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Biomarkers in Early Detection, Prognostication and Management of Gastrointestinal Tract Malignancies: A Review

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ABSTRACT: Each year the risk of cancer cases is constantly on the rise. The reoccurrence of this dilemma is due to late diagnosis, and as a result the survival rate is low. This indicates the significance of creating more efficient instruments for timely detection of cancerous cells, assessment, as well as prognosis. Hence, the objective of this paper was to provide a critical review of biomarkers in early detection, prognostication and management of gastrointestinal tract malignancies by harvesting data from online sources and libraries. Data obtained reveals that gastrointestinal tracts (GI) malignancies, encompasses malignancies that may arise from the gastric, hepatic, colonic, esophagus, gallbladder, rectal and stomach tumors are a common kind of cancer and could affect 1.400,000 - 952,000,000 people worldwide. A potential method for improving the diagnosis as well as prognosis of GI malignancy is the use of biomarkers, which are quantifiable indicators of biological processes or state of the ailments. Significant development has been made recently in detecting and validating biomarkers for various clinical procedures. This review discuss the present situation of gastrointestinal cancer biomarker research, with an emphasis on moral issues and other clinical implications that may arise from the incorporation of biomarkers in clinical practices, and also the different category of biomarkers, including genetic, epigenetic, and protein-based markers, are examined, along with their contributions to future outcomes in the management of gastrointestinal malignancies.

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Overview of malignancies of the gastrointestinal tract: Recently general cases of tumor, has been a global health concern for decades since the diagnosis of the first cases of respiratory disorders, followed by cancer which is also among the dominant cause of increased mortality globally (National Cancer Institute, 2022). All types of cancer thrives due to the unchecked growth of abnormal cells, which can invade nearby tissues and potentially spread to distant organs, all of which pose a serious risk to general health and bodily functions(Park, 2020). The biopsy of majority of human diseases related to malignant cells are caused by genomic and environmental changes; such as unhealthy habits such as obesity, smoking, high alcohol intake, exposure to harmful degree of radiation and physical inactivity(Apllebaum *et al*., 2014), all of this can stimulate the chances of cancer metastasis and death of the patient (Madizadza and Moyo, 2021)GI

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malignancy is becoming common and may have severe effect on people's health than other cancer types, gastrointestinal tract cancers have historically garnered a great deal of research attention (Coditz and Wei, 2012). Malignancies of the gastrointestinal tract is a reoccurring disease among patients of different ages ranging from children to adult, irrespective of the gender, however gastrointestinal malignancies is significant within the aging population (NCI, 2022). Malignant cells has risen to be the second global cause of death, and may result to economic crunches due to its impacts (Park, 2020). Malignancies of the gastrointestinal tract basically refers to the existence of malignant cells in the gastrointestinal tract which is otherwise known as the digestive tracts and it includes the small intestines, colon, and rectum; the stomach, liver, pancreas, and gallbladder. These malignant cells are spontaneous in their growth and may not die when there is a change in their genetic makeup (Madizadza and Moyo, 2021) malignant cells are characterize with capacity to penetrate and demolish tissues at different locations inside the body. Gastrointestinal malignancies, like other types of malignant cells, they are mainlyimpacted by genomic differenceswhich occur in aprecise genes which by design were to suppress the chances of mutations. These mutations include a complicated interaction between misfit genes, cancer-causing genes, and cancer suppressor genes (Matsuoka and Yashiro, 2018). The significantly recognized biological system created via Fearon and Vogelstein remains an ordinary instance of this case. It describes how colorectal cancer progresses in the epithelium of the colon through a series of changes, beginning with a small precursor inflammation called a benign tumor that eventually builds up to create carcinoma (Matsuoka and Yashiro, 2018). The formation of colorectal cancer is dependent on a number of genes, including TP53, adenoadmatosispolyposis coli (APC), Kirsten rat sarcoma virus oncogene homolog, and DNA mismatch repair genes including MSH2, MLH1, as well as PMS2. This pattern is marked by the accumulation of genetic alterations (Levine, 1997; Oki *et al*., 2009). GI Malignancies arise as a results ofchanges in the classical oncogenes as well as in the tumor inhibbitor genes SMAD4, TP53, PTEN, P16, and APC malignant genetic alterations are mostly responsible for the start and progression of malignant cancers. In addition to hereditary variables, environmental effects have been shown to cause the main influence on the growth of GI malignancies in recent research. Therefore, comprehending how genetics and environmental variables interact is essential when investigating the etiology of GIT cancer and creation of successful therapeutic and preventative measures. Hepatic, gastric, and colorectal cancers are diverse illnesses with a wide range of unique subtypes and molecular changes (Levine, 1997). Finding biomarkers that can accurately stratify patients into subgroups is critical to optimizing patient outcomes. These indicators eventually contribute to higher survival rates by guiding therapy choices and predicting therapeutic responses. Clinical evaluation of gastrointestinal malignancy has been carried out through physical examination, fluid test, mirror imaging and laporoscopy, majority of these clinical practices don't aid early detection of cancerous cells, these shortcomings has resulted to the advance genetic methods of diagnosis (Ceasovschih *et al*., 2022; Watanabe *et al.,* 2012). The symptoms of gastrointestinal tract malignancies is dependent on the stage and location of the cancerous cells. Malignancies of gastrointestinal tract has been shown by epidemiological studies to have relationship between various systemic and environmental factors, researchers suggested that environmental factors are the primary cause of cancer in around 80% of cancer cases (Matsuoka and Yashiro, 2018). It is important to note that gastrointestinal malignancies includes a wide range of cancers that develop in the gastrointestinal system and impact important organs such the pancreas, esophagus, colon, and rectum. Because these tumors are so common and frequently, they represent a serious threat to world health. The precise form of cancer, where it is located inside the GI region, and a number of population and regional variables all affect how common GI cancers are managed. Global Cancer Observatory (GLOBOCAN) 2020 reported that globally, it was discovered that GI malignancies have considerable prevalence fatality rates. During the period of 2020, 5.3 million new cases and 3.5 million deaths were linked to GI cancers. Here colorectal cancer (CRC) accounted for approximately 1 million new cases, and liver cancer followed (Applebaum *et al.*, 2014), the high mortality rates of gastrointestinal cancers are significantly influenced by age and gender. Research suggests that there men has high incidence of GI cancers, and that the risk of death and incidence is higher among men above 65 years of age and also in older than women than those in undeveloped age groups. Comprehending these demographic differences is vital in formulating efficacious preventive and therapeutic approaches for gastrointestinal cancers (Oki *et al*., 2009). The concept of malignant disease is being stigmatized regularly and these practices has it profound effect on communities, families, nations and even on the patient that is diagnosed with cancer4 , consequently various research were done to evaluate the effects of stigma on cancer patients, and it was indicated that stigmatization of cancer patients results to physiological and social morbidity, undermining

emotional wellbeing, may result to poor quality of life and also lessening the lifespan of it patients(Watanabe *et* al., 2012; Link and Phelan, 2001).

Environmental risk factors and unhealthy habits, Over 50% of cancers are known to be caused by risk factors including smoking and eating poorly, with tobacco accounting for 30% of cases, dietary errors for 30%, and environmental factors for the other 30% (Zhang, et al., 2005). Gastrointestinal tract tumors may also develop from preexisting cells, through the activity of molecularly altercated precancerous lesions that are stimulated by chronic inflammation and suppression of the immune system (Oliveira, et al., 2006). Therefore, non-steroidal anti-inflammatory medications may be used as a preventative measure for high-risk patients (Garber and Offit, 2005; Jasperson, et al., 2010). The current strategy of precancerous lesions must be addressed in order to avoid cancer, since this may halt the neoplastic processes before intraepithelial neoplasia progresses (Rawat and Ganesh, 2017). However, In order to implement such therapeutic treatment, there is currently insufficient knowledge on the molecular pathways behind carcinogenesis. GIT cancer-related behaviors have also drawn the attention of practitioners and academics as a potential study field. The identification of an increasing number of risk factors and the ability to prevent them would follow from advances in our understanding of carcinogenesis. Improved treatment, early diagnostic programs, screening, and a well-defined, comprehensive preventative program should all be part of cancer control efforts better treatment, screening, early diagnostic initiatives, and prevention. Secondary prevention, or the early identification of cancers by screening and treatment of lesions prior to metastasis, is another aspect of cancer prevention. Reducing exposure to environmental variables that promote cancer is part of primary prevention; this is a major challenge for organizations, public health policies, and clinicians alike. In this review we sought to spotlight advancements in biomarker discovery and ethical issue underlying the full integration of biomarkers into clinical practice, considering the facts that successful treatment of gastrointestinal malignancy is dependent on early diagnosis and proper treatments.

Importance of biomarkers in management: Biomarkers are essential indicators used to inform individualized treatment and management of negative reactions, study from National Cancer Institute recognized biomarkers as a biological molecules which identify vector in biological fluids such as blood, tissues, or tumor it also reveals if the disease is normal or aberrant (Matsuoka and Masakazu, 2024). However different researcher and publication has oriented several definitions to what biomarker is and is not, what were referred to as biomarker has changed overtime on the emergence of new sets of technologies that are prevailing in many areas of medicine especially in the aspect of disease diagnostics. With latest invention of technology imaging techniques could be used to detect the structural alterations in the human brain; these changes can be utilized as markers for certain medical disorders. In retrospect the importance of biomarkers cannot be undermine, several recommendation has been made on the relevance of biomarkers in management, offering numerous benefits in diagnosis, prognosis, and treatment, the importance includes; timely detection and diagnosis, prognosis and risk assessment, monitoring of treatment response, guiding targeted therapy, predicting treatment resistance or sensitivity and identifying respondents in clinical trials. Biomarkers are significant when selecting patients that novel clinical trials may benefits, which on the long run would accelerate the production of novel therapeutics and personalized medicine. The novel treatments in clinical trials may encompass different innovative approaches such as immunotherapies (Cancer vaccines, oncolytic viruses, tumor treating fields, and anti-angiogenic therapies) and targeting therapies (HER2- novel drugs, FGFR inhibitors). Biomarkers could also be used in early detection of cancerous cells in the body at an early stage, which it make the procedures feasible. For instance elevated levels of biomarkers like cancer antigen (CA) 19-9, also known as carcinoembryonic antigen (CEA) may indicate the presence of colorectal or pancreatic cancer (Akiyama *et al*., 1986). After detecting the cancer cells and administration of the necessary therapy, biomarkers still find usefulness in assessing the level of effectiveness of each cancer treatments, this allows healthcare practitioner to adjust treatment plan when its overactive or ineffective accordingly. And it could further be used to forecast the outcome of patients' response to a particular treatment or a resistance will be developed. This can guide treatments and avoid unnecessary side effects from ineffective therapies.

Purpose of the review article: In recent time treatments of gastrointestinal malignancies is becoming complicated due to several underlying factors which among is the mutations of cancerous cells and this may have resulted to ineffectiveness of the regular chemotherapy and pharmacokinetics among individuals with gastrointestinal malignancies differs; in most cases of cancer research, if a mutations exist that affect drug metabolism in an individual, the patient may undergo severe side effects than other patient without these mutations. If a medication's

genetic changes that result in decreased drug metabolism are understood beforehand, a lower drug dosage can be administered to the patient. Further illustration of this is a gene that produces the enzyme thiopurine methyl-transferase (TPMT). Some people are unable to metabolize the medication mercaptopurine due to mutations in this gene. One common treatment for a particular kind of juvenile leukemia is mercaptopurine. When patients with certain TPMT gene mutations are administered mercaptopurine, their bodies are unable to properly metabolize the medication, which results in a persistent decrease in white blood cell counts. It becomes expedient to assess the impact of biomarkers into clinical practice, helping to identify high-risk groups and to predict the probability of a disease making a diagnosis at an early stage. The diagnostic breakthrough that accompanied the incorporation of biomarkers as a predictive and diagnostic tools is accompanied by different thoughts, fears and perspective even though the measures bring both favorable psychological and economic outcomes, not to mention potential potent positive benefits for morbidity and extended survival. Despite considerable research efforts, biomarkers are not generalize in everyday medical practice due to their low specificity and a specificity problems in one group of patients. Consequently, the objective of this paper is to assess the common knowledge on biomarkers' function in the treatment of gastrointestinal cancers and provide an update on biomarkers and treatment selection and the Clinical implications and recommendations on the use of biomarkers.

Types of Biomarkers: Lately the use of biomarkers for research and treatment are often categorized. The concept behind the categorization is to match several potential biomarkers into a single group based on functionality. Various studies have generally classified biomarkers as Potential candidates for a cancer marker are biologically generated entities or processes that aid in the detection of cancer at the diagnostic or post-diagnosis (during the course of therapy) phases(Chatterjee and Zetter, 2005). Various types of biomarkers are used in cancer management, initialdiscovery, risk assessment, analysis, and cure (Verma and Manne, 2006).

Genetic Biomarkers: Genetic biomarkers is described as genetic materials that serve as markers for pathogenic and normal biological processes (Cancer Genome Atlas Research, 2014).

Mutations associated with gastrointestinal malignancies: Gastrointestinal malignancies that arise due to genetic mutation could be formed due to compilation of gradual changes in genes that regulates cell cycle(Grady and Markowitz, 2010) this forms of malignancies appears occasionally. Little percentage of the total occurrence of gastrointestinal malignancies possess a noticeable inherited element. The low percentage of gastrointestinal malignancies are because of specific gene alterations, these cancer forms are less common compared to other inherited cases that have high penetrants.

Single gene mutations include single nucleotide polymorphisms in genes regulated by environmental factors or involve in metabolism (Oliveira et al., 2006). Mutations in multiple susceptibility alleles may cause these tumors by producing compounding effects (Garber and Offit, 2005). To identify those who are at risk for these diseases, a comprehensive apprehension of the molecular etiology as well asbiologicalcomponent of gastrointestinal tract malignancies is necessary in the development ofpoliciesthat enhance a better cancer hindrance, diagnosis, and treatment choices (Jasperson et al., 2010). These mutations occurs in two different gene types: oncogenes, which promote cancer, and tumor suppressors, which prevent cancer, this mutations causes this cancer suppressant gene to loses it functions or misread the nucleotide(Rawat and Ganesh, 2017; Yan et al., 2018). The both genes plays an essential roles in regulating terminal division and apoptosis (Sayagues et al., 2011), thus impairment of these genes results to an uncontrolled cell division, in some cases the due to recessive mutation, the suppressing effect of the gene is entirely lost in both alleles (Blackadar, 2016). The suppressor genes' functional changes are caused by either antibody mediates tumor cell separation, deregulations of DNA replication as well as cell phase, or suppression of apoptosis (Rawat and Ganesh, 2017). The uncontrolled expansion of cells is due to functional deficiencies of the oncogenes, mutation in a single proto-oncogene allele can affect subsequent steps, such as the operation of mitogenic signals along with signaling connection (Sayagues et al., 2011). Cancergenes have dominant attributes (Sayagues et al., 2011; Blackadar, 2016). Many genes, such as PGS2 in lung cancer, XRCC1, p53, and ATM in head and neck cancers, and BRCA1, BRCA2, RAD1, and CYP1A1 in breast cancer, depend on single nucleotide mutations as critical DNA biomarkers (Hatterjee and Zetter, 2005). Nucleic acids alterations affecting genes that inhibit tumor growth (Rb, p16, p19, and p53), malignancy promoters (Ras, APC), DNA-repair associated DNA, & cellular cycles (cyclins) affect the identification and treatment of many malignancies (Bhatt et al., 2010). The malignancy attenuator APC gene has been altered in many cancers; according to

Bhatt et al. (2010), this mutation is present in 92% of cases of gastroesophageal adenocarcinoma, fifty percent induced incidences of esophageal carcinoma of squamous cells, also sixty percent of occurrences of colorectal cancer.

Germline deletions within the CDH1 genome, which encodes for the transmembrane molecule E-cadherin and exhibits a seventy to eight percent penetrance, have been associated with hereditary spread gastric cancer. Many malignancies can be connected with such alterations (Robert et al., 2012). The likelihood of diffuse cancer of the stomach and lobular cancer of the breast is elevated within cases of heterozygous mutations in the CDH1 gene. Some families that fit these criteria have mutations in CDH1, indicating that other genes may potentially play a role in the susceptibility to diffuse gastric cancer. Mutations in the germ in the CTNNA1 gene were discovered in three different families having diffuse stomach cancer (Hanrick *et al.,* 2012).

Germline CDH1 alterations were first detected in families with Maori ethnicity, due to high penetrance of Gastric cancer in this ethnic group, variety of processes and signaling pathways can be improperly activated by CDH1 mutations, which can also cause E-cadherin function to be lost. These E-cadherin mutant variants have significant structural defects that cause protein misfiling and breakdown by the endoplasmic reticulum-associated breakdown which is a protein (ERAD) pathway (Chan, 2010). This cytoplasmic catenin complex at the plasma membrane internalizes and breaks down quickly. Cell assault, movement, as well as susceptibility to apoptotic stimuli are all impacted by the abnormal amplification of both the EGFR and Notch pathways caused by the absence of e-cadherin (Chan, 2006). It has been demonstrated that EGFR including its associated downstream effects (p38 MAPK, RhoA, and Src kinase) are triggered in reaction to EGF signaling when mutations affecting the extracellular portion of E-cadherin occur (Ito, 2017). It is noteworthy that EGFR inhibitor therapy may be advantageous for individuals with inherited dispersed genetic gastrointestinal cancer alterations in exons four to thirteen of the CDH1 gene.

A relative's history of gastric cancer without a CDH1 alteration referred to as "familial gastric cancer syndrome". This is brought on by other genetic cancer predisposition syndromes like FAP or by germline changes which occur in the TP53 cancer suppressor gene, which produce Li-Fraumeni syndrome. Hereditary germ line BRCA2 alteration are linked to an even greater risk of 13% and Lynch syndrome, respectively. According to reports, there is a 5.7% chance of developing stomach cancer if a certain BRCA2 (614de1T) is present (Harinck, 2012). Recall that around 21% of those with a clan history of gastrointestinal or breast cancer are also at an increased risk of developing a GBM. Moreover, 24 percent of people having family heritage of ovarian and stomach cancer had BRCA2 abnormalities. (Jones *et al.,* 2014).

Genetic testing methods

Genetic testing methods basically refer to a specific type of clinical procedure that finds variations in genes, chromosomes, or even proteins; instances involving hereditary illnesses are the majority of which employ this kind of diagnosis. The results from such diagnosis may rule out or confirm a genetic disorder. This method of testing has become widespread especially in the treatment of gastrointestinal malignancy, although this method of diagnosis are not standardized in assessing tumor in mammary gland and non-small cell lung cancer: Standardized evaluation of these cells involves personalized treatment aimed at different drivers gene (Ceasovschih et al., 2022). Genetic testing encompasses different protein, DNA and gene sequencing techniques, which includes; Next-generation sequencing (NGS), Tissue biopsy, plasma genotyping, tumor tissue analysis, microsatellite instability (MSI) analysis and hereditary cancer testing.

Hereditary cancer testing is one of the predominant methods to identify genetic mutation, which will increase the chances of malignant cells to be form in an individual. For example the inherited kind of stomach cancer. A poorly classified disseminated gastric cancer is caused by the inherited dominant autosomal genetic factorwhich is known as hereditary diffuse gastric cancer (HDGC). Patients with linitisplastica typically appear clinically at the age of 40, without the presence of a distinct stomach tumor. Women have a comparatively higher cumulative chance of developing stomach cancer by the age of 80 (83%) than males do (67%). While no one region of the stomach is the target of tumor formation, preventive gastrectomy has shown a wide region with up to 160 separate tumor foci, in the treatment of individuals with inherited gastrointestinal cancer disorders. The first line of action should involve gathering the family history for cases of malignancies and premalignant gastrointestinal disorders. This information should be sufficient to establish a preliminary estimate of the likelihood of a hereditary cancer susceptibility. Particularly when initial and second-generation relatives are involved, all

diagnoses, together with a patient's age of assessment as well as genealogy (maternal or paternal), ought to be documented.

In order to verify identification and facilitate prognostic screening of in-danger families, DNA tests for germline mutations need to be conducted when recommended upon the most useful candidate(s) identified through family history evaluation as well as tumor analysis. To make sure the patient is making an educated choice, DNA testing ought to be performed in conjunction with pre- and following the test genetic advice. In order to reduce their overall risk of getting syndrome-specific cancers, those who fit the diagnostic requirements for a syndrome and those who are discovered to have harmful germline mutations are subject to monitoring procedures.

Next-generation sequencing (NGS) has discovered to be a new technique for genotyping genome for mutations. This method makes use of bioinformatics technologies, distinct sequencing chemistries, and various sequencing matrices (Schuster, 2008), engaging different sequencing techniques allows the sequencing of several segments of the genome in parallel arrangement, within a short amount of time. Several crucial sequencing steps are needed for NGS. In NGS, for instance, Genomic disintegration, the creation of libraries, substantially simultaneous gene sequencing, computational biology analysis, and the detection and decoding of variants and mutations are all involved. When fragmentation of DNA takes place, the target DNA strand is broken up into many, brief pieces, each consisting of 100–300 base pairs. To extract the snippets, the DNA segments might be divided mechanically, enzymatically, or by polymerase chain reaction (Knierim et al., 2011), after the hybridization capture assay,the DNA snippets are then used to prepare the libraries. During this process, the DNA snippets are altered such that each DNA sample has unique identification measure, helping in the identification of the patient from whose DNA sequencing is being done. In addition to identification, it facilitates modification, which enables all DNA segments to be bound by the sequencing primers. An NGS sequencer is used for mega identical sequencing; different sequencers have different sequencing matrices.Next generation sequencing techniques has significant advantage in clinical practices based on the fact they can check different targets at the same time within a shorter time frame than most GI malignancies diagnostic techniques (Chang and Li, 2013), The full genome can be sequenced with it. Nearly every nucleotide in the genome, including mitochondrial and chromosomal DNA, is analyzed at this level. The sequencing of complete genomes is becoming increasingly common in research contexts, while it is less common in therapeutic settings. It is more frequently employed in medical settings for fundamental genetic illnesses as opposed to somatic alterations that cause cancer. For the identification of a few uncommon genetic illnesses, it is highly helpful. For instance, when a suspected genetic problem is investigated further by analyzing a particular mutation at the molecular level. The sequencing of complete genomes may provide additional information on mutations linked to the illness under certain circumstances. Due to the fact that whole genome sequencing has a restricted broad terms, it is not as frequently used for cancer mutations in the body. Allelic mutation rates and tumor cell percentages in various specimens might differ within a same tumor. Deep sequencing is sometimes required to detect distinct mutations with varying allelic frequencies in these situations, and it is exceedingly difficult to do so using the whole genome sequencing technique (Kohlmann et al., 2001).

Protein Biomarkers: A chemical or protein that is exclusive to cancer cells and absent from healthy cells can be measured and serve as an indicator of malignancies and also to identify response to treatment. The protein is made up of several peptide and each has a mass mapping and peptide mass tandem spectrometry, these aids the analysis through the use of proteases. The presence of protein in a given disease represents a potential biomarker for that disease(Fung, et al., 2001). Example of protein biomarkers, includes markers such as CEA, CA19-9, as well as CA72-4, these are critical toward identification, prognosis, and choice of treatment for gastrointestinal cancers. Additionally, biomarkers like PD-L1 and HER2 have become viable therapeutic targets.

Tumor specific antigen (TSA): Associated antigens (TAA) exhibit expression at larger amounts in cancerous cells and at lower quantities on healthy cells, respectively. TSA essentially refers to antigens that are specific to cancer cells exclusively.. Antigens unique to tumors can aid the body's immune response to combat cancerous cells. They might be targets for immunotherapy, which would help strengthen the body's defenses against cancer, or targeted treatment. TAA are targets for immunotherapy, they helps strengthen the immune system and destroy more cancer cells, or targeted treatment. The specificity and sensitivity of protein biomarkers determine their diagnostic use. The majority of traditional cancer therapies, which include radiation, Chemotherapeutic immunotherapy using antibodies, and non-nanoparticles that can be viral or nonviral, typically lack precise locations of action, which gives rise to

concerns about safety because of ineffectiveness (Bourre, 2019). Tumor specific antigens holds great promise in terms of improving efficient diagnosis in clinical development, Alpha-fetoprotein (AFP), cancer antigen, and prostate specific antigen (PSA) are three important biomarkers for diagnosis and prognosis; Certain outputs function as serum oncomarkers when they enter the bloodstream. Proteins and macromolecules released by diseased cells into cellular fluids may be examined as indicators of malignant cells. Proteomic biomarkers, as opposed to RNA- or DNA-based biomarkers, are more significant because they are more closely linked to the onset and progression of carcinogenesis because cellular biomolecules like proteins influence these molecular mechanisms in both alteredalong the normal cells function (Zhang et al., 2006). Protein-dependent signals are produced via polyacrylamide gel electrophoresis and two-dimensional fluorescence variance gel electrophoresis analysis (Schwartz, 2004). innovative methods such as mass spectral analysis, reversed-phase microarray surface improved laser absorption ionizing flight time as well as matrix-assisted lasers desorption/ionizing time-of-flight (Schwartz, 2004). Offler et al. (2019) state that quantum dots and nanoparticles are now being utilized to evaluate potential proteins for cancer biomarkers. As of right now, the FDA has only authorized biomarkers based on molecules of protein.

Enzymes and other proteins associated with malignancies: Eukaryotic cells have developed a number of defense mechanisms to shield DNA and other essential components from externally introduced highly reactive chemicals. Several enzymes has been identified to be associated with gastrointestinal tract malignancy; they play a significant in evaluating cancer progression and may serve as a potential biomarkers.

Carcino Embryonic Antigen: CEA are proteins that specific to a particular types of cancer, CEA functionality as a biomarker is basically to evaluate the how efficiently a treatment is working in treating certain types of cancer. One effective risk factor for predicting the likelihood of a liver metastatic recurrence is CEA (Shimada et al., 2014). In advanced stages of gastrointestinal malignancies the proportions of CEA levels in the cells are measured it is observed that there is high amount of in the cells, compared to healthy cells CEA are found to be lesser; CEA levels are therefore a subpar screening method. According to research by Asao et al. (1991), CEA concentrations in peritoneal lavage solution may be a reliable indicator of peritoneal relapse following successful gastrointestinal tract cancer resection. Combining conventional cytology with immunohistochemistry CEA evaluation increased sensitivity. Using RT-PCR to measure CEA mRNA, the peritoneal cavity can be utilized to detect micrometastases (Zhang, et al., 2006). In response to the antigens the body produces antibodies to help fight the disease.

Prostate Specific Antigens (PSA): PSA is an identified enzyme produced by the prostate gland, which can utilized in detection of prostate cancer, utilization of a testing procedures, detects the pathological activities of the malignant cells. This procedure is very sensitive but not specific. Serum PSA screening is still an efficient method for the prompt identification of prostate cancer, thereby proffering supports to those who are affected with the highest chance of a cure, albeit with its dangers and potential for some "unnecessary" biopsies and over diagnosis (Michael and Stephen, 2022). In carrying out PSA testing it is recommended that digital rectal examination should be engaged because it is the most reliable diagnostic method for prostate cancer occurring in its early stages, yet investigation have indicated that the rectal examination's accuracy is not very high. Prostate-specific antigen (PSA) protein has proven to be more useful than alternative techniques for tracking prostate cancer cases that have been identified and for identifying new instances of prostate cancer. PSA is very specific to tissue around the prostate (Leslie et al., 2023).

In actuality, benign cells often produce less PSA than prostate cancer cells do. On the other hand, PSA may more readily penetrate cancerous cells' cell walls, enter the extracellular fluid around them, and ultimately enter the circulation. This is due to the fact that cancerous prostate cells are devoid of the basal layer that would normally prevent PSA from leaving the cell. Highly undifferentiated cancer cells with a very high Gleason score could not produce a noticeable quantity of PSA (Michael and Stephen, 2022).

Other Types of Biomarkers

Epigenetic markers: Epigenetic markers are modifications of DNA or proteins plays significant function in the expression of gene without causing permanent mutations on the DNA sequence in-view (Cedar and Bergman, 2009). Different kind of cancer, including gastrointestinal tract malignancies, share epigenetic changes. These modifications are often caused by histone modifications, RNA interference, and post-replicative methylation (at the DNA level) (Rawat and Ganesh, 2017; Yan et al., 2018).

DNA methylation marker: Nucleic acids methylation as the name connotes it simply refers to adding of methyl groups that can affect genetic expression, and it predominantly occur at the 5' positions of cytosine residues (CpG), followed by a guanine dinucleotide sequence(Ehrlich, 2009). The recognition of epigenetic instability as a characteristic of cancer is growing (Blackader, 2016). Data gathered over the last ten years indicates that epigenetic modifications, in addition to genetic variations, which are very important contributors to cancer (Hardy and Tollefsbol, 2011; Junker et al., 2013; Li and Robertson, 2011). The CpG islands are typically unmethylated in healthy cells, allowing the relevant gene to be actively transcribed. However, these CpG sites are often the focus of hypermethylation in cancer cells, a modification that represses the transcription of the corresponding gene, including tumor suppressors. Heritable variations may be expressed differently in somatic cells, this would results to further alterations to the original DNA base sequence (Khailany et al., 2019). The initial epigenetic signals in cancer were discovered via research on DNA methylation as well as the expression of genes. Unquestionably, DNA methylation affects the quality and functioning of genetic material, and it may also play a part in the onset of cancer. These alterations are either directly connected to the change process or represent the changed physiology of rapidly multiplying cancerous cells (Li and Robertson, 2011). Certain transcription factors can bind between residues of cytosine within the CpG dinucleotide to suppress the synthesis of specific genes, as explained by Ehrlich (2009). This process takes place in the major helix of the nucleotide double helix. Additionally, several methylation proteins bind to DNA, especially those belonging to the MECP2-mediated and MBD (Ehrlich, 2009). Cancer development frequently results in CpG island hypermethylation around seventy percent of mammalian regulators (Ehrlich, 2011). Consequently, hypermethylation indicators may be used to identify the beginning and development of cancer. For instance, recurrent colorectal cancer is closely correlated with the hyper methylation of the p16 promoter (Bhatt et al., 2010). In cancer, transcription regulatory region hypomethylation is less common than promoter CpG island hypermethylation (Pulukuri et al., 2007). However, in other situations, such as the growth of tumors which occur in breast cancer, the urokinase gene coding is overexpressed as a result of hypo methylation of transcriptgenes(Li and Robertson, 2011; Zhao and Srivastava, 2007).

Serum Markers: Serum is the liquid portion of blood that remains after the blood has clotted. When a blood sample is taken, the cells and clotting factors in the blood form a solid clot, and the remaining liquid is called serum. This liquid is rich in proteins, electrolytes, hormones, and other substances that can be measured as biomarkers to provide information about a person's health. These liquid portions of the blood can be measured as indicators of disease, response to therapy, or other biological processes. These markers providevaluedevidence about the presence, severity, and prognosis of various diseases, including GI cancers. Some examples of serum biomarkers for GI cancers include: Carcinoembryonic Antigen (CEA) a protein which often elevated in the colon, rectum, and pancreatic cancers. High carcinoembryonic antigen content can designate the occurrence of cancer or a recurrence after treatment. Biomarkers are often non-invasive diagnostic procedures that detect various bodily fluids objectively and are assessed as indicators of physiological and pathological processes. It has been established that the traditional markers employed in the management of gastrointestinal malignancies, which include CEA, Ca19-9, Ca12-5, and Ca72-4, have a poor sensitivity and specificity for gastrointestinal cancer identification and are hardly helpful for the initial identification of gastrointestinal cancer. Consequently, the pipeline of gastrointestinal cancer research now prioritizes the identification of new gastrointestinal cancer biomarkers. Serum pepsinogen (sPG) has been recognized as researched indicators for the forecast of precancerous gastric lesions. Fundic, pyloric, and Brunner's glands generate pepsinogen II (PGII), whereas the fundic glands emit pepsinogen I (PGI). The degree of serum PGI and PGII rises when gastritis worsens. The degree of stomach atrophy is measured by the serum PGI/PGII ratio (sPGr), which decreases as gastritis progresses. Serum PGI levels gradually decrease while serum PGII levels remain constant as the disease diminishes the fundic gland mucosa. Fukuda et al. proposed the ABC strategy as one of the earliest non-invasive methods. A combination of serum levels of immunoglobulin G, anti-Hp, and pepsinogen I and II (PGI and PGII). Three risk categories are identified using the ABC technique based on the serological status of the patients: (A) IgG anti Hp (−)/PG (−); (B) IgG anti Hp (+)/PG (−); and (C) IgG anti Hp (+/−)/PG (+).Evidence exists to support the accuracy of the ABC classification in classifying patients based on their risk of GC. When contrasted with radiological data, its discriminative performance was shown to be inadequate. Gastrin-17 (G-17) is a stomach acidity-dependent biomarker generated by G endocrine cells that has been associated with a condition called atrophic gastritis. A collection of biomarkers unique to the stomach, known as gastro panel and consisting of PGI, PGII, G-17, as well as HP serology, was verified

by Chapelle et al. (2012) among a sample of individuals with a greater risk of stomach cancer to predict the presence of atrophic gastritis. Gastrulate possessed an accuracy of 39.9% and a precision of 93.4%.

Short non-coding RNA Markers: Non-translated or non-coding RNA is the term used to describe transcripts via genomes that are not intended for translation. Although they are not protein coding genes, short non-coding RNA (ncRNA), they play crucial regulatory roles in cells. These indicators have been connected to a number of illnesses, including cancer (Wilusz and Sunwoo, 2009). There are 18–24 nucleotides in miRNA. They play translational inductive activities through contact through the 3'-untranslated area of mRNA (George and Mittal, 2010), and they control the targeted genes expression by tampering with the mRNA and/or inhibiting its translation (Corsini et al., 2012). For instance, it has been found that dysregulations in miRNA expression are involved with main malignancies which include lung, breastand prostate(Yarmishyn and Kurochkin, 2015). Numerous factors, such as chromosomal abnormalities, genetic mutation, polymorphism, and epigenetic alteration in miRNA synthesis, have been related to aberrant miRNA expression in malignancies. Human melanomas, the prostate, the colon, the ovarian, and other cancers are all clearly associated with increased frequency of genomic alterations in miRNA loci. Approximately 50% of human miRNA genes are often found inside genomic sequences and weak areas (Bhatt et al., 2010). The patients who suffer from cancer and the healthy group have been shown to vary statistically significantly in terms of miR-145 for breast carcinoma, miR-141 for cancer of the prostate, and miR-29a for colorectal cancer (Chervona and Costa, 2012). In cancer cells, miRNAs may be up- or down-regulated depending on their downstream signaling effects on gene derivatives (Cohen et al., 2011) down-regulated miRNAs are thought to be able to inhibit tumors, whereas up-regulated miRNAs have carcinogenic properties. The human genome has over 20,000 piRNA (PIWI-interacting RNA) genes. PiRNAs, as opposed to microRNAs, primarily interact with PIWI proteins inside the nucleus. Transposable elements are epigenetically silenced as a result of them. In a range of human somatic tissues, piRNAs express differently depending on the tissue. While abnormal piRNA expression is a common characteristic of many tumor types, their fundamental carcinogenic functions are yet unclear (Cohen et al., 2011).

Role of Biomarkers in Diagnosis: Biomarkers have played a crucial role in identifying genetic predispositions to various diseases, it also plays a vital role in identifying individuals with variants of an identified disease. Biomarkers generally play different roles ranging from selection of treatment, prediction of the patients response to chemotherapy, differential diagnosis and subtype classification of oncogene, monitoring for recurrence, and also evaluating the efficacy of a treatment plan over time (Herranz and Esteller, 2007).

Early Detection of Gastrointestinal Malignancies: Early diagnosis increases the survival rate of gastrointestinal malignancies, and the expansion of modern non-invasive diagnostic screening is essential due to high individual differences in the occurrence of oncological symptoms. Biomarkers-Epidemiology and impact Despite changes in dietary habits and lifestyle, which partially contributed to a reduction in the occurrence of gastric and colon cancer, gastrointestinal malignancies are still one of the most common types of cancer worldwide. Currently, they are the third most frequently diagnosed forms of cancer2, with around 3 million malignant tumors diagnosed every year in the gastrointestinal tract (GIT), including 1 and 2 million cases of stomach and colorectal cancer, respectively. Death from these cancers is the second most frequent among all malignancies, with about 2.5 million deaths due to gastric and colonic tumors annually (Hakami, 2024).

Biomarkers in treatment selection

Predicting response to chemotherapy: A prognostic biomarker is defined by the discovery which exists or alteration of the biomarker indicates whether a person or set of people will be more likely to suffer a negative or positive outcome from contact to a pharmaceutical or environmental factor (Madizadza and Moyo, 2021). Clinical trials must be conducted rigorously in order to demonstrate that a particular biomarker is fit for this purpose. In a perfect world, whether or not a patients have oncomarkers in their body or not, they are randomly assigned to one of two or more therapies (or a placebo comparator), and variations in the course of therapy as a consequence of treatment are closely linked to variations in the biomarker's existence, absence, or level. Thus, establishing a trustworthy predictive biomarker is a "high hurdle" to overcome. The use of predictive biomarkers in enrichment methods is crucial (Watanabe et al., 2012; Edelen et al., 2014) in the planning and execution of clinical studies. By enrolling individuals in whom the therapy is expected to "work," emphasizing the administration on participants with increased intensities of a projecting biomarker, particularly in the preliminary registration stage of growth, allows a clearer signal that the therapy really has an impact. Predictive

biomarkers seem a better targeted approach when utilized for enriching than when used for event rates, as the former may be used to identify specific individuals deemed more likely to respond to treatment or not. The same principle underpins most of the current consensus about therapy selection in clinical practice. Acute reperfusion is advised for patients with ST-segment elevation on an ECG, antihypertensive medication is prescribed for patients with high blood pressure, and blood transfusions are used to treat anemia characterized by low hemoglobin levels. These are just a few examples of biomarkers that specifically identify patients likely to benefit from therapy. In a similar vein, groups identified as requiring more intervention in population health initiatives are those who are at heightened risk because of elevated levels of predictive biomarkers that are likely to react favorably to Herceptin therapy. For instance, individuals who have elevated HbA1C levels stand to benefit the most from intensive diabetic treatment. Predictive biomarkers have also advanced significantly in the construction of genetic as well as genomic signals for precision medicine. Examples of these indicators include the ones that identify cancer patients who have a higher chance of benefiting through Herceptin medication because their HER2 receptor tests are positive. One good illustration of the intricacy of these concerns is the use of LDL cholesterol-lowering drugs based on biomarker guidance. It is evident that LDL cholesterol is a predictive as well as a susceptibility/risk biomarker. High levels of cholesterol (low-density lipoprotein) increase the risk of atherosclerosis and, once the condition is identified, an increased risk of heart attack, stroke, or even death. Lowering LDL cholesterol levels reduces mortality and significant clinical events like stroke. These three medications reduce LDL cholesterol levels: statins, ezetimibe, a particular inhibitor of cholesterol absorption, and PCSK9 inhibitors. Nonetheless, in a number of clinical studies that have involved over 100,000 patients, the proportional effect on event reduction remains constant across all levels of LDL cholesterol, including values far inside the normal range (Phelan and Link, 2001). In these clinical trials, the absolute risk of an event decreases compared to the reduction in risk, and several characteristics, including age, blood pressure, smoking status, diabetes, and LDL cholesterol levels, all play a role. Environmental exposure may have similar consequences. Certain biomarkers may be associated with certain hazards in individuals and subpopulations, such that those with increased levels of such biomarkers are most likely to benefit from preventative actions.

Prognostic Biomarkers: Prognostic biomarkers are important markers to evaluate the probability of a clinical incidence, illness recurrence, or progression in patients with a medical condition in persons with disease that needs treatment. They differ from predictive biomarkers, which link treatment efficacy to exposure or action, and susceptibility/risk biomarkers, which recognize changes from healthy to disease states. Prognostic biomarkers are frequently employed in clinical trials to enrich trial samples with higher-risk groups and define trial admission requirements. This raises the event rates and, if the therapy works, it enlarges the disparities in outcomes that are quantitative but not qualitative.

Distinctions between Prognostic and predictive biomarkers: When estimating the expected course of a disease and its response to therapy, the distinction between predictive and prognostic biomarkers is essential to be evaluated. Predictive biomarkers distinguish between patients who will react to medication and those who won't, prognostic biomarkers are linked to distinct illness outcomes.An electrocardiogram's ST-segment deviation, for instance, can be used as a prognosis biomarker. Still, a more significant prognostic biomarker is the direction of the ST-segment alterations. Furthermore, an improved response to fibrinolytic therapy is indicated by an elevated ST segment on the ECG, whereas a poor response to treatment is indicated by a depression of the ST segment. When the treatment impact differs noticeably depending on the biomarker level, as occurs in an "all-or-nothing" response scenario, the issue is easiest to understand, nonetheless, the response is frequently probabilistic.

*Monitoring biomarkers***:** Because tracking is so broad, biomarkers employed just for monitoring typically overlap with other kinds of biomarkers that were previously discussed in this book. Medical treatment may profit significantly from biomarker tracking because it has numerous applications in clinical care. For example, biomarkers can be used repeatedly to track the development of a disease or illness, look for signs of biological agent or medication interaction in the environment, or evaluate the impact of a biological element or medicinal properties product. When therapies to treat elevated blood pressure or low-density lipoprotein, or cholesterol are started, measurements of blood pressure and LDL cholesterol are monitored. Likewise, during HIV treatment, CD4 counts are tracked. Although clinical monitoring as an idea is usually well-defined, identifying which changes in the biomarker should indicate a specific shift in the clinical pattern and decision-making can be challenging and often less accurate, requiring

additional study (e.g., more testing or intervention). Given that they represent a few of our most well-known and thoroughly studied indicators, target values for hemoglobin (Hb) A1C, blood pressure, and LDL cholesterol, for example, are still up for debate. Frequently there is lack of adequate empirical support for the length of the clinical procedures that were previously carried out to fill beneficial gap between assessments. Since many of the biomarkers that are often employed in clinical practice have extremely erratic operating properties, the phrase "clinical judgment is needed" becomes a regular associate in regards to use of biomarker in a clinical "gestalt." However the exact clinical traits that should be taken into account is unclear, when a wise therapeutic choice is to be made. When developing medical products, modifications to biomarkers are commonly used to assess if critical thresholds have been reached. This allows developers to assess if the therapy had a sufficient impact on a biological target to support the product's further development. Majority of the early biomarkers employed for the purpose of monitoring, undergo the intervention's effect on the presumptive target, with the biomarker's changes indicating target engagement and associated activity.

The surveillance of biomarkers is necessary to guarantee the security of human research subjects. For instance, the legal threshold for drugs with possible liver toxicity is monitored by the serial evaluation of liver function tests, and cardiovascular events are monitored through the serial measurement of troponins.Measuring pharmacodynamics effects, seeing early signs of a therapeutic response, and identifying side effects from a treatment or illness may all be accomplished by tracking biomarkers. A traditional pharmacodynamics titration tool for warfarin anticoagulation dosage is the international normalized ratio (INR). Similar to this, if blood pressure is being treated, a drop in the blood pressure measurement indicates that the treatment is effective.

Challenges in Biomarkers utilization: Early consideration and resolution of the difficulties faced in biomarker-based trials for patients with GI malignancies is necessary during drug development to guarantee appropriate therapy and patient selection in a period that is suitable for both patient illnesses and quickly evolving oncology.

Sensitivity and Specificity Issues: The specificity of a biomarker is determined by the proportion of actual negative analytical results among a healthy population (Park, 2020). The primary purpose of diagnostic testing is to differentiate between individuals with and without a disease conditions, although different challenges are commonly encountered throughout the planning, recruiting, and evaluation of biomarker-based clinical studies for GI cancer patients. When a diagnostic biomarker has a defined context of usage and can be evaluated with a suitable degree of accuracy and reliability, its evaluation is still difficult. One objective is to establish an approved process that guarantees the biomarker can be measured accurately, consistently, and repeatedly with minimal variation. Most times when the assays are not confirmed this will engender a misleading assumptions about the value of the biomarker. The challenge of validation is demonstrated by the use of troponin, which is definitely an important biomarker for the detection of acute myocardial infarction. Considerable diversity exists in the operational features of the troponin assays, especially about regard to misinterpretation at the reduced threshold, which can significantly affect medical therapy. Additionally, even while the development of very sensitive troponin tests has made it possible to diagnose minor bouts of myocardial necrosis with greater sophistication, it has also led to increasing misunderstanding in the field. The medical consequences of minor rises in troponin at previously undetected levels are unknown. It is logical to anticipate that as measuring techniques advance, so too will our knowledge of the significance of certain diagnostic biomarkers. It is necessary to closely monitor the context of use when aanalytical biomarker is employed in clinical practice, prospective research, rather than only for differential purposes like increasing the frontiers of scientific notions. In certain clinical situations, a diagnostic biomarker with extremely poor specificity and sensitivity could be helpful, while in another, it might be totally misleading. In illnesses with limited prevalence, such as pancreatic or ovarian cancer, where an unexpected diagnosis might be obtrusive or psychologically devastating, an indicator must, for example, have an exceptionally low false-positive rate. However, larger false-positive rates are acceptable when screening for prevalent disorders like high cholesterol levels or elevated blood pressure, for which recurrent evaluations may be performed with little danger, and false-negative rates may be the main cause for worry. Receiver-operating characteristic curves have made it possible to go forward with a logical diagnostic biomarker assessment approach.

Standardization of testing methods: The process of standardizing a testing method using biomarkers, requires careful selection in considering the specificity and sensitivity. The common problem associated with standardizing of testing methods, is the lack of a historical norm for classifying a condition or sickness as present or absent. Furthermore, assessment criteria

and clinical utility are becoming increasingly important criteria for assessing a biomarker's suitability for clinical use. Though now absent, proof that a biomarker contributes to medical information may someday be required. Instead, whether the new evidence is important enough to affect clinical decision-making will be the key question. The total classification indicator is one of the many statistics being used to evaluate this issue. Initial preclinical marker investigators could profit from understanding exactly a biomarker will ultimately be appraised, much as early medication developers should take into account the medication's ultimate human usage (Oki et al., 2009). As oncology becomes more standardized, the aim is to pair each patient with the most appropriate therapeutic agent based specific characteristics of patient- and tumor. In addition to taking into account the tumor's histologic categorization and clinical presentation, several treatments under research target malignancies with particular biomarkers. Proper patient selection is essential for research studies in order to provide light on the possible efficacy of developing medicines and spare individuals who are unlikely to benefit from unsuccessful medications from the toxicities associated with them. Clinical trials utilizing biomarkers offer a means of expanding the treatment horizon beyond chemotherapeutics, including cutting-edge targeted and immunotherapeutic approaches. When creating these kinds of research, there are several things to take into account. They include everything from patient recruitment and trial availability to biomarker validity (Matsuoka and Yashiro, 2018).

Cost Effectiveness Considerations: The emergence of gastrointestinal as the fifth most re-occurring cancer is not a novel case and among the first four common causes of death caused by cancer (Siegel et al., 2022). It is essential that early screening of healthy citizens should be engage. But the challenge involve in large scale gastrointestinal endoscopies is the high cost and demands of human resources. To achieve broad testing amongst well individuals in the future, a more cost-effective and comprehensive approach is needed. Molecular indicators of cancer incidence and dissemination are called tumor markers, or cancer biomarkers. They are therefore crucial in the identification and selection of cancer therapies (Matsuoka and Yashiro, 2018). Because of developments in molecular targeting and genetic analysis technologies, their applications are growing quickly. There are currently no biomarkers that are sensitive enough or specific enough to be used in clinics to diagnose GC. To improve the clinical trajectory of GC, biomarkers are required at every step. Major advancements in cancer diagnosis and treatment have been made possible by the development of fluid biopsy technique, makes it possible to precisely identify the molecular details of solid tumors from body fluids (Alix-Panabieres and Pantel, 2021). Studies on gastrointestinal malignancy indicators for GI screening are numerous. Nevertheless, many of the potential indicators that have been identified thus far selectively manifest themselves later in life, making them inappropriate for early diagnosis. Furthermore, there is still a deficiency in a thorough review that concentrates on GC early detection. The following part provides a thorough overview of potential biomarker possibilities with an emphasis on early GC detection, including everything from laboratory testing to clinical prevalence and future directions. This data will help with future studies on GC biomarkers and their therapeutic uses.

Emerging biomarkers and technologies

Novel biomarkers under investigation: Recently, the scientific society has developed an interest in novel DNA and RNA-based molecular biomarkers for the early detection of tumors. Immediate view cancer administration, tumor burden monitoring, medication resistance prediction, little residual disease measurement, and prognostic estimation are all done on GC patients (Bourre, 2019).

Circulating Tumor Cells (CTCs): CTCs are recognized as cancer cells that circulate in the bloodstream and can be detected in the blood using specialized techniques. They may serve as biomarkers for monitoring response to therapy and detecting cancer recurrence. Some cancers have a preference for specific organs as they spread, and chemokine's like CCL21 and stromal cell-derived factor-1 (SDF-1) are accountable for this. These chemokine's are usually produced in the sites of metastasis, and the associated receptor, CXCR4, is often overexpressed in tumor cells. Because of the critical role CTCs play in the metastatic process, research on them will provide important new information about the mechanisms governing the spread of cancer. This will open up new avenues for the development of targeted therapies meant to sever the metastatic cascade and enhanced cancer patients' prognosis (Fedele et al., 2022).

Advances in biomarker detection methods: Significant progress has been made lately in the area of medical diagnosis of cancers, particularly with the creation of novel biomarkers for the detection of cancer biomarkers. The recent ground breaking technologies include new technologies such as lateral flow membrane strips, microfluidics, DNA chips, and protein chips that make it possible to effectively detect

a variety of biomarkers in the sub-nanomolar range. The uses of biosensors for the identification and measurement of biomarker proteins and nucleic acids have expanded due to developments in surface chemical modification and biomolecule conjugation. The use of protein and nucleic acid microarrays has made it possible to identify multiplex cancer biomarkers. In contrast, lateral flow and microfluidic immunoassays have made point-of-care diagnosis possible. Early cancer diagnosis, even before symptoms appear, remains quite a ways off. The trajectory of cancer therapy, the selection of efficacious options for treatment, and the success of follow-up activities are expected to be significantly impacted by the discovery of these biomarkers.

Potential future application in clinical practice: In this article the ravaging effect of gastrointestinal tracts malignancies is commonly due to the heterogeneous nature of the illness where each cancer patient has a unique molecular and genetic profile. Most older Cancer diagnostics techniques tends to focus on an aspect of the disease which may either be to evaluate the genetic profile or the molecular profile: Despite the large number of research that have been done on molecular biomarkers, though majority of the biomarkers that were found did not pass validation tests. A targeted therapy is not yet available for the majority of patients with advanced gastrointestinal malignancies, and there are no diagnostic indicators for secondary prevention. In order to employ biomarkers related to the gastrointestinal tract in patient care, a thorough analysis is necessary to ascertain the best course of action for pinpointing the exact biomarker that may be investigated for customized treatment. Compared to patients whose malignancies test negative for CDHI mutations, individuals with somatic CDH1 epigenetic and structural abnormalities may have a poorer prognosis. According to Shimada et al. (2014), this implies that the presence of CDH1 epigenetic and structural alterations in a biopsy taken for diagnostic or preoperative purposes might be a potentially useful biomarker. In blood samples from patients with GI malignancy, a recent study looked at the promoter methylation status of CDH1's diagnostic value (Asao et al., 1991). Remarkably, blood samples demonstrated a considerable facilitation of CDH1 promoter methylation, indicating that CDH1 promoter methylation may be a promising choice for biomarkers in GC patients.

Clinical implications and Recommendations

Incorporating biomarker testing into clinical guidelines: Incorporating biomarker testing into clinical guidelines can have significant implications for patient care. The following recommendations should be considered:

1) Standardization of Testing: Clinical guidelines should establish a set of standardized protocols for biomarker testing, including recommended test types, cut-off values, and interpretation criteria. This will ensure consistent and reliable results.

2) Education and Training: Healthcare professionals must be adequately trained in the use and interpretation of biomarker tests to effectively integrate them into clinical practice.

3) Cost-Effectiveness Analysis: Before biomarker tests are widely adopted, a comprehensive cost-effectiveness analysis should be conducted to determine their cost-benefit ratio and long-term value.

4) Ethical and Legal Frameworks: Clear and robust ethical and legal frameworks should be developed and implemented to address privacy, confidentiality, genetic discrimination, and other ethical concerns associated with biomarker testing.

Multidisciplinary approaches to biomarker interpretation: Newly developing multidisciplinary fields that have been internationally classified by regulatory bodies as "the investigation of how differences in DNA sequence affect the toxicity and effectiveness of drugs" (PGt) as well as "the examination of polymorphisms of both RNA and DNA properties associated with drug response" (PGx). Indeed, a growing body of research has shown that genetic variables contribute to the inter-individual heterogeneity of medication response in addition to the effects of age, illnesses, gender and other drug combinations (Wen et al., 2017). Growing genomic understanding has also led to a rise in the relevance and usage of "Genomic biomarkers" (GBs) in medication development, acceptance, and clinical implementation.

Results from biomarker tests must be accurately interpreted using multidisciplinary methods through collaborative strategy between specialists. Some examples of multidisciplinary teams in biomarker interpretation include:

1) Oncologists: Experts in cancer diagnosis, treatment, and management provide clinical context for interpreting biomarker results.

2) Genetic Counselors: Professionals trained in genetics and counseling can assist patients in making knowledgeable healthcare decisions by helping them comprehend the significance of the results of their genetic tests. One of the greatest issues is the uncertainty surrounding the accurate identifications of molecules and the use of complementary LSMC instrumentation to confirm results. Making effective biomarker validation challenging. Biomarker Identifications often rely on inferences from MS1 data

to link LCMS results with raw MALDI spectra introducing significant potential error to the final results (Park, 2020).

Patient education and shared decision making: Effective biomarker testing and interpretation need both collaborative decision-making and patient education. It may be ensured that patients are educated and actively participate in their treatment by taking into account the following factors:
Patient-Friendly Materials: Educational resources, such booklets, films, or interactive technologies, have to be presented in a way that is clear, simple to comprehend, and respectful of cultural differences.
2) Active Participation: Healthcare providers should encourage patients to make enquiries, to ensure participation in shared decision making about biomarker testing and interpretation.
3) Follow-Up Support: After biomarker testing, ongoing support and follow-up care should be provided to ensure that patients understand their results and have access to appropriate treatment options. This can include regular appointments with healthcare providers, educational programs, or support groups for patients and their families.

Ethical and Social Consideration: The integration of biomarkers into clinical practice raises several ethical and social considerations:
1) Access and Equity: If biomarker testing becomes a standard part of clinical care, it is also important to grants all patients equal access, regardless of their socioeconomic status, ethnicity, or geographic location.
2) Patient Autonomy: Patients should be empowered to make right decisions about their health, including the use of biomarker testing.
Privacy and confidentiality concerns: Privacy and confidentiality are critical concerns in the context of biomarker testing:
1) Genetic Privacy: Biomarker testing can reveal sensitive genetic information that, if not adequately protected, could be misused or exploited. This could lead to stigmatization, discrimination, or breach of privacy.
2) Data Security: Biomarker testing generates large amounts of sensitive data that must be stored and shared securely to prevent unauthorized access or theft. This includes protecting against cyber-attacks, human error, or other potential vulnerabilities.
3) Genetic Discrimination: The availability of genetic information from biomarker testing could potentially be used to discriminate against individuals in areas such as employment or insurance. Laws and rules must thus be in place to shield people from this kind of prejudice.
4) Genetic Counseling: Patients who undergo biomarker testing may benefit from genetic counseling in other to understand the implications of their genetic information and make informed decisions about their healthcare.
Equity in access to biomarker testing
1) Access and Equity: It is crucial to guarantee that all patients, irrespective of their socioeconomic level, ethnicity, or geographic location, have equitable access to biomarker testing if it becomes a routine component of clinical treatment.
2) Patient Autonomy: Patients should be empowered to make informed decisions about their healthcare, including the use of biomarker testing.

Future Directions and Research Priorities
a. Areas for further research and development
Biomarker research is a rapidly evolving field, and there are numerous areas for further research and development in GI cancer:
1) Multi-Omics Approach: By integrating data from genomic, transcriptomic, proteomic, and metabolomic analyses, GI malignancies can be better understood and new biomarkers can be found.
2) Personalized Medicine: Developing biomarker-based approaches to tailor treatment to individual patients based on their specific tumor characteristics and genetic makeup is an important area for research.
3) Early Detection: Individuals that are at higher risk of cancer, development of biomarkers employed for the early diagnosis of GI cancers, this progress will better the outcomes and effectiveness of more treatments.
4) Liquid Biopsies: Advances in liquid biopsies for the detection of tumor DNA and other biomarkers in the blood could allow for more frequent monitoring of disease progression and treatment response without invasive procedures.
5) Circulating Tumor Cells (CTCs): Isolating and characterizing CTCs from the blood can provide valuable information about tumor biology and response to therapy.
6) Microbiome Analysis: new biomarkers and possible treatment targets may result from knowledge of the gut microbiome's role in the onset and spread of GI cancer.

b. Collaborative efforts to advance biomarker science
Collaborative efforts between various stakeholders can accelerate the development of biomarker science for GI cancer:
1) Multi-Institutional Collaborations: Bringing together leading experts from different institutions to share data, ideas, and resources can lead to more comprehensive and innovative research.
2) Public-Private Partnerships: Collaboration between academic institutions, government agencies, and

private companies can lead to more efficient use of resources and accelerate the translation of research findings into clinical practice.
3) International Consortia: International collaborations can provide opportunities for large-scale genomic sequencing projects and the sharing of samples and data across countries.
4) Patient-Centered Approaches: Involving patients in the research process through initiatives such as patient advocacy groups and patient-centered clinical trials can help ensure that research is more closely aligned with patients' needs and preferences.

Potential impact on the management of gastrointestinal malignancies: The identification and utilization of biomarkers in the management of GI malignancies possess the capacity to profoundly affect patient care in a number of ways:
1) Improved Diagnosis and Prognosis: Biomarkers can provide more accurate and earlier diagnosis of GI cancers, allowing for timely and appropriate treatment interventions. They can also provide prognostic information about the likely progression and outcome of a particular cancer, which can inform treatment decisions.
2) Personalized Treatment: By identifying specific genetic or molecular features of cancer in someone with cancer, this will enable the use of biomarkers in the selection of more personalized and targeted treatment options, thereby results to fewer side effects and better outcomes.
3) Monitoring of Treatment Response and Relapse: Biomarkers can also be used to monitor reaction to medication and detect early signs of relapse, allowing for prompt adjustments to therapy if needed.
4) Identification of New Therapeutic Targets: By identifying novel biomarkers associated with GI cancers, researchers may uncover new molecular targets for the development of more effective therapies.
5) Prevention and Screening: Biomarkers may also be useful in detecting individuals that are in high risk of developing GI cancers, allowing for targeted screening and preventive measures.

Conclusion: In this article, we zeroed our focus to evaluate the impact of biomarker in the oversight of gastrointestinal tracts malignancies. The outcomes of these ongoing research will make it possible to better understand, enhance, and improve the diagnostic and treatment procedures, which will raise survival rates. Actually, stage 0–1 tumors, which have nearly 100% survival rates, will be detectable thanks to recent developments in biosensor technology. Thus, the recent advancements in biosensor technology that enable the sensitive and highly specific identification of cancer biomarkers are the main emphasis of this Research Topic.
Additionally, the study had interest in novel and cutting-edge nanomaterial-based biosensors, such as wearable technology, paper-based detection techniques, microfluidics, and micronanoscale sensors for the identification of cancer biomarkers. Additionally, we emphasize the use of special materials nanomaterials and polymers, among others that enable very precise and sensitive detection. In recent times it has been found that nano materials have profound application due to their composition, size, and adjustable attributes. They serve as markers for signal production, transduction, and amplification, or they are employed to immobilize biorecognition components. To increase the sensitivity, effectiveness, and specificity of detections in intricate biological matrices, more investigation is still needed.

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