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Quality indicators for testicular cancer: A population-based study

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ABSTRACT

Purpose: This study aimed at developing and measuring an indicator set to monitor the quality of testicular cancer care, to make comparisons over time and to support quality improvement for all practitioners and centres involved in the care of testicular cancer patients.

Methods: Quality indicators were identified from a systematic literature search and from the 2010 Belgian evidence-based clinical practice guidelines. The selection process involved an expert panel evaluating reliability, relevance, interpretability and actionability of each indicator. The quality indicators were pilot tested using the Belgian Cancer Registry (BCR) data linked with claims data for 1307 men with testicular cancer diagnosed between 2001 and 2006. The variability between centres was displayed using funnel plots.

Results: Of the 12 finally selected indicators, 5 were fully and 1 was partly measurable, while 2 indicators were measurable using proxy information. Five-year relative survival was 97%, 95% and 76% for pStage I–III, respectively. Overall 5-year survival slightly improved from 91% in 2001 to 94% in 2004. Between 2004 and 2006, 14 of 97 centres performed $\geqslant$10 orchidectomies. Large variability was found between centres. The nine centres with a 5-year observed survival below the lower limit treated less than 20 patients between 2001 and 2006.

Conclusions: The present study demonstrates the feasibility to develop a multidisciplinary set of quality indicators for testicular cancer. Using national cancer registry data linked to claims data, eight indicators were measurable, showing a mixed picture of the quality of care for testicular cancer patients in Belgium.

1. Introduction

Testicular germ cell tumours are relatively rare. In Belgium, 269 new testicular germ cell cancers were diagnosed in 2006 with an age-adjusted incidence rate of 5.2/100,000 person years.[1] Testicular cancer typically is a cancer of young men, with a peak age-standardised incidence rate of 20.9/100,000 person years in the age category 25–30 years in 2006.

The Belgian age-adjusted incidence rate is comparable to that in North-America (age-adjusted incidence rate 5.1/100,000 person years in 2008),[2] but lower than that in Western

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Europe (7.8/100,000 person years in 2008) and Northern Europe (6.7/100,000 person years in 2008).[2]

No published mortality or survival data specifically for testicular cancer are available for Belgium. However, in the period 2000–2001, the relative 5-year survival for testicular cancer was 95% in Flanders, the Northern part of the country.[3] These data are in line with those reported in the literature for other countries and regions. For example, in England and Wales, the relative 5-year survival rose from 91% between 1986 and 1990 to 97% between 1996 and 1999.[4] In the southern part of the Netherlands, the relative 5-year survival was 99% and 96% for patients with seminoma and non-seminoma germ cell cancer, respectively.[5]

The Belgian Federal Healthcare Knowledge Centre (KCE) recently issued publicly available evidence-based clinical practice guidelines (CPG) for the treatment of testicular germ cell cancer.[6] The main objective of the present study was to develop a set of process and outcome indicators to evaluate the adherence to these guidelines. In the absence of prospective data, the quality indicators were pilot tested on national cancer registry data linked with administrative claims data.

2. Methods

2.1. Indicator selection and definition

OVID Medline, the National Quality Measures Clearinghouse and websites of healthcare organisations (Agency for Healthcare Research and Quality, National Quality Measures Clearinghouse, Joint Commission, National Health Service, Clinical Indicators Support Team) were searched to identify published and validated quality indicators for testicular cancer. Furthermore, CPGs identified during the development of the Belgian testicular cancer guideline[6] were evaluated for included quality indicators. The searches were conducted in December 2009.

The list of quality indicators resulting from the literature search was complemented by quality indicators derived from the recommendations of the testicular cancer guideline.[6] To this end, most individual recommendations were translated in at least one quality indicator.

A preliminary list of 32 indicators, resulting from the literature search and addition of guideline-based indicators, was subjected to a formal assessment by six experts based on four criteria: reliability, relevance, interpretability and actionability. Measurability was no selection criterion *a priori*. Details of the selection process can be found in the Supplementary file.

For each selected quality indicator, the numerator and denominator (and their respective in- and exclusion criteria) were defined and the measurability was evaluated.

2.2. Data sources

To analyse the feasibility of the indicators, three national databases were used: the Belgian Cancer Registry (BCR) database, the Belgian population registry and a national administrative database containing claims data. More details on these databases and the linkage process can be found in the Supplementary file.

Patients with invasive testicular germ cell cancer (ICD-10 code C62) and an incidence date between 1st January 2001 and 31st December 2006 were selected from the BCR database ($N = 1337$).

2.3. Statistics

The majority of selected process indicators was binary (yes/no). These involved the definition of a numerator and denominator, and were described with percentages (N, n, %). One process indicator involved the number of times a certain procedure was performed, and was described with mean, median and standard deviation. All outcome indicators were time-to-event data, and involved the definition of a survival time until the event of interest, or until the end of follow-up. Kaplan–Meier survival functions were presented. Relative survival was computed as the ratio of observed survival to expected survival, using the Ederer II method, and based on Belgian mortality tables of 2006.[7]

A predefined algorithm was used to attribute each patient to one centre (see Supplementary file). The variability between centres was displayed using funnel plots.[8] More details are provided in the Supplementary file.

All analyses were performed with SAS 9.1.3 (SAS Institute, Cary, North Carolina, USA).

3. Results

3.1. Indicator measurability

From the original set of 32 quality indicators, 12 were finally retained (Table 1). Five of these were found to be measurable (TC1, TC4, TC6, TC7 TC9). One indicator (TC11) was only partially measurable because of the unavailability of specific administrative codes for CT and MRI imaging. Two indicators were measurable using a proxy indicator or proxy information. The relative survival (TC2, observed/expected survival) was calculated as an estimation of the disease-specific survival. For the calculation of the disease-free survival (TC3), in the absence of a specific code, recurrence was defined as the event of receiving new treatment at least 3 months after the first treatment.

The four remaining indicators were deemed not measurable. The most important reason for not being measurable was the absence of administrative codes (TC8, TC12) or the lack of specificity of the existing administrative codes (TC5, TC10).

3.2. Population characteristics

In total, the records of 1307 patients with invasive testicular germ cell cancer (97.7%) could be linked to the claims database. These patients constituted the population in the present study.

Table 2 provides an overview of the basic characteristics of the study population. The mean age of the sample was 34.5 years (SD = 12.6; range 0–95). The highest incidence of testicular germ cell cancer was found in the age category

Table 1 – Final selection of testicular cancer quality indicators.

Indicator		Type of indicator	Measurable
Generic indicators			
TC1	Overall 5-year survival by stage	Outcome	Yes
TC2	Disease-specific 5-year survival by stage	Outcome	Yes, with proxy information
TC3	Disease-free 5-year survival by stage	Outcome	Yes, with proxy information
Diagnosis and staging			
TC4	Proportion of patients with testicular cancer undergoing tumour marker assessment before any treatment	Process	Yes
TC5	Proportion of patients with testicular cancer undergoing contrast-enhanced Computed Tomography (CE-CT) or Magnetic Resonance Imaging (MRI) for primary staging	Process	No
TC6	Proportion of patients with testicular cancer discussed at the multidisciplinary team meeting (MDT)	Process	Yes
Treatment			
TC7	Number of annually surgically treated patients with testicular cancer per centre	Process	Yes
TC8	Radiation dose and field in patients with testicular cancer treated with radiotherapy by stage	Process	No
TC9	Proportion of patients with stage I non-seminoma treated with active surveillance	Process	Yes
TC10	Proportion of patients receiving CE-CT or MRI for residual disease assessment at the end of systemic treatment	Process	No
TC11	Degree and duration of active surveillance in patients with stage I non-seminoma or seminoma	Process	Partly
TC12	Proportion of patients with relapsing testicular cancer after curative treatment that are included in a clinical trial	Process	No

20–39 years (data not shown). Seminomas (53.3%) were somewhat more frequent than non-seminomas. Malignant teratomas were found to be the most common non-seminoma tumours. The number of patients with unreported pStage was 394 (30.1%). More than 88% of the patients in whom the pStage was known had pStage I.

Table 2 – Population characteristics.

Characteristic	Value
Mean age	34.5 ± 12.6
Morphology	
Non-seminoma	46.7%
Malignant teratoma	20.6%
Embryonal carcinoma	17.2%
Choriocarcinoma	2.5%
Other	6.4%
Seminoma	53.3%
pStage	
Unknown	30.1%
I	61.7%
II	5.6%
III	2.6%

3.3. *Indicator results*

3.3.1. *Survival*

For the entire population, survival measures are presented by stage in Table 3. Especially for stage I and II, 5-year relative survival was found to be high (97% and 95% respectively). For stage III disease, 5-year relative survival still was 76%. The 5-year disease-free survival for the entire cohort was estimated to be 94% for the period 2001–2004. No obvious differences in observed survival were found between seminomas and non-seminomas (Fig. 1: 5-year observed survival 94% versus 93%). All patients considered, the 5-year overall survival slightly increased between 2001 and 2004 from 91% to 94%. The 5-year relative survival increased between 2001 and 2003 from 92% to 95%.

Table 3 – Survival for testicular germ cell cancer by pStage, 2001–2006.

	pStage		
	I	II	III
5-year overall survival	0.97	0.95	0.71
5-year relative survival	0.97	0.95	0.76

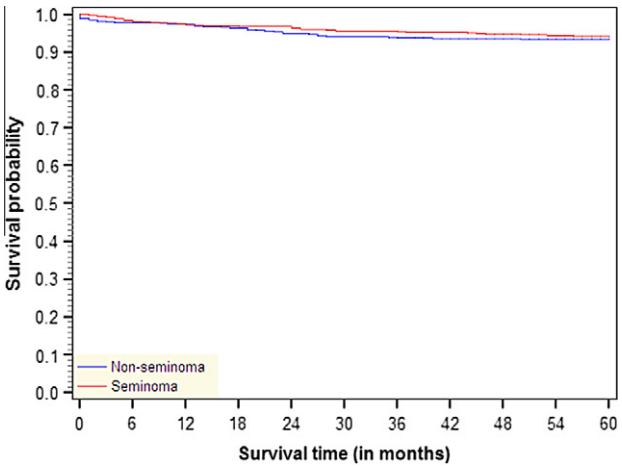

Fig. 1 – Kaplan–Meier curve for observed survival, seminoma versus non-seminoma, 2001–2006.

3.3.2. *Tumour marker assessment*

In the period 2001–2006, 73% of the treated patients underwent tumour marker assessment (alphafetoprotein [AFP] and human chorionic gonadotrophin [HCG]) within 3 months before the first treatment, while 50% underwent the measurement within 2 weeks before the first treatment. The proportion increased from 72% in 2001 to 81% in 2006 (Table 4).

3.3.3. *Multidisciplinary discussion*

Since February 2003, the reimbursement of a multidisciplinary team meeting (MDT) was introduced, enabling its monitoring using administrative data. Of all patients with an incidence date between February 1st 2003 and December 31st 2006, 58% were discussed during a MDT registered with the appropriate administrative code. Since the introduction of the reimbursement, the utilisation of the MDT increased every year, from 44% in 2003 to 67% in 2006 (Table 4).

3.3.4. *Surgical volume*

Between 2001 and 2003, 96 centres performed at least one orchidectomy for testicular cancer (Fig. 2). Only 10 centres performed at least 10 orchidectomies during this time period, representing about one-third of the surgically treated testicular cancer population. Between 2004 and 2006, 14 centres performed at least 10 orchidectomies (out of a total of 97 centres performing at least one orchidectomy during that period), representing about 40% of the surgically treated testicular cancer population during this time period.

3.3.5. *Active surveillance*

Patients with stage I disease not receiving adjuvant treatment (radiotherapy and/or chemotherapy) within 3 months after orchidectomy were considered to be under active surveillance. In the period 2001–2006, the rates of active surveillance were found to be 29% for stage I non-seminomas and 27% for stage I seminomas.

For stage I seminomas under active surveillance in the period 2001–2005, the mean number of tumour marker assessments during the first year after surgery ranged between 3.9 (SD 4.0) in 2003 and 6.8 (SD 5.5) in 2005. For stage I non-seminomas under active surveillance, the mean number of tumour marker assessments during the first year after surgery decreased from 15.9 (SD 11.7) in 2001 to 9.6 (SD 8.8) in 2005 (Table 4).

3.4. *Comparison between centres*

Using the predefined algorithm, 1260 patients (96.4%) could be attributed to one centre. Patients who could not be attributed to one centre were excluded from the analysis ($N = 47$). Funnel plots were calculated for five measurable indicators (TC1, TC2, TC4, TC6 and TC9): detailed results can be found in the Supplementary file.

A large variability was found for all five indicators. Table 5 provides an overview of the ranges of the results and the

Table 4 – Evolution of results of measurable testicular cancer quality indicators.

Indicator		2001	2006
TC1	Overall 5-year survival by stage	91%	94%[b]
TC2	Disease-specific 5-year survival by stage	92%	95%[a]
TC4	Proportion of patients with testicular cancer undergoing tumour marker assessment before any treatment	72%	81%
TC6	Proportion of patients with testicular cancer discussed at the multidisciplinary team meeting	44%[a]	67%
TC9	Proportion of patients with stage I non-seminoma treated with active surveillance	28%	20%
TC11	Degree and duration of active surveillance in patients with stage I non-seminoma or seminoma: mean number of tumour marker assessments during the first year after surgery		
	Seminoma	5.4	6.8[c]
	Non-seminoma	15.9	9.6[c]

[a] 2003 result.
[b] 2004 result.
[c] 2005 result (for patients diagnosed after December 31st 2005 follow-up data of at least 1 year were unavailable).

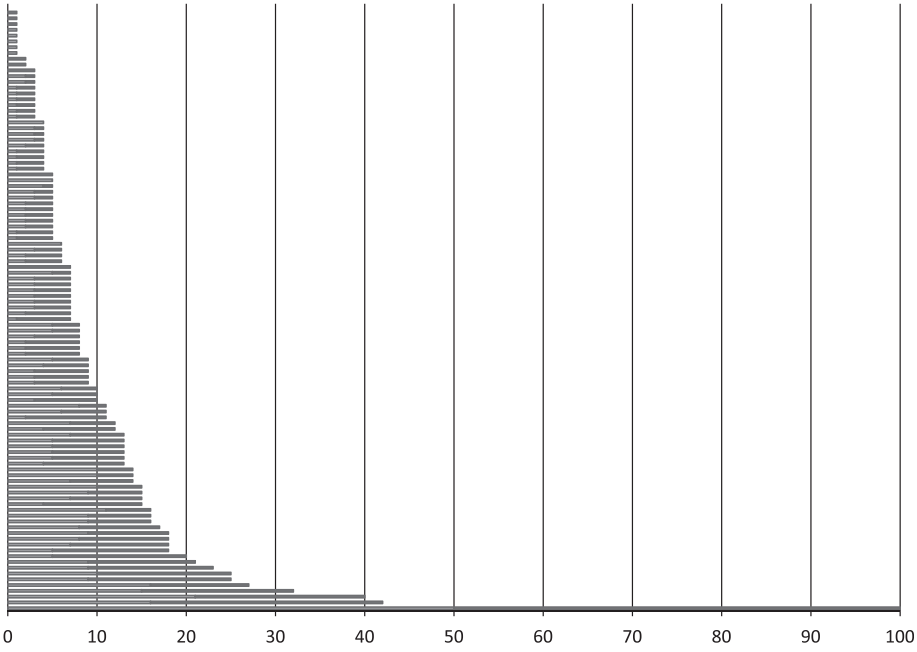

Fig. 2 – Number of orchidectomies per centre, 2001–2003 (light grey) and 2004–2006 (dark grey).

Table 5 – Variability of results and number of outlying centres per indicator.

Indicator		2001–2003				2004–2006			
		Range	*N* < lower limit	*N* > upper limit	Total *N* centres	Range	*N* < lower limit	*N* > upper limit	Total *N* centres
TC4	Proportion of patients with testicular cancer undergoing tumour marker assessment before any treatment	0–100%	15	8	95	14–100%	9	3	97
TC6	Proportion of patients with testicular cancer discussed at the multidisciplinary team meeting	–	–	–	–	0–100%	22	25	97
TC9	Proportion of patients with stage I non-seminoma treated with active surveillance	0–100%	0	21	56	0–100%	0	10	67

		2001–2006			
		Range	*N* < lower limit	*N* > upper limit	Total *N* centres
TC1	Overall 5-year survival (stage I only)	0–100%	9	0	97
TC3	Disease-free 5-year survival	50–100%	3	0	97

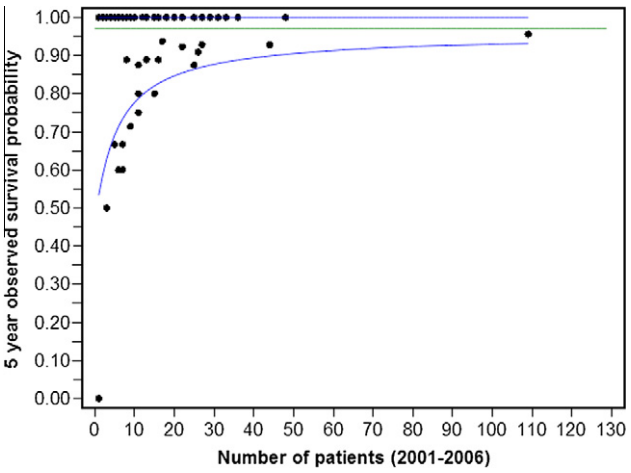

Fig. 3 – Observed 5-year survival for stage I testicular cancer, analysis by centre (N = 97), period 2001–2006.

number of outliers per indicator. Nine centres had a 5-year observed survival below the lower limit (Fig. 3). All these centres treated less than 20 patients between 2001 and 2006.

4. Discussion

To our knowledge, this is the first publication of a quality indicator set for testicular cancer in a peer-reviewed journal. For the selection of appropriate and relevant indicators, our literature search identified only one published indicator (TC4: 'Proportion of patients with testicular cancer undergoing tumour marker assessment before any treatment').[9] Of course, several countries and regions publish survival data for testicular cancer as part of a much broader reporting of survival outcomes for all cancer types. This is mainly done by national or regional cancer registries. The present study is unique in that process indicators for testicular cancer are evaluated in addition, covering the entire clinical pathway from diagnosis to follow-up.

The main strength of this study lies in its population-based approach. Although testicular cancer is a rare disease, a cohort of more than 1300 patients was studied, rendering it among the largest European cohorts on this topic.

The results of the present study show a mixed picture of the quality of care for patients with testicular cancer in Belgium for the period 2001–2006. Positive evolutions were found for the pre-treatment assessment of tumour markers and the MDT. Above this, the survival of testicular cancer patients is slightly improving since 2001. On the other hand, the proportion of stage I non-seminoma patients treated with active surveillance seems to be too low and still declining. Furthermore, the use of tumour marker assessment during active surveillance is increasing for seminomas (to a level above the recommended number), but decreasing for non-seminomas (to a level below the recommended number).

Importantly, for the interpretation of these evolutions, one should take into account the fact that a selection bias is present for the years 2001–2003 (and even 2004). In that period, mostly university hospitals participated at the cancer registration in Belgium. Also, regional differences in registration coverage were apparent at that time. Progressively, more and more smaller centres started to participate at the cancer registration, possibly resulting in a 'diluting' effect for some indicators (e.g. active surveillance). It would therefore be interesting to evaluate in how far each indicator remains stable over time on the individual centre level.

Between 2001 and 2003 the relative survival for the entire cohort rose from 92% to 95%. The survival rates found in the present study are in line with the rates reported for other countries (relative survival: The Netherlands 94% in 2003,[10] Sweden 94% 1999–2003,[11] US 96% 2001–2007[12]). However, where some reports described a difference in 5-year relative survival between seminomas and non-seminomas (France: 100% and 91%, respectively; Japan: 96% and 82%, respectively),[13,14] no such difference was found for the Belgian cohort.

In testicular cancer, the use of tumour markers is an important component of care as they impact the subsequent treatment and outcome. The proportion of patients with testicular cancer undergoing pre-treatment tumour marker assessment rose from 72% in 2001 to about 81% in 2006. In a US study using SEER data of 4742 testicular cancer cases (1998–2002), the proportion of patients undergoing tumour marker assessment (AFP and HCG) was 45%,[9] which is considerably lower than reported in the present study. In the US study, tumour marker use also varied substantially according to the SEER site.

The increase of the proportion of patients with testicular cancer discussed at an MDT meeting is not surprising, since the reimbursement was only introduced early 2003. However, in comparison to other tumour types, the proportion is rather low. For breast cancer for example, the proportion was already about 80% in 2006.[15] Importantly, the indicator only captures the billed MDT meetings. Above this, new financial incentives were adopted in 2010 to increase the use of the multidisciplinary meeting in Belgium.

Striking is the variability and dispersion of care for patients with testicular cancer. For five indicators a broad range of results were found across centres, mostly ranging between 0% and 100%. Furthermore, of all orchidectomies for testicular cancer between 2004 and 2006, 40% was performed in 14 centres, while the remaining 60% was performed in 83 centres. More than one-third of the centres treating patients with testicular cancer performed a mean of one orchidectomy or less per year between 2004 and 2006. This dispersion of care and the resulting low annual number of patients with testicular cancer in many centres renders definite comparison between centres difficult. It also raises questions about the organisation of care for these patients and the need to centralise this care in a limited number of centres. In at least one Japanese study[14] a relation between surgical volume and outcome for testicular cancer patients was suggested. Using data of 326 patients with testicular germ cell cancer diagnosed between 1993 and 1999, a significant association was found between survival and hospital procedure volume after adjustment for clinical stage, age and histology (adjusted hazard ratio for hospitals with at least 25 procedures compared to hospitals with seven or less procedures between 1993 and 1999: 0.111, 95% confidential interval (CI) 0.025–0.495). Although a volume-outcome analysis was not the

scope of this feasibility study, all nine outlying centres for the 5-year observed survival treated less than 20 patients during the 6-year period of our study.

The rates of active surveillance were found to be low in the Belgian cohort. For stage I seminomas, this can be explained by the fact that there is really a choice between active surveillance, single-dose carboplatin and radiotherapy.[6] However, for stage I non-seminomas, primary surveillance is recommended for patients *without vascular or lymphatic invasion and without a predominant embryonal component*.[6] Unfortunately, these characteristics could not be analysed in the present study to explain the low rate of active surveillance. In comparison, Osswald et al. found a rate of active surveillance of 41% for localised non-seminomas and 12% for localised seminomas.[16]

The use of retrospective administrative data can be considered a weakness of the present study. Of the 12 indicators, four were found to be not measurable, one was only partially measurable, and for two other indicators no direct information was available. To increase the number of measurable indicators, some variables would need to be registered mandatory, such as recurrence and radiation dose and field (clinical target volume). However, being a rare cancer, the impact of testicular cancer on public health is very limited. Above this, the survival data show that the prognosis of most patients with testicular cancer is already good with little room for improvement. Therefore, it may be more useful to focus on results suggesting overtreatment (e.g. the low number of patients treated with active surveillance) and on patients that died during the follow-up period. About 80 patients with testicular cancer died within 5 years after diagnosis in this cohort, which is a manageable number for a more in depth analysis of the medical file. Such an analysis of a limited number of medical files may be a more efficient alternative to the measurement of an entire quality indicator set.

This study also reports analyses based on relatively old data. Using administrative data implies a time lag of several years, which is due to delays in registration, the demand and linkage of data, and the calculation, interpretation and publication of the results. Nevertheless, the results presented in this article can serve as a baseline to follow-up the quality of care in the future in Belgium and to compare with other countries.

An additional limitation of administrative databases is that medical acts that are not billed cannot be identified. Therefore, medical acts as part of a clinical trial or medical acts that are not properly billed are not included in the claims data. This could have resulted in an underestimation of some quality indicator results.

A high percentage of missing pStages was found, being about 30% for the period 2001–2006. This is an important drawback of the present study, as the definition of many indicators involves cancer stage. Cancer stage reporting is one of the tasks of the responsible physician of the MDT meeting. One solution would be to link the reimbursement of the MDT meeting to a properly completed MDT form (including cancer stage).

Despite these limitations of administrative databases, they have the advantage of being exhaustive without extra efforts needed to register the data. Above this, this exhaustivity can be even further increased by successfully linking databases using a unique patient identifier.

5. Conclusion

The present study demonstrates the feasibility to develop a multidisciplinary set of quality indicators using a systematic approach. Using national cancer registry data linked to administrative claims data, a total of eight indicators were measurable. The results show a mixed picture of the quality of care for testicular cancer patients in Belgium. Survival is good, but there are indications of over- and underuse of certain interventions. Above this, the results suggest an important variability and dispersion of care.

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Conflict of interest statement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ejca.2011.10.023.

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