White Paper

Beyond the Bench and the Bedside: How Real-World Data Enrich Our Understanding of Oncology

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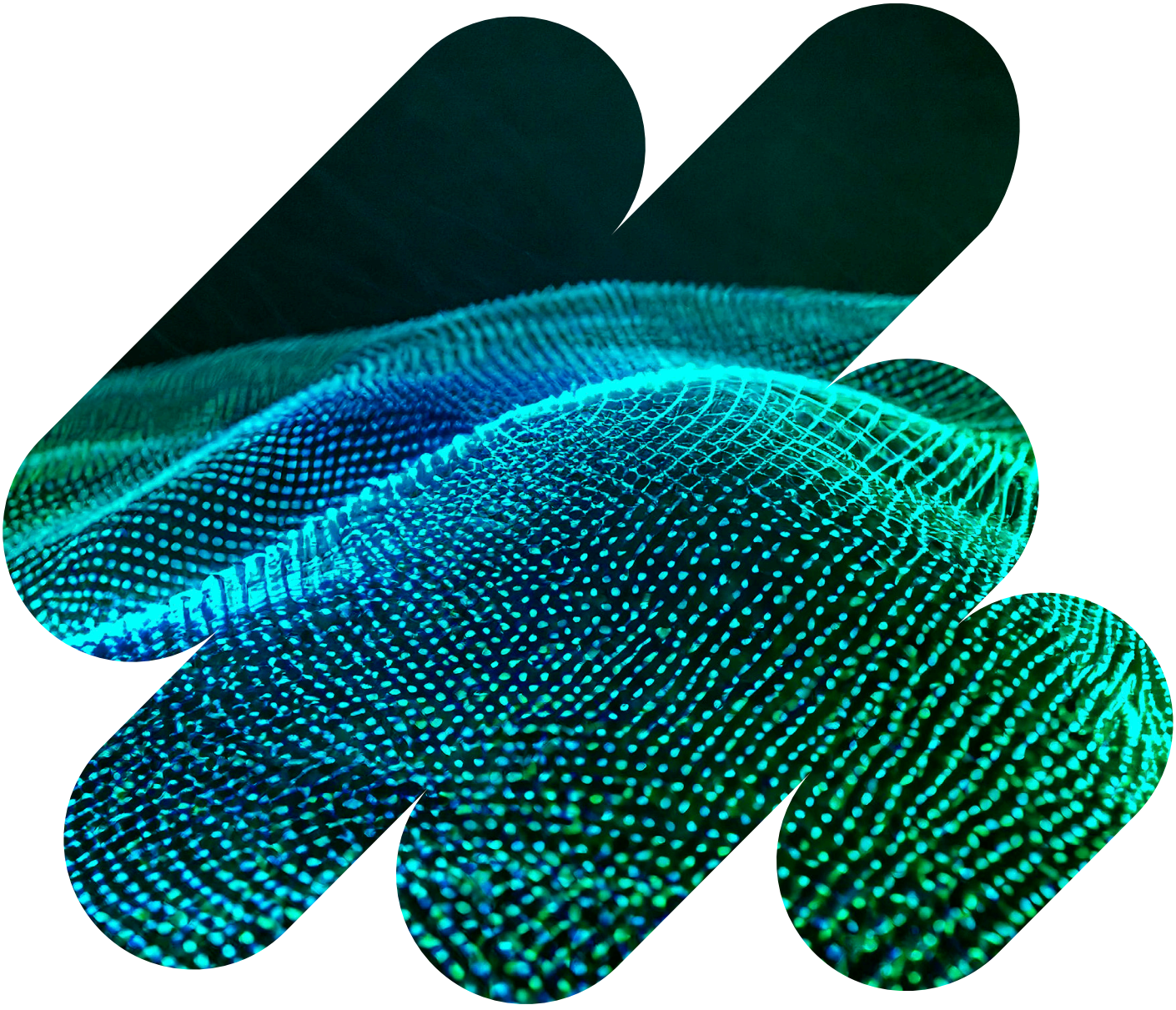

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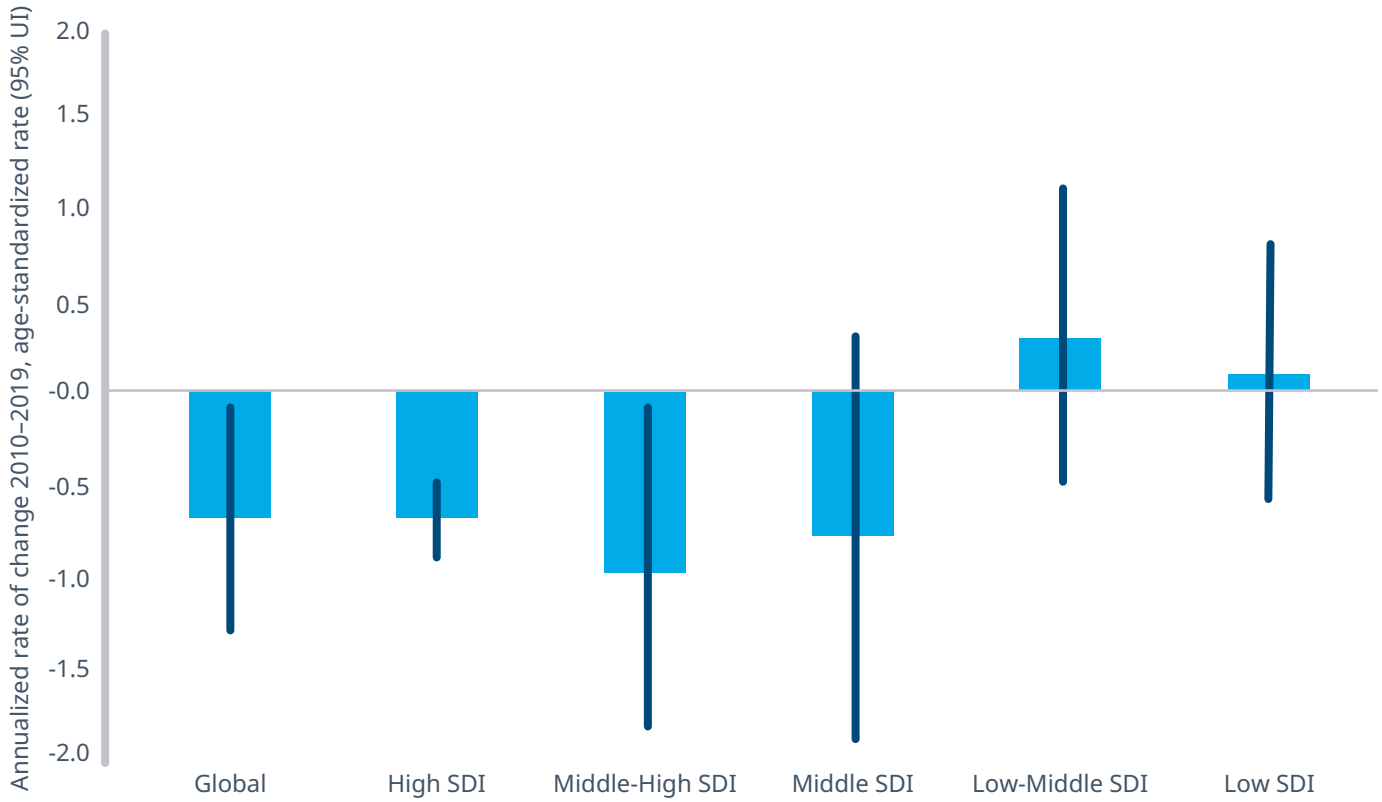
Introduction: Global cancer burden and the complexity of decision-making in oncology

The field of oncology is characterized by diagnostic and therapeutic complexity. Despite sharing a common umbrella term, each cancer type constitutes a distinct disease in its own right, affecting different populations, carrying different outcomes and risk factors. Cancer incidence is forecast to increase by over 12 million annual cases by 2050, with the highest projected increases falling on lower-income countries.[1]

The associated loss of quality of life, as well as the high treatment costs, underscore the importance of continued cancer research. Encouragingly, the Global Burden of Disease study has reported a decrease in mortality rates over the past decade, attributing this trend to advancements in cancer diagnosis and treatment methods.[2]

Mirroring the complexity of neoplasms as a disease group, the landscape of cancer treatment is diverse and dynamic, with well-established treatments gaining new indications and new drugs vying for a place in oncologists' life-extending arsenal. The variety of treatment choices, each with their own potential outcomes, side effects, and costs, creates difficulties in determining the most suitable course of treatment.[3] The decision-making may be influenced by limited scientific data, treatment availability, and individual patient considerations — see Figure 2.

Figure 1: Mean annual percentage change in age-standardized cancer mortality, 2010–2019



Data source: Global Burden of Disease 2019 Cancer Collaboration[2] (2022)

Figure 2: Conceptual model of decision-making in oncology

Adapted from Glatzer et al.[3] (2020)

In making treatment decisions, clinicians rely on the best available information, with randomized-controlled trials (RCTs) occupying the apex of the evidence hierarchy. While offering robust results, RCTs tend to be time- and cost-prohibitive and are thus primarily reserved for new drug candidates. Furthermore, the highly controlled setting of RCTs may not reflect real-world or long-term treatment usage patterns, or the contextual factors of the decision-making process in oncology. By contrast, real-world data may have less depth of detail, but offer a cost-effective and statistically powerful foundation for epidemiological research that is reflective of the treatment setting. **In this White Paper, IQVIA presents five examples of real-world data use in oncology research, showcasing some of our recent publications based on proprietary German and European datasets.**

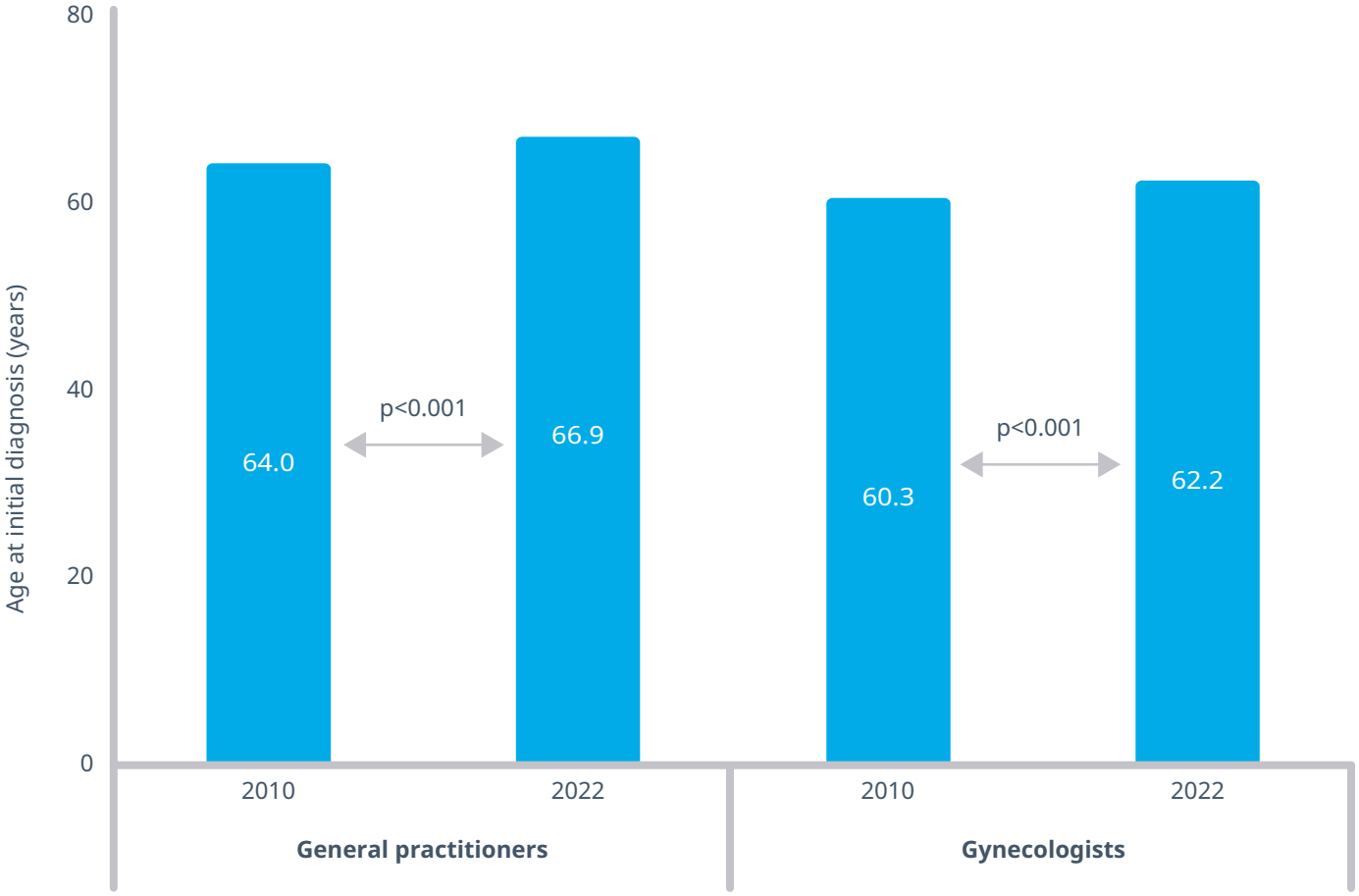
Harnessing RWD for epidemiological analyses in oncology

Newly diagnosed breast cancer: shifting age structure of the incident population

A recent study in *Breast Cancer Research and Treatment* utilized German data from IQVIA's Disease Analyzer database, which collects anonymized patient* records from a representative panel of primary care and specialty practices. IQVIA Disease Analyzer contains longitudinal records on diagnoses, prescriptions, and key demographic parameters, and has been used for numerous peer-reviewed publications. The study by Gremke et al.[4] focused on adult female patients diagnosed with breast cancer in 2010 and 2022,

* Please note: in the context of IQVIA's real-world data, terms such as "patient", "physician", etc., do not reflect usage of personal information, but exclusively anonymous information in accordance with applicable data protection laws.

Figure 3: Average age at first documented breast cancer diagnosis, Germany, 2010 vs. 2022

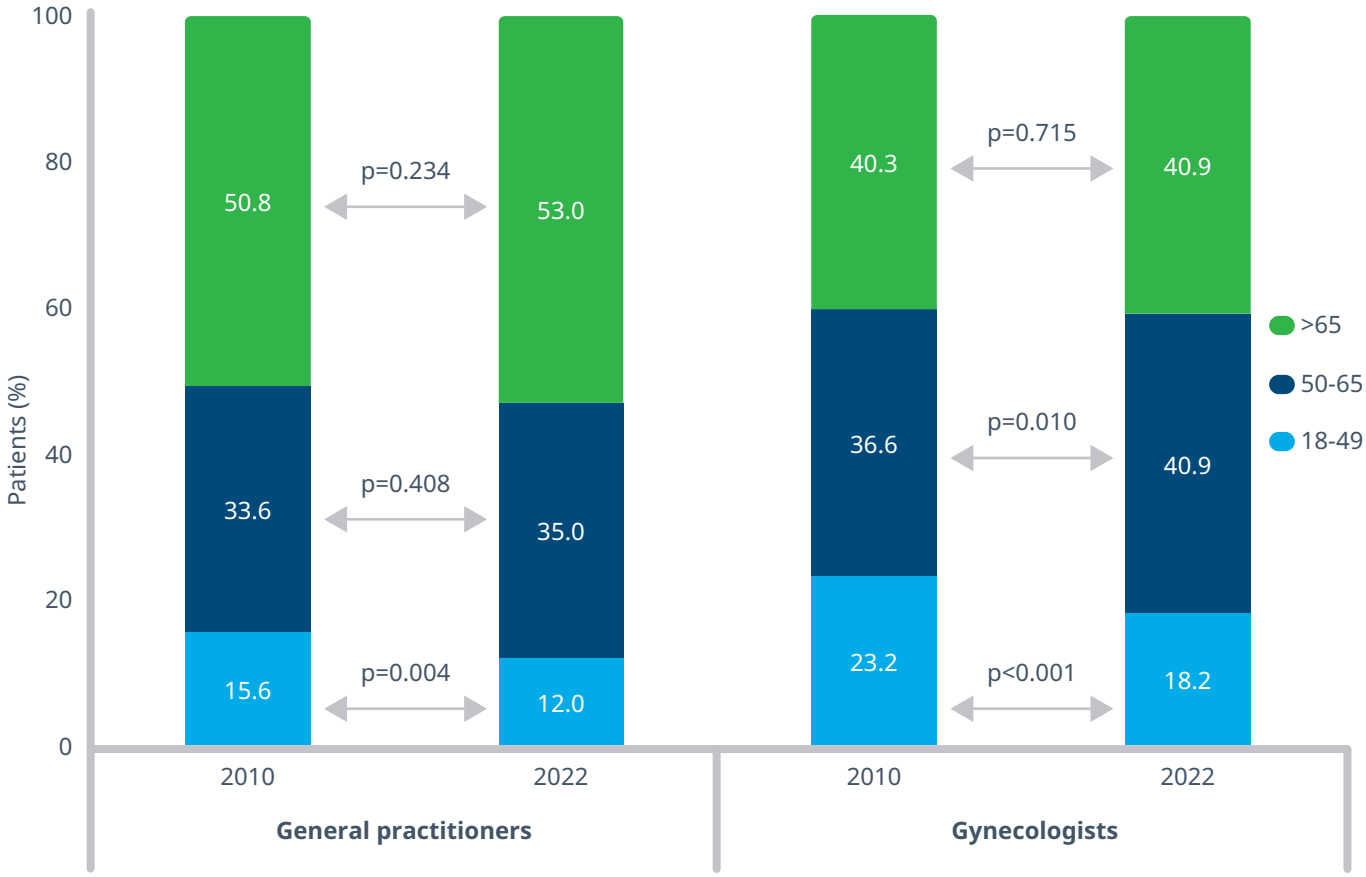


Data source: Gremke et al.[4] (2023)

addressing the average age at first cancer diagnosis and the proportion of patients in different age groups. The patient population was further stratified by setting, differentiating between patients in general and gynecologist practices. The results demonstrated a statistically significant increase in the average age at breast cancer diagnosis (from 64.0 to 66.9 years of age for general practices, from 60.3 to 62.2 for gynecologist practices).

The authors attribute the increase in the average age at first breast cancer diagnosis to the ongoing German population-based mammography screening program, which would have encouraged timely detection and treatment of precursor lesions before they had the chance to progress to invasive tumors. Additionally, population aging and a changing prevalence of risk factors such as obesity, smoking, and hormone replacement therapy were considered potential contributors to the increase in age at diagnosis. Furthermore, the study documented a statistically significant decrease in early-onset breast cancer cases in 2022 compared to 2021, defined as newly diagnosed cases among women aged 18 to 49.

Figure 4: Age group distribution of newly diagnosed breast cancer patients, Germany, 2010 vs. 2022



Data source: Gremke et al.[4] (2023)

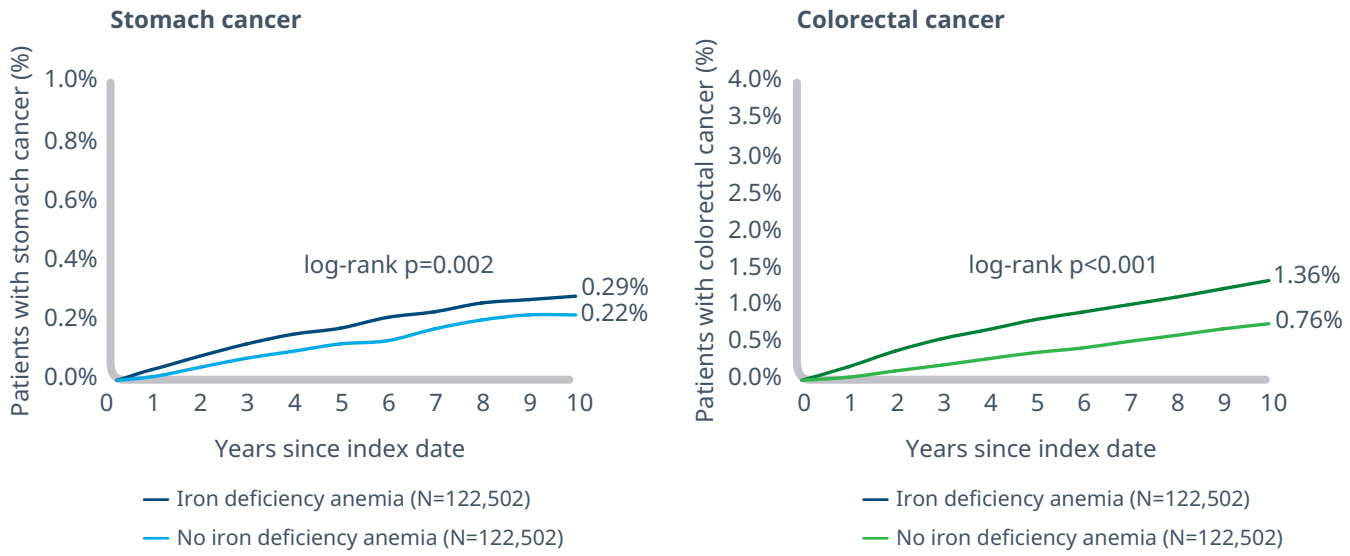
A lower proportion of early-onset cases is attributable to a decline in hormone replacement therapy utilization, better preventive management of hereditary gynecological cancers, and an increasing prevalence of obesity,[4] a condition that shares an inverse relationship with premenopausal breast cancer.[5] Further unmeasured risk factors, such as behavioral risks and socioeconomic status, should be considered in interpreting the results of both the analyses.[4]

The findings are based on data from 6,497 cases stemming from 300 general and 95 gynecological practices in Germany, selected for continuous data delivery during the study periods in 2010 and 2022. The full Disease Analyzer panel encompasses over 2,500 general and specialist practices, lending statistical power and representativeness to the analysis of interest, such as the next presented use case.

Risk factor exploration: the association between iron deficiency anemia and gastrointestinal cancers

A study by Krieg et al.[6] used IQVIA Disease Analyzer data to examine the association between iron deficiency anemia (IDA) and the incidence of stomach and colorectal cancers in a large German cohort. IDA is characterized by insufficient iron, an element essential for many bodily functions, including immune system regulation, cell proliferation, and DNA repair; etiologically, IDA is linked to various factors such as reduced dietary iron intake, impaired iron absorption, and chronic blood loss.[6] Prior research has indicated a connection between IDA and the development and progression of certain cancers, particularly those in the gastrointestinal tract.[7]

Figure 5: Cumulative incidence of stomach and colorectal cancers in patients with and without iron deficiency anemia



Data source: Krieg et al.[6] (2024)

For this study,[6] patients with and without IDA were matched 1:1 based on demographic and clinical parameters, such as age, sex, presence of metabolic conditions, and consultation frequency. The frequencies of stomach and colorectal cancer cases in the IDA and non-IDA cohorts were examined with a 10-year follow-up time frame.

The cumulative incidence curves show a positive association between IDA and both stomach and colorectal cancers. In fact, IDA patients had twice the likelihood of developing colorectal cancer compared to controls, with a Hazard Ratio (HR) of 2.05 (95% CI: 1.83–2.30). This association was particularly strong (HR: 3.07, 95% CI: 2.39–3.95) in patients over the age of 80. Additionally, IDA was linked to subsequent stomach cancer overall (HR: 1.41, 95%CI: 1.13–1.75) as well as in men (HR: 1.90, 95% CI: 1.38–2.61) and individuals over 80 (HR: 2.73, 95% CI: 1.60–4.67).

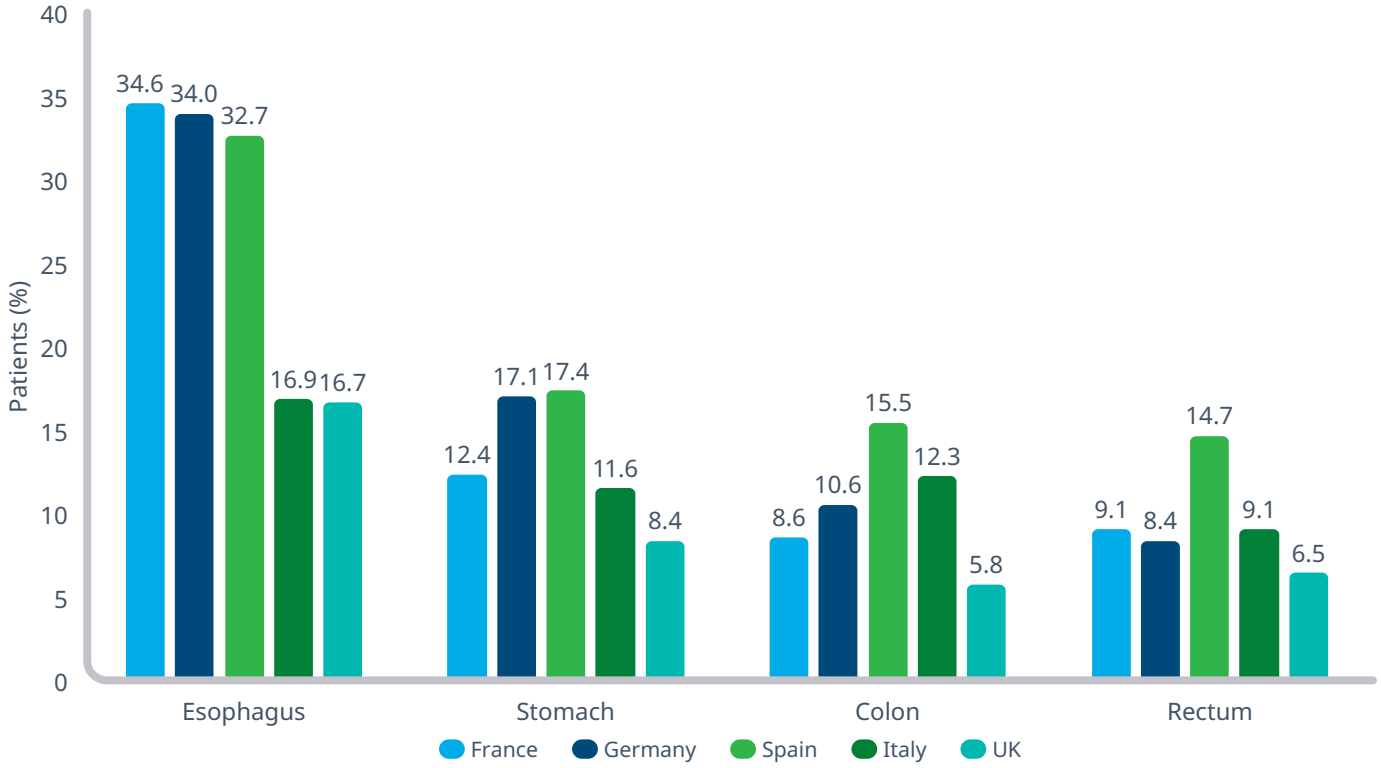
The findings are consistent with previous research, indicating a notable association between IDA and gastrointestinal cancers — this relationship could have significant implications for cancer prevention and treatment and should be further investigated in clinical and real-world settings.

The 10-year follow-up time frame, as well as the inclusion of patients with an index date of as early as 2005, were made possible by Disease Analyzer's long history of back data. To date, the dataset contains over 16 million patient records, encompassing diagnoses, therapies, laboratory values, service figures, referrals, hospital admissions, and certificates of sick leave. The panel is based on a stratified sample plan and is regularly reviewed by IQVIA's statistical office, enabling a holistic view of the outpatient practice landscape in Germany. The dataset has been validated for representativeness and has demonstrated a good correspondence with German reference literature in terms of incidence and prevalence of major chronic diseases.[8]

Prevalence of comorbidities: COPD in gastrointestinal cancer patients

Chronic obstructive pulmonary disease (COPD) and digestive tract cancers are prevalent conditions associated with considerable disease burden. A study by Loosen et al.[9] utilized IQVIA Oncology Dynamics, a global survey-based retrospective cancer database, to explore the connection between these conditions across five European countries. The analysis revealed variations in COPD prevalence across different cancer types and geographical locations: esophageal cancer patients had higher COPD rates vs. rectal cancer patients (25.5% vs. 8.8%), Spain had a noticeably higher prevalence than the UK (16.8% vs. 8.4%).

Figure 6: Prevalence of comorbid COPD among gastrointestinal cancer subpopulations in five European countries



Data source: Loosen et al.[9] (2022)

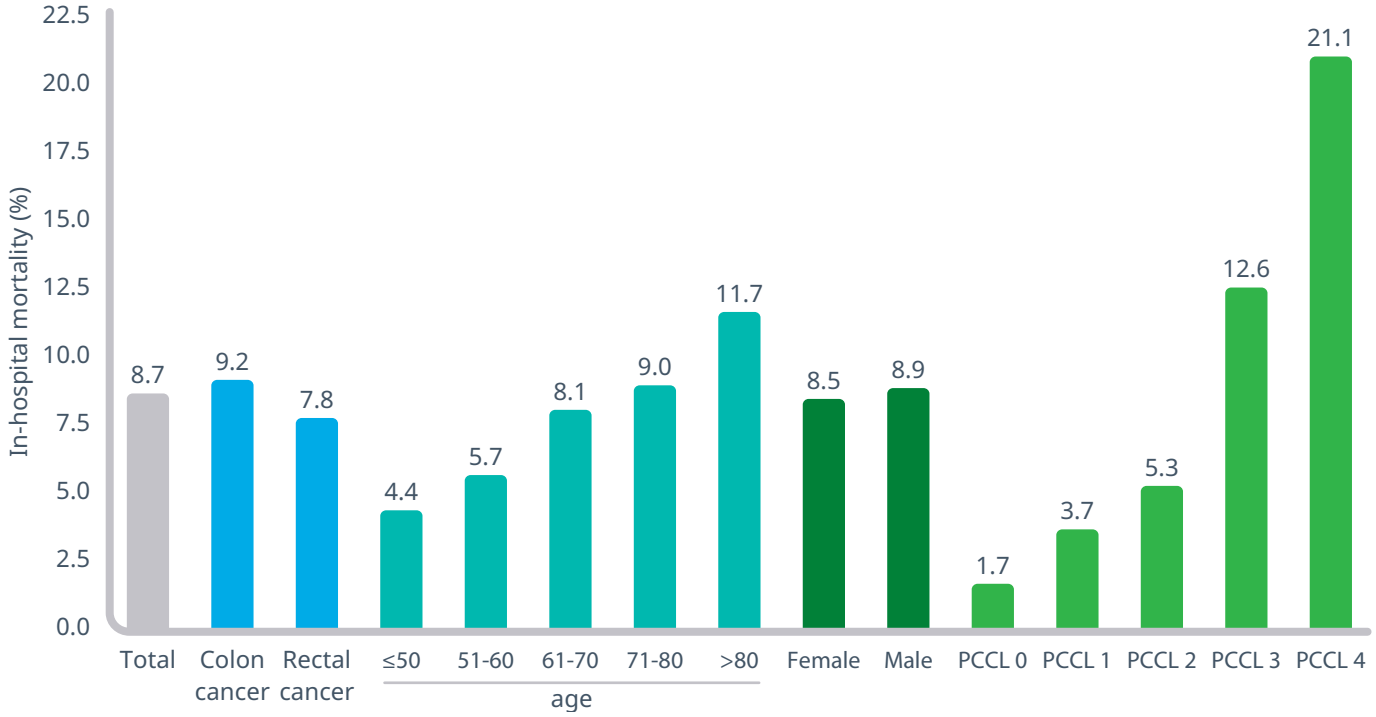
Multivariable logistic regression analysis revealed a significant association between COPD and esophageal, stomach, and colon cancers compared to the rectal cancer reference group, highlighting the varied comorbidity burden of COPD across different cancer types and underscoring the importance of considering COPD as a potential cancer-promoting factor in gastrointestinal malignancies.

This study included over 48,000 patients with esophageal, stomach, colon, and rectal cancer, documented by 811 physicians in the five European countries studied. Globally, Oncology Dynamics collects over 300,000 cases per year, spanning 18 countries. The data are collected from a representative panel of physicians (oncologists and all other cancer-treating specialties) through a survey specifically designed to document key clinical and therapeutic features of drug-treated cancer cases. Oncology Dynamics collects cancer stage and histology information, indication-specific biomarker test status and test results, and comorbidity status. Treatment information is collected for the patients' current and most recent previous anti-cancer treatments, and for several classes of supportive treatment. The representativeness of the German Oncology Dynamics database has been evaluated in a dedicated study, with the projected dataset demonstrating a cancer type distribution similar to the available prevalence literature.[10]

Setting-specific outcomes: evaluating hospital mortality in CRC subpopulations

Colorectal cancer treatment, e. g., surgery, is associated with potentially life-threatening complications. A recent study[11] in *Cancers* utilized IQVIA's PREMAX® database to analyze the prevalence of in-hospital mortality among hospitalized patients with colorectal cancers in Germany. The multicenter cross-sectional study included 4,146 colorectal cancer patients, with a mean age of 70.9 years and an average hospital stay length of 14.4 days.

Figure 7: In-hospital mortality of colorectal cancer subpopulations: by localization, age group, sex, and patient clinical complexity level (PCCL)



Data source: Kostev et al.[11] (2024)

Of the study population, 64.3% had colon cancer, 35.7% had rectal cancer; distant metastases were present in 25.1% of all cases. The results show an overall in-hospital mortality rate of 8.7%, with higher rates observed in older age groups, patients with severe complications and comorbidity effects, and those with distant metastases.

A multivariable logistic regression analysis identified several factors significantly associated with increased in-hospital mortality, including advanced age (OR: 2.44, 95% CI: 1.18–5.05 for patients over 80 vs. 50 or under), patient clinical complexity levels (OR: 3.01, 95% CI: 1.81–4.99 for PCCL 3 and OR: 3.76, 95% CI: 2.22–6.38 for PCCL 4 compared to PCCL 0), presence of distant metastases (OR: 4.95, 95% CI: 3.79–6.48), as well as certain comorbidities. The study revealed several parameters associated with an increased mortality risk, providing valuable insights into the determinants of patient outcomes in colorectal cancer care.

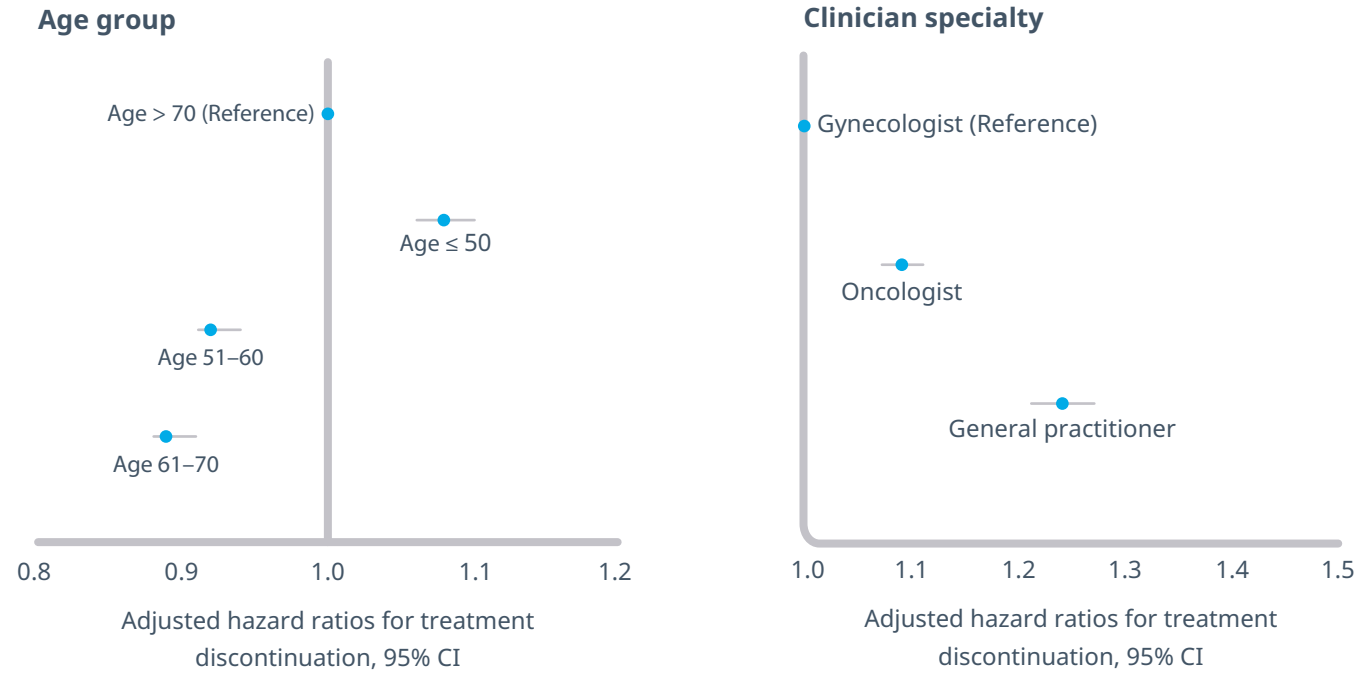
IQVIA's hospital data portfolio in Germany covers several key therapeutic areas and allows for retrospective and longitudinal real-world evidence studies with a medical science focus in the inpatient setting. Key patient characteristics, primary and secondary diagnoses, prescriptions and procedures, and outcome parameters such as stay length, reason for discharge, and mortality are available for analysis.

Real-world treatment usage: estimating persistence for endocrine therapy

Hormone-sensitive breast cancer is typically treated with endocrine therapy: either tamoxifen or aromatase inhibitors. However, despite the proven benefits of these treatments, many patients experience considerable side-effects, leading to therapy discontinuation. A study[12] in the *Journal of Cancer Research and Clinical Oncology* analyzed a breast cancer cohort from IQVIA's longitudinal prescription database *LRx*, investigating patients' persistence with endocrine therapy in Germany.

The study found that few of the patients remained on therapy after five years, with slightly higher persistence rates for aromatase inhibitors compared to tamoxifen (17.1% vs. 13.8%). Furthermore, therapy initiated by oncologists and general practitioners was associated with an increased risk of therapy discontinuation compared to gynecologists.

Figure 8: Adjusted Hazard Ratios for treatment discontinuation within 5 years of starting endocrine therapy for breast cancer



Data source: Gremke et al.[12] (2023)

The results provide patient- and setting-related insights into the challenges of persistence with endocrine therapy for breast cancer patients, highlighting the need for improved strategies to support adherence and long-term therapy continuation.

In Germany, IQVIA LRx gathers longitudinal prescription information of statutory health insurance (SHI) patients within the retail market, covering all therapy areas and physician specialties. The database covers approximately 82% of all filled SHI prescriptions in Germany, allowing for analyses within niche or subnational markets. Besides persistence and compliance, LRx can deliver insights on typical patient journeys, comedication patterns, patient demographics, and market dynamics. With its excellent coverage of the retail prescription sector and cross-specialty traceability, LRx is a promising source of longitudinal patient-level data for pharmacoepidemiological research and has been used as such in several peer-reviewed publications.[13]

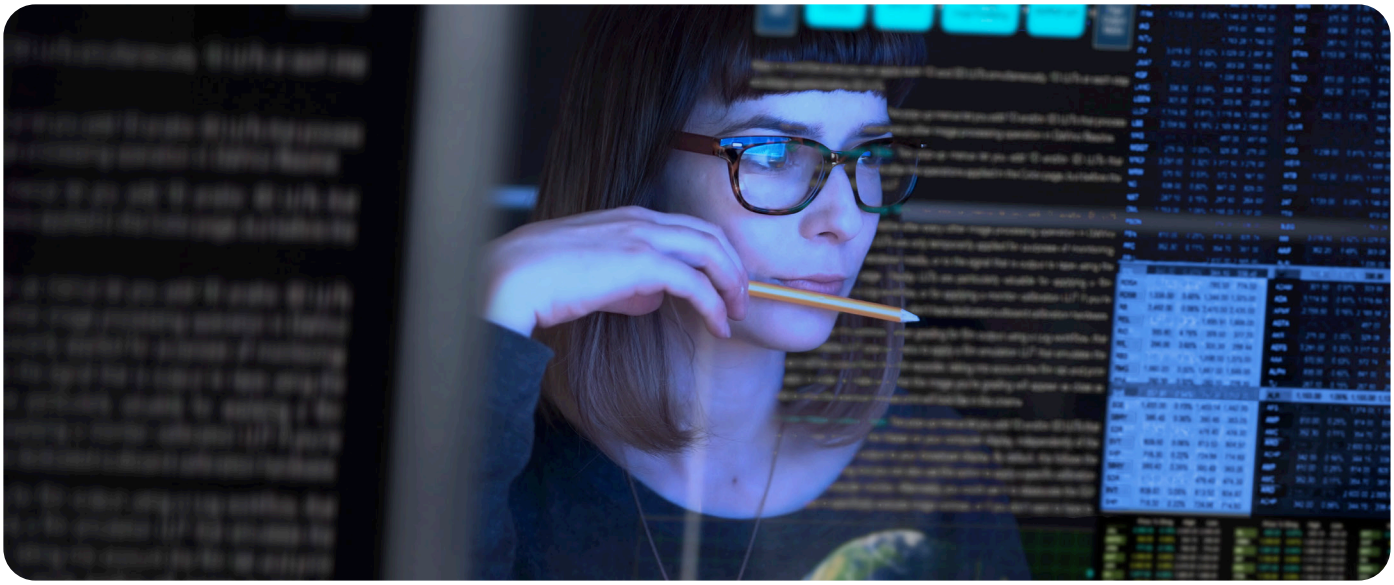
Outlook: going beyond descriptive data science

Examples above demonstrate the value of real-world data in observational cancer research. The exposure-outcome associations provide unique insights into the oncology practice and can serve as a jump-off point for further research. However, in order to take their place as an equally valuable decision-making tool in the management of cancer alongside RCTs, observational studies have to step up to the data science task of causal inference. Causal inference seeks to quantify the causal effect of the exposure on the outcome,[14] going beyond association. Key advantages of randomized trials include group comparability, both prognostically and in terms of treatment assignment.[14]

Observational studies can replicate these qualities: some techniques of ensuring group comparability have been used in studies outlined in this White Paper. For example, the cohort design in the IDA study by Krieg et al.[6] included propensity score matching based on sex, age, consultation frequency, relevant co-diagnoses, and index date as a confounding adjustment strategy. The persistence study by Gremke et al.[12] specifically included cases with an initial endocrine therapy prescription, comparing different groups of initiators rather than users, thus avoiding prevalent user bias.[15] Other studies presented[9, 11, 12] relied on multivariable regression models to adjust for confounding bias, controlling for key available parameters.

When complemented by a carefully considered study design, real-world data have exciting potential for addressing causal research questions. One framework for approaching such a design task is called Target Trial Emulation. In this approach, the causal research question is translated into a protocol for a hypothetical randomized trial, including exposure and outcome definitions, eligibility criteria, analysis plan, etc.[14] This target study is then emulated as accurately as possible using observational data.[14] This rigorous approach offers more reliable results than naïve observational studies,[15] but calls for considerable resources: the conception step requires extensive domain expertise and data science knowledge, while the application step relies on the availability of a robust dataset.

The need for wide-scale, detailed real-world data that allows for longitudinal analysis of cancer treatments and outcomes has never been higher — the use cases presented here demonstrate the powerful insights such datasets can deliver. IQVIA's Disease Analyzer dataset has grown over decades, allowing for longer follow-up and lookback periods and gaining in statistical power with the continuous accumulation of new cases in the ambulatory treatment setting. Further datasets introduced in this paper can also address oncology research questions across specialties (IQVIA LRx), countries (IQVIA Oncology Dynamics), and going beyond the outpatient sector (IQVIA PREMAX®).



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