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Research Paper

Linking clinical and population-based data in older patients with cancer in Belgium: Feasibility and clinical outcomes

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ABSTRACT

Introduction: Geriatric screening and geriatric assessment (GS/GA) have proven their benefits in the care for older patients with cancer. However, less is known about the predictive value of GS/GA for outcomes. To research this, clinical data on GS/GA can be enriched with population-based data. In this article we describe the methods and feasibility of data linkage, and first clinical outcomes (GS/GA results and overall survival).

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Overall survival

Materials and Methods: A large cohort study consisting of patients aged ≥70 years with a new cancer diagnosis was established using linked data from clinical and population-based databases. Clinical data were derived from a previous prospective study where older patients with cancer were screened with G8, followed by GA in case of an abnormal result (GS/GA study; 2009–2015). These data were linked to cancer registration data from the Belgian Cancer Registry (BCR), reimbursement data of the health insurance companies (InterMutualistic Agency, IMA), and hospital discharge data (Technical Cell, TCT). Cox regression analyses were conducted to evaluate the prognostic value of the G8 geriatric screening tool.
Results: Of the 8067 eligible patients with a new cancer diagnosis, linkage of data from the GS/GA study and data from the BCR was successful for 93.7%, resulting in a cohort of 7556 patients available for the current analysis. Further linkage with the IMA and TCT database resulted in a cohort of 7314 patients (96.8%). Based on G8 geriatric screening, 67.9% of the patients had a geriatric risk profile. Malnutrition and functional dependence were the most common GA-identified risk factors. An abnormal baseline G8 score (≤14/17) was associated with lower overall survival (adjusted HR [aHR] = 1.62 [1.50–1.75], $p < 0.001$).
Discussion: Linking clinical and population-based databases for older patients with cancer has shown to be feasible. The GS/GA results at cancer diagnosis demonstrate the vulnerability of this population and the G8 score showed prognostic value for overall survival. The established cohort of almost 8000 patients with long-term follow-up will serve as a basis in the future for detailed analyses on long-term outcomes beyond survival.

1. Introduction

Older patients with cancer represent a substantial part of the cancer population worldwide and in Belgium almost half of new cancer diagnoses are in patients aged 70 years and older [1]. It is expected that this population will keep growing due to demographic changes and increasing life expectancy [2].

Treating cancer in older patients is challenging because of their heterogeneity in health status and potential age-related conditions such as functional decline, comorbidities, and cognitive impairment [3].

Table 1
Overview of data sources that were linked to study long-term outcomes in older adults with cancer.

Source	Type of data	Information	Main variables	Remark
GS/GA study [14–16]	Primary study data	**Geriatric screening (GS) and geriatric assessment (GA) data**[a] collected in three multicenter observational cohort studies from October 2009 to February 2015	- Patient and clinical characteristics: age, sex, CCI [46], ECOG-PS [47], polypharmacy -Sociodemographics: living situation, marital status, educational level - GS: G8 [17] - GA (only if G8 score ≤ 14): functional status, falls history, pain, cognition, depression, nutrition - HRQOL (only for subgroup and if G8 score ≤ 14): EORTC QLQ-C30 GHS scale [48,49], question 29–30 combined and linearly transformed to 0–100 score	An abnormality on one of the domains is further referred to as a geriatric risk factor. The instruments and cutoff points for each domain of the GA are summarized in Supplementary Table S1.
BCR	Population-based cancer registry data	**Registry data for all invasive tumors** (except basal cell carcinomas) from 2004 up until end 2018 for all included patients + vital status available until 01/04/2020[b] + cause of death data available until end 2017[c]	Incidence date, tumor type (ICD-10), topography codes, morphology codes and behavior (ICD-O-3), clinical and pathological tumor stage (UICC TNM-6,TNM-7)	Combined stage (created for this study): pTNM > cTNM except - if cM = 1 - if pTNM = missing - if neoadjuvant treatment then cTNM priority
IMA [50]	Population-based administrative data	**Reimbursement data** for medical acts, medication and hospital stays of Belgian residents + demographic information until 01/03/2019, available in 4 databases (Healthcare, Pharmaceutical, Hospital and Population database)	Date, nomenclature code (medical act) or ATC code (medication), quantity, length of stay, prescriber type, provider type, reimbursement amount	For this article, IMA data was used to determine primary tumor-directed treatment: - surgery and radiotherapy (nomenclature) - systemic therapy: chemotherapy, targeted therapy and immunotherapy (ATC) - endocrine therapy (ATC) Reimbursement data generally lacks diagnostic information, thus timeframes around the cancer diagnosis were used to assess first line treatment (Supplementary Table S2)
TCT [51]	Population-based administrative data	**Hospital discharge data** for inpatient, day-care hospital and emergency room contacts until end 2018 (excluding year 2015)	Date of admission and discharge, main and secondary diagnoses (ICD-9-CM < 2015, ICD-10-BE >2015), specialty, procedures (ICD-9-CM < 2015, ICD-10-BE >2015)	

Abbreviations: BCR = Belgian Cancer Registry; IMA = InterMutualistic Agency; TCT = Technical Cell; CCI = Charlson Comorbidity Index; ECOG-PS = Eastern Cooperative Oncology Group Performance Status; GS = geriatric screening; GA = geriatric assessment; HRQOL = health-related quality of life; EORTC QLQ-C30 GHS = European Organization for Research and Treatment Quality of Life Questionnaire core 30 Global Health Status scale; ICD-10 = International Classification of Diseases, 10th revision; ICD-O-3 = International Classification of Diseases for Oncology, 3rd edition; UICC TNM-6 or TNM-7 = International Union Against Cancer TNM classification 6th or 7th edition; ATC = Anatomical Therapeutic Chemical codes; ICD-9-CM = The International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-BE = International Classification of Diseases, 10th Revision, Belgian Modification.

[a] More information on data collection of GS/GA and other baseline variables can be found in the original publications referenced in the table.
[b] Retrieved from the Crossroads Bank for Social Security.
[c] Retrieved from the three Belgian regional authorities.

Table 2
Patient characteristics.

Characteristic	Categories	Full cohort $n = 7556$		Solid tumors $n = 6972$		Hematologic malignancies $n = 584$	
		N	%	N	%	N	%
Solid tumor type	Breast	1974	26.1	1974	28.3		
	Colon	1132	15.0	1132	16.2		
	Lung	837	11.1	837	12.0		
	Rectum	464	6.1	464	6.7		
	Prostate	400	5.3	400	5.7		
	Pancreas	265	3.5	265	3.8		
	Esophagus	205	2.7	205	2.9		
	Bladder	201	2.7	201	2.9		
	Corpus uteri	196	2.6	196	2.8		
	Head and neck	191	2.5	191	2.7		
	Ovary	186	2.5	186	2.7		
	Stomach	123	1.6	123	1.8		
	Other [a]	798	10.6	798	11.4		
Hematologic malignancy type	Non-Hodgkin lymphoma	298	3.9			298	51.0
	Multiple myeloma	109	1.4			109	18.7
	Acute myeloid leukemia	50	0.7			50	8.6
	Chronic lymphocytic leukemia	17	0.2			17	2.9
	Hodgkin lymphoma	14	0.2			14	2.4
	Chronic myeloid leukemia	<10	<0.2			<10	<1.2
	Acute lymphoblastic leukemia	<10	<0.2			<10	<1.2
	Other	85	1.1			85	14.6
Combined stage [b]	Stage I			1324	21.6		
	Stage II			1786	29.1		
	Stage III			1468	23.9		
	Stage IV			1555	25.4		
	Missing			533			
	NA [c]			306			
History of cancer [d]	No	6578	87.1	6083	87.2	495	84.8
	Yes	978	12.9	889	12.8	89	15.2
Age	70–74	2286	30.3	2143	30.7	143	24.5
	75–79	2311	30.6	2121	30.4	190	32.5
	80–84	1791	23.7	1640	23.5	151	25.9
	≥ 85	1168	15.5	1068	15.3	100	17.1
	Median	78		78		78	
	Range	70–100		70–100		70–93	
Sex	Male	3191	42.2	2885	41.4	306	52.4
	Female	4365	57.8	4087	58.6	278	47.6
Charlson Comorbidity Index (0–37)	No comorbidities: score = 0	2418	32.2	2249	32.4	169	29.0
	Comorbidity: score ≥ 1	5099	67.8	4685	67.6	414	71.0
	Missing	39		38		1	
Polypharmacy	0–4 medications	3618	49.0	3386	49.7	232	40.6
	≥ 5 medications	3764	51.0	3425	50.3	339	59.4
	Missing	174		161		13	
ECOG-PS	Score 0–1	5142	68.2	4787	68.9	355	60.9
	Score ≥ 2	2391	31.7	2163	31.1	228	39.1
	Missing	23		22		1	
Living situation	Alone	2461	34.2	2285	34.5	176	31.0
	Not alone	4739	65.8	4347	65.5	392	69.0
	Missing	356		340		16	
Educational level	Illiterate	56	0.8	50	0.8	<10	<1.6
	Primary education	796	11.3	742	11.4	54	9.6
	Lower secondary education	2791	39.5	2556	39.3	235	42.0
	Higher secondary education	2036	28.8	1877	28.8	159	28.4
	Higher education	1328	18.8	1225	18.8	103	18.4
	Other	65	0.9	62	1.0	<10	<1.6
	Missing	484		460		24	

Footnotes: In case of missing or NA data, percentages were calculated by subtracting missing from denominator.
Cell counts <10 as well as corresponding percentages are suppressed to reduce the risk of indirect identification.
Abbreviations: NA = Not Applicable; ECOG-PS = Eastern Cooperative Oncology Group Performance Status
Source of data: Belgian Cancer Registry (tumor type, combined stage, history of cancer); Geriatric screening and assessment study (age, sex, Charlson Comorbidity index, polypharmacy, ECOG-PS, living situation, educational level)

[a] Other: numbers and percentages of other tumor types are displayed in Supplementary Table S3.

[b] Combined stage (created for this study): the pathological stage prevails over the clinical, except for cases with clinical stage IV, missing pathological stage or pathological stage defined after neoadjuvant treatment.

[c] NA: TNM staging is not applicable for certain tumor types (e.g. tumors of central nervous system) or morphology codes (e.g. angiosarcoma).

[d] History of cancer: indicates if there was an invasive tumor registered in the BCR database prior to inclusion in the study from 2004 onward.

Older patients often have deficits in multiple domains and the term frailty is used to describe this multifactorial condition [4]. Defined in literature as a state of vulnerability and increased risk of adverse health outcomes, the burden of frailty is even higher in patients with cancer [4,5].

Identifying frailty and underlying geriatric risk factors in older patients with cancer is crucial for adequate cancer management and to guide supportive geriatric interventions [6]. Geriatric screening and geriatric assessment (GS/GA) are key elements in achieving this, and their implementation is recommended by the American Society of Clinical Oncology (ASCO) [7], International Society of Geriatric Oncology (SIOG) [6], European Organization for Research and Treatment of Cancer (EORTC) [8], and National Comprehensive Cancer Network (NCCN) [9]. GS/GA in older patients with cancer has prognostic value for overall survival (OS), influences treatment decisions, predicts treatment toxicity, and facilitates communication and shared-decision making [10–13]. Yet most evidence on GS/GA is focused on short-term benefits and little is known about the predictive value of GS/GA for long-term outcomes.

The use of population-based data such as disease registry data or administrative health data, offers an opportunity to capture longitudinal data in large cohorts. Administrative databases, however, generally lack clinical and diagnostic information so linkage with clinical data such as derived from primary studies can help fill this gap. Linkage of databases does, however, require careful consideration of technical, legal, ethical and privacy aspects. Therefore, the research objectives, data sources, dataflow for linkage, applicable laws and data protection regulations should be clearly defined and explored prior to data linkage initiation.

This article describes the methods and feasibility of linking clinical and population-based databases to establish a large-sized cohort of older patients with a new cancer diagnosis. Furthermore, first clinical outcomes (i.e., GS/GA results and OS) are studied in this final cohort. In the future, this cohort will provide a solid basis to evaluate poorly explored areas in geriatric oncology, such as the care trajectory following diagnosis and end-of-life care.

2. Materials and Methods

We created a cohort of older patients with cancer linking (1) clinical data from three combined GS/GA studies [2009–2015], (2) registry data from the Belgian Cancer Registry (BCR), (3) reimbursement data from the InterMutualistic Agency (IMA), and (4) hospital discharge data from the Technical Cell (TCT). Data linkage was completed in December 2020.

2.1. Patient Selection

The patients in the current study were previously enrolled in three Belgian multicenter observational cohort studies from October 2009 to February 2015, further described as the GS/GA study [14–16]. In these studies, patients with cancer aged 70 years and older were approached for inclusion during a hospital visit at new diagnosis or at disease progression/relapse when a treatment decision had to be made. In the first study cohort (October 2009 to July 2011; ten Belgian hospitals),

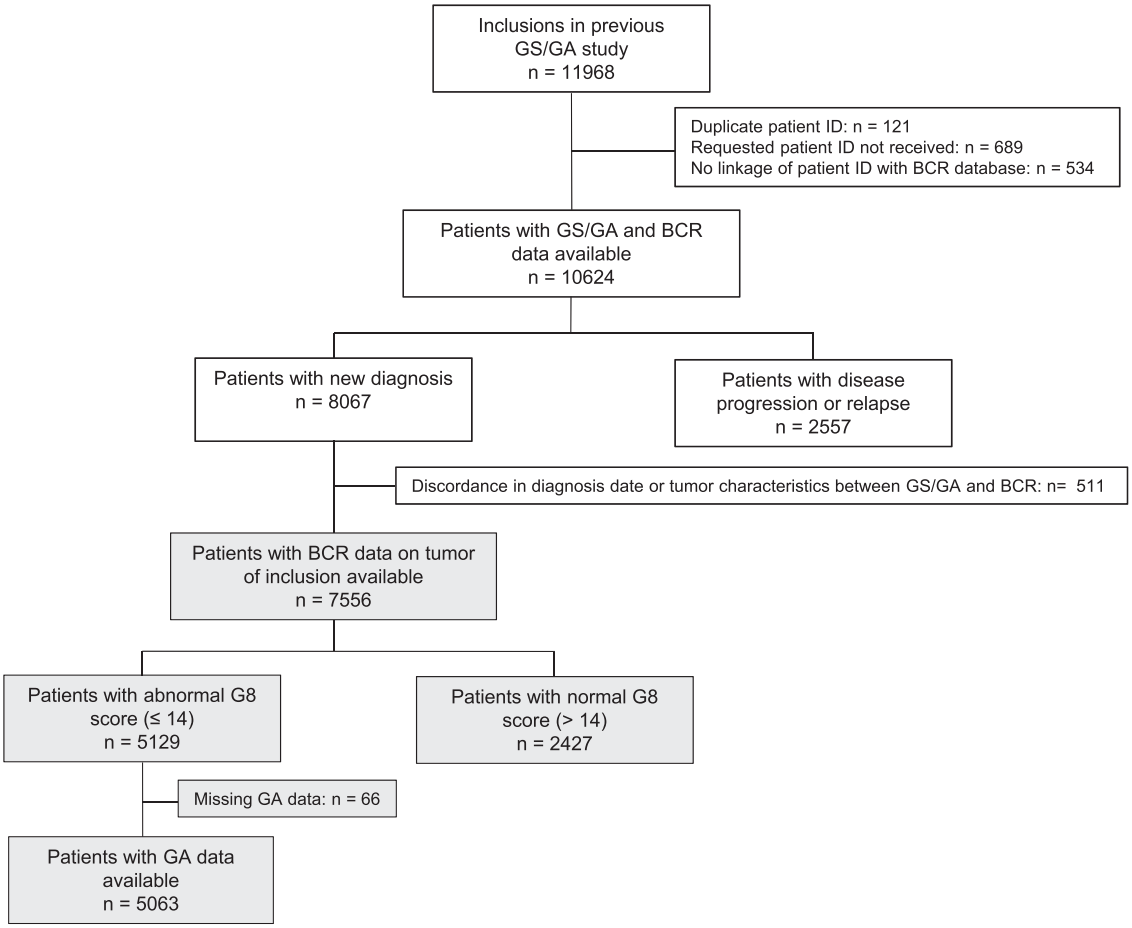


Fig. 1. Patient cohort creation flow chart.
Footnote: Grey frames indicate patients included for analysis in the current study.
Abbreviations: GS/GA = Geriatric Screening and Geriatric Assessment; Patient ID = Unique Patient Social Security Identification Number; BCR = Belgian Cancer Registry; G8 = Geriatric-8 Screening Tool

inclusion was limited to the following six tumor types: breast, colorectal, ovarian, lung, and prostate cancer and hematologic malignancies. This study focused on the implementation of GS with G8 [17] and GA [14]. In the second study cohort (August 2011 to July 2012; nine Belgian hospitals) and third study cohort (November 2012 to February 2015; 22 Belgian hospitals), patients with all tumor types were included [15,16]. These studies focused on geriatric recommendations based on GA results and more specifically on geriatric interventions in the latter.

2.2. Data Sources, Linkage and Security

Overview of the data sources and their content is provided in Table 1 and Supplementary Table S1. Linkage of GS/GA study data with BCR data, IMA reimbursement data, and TCT hospital discharge data was done deterministically, based on the patient's unique social security identification number (patient ID) that is assigned to all Belgian residents. Feasibility of linkage is assessed in percentages of successful record linkage. Selected researchers only have access to the pseudonymized linked databases that are stored on a secure server of the BCR. For the use and linkage of data through patient ID, approval of the Belgian Information Security Committee was obtained in January 2020. The study protocol of the current study was approved by the Ethics Committees of all 22 hospitals involved in the GS/GA study by April 2020. After approval the data was linked by independent 'Trusted Third Parties' in a nine-step dataflow with double coding and strict separation of patient ID and clinical/population-based data to ensure confidentiality as described in more detail elsewhere [18].

2.3. Inclusion and Exclusion Criteria

For the current study, we started from all patients included in the previous GS/GA study. If a patient was included in more than one of the GS/GA studies, only the first inclusion was taken into account. Patients were also excluded if the patient ID was not received from the hospital, if patient ID linkage with the BCR database was not possible (e.g., because of non-Belgian residency or because of patient ID mismatch) or if the tumor as defined in GS/GA study was not present in the BCR database (e.g., not registered as an invasive tumor). Furthermore, we decided to focus on patients with a new cancer diagnosis since there is no population-based registration of disease progression/relapse at the BCR.

2.4. Statistical Analysis

Descriptive statistics were used to describe baseline patient characteristics, clinical variables, and GS/GA results of the study cohort. Baseline was defined as the date of performance of GS/GA. Depending on the variable studied, descriptive statistics were performed considering the whole study cohort (GS and other baseline variables) or only patients with a G8 score $\leq$ 14/17 (additional GA variables available). To determine frequencies of geriatric risk factors, we generated dichotomous variables for each domain based on cutoff scores as summarized in Supplementary Table S1. Missing values are displayed in tables but were not considered in analyses used for figures.

Kaplan-Meier curves were computed to visualize survival probabilities from baseline to the end of follow-up on April 1, 2020. Patients still alive at end of follow-up were censored at this date. Patients lost to follow-up were censored at the date of last information on vital status. If the date of lost to follow-up was the same as the date of cancer incidence, patients were excluded for survival analyses. The follow-up time was defined as the time (median, interquartile range [IQR]) from inclusion to the last follow-up for all censored patients. Follow-up times for IMA and TCT were calculated in the same way but with end of follow-up being March 1, 2019 and January 1, 2019, respectively. Survival curves were compared using the logrank test. Hazard ratios (HR) with 95% confidence intervals (CI) were estimated using Cox proportional-hazards models. Unadjusted and adjusted analyses with age, sex, tumor type, stage, Charlson Comorbidity Index (CCI) and Eastern Cooperative Oncology Group Performance Status (ECOG-PS) as confounders were performed (categorized as displayed in Table 2). Missing information on confounders was assigned to a separate category.

All analyses were conducted in SAS Enterprise Guide (v9.4, SAS Institute Inc.).

3. Results

3.1. Patient Population and Linkage

The patient flow chart is presented in Fig. 1. In the GS/GA study, 11968 inclusions of older patients with cancer were recorded between 2009 and 2015. Of the 121 patients included in more than one study, only the first inclusion was considered. For 689 patients, we did not receive the patient ID from the original hospitals. Of the 11158 remaining patients, a link between the patient ID and the BCR database could be made for 10624 patients (95.2%). Failure of linkage can be explained by non-Belgian residency and administrative errors, but is also partly due to incomplete registration in BCR database, which is considered to be >95% complete [19]. In the current study, the target population were patients with a new cancer diagnosis. For 511 patients (on 8067 patients with new diagnosis), there was a discordance between diagnosis date or tumor characteristics in GS/GA and BCR data. Finally, a group of 7556 patients was identified with linked GS/GA and BCR data (93.7%).

Linkage between IMA reimbursement data and the final 7556 cohort was possible for 7445 patients (98.5%). Patients with missing IMA data could be exempted from mandatory health insurance (e.g., employee of European Commission, frontier workers). Median follow-up time for IMA data was 65.2 months (IQR: 56.5–81.0). Linkage between the TCT hospital discharge data and the final 7556 cohort was possible for 7361 patients (97.4%). It could be that for some patients no TCT data is available because patients have never been hospitalized or received emergency care since inclusion. Median follow-up time for TCT data was 63.5 months (IQR: 54.7–79.3). Combined GS/GA-BCR-IMA-TCT data was available for 7314 patients (96.8%).

3.2. Patient Characteristics

According to BCR data, 92.3% (n = 6972) of the 7556 patients included in this study were diagnosed with a solid tumor (Table 2). Breast (28.3%, n = 1974), colon (16.2%, n = 1132), and lung cancer (12.0%, n = 837) were the most common diagnoses. 7.7% (n = 584) of the patients were included with a hematologic malignancy. Non-Hodgkin lymphoma (51.0%, n = 298) and multiple myeloma (18.7%, n = 109) were the most common hematologic subtypes. 25.4% (n = 1555) of the patients with a solid tumor had combined stage IV disease. >10% of patients had a history of cancer as there was already an invasive tumor registered in the BCR database before registration of the tumor of inclusion.

As reported in the GS/GA study, the median age at inclusion was 78 years (range: 70–100) and the patients were divided into four age groups: 70–74 (30.3%), 75–79 (30.6%), 80–84 (23.7%), and $\geq$ 85 years (15.5%). 57.8% (n = 4365) of patients were female. Comorbidities (evaluated by Charlson Comorbidity Index) were present in 67.8% (n = 5099) of patients, and the three most prevalent comorbidities were peripheral vascular disease (26.7%, n = 2008), diabetes mellitus without complications (14.0%, n = 1054), and congestive heart failure (13.5%, n = 1017). Half of the patients took five or more different medications in the week before GS (51.0%, n = 3764). A total of 31.7% of the patients had a poor performance status (score $\geq$ 2) according to the ECOG performance score (n = 2391) and 34.2% (n = 2461) were living alone at time of diagnosis. Further patient and clinical characteristics are listed in Table 2.

For the twelve most common solid tumor types (n = 6174), the first

Table 3
First line treatment as identified through time frames around diagnosis in reimbursement data from the InterMutualistic Agency.

		12 solid tumor types [a] $n = 6174$	
		N	%
First line treatment	Surgery	3988	64.6
	Systemic therapy	2394	38.8
	Radiotherapy	2343	38.0
	Endocrine therapy	1759	28.5
	Missing	109	

[a] Only for the twelve most common solid tumor types as listed in Table 2: breast, colon, lung, rectum, prostate, pancreas, esophagus, bladder, corpus uteri, head and neck, ovary, and stomach cancer.

line treatment was identified in IMA data (Table 3). In this cohort, 64.6% had surgery, 38.8% received systemic therapy, 38.0% received radiotherapy, and 28.5% received endocrine therapy.

3.3. Geriatric Screening and Assessment

Of the 7556 patients, 5129 patients (67.9%) had an abnormal G8 score (≤14) at baseline (Fig. 2a). The percentage of patients with an abnormal G8 score clearly increased with increasing age (Supplementary Fig.S1).

For 5063 patients with abnormal G8, the results of the GA were available (Fig. 2b & Supplementary Table S4). More than half of these patients showed a functional dependence on Activities of Daily Living (ADL score ≥ 7) (56.5%) and Instrumental Activities of Daily Living (IADL score ≤ 4 for male or ≤ 7 for female) (65.3%). A fall history in the past year was present in 36.8% of the patients. Mild to severe pain (Visual Analogue Scale, score ≥ 1) was reported by 51.0% of the

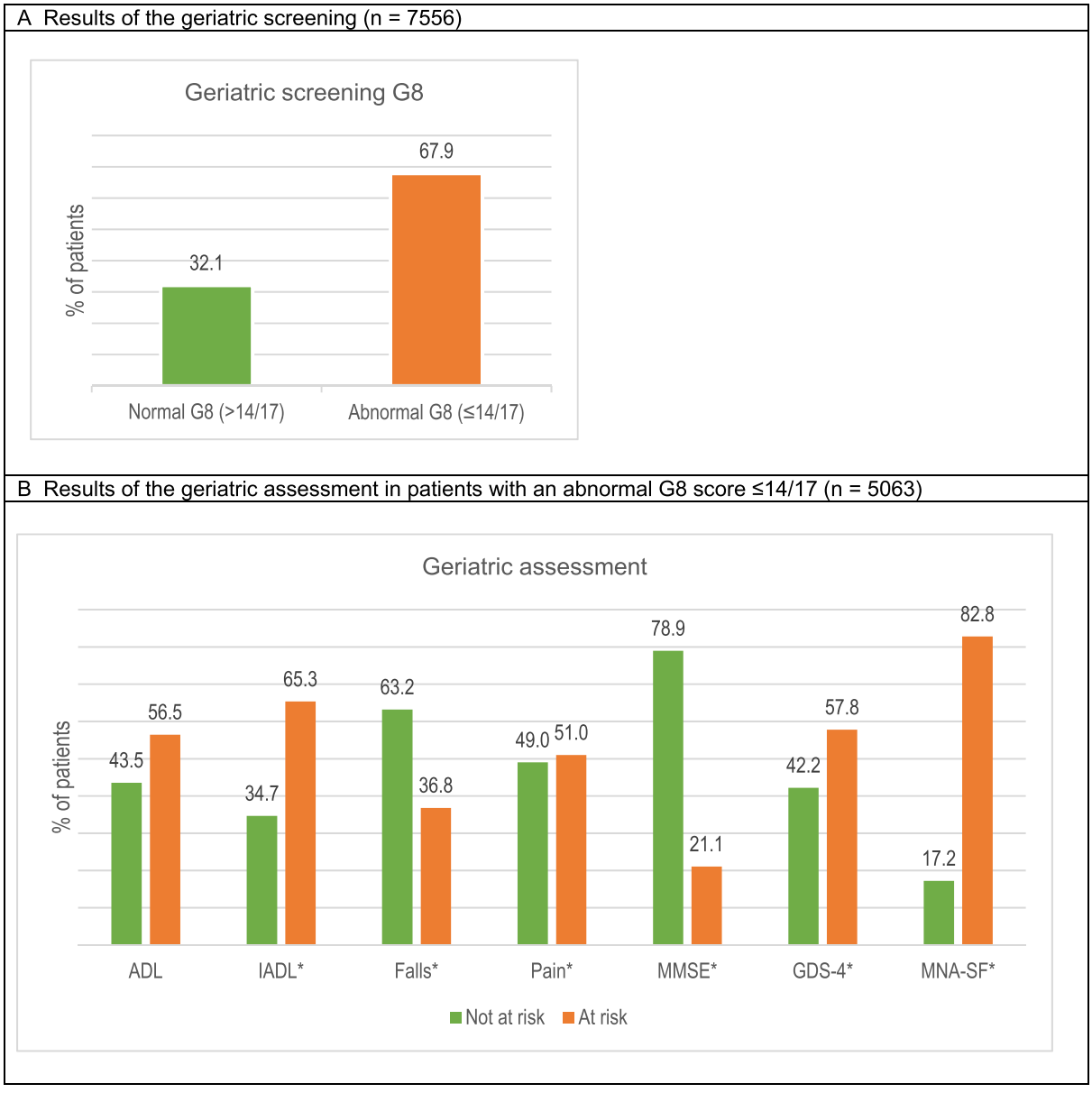


Fig. 2. Results of the baseline geriatric screening and geriatric assessment in older adults with cancer.
Footnote: *In cases of missing data, denominator was adjusted.
Abbreviations: G8 = Geriatric-8 Screening Tool; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; GDS-4 = Geriatric Depression Scale, 4-Item; MNA-SF = Mini-Nutritional Assessment – Short Form

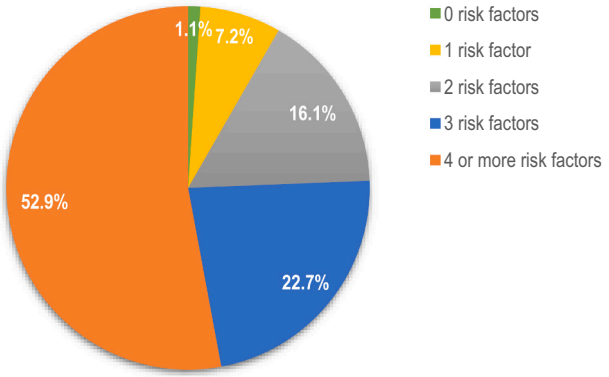


Fig. 3. Number of co-occurring geriatric risk factors in older patients with cancer and an abnormal G8 score ≤ 14/17 at baseline ($n = 5063$).
Footnote: In case of missing data in one of the GA domains, denominator was not adjusted since each patient had at least one domain available.

patients. Cognitive decline (Mini Mental State Examination, score ≤ 23) was detected in 21.1% of the patients and 57.8% were at risk for depression (4-item Geriatric Depression Scale, score ≥ 1). 82.8% of the patients were at risk for malnutrition or malnourished (Mini Nutritional Assessment Short-Form, score ≤ 11).

If the percentage at risk is compared between the age groups for each GA domain, the percentage increases with age for most domains, except for pain, depression, and nutrition (Supplementary Fig.S2).

Looking at the co-occurrence of risk factors in this cohort of patients with abnormal G8, 98.9% of patients were at risk for at least one domain (Fig. 3). More than half of the patients had minimum four or more out of seven risk factors present at time of cancer diagnosis (53.0%).

When comparing the prevalence of risk factors between the age groups, the number of patients with multiple risk factors increased with age. The prevalence of having at least four out of seven risk factors present in patients aged 70–74, 75–79, 80–84, and ≥ 85 years was 47.3%, 52.1%, 51.7%, and 61.8%, respectively (Supplementary Fig.S3).

3.4. Health-Related Quality of Life

Following the GA, the HRQOL was assessed at baseline in a subgroup of 3469 patients. The mean HRQOL for this cohort was 54.0 (SD: 22.5).

3.5. Overall Survival

Median follow-up time for OS was 78.2 months (IQR: 69.5–94.3) and median OS was 40.3 months (95%CI: 37.5–42.7). For the entire cohort, the OS rates at one, three, and five years after inclusion were 70.8%, 51.6%, and 42.0%, respectively.

When comparing the OS between patients with normal and abnormal G8 score, OS was significantly lower for patients with an abnormal G8 in all age groups (logrank $p < 0.001$, Fig. 4). For the whole cohort, the median OS for patients with a normal G8 was 115.7 months (95%CI: 105.9–122.1), whereas the median OS for patients with abnormal G8 was 21.7 months (95%CI: 20.1–23.2) (Supplementary Fig.S4). In adjusted analyses, an abnormal G8 score was associated with an increased mortality (adjusted HR [aHR] = 1.62 [1.50–1.75], $p < 0.001$) and this association remained regardless of age category (Table 4).

4. Discussion

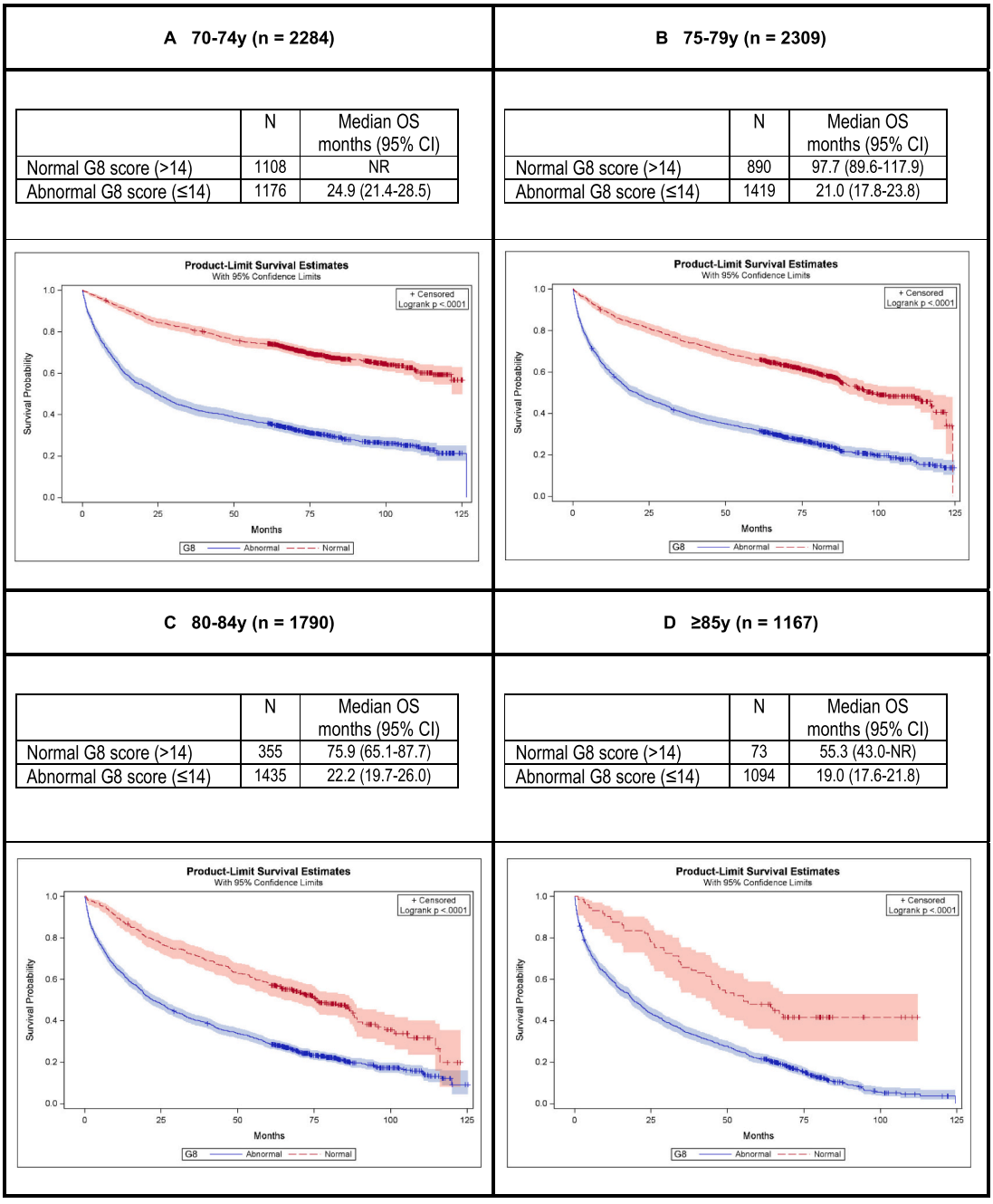
The current work describes the creation of a cohort of older patients with a new cancer diagnosis as a basis to study long-term outcomes. To this end, clinical data were individually linked with population-based registration and administrative data. The linkage process between the GS/GA study and BCR data was successful, the large majority of patients from the original clinical study could be linked with the cancer registration data resulting in a cohort of 7556 patients. Subsequent linkage to IMA and TCT also resulted in a very high coverage. To our knowledge this is the first time that clinical data from a GS/GA study is linked to population-based data for long-term follow-up on a large scale. Although challenging because of linkage constraints and strict data protection regulations, a rich dataset with baseline GS/GA and cancer registry data as well as all healthcare utilization since study inclusion, is now available for extensive outcome analyses.

According to baseline characteristics, 67.9% of the patients in this study had an abnormal G8. This result corresponds with percentages found in literature for G8 that mostly range between 60 and 94% for studies including various tumor types [17,20,21]. Within the group of patients with an abnormal G8, the prevalence of individual geriatric risk factors varied from 21% to 83%, depending on the domain. These results are more difficult to compare as the study population (age, tumor type, sex), tools, and cutoffs strongly differ between studies. Furthermore, only patients with an abnormal G8 were selected for GA so prevalence of risk factors is higher. Nutritional issues and functional dependence were the most common GA-identified risk factors, and these issues are also in other studies highly prevalent [6,22–24].

We also observed that more than half of the patients with an abnormal G8 have four or more geriatric risk factors present at diagnosis. Not many studies look at the co-occurrence of geriatric risk factors, mostly GA summary scores with dichotomous cutoff are displayed without looking at the total sum of domains. One study did compare geriatric risk factors in patients with and without cancer, and concluded that the former experienced a higher prevalence of geriatric risk factors [25]. This emphasizes the vulnerability of the older population with cancer and the importance of GS/GA. In addition, it highlights the need for management of these geriatric risk factors with tailored geriatric interventions.

If we look across different age groups, the oldest individuals were most at risk according to G8 and had the most co-occurring geriatric risk factors. This is consistent with research stating that the prevalence of frailty increases with age [26,27]. Looking at individual domains, the percentage of patients at risk increased with age for the domains functional status (ADL, IADL), falls, and cognition. For the domains pain, depression, and nutrition, the percentage of patients at risk decreased with age. One study found no significant correlation between age and geriatric risk factors in patients with gastrointestinal malignancies while others mostly observed an increase with age [28,29]. For mental status, a decrease in depressive symptoms with age in patients with cancer has been described [30,31], and may be explained by increased acceptance of the inevitable aging process and death [32]. For pain measured with VAS, this decrease could be explained by several factors, such as a decreased reactivity of the pain signaling pathway or increased erroneous answers due to increased cognitive disability with advancing age [33,34]. For nutrition, some evidence leans towards increased risk of malnutrition with aging in the general older population [35,36] while other studies report decreased risk of malnutrition with higher age [37,38](confirming our observations in this population). Possible explanations for decreased risk of malnutrition with aging might be that as the functional status decreases with age, more support such as home care or long-term care is provided that could benefit the nutritional status. Nevertheless, malnutrition is highly prevalent in all age groups and this underlines the importance of a nutritional component in the GA. Anyhow, these age-specific analyses highlight that age alone is not a reliable indicator for the presence of geriatric risk factors. Remarkable is that in the age group 70–74, also almost half of the patients with an abnormal G8 have four or more risk factors present. In the Belgian healthcare system, age 75 or higher is considered as a baseline cutoff for GA [39]. Our data indicate that in oncology also patients between 70 and 74 years old can clearly benefit from GS/GA.

Furthermore, the prognostic capacity of the G8 for long-term OS is confirmed in this study. Median OS for patients with an abnormal G8



A 70-74y (n = 2284)	N	Median OS months (95% CI)
Normal G8 score (>14)	1108	NR
Abnormal G8 score (≤14)	1176	24.9 (21.4-28.5)

B 75-79y (n = 2309)	N	Median OS months (95% CI)
Normal G8 score (>14)	890	97.7 (89.6-117.9)
Abnormal G8 score (≤14)	1419	21.0 (17.8-23.8)

C 80-84y (n = 1790)	N	Median OS months (95% CI)
Normal G8 score (>14)	355	75.9 (65.1-87.7)
Abnormal G8 score (≤14)	1435	22.2 (19.7-26.0)

D ≥85y (n = 1167)	N	Median OS months (95% CI)
Normal G8 score (>14)	73	55.3 (43.0-NR)
Abnormal G8 score (≤14)	1094	19.0 (17.6-21.8)

Fig. 4. Kaplan-Meier curves with associated logrank test showing overall survival since study inclusion according to G8 score in four age groups of older patients with cancer.
Footnote: Overall survival is displayed since the day of inclusion which is the date of screening. For the whole cohort, date of screening occurred a median of 18 days (IQR: 7–36) after cancer incidence date.
Abbreviations: G8 = Geriatric-8 screening tool; NR = not reached; CI = distribution-free confidence intervals.

(≤14/17) is less than two years whilst patients with a normal G8 (>14/17) have a median OS of more than nine years. Also in adjusted analyses, G8 remains prognostic for OS in all age categories. It's noteworthy that a simple and fast screening tool as the G8 has such strong prognostic value for OS in a heterogeneous oncologic population. These findings are consistent with other research but to our knowledge it is the first time OS according to G8 is described in such a large cohort with a minimum of five years follow-up [40–44].

The large cohort size is a major strength of this study. Furthermore, this study includes a heterogeneous population that is representative of the large population of older patients with cancer and allows a broad application of the results. On the other hand, the diversity of the cohort can be a drawback as oncologic parameters such as cancer type, stage, and treatment can influence the prevalence of geriatric risk factors. Another study limitation is that the frailty profile is determined based on the G8, which is not a perfect tool (good sensitivity, but limited specificity) and other tools exist to screen for frailty profiles [20,45]. Nevertheless, the G8 was developed to identify those patients at risk and has demonstrated good sensitivity [17].

Our future research goal is to study additional long-term outcomes in this large study cohort. These long-term outcomes are often lacking in clinical studies because long follow-up times are not feasible. In

Table 4
Prognostic value of an abnormal baseline G8 score (≤14/17) as compared to normal baseline G8 score (>14/17) for overall survival: Cox proportional-hazards regression for full cohort (all ages) and cohort stratified by age category.

	Unadjusted analysis			Adjusted analysis		
	HR	95% CI	*p*-value	aHR	95% CI	*p*-value
All ages (n = 7550)	3.12	2.90–3.34	<0.001	1.62	1.50–1.75	<0.001
70-74y (n = 2284)	3.34	2.95–3.78	<0.001	1.66	1.44–1.90	<0.001
75-79y (n = 2309)	2.73	2.42–3.06	<0.001	1.61	1.42–1.84	<0.001
80-84y (n = 1790)	2.19	1.87–2.55	<0.001	1.44	1.22–1.69	<0.001
≥85y (n = 1167)	2.48	1.82–3.38	<0.001	1.59	1.15–2.19	0.006

Abbreviations: HR = unadjusted hazard ratio; 95% CI = 95% confidence interval; aHR = adjusted hazard ratio for age, sex, tumor type, stage, Charlson Comorbidity Index and Eastern Cooperative Oncology Group Performance Status.

addition, study outcomes (such as healthcare utilization) that are nearly never covered in clinical studies on GS/GA can be explored. We aim to describe the patient's trajectory following primary treatment (e.g., number of contacts with health care professionals, number of hospitalizations, need for home care, need for institutionalization, number of diagnostic tests) and care at the end-of life (e.g., use of pain-relief medication, need for palliative care, place of death). Furthermore, we will assess the association between baseline GS/GA/HRQOL results and these endpoints to evaluate the long-term predictive value of GS/GA/HRQOL.

In conclusion, this article highlights the feasibility and potential of data linkage for studying health outcomes over time in older adults with cancer. The GS/GA and BCR-linked data were used to describe first clinical outcomes in the cohort that has been established for that purpose. The results demonstrate the vulnerability of older patients with cancer and show that the G8 is a strong independent predictor of OS in this population. This strengthens the clinical utility of GS/GA tools in geriatric oncology. In the future, the linkage to IMA and TCT data will be used to study long-term outcomes beyond survival and the association with GS/GA results.

Author Contributions

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Study design VD KVS LDC HDS KM JF CK FV HW
Data acquisition All authors
Quality control of data and algorithms VD KVS LDC CK FV HW
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Statistical analysis VD KVS LDC CK FV HW
Manuscript preparation VD KVS LDC CK FV HW
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Manuscript review All authors

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Declaration of Competing Interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

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