Extensive and Dynamic Signs and Symptoms Prior to Cancer Diagnoses

National Comprehensive Cancer Network (NCCN)
2023 Annual Conference
March 31–April 2, 2023, Orlando, FL

Ze Cong,[1] Xiangyang Ye[2] | [1]GRAIL, LLC, a subsidiary of Illumina, Inc.*, Menlo Park, CA; [2]University of Utah, Salt Lake City, Utah

INTRODUCTION

- The majority of cancer patients experience signs and symptoms prior to cancer diagnoses. It is estimated that in the US, greater than 60% of cancers are diagnosed following symptomatic presentation.[1]
- Many signs and symptoms were not specific to a certain disease type or organ system.[2-4]
- Common signs and symptoms shared by multiple cancer types contribute to complex and potentially inefficient cancer diagnoses.

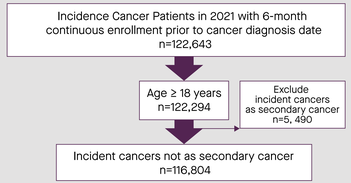
OBJECTIVES

- This study sought to characterize the flow of symptoms and signs within 6 months prior to cancer diagnoses in the US.

METHODS

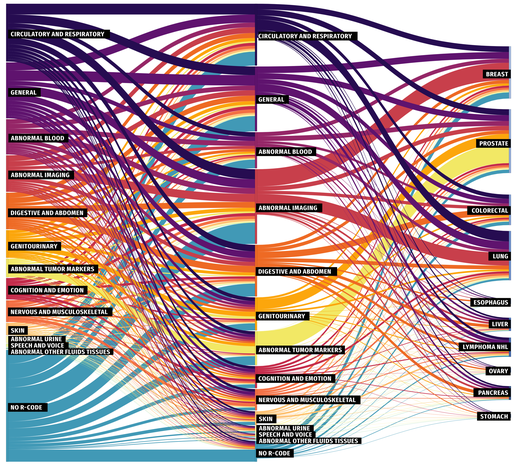
- Database: Optum's de-identified Clinformatics® Data Mart which includes Medicare Advantage and commercially insured members (**Figure 1**).
- Patients newly diagnosed with cancer in 2021 were identified by requiring two outpatient cancer claims more than 30 days apart or one inpatient claim for cancer. Inclusion criteria were:
  - 6 months continuous enrollment prior to cancer diagnosis without cancer claims
  - aged 18+ in 2021
- Patients who were diagnosed with secondary cancer in 2021 were excluded.

Figure 1. Study Schema



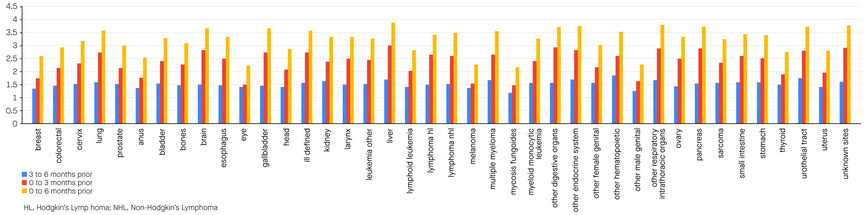
KEY RESULTS: PATIENTS WITH CANCER EXPERIENCED MULTIPLE CATEGORIES OF SIGNS AND SYMPTOMS PRIOR TO DIAGNOSIS, WITH COMMON AND DYNAMIC SIGNS AND SYMPTOMS SHARED ACROSS DIFFERENT CANCER TYPES

Figure 2. Signs and Symptoms Categories Coded 3-6 Months and 3 Months Prior to Cancer Diagnoses for 10 Cancer Types



- Signs and symptoms experienced by patients tended to be dynamic over time–patients coded to have one category of signs and symptoms during 3 to 6 months prior to cancer diagnoses could be coded to have additional/other signs and symptoms during the 0-3 months prior (**Figure 2**).
- Many cancer types shared common categories of signs and symptoms prior to diagnosis.
- More cancer patients were not coded to have signs and symptoms 3-6 months prior to cancer diagnosis than during the 0-3 months prior (50.0% vs. 18.5%).

Figure 3. Average Number of Signs and Symptoms Coded Per Patient Prior to Cancer Diagnosis by Cancer Type



HL, Hodgkin's Lymp homa; NHL, Non-Hodgkin's Lymphoma

- Patients developed more symptoms closer to cancer diagnosis (**Figure 3**).
- There is some heterogeneity among different cancer types in terms of number of signs and symptoms coded.

SUPPORTING DATA

Participants

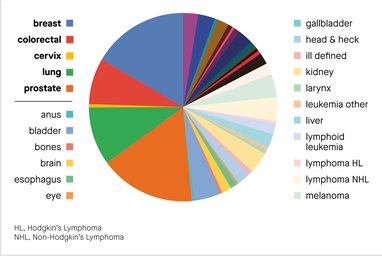
- 116,804 patients newly diagnosed with cancer in 2021 were analyzed (**Figure 1**).
- Patients had a mean age of 73 years, almost 50% were male, 11% were Black, and 9% were Hispanic (**Table 1**).

Table 1. Demographic Characteristics

	Mean/N	STD/%
Age (mean, std)	72.8	11.45
Gender		
Female	58,560	50.14
Male	58,242	49.86
Unknown	2	0.00
Race/Ethnicity		
White	82,038	70.24
Black	13,011	11.14
Asian	3,034	2.60
Hispanic	10,335	8.85
Unknown	8,386	7.18

Note: STD = standard deviation

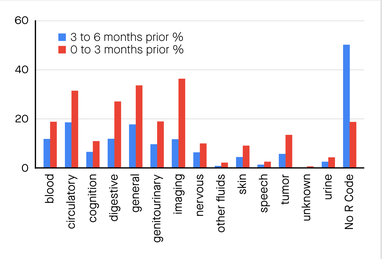
Figure 4: Distribution of Cancer Types Among All Incidence Cancers in 2021



HL, Hodgkin's Lymphoma
NHL, Non-Hodgkin's Lymphoma

- Cancers with recommended screening paradigms (breast, colorectal, cervix, lung) contributed to 35% of the total sample, whereas the remaining almost ⅔ of the total incidence of cancers do not have a USPSTF (United States Preventive Services Task Force) recommended screening (**Figure 4**).
- More patients were coded with signs and symptoms during the 3 months prior to cancer diagnoses vs. 3-6 months prior (**Figure 5**).

Figure 5: Proportion of Patients Coded With Each Signs and Symptoms Category Prior to Cancer Diagnoses



- Larger proportions of patients were coded to have digestive and abdominal symptoms, and abnormal imaging 3 months prior to cancer diagnosis vs. 3-6 months prior (**Figure 5**).

Figure 6: R-Codes Categories

R00-R09	Symptoms and Signs involving the **circulatory** and respirtatory systems
R10-R19	Symptoms and Signs involving the **digestive** system and abdomen
R20-R23	Symptoms and Signs involving the **skin** and subcutaneous tissue
R25-R29	Symptoms and Signs involving the **nervous** and musculoskeletal systems
R30-R39	Symptoms and Signs involving the **genitourinary** systems
R40-R46	Symptoms and Signs involving the **cognition**, perception, emotional state and behavior
R47-R49	Symptoms and Signs involving **speech** and voice
R50-R69	**General** symptoms and signs
R70-R79	Abnormal findings on examination of **blood** without diagnosis
R80-R82	Abnormal findings on examination of **urine** without diagnosis
R83-R89	Abnormal findings on examination of **other bodily fluids**, substances and tissues, without diagnosis
R90-R94	Abnormal findings on diagnostic **imaging** and in function studies without diagnosis
R97-R97	Abnormal **tumor** markers
R99-R99	Ill-defined and **unknown** cause of mortality

CONCLUSIONS

- Patients with cancer were reported to experience multiple categories of signs and symptoms prior to diagnosis.
- Common signs and symptoms were shared across different cancer type and were dynamic over time.
- This may lead to delayed cancer diagnosis. Tools to help streamline the diagnostic pathway can facilitate more efficient and timely cancer diagnoses.

References

1. Sarma EA et al. *Cancer Prev Res* (Phila). 2020;13(9):715-720.
2. Næser E, et al. *Cancer Epidemiol*. 2017;50(Pt A):158-165.
3. Lyratzopoulos G, et al. *Br J Cancer*. 2015;31;112 Suppl 1(Suppl 1):S84-91.
4. Koo MM et al. *Neoplasia*. 2018;20(2):165-174.

Disclosures

Study funded by GRAIL, LLC, a subsidiary of Illumina, Inc.* ZC is an employee of GRAIL, LLC, a subsidiary of Illumina, Inc.*, with equity in Illumina, Inc. XY is a consultant to GRAIL, LLC, a subsidiary of Illumina, Inc.* and received funding from GRAIL, LLC, a subsidiary of Illumina, Inc.* to conduct this study. All financial relationships disclosed at abstract submission.

Acknowledgements

Study funded by GRAIL, LLC, a subsidiary of Illumina, Inc.*Graphic assistance provided by Prescott Medical Communications Group (Chicago, IL). *GRAIL, LLC, is currently held separate from Illumina Inc. under the terms of the Interim Measures Order of the European Commission dated October 2021.