

Drug Safety Studies Using Cancer Registry Data: Confluence of Elements Impacting the Interview Response Rate

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ABSTRACT

Background: Conducting research with patients identified through US cancer registries is challenging in the context of current privacy regulations, and cancer registries may lack internal resources to participate in outside research. An ongoing 15-year surveillance program, initiated in 2002, provides an opportunity to share lessons learned relating to these challenges.

Objectives: To examine the impact of patient privacy requirements and other factors at cancer registries on interview response rates in an ongoing safety surveillance study.

Methods: Participating cancer registries were grouped into categories by patient access pathway (i.e., steps required by the local cancer registry to be completed prior to direct patient contact). A descriptive analysis examined telephone interview response rates, stratified by type of access pathway and time from diagnosis to reporting to researcher. In addition, other factors reported by individual registries that may impact response rate were examined.

Results: As of September 2010, 16 cancer registries, with 5 distinct pathways for accessing patients, had identified 1,236 patients; of these, 449 were interviewed. The highest interview rate (46%) occurred when the patient's physician was notified and allowed to decline before the patient was contacted. Interview response rates among cases with contact information (n = 969) were inversely related to time from diagnosis to time reported to researcher: 0-1 year (55%), 1-2 years (45%), 2-3 years (41%), > 3 years (38%). Other factors reported by individual registries included restrictions on use of nonpublic databases and lack of internal resources, which impede the registry's ability to maintain updated contact information for patients, proxies, and physicians.

Conclusions: In the US, current procedures and policies in place regarding patient privacy hinder the ability to conduct observational research and have been demonstrated to be associated with lower interview response rates in this safety surveillance study.

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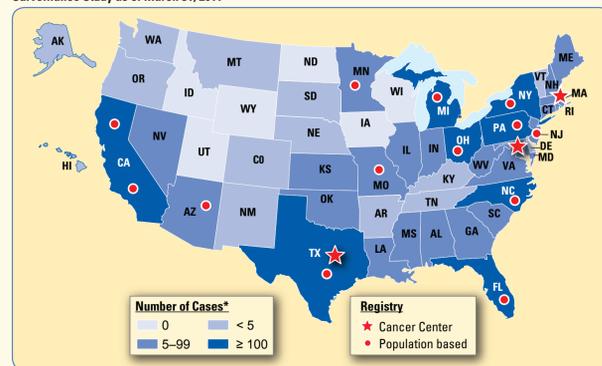
BACKGROUND

- The implementation of the HIPAA Privacy Rule has had a measurable impact on the ability to conduct multi-site research studies with patients.¹
- United States (US) cancer registries are considered a gold standard for identification of incident cancers because of the high proportion of cases they capture in the catchment area and the documentation they require to confirm a cancer case; however, they often have administrative, legal, or resource constraints that can impede their ability to participate in research beyond characterizing the cancer burden in their catchment area.
- An ongoing 15-year surveillance program provides a unique opportunity to evaluate and characterize individual patient and institutional level factors that may affect participation in an epidemiologic study requiring direct contact with patients.

US Adult Osteosarcoma Surveillance Study

- At the request of the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), a safety surveillance study was initiated in the US and Europe.²
- The study was initiated in 2002 to monitor for a signal of a possible association between teriparatide, an injectable treatment for osteoporosis, and adult osteosarcoma.
- Current primary objectives:
 - To identify and interview 33% of newly diagnosed cases of osteosarcoma in adults aged 40 years and older in the US, for a duration of 15 years.
 - To determine incident cases, if any, in those who have a history of treatment with teriparatide.
- Case ascertainment: Conducted by cancer registries and cancer information sent to RTI.
- Information transfer to RTI: Cancer registries use locally approved patient access pathways prior to sending patient contact information for identified cases.
- Exposure ascertainment: RTI conducts telephone interviews with the identified patient or, if deceased, his or her proxy.
- Analysis: Compare observed versus expected exposure in osteosarcoma patients.
- Precision: Sufficient size to detect a tripling in the risk compared with the general population of similar age and sex by the end of the study.

Figure 1. US Registries Contributing Data and Residence of Cases Identified in the US Adult Osteosarcoma Surveillance Study as of March 31, 2011



OBJECTIVE

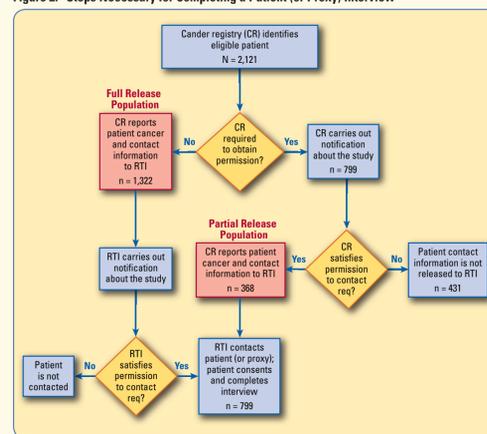
- To examine the impact of patient access pathway, lag time, vital status, sex, cancer type, and introduction of participant compensation on interview rates in an ongoing safety surveillance study.

METHODS

Design

- We conducted descriptive and multivariate analyses to identify registry and patient factors associated with successful completion of a telephone interview.
 - Descriptive Analysis #1: The interview rate was stratified by the patient access pathways described above for all patients identified by contributing cancer registries.
 - Descriptive Analysis #2: The interview rate was stratified by lag time for the Full Release and Partial Release Populations combined (Figure 2).
- Cancer registries with more restrictive patient access pathways were added later during implementation of the study; hence, patients from registries added later have a longer average lag time. We attempted to account for this impact by further limiting the lag-time analysis to the Full Release Population (Figure 2).
- Multivariate analysis: Using stepwise logistic regression we evaluated impact of the explanatory variables (listed below) on the dependent binary variable of whether an interview was completed (yes/no). Because some cancer registries cannot provide the explanatory variables in a manner that allows them to be linked to whether an interview was completed, this analysis was limited to the Full Release Population. Due to this restriction, the pathways of MD Notify and Patient Release, and MD Permission and Patient Release could not be considered in the model, because these two pathways are only associated with cancer registries that provide the Partial Release Population.
- Explanatory variables considered included the following:
 - Patient access pathway (from most restrictive to least restrictive: MD Notification, Patient Release Required, and MD Permission Required)
 - Lag time: ≤ 1 year or > 1 year)
 - Vital status at time the case is identified by the cancer registry: alive vs. deceased
 - Sex
 - ICD-0-3 group (osteosarcoma vs. other protocol defined cancers)
 - Date case reported to RTI before or after September 2008 (Proxy variable for receipt of \$25 incentive implemented fall 2008).

Figure 2. Steps Necessary for Completing a Patient (or Proxy) Interview



CR = cancer registry.

Definitions

- Some cancer registries may release contact information to RTI for the entire study population covered (Figure 2, **Full Release Population**), while other cancer registries may only release contact information to RTI after local release requirements have been fulfilled (Figure 2, **Partial Release Population**). Therefore, data on all potentially eligible patients can only be captured and analyzed for the Full Release Population.
- Patient access pathways:** The series of steps (notifications that must be carried out and permissions obtained) completed by the local cancer registry before patient contact information can be released to RTI. Pathways also include the steps RTI must complete before contacting a patient regarding his or her interest in participating in the study.
 - Notification (MD) notification (n = 4) (least restrictive):** RTI sends a notification about the study to the patient's physician. If the physician does not object to the patient being contacted for the study within a set time period, RTI is allowed to initiate contact with the patient. No physician or patient release is required.
 - Patient release required (n = 4):** A patient permission form must be obtained by the cancer registry or RTI before RTI can contact the patient. No physician notification is carried out.
 - MD notification and patient release required (n = 3):** The physician is notified, and the cancer registry must obtain a permission form from the patient before RTI may contact the patient to participate in the study.
 - MD permission required (n = 4):** The registry or RTI must contact and obtain permission from the physician before RTI may contact the patient to participate in the study. No patient release is required.
 - MD permission and patient release required (n = 1) (most restrictive):** The registry must obtain permission from both the physician and the patient before RTI may contact the patient to participate in the study.
- Lag Time:** The time between the date of diagnosis and the date the contact information is released to RTI.

RESULTS

- For this ongoing study, results for this analysis have been updated since the abstract was submitted to include osteosarcoma and other cancers as defined in the study protocol and the most recent data available (March 31, 2011).

Descriptive Analysis #1

- Table 1 depicts the results of the interview rate stratified by the patient access pathways for all patients identified by contributing cancer registries. Cancer registries with the least restrictive pathway, MD notification, collectively had the highest interview rate.

Table 1. Interview Rate Among All Cases Identified by Contributing Registries, Stratified by Patient Access Pathway, in Descending Order of Interview Rate (N = 2,121)

Registry	Type of Patient Access Pathway	Total Identified	Total Interviewed	Interview Rate, ^a %
North Carolina	MD notify only	121	71	59
New York	MD notify and patient release	231	108	47
California - LA SEER	MD notify only	81	36	44
California (excluding LA)	MD notify only	323	141	44
Michigan	MD notify and patient release	122	51	42
Pennsylvania	Patient release only	183	70	38
Arizona	MD notify only	36	13	36
Harvard and Hopkins	MD permission	111	40	36
MD Anderson	Patient release only	154	51	33
Missouri	Patient release only	63	21	33
New Jersey	MD permission and patient release	67	22	33
Florida	Patient release only	269	86	32
Ohio	MD permission	100	32	32
Minnesota	MD notify and patient release	88	24	27
Texas	MD permission	172	33	19

LA = Los Angeles; SEER = Surveillance, Epidemiology, and End Results.

^a Interview rate among identified cases = (# interviewed)/(# identified by participating registries).

Descriptive Analysis #2

- Table 2 depicts the impact of increased lag time on the interview rate for the Full Release and Partial Release Populations combined. These data include all registries, even those added much later during implementation of the study. Results show somewhat higher interview rates with shorter lag time.

Table 2. Interview Rate by Lag Time Among All Cases Reported to RTI With Contact Information (n = 1,690^a)

Lag Time, Years	Total Reported to RTI With Contact Information	Total Interviewed	Interview Rate, ^b %
0-1	575	298	52
1-2	570	252	44
2-3	234	103	44
> 3	310	145	47

^a One case was excluded due to missing data for lag time.

^b Interview rate among identified cases = (# interviewed)/(# reported to RTI with contact information).

- Table 3 displays the results when limiting the lag-time analysis to the Full Release Population. These data show a strong relationship between the interview rate and lag time.

Table 3. Interview Rate by Lag Time for the Full Release Population (n = 1,322)

Lag Time, Years	Total Reported to RTI With Contact Information	Total Interviewed	Interview Rate, ^a %
0-1	500	238	48
1-2	451	163	36
2-3	174	55	32
> 3	197	50	25

^a Interview rate among identified cases = (# interviewed)/(# reported to RTI with contact information).

Multivariate Analysis

- Table 4 displays the factors impacting the probability of a patient (or proxy) completing a telephone interview among patients reported to RTI for the Full Release Population. Less restrictive patient access pathway, shorter lag time, and patient vital status as alive at diagnosis were important predictors of interview success. Other factors (patient sex, ICDO code group, year following introduction of the patient incentive) were not statistically significant predictors in the stepwise prediction model.

Table 4. Factors Impacting Probability of Being Interviewed for Patients in the Full Release Population Reported to RTI With Contact Information (n = 1,322^a)

Factors	Effect	OR (95% CI)
Patient access pathway	MD permission	1.00 (ref.)
	Patient release	1.02 (0.74-1.43)
	MD notify only	1.72 (1.25-2.35)
Lag time	> 1 year	1.00 (ref.)
	≤ 1 year	1.47 (1.15-1.89)
Vital status at time identified by registry	Deceased	1.00 (ref.)
	Alive	2.53 (1.96-3.25)

OR = odds ratio; CI = confidence interval.

^a Nine cases were excluded due to missing data for vital status.

CONCLUSIONS

- In the descriptive analysis of patient access pathways, interview rates decreased as the complexity of the patient access pathway increased.
- Interview rates tended to be lower at registries where MD permission and/or a patient release were required to be obtained compared with registries where these steps were not required.
- Among the Full Release Population, the interview rates consistently decreased as lag time between the date of diagnosis and the date reported to RTI increased.
- Among the Full Release Population, the probability of completing an interview with a patient (or proxy) increased if the patient access pathway was the least restrictive (MD notification only), there was < 1 year of lag time between the date of diagnosis and the date the case information was reported to RTI, and the patient was alive at the time the case was identified by the cancer registry.

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