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RESEARCH ARTICLE

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Describing adverse events in Swiss hospitalized oncology patients using the Global Trigger Tool

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Abstract

Background and aims: The occurrence rate of adverse events (AEs) related to care among hospitalized oncology patients in Switzerland remains unknown. The primary objective of this study was to describe, for the first time, the occurrence rate, type, severity of harm, and preventability of AEs related to care, reported in health records of hospitalized hematological and solid-tumor cancer patients in three Swiss hospitals.

Methods: Using an adapted version of the validated Global Trigger Tool (GTT) from the Institute for Healthcare Improvement, we conducted a retrospective record review of patients discharged from oncology units over a 6-week period during 2018. Our convenience sample included all records from adult patients (≥18 years of age), diagnosed with cancer, and hospitalized (>24 hours). Per the GTT method, two trained nurses independently assessed patient records to identify AEs using triggers, and physicians from the included units analyzed the consensus of the two nurses. Together, they assessed the severity and preventability of each AE.

Results: From the sample of 224 reviewed records, we identified 661 triggers and 169 AEs in 94 of them (42%). Pain related to care was the most frequent AE (n = 29), followed by constipation (n = 17). AEs rates were 75.4 per 100 admissions and 106.6 per 1000 patient days. Most of the identified AEs (78%) caused temporary harm to the patient and required an intervention. Among AEs during hospitalization (n = 125), 76 (61%) were considered not preventable, 28 (22%) preventable, and 21 (17%) undetermined.

Conclusion: About half of the hospitalized oncology patients suffered from at least one AE related to care during their hospitalization. Pain, constipation, and nosocomial infections were the most frequent AEs. It is, therefore, essential to identify AEs to guide future clinical practice initiatives to ensure patient safety.

KEYWORDS
adverse events, Global Trigger Tool, hematological cancer, medical errors, oncology, patient safety

1 | INTRODUCTION

Hospitalized oncology patients are particularly vulnerable to adverse events (AEs), mainly due to the complexity of cancer disease and toxic treatments.[1-3] AEs are a major cause of patient harm, resulting in temporary or permanent disability as well as increased morbidity and mortality.[4,5]

Measuring AEs is considered a minimum standard of care and central to patient safety programs.[6] Most existing methods measuring AEs require considerable time and resources.[7,8] So-called "trigger tools" based on record review have shown promising efficiency.[9] Triggers are clues in the health record suggesting a higher likelihood that a patient experienced harm.[5] For example, receiving a blood transfusion is a trigger that could indicate an AE such as a hemorrhage, which could be related to the insertion of a catheter. The Institute for Healthcare Improvement (IHI) Global Trigger Tool (GTT) is among the most widely used trigger tools for measuring AEs.[10,7] The GTT has been used in a variety of settings and detects minor AEs with greater sensitivity compared to other methods such as voluntary reporting systems.[11] The GTT demonstrates promising inter- and intra-rater reliability and good sensitivity and specificity compared to traditional record review.[9,12] The original version of the GTT has been adapted to capture oncology-specific AEs.[13,14] Mattsson et al used the oncology module developed by the Velindre Cancer Centre[15] to supplement the GTT.[14] However, this adapted tool did not identify additional AEs specific to the oncology setting.[14] Lipitz-Snyderman et al[13] developed an oncology-specific trigger tool to describe harm (beyond toxicity) in outpatient and inpatient cancer care settings. The tool includes a longer list of triggers, yet does not strictly follow the GTT method and is more time-consuming.[13] Using the combination of these two approaches, and as requested by the IHI, we adapted the GTT to our local context and named the adjusted tool Swiss Oncology Trigger Tool (SOTT). To our knowledge, only one study[16] has been conducted in Switzerland applying an adapted GTT method so far. This analysis of 240 patient charts identified an AE rate of 95.7 AEs per 1000 patient-days. However, that study was conducted in the Department of General Internal Medicine at a university hospital and not specifically in an oncology setting.

In order to improve quality of care and patient safety in oncology, an effective and reliable monitoring of AEs is necessary. The primary objective of this study was to describe the occurrence rate, type, severity of harm, and preventability of AEs related to care reported in health records of Swiss hospitalized hematological and solid-tumor cancer patients. As a secondary objective, the GTT was adapted to the local context and used in hematological and solid-tumor cancer patients.

2 | METHODS

This descriptive, retrospective study was part of a larger quality and safety investigation in four oncology units of three large hospitals in Switzerland. It was reviewed by the local Ethics Committee and was deemed beyond the scope of the Federal Act on Research involving Human Beings.[17] This study used routinely collected data. Patients provided consent for its use in clinical trials upon their admission to the hospital.

An interprofessional team of experts (four physicians, six nurses, and one researcher) from all three hospitals were involved in the development/application of the SOTT and chart review/data analysis. Based on the GTT method, the team consisted of two primary record reviewers (nurses) and at least one physician who confirmed the consensus of the two primary reviewers.[5] The two primary reviewers had extensive experience in oncology and surgery, and knowledge about the electronic health records (EHRs) of the included hospitals. Primary reviewers remained the same across hospitals; secondary reviewers were four physicians working in the included oncology units.

2.1 | Swiss oncology trigger tool development

The instrument was developed in three stages: (a) research and initial design of the adapted tool, (b) getting expert feedback and refining the tool, and (c) reaching consensus and validation of the final tool (Table S1). The IHI-GTT includes 53 triggers grouped in two general modules (cares and medication) and four specific modules (intensive care unit, surgery, emergency department, and perinatal unit).[5] We used an iterative expert consensus method with the interprofessional expert team to adapt the two general modules to our local setting and to create an additional oncology module without a formal rating procedure. The triggers comprised in the newly developed SOTT included all aspects related to care independent of the type of healthcare profession. Trigger definitions, sources used to guide definitions, and the final SOTT version are provided in Table S2. We were broad in our definition of triggers to make sure we captured a large scope of AEs.

2.2 | Training and pilot testing

As recommended by the IHI for the GTT, a training phase was completed before data collection to improve inter-rater reliability (IRR).[5,12] First, both primary and secondary reviewers independently studied the GTT documentation provided by the IHI.[5] Next, five health records were randomly selected from each site, using the same criteria as for the sample in the study, and were reviewed by primary and secondary reviewers. This allowed

researchers to create a record review flowchart (Figure S1) to guide and standardize the review process.

2.3 | Data collection and screening procedure

The screening process consisted of one primary and one secondary review. Primary reviewers (nurses) reviewed patient records using the EHR review flowchart (Figure S1). Per the GTT method, a 20-minute time limit was set for record review. AEs were identified on admission, during hospitalization, or as a cause of readmission. Secondary reviewers (physicians) evaluated and analyzed the consensus of the primary reviewers to reach a final decision on the frequency, type, severity of harm, and preventability of each AE identified during hospitalization (Figure 1). If there were disagreements among the reviewers, a discussion would take place until a consensus was reached. Due to insufficient contextual data, neither preventability nor severity of harm was assessed for AEs identified for admission or as a cause for readmission.

2.4 | Setting and sample

This study was performed in two university hospitals (1550-1900 hospital beds) and one urban tertiary hospital (570 hospital beds) in Switzerland. One hematological unit, one unit with solid-tumor cancer patients, and two mixed units (hematological and solid-tumor) were included in the study, which are the four largest oncology units in the French-speaking part of Switzerland. Due to differences in the average length of stay, the nature of the disease, and the types of treatment, we divided our sample in two groups: hematological and solid-tumors cancer patients. The units varied in size, ranging between 9 and 23 beds. These wards covered all types of cancer treatment (chemotherapy, radiotherapy, immunotherapy, bone marrow transplant, hormonotherapy, and targeted molecular therapy) and severity levels.

We retrospectively reviewed EHRs of patients discharged over a 6-week period, between January 22nd and March 4th for the first hospital, between February 5th and March 18th for the second hospital, and between May 23rd and June 27th for the third hospital, in 2018. Our convenience sample included all records from adult patients who were diagnosed with cancer and hospitalized (>24 hours) in a participating oncology unit. All records documenting hospital readmission, as defined by Diagnosis Related Groups[18] (within 18 days following discharge), were also reviewed. Records of cancer patients in complete remission, hospitalized for surgery/rehabilitation, or not under the responsibility of the oncology medical team were excluded from the analysis. The latter concerned cancer patients receiving treatment in the oncology department but hospitalized in other units (ie, medicine or surgery; Figure 2).[19]

2.5 | Patient demographics and administrative variables

Patient age, sex, length of hospital stay, cancer patient group (solid-tumor or hematological), and cancer type were collected and coded from EHRs at participating sites. We manually registered the date and time of hospitalization and of transfer/discharge.

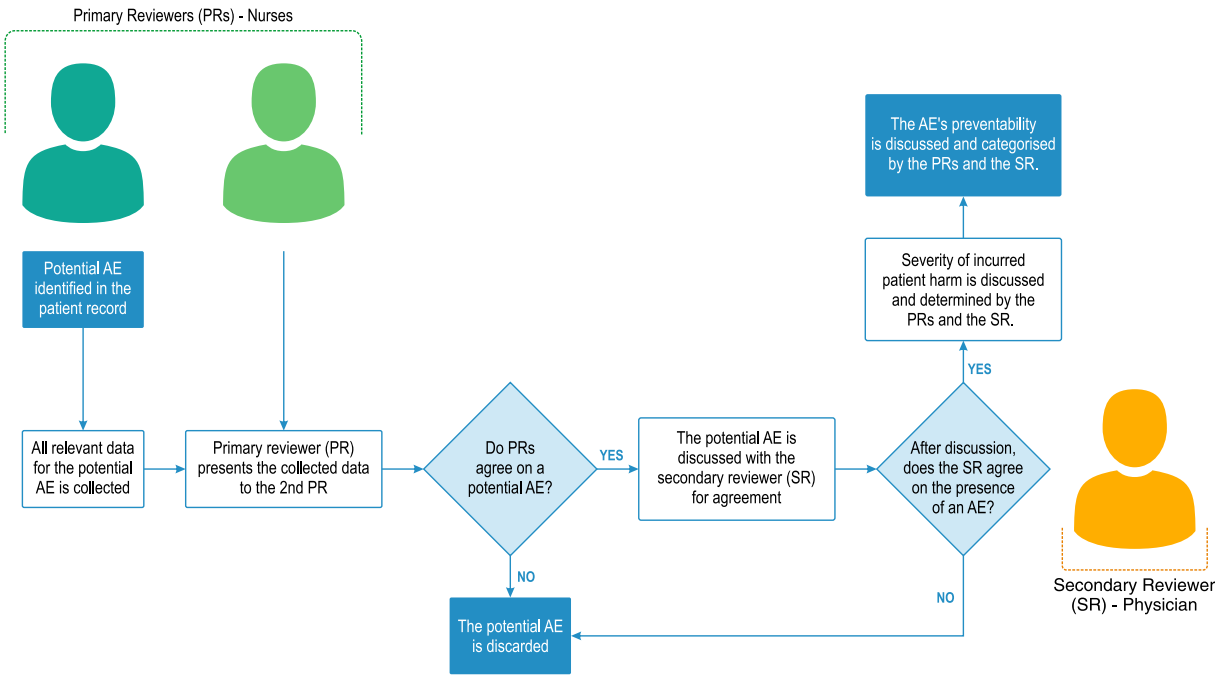

FIGURE 1 Adverse events identification flowchart

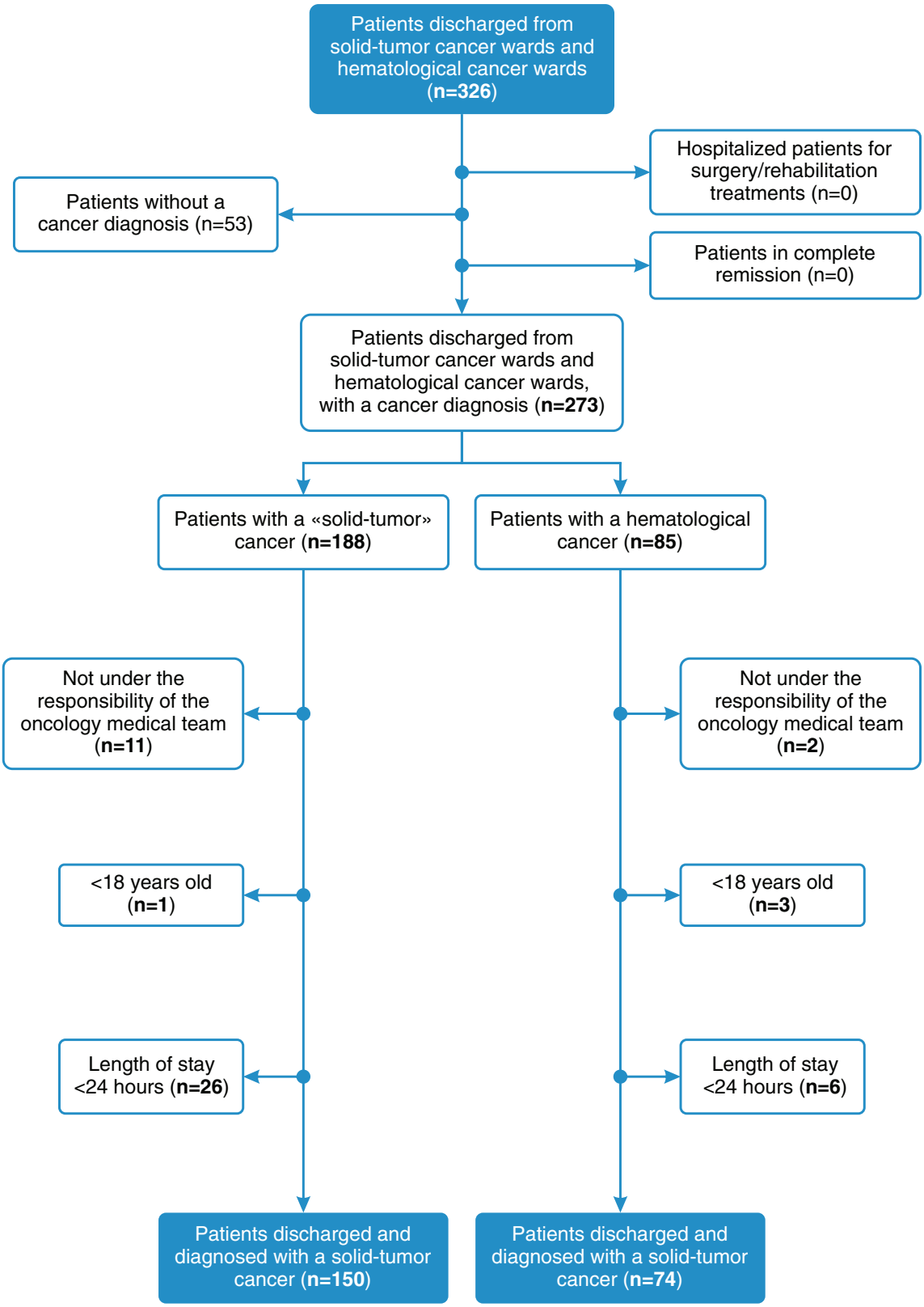

FIGURE 2 Patient record sampling flowchart[19]

2.6 | Study outcomes

2.6.1 | Adverse events

The IHI considers an AE "an unintended physical injury resulting from or contributed by medical care, that requires additional monitoring, treatment, or hospitalization, or that results in death".[20] Notably, the IHI definition excludes diagnostic error and harm related to the omission of care.[5] In our study, an AE was only considered if a clear cause related to care could be established. Here, we listed all different types of AE to avoid losing relevant information due to bundling.

Based on the IHI definition of AE,[5] we decided to include *pain related to care*, *persistent fatigue*, and *psychological distress* as AEs since they are associated to substantial suffering of cancer patients.[21-24] In our study, *pain* was considered as AE if it was determined to have been related to care such as puncture/bone marrow biopsy, peripheral, central, or urinary catheter placement, dressing change, mobilization, paracentesis, and chemotherapy. *Persistent fatigue* was considered as an AE if a relation to the treatment (eg, chemotherapy or radiotherapy) could be identified. *Psychological distress* was considered as AE when it could be directly associated to care interventions (invasive or noninvasive, e.g., breaking bad news to patients), or when patients related their own distress to a care intervention. We analyzed the AEs by cancer group to refine the analysis and to see if they differed between the two groups.

2.6.2 | Severity of harm

The severity of harm related to the AEs was categorized following the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index.[25] We used the categories E, F, G, H, and I, that focused on harm.

2.6.3 | Preventability

Several authors state that assessing preventability can inform about quality improvement priorities.[7,26,27] Thus, we assessed preventability in this study (Figure 1). Preventability was defined as failure to apply known methods to avert an injury or harm, and took into account the clarified cause of the AE.[28] An AE was considered preventable if it would not have occurred if the patient had received standards of care appropriate at the time of the study.[28,29] Preventability judgement was performed by the secondary reviewers based on the discussion with primary reviewers. An AE was considered as "not preventable" if no additional preventive measures could have been put into place to avoid harm. An AE was classified as "undetermined" if available data were not sufficient to determine preventability, or if it was due to an act of omission.

2.7 | Statistical analyses

Patient demographics and clinical data, number of rehospitalizations due to an AE, category of harm, and preventability of AEs were reported using descriptive statistics. To assess the incidence and type of AEs between cancer patient groups (ie, solid-tumor and hematological cancers), comparisons were performed using the Wilcoxon-Mann-Whitney test (age), and proportions test (AE rates, sex). Lengths of stay were analyzed with the Wilcoxon-Mann-Whitney test. Absolute and relative frequency of AEs by cancer patient group were determined. We calculated AEs per 1000 patient-days using length of stay data and AEs per 100 admissions using total admissions (including AEs present-on-admission, during hospitalization, and leading to a readmission). Generalized linear model with Poisson distribution was conducted to assess how many AEs could be explained by age, sex, length of stay, or cancer patient group (solid-tumor vs hematological cancer). We tested the interaction effect between length of stay and cancer patient group using R version 5.3.2 and the "plot_model" function from the "sjplot" package.

To monitor the quality of the screening process, IRR for trigger identification between primary reviewers was determined using unweighted Cohen's Kappa statistic.[30] Due to the large number of patient records and limited number of primary reviewers (two nurses), IRR was calculated every 10 records.[5]

For each trigger, a positive predictive value (PPV) was calculated to assess the trigger's performance[31] by dividing the number of times the trigger led to an identified AE by the total number of times it was identified.[13] Each trigger that indicated zero or more AEs was counted. Median PPVs for each module were calculated. Weingart et al[32] cite PPVs of 17% to 45% using physician chart review as the gold standard, in general medicine literature. Data were analyzed with Stata 14. For the Poisson model, we used the general linear model (glm) function of R (version 3.5.2).

3 | RESULTS

A total of 224 patient records (solid-tumor cancer: n = 150, hematological cancer: n = 74, representing 1585 patient-days) were included. Patient characteristics are shown in Table 1. Median length of stay was 3 (IQR 2-8) days for haemato-oncology patients and 3 (IQR 2-6) for solid-tumor patients; this difference was not statistically significant difference (*P*-value = .62, Wilcoxon-Mann-Whitney).

3.1 | AE rates

Overall, 94/224 (42%) of the analyzed EHRs contained at least one AE. We identified 169 AEs, including 34 AEs on admission, 125 during hospitalization, and 10 leading to a readmission (Table 3). Forty-nine patients (49/224, 22%) suffered from one AE and 45 patients (45/224, 20%) had two or more AEs. A maximum of seven AEs were identified in a patient during hospitalization (Table S3). A total of 144 AEs were identified by at least one trigger and 25 were identified without an attributable trigger, through the discharge notes. The most

TABLE 1 Patient characteristics (N = 224)

	Total records (*N* = 224)	Solid-tumor cancer patients (n = 150)	Hemato-logical cancer patients (n = 74)	*P* value
Age, median (years) [IQR]	61 [52–70]	61 [52–70]	61 [52–70]	.80
Sex % (n)				.17
Female	100 (104)	72.1	27.9	
Male	100 (120)	62.5	37.5	
Length of stay, total (days)	1585	852	733	
Length of stay, median (days) [IQR]	3 [2–7]	3 [2–6]	3 [2–8]	.62
Cancer type, n (%)				
Gastrointestinal		43 (29)	-	
Head and neck		23 (15)	-	
Pulmonary		21 (14)	-	
Urological		16 (11)	-	
Sarcoma		13 (9)	-	
Breast		10 (7)	-	
Melanoma		9 (6)	-	
Central nervous system (CNS)		8 (5)	-	
Gynecological		7 (4)	-	
Lymphoma		-	46 (62)	
Leukaemia		-	15 (20)	
Myeloma		-	13 (18)	

TABLE 2 Incidence rate for AEs of a corrected *z*-test

				AEs per 100 admissions			AEs per 1000 patient days		
	Number of patient records	Number of AEs	Length of stay, total (days)	Rate %	Difference in proportions in absolute value (CI 95%)	*P* value	Rate ‰	Difference in proportions in absolute value (CI 95%)	*P* value
Solid-tumor cancer	150	100	852	67	26.5 (16.1-37)	<.001	117	23.2 (−54.7 to 8.3)	.157
Hematological cancer	74	69	733	93			94		

Abbreviation: AEs, adverse events.

frequent cause for readmission was *febrile agranulocytosis* (3/5; Table 3). The overall AE rate was 75.4 per 100 hospital admissions and 106.6/1000 patient-days.

Most AEs (100/169, 59%) were identified in patients with solid-tumors, while hematological cancer patients had 69 total AEs (41%). The AE rate was 93 per 100 admissions for hematological cancer and 94 per 1000 patient-days, whereas solid-tumor patients experienced a rate of 67 per 100 admissions and 117 per 1000 patient-days. The rate of AE per 100 admissions was significantly different between the cancer patient groups (difference in proportions in absolute value, 26.5, 95% CI, 16.1-37, $P < .001$); the rate of AE per 1000 patient-days was not (difference in proportions in absolute value, 23.2, 95% CI, −54.7-8.3, $P = .157$; Table 2).

3.2 | AE Harm severity and type

The majority of AEs occurring during hospitalization caused temporary harm that required an intervention (98/125, 78%; Category E; Figure 3). This severity of harm was most often observed among solid-tumor patients (67/79, 85%). Of those AEs that required initial/prolonged hospitalization (category F), hematological cancer patients had 14/46 (30%) AEs compared to solid-tumor cancer patients with

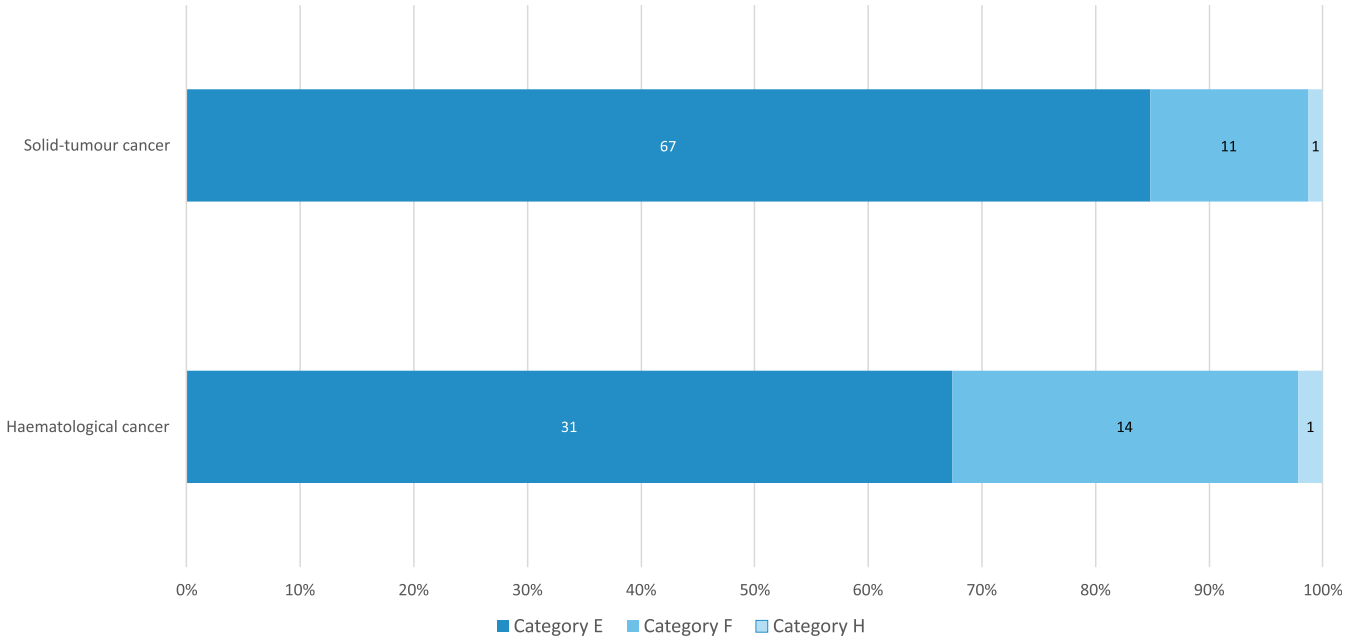

FIGURE 3 Harm severity of identified adverse events (AEs; n = 125). Harm severity scoring denotes an AE that may have contributed to or resulted in harm to the patient. Category E represents temporary harm that required an intervention; category F was temporary harm that required initial/prolonged hospitalization and category H an intervention to sustain life was required

11/79 (14%). *Pain related to care* was the most frequent AE in the category E for solid-tumor cancer patients (19/67, 28%) and for hematological cancer patients (6/31, 19%), followed by *constipation* (13/67, 19% and 3/31, 10%, respectively). The three most prevalent AEs in category F for solid-tumor and hematological cancer patients were: *nosocomial infection* (2/11.18% and 2/14.14%, respectively), *respiratory distress* (2/11, 18% and 1/14, 7%), *reaction to a drug* (2/11, 18% and 2/14, 14%).

One solid-tumor cancer patient required an intervention to sustain life (category H) following *drug-related kidney failure* (*acute*; 1/1, 100%), and one hematological cancer patient required an intervention to sustain life following *surgery* (1/1, 100%).

Types of AEs per cancer patient group are presented in Table 3.

3.3 | AE preventability

In a secondary review, primary and secondary reviewers considered 76/125 (61%) AEs during hospitalization were not preventable and 28/125 (22%) preventable (Table S4). The remaining 21 AEs were classified as "undetermined." The most common preventable AEs included *constipation* (9/28, 32%), *pain related to care* (5/28, 19%), and *pressure ulcer* (3/28, 11%).

3.4 | AE triggers

Approximately, one-fifth of triggers (140/661, 21%) identified at least one AE. Trigger PPVs ranged from 0% to 86% (median 26%; Table 4). Median PPVs of the new oncology module and adapted GTT modules (cares, medication) were 23%, 46%, and 21%, respectively. IRR between primary reviewers was high (Cohen's kappa = 0.9).

3.5 | Factors associated with AEs

The Poisson model showed that the number of AEs exhibited a statistically significant increase for both cancer patient groups by length of stay (Table S5). However, an interaction effect indicated a steeper slope for patients with solid-tumor cancer. Notably, the number of AEs increased exponentially for solid-tumor cancer patients compared to hematological cancer patients (Figure 4).

4 | DISCUSSION

The results of this study using a newly developed tool revealed that 42% of hospitalized Swiss oncology patients experienced at least one AE. The majority of AEs that occurred during hospitalization caused temporary harm that required intervention. *Pain related to care* and *constipation* were the most common AEs identified. Most AEs were deemed not preventable. The majority of AEs were identified by a trigger. Comparing the two groups, 59% of AEs were identified in patients with solid-tumors while 41% were in hematological cancer patients.

4.1 | Triggers

In this study, the PPVs ranged from 0% to 86%. Higher results were reported by one US[13] and one Swiss[16] study. PPVs vary

TABLE 3 AE types by occurrence

		AEs during hospital stay n (%)		AEs present on admission n (%)		AEs leading to a readmission n (%)	
AE types (n = 169)	Total n	H[a]	S[b]	H[a]	S[b]	H[a]	S[b]
Pain related to care	29	6 (21)	19 (66)	3 (10)	1 (3)	-	-
Constipation	17	3 (18)	13 (76)	-	1 (6)	-	-
Anemia	9	1 (11)	2 (22)	2 (22)	4 (44)	-	-
Nosocomial infection	8	4 (50)	3 (38)	1 (13)	-	-	-
Anaphylactic reaction to a drug	6	3 (50)	3 (50)	-	-	-	-
Pressure ulcer	6	0 (0)	3 (50)	2 (33)	1 (17)	-	-
Psychological distress	5	1 (20)	3 (60)	1 (20)	-	-	-
Hypotension	5	2 (40)	3 (60)	-	-	-	-
Drug-related mucositis	5	2 (40)	1 (20)	2 (40)	-	-	-
Febrile agranulocytosis	5	1 (20)	1 (20)	-	-	1 (20)	2 (40)
Fall with injury	4	1 (25)	3 (75)	-	-	-	-
Dehydration	4	2 (50)	1 (25)	-	1 (25)	-	-
Adverse drug reaction	4	1 (25)	2 (50)	-	1 (25)	-	-
Vomiting	4	2 (50)	2 (50)	-	-	-	-
Respiratory distress	3	1 (33)	2 (67)	-	-	-	-
Thrombocytopenia	3	-	1 (33)	1 (33)	1 (33)	-	-
Port-a-Cath thrombosis (partial)	3	1 (33)	1 (33)	1 (33)	-	-	-
Anorexia	2	1 (50)	-	1 (50)	-	-	-
Confused state (acute)	2	-	2 (100)	-	-	-	-
Infiltration/extravasation (i.v.)	2	1 (50)	1 (50)	-	-	-	-
Drug-related kidney failure (acute)	2	2 (100)	-	-	-	-	-
Drug-related neutropenia	2	-	2 (100)	-	-	-	-
Deep vein thrombosis	2	-	2 (100)	-	-	-	-
Diabetic ketoacidosis	1	1 (100)	-	-	-	-	-
Acute kidney failure	1	-	-	-	-	1 (100)	-
Anorexia	1	-	-	-	-	-	1 (100)
Dehydration	1	-	-	-	-	-	1 (100)
Insufficient pain management	1	-	-	-	-	-	1 (100)
Pleural effusion	1	-	-	-	-	-	1 (100)
Pneumonia	1	-	-	-	-	1 (100)	-
Postembolization syndrome with electrolyte imbalance	1	-	-	-	-	-	1 (100)
Other[c]	30	11 (37)	9 (30)	6 (20)	4 (13)	-	-
Total	169	46 (27)	79 (47)	20 (12)	14 (8)	3 (2)	7 (4)

[a]Hematological cancer patient group.
[b]Solid-tumor cancer patient group.
[c]Please consult Table S6.

depending on the context and patient populations.[31] For a PPV of 100%, the trigger itself can be the AE, leaving little room for other AEs to be associated with that trigger. The calculation of the PPV does not provide any measure on how many events the trigger identifies but reflects the rate of positive triggers that raise one or more AEs.[31] Therefore, a low PPV may be due to poor trigger performance and/or low event rates.[31] Further research is needed to define the best performing triggers in a given context with a given type of population in order to widen the scope for identifying AEs.

4.2 | Adverse events

One Swiss study using the GTT analyzed 240 patients' charts over 1 year and found that about two thirds of patients suffered from AEs

TABLE 4 Trigger frequencies and positive predictive value (PPV) of triggers

Triggers			Associated with at least 1 AE n	Total positive triggers n	PPV[a] (%)
"Cares" module	C1	Blood transfusion or use of other blood products	11	31	35
	C2	Cardiopulmonary resuscitation, cardiac and/or pulmonary arrest, or rapid response team activation	-	1	-
	C3	Positive blood culture/infections related to care	3	7	43
	C4	Decrease in hemoglobin or hematocrit of 25% or greater over previous value	-	2	-
	C5	Fall	4	8	50
	C6	Pressure ulcers	5	7	71
	C7	Readmission	7	14	50
	C8	Physical restraints use	2	4	50
	C9	Hyperthermia	9	38	24
	C10	Transfer to higher level of care	6	7	86
Module PPV[b] (median)					46
"Medication" module	M1	Diarrhea	3	31	10
	M2	Hyperglycemia	4	12	33
	M3	Hypoglycemia	-	3	-
	M4	Serum creatinine	1	4	25
	M5	Vitamin K administration	1	6	17
	M6	Antihistaminic administration	4	12	33
	M7	Naloxone administration	-	-	-
	M8	Nausea	6	45	13
	M9	Over-sedation/symptomatic hypotension	4	10	40
Module PPV[b] (median)					21
"Oncology" module	O1	Pain	29	108	27
	O2	Acute or unusual dyspnea, respiratory physiotherapy, use of noninvasive ventilation	3	13	23
	O3	Extravasation	2	4	50
	O4	Port (Port-a-Cath)	5	65	8
	O5	Fatigue	2	36	6
	O6	Tumor lysis syndrome	-	2	-
	O7	Anticoagulation	4	100	4
	O8	High potassium levels	2	4	50
	O9	Constipation	16	46	35
	O10	Psychiatrist consultation	2	9	22
	O11	Mucositis	4	8	50
	O12	Agranulocytosis	1	24	4
Module PPV[b] (median)					23

Abbreviations: AEs, adverse events; PPV, positive predictive value.

[a]PPV was calculated by dividing the number of times the trigger led to the identification of an AE by the total number of times the trigger was identified.

[b]Median PPV of each module was calculated by determining the median PPV of all triggers within the module.

with harm, during hospitalization.[16] This rate of AEs of hospitalized patients in an internal medicine unit is higher than in our study. Other studies have found lower rates of AEs in comparison to our findings. For instance, a Norwegian study using the IHI GTT found that 24.2% of cancer patients had experienced at least one AE.[1] An analysis of AEs in 400 surgical and 600 medical records of hospitalized patients in Switzerland showed that 12.3% of these patients had at least one AE.[33] The latter study used the Adverse Patient Occurrence inventory tool to screen patient records. Nevertheless, the three studies cannot be directly compared to our study due to differences in study populations, settings, or methods applied.

We found an overall rate of 106.6 AEs per 1000 patient-days, including both solid-tumor and hematological cancer patients. In comparison, Lipitz-Snyderman et al[2] observed 91.2 AEs per 1000 patient-

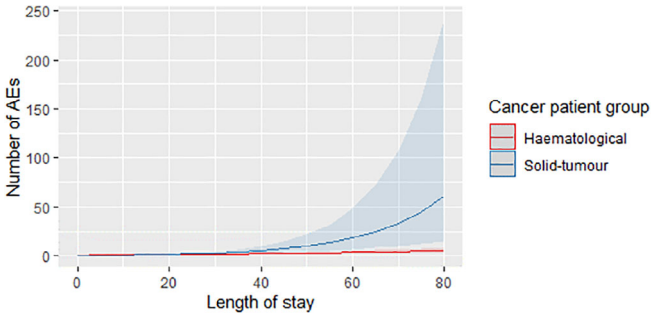

FIGURE 4 Number of adverse events (AEs) as a function of the length of stay predicted by the model in Table S5, line 12, with a 95% confidence band

days for hospitalized solid-tumor cancer patients, and Classen et al[11] revealed 91 events per 1000 patient-days (range: 89-106) including all adult inpatients of three hospitals during a 1 month period. In contrast, Haukland et al[1] found in their study 37.1 AEs per 1000 patient-days for both groups of cancer patients. A meta-analysis of AEs measured by the GTT revealed an average of 61 AEs per 1000 patient days for a hospitalized patients.[31] These findings suggest that the number of AEs per 1000 patient-days considerably varied between the different studies, making comparisons difficult. These discrepancies may be due to several factors: first, the populations/samples of the different GTT studies, the quality of the documentation, and the training/experience of reviewers. Second, the restricted time period; in our study, we did not capture variations like staffing conditions (eg, illness, maternity leave, personal turnover) and seasonal factors (eg, "common cold" season) that could have impacted the occurrence of AEs. Although the IHI recommends an analysis of 20 patient records per month over a full year,[5] we reviewed EHRs of patients discharged over only a 6-week period, because this study is part of a larger investigation. Third, we used the SOTT which includes a specific oncology module, which was not the case in the study from Haukland et al.[1] Triggers in the new oncology module were developed based on the participating institutions' care guidelines, both medical and nursing, thus increasing the likelihood of identifying more AEs in this specific setting. Fourth, despite being considered the "fifth vital sign",[34] pain has not been universally considered as an AE in prior studies. Pain is described as a physical and emotional experience associated with actual and potential tissue damage.[34] We found that *pain related to care* interventions was the most frequent AE. The care interventions that originated pain were sufficiently described in the EHRs to attribute the pain stemming from care. Furthermore, the National Comprehensive Cancer Network recognizes psychological distress as interfering with effective coping with cancer physical symptoms and treatment.[23] We believe excluding psychological harm as an AE may result in underestimating important sources of cancer patients suffering. Therefore, we considered it as an AE and posit that the conceptual definition of AE may require revision. When *psychological distress* and *pain* AEs are excluded from the analysis, rates decrease from 75,4 to 60/100 admissions and 106,6 to 85/1000 patient-days. Regarding the harm severity of AEs, our findings are consistent with previous studies, most of them showing temporary harm (Categories E and F).[1,2,26,35]

To our knowledge, this is the first study to compare AEs between patients with solid-tumors and hematological cancers. Per 1000 patient-days, we observed that the number of AEs was higher for patients with solid-tumors compared to patients with hematological cancer. This could be due to the higher number of patients with solid-tumors per 1000 patient days, as their length of stay is shorter than for patients with hematological cancer. This hypothesis should be verified. We observed that patients in our cohort with a solid-tumor were more likely to suffer from AE related to length of stay compared to hematological cancer patients. Length of stay has already been correlated with AEs in other studies. Patients with solid-tumors suffered more AEs related to *pain* and *constipation* than hematological cancer patients. Patients with hematological cancer suffered more AEs related to *nosocomial infections* than solid-tumors cancer patients. Several studies[1,2,14] have identified *infections* as the most common AE. The proportion of AEs classified in category F was higher in patients with hematological cancer compared to solid-tumor cancer. The highest proportion of overall AEs in this category was nosocomial infections, with 14% for hematological cancer and 18% for solid-tumor cancer. This result is in line with Lipitz-Snyderman et al.[2] stating that 16% of AEs are related to infections for solid-tumor cancer patients.

We determined a lower percentage of preventable AEs (22% vs 32%) compared to prior reports.[2] However, the subjective nature of this type of assessment and the diverse definitions of this concept make comparisons among studies difficult.[13,36] Interestingly, more than half of the AEs related to *pain related to care*, *dehydration*, and *falls with injury* were considered by the reviewers as not preventable. A clinician working in the oncology unit has certainly a deep and valuable insight on the AE's context, but a risk of bias remains when reflecting on the causes of the AE, as well as on their preventability. Regardless, the understanding of preventable AEs can be key to prioritize improvement measures.[27]

4.3 | Implications

The SOTT based on the methods used by the IHI for the GTT proves to be a complement to existing approaches in Switzerland.[37,38] This study has shown that the SOTT allows a comprehensive detection of AEs in oncology units. As recommended, triggers must be adapted to local practice and settings to achieve a standardized approach.[7,31] We are aware that additional work is needed to apply the SOTT more widely, such as a uniform definition of AEs and processes to define the level of harm and preventability. However, SOTT allows the detection of additional types of AEs compared to commonly used tools and can open new perspectives in automating trigger events detection.

4.4 | Strengths and Limitations

This study provides first data on the occurrence rate, type, harm severity, and preventability of AEs related to care for oncology units

in Switzerland, comparing solid-tumors and hematological cancer patients. However, we also note several limitations. First, the record review is subject to documentation bias as AEs were determined based on information in the EHR. Second, the 6-week data collection period does not provide insights into how AEs may change over time, particularly in terms of type and prevalence. Third, preventability or harm severity of AEs was a subjective assessment by primary and secondary reviewers and did not follow a standardized and objective assessment. Secondary reviewers cared for some of the patients included in this study, which could have biased judgement and agreement between reviewers on preventability. To minimize bias and inaccuracy in future studies, we propose to define objective criteria for preventability and to trace the reviewer's position on each criterion, thereby ensuring reproducibility (typically measured with a chance-adjusted measure such as the kappa statistic).[36] Fourth, demographic data were not collected on patients' active cancer treatment protocols. Such a level of detail may provide further insights into treatment-specific AEs. Fifth, this study is part of a larger investigation on the quality and safety of nursing care in Swiss oncology units. Therefore, the study time was limited to 6 weeks, all EHRs that met the inclusion criteria were analyzed during this time period, and no power estimation was calculated. Sixth, the exclusion of patients not under the full responsibility of the oncology units might have resulted in an underestimation of the number of AEs (even though such selection criteria was in line with the IHI's recommendation). Finally, the observational nature of the study precludes conclusions on causal links between the type of AEs and the factors that contributed to these AEs. The adaptation of the tool to our local context does not make it generalizable at this stage. Further testing on the sensitivity and specificity of the SOTT is thus required before generalizing the present approach to other oncology units.

5 | CONCLUSION

The SOTT offers a thorough method and led to the identification of 661 triggers indicating 169 in-hospital AEs in 240 oncology patient records in three hospitals in Switzerland.

The SOTT is a contribution to GTT's measurements of AE in oncology patients and may advance the study of cancer patients' safety and quality of care. Most AEs identified, like *pain*, *constipation*, and *nosocomial infections* are already well-known in clinical practice. Measures to prevent and limit their impact are readily available.

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All authors have read and approved the final version of the manuscript. Manuela Eicher had full access to all of the data in this study and takes complete.

CONFLICT OF INTEREST

Dr. Manuela Eicher reports grants from Krebsliga Schweiz, grants from Altschüler Stiftung, personal fees from Vifor, grants from Roche, grants from Bristol Meyers Squibb, during the conduct of the study. Dr. Sara Colomer-Lahiguera received honoraria from Vifor Pharma and research grants from Roche and Bristol Meyers Squibb. Prof. Solange Peters has received education grants, provided consultation, attended advisory boards, and/or provided lectures for: Abbvie, Amgen, AstraZeneca, Bayer, Biocartis, Boehringer-Ingelheim, Bristol-Myers Squibb, Clovis, Daiichi Sankyo, Debiopharm, Eli Lilly, F. Hoffmann-La Roche, Foundation Medicine, Illumina, Janssen, Merck Sharp and Dohme, Merck Serono, Merrimack, Novartis, Pharma Mar, Pfizer, Regeneron, Sanofi, Seattle Genetics and Takeda, from whom she has received honoraria. The supporting source/financial relationship had no role in the study. All remaining authors have declared no conflicts of interest.

TRANSPARENCY STATEMENT

The corresponding author (Manuela Eicher) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

Manuela Eicher had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Haukland EC, von Plessen C, Nieder C, Vonen B. Adverse events in hospitalised cancer patients: a comparison to a general hospital population. *Acta Oncol*. 2017;56(9):1218-1223.
2. Lipitz-Snyderman A, Pfister D, Classen D, et al. Preventable and mitigable adverse events in cancer care: measuring risk and harm across the continuum. *Cancer*. 2017;123(23):4728-4736.
3. Lipczak H, Knudsen JL, Nissen A. Safety hazards in cancer care: findings using three different methods. *BMJ Qual Saf*. 2011;20(12):1052-1056.
4. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. *BMJ Qual Saf*. 2008;17(3):216-223.
5. Griffin FA, Resar RK. *IHI Global Trigger Tool for Measuring Adverse Events*. 2nd ed. Cambridge, MA: Institute for Healthcare Improvement; 2009 http://www.ihi.org/resources/Pages/IHIWhitePapers/IHIGlobalTriggerToolWhitePaper.aspx (Accessed July 5, 2019).
6. Organisation for Economic Co-operation and Development. *Measuring Patient Safety: Opening the Black Box*. Paris, France: OECD; 2018 https://www.oecd.org/health/health-systems/Measuring-Patient-Safety-April-2018.pdf (Accessed July 5, 2019).
7. Hibbert PD, Molloy CJ, Hooper TD, et al. The application of the Global Trigger Tool: a systematic review. *Int J Qual Health Care*. 2016;28(6):640-649.
8. Naessens JM, O'byrne TJ, Johnson MG, Vansuch MB, McGlone CM, Huddleston JM. Measuring hospital adverse events: assessing inter-rater reliability and trigger performance of the Global Trigger Tool. *Int J Qual Health Care*. 2010;22(4):266-274.
9. Sharek PJ. The emergence of the trigger tool as the premier measurement strategy for patient safety. *AHRQ WebM&M*. 2012;2012(5):120.
10. Doupi P, Svaar H, Bjørn B, et al. Use of the Global Trigger Tool in patient safety improvement efforts: nordic experiences. 2015;17(1):45-54.
11. Classen DC, Resar R, Griffin F, et al. 'Global trigger tool' shows that adverse events in hospitals may be ten times greater than previously measured. *Health Aff (Millwood)*. 2011;30(4):581-589.
12. Classen DC, Lloyd RC, Provost L, Griffin FA, Resar R. Development and evaluation of the institute for healthcare improvement global trigger tool. *J Patient Saf*. 2008;4(3):169-177.
13. Lipitz-Snyderman A, Classen D, Pfister D, et al. Performance of a trigger tool for identifying adverse events in oncology. *J Oncol Pract*. 2017;13(3):e223-e230.
14. Mattsson TO, Knudsen JL, Brixen K, Herrstedt J. Does adding an appended oncology module to the Global Trigger Tool increase its value? *Int J Qual Health Care*. 2014;26(5):553-560.
15. 1000 Lives Plus. How to use trigger tools England: National Health Services Wales; 2012. http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/T4I%20%284%29%20How%20to%20use%20Trigger%20Tools%20%28Feb%202011%29%20Web.pdf (Accessed September 9, 2019).
16. Grossmann N, Gratwohl F, Musy SN, Nielen NM, Simon M, Donze J. Describing adverse events in medical inpatients using the Global Trigger Tool. *Swiss Med Wkly*. 2019;149:w20149.
17. Federal Assembly of the Swiss Confederation. Federal Act on Research involving Human Beings (RS 810.30); 2014. https://www.admin.ch/opc/en/classified-compilation/20061313/index.html (Accessed July 5, 2019).
18. Pellegrini S. Évolution des coûts et du financement dans le système de soins depuis la révision du financement hospitalier; 2018.
19. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *PLoS Med*. 2007;4(10):e297.
20. Adler L, Moore J, Federico F. *IHI Skilled Nursing Facility Trigger Tool for Measuring Adverse Events*. Cambridge, MA: Institute for Healthcare Improvement; 2015 http://www.ihi.org/resources/Pages/Tools/SkilledNursingFacilityTriggerTool.aspx (Accessed July 5, 2019).
21. National Comprehensive Cancer Network. NCNN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue. NCNN; 2019: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf.
22. National Comprehensive Cancer Network NCCN Clinical practice Guidelines in Oncology: Adult Cancer Pain (Version June 3, 2019 24, 2019). National Comprehensive Cancer Network; 2019: https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Distress Management (Version 3.2019-May 6, 2019). Plymouth Meeting, PA: National Comprehensive Cancer Network; 2019: https://www.nccn.org/professionals/physician_gls/pdf/distress.pdf (Accessed July 5, 2019).
24. Absolom K, Gibson A, Velikova G. Engaging patients and clinicians in online reporting of adverse effects during chemotherapy for cancer: the eRAPID system (electronic patient self-reporting of adverse events: patient information and aDvice). *Med Care*. 2019;57(Suppl 1):S59-s65.
25. National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP Index for Categorizing Medication Errors. NCC MERP; 2001: www.nccmerp.org/sites/default/files/indexColor2001-06-12.pdf (Accessed July 5, 2019).
26. Good VS, Saldaña M, Gilder R, Nicewander D, Kennerly DA. Large-scale deployment of the Global Trigger Tool across a large hospital system: refinements for the characterisation of adverse events to support patient safety learning opportunities. *BMJ Qual Saf*. 2011;20(1):25-30.
27. Panagioti M, Khan K, Keers RN, et al. Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. 2019;366:l4185.
28. *World Health Organization. Conceptual Framework for the International Classification for Patient Safety: version 1.1*. Geneva: World Health Organization; 2009 https://apps.who.int/iris/handle/10665/70882 (Accessed July 5, 2019).
29. Committee of Experts on Management of Safety and Quality in Health Care. Glossary of terms related to patient and medication safety. Strasbourg, France: Council of Europe; 2005: https://www.who.int/patientsafety/highlights/COE_patient_and_medication_safety_gl.pdf (Accessed July 5, 2019).
30. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med*. 2012;22(3):276-282.
31. Health Quality & Safety Commission. *The Gobal Trigger Tool: A Review of the Evidence*. 2016th ed. Wellington: Health Quality & Safety Commission; 2016 https://www.hqsc.govt.nz/assets/GTT/PR/GTT-evidence-review-Jan-2016.pdf (Accessed July 5, 2019).
32. Weingart SN, Nelson J, Koethe B, et al. Developing a cancer-specific trigger tool to identify treatment-related adverse events using administrative data. *Cancer Med*. 2020;9:1462-1472.
33. Halfon P, Staines A, Burnand B. Adverse events related to hospital care: a retrospective medical records review in a Swiss hospital. *Int J Qual Health Care*. 2017;29(4):527-533.
34. National Pain Management Coordinating Committee. *Pain as the 5th Vital Sign Toolkit*. Washington, DC: Veterans Health Administration; 2000 https://www.va.gov/PAINMANAGEMENT/docs/Pain_As_the_5th_Vital_Sign_Toolkit.pdf (Accessed December 18, 2019).

35. von Plessen C, Kodal AM, Anhøj J. Experiences with global trigger tool reviews in five Danish hospitals: an implementation study. 2012; 2(5):e001324.
36. Nabhan M, Elraiyah T, Brown DR, et al. What is preventable harm in healthcare? A systematic review of definitions. *BMC Health Services Res*. 2012;12:128.
37. Swissnoso. SSI Surveillance; 2020. https://www.swissnoso.ch/fr/modules/ssi-surveillance/au-sujet-de-la-surveillance-des-ssi/le-module/ (Accessed February 17, 2020).
38. Sécurité des patients Suisse. CIRRNET: Critical Incident Reporting & Reacting NETwork; 2020. https://www.securitedespatients.ch/cirrnet/ (Accessed February 17, 2020).

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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