Support Care Cancer (2015) 23:3025–3032
DOI 10.1007/s00520-015-2671-3

ORIGINAL ARTICLE

Does routine symptom screening with ESAS decrease ED visits in breast cancer patients undergoing adjuvant chemotherapy?

L. Barbera · R. Sutradhar · D. Howell · J. Sussman · H. Seow · D. Dudgeon · C. Atzema · C. Earle · A. Husain · Y. Liu · M. K. Krzyzanowska

Received: 2 December 2014 / Accepted: 15 February 2015 / Published online: 26 February 2015

Abstract
Background In 2007, the provincial cancer agency in Ontario, Canada initiated a wide-scale program to screen for symptoms in the cancer population using the Edmonton Symptom Assessment Scale (ESAS). The purpose of this study is to evaluate the impact of screening with ESAS on emergency department (ED) visit rates in women with breast cancer receiving adjuvant chemotherapy.
Patients and methods This retrospective cohort study used linked administrative health care data from across the province of Ontario, Canada. The cohort included all women aged ≥18 who were diagnosed with stage I–III breast cancer between January 2007 and December 2009 and received adjuvant chemotherapy within 6 months of diagnosis. Using an adjusted recurrent event model, we examined the association of screening with ESAS at a clinic visit on the ED visit rate.
Results The relative rate of ED visits was 0.57 when prior ESAS screening occurred compared to when it did not. The relative rate of ED visits was 0.83 when the prior number of ESAS screens was modeled as a continuous variable. Alternatively stated, the rate of ED visits was 43 % lower among patients previously screened with ESAS compared to those not previously screened. For each additional prior ESAS assessment, there was a 17 % decreased rate of ED visits.
Conclusions Our results demonstrate that screening with ESAS is associated with decreased ED visits. To our

An abstract of this work was presented at the 2014 ASCO Annual Meeting.

L. Barbera (✉)
Odette Cancer Centre, 2075 Bayview Avenue,
Toronto, Ontario M4N 3M5, Canada
e-mail: lisa.barbera@sunnybrook.ca

L. Barbera
Department of Radiation Oncology, University of Toronto,
Toronto, Ontario, Canada

L. Barbera · R. Sutradhar · H. Seow · C. Atzema · C. Earle · Y. Liu · M. K. Krzyzanowska
Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada

R. Sutradhar
Department of Biostatistics, Dalla Lana School of Public Health,
University of Toronto, Toronto, Ontario, Canada

D. Howell
Faculty of Nursing, University of Toronto, Toronto, Ontario, Canada

D. Howell · M. K. Krzyzanowska
University Health Network, Princess Margaret Hospital,
Toronto, Ontario, Canada

J. Sussman · H. Seow
Department of Oncology, McMaster University, Hamilton, Ontario,
Canada

J. Sussman · H. Seow
Supportive Cancer Care Research Unit, Hamilton, Ontario, Canada

D. Dudgeon
Departments of Medicine and Oncology, Queen's University,
Kingston, Ontario, Canada

C. Atzema · C. Earle · M. K. Krzyzanowska
Department of Medicine, University of Toronto, Toronto, Ontario,
Canada

A. Husain
Department of Family and Community Medicine, University of
Toronto, Toronto, Ontario, Canada

knowledge, this is the first report on the effectiveness of routinely documenting a patient reported outcome on ED visits, in a real-world setting.

Keywords ESAS · Emergency department visits · Adjuvant chemotherapy · Breast cancer

Introduction

Breast cancer is the most common cancer in women [1]. Indications for adjuvant chemotherapy are broad, so many women receive a recommendation for adjuvant chemotherapy of some type. Unfortunately, many of the regimens can be quite toxic which may impact on several different outcomes. Unplanned visits to the emergency department (ED) and/or hospitalization, for example, may occur in as many as 42–60 % of these women, reflecting the magnitude of acute toxicity experienced by these patients [2, 3].

Documentation of patient-reported outcomes (PROs) as a part of routine clinical care is gaining increasing interest amongst many cancer health care providers. Several randomized clinical trials have demonstrated improved outcomes with routinely collected PROs compared to usual care, including communication and patient satisfaction [4–8]. Many large academic centers have started implementing routine collection of PROs [9–11].

Since 2007, Cancer Care Ontario, the cancer agency in Ontario, Canada, has systematically collected symptom scores in cancer outpatients by implementing the Edmonton Symptom Assessment System (ESAS) as a standardized tool in all cancer centers. One of the goals of this initiative is to improve symptom management through earlier identification, documentation, and communication of patients' symptoms. The ESAS is a well known and validated tool to screen for the presence and severity of symptoms [12]. The identification of symptoms with this screening tool is meant to prompt a further detailed assessment, with possible intervention depending on the findings. In essence, Ontario has implemented population-wide standardized symptom assessment for cancer outpatients.

The purpose of this study is to evaluate the impact of screening with ESAS through the Ontario Symptom Management Collaborative (OCSMC) on ED visit rates in women with breast cancer receiving adjuvant chemotherapy. We hypothesized that when women are screened with ESAS as part of the screening program, they would experience fewer ED visits, presumably on the basis of improved symptom control.

Methods

Study design

This retrospective cohort study used linked administrative health care data from across the province of Ontario, Canada. Data linkage was completed using a unique encrypted patient identifier. The study was approved by the privacy office of the Institute for Clinical Evaluative Sciences (ICES) and complied with its' stringent data confidentiality and privacy guidelines.

Study population

The cohort included all women aged ≥18 in Ontario diagnosed with stage I–III breast cancer between January 2007 and December 2009 who received adjuvant chemotherapy within 6 months of diagnosis. This is a population at high risk of experiencing the outcome but otherwise homogeneous allowing us to better control for confounders.

Patients were excluded if they had an invalid or missing provincial health insurance number (which precluded linkage). Other exclusion criteria were male sex and any prior history of cancer or another cancer diagnosis (different primary site) within 14 months of the breast cancer diagnosis.

The observation window for individuals in the cohort started on the first day of chemotherapy and ended 30 days after the last day of chemotherapy.

Study setting

The study setting was the province of Ontario, Canada, whose population exceeds 13 million people. Chemotherapy is provided to women in regional cancer centers or cancer clinics in community hospitals. All care is provided by a government-funded single-payer health plan. During the time of this study, the OCSMC was predominantly active in regional cancer centers.

Details of the provincial initiative to routinely collect ESAS scores have been previously reported [13–15]. Briefly, standardized assessment using ESAS is completed at each patient's cancer center visit. Typically, patients complete the ESAS via a web-based tool that allows patients to enter their own scores at a touch screen kiosk in the clinic waiting area. Alternatively, the scores can be completed on paper which is then entered into an electronic database. A printed summary of the symptom scores, including those from previous visits, is then provided to the primary clinical team, the aim being to facilitate discussion of any potentially problematic symptoms.

Patients eligible for symptom screening included those living in all regions of the province, with any cancer diagnoses, of any age, with any treatment intent, and receiving care in the ambulatory setting. Assessments happened on an

opportunistic basis depending on how each cancer center implemented the standardized tool. Ideally, all patients were screened at every cancer clinic visit; however, this is not the same as being systematically screened at regular intervals as one would do in a research study. Participating centers gradually increased their screened population as they were able. In 2008, about 45 % of the lung cancer population and 15 % of the remaining cancer patients in Ontario were screened [16].

Data sources

The data source used to identify screening with ESAS is the Symptom Management Reporting Database (SMRD) held by Cancer Care Ontario. Emergency department visits are captured in the Canadian Institute for Health Information National Ambulatory Care Reporting System (CIHI-NACRS). As well, the study utilized other administrative databases: the Ontario Cancer Registry, a comprehensive population-based cancer registry created to capture all incident cases of cancer in the province [17, 18]; the Collaborative Staging Database which captures stage; the Registered Persons Database, contains sociodemographic information on all residents of Ontario who are eligible for the universal government-funded health care plan [19]; the Canadian Institute for Health Information's Discharge Abstract Database which lists diagnostic and procedure codes from all inpatient and outpatient hospital admissions [20]; the Ontario Health Insurance Plan (OHIP) which reimburses physicians for their work and has claims for all visits; and the New Drug Funding Program (NDFP) which contains records documenting chemotherapy drug regimens prescribed and dates. Older inexpensive drugs are not covered by NDFP (e.g., cyclophosphamide, adriamycin) and for these patients, chemotherapy use was identified using physician billing claims (OHIP).

Exposure definition

The exposure for this study was whether or not an ESAS assessment was completed at a visit to the clinic. All eligible clinic visits were identified (described in next paragraph). For each visit date, a flag was created to indicate if an ESAS happened that day. A single patient may have no ESAS assessments, a single assessment, or several assessments during the observation window.

All clinic visits eligible for an ESAS screen were identified for each woman in the cohort. These visits were divided into three types: (1) visits for a chemotherapy injection, date from NDFP or OHIP; (2) visits to the chemotherapy provider for purposes other than a chemotherapy injection; (3) visits to a radiation oncologist. While other providers were involved in the care of these women, the visits could not be reliably identified as a visit where an ESAS exposure could have occurred. Together, the dates of these three types of visits were then linked back to the SMRD. We were able to match 90 % of the ESAS assessment dates known to occur during the observation window to identified clinic visit dates. The remaining 10 % of the ESAS assessments were omitted from the analysis.

Outcome definitions

The outcome was unplanned emergency department visits during the observation window. NACRS codes visits as planned or unplanned (for example, a patient with a lacerated leg who is instructed to return the following day for a dressing change). Planned visits occur very infrequently.

Covariate definitions

Age, region, and neighborhood income quintile (based on postal code linkage [21]) were taken from the Registered Persons Database. "Best stage" was obtained from the Collaborative Staging Database. Comorbidity was calculated using the Deyo modification of the Charlson score based on diagnoses coded in Discharge Abstract Database in the 5 years prior to surgery with scores for primary cancer subtracted [22]. Previous analysis with this cohort [3] has demonstrated that chemotherapy regimens containing docetaxel were associated with increased ED use. We therefore controlled for this variable in our analysis. It was assumed that patients whose regimens were not documented in NDFP received older chemotherapy regimens without a taxane.

Statistical analysis

As each patient may experience multiple unplanned emergency department visits, we modeled the association between covariates and the rate of ED visits using an Andersen-Gill [23] recurrent event model under a counting process framework [24]. The recurrent event model has been well studied in the statistical literature [25, 26]. It is similar in concept to the Cox model, but it allows for the outcome to occur multiple times during the observation window. To address correlation among ED visits from the same patient, robust standard errors of the model parameter estimates were calculated using a sandwich approach. ESAS exposure was incorporated into the recurrent event model as a time-varying covariate using two different techniques. The first technique captured prior ESAS exposure as binary time-varying covariate. That is, for each patient, at any given time t, this covariate reflected whether or not there was ESAS exposure prior to this time. The second technique captured prior cumulative ESAS exposure as a continuous time-varying covariate. That is, for each patient, at any given time t, this covariate reflected the cumulative number of visits with ESAS screening prior to this time. Using the binary technique, the resultant relative rate at any

given time t provides the adjusted ED rate for a patient who was exposed to ESAS (by time t) compared to the adjusted ED rate for a patient who was not yet exposed to ESAS (by time t). The statistical and clinical literature offer several examples on the implementation of such time-varying covariates in a recurrent event model [24, 27–29].

To visualize the data, we first plotted the unadjusted expected cumulative number of ED visits over time, also known as the mean cumulative function plot [24]. This was done for women with and without prior ESAS exposure. Since this exposure was time-varying, a woman only contributed to the prior ESAS exposure "yes" curve once that had experienced at least one ESAS assessment. A series of univariate and multivariable recurrent event models were performed. The main covariate of interest was time-varying ESAS exposure, defined using the two techniques described above. Under each technique, the multivariable model adjusted for baseline/time-fixed characteristics (age as a continuous variable, region,

Table 1 Characteristics of women in cohort

Variable	Value	Total cohort	With ESAS screening	Without ESAS screening
		N=8359	*N*=2541	*N*=5818
Age	Mean	53.7	53.22±10.44	53.87±10.57
	18–29	59 (0.7 %)	20 (0.8 %)	39 (0.7 %)
	30–39	663 (7.9 %)	217 (8.5 %)	446 (7.7 %)
	40–49	2333 (27.9 %)	724 (28.5 %)	1609 (27.7 %)
	50–59	2764 (33.1 %)	847 (33.3 %)	1917 (32.9 %)
	60–69	1967 (23.5 %)	584 (23.0 %)	1383 (23.8 %)
	70–79	521 (6.2 %)	134 (5.3 %)	387 (6.7 %)
	80–89	50 (0.6 %)	15 (0.6 %)	35 (0.6 %)
	90–99	2 (0.02 %)	0 (0.0 %)	<6 (0.0 %)
Stage	I	1844 (22.1 %)	539 (21.2 %)	1305 (22.4 %)
	II	4477 (53.6 %)	1384 (54.5 %)	3093 (53.2 %)
	III	1587 (19.0 %)	521 (20.5 %)	1066 (18.3 %)
	Unknown	451 (5.4 %)	97 (3.8 %)	354 (6.1 %)
Regimen	Docetaxol yes	5096 (61.0 %)	1460 (57.5 %)	3636 (62.5 %)
	Docetaxol no	3263 (39.0 %)	1080 (42.5 %)	2182 (37.5 %)
Charlson	0	7685 (91.9 %)	2328 (91.6 %)	5357 (92.1 %)
	1+	674 (8.1 %)	231 (8.4 %)	461 (7.9)
Income quintile	1	1294 (15.5 %)	324 (12.8 %)	970 (16.7 %)
	2	1543 (18.5 %)	436 (17.2 %)	1107 (19.0 %)
	3	1720 (20.6 %)	539 (21.2 %)	1181 (20.3 %)
	4	1877 (22.4 %)	624 (24.6 %)	1253 (21.5 %)
	5	1925 (23.0 %)	618 (24.3 %)	1307 (22.5 %)
Region	1	416 (5.0 %)	260 (10.2 %)	156 (2.7 %)
	2	616 (7.4 %)	232 (9.1 %)	384 (6.6 %)
	3	403 (4.8 %)	168 (6.6 %)	235 (4.0 %)
	4	922 (11.0 %)	272 (10.7 %)	650 (11.2 %)
	5	518 (6.2 %)	185 (7.3 %)	333 (5.7 %)
	6	686 (8.2 %)	309 (12.2 %)	377 (6.5 %)
	7	614 (7.4 %)	20 (0.8 %)	594 (10.2 %)
	8	1093 (13.1 %)	142 (5.6 %)	951 (16.3 %)
	9	1041 (12.5 %)	79 (3.1 %)	962 (16.5 %)
	10	312 (3.7 %)	130 (5.1 %)	182 (3.1 %)
	11	821 (9.8 %)	351 (13.8 %)	470 (8.1 %)
	12	328 (3.9 %)	218 (8.6 %)	110 (1.9 %)
	13	429 (5.1 %)	76 (3.0 %)	353 (6.1 %)
	14	159 (1.9 %)	99 (3.9 %)	60 (1.0 %)
	Missing	<6	0	<6

neighborhood income quintile and Charlson score, stage). The three other types of clinic visits were incorporated into the model as time-varying cumulative count covariates. We adjusted for the use of docetaxel-containing regimens as a binary time-varying covariate. That is, the variable was "switched on" the first date the docetaxel chemotherapy occurred and left "on" for the remainder of the analysis. Similar to previous work [28], since prior ED visits may be associated with subsequent ED visits, we also adjusted for the prior number ED visits as a time-varying covariate. Analysis was completed using SAS 9.2 (Carey, NC).

Results

We identified 8359 women with stage I–III breast cancer who received adjuvant chemotherapy. One third of these women were screened with at least one ESAS assessment. The cohort is described in Table 1. Although the regression analyses do not directly compare individuals screened with ESAS to those without, we have included this description to provide more details about the two groups. The differences observed between groups that may be clinically important are stage (more unknown for group without ESAS), docetaxel chemotherapy (more common in group without ESAS), and region.

Table 2 shows the mean and median number of ESAS assessments, clinic visits, and ED visits over the entire observation window. For example, the mean number of ESAS assessments for the 2541 women who had at least one ESAS was 3.82. The median number of radiation oncologist visits for the 5273 women who had such a visit was 1.

Figure 1 presents the unadjusted expected cumulative number of ED events over time for women with and without prior ESAS assessments (a patient only contributes to the ESAS exposure "yes" curve once they had at least one ESAS visit). This initial analysis clearly demonstrates that the expected cumulative number of ED events by any time t is consistently higher among women who have not yet been exposed to ESAS compared to women who have been exposed to ESAS by this time.

Table 3 shows the results for the univariate and adjusted models examining the association between ESAS exposure and ED visit rates. Regardless of technique used to capture ESAS exposure, being screened with ESAS was associated with a decreased ED visit rate. The relative rate of ED visits was 0.57 when prior ESAS screening occurred compared to when it did not. Alternatively stated, the rate of ED visits was 43 % lower among patients who had been previously screened for ESAS at least once compared to those who had not. Likewise, for each additional prior ESAS assessment, there was a 17 % decreased rate of ED visits. We further observed that additional visits to clinic (regardless of type) also protected against ED visits. It should be noted that the preventative association of screening with ESAS on ED visits was maintained even while controlling for these other visits. Finally, regional variation was observed in the adjusted analyses with some regions having a relative rate of up to 2.0.

Discussion

This study demonstrates that screening with ESAS is associated with a decrease in ED visits in women with breast cancer receiving adjuvant chemotherapy. The rate of ED visits was 43 % lower among women previously screened for ESAS compared to women who were not. Each additional prior ESAS assessment decreased the ED visit rate by 17 %. To our knowledge, this is the first study to suggest a positive effect of a routinely documented PRO on health service utilization. In addition, we are unaware of another study evaluating the effectiveness of a large-scale programmatic change using PROs, like OCSMC.

Our results do not prove causality between screening with ESAS and decreased ED visits, only an association. Possible mechanisms by which symptom screening could decrease ED visits include improved identification of symptoms, more timely identification of symptoms, improved symptom management, improved timeliness of symptom management, or improved patient willingness to report symptoms. It is also possible that the ESAS itself is not solely responsible for the decreased ED visits but rather a marker for other changes in how patients are being managed. In the context of Anderson's model of health service use, symptom screening may result in a better characterization of need resulting in a different response from the health care system and subsequent change in health service utilization [30].

Table 2 Crude number of events (ESAS assessments, clinic visits by type, or ED visits) over entire observation interval, for the cohort of N=8359

	ESAS assessments	Chemotherapy delivery visits	Radiation oncologist visits	Chemoprovider visits	ED
Number of people without event	5818	0	3086	1362	5186
Number of people with event	2541	8359	5273	6997	3173
Mean±SD[a]	3.82±3.08	5.38±2.1	1.47±0.91	3.8±2.38	1.62±1.12
Median (IQR)[a]	3 (1–5)	6 (4–6)	1 (1–2)	3 (2–5)	1 (1–2)

[a] Among those with event

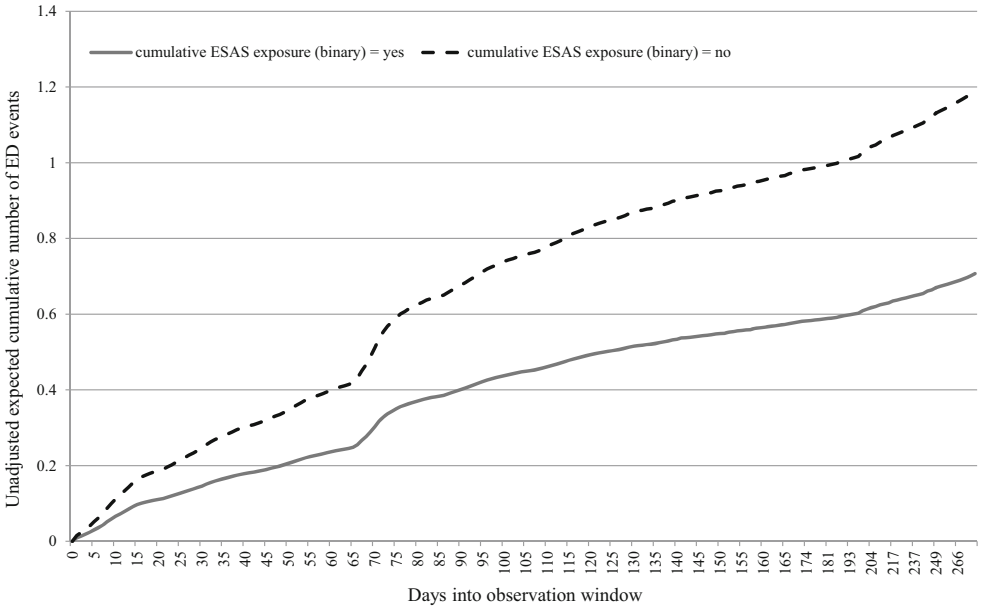

Fig. 1 Mean cumulative unadjusted ED rate by ESAS exposure

It is important to note that ESAS was originally developed in advanced cancer patients [12]. It was subsequently validated in a more general oncology population, which did not include breast cancer [31]. This study demonstrates the

Table 3 Univariate and adjusted model results for relative rate of ED visit

Variable	Value	Univariate			Adjusted					
					ESAS (Y/N)			ESAS (Continuous)		
		RR	LCL	UCL	RR	LCL	UCL	RR	LCL	UCL
Age	Continuous	1.00	1.00	1.01	0.99	0.99	0.99	0.99	0.99	0.99
Income quintile	1	1.26	1.13	1.40	1.12	1.01	1.25	1.12	1.01	1.24
	2	1.16	1.04	1.28	0.95	0.85	1.06	0.94	0.84	1.05
	3	1.24	1.12	1.37	0.98	0.88	1.10	0.97	0.87	1.08
	4	1.11	1.01	1.22	1.03	0.93	1.14	1.03	0.93	1.13
	5	1			1		1			
Charlson	0	1			1		1			
	1	1.35	1.22	1.51	1.01	0.90	1.14	1.03	0.92	1.16
Stage	I	1			1			1		
	II	1.09	1.00	1.19	1.21	1.11	1.32	1.22	1.12	1.33
	III	1.14	1.02	1.27	1.31	1.17	1.48	1.31	1.17	1.48
	Unknown	1.37	1.19	1.59	1.46	1.24	1.72	1.47	1.25	1.73
Docetaxol regimen	Yes	1.99	1.85	2.14	5.17	4.70	5.68	5.08	4.62	5.58
	No	1				1		1		
RO visit	Continuous	0.42	0.39	0.45	0.60	0.56	0.65	0.60	0.56	0.65
CT delivery visit	Continuous	0.51	0.49	0.52	0.40	0.38	0.42	0.40	0.38	0.42
CP visit	Continuous	0.76	0.75	0.78	0.79	0.77	0.81	0.79	0.77	0.81
Prior ED	Continuous	1.41	1.35	1.46	1.31	1.27	1.35	1.31	1.27	1.35
ESAS exposure	Yes	0.59	0.55	0.64	0.57	0.52	0.63	–	–	–
	No	1								
	Continuous	0.84	0.82	0.86	–	–	–	0.83	0.81	0.86

Exposure to ESAS during chemotherapy is defined alternately as either as a dichotomous (Y/N) or continuous variable (model also adjusted for region)
RR relative rate, *LCL* lower confidence limit, *UCL* upper confidence limit, *RO* radiation oncologist, *CT* chemotherapy, *CP* chemotherapy provider

potential utility of ESAS for breast cancer patients and in the adjuvant treatment setting. This may allay some concerns about using a generic PRO in this population.

A comprehensive review of the impact of routine collection of PROs on patients, providers, and health organizations in an oncologic setting was recently published [32]. The authors identified 27 studies showing strong evidence that routinely collected PROs, with feedback, improves patient-provider communication and increases patient satisfaction. They further comment that there was little or no evidence that routinely collected PROs have led to improvements in many areas including quality improvement or system performance at a population level. Our study makes a significant contribution to this area of study. A more recent review of randomized controlled trials identified five trials that included health service use as an outcome, but none evaluated emergency department visits [33].

Prior research has demonstrated the frequency of chemotherapy toxicity-related emergency department visits [2, 3]. Emerging literature is examining interventions that include PROs, to improve chemotherapy-related toxicity. For example, a cellphone for symptom reporting with nurse monitoring has been successfully developed in the UK [34]. Results from the current study are consistent with the concept of routinely report patient outcomes improving toxicity outcomes.

The strengths of this study include the rigorous analytic method used. The analytic approach was best suited to the structure of the data, and we controlled for several possible confounders.

The study has several limitations. Modest differences were observed between those who were screened and those who were not. The model was adjusted for all of these differences, including comorbidity, stage, type of chemotherapy, and number of visits to the clinic. In spite of adjustments made, there may be confounders for which we were unable to adjust, that are contributing to the observed outcome in this otherwise homogeneous cohort. We are unable to comment if the effect of ESAS screening would be observed in other patient populations, especially those whose baseline risk of ED visits is low. We are also unable to draw conclusions about the ability of other instruments or tools to have same effect in this population. Finally, because we omitted 10 % of the ESAS assessments, these results may underestimate the magnitude of the association.

Provincial implementation of OSCMC was based on a successful pilot, which suggested decreased ED visits [14]. The results of this large-scale investigation of the same endpoint, albeit in a different subgroup of patients, are consistent with the original pilot findings.

Acknowledgments This study was conducted with the support of the Ontario Institute for Cancer Research through funding provided by the Government of Ontario. This study was supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the MOHLTC is intended or should be inferred. The authors would like to thank Sean Molloy and Jose Pereira for their insight and explanations regarding the SMDB and Joan Porter for her comments on the manuscript.

Funding source This study was conducted with the support of the Ontario Institute for Cancer Research through funding provided by the Government of Ontario.

Conflict of interest The authors have declared no conflicts of interest.

References

1. Canadian Cancer Society/National Cancer Institute of Canada (2013) Canadian Cancer Statistics 2013. Toronto
2. Hassett MJ, O'Malley AJ, Pakes JR, Newhouse JP, Earle CC (2006) Frequency and cost of chemotherapy-related serious adverse effects in a population sample of women with breast cancer. J Natl Cancer Inst 98:1108–1117
3. Enright K, Grunfeld E, Yun L, Moineddin R, Ghannam M, Dent S et al (2015) Population-based assessment of emergency room visits and hospitalizations among women receiving adjuvant chemotherapy for early breast cancer. J Oncol Pract. doi:10.1200/JOP.2014.001073
4. Detmar SB, Muller MJ, Schornagel JH, Wever LD, Aaronson NK (2002) Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. JAMA 288:3027–3034
5. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM et al (2004) Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol 22:714–724
6. Taenzer P, Bultz BD, Carlson LE, Speca M, DeGagne T, Olson K et al (2000) Impact of computerized quality of life screening on physician behaviour and patient satisfaction in lung cancer outpatients. Psychooncology 9:203–213
7. Cleeland CS, Wang XS, Shi Q, Mendoza TR, Wright SL, Berry MD et al (2011) Automated symptom alerts reduce postoperative symptom severity after cancer surgery: a randomized controlled clinical trial. J Clin Oncol 29:994–1000
8. Berry DL, Blumenstein BA, Halpenny B, Wolpin S, Fann JR, Austin-Seymour M et al (2011) Enhancing patient-provider communication with the electronic self-report assessment for cancer: a randomized trial. J Clin Oncol 29:1029–1035
9. Snyder CF, Jensen R, Courtin SO, Wu AW (2009) PatientViewpoint: a website for patient-reported outcomes assessment. Qual Life Res 18:793–800
10. Basch E, Artz D, Iasonos A, Speakman J, Shannon K, Lin K et al (2007) Evaluation of an online platform for cancer patient self-reporting of chemotherapy toxicities. J Am Med Inform Assoc 14: 264–268
11. Abernethy AP, Herndon JE, Wheeler JL, Patwardhan M, Shaw H, Lyerly HK et al (2008) Improving health care efficiency and quality using tablet personal computers to collect research-quality, patient-reported data. Health Serv Res 43:1975–1991
12. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K (1991) The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. J Palliat Care 7:6–9

13. Barbera L, Seow H, Howell D, Sutradhar R, Earle C, Liu Y et al (2010) Symptom burden and performance status in a population-based cohort of ambulatory cancer patients. Cancer 116:5767–5776
14. Dudgeon DJ, Knott C, Eichholz M, Gerlach JL, Chapman C, Viola R et al (2008) Palliative Care Integration Project (PCIP) quality improvement strategy evaluation. J Pain Symptom Manag 35:573–582
15. Dudgeon DJ, Knott C, Chapman C, Coulson K, Jeffery E, Preston S et al (2009) Development, implementation, and process evaluation of a regional palliative care quality improvement project. J Pain Symptom Manag 38:483–495
16. Cancer Care Ontario. Cancer System Quality Index. http://csqi.cancercare.on.ca/
17. Clarke EA, Marrett LD, Kreiger N (1991) Cancer registration in Ontario: a computer approach. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG (eds) Cancer registration principles and methods. IARC Pub, Lyon, pp 246–257
18. Robles SC, Marrett LD, Clarke EA, Risch HA (1988) An application of capture-recapture methods to the estimation of completeness of cancer registration. J Clin Epidemiol 41:495–501
19. Iron K, Zagorski BM, Sykora K, Manuel DG (2008) Living and dying in Ontario: an opportunity for improved health information. ICES investigative report. Institute for Clinical Evaluative Sciences, Toronto
20. Canadian Institute for Health Information (2004) Data quality of the discharge abstract database following the first year implementation of ICD-10-CA/CCI-Final Report. CIHI, Ottawa
21. Wilkins R (2001) PCCF + Version 3G users guide: automated geographic coding based on the statistics canada postal code conversions files. Statistics Canada, Ottawa
22. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 45:613–619
23. Andersen PK, Gill RD (1982) Cox's regression model for counting processes: a large sample study. Ann Stat 10:1100–1120
24. Therneau TM, Grambsch PM (2000) Modeling survival data: extending the Cox model. Springer, New York
25. Cook RJ, Lawless JF (2002) Analysis of repeated events. Stat Methods Med Res 11:141–166
26. Twisk JW, Smidt N, de Vente W (2005) Applied analysis of recurrent events: a practical overview. J Epidemiol Community Health 59: 706–710
27. Sorup S, Benn CS, Poulsen A, Krause TG, Aaby P, Ravn H (2014) Live vaccine against measles, mumps, and rubella and the risk of hospital admissions for nontargeted infections. JAMA 311:826–835
28. Guo Z, Gill TM, Allore HG (2008) Modeling repeated time-to-event health conditions with discontinuous risk intervals. An example of a longitudinal study of functional disability among older persons. Methods Inf Med 47:107–116
29. Arneson TJ, Liu J, Qiu Y, Gilbertson DT, Foley RN, Collins AJ (2010) Hospital treatment for fluid overload in the Medicare hemodialysis population. Clin J Am Soc Nephrol 5:1054–1063
30. Andersen RM (1995) Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav 36:1–10
31. Chang VT, Hwang SS, Feuerman M (2000) Validation of the Edmonton symptom assessment scale. Cancer 88:2164–2171
32. Chen J, Ou L, Hollis SJ (2013) A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. BMC Health Serv Res 13:211
33. Kotronoulas G, Kearney N, Maguire R, Harrow A, Di Domenico D, Croy S et al (2014) What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 32:1480–1501
34. McCann L, Maguire R, Miller M, Kearney N (2009) Patients' perceptions and experiences of using a mobile phone-based advanced symptom management system (ASyMS) to monitor and manage chemotherapy related toxicity. Eur J Cancer Care (Engl) 18:156–164