A systematic review of the economic impact of the centralisation of cancer services

Ke, K.M.*, Hollingworth, W.** and Ness, A.R.*

Address:
* School of Oral and Dental Sciences, University of Bristol, Lower Maudlin Street, Bristol, BS1 2LY, United Kingdom
** School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, United Kingdom

Abstract

Background: The centralisation of cancer services has been shown to improve the outcome and quality of care for people with some tumours. The NHS has recommended centralisation of cancer services particularly for less common cancers. However, there is uncertainty about the economic impact of centralisation on the health service and patients. We identified published papers that have investigated whether or not the centralisation of cancer services results in economies of scale, is cost-effective, or transfers costs of care from the healthcare system to patients and their carers.

Methods: We conducted a systematic review of journal articles based on a comprehensive keyword based search in Embase, Medline, NHS EED, and CINAHL.

Results: Nineteen studies (one randomised crossover trial, two prospective cohort, eleven cross-sectional, five modelling) fulfilled the eligibility criteria. Thirteen studies were US-based, three were UK-based, two were in Taiwan, and one in the Netherlands. Evidence from thirteen studies suggests that increasing surgeon volumes are associated with cost reductions, though one study suggested that this relationship is U-shaped and the evidence is not consistent for hospital volumes and costs. Of the four studies that investigated cost-effectiveness, only one study demonstrated that centralisation was cost-effective with an incremental cost utility ratio of US$5,029/QALY gained. Consistent evidence from four studies suggested that centralised services shift the costs of care to patients.

Conclusion: Current evidence on the economic impact of centralisation of cancer services on the health service and patients is limited and of poor quality. Therefore, it remains unclear whether centralisation results in economies of scale and is cost-effective. Future research should be based on a clear definition of the different components of centralisation in order to determine which aspects of centralisation are efficient and for which cancer subgroups.

1. Introduction

Since the publication of the seminal paper by Luft *et al*.(1979)[1] a number of studies have investigated the association between surgical volume and clinical outcomes for various diseases including cancer. Studies reporting improved clinical outcomes with increasing operative volume have led many to advocate centralisation of cancer services.[2-6] This is typically characterised by a reorganisation of care onto fewer sites, with care provided by a multidisciplinary team of specialists with higher throughput of patients.[7]

In the UK, the Calman-Hine report[8] recommended concentration of cancer care and the creation of site-specialist multidisciplinary teams. The report also recommended that treatment for less common cancers and those where treatment is technically demanding or capital intensive should be offered in regional cancer centres. The more recent Cancer Reform Strategy[9] reinforced this policy by stating that services should be centralised where it was necessary to improve patient outcomes. Comparable trends of centralisation have occurred in some parts of the United States and Europe.[10-11]

An important consideration in this reorganisation of cancer services that has been neglected is its economic implications. There are three main economic questions that are relevant in this context. Firstly, to what extent does the centralisation of cancer services increase or decrease costs to the health care system? Cost savings could arguably come about as a result of improved efficiency due to economies of scale, whereby the average cost per patient treated decreases as the volume of activity increases. However, increasing scale also brings additional costs (diseconomies), such as additional bureaucracy associated with managing a larger organisation. Secondly, to what extent is the centralisation of cancer services cost-effective? In the introduction of any new strategy, be it technological or organisational, it is crucial to establish if resources have been utilised in a worthwhile manner in terms of the balance between benefits and costs. Thirdly, to what extent does the centralisation of cancer services shift the costs of care from the health care system to patients and their carers? These costs include transport expenses and time spent travelling longer distances to receive treatment.

We conducted a systematic review of economic studies of centralisation of cancer care to summarise the evidence on cost reduction, cost effectiveness and shifting of costs to patients or carers.

2. Methods

The aim of our systematic review was to examine research that has investigated the economic implications of the centralisation of cancer care in order to address the following three review questions:

1. Does centralisation of cancer services reduce health service cost per patient treated?
2. To what extent is the centralisation of cancer services cost-effective?
3. Has centralisation of cancer services shifted costs of care onto patients and their carers?

Search strategy

We searched the databases Embase and Medline (both via the Ovid interface), NHS EED, and CINAHL for relevant articles published from the date of inception of each database to July 2010. The search strategy consisted of combinations of free text and MeSH terms related to the economics of centralisation of cancer care services (see Appendix 1). The search was limited to journal articles published in the English language. Reference lists from included studies and other relevant publications, including reviews, were manually checked for citations missed by the electronic search.

Selection process

Initially, titles and abstracts of the retrieved studies were scanned by one author (KMK) to assess their suitability for inclusion. When a study appeared to meet the eligibility criteria (Table 1) or information was insufficient to exclude it, full text articles were obtained for further review. Studies which included patients from many different diagnostic groups, including cancer, were excluded unless costs or cost-effectiveness were reported separately for cancer patients. The final selection of papers for inclusion in the review was established through discussion and consensus by two authors (KMK and WH).

Data extraction and critical appraisal

A data extraction template, developed using the guidelines provided by the Centre for Reviews and Dissemination,[12] was used to extract the following data alongside the critical appraisal of original studies: country of investigation; objective of the study; study intervention and comparator; study design and setting; target population characteristics; sources and quality of clinical data, if applicable; sources and quality of cost data; methods for dealing with uncertainty; and study results.

Due to the varied nature of the studies, we provide a narrative summary of the study results for each objective of our review rather than a formal meta-analysis and pooling of results.

Table 1: Inclusion and exclusion criteria for systematic review

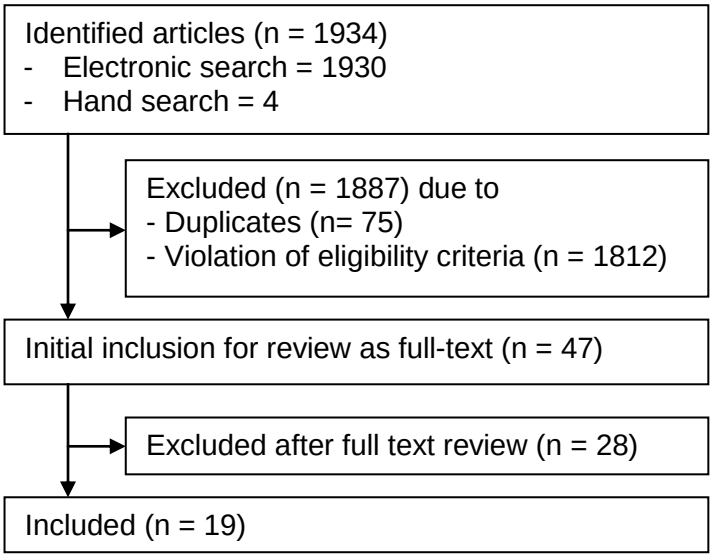
Inclusion criteria	Exclusion criteria
Studies comparing centralised with non-centralised cancer services in entirety, or expert/specialised versus less-experienced/less-specialised/general centres, high-volume versus low-volume centres, or multidisciplinary care versus non-multidisciplinary care	Studies that focus on one centre or unit
Cancer services providing initial diagnosis and treatment	Cancer services providing screening and follow-up treatment
Population – persons diagnosed with cancer.	
Outcomes – average cost per patient treated, or incremental cost effectiveness ratios, or additional travel costs incurred or extra distance travelled by patients to centralised cancer services	
Study design – randomised controlled trials, cohort, case-control, before and after, cross-sectional studies, or modelling studies	Ecological studies, case reports
Applied study (i.e. studies generating primary data or modelling of secondary data)	Methodological and general articles, expert opinion, letters and abstracts
Study setting – any country	
Journal articles	Books, grey literature
English language	Foreign languages

3. Results

Our systematic literature search identified 1,930 articles electronically and 4 articles by hand search (Figure 1). Of the 47 articles selected for full text retrieval, 28 were excluded after critical appraisal because they failed one or more eligibility criteria. Of the nineteen studies included in the final analysis (Table 2), thirteen studies related to health service costs,[13-25] four to cost-effectiveness,[13, 26-28] and four to costs shifts to patients and carers.[25, 29-31] Two studies contributed results to more than one review question.[13, 25]

First, we report results relating to the first review question on health care costs. We have sub-categorised these into costs in association with surgeon volumes (Table 3a), hospital volumes (Table 3b), and hospital locations (Table 3c); second, we report results for the second review question on cost-effectiveness (Table 4); finally we report results on patient costs (Table 5).

Figure 1: Review profile and study selection process



Healthcare costs

All except two[13, 25] of the thirteen studies that investigated the impact of centralisation on healthcare costs were cross-sectional (Table 3a-c). Oesophageal[13, 17, 19, 24] and pancreatic[13, 17, 23, 25] cancers were most frequently studied. Nine out of the thirteen studies were based in the US. Studies adopted a health care payer cost perspective with the exception of Pace *et al.* (2009)[25] who also included patient costs. Surgeon or hospital volume was used as a proxy measurement of centralisation of cancer services in almost

all of the studies. However there were wide variations in the definition of high volume surgeon (mean values ranged from 1.5 to 100 procedures per year) and high volume hospital (mean values ranged from 2.75 to 230 cases per year).

Table 2: Summary of key characteristics of review studies (n = 19)

	Review question 1: Healthcare costs (n = 13)	Review question 2: Cost-effectiveness (n = 4)	Review question 3: Patient costs (n = 4)
Study country			
UK	2	1	2
USA	9	2	2
Europe	-	1	-
Rest of the world	2	-	-
Study design			
Randomised crossover	1	-	1
Cohort	1	2	-
Cross-sectional	11	-	-
Modelling	-	2	3
Cancer type*			
Bladder	1	-	-
Breast	1	-	1
Colorectal	2	-	1
Gastric	1	1	-
Head and neck	-	-	1
Lung	1	-	-
Melanoma	1	1	1
Oesophageal	4	1	2
Oral	2	-	-
Ovarian	-	2	-
Pancreatic	4	1	3
Prostate	3	-	1
Uterine	1	-	-
Study perspective			
Health care payer	13	3	-
Patient	1	-	4
Societal	-	1	-
Aspect(s) of centralisation studied*			
Surgeon volume	8	1	-
Hospital volume	8	-	2
Hospital location	2	1	2
Degree of specialisation	-	1	-
Multidisciplinary care	-	1	-

* The numbers do not add up to the total number of studies for each review question because some studies had examined more than one type of cancer, considered costs from different perspectives, or conceptualised centralisation in more than one way.

Surgeon volumes and costs

Seven out of eight studies showed that there was an inverse relationship between surgeon volumes and healthcare costs (Table 3a). In a UK cohort study measuring hospital costs of

patients with oesophageal, gastric or pancreatic cancer, Bachmann et al. (2003)[13] found a U-shaped association between mean hospital cost per patient and surgeon volume per year. Ramirez et al. (2006)[22] concluded that a surgical volume increase corresponding to one radical prostatectomy (RP) per year was associated with a US$25 decrease in hospital charges. Five other studies covering a range of cancers, also reported that mean costs were generally lower for surgeons with a higher operative volume.[16-18, 20-21] However, one study in the US found that for the treatment of uterine cancer among an older population adjusted median costs associated with high volume surgeons (HVS) were 35% higher than low volume surgeons (LVS).[14]

Hospital volumes and costs

There was mixed evidence on the relationship between hospital surgical volumes and cost per patient treated (Table 3b). Six studies reported that mean costs were lower for hospitals with a higher surgical volume, with cost differences ranging from 2% to 50%.[15-18, 23-24] However, Kuo *et al*. (2001)[19] found no evidence of a real difference in adjusted costs for oesophageal cancer treatment between high volume hospitals (HVH) and low volume hospitals (LVH). Three other studies[14, 18, 23] found some evidence that HVH were associated with higher costs.

Hospital locations and costs

Both studies that reported healthcare costs and hospital location, showed that lower costs were associated with the centralised location (Table 3c).[24-25]

Cost-effectiveness

Four observational and modelling studies, which had each focused on a different aspect of centralisation, reported mixed evidence on the cost-effectiveness of the centralisation of cancer services (Table 4).[13, 26-28] Only one modelling study, in patients with ovarian cancer, came to a firm conclusion that centralisation was cost-effective with an incremental cost effectiveness ratio of US$5,029 per quality adjusted life year (QALY) gained.[26]

Patient costs

Of the four studies that evaluated the patient costs of centralisation,[25, 29-31] one study involved a small randomised crossover design (Table 5).[25] Except for the study by Patel *et al.*,[30] which studied head and neck cancer, the other three studies considered a range of

Table 3a: Studies included in the systematic review relating to the impact of centralisation of cancer services on health care costs in relation to surgeon volume

Authors, date, and country	Aspect(s) of centralisation evaluated	Cancer type	Total Sample size	Study design	HVS vs. LVS*	Notes
Bachmann *et al*., 2003,[13] UK	Surgeon volumes	Pancreatic, oesophageal and gastric	2,294	Prospective cohort	n.c.	U-shaped relationship between hospital cost per patient and surgeon volume; lowest cost at volumes of 10 - 20 procedures per year.
Ramirez *et al.,* 2006,[22] US	Surgeon volumes	Prostate	3,167	Cross-sectional	n.c.	A surgical volume increase corresponding to one radical prostatectomy was associated with a US$25 decrease in hospital charges.
Lin *et al.,* 2008,[21] Taiwan	Surgeon volumes	Oral	2,325	Cross-sectional	n.c.	LVS US$995 higher than HVS LVS US$2,138 higher than very HVS.
Lee *et al.,* 2010,[20] Taiwan	Surgeon volumes	Oral	2,663	Cross-sectional	n.c.	LVS US$1,546 higher than HVS LVS US$1,820 higher than very HVS.
Harmon *et al*., 1999[16], US	Hospital and surgeon volumes	Colorectal	9,739	Cross-sectional	-11%	
Konety et al., 2004,[18] US	Hospital and surgeon volumes	Bladder	13,904	Cross-sectional	TURBT= -13%	
Diaz-Montes et al., 2007,[14] US	Hospital and surgeon volumes	Uterine	656	Cross-sectional	+35%	
Ho and Aloia, 2008,[17] US	Hospital and surgeon volumes	Colorectal, lung, oesophageal, pancreatic	266,648	Cross-sectional	-4% to -26%	Cost difference varied by time periods and cancer surgeries

HVS – high volume surgeons, LVS – low volume surgeons, n.c. – cannot be computed, TURBT - transurethral bladder tumour resection, * refers to percentage of costs difference with plus sign indicating costs being greater for HVS than LVS and minus sign indicating costs being lesser for HVS than LVS

Table 3b: Studies included in the systematic review relating to the impact of centralisation of cancer services on health care costs in relation to hospital volume

Authors, date, and country	Aspect(s) of centralisation evaluated	Cancer type	Total Sample size	Study design	HVH vs. LVH*	Notes
Sosa *et al.,* 1998,[23] US	Hospital volumes	Pancreas	1,236	Cross-sectional	PR = -24% BP = +27%	
Ellison *et al*., 2000,[15] US	Hospital volumes	Prostate	66,693	Cross-sectional	-13%	
Kuo *et al.*, 2001,[19] US	Hospital volumes	Oesophagus	1,193	Cross-sectional	n.c.	No evidence of cost difference between HVH and LVH (p = 0.33).
Harmon *et al*., 1999,[16] US	Hospital and surgeon volumes	Colorectal	9,739	Cross-sectional	-6%	
Konety et al., 2004,[18] US	Hospital and surgeon volumes	Bladder	13,904	Cross-sectional	RC = -11% TURBT = +23%	
Diaz-Montes et al., 2007,[14] US	Hospital and surgeon volumes	Uterine	656	Cross-sectional	+13%	
Ho and Aloia, 2008,[17] US	Hospital and surgeon volumes	Colorectal, lung, oesophageal, pancreatic	266,648	Cross-sectional	CL = -2%	Cost difference varied by time periods and cancer surgeries
Swisher *et al.,* 2000,[24] US	Hospital volume and hospital location	Oesophagus	340	Cross-sectional	-50%	

BP - palliative bypasses, CL – colectomy, HVH – high volume hospitals, LVH – low volume hospitals, n.c. – cannot be computed, PR - pancreatic resection, RC - radical cystectomy, TURBT - transurethral bladder tumour resection, * refers to percentage of costs difference with plus sign indicating costs being greater for HVH than LVH and minus sign indicating costs being lesser for HVH than LVH

Table 3c: Studies included in the systematic review relating to the impact of centralisation of cancer services on health care costs in relation to hospital location

Authors, date, and country	Aspect(s) of centralisation evaluated	Cancer type	Total Sample size	Study design	Findings
Pace *et al.,* 2009,[25] UK	Hospital location	Breast, melanoma, pancreas, prostate	31	Randomised crossover	Incremental cost of chemotherapy at community hospitals per clinic = £77
Swisher *et al.,* 2000,[24] US	Hospital volume and hospital location	Oesophagus	340	Cross-sectional	% cost difference national cancer institutions vs. community hospitals = 61%

Table 4: Studies included in the systematic review relating to cost-effectiveness of centralisation of cancer services

Authors, date, and country	Aspect(s) of centralisation evaluated	Cancer type	Total sample size	Study design	Intervention and comparator	Discounting and base year	Findings
Fader *et al.,* 1998[27], US	Multidisciplinary care	Melanoma	208	Retrospective cohort	MDT vs. traditional non-MDT care	Not stated	MDT care resulted in equivalent clinical outcomes as traditional non-MDT care. Average (SD) difference (saving due to the use of MDT care) in per patient costs = US$1,595 (US$643).
Bachmann *et al*., 2003,[13] UK	Surgeon volume	Pancreatic, oesophageal and gastric	2,294	Prospective cohort	n.a.	Base year = 1996/7. No discounting used.	U-shaped relationship between mean hospital cost per day of life and doctor volume per year with lowest cost of approximately £45, £30, and £35 at doctor volumes of about 11, 13 and 27 per year for pancreatic, gastric, and oesophageal cancers respectively.
Bristow *et al.,* 2007,[26] US	Degree of specialisation	Ovarian	n.a.	Decision analytic modelling	Expert vs. less experienced centre	Base year = 2006. No discounting used.	When benefits were not discounted ICER was US$3,809/QALY gained, whereas when the benefits were discounted, ICER was $5,029/QALY gained.
Greving *et al.,* 2009,[28] the Netherlands	Hospital location	Ovarian	879	Decision analytic modelling	Tertiary hospital vs. general and semi-specialised hospitals	Base year is 2006 and discount rate is 4%.	SSH vs GH – ICER €7,135/QALY TH vs SSH – ICER €102,642/QALY.

GH – general hospitals, ICER – incremental cost-effectiveness ratio, MDT – multidisciplinary team, n.a. – not applicable, QALY – quality adjusted life years, SD – standard deviation, SSH – semi-specialised hospitals, TH – tertiary hospitals

Table 5: Studies included in the systematic review relating to the impact of centralisation of cancer services on patient costs

Authors, date, and country	Aspect(s) of centralisation evaluated	Cancer type	Sample size	Study design	Method of distance measurement	Findings
Birkmeyer *et al*., 2003,[29] US	Hospital volume	Oesophagus, pancreas	15,796	Modelling	Straight line	• If minimum volume is low (1/year for pancreatectomy; 2/year for oesophagectomy), about 15% of patients would need to change to HVH, with negligible effect on their travel times. • If minimum volume is high (>16/year for pancreatectomy; >19/year for oesophagectomy), about 80% of patients would need to change to HVH and more than 50% would increase their travel time by more than one hour,
Stitzenberg *et al.,* 2009,[31] US	Hospital volume	Oesophagus, pancreas, colon, rectum	272,886	Modelling	Straight line	Increase in travel distance attributed directly to centralization - 0.73 miles for rectal cancer, 5.02 miles for oesophageal cancer, 3.14 miles for pancreatic cancer, and 0.47 miles for colon cancer.
Patel *et al.,* 2004,[30] UK	Hospital location	Head and neck	85	Modelling	RAC route planner	Patients have to travel on average an extra 201 miles (range, 191 to 206) per round trip to the centralised service.
Pace *et al.,* 2009,[25] UK	Hospital location	Breast, melanoma, pancreas, prostate	31	Randomised crossover	Actual distance travelled by private car and public transport	• Incremental cost of attending the cancer centre rather than the community hospital is £6.29 per visit. • Patients lived closer to the community hospital (average distance 10.25 miles) than the cancer centre (average distance 19.00 miles).

HVH – high volume hospitals, RAC – Royal Automobile Clu

cancers. The findings from these four studies (two of which reported costs in relation to hospital location[25, 30] and two to hospital volume) suggested that centralised services would shift the costs of care to patients.[29, 31]

4. Discussion

Summary of findings

In this systematic review we identified nineteen studies on the economic impact of the centralisation of cancer services. The evidence available was limited and generally of low quality. Most did not involve a longitudinal element to their design. There was evidence that higher surgeon volumes are associated with lower costs per patient, but one study suggested that costs may increase again in the highest volume surgeons. However, existing evidence on the relationship between hospital volume and treatment costs is mixed. We only found one non-randomised study that came to a firm conclusion that centralisation of cancer services is cost-effective. We also found that there is consistent evidence that centralisation of cancer services increased patient travel costs, time and distance.

Strengths and weaknesses of the systematic review

To our knowledge, we present the first systematic review of the evidence on the economic effects of centralisation of cancer services. The limitations of this review need to be borne in mind. Firstly, the literature search was limited to databases of peer-reviewed research. Therefore, we have not included evidence from the grey literature. Secondly, as with any systematic review, publication bias might be a problem if studies with null findings are not published. Whether the omission of grey literature has materially affected the key issue of study quality and the extent to which publication bias has occurred in the context of such studies are in our view both questionable. Finally, this review was not restricted to a particular country or cancer type. While this approach is valuable in describing the available evidence from a wide perspective, it restricts the comparability across studies. Given that the studies were diverse in terms of their characteristics, the findings may not be applicable across different healthcare settings where different clinical practices and geographical constraints operate.

Weaknesses of the evidence

We have identified three key weaknesses in the current evidence base for the economic impact of centralisation of cancer services. Firstly, the definition of centralisation used has generally been a narrow one which does not reflect the multi-faceted nature of centralisation. While various working definitions of 'centralisation' including high volume surgeons, high volume hospitals, multidisciplinary treatment decisions, and regional or tertiary cancer centres were used in the studies included in our systematic review, most had examined centralisation using a volume-based definition. Secondly, the existing evidence was of relatively low quality. Eleven of the nineteen studies identified were cross-sectional. Such studies are particularly vulnerable to bias and unclear directionality of effects, even after adjustment for potential confounders. Furthermore, five other studies were based on modelling, which are only as valid as the evidence and assumptions upon which they are based. Thirdly, the available evidence was limited so that it was not possible to be conclusive about which aspects of centralisation would lead to efficient care in specific cancer subgroups.

Consistency with other studies

The positive association between surgical volume and outcome has been relatively consistently observed across a wide range of procedures.[32] However, it has been argued that this should not lead to the general presumption that larger hospitals benefit from economies of scale or that service concentration necessarily leads to improved outcomes for patients.[33-34] Our systematic review has shown that existing evidence is very limited and therefore it is not possible to conclude whether specific cancer services have become more efficient as a result of increasing centralisation.

Future research

Based on our systematic review findings, we propose that one key focus of future research in this area should be the determination of the most cost-effective model of care for any given type of cancer with its specific characteristics and treatment options in a given geographical area. Such attempts should take into account the following issues. Firstly, clear definitions are needed of what centralisation actually entails and what are its boundaries. For example, aspects of centralisation could include the practice of multidisciplinary treatment decision-making and high volume

surgeons working at specialised hospitals. It may be more beneficial to provide other less complex aspects of cancer care such as chemotherapy in community settings. Secondly, once the different aspects of centralisation have been clearly defined, it would then be possible to determine the efficiency of each aspect for different cancer subgroups using strong study designs. Although well-conducted randomised trials provide the most reliable evidence on the cost-effectiveness of interventions, these are not always feasible for assessing the impact of an organisational change such as centralisation. Alternative methods that have been recognised as acceptable for the evaluation of organisational interventions are randomised or non-randomised cluster controlled trials/studies, interrupted time series, and controlled before and after studies.[35]

Policy implications

The economic impact of centralisation of cancer services is likely to vary according to many factors, such as tumour type, treatment selected and geographical location. It is possible that costs may be reduced with higher surgeon volume but it is not clear from the current evidence base what the optimum volume would be. Even if centralisation of cancer services results in cost savings for healthcare providers and patients (in terms of improved health outcomes), this may be offset by the transferring of costs to patients in terms of longer travel time and distance. Several studies have shown that increased distance and travel time from patients' homes to centralised cancer services reduced the likelihood of compliance with and take-up of treatment.[36-40] Taking into consideration all these issues, it is likely that there is no 'one-size-fits-all' model of centralisation to suit all cancers, treatment modalities and locations.

Conclusions

Recent trends towards centralisation of cancer services have taken place despite incomplete evidence that such service reorganisation will lead to cost-effective care. While existing evidence suggests that increasing surgeon volume can reduce cost-per-patient up to a point, this might be at least partly counterbalanced by diseconomies of scale in very high surgical volumes and by the shifting of costs onto patients and carers. Further studies utilising stronger study designs aimed at understanding which aspects of centralisation would lead to efficient care in specific

cancer subgroups would help to inform policy decision-making in the delivery of cancer services.

Authors' contributions

KMK, WH and ARN conceived of the study and participated in its design. KMK conducted the initial retrieval and scanning of papers for inclusion. KMK and WH performed the final selection of papers for review. KMK coordinated data retrieval and extraction. All authors drafted the manuscript, and read and approved the final manuscript.

Acknowledgements

The authors would like to thank Professor Tim J. Peters for his comments that have helped to improve this manuscript. This work presents independent research commissioned by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research scheme (RP-PG-0707-10034). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

References

1. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. N Engl J Med. 1979 Dec 20;301(25):1364-9.
2. Birkmeyer JD, Sun Y, Wong SL, Stukel TA. Hospital volume and late survival after cancer surgery. Ann Surg. 2007 May;245(5):777-83.
3. Forshaw MJ, Gossage JA, Stephens J, Strauss D, Botha AJ, Atkinson S, et al. Centralisation of oesophagogastric cancer services: can specialist units deliver? Ann R Coll Surg Engl. 2006 Oct;88(6):566-70.
4. Tingulstad S, Skjeldestad FE, Hagen B. The effect of centralization of primary surgery on survival in ovarian cancer patients. Obstet Gynecol. 2003 Sep;102(3):499-505.
5. Weitz J, Koch M, Friess H, Buchler MW. Impact of volume and specialization for cancer surgery. Dig Surg. 2004;21(4):253-61.
6. Wouters MW, Karim-Kos HE, le Cessie S, Wijnhoven BP, Stassen LP, Steup WH, et al. Centralization of esophageal cancer surgery: does it improve clinical outcome? Ann Surg Oncol. 2009 Jul;16(7):1789-98.
7. Selby P, Gillis C, Haward R. Benefits from specialised cancer care. Lancet. 1996 Aug 3;348(9023):313-8.
8. Expert Advisory Group on Cancer. A policy framework for commissioning cancer services: A report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. Department of Helath, London: HM Stationery Office; 1995.
9. Department of Health UK. Cancer Reform Strategy. London: HM Stationery Office; 2007.

10. Atun R, Ogawa T, Martin-Moreno JM. Analysis of National Cancer Control Programmes in Europe.
. London: Imperial College London; 2009.
11. Stitzenberg KB, Meropol NJ. Trends in Centralization of Cancer Surgery. Ann Surg Oncol. 2010 Jun 18.
12. Centre for Reviews and Dissemination. Systematic reviews: CRD's guidance for undertaking reviews in health care. York: CRD, University of York; 2009.
13. Bachmann M, Peters T, Harvey I. Costs and concentration of cancer care: evidence for pancreatic, oesophageal and gastric cancers in National Health Service hospitals. J Health Serv Res Policy. 2003 Apr;8(2):75-82.
14. Diaz-Montes TP, Zahurak ML, Giuntoli RL, 2nd, Bristow RE. Concentration of uterine cancer surgical care among the elderly: a population-based perspective. Gynecol Oncol. 2007 Dec;107(3):436-40.
15. Ellison LM, Heaney JA, Birkmeyer JD. The effect of hospital volume on mortality and resource use after radical prostatectomy. J Urol. 2000 Mar;163(3):867-9.
16. Harmon JW, Tang DG, Gordon TA, Bowman HM, Choti MA, Kaufman HS, et al. Hospital volume can serve as a surrogate for surgeon volume for achieving excellent outcomes in colorectal resection. Ann Surg. 1999 Sep;230(3):404-11; discussion 11-3.
17. Ho V, Aloia T. Hospital volume, surgeon volume, and patient costs for cancer surgery. Med Care. 2008 Jul;46(7):718-25.
18. Konety BR, Dhawan V, Allareddy V, O'Donnell MA. Association between volume and charges for most frequently performed ambulatory and nonambulatory surgery for bladder cancer. Is more cheaper? J Urol. 2004 Sep;172(3):1056-61.
19. Kuo EY, Chang Y, Wright CD. Impact of hospital volume on clinical and economic outcomes for esophagectomy. Ann Thorac Surg. 2001 Oct;72(4):1118-24.
20. Lee CC, Ho HC, Jack LC, Su YC, Lee MS, Hung SK, et al. Association between surgeon volume and hospitalisation costs for patients with oral cancer: a nationwide population base study in Taiwan. Clin Otolaryngol. 2010 Feb;35(1):46-52.
21. Lin CS, Lee HC, Lin CT, Lin HC. The association between surgeon case volume and hospitalization costs in free flap oral cancer reconstruction operations. Plast Reconstr Surg. 2008 Jul;122(1):133-9.
22. Ramirez A, Benayoun S, Briganti A, Chun J, Perrotte P, Kattan MW, et al. High radical prostatectomy surgical volume is related to lower radical prostatectomy total hospital charges. Eur Urol. 2006 Jul;50(1):58-62; discussion -3.
23. Sosa JA, Bowman HM, Gordon TA, Bass EB, Yeo CJ, Lillemoe KD, et al. Importance of hospital volume in the overall management of pancreatic cancer. Ann Surg. 1998 Sep;228(3):429-38.
24. Swisher SG, Deford L, Merriman KW, Walsh GL, Smythe R, Vaporicyan A, et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. J Thorac Cardiovasc Surg. 2000 Jun;119(6):1126-32.
25. Pace E, Dennison S, Morris J, Barton A, Pritchard C, Rule SA. Chemotherapy in the community: what do patients want? Eur J Cancer Care (Engl). 2009 Mar;18(2):209-15.
26. Bristow RE, Santillan A, Diaz-Montes TP, Gardner GJ, Giuntoli RL, 2nd, Meisner BC, et al. Centralization of care for patients with advanced-stage ovarian cancer: a cost-effectiveness analysis. Cancer. 2007 Apr 15;109(8):1513-22.
27. Fader DJ, Wise CG, Normolle DP, Johnson TM. The multidisciplinary melanoma clinic: a cost outcomes analysis of specialty care. J Am Acad Dermatol. 1998 May;38(5 Pt 1):742-51.

28. Greving JP, Vernooij F, Heintz AP, van der Graaf Y, Buskens E. Is centralization of ovarian cancer care warranted? A cost-effectiveness analysis. Gynecol Oncol. 2009 Apr;113(1):68-74.
29. Birkmeyer JD, Siewers AE, Marth NJ, Goodman DC. Regionalization of high-risk surgery and implications for patient travel times. JAMA. 2003 Nov 26;290(20):2703-8.
30. Patel RS, Hewett J, Hickey SA. Patient burden of centralization of head and neck cancer surgery. J Laryngol Otol. 2004 Jul;118(7):528-31.
31. Stitzenberg KB, Sigurdson ER, Egleston BL, Starkey RB, Meropol NJ. Centralization of cancer surgery: implications for patient access to optimal care. J Clin Oncol. 2009 Oct 1;27(28):4671-8.
32. Dudley RA, Johansen KL, Brand R, Rennie DJ, Milstein A. Selective referral to high-volume hospitals: estimating potentially avoidable deaths. JAMA. 2000 Mar 1;283(9):1159-66.
33. Posnett J. Is bigger better? Concentration in the provision of secondary care. BMJ. 1999 Oct 16;319(7216):1063-5.
34. Birkmeyer JD, Skinner JS, Wennberg DE. Will volume-based referral strategies reduce costs or just save lives? Health Aff (Millwood). 2002 Sep-Oct;21(5):234-41.
35. Cochrane Effective Practice and Organisation of Care Group. Study designs for EPOC reviews. [cited 2010 22 October]; Available from: http://epoc.cochrane.org/epoc-resources-review-authors
36. Baird G, Flynn R, Baxter G, Donnelly M, Lawrence J. Travel time and cancer care: an example of the inverse care law? Rural Remote Health. 2008 Oct-Dec;8(4):1003.
37. Blais S, Dejardin O, Boutreux S, Launoy G. Social determinants of access to reference care centres for patients with colorectal cancer--a multilevel analysis. Eur J Cancer. 2006 Nov;42(17):3041-8.
38. Dejardin O, Bouvier AM, Herbert C, Velten M, Buemi A, Delafosse P, et al. Social and geographic disparities in access to reference care site for patients with colorectal cancer in France. Br J Cancer. 2005 May 23;92(10):1842-5.
39. Jones AP, Haynes R, Sauerzapf V, Crawford SM, Zhao H, Forman D. Travel time to hospital and treatment for breast, colon, rectum, lung, ovary and prostate cancer. Eur J Cancer. 2008 May;44(7):992-9.
40. Onega T, Duell EJ, Shi X, Demidenko E, Goodman D. Determinants of NCI Cancer Center attendance in Medicare patients with lung, breast, colorectal, or prostate cancer. J Gen Intern Med. 2009 Feb;24(2):205-10.

Appendix 1: Search strategy

EMBASE
#1 cancer OR neoplasm
#2 centrali* OR concentration OR volume OR speciali* OR regionali* OR multidisciplinary
#3 1 AND 2
#4 “cost savings" OR "cost-effective*" OR "cost-benefit" OR "cost-utility" OR "economic evaluation" OR economic OR "cost analysis" OR ‘health care costs’ OR access* OR travel OR burden
#5 3 AND 4
#6 limit to (human and English language) AND (article or conference paper)

MEDLINE (MeSH terms used)
#1 cancer OR neoplasm
#2 ((Centralized Hospital Services) OR (Cancer Care Facilities) OR (Oncology Service, Hospital))
#3 1 AND 2
#4 ((Costs and Cost Analysis) OR (Economic*) OR (Cost-Benefit Analysis) OR (Cost Savings) OR (Health Care Costs) OR (Cost of Illness) OR (Health Services Accessibility) OR (Patient Transfer) OR (Travel) OR (Transportation of Patients)
#5 3 AND 4
#6 limit 5 to (English language and humans)

NHS EED
((centrali* OR concentration OR volume OR speciali* OR regionali* OR multidisciplinary OR access* OR travel OR burden) AND (cancer))(english:la NOT review:ty)

CINAHL
#1 cancer OR neoplasm
#2 centrali* OR concentration OR volume OR speciali* OR regionali* OR multidisciplinary
#3 1 AND 2
#4 “cost savings" OR "cost-effective*" OR "cost-benefit" OR "cost-utility" OR "economic evaluation" OR economic OR "cost analysis" OR ‘health care costs’ OR access* OR travel OR burden
#5 3 AND 4
#6 limit to English Language; Peer Reviewed; Research Article; Exclude MEDLINE records