated course. A considerable variation of these casemix factors among hospital populations was observed, with the expected mortality and complicated course per hospital ranging from 1.4% to 3.2% and from 11.5% to 17.1%, respectively.

Conclusions | The between-hospital variation in casemix of patients undergoing surgical treatment for non-small cell lung cancer emphasizes the importance of proper adjustment when comparing hospitals on outcome indicators.

INTRODUCTION

Lung cancer is the most common cause of cancer-related death in Europe and the United States.[1] Upfront surgery is the cornerstone of curative treatment in patients with non-small cell lung cancer (NSCLC) stage I to II, which accounts for about one third of the clinical stages.[2,3] Additionally, about 15% of patients with stage III disease are treated surgically, with or without (neo)adjuvant therapy.[4]

In 2012 the Dutch Lung Cancer Audit for Surgery (DLCA-S) was started.[5,6] This nationwide, mandatory clinical registry includes all patients undergoing surgical treatment for lung cancer. The main purpose is to provide caregivers with feedback on quality of care and thus enable a national benchmark.

Interest in using outcome measures, such as mortality, as public information is increasing. To facilitate meaningful between-hospital comparisons, it is important to take the 'casemix' (a combination of patient and disease characteristics that displays disease burden) into account. A casemix factor can affect outcomes but is not part of the decision made for the specific intervention.

Previous studies investigated the effect of patient, disease, and treatment characteristics on outcomes in lung surgery, but they did not provide insight into whether hospitals differ in casemix and how this could influence outcomes of these hospitals.[7–9]

This study, in patients undergoing surgical treatment for NSCLC, aimed to:

1. Validate risk factors for 'postoperative mortality' and 'complicated course'.
2. Examine differences in casemix between hospitals.
3. Develop a casemix adjustment model useful in practice for both outcome indicators.

PATIENTS AND METHODS

Data source and study population

Data were derived from the DLCA-S.[5] The database includes information on patient and tumour characteristics, diagnostic workup, surgical procedure, postoperative outcomes, and pathologic features. Data are collected through a secured Web-based system. Participating hospitals receive weekly updated feedback, benchmarked to the national average. In-hospital data verification by an independent third party is part of the evaluation cycle. The last verification, completed in July 2016, shows sufficient data quality, with 99.4% complete patient inclusion and 0.0% under-registration of 'postoperative mortality' and 'complicated course'.[10]

Patients undergoing NSCLC surgery between January 2012 and December 2016 were included. Minimum data registry criteria –to be eligible for analysis – included information on age, sex, operation date, type of surgical procedure, and vital status 30 days postoperatively or at the time of discharge.

Main outcomes

The outcomes assessed were postoperative mortality and complicated course. Postoperative mortality was defined as mortality within 30 days after surgical treatment or during the primary hospital admission. The composite measure postoperative complicated course was defined as a complication leading to a prolonged hospital stay (≥14 days),[11] unplanned reintervention, or death, and it was used to reflect only severe complications.

Casemix factors

Selected casemix factors were determined on the basis of literature and expert opinion (DLCA-S Scientific Committee) and included the following: age; sex; comorbidities; previous thoracic surgical procedure; Eastern Cooperative Oncology

Group Performance Score (ECOG PS); American Society of Anesthesiologists (ASA) classification; lung function (forced expiratory volume in 1 second percentage of normal [FEV1%]; diffusing lung capacity for oxygen percentage of normal [DLCO%]); tumour, node, metastasis (TNM) stage (TNM7);[2] primary or recurrent disease; induction therapy; extent of resection; and histopathologic findings.

Statistical analysis

The association of selected casemix factors on postoperative mortality and complicated course was investigated by two separate multivariable adjustment models. For this multivariable model, factors from univariable logistic regression (P<0.10) were selected after controlling for collinearity. Model discrimination was assessed by the C-statistic.

The effect of age was calculated as an increase per decade. Lung function was analysed as a composite measure of FEV1% and DLCO%, divided in three categories: (1) FEV1 and DLCO ≥80% or one of the values missing, (2) FEV1 or DLCO <80%, and (3) both FEV1 and DLCO values missing. These cut-off values are in accordance with the evidence-based Dutch guideline.[3,12] Using a composite measure reduced the missing data on lung function from 20.2% (1628 of 8040) to 6.5% (521 of 8040). Missing items were analysed as a separate group if they exceeded 5%, and subgroups of missing items ≤5% were excluded from logistic regression analyses.[13]

To study between-hospital variations in patient population, medians, interquartile ranges, and minimum and maximum values for selected patient and tumour characteristics were calculated on a hospital level.

Using coefficients from the multivariable model, 'expected' mortality was calculated per patient. On the basis of all patients in one hospital, the expected and observed mortality rate was calculated per hospital. The adjusted mortality per hospital was calculated as follows: (observed/expected)*mean. The same was done for postoperative complicated course.

Because of statistical restriction of multivariable regression models, the number of events limits the number of casemix factors one can adjust for.[14] When needed, models were restricted by selecting factors on the basis of expert opinion.

To minimize statistical artifacts resulting from small sample size, only hospitals that performed ≥20 parenchymal resections per year (the minimum volume standard according to the Association of Surgeons in The Netherlands)[15] were included in the calculations for between-hospital variation.

Statistical significance was set at a threshold of 0.05, with p values calculated by two-sided tests. Statistical analyses were performed using SPSS (IBM SPSS Statistics for Macintosh, Version 23.0, IBM Corp, Armonk, New York).

RESULTS

Population characteristics

A total of 8040 patients, distributed over 51 hospitals, who underwent NSCLC surgical procedures were eligible for analyses. Baseline characteristics are displayed in **Table 1**. Median age was 67 years, and 56.1% (n = 4508) of patients were male. More than one half of all patients had clinical stage I (n = 4379; 54.5%). Lobectomy was the most commonly performed resection type (n = 6203; 77.2%). Most operations (5366; 66.8%) started using a minimally invasive technique, and 787 (14.7%) were converted to thoracotomy.

The average postoperative mortality was 2.2% (n = 176). The average postoperative complicated course was 13.6% (n = 1094). The overall complication rate, regardless of complication severity, was 34.4% (n = 2763).

Predictors of postoperative mortality and complicated course

In 358 patients information on ASA classification (n = 285; 3.5%) or pathologic T-stage (n = 79; 1.0%) was missing. After excluding these patients, 7682 patients were included for univariable and multivariable logistic regression analyses.

Table 1. Population characteristics. Hospitals: N = 51, patients: n = 8040

	N	%
Age, y, median[IQR]	67[60 - 73]	
Gender		
Male	4508	56.1
ASA-classification		
I-II	5634	70.1
III+	2121	26.4
Unknown	285	3.5
ECOG PS		
0-I	6117	76.1
II+	314	3.9
Unknown	1609	20.0
Charlson comorbidity index		
0	2546	31.7
1	2270	28.2
2+	3224	40.1
Cardiac comorbidity [a]		
Yes	2135	26.6
Lung function		
FEV1 and DLCO ≥80% [b]	2474	30.8
FEV1 or DLCO <80%	5045	62.7
FEV1 and DLCO unknown	521	6.5
Primary tumour/ recurrence		
Primary [c]	7905	98.3
Recurrence	135	1.7
Induction		
No/unknown	7502	93.5
Chemoradiotherapy	298	3.7
Different [d]	228	2.8
Urgency		
Elective	7726	96.1
Urgent/acute [e]	197	2.4
Unknown	117	1.5
Approach		
Minimally-invasive	5366	66.8
Primary thoracotomy	2640	32.8
Different/unknown	34	0.4

Table 1. (continued)

	N	%
Side		
Left	3475	43.2
Right	4565	56.8
Extent of surgery		
Pneumonectomy	641	8.0
Bilobectomy	450	5.6
Lobectomy	6203	77.1
Segmentresection	151	1.9
Wedge resection	495	6.2
No resection	100	1.2
Pathological stage [f]		
Stage I/occult	4258	53.0
Stage II	2112	26.3
Stage IIIa+	1283	15.9
Unknown	387	4.8
Pathological T-stage [f]		
pT1a-b(/To/Tis)	3215	40.0
pT2a-b	3167	39.4
pT3	1271	15.8
pT4	308	3.8
Unknown/Tx	79	1.0
Pathological N-stage [f]		
No	5816	72.3
N1	1325	16.5
N2	717	8.9
N3	13	0.2
Unknown	169	2.1
Postoperative histopathology		
Adenocarcinoma	4762	59.2
Squamous cell	2742	34.1
Adenosquamous	105	1.3
Different [g]	431	5.4

[a] Missing was considered as 'no'
[b] FEV1 and DLCO ≥80% or one of the values missing
[c] Including second primary tumours
[d] Chemotherapy/radiotherapy alone
[e] Surgery performed <12 (urgent) <6 (acute) hours after indication
[f] TNM7
[g] Large-cell carcinoma and neuro-endocrine tumour

Age, ASA classification, ECOG PS, lung function, extent of resection, pathologic T-stage, and histopathologic findings were individual significant predictors of postoperative mortality (**Table 2**). The C-statistic (95% confidence interval [CI]) of the model was 0.81 (0.77 to 0.84).

For postoperative complicated course, individual significant predictors were age, sex, ASA classification, ECOG PS, lung function, induction therapy, extent of resection, pathologic T-stage, and histopathologic findings (**Table 2**). The C-statistic (95% CI) of the model was 0.66 (0.64 to 0.68).

Between-hospital variation

After excluding hospitals performing <20 parenchymal resections per year, 6600 patients across 37 hospitals were selected to analyse between-hospital variation in casemix characteristics. Of the 14 excluded hospitals, 11 stopped performing lung cancer surgery, and three hospitals were excluded on the basis of annual volume (on average seven, nine, and 19).

Considerable between-hospital variation in casemix was observed (**Figure 1, Supplemental Table 1**). For example, the proportion of patients with pathologic T-stage 3 to 4 was 10.3% in one hospital and 31.8% in another. Significant between-hospital variations were also seen in age 80+ years (0.5% to 16.7%), ASA classification III+ (6.5% to 65.2%), induction chemoradiotherapy (0% to 24.8%), and pneumonectomy (3.0% to 21.6%). Expected mortality and complicated course per hospital ranged from 1.4% to 3.2% and from 11.5% to 17.1%, respectively (**Figure 2a-b**).

Table 2. Factors associated with postoperative mortality and complicated course after NSCLC surgery. Hospitals: N = 50, patients: n = 7682.

	Mortality						Complicated course					
	Unadjusted OR			Adjusted OR			Unadjusted OR			Adjusted OR		
	OR	95%-CI		OR	95%-CI		OR	95%-CI		OR	95%-CI	
Age per decade	**2.04**	**1.68**	**2.49**	**1.88**	**1.52**	**2.33**	**1.21**	**1.12**	**1.30**	**1.15**	**1.06**	**1.25**
Gender												
Male	**2.29**	**1.62**	**3.23**	1.41	0.98	2.04	**1.51**	**1.32**	**1.73**	**1.30**	**1.12**	**1.50**
Female	ref			ref			ref			ref		
ASA-classification												
I-II	ref			ref			ref			ref		
III+	**2.31**	**1.70**	**3.13**	**1.51**	**1.08**	**2.10**	**1.88**	**1.64**	**2.15**	**1.59**	**1.38**	**1.85**
ECOG PS												
0-1	ref			ref			ref			ref		
2+	**4.25**	**2.70**	**6.70**	**2.65**	**1.62**	**4.34**	**2.77**	**2.14**	**3.58**	**2.06**	**1.57**	**2.70**
Unknown	0.96	0.63	1.48	0.87	0.56	1.35	0.94	0.79	1.12	0.88	0.73	1.05
Cardiac comorbidity												
No	ref			ref			ref			ref		
Yes	**1.83**	**1.34**	**2.49**	1.20	0.85	1.69	**1.26**	**1.09**	**1.45**	0.99	0.85	1.16
Lung function												
FEV1 or DLCO ≥80% [a]	ref			ref			ref			ref		
FEV1 and DLCO <80%	**1.70**	**1.17**	**2.47**	**1.54**	**1.05**	**2.27**	**1.81**	**1.55**	**2.12**	**1.72**	**1.47**	**2.03**
Unknown	1.53	0.75	3.10	1.36	0.65	2.86	**1.39**	**1.02**	**1.91**	1.36	0.99	1.88
Primary tumour or recurrence												
Primary [b]	ref			ref			ref			N.A.		
Recurrence	**3.12**	**1.50**	**6.50**	1.80	0.81	3.99	1.43	0.91	2.27	N.A.		

Table 2. (continued)

Induction therapy																
No	ref				N.A.					ref				ref				
Chemoradiotherapy	1.50	0.76	-	2.97	N.A.					**1.57**	**1.16**	-	**2.12**	**1.63**	**1.19**	-	**2.24**
Different [c]	1.51	0.70	-	3.27	N.A.					1.20	0.83	-	1.74	1.02	0.69	-	1.49
Extent of resection																
Pneumonectomy	**5.16**	**3.57**	-	**7.46**	**3.74**	**2.47**	-	**5.65**		**1.73**	**1.40**	-	**2.14**	**1.43**	**1.14**	-	**1.79**
Bilobectomy	**3.95**	**2.51**	-	**6.22**	**3.25**	**2.03**	-	**5.21**		**2.03**	**1.60**	-	**2.57**	**1.83**	**1.44**	-	**2.34**
Lobectomy	ref				ref					ref				ref			
Segment resection	1.33	0.42	-	4.26	1.55	0.48	-	5.04		0.70	0.40	-	1.21	0.72	0.41	-	1.27
Wedge resection	0.90	0.39	-	2.06	0.95	0.41	-	2.20		**0.58**	**0.41**	-	**0.83**	**0.59**	**0.41**	-	**0.84**
No resection	0.92	0.13	-	6.69	0.47	0.06	-	3.46		0.51	0.20	-	1.26	0.38	0.15	-	0.95
Pathological T-stage [d]																
≤pT2a-b	ref				ref					ref				ref			
pT3-pT4	**2.85**	**2.09**	-	**3.90**	**1.85**	**1.32**	-	**2.59**		**1.53**	**1.32**	-	**1.78**	**1.29**	**1.10**	-	**1.51**
Postoperative histology																
Adenocarcinoma	ref				ref					ref				ref			
Squamous cell carcinoma	**2.89**	**2.08**	-	**4.01**	**1.50**	**1.06**	-	**2.14**		**1.56**	**1.36**	-	**1.78**	**1.16**	**1.00**	-	**1.35**
Different [e]	**2.35**	**1.32**	-	**4.18**	**1.98**	**1.10**	-	**3.57**		1.15	0.87	-	1.51	1.02	0.77	-	1.35

[a] FEV1 and DLCO ≥80% or one of the values missing

[b] Including second primary tumours

[c] Chemotherapy or radiotherapy alone

[d] TNM7

[e] Adenosquameus or large cell carcinoma

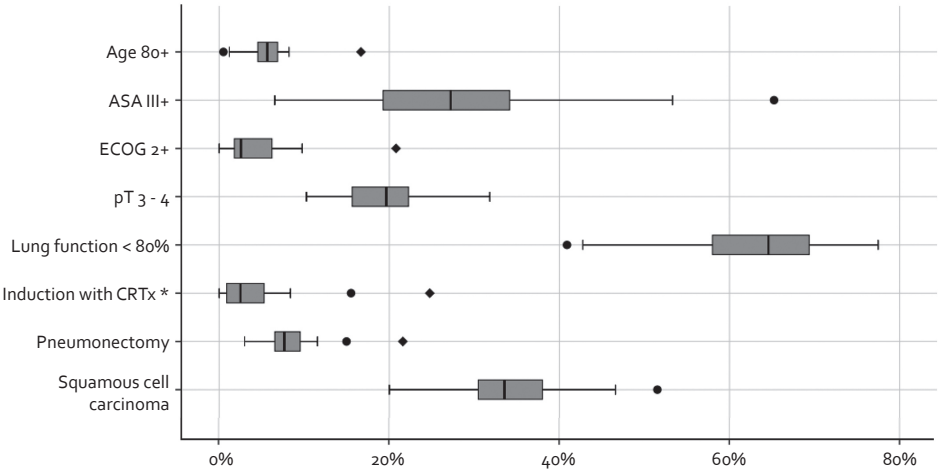

Figure 1. Boxplot illustrating between-hospital variation of specific casemix characteristics of patients undergoing surgical treatment for NSCLC. Hospitals: N = 37, patients: n = 6600.
● Hospital outside 95% C.I.
◆ Hospital outside 99% C.I.
|—| Hospitals within the 95% C.I.
* CRTx = chemoradiotherapy

Casemix adjustment in practice

With an event rate of postoperative mortality of 70 per 2 years, the casemix adjustment model – to be useful for audit purposes – had to be restricted to age, ECOG PS, ASA classification, extent of resection, pathologic T-stage, and histopathologic findings. Because of a higher event rate of complicated course (±435 per 2 years), further restriction of the casemix adjustment model was not necessary. In the DLCA-S, postoperative mortality and complicated course are evaluated over a 2-year period and are presented using funnel plots with 95% CIs. Depending on the expected outcome (representing the complexity of patient population per hospital) the adjusted percentage can be higher or lower than or equal to the observed percentage. This is demonstrated for complicated course in **Figure 3**.

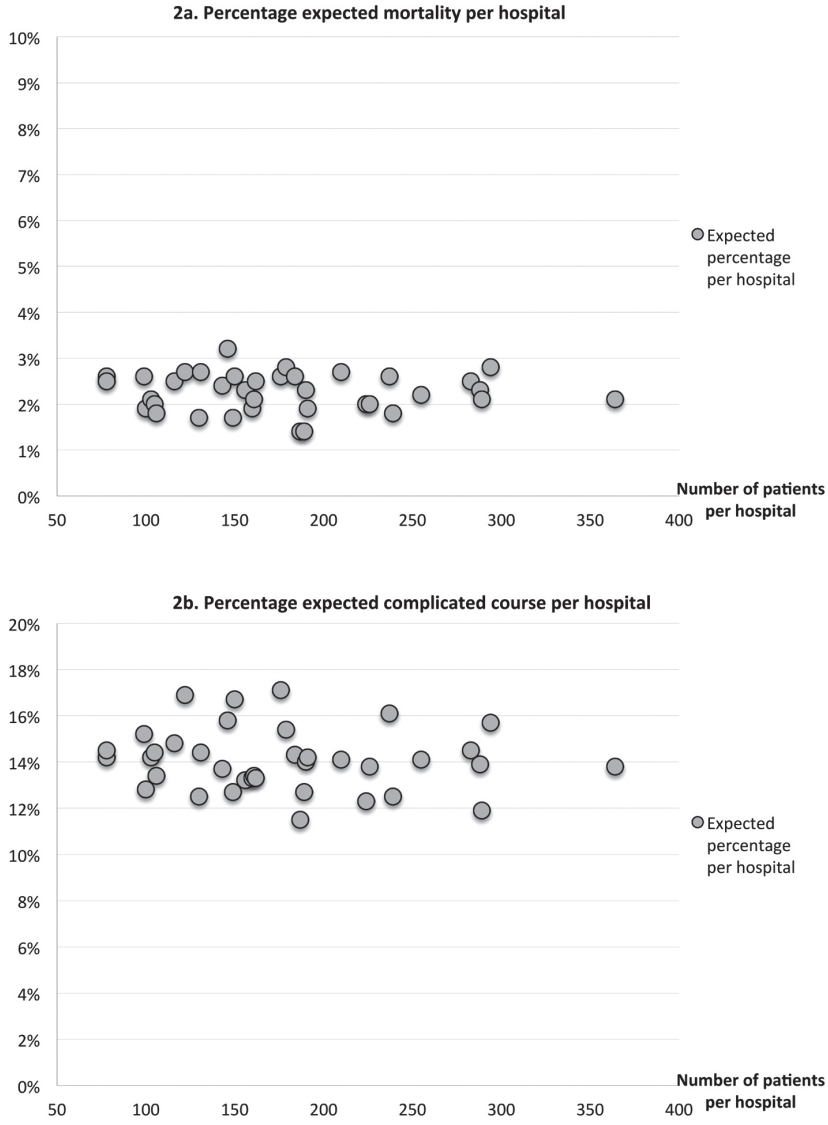

Figure 2. Scatterplots of the percentage of (a) expected mortality and (b) complicated course per hospital. Hospitals: N = 37, patients: n = 6600.

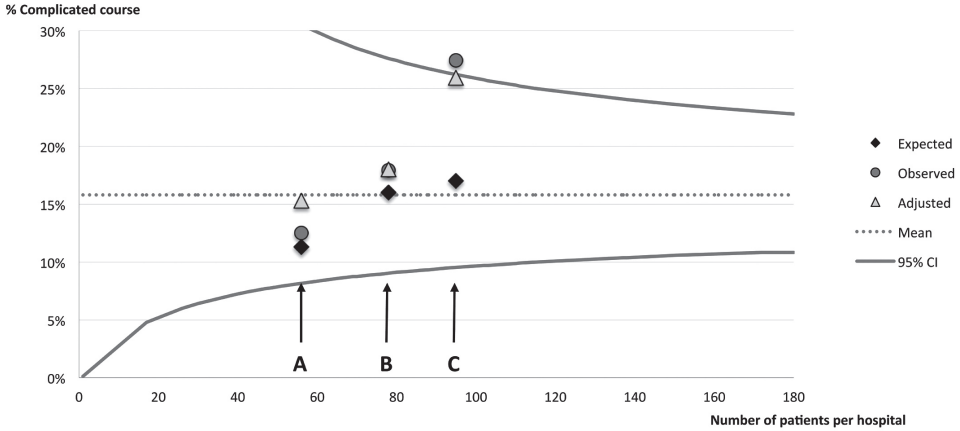

Figure 3. Illustration of a funnelplot with casemix adjustment in practice.
X-axis: number of patients undergoing surgery per hospital (2015-2016).
Y-axis: percentage complicated course per hospital (expected ◆, observed ●, adjusted △).
◆ = Based on: age, gender, ECOG PS, ASA-classification, lung function, induction therapy, extent of resection, pathological tumour stage and postoperative pathology.
△ = Calculated by: (observed/expected)*mean.
A, **B** and **C** are examples of hospitals. The expected percentage of patients with a 'complicated course' in hospital **A** is lower than the mean. Based on the selected casemix factors, this hospital has a less complex patient population. In the 'adjusted' calculation the denominator is smaller and the 'adjusted' becomes higher than the 'observed'. The opposite applies to hospital **C**. The 'expected' in hospital **B** is similar to the national average so the 'observed' and 'adjusted' values are equal. (CI = confidence interval.)

COMMENT

Using a nationwide mandatory registry, this study emphasized the importance of casemix adjustment when benchmarking hospitals on outcome measures in NSCLC surgery. Age, ECOG PS, ASA classification, lung function, extent of resection, pathologic tumour stage, and histopathologic findings were confirmed as individual significant predictors for both postoperative mortality and complicated course. Postoperative complicated course was also influenced by sex and induction chemoradiotherapy. Considerable variation of casemix among hospital populations

was observed, with expected outcomes for mortality and complicated course varying, respectively, between 1.4% to 3.2% and 11.5% to 17.1%. Given the low event rate of mortality, for the casemix adjustment model to be usable for audit purposes it was restricted to age, ECOG PS, ASA classification, extent of resection, pathologic tumour stage, and histopathologic findings.

Risk stratification in lung (cancer) surgery is a popular topic that may have been studied in cohorts larger than the current study.[7–9] However, the basis of the current study is a registry with mandatory participation for all Dutch hospitals, with resulting national complete coverage.[5] Participation in other databases is usually on a voluntary basis and thus is prone to selection bias.

Previous studies focused on prediction for individual patients, but they did not study between-hospital differences in casemix, relevant for outcome adjustment. The current study adds this information, combined with practical implications of casemix adjustment in national audit data and benchmarking.

The observed unequal distribution of patients over Dutch hospitals in this study is not entirely unexpected, given the structure of oncologic care in The Netherlands and in line with similar studies on colorectal carcinoma.[3,16] Factors associated with the postoperative outcomes in this study are comparable to those used in previous studies.[7–9] In other studies, associated factors also included body mass index, dyspnoea grade, and steroid use. A one-on-one adoption of previous models on DLCA-S data was not possible because registered data items differ among databases.

In addition, casemix adjustment models intended for between-hospital quality of care comparison should include as few factors in the decisional pathway or attributable to hospital characteristics (e.g., case volume) as possible. If these factors are included in the adjustment model, the effect of what one wants to measure (quality of care delivered by the hospital) can be distorted or even nullified.[17]

Extent of resection is shown to influence postoperative outcomes. The extent of resection partly depends on preoperative decisions of surgical teams or occasionally on preoperative events and hence is not purely a casemix characteristic. However, extent of resection was chosen as proxy measure because the used data set lacks information on central tumour location or extension into an adjacent lobe.

Similarly, one could state that 'surgical approach' (minimally invasive or open) is a proxy for complexity. However, whether a procedure is started and is successfully performed minimally invasively depends on correct patient selection by the (surgical) team and ultimately the team's technical skills. Therefore, surgical approach was not included in the model.

From 2017 on, data on tumour location are registered. When this or other new information contributes to the casemix adjustment models, models will be taken into reconsideration.

Postoperative mortality is the most unfavourable event. Providing caregivers with insight into this outcome is of great importance. However, an event rate of 2% means that in the largest-volume hospitals, with 160 resections per 2 years, about 3 patients die within 30 days or during primary admission. One can discuss whether this information lacks discriminative power for hospital comparison. In low-volume hospitals, outliers can be determined by chance and not by excellent or substandard performance. For this reason benchmark information is always provided with a 95% CI.

Because an inverse relationship between postoperative mortality and hospital volume was shown,[18] it is also questionable whether a volume standard of 20 resections is sufficient. However, the cut-off value for high-volume is unclear. Currently, the Association of Surgeons in The Netherlands visits hospitals structurally not complying with standards, as well as structurally underperforming hospitals. Additionally, the Dutch Health Care Inspectorate and the National Health

Care Institute monitor volume and quality standards. On indication, assistance for improvements is provided.

Composite measures, such as complicated course, typically have a higher event rate and can be more distinctive in hospital comparisons. Event rate can also be increased by extending the follow-up (e.g., 1-year mortality). However, this is less usable for audit purposes focused on enabling rapid insight and improvement of outcomes. Long-term follow-up is also more likely to be affected by other (nonsurgical) treatments. Other potential outcomes for quality of (surgical-oncologic) care evaluation are resection completeness, disease recurrence, and patient-reported outcome measures. In this study, the outcomes postoperative mortality and complicated course were chosen to mainly reflect the quality of the (peri)surgical process.

Although casemix does influence postoperative outcomes and should be taken into consideration in quality of care comparisons among hospitals, it remains essential to provide caregivers with their own unadjusted data. Every adverse outcome, regardless of patients' characteristics, should trigger opportunities to improve care processes.

A strength of this study is the large, national cohort that was investigated. National audit data enable analysis of information without patient selection such as in randomized studies with strict inclusion protocols and are therefore highly representative of current national practice.

On the downside, there may be less insight in patients who are falsely not registered or incorrectly registered. Therefore, in-hospital data verification by an independent third party is incorporated into the DLCA-S.[10]

Another limitation, related to (large) data sets in general, is missing data. Overall, the percentage of exclusion for the multivariable logistic regression resulting from missing data was considered acceptable (358 of 8040; 4.5%). Imputation to

handle missing data seemed less desirable because the study focused on practical implications of casemix adjustment in a national quality registration with weekly updated feedback and benchmark information. Techniques to handle missing data in this study were categorization of missing data in a separate subgroup and exclusion.[13] Participating hospitals should be stimulated to register data that are as complete as possible.

Future research should focus on developing informative outcome indicators that provide caregivers with information to implement changes and simultaneously have sufficient discriminative power for hospital comparisons. Minimization of registration burden with maximized reliability and data quality should be another focus. Finally, if comparisons on an international level are made, consensus should be reached on what casemix adjustment model can be used best.

In conclusion, the large between-hospital variation in population demographics and disease burden of patients undergoing surgical treatment for NSCLC emphasizes the importance of proper casemix adjustment when comparing hospitals on outcome indicators.

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APPENDICES

Supplemental Table 1. Variation between hospital populations in casemix. Hospitals: N = 37, patients: n = 6600.

	Between hospital comparison		
	Median	**IQR** [h]	**Min - Max**
Age	66	66 - 67	63 - 70
Age categories			
<60	21.8%	18.7% - 23.9%	14.0% - 34.2%
60-69	38.4%	35.3% - 40.7%	24.4% - 48.5%
70-79	34.5%	29.8% - 38.2%	24.5% - 46.0%
80+	5.7%	4.5% - 6.9%	0.5% - 16.7%
Gender			
Male	56.2%	53.4% - 59.9%	40.5% - 65.9%
ASA [a] score			
I-II	71.7%	65.4% - 77.1%	14.1% - 93.1%
III+	27.2%	19.3% - 34.1%	6.5% - 65.2%
ECOG score			
0-I	88.2%	56.2% - 93.4%	2.8% - 100.0%
II+	2.6%	1.8% - 6.2%	0.0% - 20.8%
Unknown	6.3%	1.5% - 41.9%	0.0% - 97.2%
Lung function			
FEV1 [b] and DLCO [c] ≥80% [d]	29.5%	27.2% - 35.1%	19.6% - 50.0%
FEV1 [b] or DLCO [c] <80%	64.6%	58.0% - 69.4%	40.9% - 77.5%
FEV1 [b] and DLCO [c] unknown	4.1%	2.4% - 6.0%	0.0% - 35.6%
Induction therapy			
No	95.4%	91.4% - 96.6%	68.8% - 100.0%
Chemoradiotherapy	2.5%	0.9% - 5.3%	0.0% - 24.8%
Different [e]	2.0%	1.1% - 3.4%	0.0% - 10.1%
Size of resection			
Pneumonectomy	7.7%	6.5% - 9.5%	3.0% - 21.6%
Bilobectomy	5.1%	3.8% - 6.9%	2.0% - 10.6%
Lobectomy	77.1%	74.8% - 81.5%	62.2% - 87.2%
Segmentresection	1.1%	0.0% - 2.5%	0.0% - 10.5%
Wedge resection	4.8%	2.7% - 7.8%	0.0% - 20.4%
No resection	0.9%	0.0% - 1.6%	0.0% - 5.0%

Supplemental Table 1. (continued)

	Between hospital comparison		
	Median	**IQR** [h]	**Min - Max**
Pathologic T-stage [f]			
≤pT2	80.4%	77.5% - 83.1%	65.7% - 89.7%
pT3-pT4	19.6%	15.6% - 22.3%	10.3% - 31.8%
Postoperative histology			
Adenocarcinoma	58.7%	55.2% - 63.6%	43.9% - 71.0%
Squamous cell	33.5%	30.5% - 38.0%	20.0% - 51.5%
Different [g]	6.4%	4.3% - 8.0%	1.4% - 11.7%

[a] American Society of Anaesthesiologists score

[b] Forced Expiratory Volume in 1 second, percentage of expected

[c] Diffuse Lung Capacity for Oxygen, percentage of expected

[d] FEV1 and DLCO ≥80% or one of the values missing

[e] Chemotherapy or radiotherapy alone

[f] TNM7 staging

[g] Adenosquamous or large-cell carcinoma

[h] Interquartile range

Supplemental Table 2. Abbreviations and acronyms.

ASA	=	American Society of Anaesthesiologists
CI	=	Confidence Interval
DICA	=	Dutch Institute for Clinical Auditing
DLCA-S	=	Dutch Lung Cancer Audit for Surgery
DLCO%	=	Diffusing Lung Capacity for Oxygen percentage of normal
ECOG PS	=	Eastern Cooperative Oncology Group Performance Score
FEV1%	=	Forced Expiratory Volume in 1 second percentage of normal
IQR	=	Inter Quartile Range
NSCLC	=	Non-Small Cell Lung Cancer
OR	=	Odds Ratio

PART II

VARIATION IN MULTIDISCIPLINARY CANCER TREATMENT

CHAPTER 5

Pneumonectomy for lung cancer treatment in the Netherlands: between-hospital variation and outcomes

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ABSTRACT

Background | Pneumonectomy in lung cancer treatment is associated with considerable morbidity and mortality. Its use is reserved only for patients in whom a complete oncological resection by (sleeve) lobectomy is not possible. It is unclear whether a patients' risk of receiving a pneumonectomy is equally distributed. This study examined between-hospital variation of pneumonectomy use for primary lung cancer in the Netherlands.

Methods | Data from the Dutch Lung Cancer Audit for Surgery from 2012-2016 was used to study the use of pneumonectomy for primary lung cancer in the Netherlands. Using multivariable logistic regression, factors associated with pneumonectomy use were identified and the expected number of pneumonectomies per hospital was determined. Subsequently the observed/expected-ratio (O/E-ratio) per hospital was calculated to study between-hospital differences.

Results | Of the 8,446 included patients, 659 (7.8%) underwent a pneumonectomy with a mean postoperative mortality of 7.1% (n = 47). Factors associated with receiving a pneumonectomy were age, gender, cardiac and pulmonary comorbidities, tumour side, size and histopathology. The pneumonectomy use in the Netherlands varied considerably between hospitals (IQR 5.5-10.1%). Three hospitals out of 51 performed significantly less pneumonectomies than expected (O/E-ratio<0.5) and three significantly more (O/E-ratio>1.7). In the latter group severe complications were more frequent, taking other influencing factors into account (OR 1.51, 95%-CI 1.05-2.19).

Conclusions | There is a considerable between-hospital variation in pneumonectomy use in lung cancer treatment. To further optimise surgical lung cancer care we suggest centre specific feedback on pneumonectomy use and the development of a risk-adjusted pneumonectomy indicator.

INTRODUCTION

Anatomical parenchymal resection is the cornerstone in curative treatment for primary lung cancer. In certain cases a complete oncologic resection cannot be obtained by a (sleeve) lobectomy and a pneumonectomy is considered the resection of choice. However, pneumonectomy is associated with considerable postoperative morbidity and mortality compared to less extensive resections and is an individual predictor of these negative outcomes.[1–5] Reduction in adverse outcomes of lung surgery may therefore be achieved by decreasing the number of pneumonectomies.

Several nationwide registries reported on the national pneumonectomy use.[6–12] Although the optimal target proportion of pneumonectomies is unclear and partly depends on casemix, differences in the threshold at which a pneumonectomy is performed may identify improvement potential. As suggested by Jakobsen et al. the proportion of pneumonectomies could eventually function as a quality indicator in surgical lung cancer care.[6]

To apply such a quality indicator, between-hospital variation in pneumonectomy use and possibilities for proper casemix adjustment first need to be studied. Therefore, the aim of this study was to investigate between-hospital variation in the use and outcomes of pneumonectomies for primary lung cancer in the Netherlands and to identify factors associated with pneumonectomy use

METHODS

Data source and study population

Data was derived from the Dutch Lung Cancer Audit for Surgery (DLCA-S).[13] The DLCA-S is a nationwide mandatory registry including all patients undergoing

surgery for lung cancer and is part of the multidisciplinary Dutch Lung Cancer Audit (DLCA), in which all major treatment disciplines evaluate care.[13]

In the DLCA-S, data are collected on hospital level. Distinction on individual surgeon level is not possible. In cases of a surgeon operating in different hospitals, the procedure is attributed to the hospital where it was performed. Collected data includes information on patient- and tumour characteristics, diagnostic work-up (e.g. discussion in a multidisciplinary meeting), surgical procedure, postoperative outcomes and pathology.[14] Independent on-site data verification processes are used to ensure data quality.[15] From 2015 on there is a 100% coverage of NSCLC resection registration.[14]

For this study, no ethical approval or informed consent was required under Dutch law.

Patients with a primary lung cancer resection between January 2012 and December 2016 were included. Minimum data registry criteria to be eligible for analyses included: age, gender, operation-date, type of surgery, tumour side, postoperative histology and vital status 30 days after surgery and/or at time of discharge.

Wedge excisions were excluded for the analysis of anatomical resections, since these are considered oncologically insufficient. Primary lung cancer comprised a postoperative histology of: adenocarcinoma, squamous cell carcinoma, carcinoid, large cell carcinoma, small cell carcinoma and non-small cell carcinoma not otherwise specified.

Population characteristics and main outcomes

Analysed patient characteristics were: age at time of surgery, gender, lung function, ECOG performance status and ASA-classification. Preoperative lung function was analysed as a composite measure of FEV1% (forced expiratory volume in 1 second percentage of normal) and DLCO% (diffusing lung capacity for oxygen percentage of normal), in three categories: FEV1% and DLCO% ≥ 80% or one of the values

not-registered (1), FEV1% or DLCO% < 80% (2) and both FEV1% and DLCO% not-registered (3). These cut-off values are in accordance with the evidence-based Dutch guideline.[16,17]

Disease characteristics and pre-surgical treatment characteristics were: tumour side, induction therapy (none/unknown, chemotherapy, radiotherapy and chemoradiotherapy), tumour stage (according to the 7th edition of the TNM staging system) and postoperative histology.

The outcomes assessed were postoperative mortality and postoperative complicated course. Postoperative mortality was defined as mortality within 30 days after surgery or during the primary hospital admission. Postoperative complicated course was defined as any complication leading to prolonged hospital stay (≥14 days), unplanned re-intervention or mortality, and was used to reflect only severe complications.

Between-hospital variation in applying pneumonectomy

Between-hospital variation in applying pneumonectomy was studied by comparing the observed with the expected number of pneumonectomies per hospital. With a multivariable logistic regression model, after controlling for collinearity, patient and tumour characteristics associated with the risk of undergoing pneumonectomy were identified. Discriminative ability of the model was assessed by area under the ROC-curve (AUC).

Subsequently, by using the coefficients of this multivariable model the expected 'pneumonectomy risk' per patient was calculated, which in turn was used to calculate the expected number of pneumonectomies on hospital level. Then, by dividing the number of observed by the number of expected pneumonectomies per hospital, the observed/expected-ratio (O/E-ratio) was calculated per hospital. An O/E-ratio >1 indicates that the hospital performed more pneumonectomies than expected based on the hospital population, whereas an O/E-ratio <1 indicates a

lower pneumonectomy use than expected. Between-hospital variation in O/E-ratio was displayed using a funnel-plot, with 95% confidence intervals (95%-CI)[18].
Hospital characteristics (e.g. case volume or type of hospital) were not included in the model since the chance of undergoing a pneumonectomy or a different resection type should not depend on that. If these factors would be included in the model, the effect can be distorted or even nullified.[19]

Pneumonectomy/sleeve-resection-ratio

From 2015 on, the DLCA-S contains information on sleeve-resections. Hypothesizing that sleeve-lobectomies and pneumonectomies are performed in similar patient populations, a ratio between these two operation types could demonstrate differences in preference of indication per hospital.

Statistical significance was set at a threshold of 0.05, with P values calculated by two-sided tests. Statistical analyses were performed using SPSS (IBM SPSS Statistics for Macintosh, Version 23.0).

RESULTS

Population characteristics

A total of 8446 patients underwent a primary lung cancer resection and were eligible for analyses. Of these, 659 (7.8%) underwent pneumonectomy, 7226 (85.6%) (bi) lobectomy or anatomical segment-resection and 561 (6.6%) wedge-excision.
After excluding the wedge-excisions, 7885 patients with an anatomical resection remained, of which 8.4% (659) underwent pneumonectomy. These 7885 patients were divided over 51 hospitals, with a mean number of patients per hospital of 155, SD 97, range: 8-377.

Of patients with an anatomical resection, mean age was 66 years, 55.7% was male (n = 4395), 76.6% had an ECOG performance score 0-1 (n = 6040), 70.9% had an ASA score I-II (n = 5587), 6.3% received induction therapy (n = 498), 43.1% had a left-sided tumour (n = 3399), 81.5% had a pathological stage ≤II (n = 6421) and 55.2% had an adenocarcinoma (n = 4352).

Table 1 displays the characteristics of all patients undergoing pneumonectomy. Compared to the total anatomical resection group, pneumonectomies were performed in slightly younger patients, more often of male sex, in more advanced disease stages, left-sided tumours and squamous cell carcinomas.

Of all anatomical resections 5.3% (n = 417) was performed in hospitals with less than 20 resections a year (low volume considering the minimum annual volume standards set by the Association of Surgeons in the Netherlands), 56.0% (n = 4416) in hospitals with 20 to 49 resections a year, and 38.7% (n = 3052) in hospitals with 50 or more resections a year. The percentage of pneumonectomies in these three hospital volume categories were respectively 8.9%, 7.9% and 8.9%.

Factors associated with pneumonectomy

Age, gender, cardiac and pulmonary comorbidities, tumour side, clinical tumour stage (cT) and histopathology are individual factors significantly associated with receiving a pneumonectomy (**Table 2**). The discriminative ability of a multivariable model with these factors was fairly-good (AUC); 0.80, 95%-CI 0.78-0.82.

Supplemental Figure 1 visually demonstrates the association between cT and histopathology and the pneumonectomy-proportion.

Between-hospital variation

The use of pneumonectomy as an anatomical resection for primary lung cancer per hospital ranged from 0.0 to 25.3% (national mean 8.4%). Fifty per cent of hospitals (Inter Quartile Range – IQR) performed a pneumonectomy in 5.5-10.1% of their patients.

Table 1. Population characteristics and postoperative outcomes of patients with primary lung cancer undergoing an anatomical parenchymal resection, stratified for resection type.

	Pneumonectomy		(Bi)lobectomy and segmentectomy		
	N	**%**	**N**	**%**	**P value**
Of total anatomical parenchymal resections	659	8.4%	7226	91.6%	-
Gender					<0.001
Male	452	68.6%	3943	54.6%	
Female	207	31.4%	3283	45.4%	
Age mean [median] (±SD)	65 [66] (±8.8)		66 [67] ± 9.4		
Age (years)					<0.001
<60	143	21.7%	1681	23.3%	
60-64	144	21.9%	1256	17.4%	
65-69	143	21.7%	1491	20.6%	
70-74	145	22.0%	1433	19.8%	
75+	84	12.7%	1365	18.9%	
Lung function					
FEV1% and DLCO% ≥80%	173	26.3%	2358	32.6%	0.004
FEV1% or DLCO% <80%	443	67.2%	4439	61.4%	
Unknown	43	6.5%	429	5.9%	
Performance score[a]					0.063
< 2	489	74.2%	5551	76.8%	
≥ 2	35	5.3%	260	3.6%	
Unknown	135	20.5%	1415	19.6%	
ASA score					0.323
I-II	451	68.4%	5136	71.1%	
III+	186	28.2%	1847	25.6%	
Unknown	22	3.3%	243	3.4%	
Side					0.001
Left	408	61.9%	2991	41.4%	
Right	251	38.1%	4235	58.6%	
Induction therapy					<0.001
No	589	89.4%	6798	94.1%	
Chemoradiotherapy	31	4.7%	265	3.7%	
Chemotherapy	1	0.2%	137	1.9%	
Radiotherapy	38	5.8%	26	0.4%	

Table 1. (continued)

	Pneumonectomy		(Bi)lobectomy and segmentectomy		
	N	**%**	**N**	**%**	**P value**
Pathological stage					<0.001
Stage I and occult	107	16.2%	4155	57.5%	
Stage II	266	40.4%	1893	26.2%	
Stage III+	255	38.7%	939	13.0%	
Unknown	31	4.7%	239	3.3%	
Pathological T-stage					<0.001
T1 (To, Tis, Tx)	89	13.5%	3087	42.7%	
T2	274	41.6%	2915	40.3%	
T3	214	32.5%	1048	14.5%	
T4	80	12.1%	152	2.1%	
Unknown	2	0.3%	24	0.3%	
Postoperative histology					<0.001
Adenocarcinoma	189	28.7%	4163	57.6%	
Squamous cell	410	62.2%	2194	30.4%	
Different[b]	60	9.1%	869	12.0%	
Postoperative mortality[c]	47	7.1%	123	1.7%	

[a] Performance score using ECOG / WHO

[b] Different: SCLC, carcinoid, adenosquamous, large cell (NET) and not otherwise specified

[c] Defined as postoperative 30-day or in-hospital mortality

Table 2. Factors associated with receiving a pneumonectomy. Number of patients included: N = 7885.

	Resection using pneumonectomy					
	Unadjusted*			Adjusted**		
	OR^	95% CI^		OR^	95% CI^	
Age						
<60	ref			ref		
60-64	**1.35**	**1.06**	**1.72**	1.16	0.89	1.50
65-69	1.13	0.89	1.44	0.88	0.67	1.14
70-74	1.19	0.93	1.51	0.81	0.62	1.06
75+	**0.72**	**0.55**	**0.96**	**0.47**	**0.34**	**0.64**
Gender						
Male	ref			ref		
Female	**0.55**	**0.46**	**0.65**	**0.72**	**0.60**	**0.87**
Cardiac comorbidity						
No	ref			ref		
Yes	**0.74**	**0.61**	**0.90**	**0.75**	**0.60**	**0.92**
Pulmonary comorbidity						
No	ref			ref		
Yes	0.75	0.63	0.89	0.69	0.57	0.83
Lung function						
FEV1 [a] or DLCO [b] ≥80%	ref			NA		
FEV1 and DLCO <80%	1.36	1.13	1.63	NA		
FEV1 and DLCO unknown	1.37	0.96	1.94	NA		
Side of tumour						
Left	ref			ref		
Right	**0.44**	**0.37**	**0.51**	**0.43**	**0.36**	**0.52**
Clinical T-stage [c]						
≤ T1	ref			ref		
T2	**3.54**	**2.76**	**4.54**	**2.86**	**2.21**	**3.69**
T3	**8.23**	**6.36**	**10.64**	**6.75**	**5.18**	**8.80**
T4	**15.51**	**10.94**	**21.98**	**14.74**	**10.20**	**21.30**
Unknown	**4.08**	**2.75**	**6.04**	**3.78**	**2.52**	**5.65**

Table 2. (continued)

	Resection using pneumonectomy			
	Unadjusted*		Adjusted**	
	OR^	95% CI^	OR^	95% CI^
Postoperative histology				
Adenocarcinoma	ref		ref	
Squamous cell carcinoma	**4.12**	**3.44 - 4.93**	**3.58**	**2.94 - 4.35**
Different [d]	**1.52**	**1.13 - 2.06**	**1.49**	**1.09 - 2.03**

[a] Forced Expiratory Volume in 1 second, percentage of expected

[b] Diffuse Lung Capacity for Oxygen, percentage of expected

[c] According to TNM 7 staging

[d] Adenosquameus or large cell carcinoma

* Univariable

** Multivariable

^ OR = odds ratio, CI = confidence interval. A confidence interval excluding 1.00 indicates statistical significance

Between-hospital variation remained after adjustment for relevant factors (**Figure 1**). Out of 51 hospitals, three performed significantly more pneumonectomies than expected (O/E-ratio>1.7) Three performed significantly less pneumonectomies than expected, with an O/E-ratio<0.5 the percentage of pneumonectomies performed is >50% less than expected. All six hospitals were middle sized non-academic centres. After adjustment for relevant factors,[5] there were no significant differences in postoperative mortality and complicated course after a pneumonectomy performed in the three hospitals with more pneumonectomies (71 patients included) compared to the three hospitals with less pneumonectomies (19 patients included) than expected (mortality: OR 0.28, 95%-CI 0.05-1.45, complicated course: OR 1.42, 95%-CI 0.40-5.05).

When considering all anatomical resections, there were significantly more patients with a postoperative complicated course in the three hospitals with more pneumonectomies (430 patients included) compared to the three hospitals with less pneumonectomies (557 patients included) than expected (OR 1.51, 95%-CI 1.05-

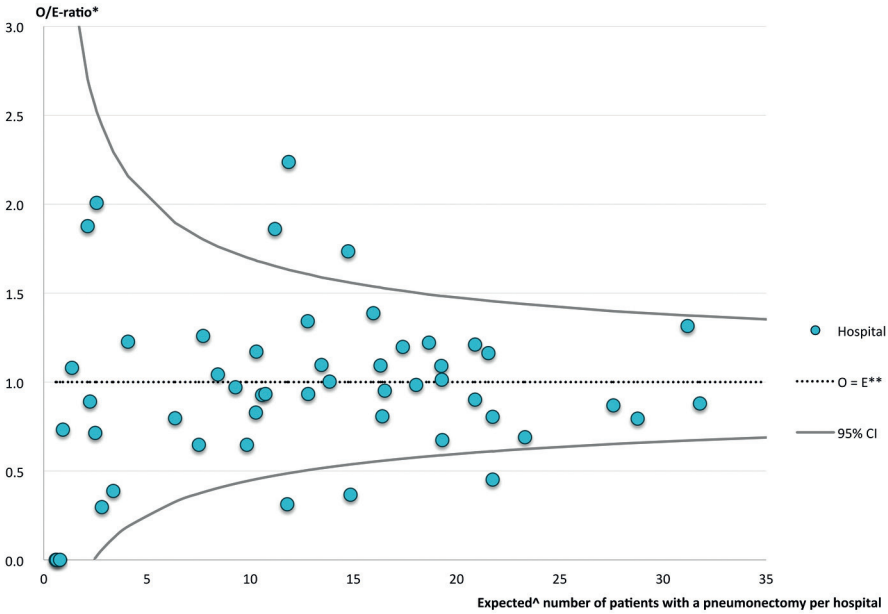

Figure 1. Funnel-plot of between-hospital variation in the use of pneumonectomy (2012-2016).
* O/E-ratio: observed number of pneumonectomies divided by expected^ number of pneumonectomies.
** O = E: the observed number equals the expected^ number of pneumonectomies.
^ Expected number of pneumonectomies per hospital based on hospital population characteristics (age, gender, cardiac and pulmonary comorbidity, side of malignancy, clinical T-stage, histopathology).
Number of hospitals included N = 51, number of patients included n = 7885.

2.19), after adjustment for relevant factors. There was no significant difference in postoperative mortality between these groups (OR 0.66, 95%-CI 0.28-1.54).

From 2015 on, the DLCA-S contains information on sleeve-resections. Subgroup analysis of resections between 2015-2016 showed wide variation in the pneumonectomy/sleeve-resection-ratio per hospital (**Figure 2**). Eight hospitals performed no sleeve-resection and up to 10.9% pneumonectomies. Two hospitals performed up to 7.7% sleeve-resections and no pneumonectomies.

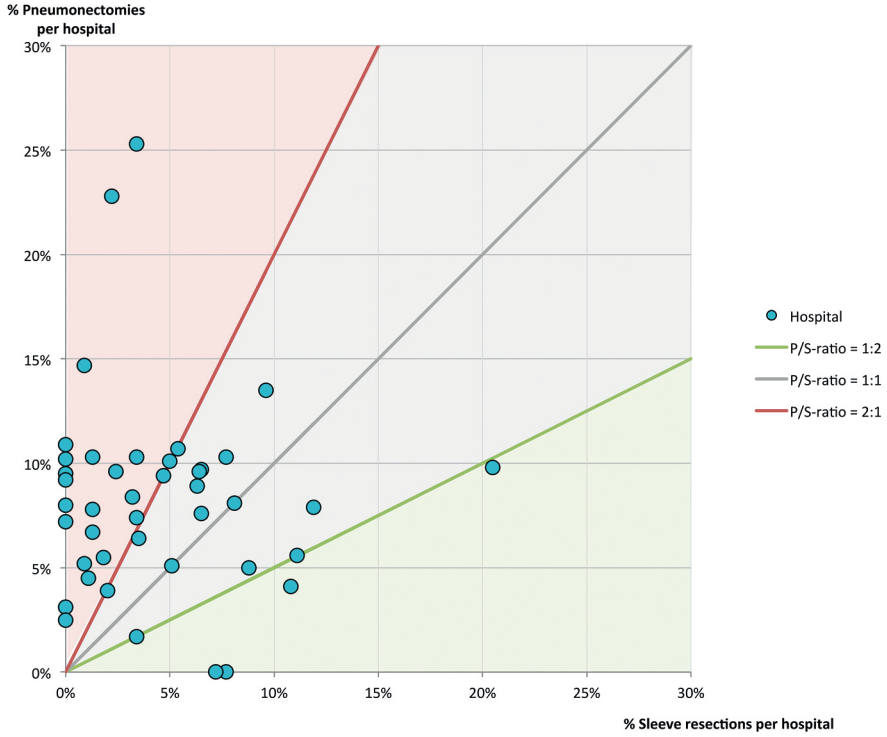

Figure 2. Scatter of P/S-ratio* per hospital (2015-2016).
* P/S-ratio = number of pneumonectomies devided by number of sleeve resections per hospital. Number of hospitals included N = 42, number of patients included n = 3790.

COMMENT

This study is the first to report on both the national practice of pneumonectomy use and between-hospital variation by using Dutch nationwide registry data with centre-specific information. Considerable between-hospital variation exists in the use of pneumonectomy for primary lung cancer in the Netherlands, even after adjustment for patient- and disease characteristics.

National variation

In the current study, age, gender, cardiac and pulmonary comorbidities, tumour side, cT and histopathology were individual factors significantly associated with receiving a pneumonectomy. This is in line with previous studies, although the current study was the first to perform multivariable analyses.[20,21]

Between-hospital variation in pneumonectomy use in the Netherlands ranged from 0.0-25.3% (IQR: 5.5-10.1%). After adjustment for relevant factors, out of 51 hospitals, three hospitals performed significantly more and three significantly less pneumonectomies than expected based on predetermined patient-/disease characteristics.

The proportion of severe postoperative complications was higher in the hospitals with significantly more pneumonectomies. There were no significant differences in postoperative mortality between the hospitals performing significantly more or significantly less pneumonectomies. However, pneumonectomy-related mortality and morbidity often expresses beyond the 30-day follow-up period,[1,8,10] thus the outcomes reported in this study could be an underestimation.

The existence of between-hospital variation suggests that for individual patients the risk to receive a pneumonectomy, and its related morbidity, could depend on the hospital of choice. Pneumonectomies may be performed on lower thresholds in some hospitals whereas others might perform sleeve-lobectomies or no resection at all. Off course one cannot simply assume that every sleeve-resection is an averted pneumonectomy, however the varying pneumonectomy/sleeve-resection-ratio does indicate that considerations per hospital vary. The proportion of pneumonectomies per hospital might also be influenced by the availability of alternative treatment strategies (e.g. chemo(radiotherapy) instead of surgery in T_3/T_4-tumours) or the preference of local multidisciplinary teams. Whether referral

patterns or patient preferences influence the between-hospital differences could not be studied, since this data was not available from the DLCA-S. However, the fact that all six 'outlying' hospitals are medium-sized non-academic centres lowers the presumption of referral bias. In addition, potential bias was reduced by the casemix adjustment.

Unlike previous literature and the intuitive expectation that centres with a high pneumonectomy proportion would have better post-operative outcomes after a pneumonectomy, in this study no significant differences were observed in postoperative mortality and complicated course after a pneumonectomy performed in hospitals with a high versus low pneumonectomy proportion. This could suggest that high pneumonectomy proportions are rather an expression of varying treatment considerations per hospital than the result of referral to expertise centres. It can also be hypothesised that higher pneumonectomy percentages could be the result of more unplanned pneumonectomies due to intra-operative complications or a pre-operatively underestimated tumour stage.

Centralisation of care

In the past years the number of hospitals providing surgical lung cancer care declined from 79 in 2005 to 43 hospitals in 2015, signifying a 45% reduction.[14,22] In the current study there were 42 hospitals performing sleeve resections or pneumonectomies in 2015-2016. In this period there were 30 hospitals performing between 1 and 10 sleeve resections and 28 hospitals performing between 1 and 10 pneumonectomies. Although a considerable centralisation has been achieved, a further centralisation might be necessary for the technically difficult or high-risk procedures as sleeve resections or pneumonectomies, since it is know that volume could influence surgical outcomes.[23]

International comparison

The pneumonectomy proportion in the Netherlands (7.8%) is lower than most European countries (7.4-19.6%), but higher than the United States (4.8%) (**Supplemental Table 1**).[6–12] A pneumonectomy proportion as high as 34.6% was reported by a regional cohort study from the Netherlands (1984-1992).[24] More historical English and Danish registry data show significant decrease in pneumonectomy proportion over time.[6,7] The study by Jakobsen et al. reports a national decrease from 23% to 11% (2000-2007).[6] Postoperative mortality after pneumonectomy in the Netherlands (7.1%) is similar to other European countries (5.9-8.0%), but slightly higher than the United States (4.9%).

Making these international comparisons, one should keep in mind that studied populations differ. The Society of Thoracic Surgeons - General Thoracic Surgery Database (GTSD) and the European Society of Thoracic Surgeons GTSD data not only included resections for primary lung cancer (87.0-94.5%), but also for metastasis (1.9-4.5%) and benign diseases (3.6-3.8%).[20] Besides, the Dutch population is older, less frequently treated with induction therapy and tumour (pT) stage is less frequently missing, though comparable to European and American populations.[9,20]

Although there are previous studies reporting on the national pneumonectomy proportion and regional variation, this study is the first to report between-hospital variation. What also distinguishes the current study from previous ones is the way data is collected and used, influencing data quality, completeness and analytic possibilities. Data for this study was collected using a national prospective audit system.[13,25] The audit itself is designed and maintained by clinicians, therefor including clinically most relevant information. Clinicians receive weekly updated feedback information, thereby enhancing data quality. Participation in the audit is incorporated in the professional quality system and registered data are regularly checked by external data verification, thereby stimulating unbiased

information. This is in contrast with registries with a more voluntary nature or a pure retrospectively registration.

Study limitations

A limitation of the DLCA-S is that it does not provide information on non-operated patients, thus resection rates cannot be calculated, nor could the indication for (not) operating be studied. In accordance with English and Danish registry data,[6,7] another study showed an increasing lung cancer resection rate in the Netherlands.[26] This, together with stable pneumonectomy rates and population characteristics during the existence of the DLCA-S, suggests that the relatively low pneumonectomy proportion in the Netherlands is not due to risk-averse behaviour. The DLCA-S data 2012-2016 did not provide information whether a tumour is centrally located or extends beyond fissures. This is registered from 2017 onwards. Proxy information used in this study are tumour (T-) stage and histopathology, since squamous cell carcinoma is more often centrally located.[27] Also, the DLCA-S does not provide information on the percentage of aborted procedures stratified by the extent of surgery. A probably underestimated percentage of 1.2% of all patients undergoing surgery for NSCLC in the DLCA-S with no resection in the end is reported previously.[5] Due to differences in definitions (e.g. mortality) and applied in- and exclusion criteria, it is challenging to generate true international comparisons. Consensus on key data items therefore should be a shared objective.

Future perspectives

Awareness among caregivers on pneumonectomy use in practice can increase by providing benchmarked information regarding the pneumonectomy proportion per hospital in indicator format.

National data can be used to evaluate current clinical practice and trigger improvement initiatives. In colorectal cancer surgery for example, data from the

clinical audit led to a modification of the national guideline adjustment and leading to remarkable changes in clinical practice.[28]

In addition, indicator results and between-hospital variation can be used to support a more solid quality of care discussion. Adjustment for patient-/disease characteristics can place this information in context.

The DLCA-S scientific committee will work towards providing caregivers with this information. Since a pneumonectomy remains necessary to obtain complete oncologic resection in certain cases a percentage of 0.0 pneumonectomies is not aspired. What the ideal 'target' pneumonectomy proportion would be is not yet clear. This will be subject of debate for the DLCA-S scientific committee and affiliated professional associations. Another point of discussion will be whether further concentration of high-risk procedures into expertise centres (with expertise in sleeve-resections, high-volume and optimal post-operative care) may be beneficial. Organizing this optimal care, equally accessible to all patients, is a combined responsibility of healthcare government and caregivers.

Conclusions

This study demonstrates that there is a considerable nationwide between-hospital variation in pneumonectomy use in surgical lung cancer treatment, even after adjustment for patient- and disease characteristics. Variation could be the result of varying treatment considerations or unplanned pneumonectomies. Nationwide registries and the development of specifically focused pneumonectomy indicators could be improvement-tools to further optimise surgical lung cancer care.

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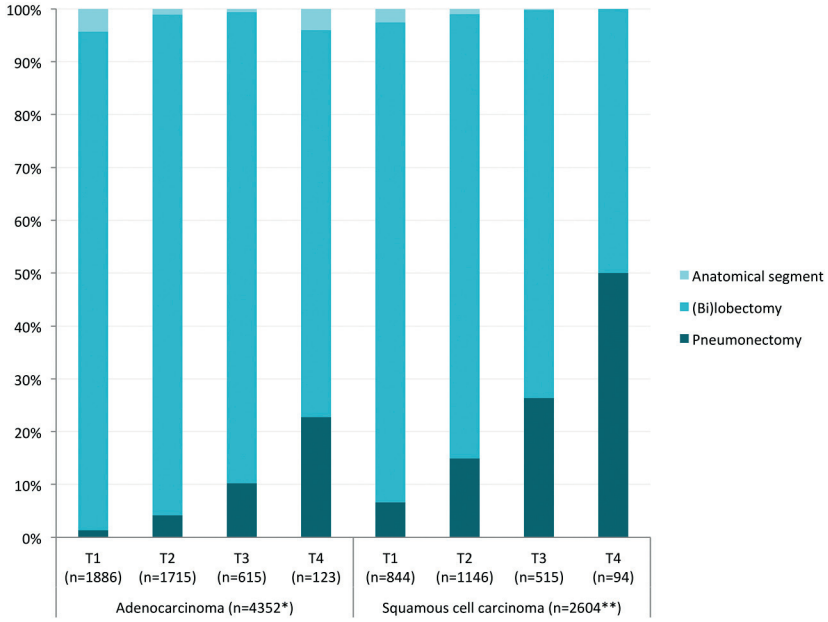

Supplemental figure 1. Type of parenchymal resection according to pathological tumour stage (TNM7) stratified for adenocarcinoma and squamous cell carcinoma.
*T-stage unknown n = 13, **T-stage unknown n = 5.

Supplemental table 1. Percentage of patients undergoing a pneumonectomy for primary lung cancer and postoperative mortality compared to other (inter)national studies.

Country / region (database)	Study period	% pneumonectomies of parenchymal resections	% pneumonectomies of all resections	Mortality pneumonectomies	Mortality all resections	Reference
Netherlands, Region (Rotterdam Cancer Registry)	1984-1992	NA	34.6% (530/1577)	5.7%* (given)	3.1% (49/1577)	Damhuis et al.[24]
England (National Cancer Data Repository)	1998-2008	NA	15.7% (4201/26799)	NA	NA	Riaz et al.[7]
Denmark (Danish Lung Cancer Registry)	2000-2007	NA	19.6% (868/4428)	8.0%* (given)	NA	Jakobsen et al.[6]
England (National Lung Cancer Audit)	2004-2010	NA	10.9% (1121/10274)	7.0%* (78/1121)	3.0% (334/10991)	Powell et al.[8]
France (Epithor)	2003-2013	NA	12.3% (4820/39030)	7.8%^ (351/4498)	NA	Thomas et al.[9]
Denmark (Danish Lung Cancer Registry)	2007-2011	NA	7.4% (250/3359)	7.2%* (18/250)	2.1% (72/3359)	Green et al.[10]
France (Epithor)	2005-2012	14.7% (4478/30527)	13.2% (4478 / 34006)	NA	3.0% (1037/34006)	Morgant et al.[11]
France (Epithor)	2005-2014	NA	NA	5.9%^ (313/5318)	NA	Pagès et al.[21]
Europe (ESTS database)	2010-2013	10.9% (2151/19699)	10.0% (2151/21509)	7.3% ∫ (given)	2.3% ∫ (700/30830)	Seder et al.[20]
United States (STS database)	2010-2013	4.8% (1164/24072)	4.0% (1164/29120)	4.9% ∫ (given)	1.7% ∫ (799/47539)	Seder et al.[20]
Netherlands (DLCA-S)	2012-2016	8.4% (659/7885)	7.8% (659/8446)	7.1%^ (47/659)	2.1% (177/8446)	Current study

* 30-day mortality

^ 30-day and/or in hospital mortality

∫ 30-day mortality, calculated including pathologies other than primary lung cancer

CHAPTER 6

Factors contributing to variation in the use of multimodality treatment in patients with gastric cancer: a Dutch population based study

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** Can be found under the heading 'Collaborators'

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ABSTRACT

Background | Substantial variation in the use of (neo)adjuvant treatment in patients with gastric cancer exists. The aim of this study was to identify underlying (organisational and process) factors associated with the use of perioperative therapy.

Patients and methods | Patients with resectable gastric cancer who underwent surgery between 2012-2014 were selected from the Dutch Upper gastrointestinal Cancer Audit (DUCA). The proportion of perioperatively treated patients was defined per hospital. Five hospitals with the lowest percentage (LP group) and 5 hospitals with the highest percentage (HP group) of perioperative therapy were identified. In the selected hospitals additional information was obtained from patients' medical records using a structured list with predefined variables.

Results | In total, 429 patients (231 in LP group, 198 in HP group) from 9 different hospitals were included. Perioperative therapy was given in 16.0% of patients in the LP group compared to 40.4% in the HP group. In the LP group, patients were enrolled in a clinical trial less frequently (10.8% versus 26.8%, P<0.001), and a higher percentage grade III-IV toxicity was observed during neoadjuvant treatment (25.7% versus 46.3%, P = 0.007). Multivariable analysis showed that, besides known casemix factors, consultation with ≥3 upper GI specialists prior to treatment decision was positively associated with initiating perioperative therapy (OR 2.08, 95% CI 1.19 - 3.66).

Conclusion | Results of this study confirm considerable hospital variation in the use of perioperative therapy in patients with gastric cancer. Besides known casemix factors, use of perioperative therapy was associated with the level of involvement of multidisciplinary care.

INTRODUCTION

Surgery is the cornerstone in the curative treatment of resectable gastric cancer. Despite improvements in postoperative mortality, prognosis remains poor with 5-year overall survival rates of 33-50 % for patients with stage I-III gastric cancer that underwent a resection.[1,2]

Multimodality treatment improves disease-free and overall survival.[3–5] However, an international consensus on the best approach has not been reached. Perioperative chemotherapy is favoured in Northern Europe, adjuvant chemoradiotherapy or perioperative chemotherapy in North America and adjuvant chemotherapy in Japan.[6–8] In the Netherlands, the use of perioperative chemotherapy (according to the MAGIC study) is recommended for all patients with non-metastasised resectable gastric cancer (excluding stage I) as of 2009, provided that the patient is in good condition in terms of fitness and comorbidity.[9]

In 2011, the Dutch Upper Gastrointestinal Cancer Audit (DUCA) group initiated a nationwide surgical audit, including all patients that underwent surgery with the intent of a resection for oesophageal or gastric cancer in the Netherlands. This registry is used for quality assessment and it facilitates potential improvements by providing stakeholders with casemix corrected and benchmarked information on the process and short term outcomes of care.[1] Results of a previous study using DUCA data showed that 50-55 per cent of the patients with resectable gastric cancer received neoadjuvant chemotherapy.[1] Adjuvant chemotherapy was given to 26-32 per cent of all patients, who underwent a resection with curative intent. In a subsequent study, considerable hospital variation in the use of neoadjuvant and adjuvant treatment was observed, even after casemix correction.[10] This suggests that other factors than the generally known casemix factors play a role in the decision to prescribe perioperative treatment.

The aim of this retrospective cross-sectional study was to identify organisational and process factors associated with the use of multimodality treatment in patients with gastric cancer in the Netherlands.

METHODS

For this study, multiple data sources were combined, as explained below.

Patient selection and definitions

All patients with gastric cancer, who underwent surgery with the intention of a curative resection between 2012-2014, were identified from the DUCA database. Patients with non-epithelial tumours and patients undergoing non-surgical treatment (such as definitive chemoradiotherapy) are not included in this registry. Verification of data registered in 2013 showed that data entry was complete and reliable.[1]

Patients with stage I or IV disease (clinical tumour staging) were excluded for this study, as they are not candidates for perioperative chemotherapy according to Dutch guidelines. Minimal data requirements to consider a patient eligible for analyses were information on date of birth, date of surgery, tumour location, intent of surgery (potentially curative, palliative or no resection) and the patient's vital status 30 days after surgery and / or at time of discharge. For all selected patients, data on patient and tumour characteristics, treatment, morbidity and mortality were retrieved from the DUCA. Patients were classified according to the hospital of surgery, since hospital of diagnosis or the hospital administering perioperative treatment is not registered. Clinical tumour stage was defined according to the seventh edition of the International Union Against Cancer tumour node metastasis (TNM) classification.[11] No ethical approval or informed consent was required for this study under Dutch law.

Hospital selection

Between January 1st 2012 and December 31st 2014, 45 hospitals performing gastric cancer surgery participated in the DUCA. All hospitals that were no longer performing gastric cancer resections at the end of the study period were excluded (N = 18). To minimise statistical artefacts as a result of small sample size (based on surgical volume), hospitals registering < 25 patients were excluded (N = 5). Among the remaining hospitals (N = 22) the proportion of patients treated with perioperative therapy per hospital was analysed (**Figure 1 and 2**). Subsequently, 5 hospitals with lowest percentages of perioperative therapy (LP group) and 5 hospitals with highest percentages of perioperative therapy (HP group) were approached for in-depth investigation of patient's medical records based on feasibility. By comparing two groups at opposite ends of the spectrum, potential explanatory factors were analysed and differences were more likely to be found. Nine hospitals participated, as one hospital was not able to facilitate in-depth investigation within the study period (**Figure 1 and 2**). Medical records of all included patients in the selected hospitals were studied using a structured variable list with predefined variables. This data was combined with data from DUCA and served as an extended dataset.

Perioperative therapy

Between 2007-2015, the CRITICS study was on-going in the Netherlands, investigating the role of postoperative chemoradiotherapy versus chemotherapy in patients with gastric cancer who received neoadjuvant chemotherapy.[12] Therefore, both perioperative chemotherapy (as recommended in Dutch treatment guidelines)[3] and neoadjuvant chemotherapy combined with adjuvant chemoradiotherapy (as part of the CRITICS study)[12] were considered as perioperative therapy. Additionally, at least one cycle before the operation and one cycle after the operation had to be completed.

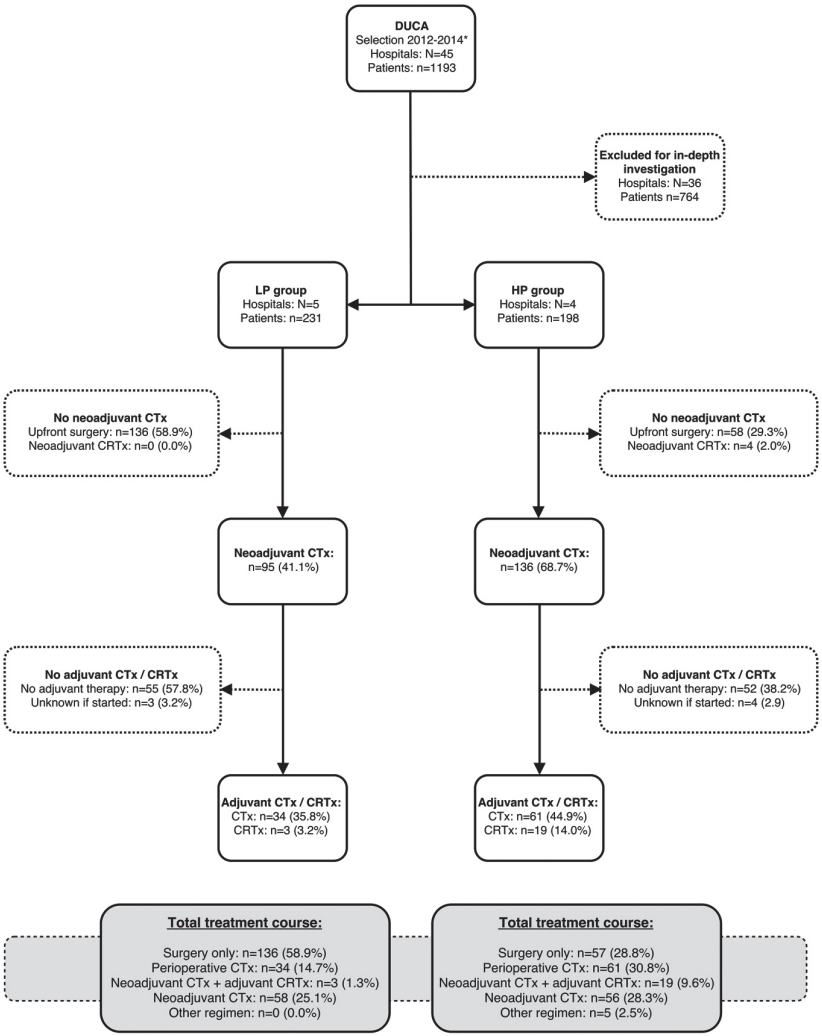

Figure 1. Flowchart describing different steps of multimodal treatment of patients in both LP and HP group. DUCA = Dutch Upper Gastrointestinal (GI) cancer Audit. CTx = chemotherapy, CRTx = chemoradiotherapy. LP group = group of hospitals with low percentage of perioperative therapy. HP group = group of hospitals with high percentage op perioperative therapy.

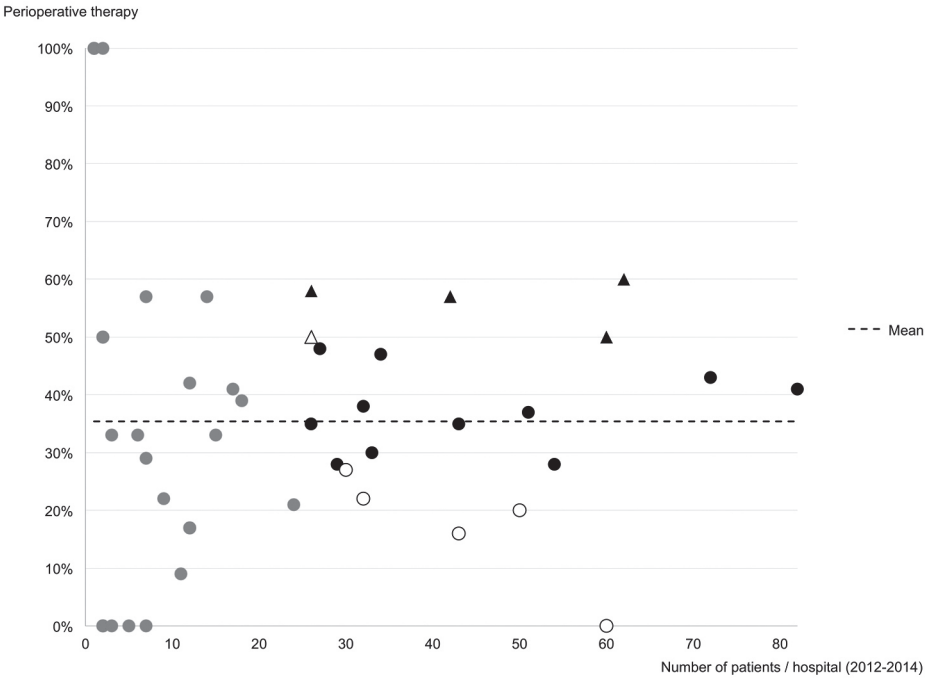

Figure 2. Plot displaying selection of hospitals for in-depth investigation.
● = Hospitals stopped performing gastric cancer surgery in 2014 or with < 25 patients registered; ○ = Hospitals selected in the low percentage of perioperative therapy (LP) group; ▲ = Hospitals selected in the high percentage of perioperative therapy (HP) group; △ = Non participating hospital in the HP group; ● = Other hospitals.

Structured variable list

Based on literature[13–16] and expert opinion, a list of potential variables associated with the use of perioperative therapy was created. An expert panel formed by health care professionals in the field of medical oncology (AC), surgery (JvS, MvBH, BW), and radiation oncology (FV), reviewed the list. The list was evaluated during a consensus meeting with the scientific committee of DUCA and finalised after a pilot study in one of the selected hospitals. Studied variables used for the final list were grouped into different subgroups including factors prior to treatment decision,

study participation, neoadjuvant course, surgical procedure and postoperative course, and adjuvant course based on timing in treatment.

Statistical analysis

Differences in patient, tumour and treatment characteristics were analysed using chi square tests (categorical variables) and T-tests (continuous variables). A multivariable logistic regression model for the intention of perioperative treatment (yes/no) was employed to study the association between outcome, patient characteristics (sex, age, American Society of Anaesthesiologists (ASA) score and amount of weight loss), tumour (tumour stage and nodal stage)[11] and treatment characteristics prior to treatment decision (referral from another hospital for surgery and the number of specialist consulted in the hospital of surgery). When using covariates with >2 categories, the first category was chosen as reference category (age, clinical tumour and nodal stage, amount of weight loss, number of consulted specialists). Missing items were included in the analysis as a separate category if > 5.0%. Statistical significance was set at a threshold of 0.05. Statistical analyses were performed using SPSS (IBM SPSS Statistics for Macintosh, Version 22.0).

RESULTS

Patients, treatment and hospitals

A total of 429 patients from 9 hospitals were included: 231 patients in the LP group and 198 patients in the HP group. The LP group consisted of 1 university hospital and 4 teaching hospitals. The HP group consisted of 2 university hospitals, 1 teaching- and 1 non-teaching hospital.

Overall hospital volumes ranged from 30-60 resections in the LP group (median 43) and from 26-62 (median 51) resections in the HP group. Perioperative therapy was administered to 37 of 231 patients (16.0%) in the LP group, and to 80 of 198 patients

(40.4%) in the HP group (**Figure 1**). Of these patients, in the LP group, 5 patients (13.5%) completed two-thirds or less of all perioperative cycles. In the HP group, 11 patients (13.8%) completed two-thirds or less of all perioperative cycles.

In the LP group, patients were older and nodal (N) stage was more frequently unknown (**Table 1**). There were no significant differences between the groups for other patient and tumour characteristics.

Patients in the LP group were referred less frequently for surgical treatment from another hospital (50.6% versus 81.8%, P<0.001) and participated less frequently in a clinical trial compared to patients in the HP group (10.8% versus 26.8%; P <0.001). In the LP group, a smaller proportion of patients visited multiple upper GI specialists prior to the multi-disciplinary team (MDT) meeting during which the treatment plan was determined (**Table 1**).

No differences were observed regarding type of surgery performed, postoperative complications and mortality.

Perioperative therapy

On a national average, in the DUCA database, 35.4% of patients receive perioperative treatment, varying from 0-60% per hospital (**Figure 2**).

In the selected hospitals for the current study, in the LP group, 95 patients (41.1%) were scheduled for perioperative therapy compared to 136 (68.7%) in the HP group (**Table 2**). In the LP group, 67 of 95 patients (70.5%) receiving neoadjuvant chemotherapy completed all cycles, compared to 108 of 136 patients (79.4%) in the HP group. During neoadjuvant treatment, a higher percentage of grade III-V toxicity was observed in the LP group (P = 0.004) (**Table 2**). Thirty-seven of 95 patients (38.9%) scheduled for perioperative therapy in the LP group also started adjuvant therapy compared to 80 of 136 patients (58.8%) in the HP group (P = 0.005) (**Figure 1, Table 2**).

Reasons to omit (neo)adjuvant treatment are shown in **Supplemental Table 1**.

Table 1. Patient, tumour and treatment characteristics of 429 patients stratified in two groups according to the proportion of patients treated with perioperative therapy per hospital.

	Low perioperative therapy (LP) group (N = 231)		High perioperative therapy (HP) group (N = 198)		P value
	N	%	N	%	
Age (years), mean [SD]	70.2 [10.0]		66.2 [13.0]		<0.001
Age (years)					
<65	58	25.1%	74	37.4%	0.015
65-74	85	36.8%	68	34.3%	
75+	88	38.1%	56	28.3%	
Sex					
Male	144	62.3%	127	64.1%	0.699
Female	87	37.7%	71	35.9%	
ASA score [a]					
I-II	163	70.6%	133	67.2%	0.449
III+	68	29.4%	65	32.8%	
Charlson Comorbidity Index					
0	102	44.2%	94	47.5%	0.664
1	46	19.9%	41	20.7%	
2+	83	35.9%	63	31.8%	
Preoperative weight loss					
None	53	22.9%	40	20.2%	0.442
1-10 kg	101	43.7%	94	47.5%	
>10 kg	33	14.3%	35	17.7%	
Unknown	44	19.0%	29	14.6%	
Clinical tumour stage [b]					
T1-T2	25	10.8%	14	7.1%	0.119
T3-T4	115	49.8%	117	59.1%	
Unknown	91	39.4%	67	33.8%	
Clinical nodal stage [b]					
No	74	32.0%	82	41.4%	0.004
N+	103	44.6%	93	47.0%	
Unknown	54	23.4%	23	11.6%	

Table 1. (continued)

	Low perioperative therapy (LP) group (N = 231)		High perioperative therapy (HP) group (N = 198)		P value
	N	%	N	%	
Referred from other hospital for surgery §	117	50.6%	162	81.8%	<0.001
Consultation with§: (prior to treatment planning, in hospital of surgery)					
Gastroenterologist	123	53.2%	145	73.2%	<0.001
Medical-oncologist	28	12.1%	94	47.5%	<0.001
Surgeon	120	51.9%	164	82.8%	<0.001
Radiation oncologist	0	0.0%	30	15.2%	<0.001
Specialised nurse	80	34.6%	36	18.2%	<0.001
Enrolled in clinical trial§	25	10.8%	53	26.8%	<0.001
Type of surgery					
Total gastrectomy	76	32.9%	82	41.4%	0.190
Partial gastrectomy	116	50.2%	87	43.9%	
Other	39	16.9%	29	14.6%	
Tumour negative resection margins (R0)¶§	172	88.2%	156	91.2%	0.151
No. of resected lymph nodes, mean [SD]¶	23.3 [15.2]		26.5 [12.7]		0.039
Major postoperative complication§	44	19.0%	37	18.7%	0.840
In-hospital / 30-day mortality§	10	4.3%	5	2.5%	0.311

[a] American Society of Anaesthesiologists score

[b] According to Tumour Node Metastasis (TNM) system (7th edition)

§ In case of yes/no variables only the option yes is shown

¶ Of patients who underwent tumour resection

Table 2. Characteristics of perioperative therapy for 429 patients stratified in two groups according to the proportion of patients treated with perioperative therapy per hospital.

	Low perioperative therapy (LP) group (N = 231)		High perioperative therapy (HP) group (N = 198)		P value
	N	%	N	%	
Perioperative course as decided in MDT					
Upfront surgery	136	58.9%	58	29.3%	<0.001
Neoadjuvant CTx and Adjuvant C(R)Tx	95	41.1%	136	68.7%	
Neoadjuvant CRTx	0	0.0%	4	2.0%	
Neoadjuvant treatment completed [a]					
No / unknown	28	29.5%	28	20.6%	0.121
Yes	67	70.5%	108	79.4%	
Toxicity in neoadjuvant course, highest grade [a]					
None	14	14.7%	37	27.2%	0.004
Grade I-II	30	31.6%	44	32.4%	
Grade III-V	44	46.3%	35	25.7%	
Unknown grade	7	7.4%	20	14.7%	
Start of adjuvant treatment [a]					
No	55	57.9%	52	38.2%	0.005
Yes	37	38.9%	80	58.8%	
Unknown	3	3.2%	4	2.9%	

CTx = chemotherapy; C(R)Tx = chemotherapy or chemoradiotherapy; CRTx = chemoradiotherapy; MDT = multidisciplinary team.

[a] Subgroup consisting of all patients planned for neoadjuvant CTx and adjuvant C(R)Tx (LP group N = 95, HP group N = 136).

Multivariable analysis showed that age, sex, ASA status, clinical N-stage and the number of upper GI specialists consulted prior to treatment decision in a multidisciplinary team (MDT) meeting were independently associated with the start of perioperative treatment (**Table 3**). Clinical tumour stage, amount of weight loss and referral for surgery were not independently associated with the start of perioperative treatment.

Table 3. Risk factors associated with initiating perioperative therapy (neoadjuvant CTx and adjuvant C(R)Tx) in 429 patients included for in-depth investigation.

	OR for starting Neoadjuvant CTx and adjuvant C(R)Tx	
	OR	**95% CI**
Age (years)		
<65	ref	
65-74	0.79	0.45 - 1.38
75+	0.12	0.06 - 0.21
Sex		
Male	ref	
Female	0.61	0.38 - 0.97
ASA score [a]		
ASA I-II	ref	
ASA III+	0.42	0.25 - 0.69
Clinical tumour stage [b]		
1-2	ref	
3-4	0.91	0.40 - 2.05
Unknown	0.81	0.33 - 1.95
Clinical Nodal stage [b]		
0	ref	
1-3	1.21	0.70 - 2.08
Unknown	0.44	0.23 - 0.84
Weight loss		
0 kg	ref	
1-10 kg	0.96	0.53 - 1.72
>10 kg	0.57	0.27 - 1.20
Unknown	0.89	0.43 - 1.86
Referred from other hospital for surgery		
No	ref	
Yes	1.62	1.00 - 2.63
Number of upper GI specialists consulted [c]		
0-1	ref	
2	1.36	0.80 - 2.32
3+	2.08	1.19 - 3.66

CTx = chemotherapy; C(R)Tx = chemotherapy or chemoradiotherapy; GI = gastro intestinal

[a] American Society of Anaesthesiologists score

[b] According to the Tumour Node Metastasis system (7th edition)

[c] Prior to therapy decision in the Multidisciplinary Team (MDT) meeting

DISCUSSION

Results of this study confirm considerable hospital variation in the use of perioperative therapy in patients with resectable gastric cancer. Perioperative therapy was administered 2.5 times more frequently in the HP group compared to the LP group (40.4% versus 16.0%). In the LP group, a smaller proportion of patients was enrolled in a clinical trial. Besides known casemix factors, the number of consulted upper GI specialists prior to treatment decision in a MDT meeting was independently associated with the probability of starting with perioperative therapy.

Several studies have shown a benefit of multimodality treatment (perioperative chemotherapy, adjuvant chemoradiotherapy and adjuvant chemotherapy) in patients with stage II-III gastric cancer.[3–5,17] This has resulted in various recommendations regarding optimal treatment.[18,19] Absence of an international consensus may be one of the reasons why only subgroups of the patients with gastric cancer received treatment as recommended by the national guideline.[1,9,10]

Apart from this, there are a number of other potential reasons that could explain variation of patients with gastric cancer. Results of previous studies using data from surveillance programs, audits or cancer registries have shown that younger age, a lower Charlson Comorbidity Index and higher disease stage are associated with a higher likelihood of receiving multimodality therapy in patients with gastric cancer.[10,13–16,20] Results of this study confirm such an association between patient and tumour characteristics, and the probability to receive perioperative treatment. Multivariable analyses in the current study did not show significant influence of the clinical tumour stage on the start of perioperative treatment, probably because the overall proportion of patients with a low T-stage was small (39 of 429 patients, 9.1%).

In addition, hospital characteristics related to the decision-making with respect to perioperative treatment were investigated. Patients who were seen by ≥3 upper GI specialists prior to the treatment decision in a MDT meeting had a 2 times higher likelihood of receiving perioperative treatment. This corresponds with recommendations from previous studies, underlining the importance of multidisciplinary assessment and the role of a MDT in determining the most optimal treatment strategy in patients with gastric cancer.[16,21] The proportion of patients referred from another hospital was significantly lower in the LP group compared to the HP group, suggesting a higher level of expertise in the treatment of gastric cancer in these hospitals. However, both the LP and the HP group consisted of a mixture of university hospitals and teaching hospitals, and hospital volumes were different within both groups.

Also other differences between the LP and HP group point towards differences in dedicated multidisciplinary assessment of patients with gastric cancer. Nodal (N) stage was more frequently unknown in the LP group. This could reflect less adequate clinical staging due to different staging methods that are used or effort put into adequate clinical staging. On the other hand, if a patient is found to be fit for surgery, but not eligible for perioperative treatment, nodal staging might be less relevant. Secondly, the number of resected lymph nodes was significantly higher in the HP group compared to the LP group (mean 26.5 versus 23.3 resected lymph nodes). This could be explained by differences in patient and tumour characteristics. On the other hand, a higher number of resected lymph nodes found in the resected specimen might reflect the (surgical) quality of oncological care, in which both the surgeon and pathologist are of importance. These findings correspond with findings from a previous study reporting an association between a higher lymph node yield and evidence based care.[16] A minimum of 15 lymph nodes in the resected specimen is recommended by Dutch guidelines for adequate staging.[9, 22, 23] Finally, compliance

to perioperative chemotherapy in patients with gastric cancer is known to be difficult, even in selected trial populations. Only 40-60% of all patients complete the entire course.[3,5] In the present study, 70-80% of patients received all neoadjuvant cycles and only 40-60% started adjuvant chemo(radio)therapy. The proportion of patients experiencing toxicity grade ≥III was significantly higher in the LP group. Besides differences in patient characteristics, experience of a medical team with administration of chemotherapy could play a role resulting in early recognition and adequate anticipation e.g. switching to a different type of chemotherapy in the case of potential side effects.

This study has some limitations. Although the DUCA is a prospective quality registry, in-depth investigation of medical records was performed retrospectively. This could affect completeness of included data. However, no large amounts of missing data were observed in this study. Secondly, the DUCA is a surgical audit and only contains information on patients who underwent surgical treatment. For instance, if a patient was eligible for surgical treatment in the first place, but developed serious toxicity during neoadjuvant therapy and eventually did not proceed to surgery, this patient was not included in the DUCA. Furthermore, due to centralisation, an increasing number of patients with resectable gastric cancer was referred to another hospital for surgical treatment (reference hospital) whilst receiving perioperative treatment in the referring hospital. As the referring hospital is not registered in the DUCA, in-depth investigation of medical records took place in the reference hospital. Reliability and completeness of the collected data therefore relies on adequate transfer of all essential information between both hospitals. Standardisation of operative reports and reports from MDT meetings are crucial in this process, but not yet widely used. Finally, the effect of an evidence-based treatment may differ in a nationwide population. However, as the DUCA does not contain information about long-term follow-up, the beneficial survival effect of multimodality therapy

could not be investigated in this study. Future links between other databases that include survival data could resolve this issue, making all individual registries more meaningful.

In conclusion, results of this study confirm considerable hospital variation in the use of perioperative therapy in the Netherlands. Variation in multimodality treatment on both a national and international level underlines the importance of national and international consensus regarding optimal treatment. The likelihood of initiating perioperative therapy is not only associated with patient and tumour characteristics, but also with hospital characteristics regarding multidisciplinary care. Results from this study may have implications for the standard care path of newly diagnosed patients. Not only should they be discussed in a multidisciplinary meeting; also, a clinical evaluation of these patients by several specialists from different disciplines should take place before a final treatment plan is made.
This emphasises the importance of a dedicated MDT in oncological care.

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APPENDICES

Supplemental Table 1. Reasons to refrain from initiating perioperative therapy or adjuvant therapy for patients stratified in two groups according to the proportion of patients treated with perioperative therapy per hospital.

	Low perioperative therapy (LP) group		High perioperative therapy (HP) group	
	N	**%**	**N**	**%**
Reasons to refrain perioperative therapy [a]				
Patient preference	9	6.6%	8	13.8%
Patient factors (age, performance score, comorbidities)	58	42.6%	21	36.2%
Tumour factors (tumour stage, differentiation)	15	11.0%	3	5.2%
Urgency of procedure (haemorrhage, perforation, obstruction)	25	18.4%	16	27.6%
Different treatment due to tumour location / pathology [b]	15	11.0%	3	5.2%
Unknown	14	10.3%	7	12.1%
Reasons to refrain adjuvant therapy [c]				
Toxicity neoadjuvant CTx	17	30.9%	9	17.3%
Poor tumour response after neoadjuvant treatment	3	5.5%	1	1.9%
Progressive disease / non curative resection	17	30.9%	24	46.2%
Postoperative complicated course	4	7.3%	7	13.5%
Patient preference	8	14.5%	5	9.6%
Other	3	5.5%	2	3.8%
Unknown	3	5.5%	4	7.7%

CTx = chemotherapy

[a] Calculated from the number of patients with upfront surgery (LP group N = 136, HP group N = 58)

[b] e.g. neuroendocrine tumours or gastro-intestinal stoma cell tumours (GIST)

[c] Subgroup consisting of all patients not starting adjuvant therapy (LP group N = 55, HP group N = 52)

CHAPTER 7

Between-hospital variation in the use of perioperative therapy in gastric cancer: identifying barriers and facilitators using a qualitative approach

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* Can be found under the heading 'Collaborators'

Submitted

ABSTRACT

Background | Previous results from the Dutch Upper Gastrointestinal Cancer Audit (DUCA) have shown substantial hospital variation in use of perioperative therapy in patients with potentially resectable gastric cancer. This variation is not fully explained by patient and tumour characteristics, but could be due to variation in treatment preferences. The aim of this study was to explore potential barriers and facilitators for the use of perioperative therapy.

Methods | In-depth semi-structured interviews with surgical and medical oncologists (n = 17) were conducted in five hospitals with the lowest and four hospitals with the highest percentage of perioperative therapy use as identified from DUCA. Data were analysed using inductive content analysis guided by a pre-existing implementation framework.

Results | A total of 33 factors, including 18 barriers and 15 facilitators, were identified. Most concerned the individual professional level. Themes of barriers and facilitators varied from '(dis)believe in added value of therapy', 'burden of therapy' and 'difficult extrapolation of study results' to 'specialist dedication', 'centralisation' and 'regional collaboration'. Although there were no big differences between hospital groups in themes reported or the number of barriers or facilitators, the quoted answers did differ in a nuanced way.

Conclusions | Potential barriers and facilitators for use of perioperative therapy in patients with gastric cancer were identified. It is suggested that between-hospital variation can be reduced by an up-to-date national guideline, earlier consensus on implementation of study results, concentration of perioperative care (leading to more exposure) and close (regional) collaboration.

INTRODUCTION

In non-metastatic, locally advanced, resectable gastric cancer (neo)adjuvant chemo(radio)therapy improves disease-free and overall survival compared to surgery alone.[1–3] However, there is no international consensus on the best multimodality treatment. In North America adjuvant chemo-radiotherapy is preferred and in Japan adjuvant chemotherapy is favoured.[4,5] In Northern Europe, the use of perioperative chemotherapy (according to the MAGIC study[1]) is recommended.[6,7]

Previous studies, using data from the nationwide surgical Dutch Upper Gastrointestinal Cancer Audit (DUCA) showed that the use of perioperative chemo(radio)therapy varied considerably between hospitals.[8–10] Differences in treatment strategies between hospitals could not be explained by patient and tumour characteristics alone and the use of perioperative therapy was associated with the level of involvement of multidisciplinary care.[10] In addition, postoperative complications were associated with omission of adjuvant therapy.[9]

From these previous studies it was clear that quantitative measurable factors did not fully explain between-hospital differences in perioperative treatment strategies. It was hypothesised that variation could be the result of variation in treatment preferences. The aim of this study was to explore and categorise barriers and facilitators for perioperative therapy use in patients with gastric cancer, as perceived by surgical and medical oncologists in the Netherlands.

METHODS

To identify barriers and facilitators for perioperative therapy use in patients with gastric cancer, a qualitative approach with semi-structured interviews among surgical and medical oncologists was used. Qualitative data analyses (for example by analysing interviews or videos) can reveal information not retrieved from quantitative analyses, since opinions and behaviours are often not entirely encapsulated in responses to direct questions, and can therefore provide information about motivations, perceptions and experiences of individuals.[11] In this specific setting, identification of barriers and facilitators for the use of perioperative therapy could contribute to a further understanding why between-hospital variation exists and could potentially reduce unwarranted variation.

Selection of participants

The DUCA was initiated in 2011 with the main aim to improve quality of care for patients undergoing surgery for oesophageal or gastric cancer.[8] From DUCA data, the proportion of patients with gastric cancer receiving perioperative therapy in 2012-2014 was calculated per hospital. Five hospitals with the lowest percentage (LP group) and four hospitals with the highest percentage (HP group) of perioperative therapy were included in this study. Because of the CRITICS study, both perioperative chemotherapy (recommended by current Dutch guidelines[6]) and neoadjuvant chemotherapy combined with adjuvant chemoradiotherapy (CRITICS intervention arm[12]), were considered as "perioperative therapy". The selection methods of the LP and HP group have previously been described in full.[10] From each selected hospital, one surgical oncologist and one medical oncologist (both referred to as 'specialist') involved in treatment of patients with gastric cancer were asked to represent their hospitals multidisciplinary team (MDT).

Data collection

All specialists were invited for interviews by e-mail, which provided an explanation of the study purpose. Between October 2015 and April 2016, 17 of the 18 scheduled interviews were conducted. One interview could not be facilitated within the study period. All interviewees are included in the list of Collaborators.

Prior to the interview, participants were informed about study objectives and design. A topic guide for the interviews was developed in collaboration with a panel of health care professionals in the field of medical oncology, surgery, and radiation oncology and was based on literature[13–15] and expert opinion (**appendix 1**). Included topics were hypothesised as important in treatment decision-making. Interviewees were encouraged to share their views on optimal curative treatment for gastric cancer as well as on the current national guideline and potentially explanatory factors for between-hospital variation in perioperative therapy.

Interviews were one-on-one, either face-to-face or by telephone, performed by one interviewer (NB: MD, PhD student) and audio recorded. The interviewer was not involved in clinical work when the interviews were conducted. Although the interviewer knew the performance of the hospitals being part of the LP or HP group, both groups were approached equally

Analysis

All audio-recorded interviews were transcribed in full. Transcripts were not returned to interviewees for correction. Anonymised transcripts were analysed with inductive content analysis using the software package ATLAS.ti version 8 (GmbH, Berlin, Germany) by the researcher who also conducted interviews.[16] Data driven, open coding was performed on all transcripts. A pre-existing implementation framework was used to guide identification and classification of possible barriers and facilitators for the use of perioperative therapy.[17]

Barriers and facilitators were categorised in five levels of this framework: individual professional, patient, social context, organisational context and innovation. Since our previous study emphasised the importance of multidisciplinary care for the administration of perioperative therapy, there was a special focus on implementation of a multidisciplinary outpatient clinic within the organisational level.[10]

All interviews were coded. Data saturation was reached at interview thirteen. A second coder (SV: MD, PhD student) experienced in interview analyses, independently reviewed transcripts 5-13 (n = 9) for continuity of data interpretation, miscoded statements and inappropriately uncoded segments. Discrepancies were discussed until consensus was reached. Subsequently, the first coder (NB) re-evaluated all codes in the remaining transcripts 1-4 and 14-17 (n = 8).

After coding, the anonymised transcripts were classified to the LP or HP group to facilitate comparison between both groups. Representative quotes for the coded barriers and facilitators were extracted from interviews from both groups.

RESULTS

Seventeen interviews were completed in nine hospitals. Characteristics of the interviewed specialists and their hospitals are described in **Table 1**. In total, 33 barriers (n = 18) and facilitators (n = 15) for perioperative therapy use were extracted (**Table 2**). When classified into the 5 levels of the framework, most barriers and facilitators were reported at the individual professional level. In some cases, the same theme could be reported both as a barrier and a facilitator, depending on the presence or absence of this factor. In the LP group 12 barriers and 13 facilitators were mentioned, while in the HP group 15 barriers and 14 facilitators were mentioned. Although themes can be classified into multiple levels of the framework and are likely to be interdependent, for the ease of interpretation they will be discussed per level and more or less separate from the context.

Table 1. Participant characteristics at hospital and interviewee level.

	LP group		HP group	
	N	%	N	%
Hospital level	(N = 5)		(N = 4)	
Hospital type				
Academic	1	20%	2	50%
Teaching	4	80%	2	50%
Median volume of patients *	43		51	
Median percentage perioperative therapy use *	20%		58%	
Interviewee level	(N = 9)		(N = 8)	
Discipline				
Surgeon	5	56%	4	50%
Medical oncologist	4	44%	4	50%
Gender				
Male	8	89%	3	38%
Female	1	11%	5	63%
Conduction				
Face-to-face	7	78%	6	75%
Telephone	2	22%	2	25%
Median duration, minutes [IQR]	32 [18-40]		33 [31-35]	
Transcript numbers	1; 3; 4; 7; 10; 12; 14; 15; 17		2; 5; 6; 8; 9; 11; 13; 16	

* In the years 2012-2014
IQR = Inter-Quartile Range
LP group = group of hospitals with low percentage of perioperative therapy use
HP group = group of hospitals with high percentage of perioperative therapy use

Individual-professional level

Five themes were mentioned by interviewees in both the LP group and HP group. Interviewees in the HP group also specifically mentioned believes or disbelieves of individual clinicians or the entire team in a certain treatment.

Regarding the evidence supporting perioperative therapy use, most interviewees felt this evidence was clear, thereby acting as a facilitator. However, quotes from interviewees in the LP group tended to be more sceptical on the added value of perioperative therapy, with 4 of 9 even doubting the evidence (versus 1 of 8 in HP group), and thus acting as a potential barrier.

Table 2. Barriers and facilitators to apply perioperative therapy in patients with gastric cancer.

		LP-group			HP-group		
Level	**Theme**	**B**	**F**	**I**	**B**	**F**	**I**
Individual professional	Evidence of added value clear (F) / doubted (B)	+	+		+	+	
	Being less / more conservative (F / B)	+	+		+	+	
	Dedication / superspecialisation		+	+		+	
	Experience (F) / lack of experience (B) due to volume		+	+	+	+	
	Difficulties extrapolating study results to clinic	+			+		
	Emphasis on only certain part of treatment	+					
	Believe (F) / disbelieve (B) of individual clinician(s)				+	+	
Patient	Patients preference not to start perioperative therapy	+			+		
	Restricting patient factors (condition / comorbidity)	+			+		
	Optimisation of patients condition pre-treatment		+			+	
	Restricting tumour factors (bleeding / obstruction)	+			+		
	Burden of therapy (B) is manageable (F)	+	+		+		
Social context	Good interdisciplinary collaboration		+			+	
	Good (F) / difficult (B) collaboration with referring hospitals	+	+		+	+	
Organisational context*	Centralisation of perioperative therapy		+	+		+	
	Clustering (F) / division (B) of oesophagogastric cancer care	+	+			+	
	Optimising diagnostic information before treatment planning		+			+	
	MDT as a quality controlling moment		+			+	
	Quality of MDT depends too much on individual specialists				+		
	Fragmentation of care				+		

Table 2. (continued)

		LP-group			HP-group		
Level	**Theme**	**B**	**F**	**I**	**B**	**F**	**I**
Innovation	Guideline out of date	+			+		
	Differences in (inter)national guidelines or local treatment protocols	+			+		
	Study participation by the hospital does (not) create awareness among clinicians on standard of care		+	+		+	+
	Study participation stimulates persistency to complete treatment					+	
	Implementation of novel treatment ahead of the guideline				+		

LP group = group of hospitals with low percentage of perioperative therapy use
HP group = group of hospitals with high percentage of perioperative therapy use
B = barrier; F = facilitator; I = indifferent, signifying a theme was indicated without a clear direction
* Special focus on the implementation of a multidisciplinary outpatient clinic in Table 3

"Let's face it, neoadjuvant -or perioperative- chemotherapy improves survival. And improves survival with such a percentage that we all decided it to be valuable." (#8, HP group)

"Sometimes you hear one question 'does that chemo really have an effect, or is it compensating for relatively bad surgery?'." (#17, LP group)

In both groups the level of conservativeness of clinicians was regarded as potentially influencing the use of perioperative therapy on hospital level.

"One doctor differs from the other. One person will have a little more courage, or takes a little more risk, or makes a slightly different assessment than another doctor." (#4, LP group)

In the LP group there were numerous interviewees that valued only a specific element in the total multimodal gastric cancer treatment. Some for example emphasised neoadjuvant or surgical treatment only.

"Excellent surgery is in any case the most important thing. Completely standardised, excellent surgery, for which we proctor each other. [...]" (#12, LP group)

The level of experience of clinicians was indicated in both groups as influencing the use of any specific treatment. Interviewees from both groups indicated that the low prevalence of gastric cancer makes it difficult to gain sufficient experience in this specific patient population. Super-specialisation of clinicians or establishing dedicated teams with a higher patient-volume could enhance experience.

"Now I notice that I am really only concerned with the upper-GI. This ensures your focus. You deal with the subject, and the guidelines, in such depth. If this is all you do, I think it does have an effect." (#6, HP group)

In addition, interviewees in both groups indicated to experience difficulties to extrapolate study results into daily practice. The guideline is based on studies performed in a selected group of patients. In clinical practice however, many patients do not meet these inclusion criteria, making it harder to choose the best treatment.

Patient level

At patient level, mainly barriers for perioperative therapy use were reported. One of these was 'patient preference not to start therapy'. Both patient (such as age, comorbidities or general condition) and tumour related factors (such as an obstructing or bleeding tumour requiring urgent surgery) were found to restrict therapeutic options. All interviewees mentioned such patient level barriers.

> "Quite a lot of patients are not suitable [for the chemotherapy], because they are too old, or have too many comorbidities." (#3 LP group)

Optimisation of the patients' condition to enable perioperative therapy was named to potentially facilitate perioperative treatment use. Optimisation of the patients' condition (for example by tube feeding or radiotherapy for tumour bleeding) was more frequently mentioned as a facilitator in the HP group (6 of 8 interviewees versus 4 of 9 in the LP group).

The burden of perioperative therapy was emphasised frequently (all 9 interviewees in the LP group and 4 of 8 in the HP group). Interviewees also mentioned neoadjuvant therapy could negatively impact patients' per-operative condition and in some cases withhold patients from surgery due to severe side effects like sepsis, arterial occlusion or even death. Only one interviewee thought of the potential toxicity as negligible.

> "A few years ago, a patient was admitted to the ICU [during neoadjuvant treatment] and was in such a condition that he could not undergo surgery. Of course, then you have totally failed." (#2 HP group)

Social context level

Collaboration and/or communication between various disciplines within the hospital and, when referring patients, between hospitals were mentioned both as potential facilitators and barriers in both groups. Especially, good collaboration in MDT meetings was mentioned to positively affect quality of decision-making.

Also, other disciplines being easily approachable outside the MDT meeting was indicated to facilitate multimodal treatment. In case of referred patients, specific barriers were encountered influencing collaboration and communication between hospitals. Clinicians experienced that information of referred patients was often incomplete or harder to rely on compared to information from one's own hospital, and that referral can cause delay in the progress and treatment.

> "Our patients are often diagnosed in another hospital. Then already a week has passed before all diagnostic information is sent. Then only half of it turns out to be complete. And so on. So, it often takes two to three weeks before we actually see the patient." (#8, HP group)

Organisational level

Most themes reported at the organisational level were considered to act as a facilitator. Interviewees suggested centralising perioperative therapy to fewer hospitals, in addition to the already centralised surgical procedures. Clustering of oesophagogastric cancer care was proposed, with interviewees pleading that hospitals should treat the entire spectrum of oesophagogastric cancer instead of only oesophageal or gastric cancer.

> "It is a heavy chemo with considerable toxicity, potentially fatal. Just like we – surgeons – have our sub-specialisations, maybe this kind of care should also be done by a limited number of oncologists. And not by just anyone, in every hospital in the Netherlands." (#17, LP group)

Both groups identified the MDT-meeting as an important quality control moment, provided that all MDT participants are well prepared.

Another facilitator was optimisation of diagnostic information prior to treatment planning, for which some hospitals have a specific 'fast-track' diagnostic pathway.

For the implementation of a structured multidisciplinary outpatient clinic, 3 barriers and 4 facilitators were identified (**Table 3**). Both groups considered a

Table 3. Barriers and facilitators to implement a multidisciplinary outpatient clininc into practice as part of the orginasitional context.

	LP-group		HP-group	
Theme	**B**	**F**	**B**	**F**
Patient (un)friendly	+	+	+	+
Does not have influence on quality of decision	+		+	+
Saves (F) / costs time for specialists (B)	+	+	+	+
Stimulates multidisciplinary team work		+		+

LP group = group of hospitals with low percentage of perioperative therapy use
HP group = group of hospitals with high percentage of perioperative therapy use
B = barrier; F = facilitator

multidisciplinary outpatient clinic both demanding for patients as well as patient-friendly. In terms of efficiency for specialists, some interviewees expect it to be time consuming, especially if they are not part of the treatment strategy, while others expect to save time because all specialists are well prepared. Both groups expect a structured multidisciplinary outpatient clinic to stimulate multidisciplinary teamwork, however only interviewees in the HP group expect it to positively affect decision-making quality (5 of 8 interviewees).

Pre-set conditions were named to maximise advantage of a multidisciplinary outpatient clinic, such as a sufficient number of patients, to utilise waiting time for patients and proper patient preparation and information.

Innovation level

More barriers than facilitators were identified at the level of the innovation. The current guideline being out-of-date was a frequently stated barrier (6 of 9 interviewees in the LP group, all interviewees in the HP group), with the process of new guideline composition being perceived too demanding and time-intensive. Also, differences in (inter)national guidelines and/or local treatment protocols were mentioned to potentially play a role in hospital differences. Additionally, some hospitals tend to implement certain treatments ahead of the guideline, while

others are await the formal guideline changes. Implementing certain innovative treatments ahead of formal guidelines could be a barrier to adhere to the current guideline.

> "Sometimes people have the idea 'this is better' and already implement it, rather than implementing it nationwide, then of course you get differences in approach. I don't think that is desirable." (#4, LP group)

A number of interviewees indicated study participation as a facilitator. It could induce clinicians to become more aware of the standard of care, being more up-to-date with the literature and being more critical (for example, more accurate patient selection and evaluation before start of treatment). In addition, some interviewees in the HP group stated that study participation could stimulate adherence to protocols due to structure and persistence to complete a certain treatment.

> "I think that clinicians that participate in studies are forerunners in innovation. They also keep up with the literature better and have more frequent discussions with other colleagues in the country." (#13, HP group)

DISCUSSION

In the present study, 33 potential barriers and facilitators for perioperative therapy use in patients with gastric cancer, as perceived by surgical and medical oncologists, were identified. These factors might contribute to the between-hospital variation. Most barriers and facilitators were encountered at the individual professional level. At the organisational level, mostly facilitators were identified, whereas more barriers were identified at the patient level. Although there were no big differences between the LP and HP group in the themes reported or the number of barriers or facilitators, the nuances in the quoted answers were quite different. While interviewees in the LP group emphasised the burden of perioperative therapy more frequently, optimisation of patients' condition was more often mentioned in the HP

group. In addition, quotes from interviewees in the LP group tended to be more sceptical on the added value of perioperative therapy or appeared to emphasise only a specific element in the total multimodal treatment.

Annual exposure per hospital

The incidence of gastric cancer in the Netherlands is low and declining. Each year there are around 1200 new gastric cancer patients, of whom less than half undergo surgical treatment.[8,18,19] In 2014, gastric cancer surgery was performed by 27 hospitals. Of the surgically treated patients about two-thirds start perioperative chemo(radio)therapy, i.e. about fifteen patients per hospital per year. Due to these low numbers it could be difficult to gain experience with this specific cancer care. This lack of experience was identified as a potential barrier for perioperative therapy. Experience (and thereby the quality of decision-making) could be improved by collaboration in (regional) MDTs by centralising care.

Extrapolation of study results into daily practice

Interviewees in both groups reported difficulties to extrapolate results of the MAGIC study (underlying the current guideline) into clinical practice. In the MAGIC trial, about 20% of patients was over 70 years, while this was about 48% according national DUCA data.[1,8] Also, in the MAGIC trial a WHO performance status of 0-1 was necessary for inclusion. WHO performance status is not recorded, but ASA classification was III or higher in 30% of all operated patients.[8] It is known that study patients often represent only a subpopulation of the actual patient group.

Guideline and study interpretation

Varying confidence in the current national guideline was reported as another reason for between-hospital differences in perioperative therapy use. Generally speaking, interviewees reported the guideline to be out-of-date and that updating the guideline is a time-consuming process.

Some interviewees, especially in the LP group, doubted the beneficial value of perioperative therapy or emphasised only a specific element, e.g. only the neoadjuvant part. Additionally, at the time of the interviews, results from the CRITICS study were being analysed.[20] Some interviewees indicated to already use post-operative chemo-radiotherapy in selected patient groups outside the study context. In May 2018 it was documented that there was no survival benefit of postoperative chemoradiotherapy over postoperative chemotherapy.[21] Implementing treatments still being studied, in this case was not beneficial for patients. Also, doing so was indicated as a potential barrier by some interviewees.

Burden of therapy for specific patients

Previous studies demonstrated patient and tumour characteristics as influential factors for treatment decisions.[9,10,19] Differences in the perceived burden of perioperative therapy could be an explanation for the varying use between hospitals. In the LP group all interviewees emphasised its' burden, influence on patient condition and risks of toxicity. In the HP group, half of the interviewees mentioned this burden, but also mentioned techniques to optimise patients' condition.

Multidisciplinary approach

Between-hospital variation in perioperative therapy was associated with the level of involvement of multidisciplinary care.[10] Given that the level of multidisciplinary care influences treatment decisions,[15,22,23] a multidisciplinary outpatient clinic could enhance decision quality. While half of the clinicians in the HP group judged it to positively influence decision quality, none of the clinicians in the LP group did. Also, clinicians in the LP group named more barriers and less facilitators than those in the HP group.

Strengths and limitations

An important strength of this study is its' qualitative approach. Qualitative analyses can be used to reveal the complexity of influencing factors that would not be revealed by quantitative data. Though qualitative research does not validate or invalidate certain hypotheses, it has an explorative nature and can be used to generate hypotheses. Data saturation was reached, signifying an appropriate number of interviewees.

An important limitation in this study is that per hospital only one clinician per specialty was selected for the interviews, assuming that their response would be representative for the team. As interviewees mentioned, opinions can differ between specialists within the same hospital. Although the current study investigated an extended list of barriers and facilitators, it might be possible that certain themes were missed. Also, it occurred that a theme would match multiple levels of the pre-existing framework, while could only be categorised into one. For example, the barrier 'difficulties extrapolating study results to clinic' was classified at the individual professional level, since it was regarded as limited knowledge of the clinician. However, one could also consider it as an ambiguity in study results, thus at the level of innovation. To pursue objectivity, all discrepancies were discussed until consensus was reached. Lastly, this study does not provide insight in to what extent the themes actually contribute to the between-hospital variation.

Conclusion and future perspectives

In this study barriers and facilitators for perioperative therapy use in gastric cancer treatment were identified. These may partly explain the between-hospital variation. Although there were no striking differences between interviewees in the LP and HP group, their quoted answers did differ in a nuanced way. Interviewees in the LP group tended to be more sceptical on the added value of perioperative therapy, emphasised only a specific element in the multimodal treatment, or indicated the

burden of perioperative therapy more frequently. Based on the findings in this study, it is suggested that between-hospital variation can be reduced by an up-to-date national guideline and earlier consensus on the implementation of (inter)national study results. Concentration of perioperative care could lead to more experience. Together with the advanced collaboration in (regional) MDTs, this could minimise between-hospital variation and improve the quality of uniform decision-making.

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APPENDICES

Appendix 1. Topic list for semi-structured interviews with surgical- and medical oncologists working in the field of gastric cancer treatment

Introduction

- Background and objectives
- Information about interview (anonymity, safety)

General information

- Information about participant: other medical specialisation area(s), percentage of work time spent on gastric cancer care.
- Information about participants hospital: type of hospital (incl. residential training), possibilities for oesophageal cancer treatment, diagnostic and treatment facilities, study participation

In-depth investigation

- Diagnostic and treatment pathway for patients with gastric cancer (both new and referred)
  - Type of specialists involved in gastric cancer care
  - Role of multidisciplinary team (meeting) and influence of multidisciplinary collaboration
  - Influence of patient referral
  - Local / regional guidelines used
- View on the optimal potentially curative treatment of gastric cancer
- View on the current national guideline
- Potential explanation for between-hospital variation in perioperative therapy
- Use of perioperative therapy suitable as a quality indicator

CHAPTER 8

General discussion and future perspectives

DISCUSSION

Worldwide, the quality and sustainability of health care is considered a priority on the political agenda. This is of special importance in cancer care, due to the growing burden of disease, the rising complexity of care, which increasingly involves a multidisciplinary approach, and the expanding availability of expensive therapies. Despite the best intentions of well-trained clinicians and policy makers the quality of care and resources are not evenly distributed.[1]

Partly this might be overcome by the use of clinical auditing. Clinical audits are used as a tool to gain insight in quality of care, facilitate improvement initiatives, increase efficiency of care, thereby reducing healthcare costs, and reducing variation.[2] In the last decades another effort to improve overall quality of oncologic care and reduce undesirable variation was made by incorporating multidisciplinary teams (MDTs) in the standard care. MDTs are considered to improve overall quality and reduce variation by better communication, patient coordination, clinical decision-making and practice of evidence-based medicine.[3,4]

Facing these trends to increase overall quality and reduce undesirable variation in cancer care, this thesis focused on the development and implementation of clinical audits for the evaluation of multidisciplinary cancer care in **Part I** and variation in surgical oncological treatment in **Part II**. For the latter, two eminently multimodal treated cancer types were highlighted.

Evaluating quality of cancer care using clinical auditing

Clinical auditing is a process of systematic analysis of quality of healthcare, with the aim to improve outcomes. With this tool participating hospitals can be provided with feedback information on population and performance (mirror information) and

comparison with other hospitals, the national mean or any set value (benchmark information).[5]

The fundamental thoughts for 'clinical auditing' have already been set a century ago.[6,7] However, the use of data to monitor healthcare quality has only been a development of the last decades, partly facilitated by the increasing digitalisation of healthcare. Many initiatives have been developed either by professional associations or government authorities.[2,8–11] In the Netherlands, one of the leading organisations facilitating clinical auditing is the Dutch Institute for Clinical Auditing (DICA). **Chapter II** of this thesis provides insight into the development of DICA and the nationwide implementation of clinical audits. With a narrative review of individual audits, the effects on care processes and outcomes for patients are described.

One of the main features is the central role for clinicians in the determination of the audits' objectives and dataset content. Frequently updated quality of care information at hospital level is used to stimulate local improvement initiatives. By discussing audit results in scientific medical conferences and reporting areas for improvement in the annual report and congresses, clinicians have the chance to share their expertise and their ideas for quality improvement. Simultaneously, quality indicators – defined in a national collaboration between patient representatives, professionals, payers and government organisations – are used for public transparency.

Integrating audits into existing quality systems and stepwise transparency of quality indicator results, stimulated participation by all hospitals and rapid nationwide implementation. Although all audits and affiliated clinicians have their own learning curve, an overarching organisation has the advantage to enable building on the foundations, structures and knowledge of already existing audits. In less than ten years, over 20 nationwide audits were implemented in various clinical fields. Valuable

insights were gained in the development of quality indicators, casemix adjustment models, hospital variation analysis and evaluation of real world clinical practice.[12–15] Evaluation of national data even initiated national guideline adjustments.[16,17] On numerous process and outcome indicators positive effects were observed, with reduction of variation and improvement of the national average.[18–22] In addition, clinical auditing was associated with healthcare cost reduction.[23]

Although the observed improvements are likely to be multifactorial – with simultaneous centralisation, specialisation and introduction of new techniques – and not solely attributable to the audits, the audits provided insights into performance of the national healthcare system and individual providers that were previously not available. Of vital importance is the central role of the clinicians in the processes of development of the audits and evaluation of results, since the cultural component of constant commitment is critical in improving healthcare.[24,25] Also, their continuous input is required to keep the audits up-to-date and relevant, as the concept of what presents state of the art care changes over the years.

The evolution of multidisciplinary cancer care

In most solid cancers there is a growing evidence for the added value of treatments besides or even replacing surgery to improve outcomes. With this growing number of treatment possibilities multidisciplinary team meetings (MDTs) are incorporated in the standard of care for patients with cancer in most countries across Europe and the USA. The rationale for working with MDTs is that it is important to involve all key professionals in making complex decisions.[26] In the Netherlands, oncological MDTs are therefore considered mandatory and take place in a fixed frequency.[27–29] They typically consist of surgeons, medical oncologists, radiotherapists, radiologists, pathologists and a case-manager or specialised nurse. MDTs are considered to tailor holistic treatment plans to patients' by improving communication, coordination, evidence-based medicine and clinical decision-making. In certain studies the

discussion of patients in an MDT was associated with an improved survival.[30,31]

While the decision on how to treat patients with cancer is becoming more of a shared effort, the actual path from diagnoses to treatment and eventually follow-up is still rather fragmented. The reorganisation of care into integrated practice units around medical conditions, instead of procedures, is suggested by various healthcare and business professionals.[25,32] As Michael Porter stated "Value for patients comes from the overall effect of the entire sequence of activities, not from any individual service."[25] He also advocates measuring outcomes for a given medical condition over the full cycle of care.

The evolution of multidisciplinary care evaluation

The importance of integrated care evaluation is also emphasised by the fact that outcomes can transcend disciplines. For example in patients with gastric cancer, severe postoperative complications were associated with the omissions of adjuvant therapy.[33] Conversely, in lung cancer, the administration of neoadjuvant chemoradiotherapy was associated with severe postoperative complications.[34] Likewise in rectal cancer treatment, neoadjuvant chemoradiotherapy can improve recurrence rates, while it may lead to more postoperative complications, such as anastomotic or perineal wound complications. This indicates that a more comprehensive approach is preferably used in interpretation of outcomes. Simultaneously, involving multiple disciplines in the interpretation of results could lead to a broader perspective of indicator scores and potentially leads to further improvement.

Initially, DICA audits were initiated by members of the Association of Surgeons in the Netherlands (ASN) and focused on the quality of (mainly colorectal, upper gastro-intestinal and lung) cancer surgery. Over time, the interest for quality evaluation

expanded among other professional associations and the audit subjects extended to surgical treatment of non-malignant diseases, non-surgical treatments of malignant diseases and non-surgical treatments of non-malignant diseases. Still, most audits were mainly mono-disciplinary and treatment-specific instead of condition-specific. The first step to enable the evaluation of the entire multidisciplinary care pathway by clinical auditing in the Netherlands was set in 2016 by the implementation of the Dutch Lung Cancer Audit (DLCA). The DLCA is a product of a close cooperation between members of various professional associations (the Dutch Society of Physicians for Lung Diseases and Tuberculosis - NVALT, the Netherlands Association for Cardio-Thoracic Surgery - NvT, the Dutch Society for Lung Surgery - NVvL-NVvH and the Dutch Society for Radiotherapy and Oncology - NVRO). In **Chapter III** of this thesis the core concepts, phased implementation and very first results of this multidisciplinary audit are presented. Although in its current format the audit is not at the level of an entirely integrated evaluation of care around the medical condition of lung cancer, the structural gathering of key professionals already seems beneficial in the progress of integration. One of the biggest challenges of the DLCA and other future multidisciplinary audits is the fact that in clinical practice diagnoses and treatment of patients often transcends multiple centres, in which data collection and display is complicated by (medical) information laws like the EU General Data Protection Regulation (GDPR).

However, an advantage of the multidisciplinary audit, experienced by all specialisms was the opportunity to address overarching issues and the quick implementation of new knowledge into national clinical practice; for example the nationwide in-hospital adoption of TNM8, only a few months after publication. Related to this subject is the unfavourable quality of lung cancer staging that was demonstrated using surgical audit data.[14,35] Staging is an issue of importance to all specialists, since it determines optimal treatment strategy. To improve pre-treatment staging, a multidisciplinary approach is essential.

Although the debate remains on which indicators best reflect health care quality, it is known that with the use of only single parameter indicators the total aspect of care is not valued. To place single parameter measures in a broader context, most surgically focused audits incorporated composite measures such as failure-to-rescue or textbook-outcome.[15,36–39] Still, these measures only reflect part of the cycle of care. The main aim, and at the same time a challenge, for the DLCA is therefore to truly integrate quality information in a way that it enables multidimensional quality evaluation of the entire care spectrum, from prevention, diagnosis and treatment to end-of-life care. Because ultimately this is the bigger picture that matters to the patient. To facilitate this for the future, the International Consortium of Health Outcome Measurement (ICHOM)[40] standard dataset was adopted as much as possible

Conditions for quality evaluation and comparison

The interest in using clinical audit data to analyse healthcare quality is growing among different stakeholders. As described, clinicians use it to gain insight in performance in order to improve quality. Besides this internal use of information, there is a growing demand for externally transparent information for government organisations, insurance companies and patients. Incentives vary from quality control and regulation to steering information for contracts or shared decision-making. With this wide use of information and potential consequences, it is of utter importance to generate correct and meaningful information.

While indicators are typically classified as 'structure', 'process' or 'outcome', outcome indicators are thought to matter most for patients and reflect all (underlying) aspects of care.[41] Criteria used to assess the suitability of indicators for quality evaluation purposes include relevance, usability (understand-ability and action-ability), feasibility, discriminative capability, reliability and validity.[42]

Reliability (repeated measures will lead to the same result) compromises data quality and uniform definitions. Validity refers to whether an indicator measures what it claims to measure.

An important part of validity when using outcome indicators to compare hospital care is the adjustment for casemix (a combination of patient- and disease characteristics). As one can imagine, the risk on postoperative mortality for example differs between a healthy 60-year old woman and a 75-year old man with diabetes, hypertension and cardiac failure. Similarly, disease specific characteristics influence outcomes. For example a patient using systemic steroids that received neoadjuvant therapy will have a higher risk on postoperative complications compared to a patient with a lower stage tumour without indication for neoadjuvant therapy. Risk differences between patients would not be of importance if patients were randomly distributed over hospitals. However, this is not the case.[43] Regional differences in patient population and referral of more complex cases to expertise centres cause unequal distribution of patients and their risks over various hospitals.

In **Chapter IV** of this thesis, the need for proper casemix adjustment when comparing hospitals on outcome indicators in the surgical treatment of NSCLC was emphasised and a casemix adjustment model useful in practice was developed.[34] A large between-hospital variation in patients undergoing lung cancer surgery was seen, both in individual parameters (e.g. ASA-classification and neoadjuvant therapy) as in more composite measures. The risk on postoperative mortality in the hospital with the highest risk population was 2.3 times higher than in the hospital with the lowest risk populations.

To enable between-hospital comparisons or when using outcome indicators as transparent information to patients, policy makers or insurers ('external

accountability'), this thesis shows that a proper casemix adjustment is indispensable. However, when feedback information is presented to caregivers ('internal quality improvement'), unadjusted data and the ability to evaluate raw data is essential. Every adverse outcome, regardless of the patients' characteristics, should trigger the opportunity to improve care processes. Also, the possibility for caregivers to stratify their outcomes for various patient- or disease characteristics can be informative in the process of quality improvement, especially when a specific patient population can be identified as a target for improvement. The purpose with which information is displayed ('external accountability' versus 'internal quality improvement') thus determines the context at which information is presented (casemix adjusted versus unadjusted raw data). However, for both aims detailed information on patient and disease characteristics is indispensable and therefore needs to be included in clinical audits.

Quality assurance using (publicly available) indicators

As noticed, indicator results should always be seen in context of population characteristics. Often they should also be seen in the context of other indicator results. Most single-measure indicators are hard to interpret separately and do not always provide a one-to-one answer on what is 'right' or 'wrong', high or low quality of care. For instance, in rectal cancer surgery the 'anastomotic leakage' rate as an undesired postoperative outcome, can be influenced by the construction of a stoma. When postoperative complication rate is used as a publicly transparent indicator, clinicians might have the tendency to be more risk-averse and construct a stoma in more cases to prevent anastomotic leakages. Analysis of nationwide audit data demonstrated significant differences between hospitals in the use of stomas.[13,44] Counterintuitive, a high tendency towards stoma construction did not result in lower overall anastomotic leakage or mortality rates, which was a real eye-opener for the colorectal surgeons participating in the audit. The ability to select

the right patients for stoma construction appeared to be the key towards preferable outcomes for rectal cancer resections: low anastomotic leakage rates combined with low stoma rates.

Single-measure indicator results thus should be evaluated and interpreted in the context of other indicators. Another possibility lies in the use of composite measures, preferably transcending disciplines, to evaluate overall quality of care. Composite measures, such as "textbook outcome" are therefore studied as potential indicators involving both process and outcome measures.[15,39] If all individual parameters are correctly weighed into the composite measure, it could be of added value in the evaluation of hospital performance and variation.

Critics of the public reporting of outcome measures argue that transparency of outcome measures might cause risk-averse behaviour of clinicians, such as omitting high-risk patients for certain treatments or making more conservative treatment choices. Fortunately, a recent study from the United Kingdom, where outcomes on individual clinician level are publicly available, could not detect indications for risk-averse behaviour.[45] After the introduction of public reporting no decrease in the number of patients at high risk undergoing a major resection was observed. What was observed was an improvement in surgical mortality in eligible patients.

Quality assurance by learning from variation

While it remains a subject of debate, mostly among opponents of public transparency, whether the provision of outcome measures induces risk-averse behaviour, variation on indicator scores does provide an insight into current practice. Observed variation should always trigger a discussion on why the variation exists, whether it is desired or undesired variation and if it is the latter, how it should be reduced. In some cases reasons for variation cannot be distilled from the available

data. In these circumstances more information can be gained by performing in-depth investigations.

Often, caregivers do not know that they differ in the use of diagnostic modalities or treatment techniques or have different outcomes compared to their peers. Simply because they have a different perspective on their own practice, the information is not available, or because they do not often compare their outcomes with other clinicians or other clinics. In a recent study evaluating guideline deviation in aneurysm diameter thresholds, that included questionnaires among vascular surgeons, the majority of surgeons estimated to deviate from the guideline in less than 5% of their patients, while national audit data demonstrated a 15% guideline deviation ranging from 2-40% between hospitals.[46]

Feedback of performance information could lead to more realistic perspectives on the area that is now sometimes considered as 'a black box'. Especially in high-risk procedures or therapies with potential adverse outcomes, it is important to contemplate the potential expected harms and benefits. Guidelines and keynote studies do provide guidance in this decision-making. However, there often remains a fair amount of 'grey area'. For individual patients that fall outside the scope of the studied population, decisions often depend on MDTs or individual clinicians and it is plausible that varying perspectives or preferences can result in differences in treatment decisions.

In the treatment of lung cancer, such a high-risk procedure in which a careful consideration of potential harms and benefits is of utter importance is the pneumonectomy, the removal of an entire lung. While performing a pneumonectomy might lead to a curative treatment, it is known as a procedure that independently increases the risk on postoperative (mainly cardiopulmonary)

morbidity and mortality, due to the large resected volume and subsequently anatomical changes.[47–49] The estimation whether or not a pneumonectomy should and could be performed is typically a multidisciplinary matter, to which expertise of pulmonologists, surgeons and radiotherapists contribute. In **Chapter V** of this thesis, using nationwide data, a considerable between-hospital variation in the use of pneumonectomy for primary lung cancer was observed.[50] Hospital-specific results ranged from 0.0% to 25.3% pneumonectomies as a proportion of all anatomic resections, with six out of 51 hospitals identified as a significant outlier. This suggests that for individual patients the risk to receive a pneumonectomy, and its related morbidity, could depend on the hospital of choice. Variation could be the result of varying treatment considerations or unplanned pneumonectomies, reflecting surgical quality, per hospital. Potentially a further concentration of these high-risk procedures into expertise centres may be beneficial.[51,52] Centralisation of surgical lung cancer care has already been implemented in Denmark, where lung surgery is performed in four hospitals, resulting in an average volume per hospital per year five times as high as in the Netherlands.[53] Over the period of centralisation in Denmark a decrease in both the use of pneumonectomies and an improvement in 5-year survival after all surgical resections was observed, while the proportion of surgical resections increased.[11]

Another potentially harmful therapy in which substantial between-hospital variation was observed using nationwide audit data, was the use of adjuvant chemotherapy in gastric cancer.[33] Although the Dutch guidelines recommend perioperative chemotherapy in all patients with potentially resectable gastric cancer, it is considered as a burdensome therapy with only 40-60% patients completing the comply cycle of therapy in selected study populations.[54,55] Observations from the national data initiated an in-depth investigation to identify reasons for this variation. In **Chapter VI** it was demonstrated that, in addition to the

known casemix and surgical treatment factors known from the existing database, the extent of multidisciplinary care was associated with the chance to receive perioperative therapy.[33,56] In addition to this, a study using a qualitative approach with semi-structured interviews supported the hypothesis that varying perspectives or preferences of doctors can be associated with differences in treatment decisions between hospitals (**Chapter VII**).

Although for both pneumonectomies and the use of (neo)adjuvant therapy there is no set 'target' proportion to which caregivers can strive up to, information in indicator format enhances awareness among individual caregivers and MDTs. Within professional associations or expert groups, between-hospital variation can be used to support a more solid quality of care discussion contributing to quality improvement. Variation between countries in the use of neoadjuvant radiotherapy for rectal cancer was observed compared to other countries, with a relatively high nationwide use in the Netherlands.[16] National debate on this finding led to a guideline adjustment. Effects of this adjustment were evaluated, again using clinical audit data. This demonstrated a decrease in radiotherapy use from 84.2% to 64.4% in two years without compromising oncologic outcomes.[17]

Recapitulating the evolution of quality assurance in medicine

In the end of the 20th century a shift from 'authority-based medicine', in which the expertise of individual specialists had a prominent role, to 'evidence-based medicine' in which treatment decisions rely largely on scientific evidence, has taken place.[57,58] To translate the large amounts of study results into information useful in clinical practice, guidelines for the diagnosis and treatment of specific medical conditions are designed to support decision-making in order to secure quality. Parallel to this movement is the increasing use and dependency on technology, with the replacement of written medical records by electronic medical records being just one of the recent transitions in modern medical practice.[32,59] Data collection and

analysis in medicine has taken an enormous flight due to the rapid evolution in data storage and processing speed. Increased accessibility of these data enables insights into 'real-world' daily medical practice. Consequently it became clear that in daily practice there is variation of care between individual caregivers, hospitals, regions or countries.[1]

Both the increasing availability of guidelines and the insights into practice variation have triggered the debate on standardisation of care. In this on-going discussion, medical professionals are accompanied by other stakeholders in health care such as patients, policy makers, insures, and regulators. One of the controversies in standardisation of care debate is to which degree variation is acceptable or justified. In other words; which variation is harmful and which is beneficial for patients. If practice variation is the result of subjectivity or ignorance, standardisation could help to reduce unjustifiable differences. On the other hand, a strict adherence to standardisation by guidelines could suppress professional expertise or experience and patient preferences by not taking the contextual factors sufficiently into account. These contextual factors seem to become more and more important with the increasing complexity of daily medical practice with on the one hand the aging population with an increasing number of comorbidities and on the other hand the growing possibilities in diagnostic tools and combinations of treatments.

It is thus becoming clearer that the elimination of variation is not an established goal in itself. In the early years of the audits, clinicians were confronted with the existence of variation and their own performance data. There was a particular focus on care processes often defined by the medical guideline (e.g. discussion of patients in a MDT) and reduction of variation, with an important role for quality indicators. With the increasing complexity of patient populations and treatment options, making it difficult to capture within a guideline, it seems to be time to use clinical

data to study exactly those populations not captured by guidelines. Clinical data could provide valuable insights into how treatment takes place for these patients and can therefore be a tool for complex or relatively small subgroups of patients. To be of value, there should be a central role for clinicians of various medical specialisms from different locations. After the transition from "unregulated inconsistent care" to "(external) accountability" starting the end of the 20th century, it now seems time to shift the weight of data use to the core business of being a medical professional; providing the best treatment tailored to the individual patient.

FUTURE PERSPECTIVES

Although the collection of data is not a goal in itself, clinical data can help to improve the care and optimal treatment for individual patients. Following the above stated shift there are some challenges and major transitions need to be made.

Multidisciplinary evaluation of quality of care evaluation

The increasingly multidisciplinary approach of cancer treatment and the knowledge that outcomes transcend across disciplines advocates the importance of multidisciplinary evaluation of care. First of all because for patients it is the bigger picture that matters, from diagnoses (or even prevention) to treatment, recovery, recurrence and end of life, and not just any fragment of this path. Second, the parameters of various interventions need to be known to give context to outcomes of others. For example the use of neoadjuvant therapy generally increases the chance of radical resection but also on postoperative complications or in some cases even the chance of receiving surgical therapy at all. Third, with a multidisciplinary collaboration, overarching issues can be identified and addressed. For example the quality of staging before treatment, or the identification of patient groups that fall outside the scope of clinical trials and guidelines. Lastly, with each specialism

contributing to data collection the administrative burden per participating specialism could be reduced and data quality could improve.

Excellent support of technology and legalisation

The burden associated with collecting data, is one of the most prominent downsides of clinical auditing these days. It is noted that a significant proportion of data collection is performed by clinicians or paramedics themselves, therefore distracting them from direct patient care. Distributing the registration burden among various physicians in a multidisciplinary data collection could be an interim solution, however preferably to be skipped. Ideally, data should be used from already existing databases, as close to the original source as possible. The most evident source is the electronic medical record (EMR) of patients in hospital. Some hospitals already use automatic extraction of EMR data for personal quality evaluation or research. On a national or even international level, however it is still difficult to use automated data extraction, due to IT-systems varying between hospitals and systems not being designed for quality evaluation purposes or changes to do so are too costly. Maybe an even more important barrier to unlock and link already existing data for audit purposes is the increasingly stringent privacy legislation in Europe. Today, in the Netherlands, it is even not allowed to share certain information between caregivers on various locations (e.g. general practitioner, the emergency post and the hospital) or clinical practice use.[60] Legislation aiming to protect the peoples' privacy in this case hampers the linking of data and exchange of important information, thereby restricting the use of data in direct patient care and in shared audit systems (indirect patient care).

In order to achieve a more automated data collection, strict agreements on uniform definitions and structured reporting by clinicians is required, in-hospital workflow redesign will be necessary and close cooperation between doctors and hospital IT providers is indispensable. Possibilities in this field are examined by collaborating

initiatives as "registration at the source".[61] Other advances in data extraction in the medical field are the development of rapid-learning or deep-learning systems, in which unstructured data from various sources (including unstructured free text and images) are combined for automatic analyses.[62]

However, the maximum benefit from these more technical developments can only be achieved if there is legal support. This was emphasised recently in the advisory report "governance of quality registrations". In this report the committee, led by Van der Zande, proposes an amendment in the law to support the processing, storage, linking and use of data for quality registrations.[63] To advance health care quality improvement through clinical auditing, excellent support is needed through both technology and legislation.

Integrating quality evaluation and improvement in daily practice of professionals

Clinicians and other stakeholders involved in healthcare provision need time and education in order to be able to use clinical practice data to improve their care. Like EBM, which is nowadays incorporated in the training of medical students and medical specialists, the analysis or at least the interpretation of clinical practice data are skills doctors should acquire. Currently, most local and national healthcare quality improvement initiatives involving clinicians largely depend on their personal interest, initiative and willingness to invest private time in these projects. If quality improvement is to be considered a part of medical practice, clinicians should be offered the opportunities to truly incorporate it into their practice. While feedback data offered by audit systems are traditionally offered in a fixed format, more dynamic, interactive systems should be developed to optimise information provision for clinicians and stimulate the internal use of data for quality improvement cycles. Medical teams can use this system to facilitate a feedback culture in their hospital through data-driven discussions ('Codman sessions') or to integrate in other quality

focussed meetings such as the morbidity and mortality conferences. As other studies investigating quality assurance tools demonstrate, a true culture focussed on quality improvement might be the most vital ingredient to achieve the greatest possible success for clinical auditing.[25,64]

CONCLUSION

In this thesis the development of clinical audit systems as tools to evaluate quality of care of various diseases and multidisciplinary treatments is demonstrated. They have the potential to catalyse improvement on both local and national level. With the rising complexity of cancer care and increasing use of multidisciplinary treatment strategies, evaluation of the 'bigger picture' should be maximised with taking contextual factors into account. In complex populations, treatment variation between hospitals can partly be explained by the degree of multidisciplinarity of care, but also seems to depend on individual choices or preferences of doctors. Especially in specific patient populations that are typically underrepresented in the more 'traditional' clinical trials (e.g. patients with multi-morbidity or combinations of treatments), population-based clinical data can have an additional value for more personalised treatments. When challenges of registration burden, largely concerning information technology and privacy legalisation are solved, discipline- and hospital- transcending quality information can release the true improvement potential in cancer care. In the next years focus should shift from merely the reduction of variation to the rational or value of variation. To consider continuous quality improvement as an essential part of medicine, all stakeholders in healthcare have to be willing to truly incorporate data-driven improvement cycles into daily clinical practice.

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CHAPTER 9

Dutch summary

WAARBORGING VAN KWALITEIT IN DE ONCOLOGISCHE ZORG; EEN UITDAGENDE MULTIDISCIPLINAIRE VERANTWOORDELIJKHEID

Zowel in Nederland als in de rest van de wereld neemt het aantal patiënten met kanker toe. Wereldwijd steeg het aantal nieuwe patiënten met kanker van ongeveer 14 miljoen in 2012 naar 18 miljoen in 2018. De meest voorkomende vormen van kanker waren: borst-, long-, dikke darm- en maagkanker, waarbij long- en maagkanker samen verantwoordelijk waren voor ongeveer een kwart van de sterfte door kanker. Naar verwachting zal het aantal nieuwe patiënten met kanker doorstijgen naar 24 miljoen in 2035.

Multidisciplinaire oncologische zorg

Chirurgie speelt een belangrijke rol in de behandeling van veel kankersoorten. Echter wordt het steeds duidelijker dat andere behandelingen hiernaast bijdragen aan een langere overleving of zelfs een betere kans op genezing. Het gaat dan om behandelingen zoals chemotherapie, radiotherapie (bestraling), hormoontherapie, immunotherapie, doelgerichte therapie, of combinaties van behandelingen. Deze behandelingen kunnen voor (neoadjuvant) of na de operatie (adjuvant) worden gegeven. In sommige gevallen wordt de operatieve behandeling in zijn geheel vervangen door een ander type behandeling.

Met deze ontwikkelingen is de zorg voor patiënten met kanker een steeds complexere medische discipline, waarbij in het zorgproces steeds meer verschillende specialismen en paramedici betrokken zijn. Het werken in multidisciplinaire teams en houden van Multidisciplinaire Overleggen (MDO's) is daarom een gebruikelijk en essentieel onderdeel geworden van de standaard oncologische zorg.

Kwaliteitsevaluatie in de multidisciplinaire oncologische zorg

In Nederland werd een aanzienlijke variatie in de behandeling en uitkomsten van verschillende kankersoorten op ziekenhuisniveau voor het eerst aangetoond in

het rapport 'Kwaliteit van Kankerzorg'. Redenen voor de variatie konden, door de beperkte gegevens die er bekend waren, nauwelijks achterhaald worden. Om een structureler inzicht hierin te krijgen werden landelijke 'Clinical Audits' opgezet. Een Clinical Audit is een systematische analyse van zorgprocessen en de resultaten daarvan, met het doel deze inzichtelijk te maken en continue te kunnen verbeteren. In dit systeem worden gegevens uit de praktijk vergeleken met vooraf gedefinieerde kwaliteitsindicatoren en wordt deze informatie continue teruggekoppeld aan deelnemende zorgverleners.
In de afgelopen jaren is er met behulp van Audit gegevens met name onderzoek gedaan naar – de kwaliteit van en variatie in – de chirurgische behandeling van patiënten met kanker. Ook het gebruik van Clinical Auditing als kwaliteitsinstrument was voornamelijk gericht op de chirurgisch zorg. Over de kwaliteit en variatie van de andere oncologische behandelingen en combinaties ervan (multimodale therapie) is echter betrekkelijk weinig bekend.

Dit proefschrift richt zich daarom in **deel I** op de ontwikkeling van Clinical Audits voor de evaluatie van multidisciplinaire oncologische zorg en in **deel II** op de variatie in multimodale behandelstrategieën tussen ziekenhuizen. Voor dit laatste werden twee bij uitstek multidisciplinair behandelde typen kanker uitgelicht: long- en maagkanker.

Deel I. Kwaliteitsevaluatie in multidisciplinaire oncologische zorg

De fundamentele gedachten waarop Clinical Auditing is gebaseerd gaan terug naar meer dan 100 jaar geleden, met ideeën van onder andere arts Thomas Percival (1803), verpleegster Florence Nightingale (1820) en arts Ernest Codman (1869). Het gedachtegoed van Codman – waarbij "ieder ziekenhuis de behandelde patiënten dient te vervolgen zo lang als nodig is om te weten of de behandeling succesvol

is geweest en indien het niet succesvol was waarom niet, om soortgelijke fouten in de toekomst te doen voorkomen" – wordt beschouwd als de basis voor de hedendaagse Clinical Audits.

De opzet van landelijke Clinical Audits

Hoofdstuk 2 geeft inzicht in hoe Codmans concept landelijk is geïmplementeerd in de Nederlandse gezondheidszorg. De in 2009 vanuit de beroepsgroep opgerichte Dutch ColoRectal Audit (DCRA, voorheen de Dutch Surgical Colorectal cancer Audit - DSCA) was het eerste landelijke initiatief om de chirurgische kwaliteit van zorg, in dit geval voor patiënten met darmkanker, te kunnen monitoren en verbeteren. Het bleek een succesvol initiatief; binnen enkele jaren werden er landelijke verbeteringen in processen en uitkomsten van zorg voor deze groep patiënten gezien. Op basis van de blauwdruk van de DCRA werden vervolgens andere landelijke audits opgericht, waarbij het Dutch Institute for Clinical Auditing (DICA, opgericht in 2010) als overkoepelende faciliterende organisatie optrad. Wat kenmerkend is voor deze audits is de centrale rol van artsen in de opzet en onderhoud ervan, de nauwe samenwerking met andere partijen in de gezondheidszorg (zoals patiëntenverenigingen en zorgverzekeraars), de kort-cyclische feedback informatie die geboden wordt, met de mogelijkheid om te spiegelen aan andere zorgverleners en de landelijke dekking van het systeem. De leidende rol van artsen en de samenwerking met andere partijen is hierbij essentieel om betekenisvolle kwaliteitsinformatie te verkrijgen.

In minder dan 10 jaar tijd werden meer dan 20 landelijke audits opgericht, waarbij ook een steeds groter aantal en meer diverse groep van artsen betrokken is. In deze jaren werden voor meerdere ziektebeelden en behandelingen verbeteringen op landelijk niveau waargenomen en nam de variatie tussen ziekenhuizen af. Met de grote hoeveelheid gegevens uit de klinische praktijk bleek het goed mogelijk om wetenschappelijk onderzoek te doen, waarbij deze 'real-world data' een

waardevolle aanvulling vormen op de meer traditionele studies (trials) in vooraf geselecteerde patiëntengroepen. Bovendien vormen de gegevens een basis voor een meer gegronde discussie over de kwaliteit van zorg.

De opzet van multidisciplinaire Clinical Audits

Initieel werden de meeste audits opgezet voor de evaluatie van de chirurgische behandeling van kanker. In de loop van de jaren is het interessegebied uitgebreid naar de evaluatie van niet-kwaadaardige ziekten (bijvoorbeeld vaatziekten of aandoeningen van het zenuwstelsel) en ook niet-chirurgische behandelingen. In navolging van het toenemende belang van multidisciplinaire zorg streven audits steeds meer naar een integrale evaluatie van het gehele zorgtraject. Een van de eerste Nederlandse nationale audits die dit in praktijk bracht was de Dutch Lung Cancer Audit (DLCA). In **hoofdstuk 3** beschrijven we hoe deze is ontstaan en welke informatie de audit de eerste jaren heeft opgeleverd. De eerste subregistratie van de DLCA werd al in 2012 gestart. Deze was met name gericht op de chirurgische behandeling van longkanker. In 2014 werd hiernaast een subregistratie gestart om de behandeling middels radiotherapie te evalueren. De longartsen, die een belangrijke rol spelen in de diagnosestelling en behandeling middels o.a. chemo- en immunotherapie, hebben sinds 2016 een subregistratie om hun zorg te kunnen evalueren. Sinds 2016 zijn dus alle behandelende specialismen vertegenwoordigd en actief betrokken om de kwaliteit van zorg te monitoren en te verbeteren.

De DLCA werd in korte tijd landelijk geïmplementeerd, waarbij in de eerste jaren een groei werd gezien in het aantal deelnemende ziekenhuizen en het aantal geregistreerde patiënten. Hoewel er het eerste jaar zeker nog geen complete registratie was van alle patiënten met longkanker (ongeveer 40% van de landelijke incidentie), gaf het al wel een goed inzicht in de dagelijkse praktijk van longkankerzorg. Bijvoorbeeld in het gebruik van minimaal-invasieve operatietechnieken (kijkoperaties) om de tumor te verwijderen lijkt Nederland

voor te lopen op andere landen, waarbij uitkomsten zoals postoperatieve sterfte vergelijkbaar zijn. In het correct stadiëren van de tumor voorafgaand aan de behandeling lijken dan weer verbetermogelijkheden te liggen. Daarnaast werd het duidelijk dat de multidisciplinaire samenwerking in de DLCA het mogelijk maakt om nieuwe kennis gemakkelijker op een landelijk niveau te implementeren. Zo is bijvoorbeeld de invoering van de nieuwe indeling voor tumorstadiëring (TNM-stadiëring) al enkele maanden na de internationale publicatie ervan in gebruik genomen in de Nederlandse praktijk.

Hoewel de eerste stappen in de ontwikkeling van een multidisciplinaire audit zijn gezet, is de belangrijkste uitdaging van de DLCA om de subregistraties zodanig te integreren dat zowel de verzameling als het gebruik van gegevens mogelijk is vanuit verschillende specialismen uit verschillende ziekenhuizen, leidend tot maximale mogelijkheden wat betreft kwaliteitsevaluatie voor een zo minimaal mogelijke inspanning.

Succesfactoren en valkuilen

Wat kenmerkend is voor de in **hoofdstuk 2 en 3** omschreven audits is de centrale rol die artsen in het proces spelen, dit in tegenstelling tot veel buitenlandse systemen waarbij de overheid of externe organisaties sturend zijn. Zowel in de ontwikkeling en implementatie ervan als in de verdere ontwikkeling zijn clinici de drijvende krachten. Zij vormen de verbinding met de praktijk en weten welke vraagstukken er spelen in de beroepsgroep. Hiernaast is ook de samenwerking met de andere partijen in de gezondheidszorg belangrijk om kwaliteitsinformatie te verkrijgen die voor meerdere groepen van betekenis is. Gegevens uit de audits worden door die andere partijen gezien als een belangrijke bron om verder beleid te voeren.

De grote stimulans voor clinici om deel te nemen aan de audits is de feedback-informatie die zij krijgen over de kwaliteit van de door hen geleverde zorg. Het integreren van de audits in het landelijke kwaliteitsbeleid van beroepsverenigingen

van medisch specialisten, bijvoorbeeld via de aanlevering van informatie over 'participatie-indicatoren', en het stapsgewijs vrijgeven van bepaalde indicatoruitkomsten op ziekenhuisniveau hebben een snelle implementatie van de audits gestimuleerd. Hierdoor zijn de gegevens vollediger, beter bruikbaar en leveren ze belangrijke benchmarkinformatie, in vergelijking met initiatieven waarbij ziekenhuizen ieder voor zich, op eigen initiatief, gegevens registreren.
Voordelen voor de beroepsgroepen, wetenschappelijke verenigingen van medisch specialisten, om zich aan te sluiten bij een overkoepelende organisatie zoals DICA zijn: de ervaring op het gebied van methodologie en logistiek, de aanwezige data-infrastructuur (en de juridische- en privacyaspecten die hiermee samenhangen), een reeds gevormd netwerk van medisch specialisten en ziekenhuizen (en de afspraken die daar mee samenhangen) en het vermijden van dubbele verzameling van gegevens.

De huidige audits hebben vooralsnog wel enkele punten die verbetering behoeven. Een belangrijk en veelgenoemd knelpunt is de administratieve last die gepaard gaat met het verzamelen van de gegevens voor de audit, wat voor een deel door zorgverleners zelf gedaan wordt. Een oplossing hiervoor is de automatische extractie van gegevens uit de reeds bestaande informatie, vastgelegd in de elektronische patiëntendossiers in ziekenhuizen. Echter vormt de steeds strengere Nederlandse en internationale privacy wetgeving hier wel een moeilijkheid in, met name in het combineren en delen van medische gegevens tussen verschillende ziekenhuizen. Daarnaast zijn strikte afspraken met IT-leveranciers (hoe worden gegevens verzameld, opgeslagen en uitgewisseld) en tussen verschillende specialismen (wie is verantwoordelijk voor het vastleggen van welke gegevens op welke wijze) noodzakelijk om dergelijke geautomatiseerde gegevensextractie mogelijk te maken.

IT kan ook een belangrijke rol spelen om de gegevens makkelijker bruikbaar te maken voor artsen, bijvoorbeeld door de ontwikkeling van gebruiksvriendelijke interactieve systemen, waarbij het voor de arts mogelijk is om met een aantal muisklikken zijn klinische vraagstukken te beantwoorden. Hierin worden momenteel de eerste stappen gezet.

Een ander continue spanningsveld is de mate waarin gegevens gedeeld worden met andere partijen in de gezondheidszorg. In eerste instantie dienen gegevens uit de audit verbeterdoeleinden voor artsen. Maar zoals gezegd is er ook vanuit andere partijen grote interesse voor deze gegevens. In potentie zou het kunnen delen van uitkomsten risicomijdend gedrag in de hand kunnen werken, zoals bijvoorbeeld het niet meer opereren van patiënten met een complexere problematiek, zowel wat betreft hun performance status, comorbiditeiten of leeftijd, als een gevorderd stadium van de ziekte. Gelukkig laten zowel evaluaties van de audit data over de jaren als internationale onderzoeken geen aanwijzingen zien die wijzen op dergelijk risico-avers gedrag. Voor zorgverleners moet het echter altijd mogelijk blijven om hun gegevens in een veilige omgeving met elkaar te delen en te evalueren voordat ze met andere partijen gedeeld worden.

Uitkomsten vergelijken

Om ziekenhuizen betrouwbaar te kunnen vergelijken, en bijvoorbeeld het eerder genoemde risicomijdend gedrag te voorkomen, is het belangrijk om rekening te houden met de zorgzwaarte van de patiënten in dat ziekenhuis. Die zorgzwaarte wordt bepaald door een combinatie van patiënt- en ziektekenmerken die samen 'casemix' worden genoemd. In **hoofdstuk 4** hebben we onderzocht in welke mate het corrigeren voor deze casemix factoren van belang is bij het evalueren van longkankerchirurgie. Welke factoren in de casemix worden meegenomen wordt bepaald op basis van eerder onderzoek, kennis van experts en statistische methoden. Voor dit onderzoek hebben we gebruik gemaakt van gegevens uit het

chirurgische gedeelte van de DLCA. In totaal werden gegevens van 8040 patiënten, verspreid over 51 Nederlandse ziekenhuizen meegenomen in de analyse.

Factoren die van invloed bleken op de uitkomstmaten postoperatief overlijden en gecompliceerd beloop waren: leeftijd, twee fitheidsscores (ASA-classificatie en ECOG-score), longfunctie, de hoeveelheid longweefsel die verwijderd moest worden om de tumor te verwijderen, het tumorstadium en het type longkanker dat uit het postoperatieve weefselonderzoek bleek. Tussen de verschillende ziekenhuizen was er een aanzienlijke variatie in de individuele factoren. Op basis van de combinatie van deze factoren, de algehele zorgzwaarte in een ziekenhuisgroep, werden de kansen voorspeld op overlijden of een gecompliceerd beloop na de operatie. Ook dit berekende risico varieerde beduidend tussen de ziekenhuizen, waarbij de risico's uiteenliepen van 1.4% tot 3.2% voor postoperatief overlijden en 11.5% tot 17.1% voor een postoperatief gecompliceerd beloop. Door de zorgzwaarte van de patiëntpopulatie in het ene ziekenhuis was de kans op overlijden bij voorbaat dus al twee keer zo hoog als in het andere ziekenhuis. Deze variatie in casemix tussen ziekenhuizen benadrukt het belang van een juist correctiemodel, wanneer ziekenhuizen vergeleken worden op uitkomstindicatoren. Aansluitend werden in deze studie modellen voorgesteld die bruikbaar zijn voor casemix correctie in de huidige audit.

Wel moet opgemerkt worden dat er om te kunnen corrigeren een uitgebreidere gegevensuitvraag nodig is (dus meer registratielast) en dat men moet waken voor 'over-correctie', waarbij er bijvoorbeeld keuzes die de zorgverlener in het proces maakt worden weg gecorrigeerd. Daarnaast blijft het voor individuele ziekenhuizen altijd van belang om zelf ook naar hun ongecorrigeerde uitkomsten te blijven kijken.

Deel II. Variatie in de multidisciplinaire oncologische zorg

Waar er voorheen weinig bekend was over hoe de zorg in de praktijk daadwerkelijk werd geleverd, hebben audits hier nieuwe inzichten in gegeven. Zorgverleners zijn zich niet altijd bewust van hun eigen prestaties en of ze verschillen van collega's of andere ziekenhuizen in het gebruik van bepaalde diagnostiek, behandelmethoden of uitkomsten. Dit omdat de informatie niet beschikbaar is of niet wordt gebruikt om naar verschillen te kijken. Het perspectief dat clinici hebben op hun zorg in de praktijk kan daardoor behoorlijk afwijken van wat data laat zien. Zo schatte, in een recent gepubliceerde studie, meer dan driekwart van de 44 ondervraagde vaatchirurgen in dat ze bij minder dan 5% van de door hun geopereerde patiënten afweken van de richtlijn, terwijl dit uit de landelijke data bij 15% het geval bleek te zijn, variërend van 2-40% van de deelnemende ziekenhuizen.

Variatie gebruiken voor verbeteringen

Met de gegevens uit de audit is het niet alleen mogelijk voor individuele zorgverleners of ziekenhuizen om zichzelf te monitoren en te verbeteren, ook op landelijk niveau of zelfs internationaal kan er gekeken worden naar mogelijkheden voor verbetering. Het bestaan van verschillen in gebruik van diagnostiek, bepaalde behandelmethoden of uitkomsten tussen ziekenhuizen, regio's of landen kan er op wijzen dat de zorg op de ene plek efficiënter is ingericht of van betere kwaliteit is dan op een andere plek. Een internationale vergelijking die werd gemaakt in het gebruik van neoadjuvante radiotherapie bij endeldarmkanker liet bijvoorbeeld zien dat het gebruik in Nederland aanzienlijk hoger was dan in andere landen. Dit bracht een discussie op gang of deze behandeling, met risico op bijwerkingen, daadwerkelijk voor alle patiënten aan wie deze gegeven werd noodzakelijk was en werd de Nederlandse richtlijn aangepast.

Het geven van terugkoppeling over eigen prestaties geeft meer realistische perspectieven op de geleverde zorg. Met name bij risicovolle procedures of behandelingen in groepen kan deze informatie van belang zijn, om een goede afweging van de voor- en nadelen te maken. Onderzoeksresultaten van gerandomiseerde studies geven vaak een richtlijn voor de besluitvorming, echter is dit vaak gebaseerd op een zeer geselecteerde groep patiënten, die aan de vaak strenge inclusiecriteria van de studie voldeden. Hierdoor blijft er een behoorlijk grijs gebied over voor patiënten die qua karakteristieken buiten de studies vallen. Het is niet gek om te bedenken dat beslissingen die voor deze patiënten genomen worden, tussen de verschillende ziekenhuizen en zorgverleners kunnen verschillen. Door op verschillen in te zoomen kan er een discussie op gang gebracht worden of het gaat om gewenste of ongewenste variatie en als de variatie ongewenst is hoe deze kan worden verminderd. Soms zijn de beschikbare gegevens ontoereikend en is meer diepgaand onderzoek nodig.

Variatie in gebruik hoog-risico operatie voor longkanker

In de behandeling van longkanker is een dergelijke risicovolle procedure de pneumonectomie, het verwijderen van een gehele long. De kans om postoperatief te overlijden na deze procedure is ongeveer drie keer hoger in vergelijking met minder invasieve operaties. De kans op ernstige complicaties is na een pneumonectomie ook aanzienlijk hoger. Het gebruik van dit type operatie is daarom voorbehouden aan patiënten met een voldoende conditie, bij wie het niet mogelijk is om de tumor volledig te verwijderen middels een kleinere operatie. Een zorgvuldige afweging van mogelijke voor- en nadelen is bij dit type operatie van groot belang en is vrijwel altijd een multidisciplinaire kwestie.

Het was onduidelijk of het risico van patiënten op het ondergaan van een pneumonectomie gelijk is in de Nederlandse ziekenhuizen die longkankeroperaties doen. In **hoofdstuk 5** onderzochten we daarom wat de Nederlandse praktijk is in

het gebruik van de pneumonectomie als behandeling van longkanker en bekeken we of er verschillen waren tussen ziekenhuizen in het gebruik ervan. Gegevens van meer dan 8.400 patiënten, geopereerd tussen 2012-2016, werden geanalyseerd. Op landelijk niveau onderging 7,8% van al deze patiënten een pneumonectomie. Per ziekenhuis varieerde dit aantal van 0,0% tot 25,3%. De landelijke postoperatieve sterfte na een pneumonectomie was 7,1%, terwijl dit bij kleinere operaties 1,7% was. Factoren geassocieerd met een grotere kans op het ondergaan van een pneumonectomie waren: lagere leeftijd, mannelijk geslacht, geen hart- of longaandoeningen in de voorgeschiedenis, een tumor die zich in de linker long bevindt, een verder gevorderd tumorstadium en een tumor van het type plaveiselcelcarcinoom. Op basis van deze factoren werd berekend wat het verwachtte aantal patiënten per ziekenhuis zou zijn dat een pneumonectomie zou ondergaan. Dit aantal hebben we vergeleken met het aantal patiënten dat daadwerkelijk een pneumonectomie onderging. Van de 51 ziekenhuizen, bleken er 3 te zijn die significant meer pneumonectomieën uitvoerden dan op voorhand verwacht werd en 3 die er significant minder uitvoerden. Deze laatste 3 ziekenhuizen voerden minder dan de helft van het vooraf verwachtte aantal pneumonectomieën uit en wisten dus meer patiënten te opereren met een minder belastende operatie. Variatie in het gebruik van deze operatie tussen ziekenhuizen zou een gevolg kunnen zijn van verschillen in behandelingsoverwegingen tussen behandelaars uit de verschillende ziekenhuizen. Ook zou het kunnen zijn dat in sommige ziekenhuizen tijdens de operatie vaker moet worden uitgeweken naar een pneumonectomie, bijvoorbeeld omdat er tijdens de operatie complicaties optreden. Door het aanbieden van informatie in indicator-vorm, specifiek gericht op het pneumonectomie-gebruik, willen we behandelaars bewust maken van de verschillen en hun eigen presteren hierin, om zo de zorg te verbeteren.

Variatie in gebruik van chemotherapie rondom maagkanker operaties

Een andere behandeling waarbij het – gezien de grote potentiële voor- en nadelen – belangrijk is om een goede afweging te maken, is (neo)adjuvante chemotherapie in de behandeling van maagkanker. Studies wijzen uit dat het geven van chemotherapie zowel voor als na de operatie een winst in overleving oplevert. Echter is ook bekend dat deze behandeling aanzienlijke bijwerkingen kan hebben. Zelfs in studieverband, wat doorgaans gezondere patiënten zijn, volbrengt slechts 40-60% van alle patiënten de gehele behandeling. Het advies in de Nederlandse richtlijn is dan ook om alle patiënten – met een in opzet curatieve behandeling van maagkanker – perioperatief (zowel voor- als na de operatie) te behandelen, "mits de verwachting is dat de patiënt dit qua conditie en comorbiditeit aankan".

Uit gegevens van de landelijke audit voor maag- en slokdarmkanker, de DUCA, blijkt het percentage patiënten dat in de dagelijkse praktijk perioperatieve behandeling krijgt, circa 35%, lager dan de genoemde studies. Daarnaast bleek er een aanzienlijke variatie te bestaan tussen ziekenhuizen in de mate waarin ze deze perioperatieve chemotherapie toepassen. Zoals verwacht speelden casemix factoren hierbij een rol. Echter was de variatie tussen de ziekenhuizen hiermee niet geheel verklaard.
In **hoofdstuk 6 en 7** hebben we onderzoek gedaan naar onderliggende verklaringen voor de ziekenhuisverschillen in het gebruik van perioperatieve therapie. Aangezien de DUCA vooral gericht was op de evaluatie van de operatieve behandeling van maagkanker, kon uit de gegevens van de DUCA onvoldoende informatie gehaald worden over andere vormen van behandeling en het besluit daartoe. In het onderzoek voor **hoofdstuk 6** hebben we aanvullende gegevens verzameld uit de medische dossiers van patiënten in een aantal ziekenhuizen, die waren geselecteerd op basis van het percentage patiënten dat perioperatieve behandeling onderging, waarbij we de twee uiterste groepen met elkaar vergeleken hebben. Dossiers van 429 patiënten werden onderzocht. In de 4 ziekenhuizen met het hoogste percentage

perioperatieve therapie onderging 40,4% van de patiënten perioperatieve therapie, tegenover 16,0% in de 5 ziekenhuizen met het laagste percentage. Uit deze studie bleek een verband tussen de mate van multidisciplinariteit van zorg en het geven van perioperatieve behandeling. Wanneer een patiënt drie of meer verschillende specialismen had gezien voorafgaand aan het MDO was de kans op het starten van perioperatieve behandeling meer dan twee maal zo groot. Verder zaten er tussen de ziekenhuisgroepen onder andere verschillen in het aantal patiënten dat deelnam aan een studie en bleken in de groep ziekenhuizen met het laagste percentage perioperatieve therapie meer patiënten een ernstige bijwerking van de chemotherapie te ervaren (46,3% versus 25,7%). Op basis van deze studie lijkt het dus niet alleen van belang om patiënten multidisciplinair te bespreken, maar ook om de patiënt daadwerkelijk door meerdere specialismen te beoordelen, om zo een goede inschatting te kunnen maken voorafgaand aan de behandeling.

Hiernaast bestond het vermoeden dat de variatie tussen ziekenhuizen zou kunnen berusten op verschillen in voorkeuren tussen behandelaars. Dit is echter lastig te toetsen met het kwantitatieve onderzoek dat met behulp van databases of patiëntendossiers gedaan kan worden, aangezien overtuigingen en gedrag hierin niet goed te vatten zijn. In **hoofdstuk 7** beschrijven we hoe we middels interviews (een kwalitatieve onderzoeksmethode) met in totaal 17 chirurgen en oncologen, deze hypothese hebben kunnen exploreren.

In totaal werden er 33 verschillende barrières en stimuli genoemd voor het geven van perioperatieve therapie in de behandeling van maagkanker, waarbij er meer barrières werden benoemd. Een aantal barrières en stimuli die uit dit onderzoek kwamen: '(on)geloof in de behandeling', 'zwaarte van de behandeling', 'moeilijke implementatie van de studieresultaten', 'toewijding van specialisten', 'centralisatie van zorg' en 'regionale samenwerking'. Hoewel er geen grote verschillen tussen de twee ziekenhuisgroepen waren wat betreft het aantal genoemde barrières en

stimuli en de thema's die deze omvatten, leken er wel genuanceerde verschillen te bestaan in de geciteerde antwoorden.

Suggesties om ongewenste variatie tussen ziekenhuizen te beperken op basis van dit onderzoek zijn: streven naar een actuele (inter)nationale richtlijn, vlottere consensus over de implementatie van nieuwe onderzoeksresultaten, concentratie van ook de perioperatieve zorg en geoptimaliseerde (regionale) samenwerking.

Conclusie en toekomstperspectief

Dit proefschrift geeft inzicht in de ontwikkeling van Clinical Audits voor de evaluatie van – multidisciplinaire – kwaliteit van zorg en als katalysator van zowel lokale als landelijke verbeteringen. Met de toenemende complexiteit van de oncologische zorg, waarbij de zorg voor patiënten een steeds meer multidisciplinaire verantwoordelijkheid wordt, is het van belang om een geïntegreerde multidisciplinaire evaluatie mogelijk te maken. In complexe populaties of behandelingen kan ziekenhuisvariatie samenhangen met de mate van multidisciplinariteit van de zorg. Daarnaast lijkt ook de voorkeur van individuele behandelaars een rol te spelen in ziekenhuisvariatie.

Er is een aantal stappen te nemen om de Clinical Audits van maximale waarde te kunnen laten zijn in de kwaliteitsborging van multidisciplinaire oncologische zorg. Het verminderen van de registratielast voor zorgverleners is één van de belangrijkste punten. Om tot een geïntegreerde multidisciplinaire gegevensverzameling en -evaluatie te komen moeten vraagstukken opgelost worden op het gebied van o.a. privacywetgeving, eenduidige gegevensverzameling en overeenkomsten tussen specialismen en ziekenhuizen. De focus die in de beginjaren van Clinical Auditing met name heeft gelegen op reductie van variatie zal in de komende periode moeten verschuiven naar meer focus op de rationale achter variatie, het onderscheid tussen gewenste en ongewenste variatie en de waarde van juist gewenste variatie. Het daadwerkelijk integreren van kwaliteitsevaluatie in de dagelijkse praktijk van

zorgverleners en het opnemen als onderdeel van de moderne geneeskunde is van belang om de volledige potentie te kunnen benutten voor de verbetering van de patiëntenzorg.

APPENDICES 10

Curriculum vitae

List of publications

Dankwoord

CURRICULUM VITAE

Naomi Beck was born on the 1st of August 1988 in Leiden. With her family she lived in Yogyakarta, Indonesia, for two and a half years. The rest of her childhood she spent in Hilvarenbeek, Noord-Brabant. After graduating from the Odulphuslyceum (Tilburg) in 2006, she first travelled through Middle and South America for eight months, volunteering, studying Spanish and learning about the world.

Being unfortunately excluded to study Medicine, she studied Human Movement Science for one year. In 2008 she started studying Medicine at the Erasmus University in Rotterdam (EUR). Combining her interests for scientific research and surgery with her passions for travelling and sports, she started a research project studying knee-osteoarthritis after ACL-reconstruction at the University of Queensland (UQ), Brisbane, Australia. This project, supervised by dr. K.M. Crossley and dr. M. van Middelkoop, was the start of a still standing research collaboration between the UQ and the EUR.

After graduating Medical School in 2015, she got the opportunity to focus on research with a combined PhD program at the Leiden University Medical Centre and the Dutch Institute of Clinical Auditing under the supervision of promotor prof. R.A.E.M. Tollenaar and co-promotores dr. W.H. Schreurs and dr. M.W.J.M. Wouters. Her research was focussed on the evaluation of multidisciplinary cancer care and partly funded by the Dutch Cancer Society (KWF kankerbestrijding). Simultaneously she developed and coordinated multiple clinical audits as a part of national quality improvement projects.

While finishing her PhD thesis, she started as a Medical Doctor at the Surgical Department in 2018, first in the Dijklander Hospital in Hoorn and later in the Amsterdam UMC, where she is currently working.

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