



Gastrointestinal cancers: an urgent need

INTRODUCTION

Scope of problem:

Gastrointestinal (GI) cancers—including cancers of the colon and rectum (colorectal cancers), esophagus and stomach (gastroesophageal cancers), liver, gallbladder, pancreas, small intestine, appendix, and anus—collectively represent one of the greatest public health issues in the US and, indeed, worldwide—leading to almost 4.5 million global deaths in (latest data from 2013). According to American Cancer Society (ACS) reported statistics (www.cancer.org), taken as a whole, ***gastrointestinal (GI) cancers have the highest incidence*** and are the second leading cause of cancer death (after lung cancer) in the United States (Figure 1). However, the relative proportion of government and private funding for GI cancer research does not match the problem—for example, in 2013, the NCI allocated over \$100 m more to breast cancer than to GI cancer research (approximately 11.7% compared with 8.6% of their total budget) and, in 2015, ACS total funding amount by percent relevance for breast cancer was approximately \$62 m compared with \$43 m for GI cancers. These amounts were awarded despite the fact that, during those years, approximately 3.6 times more patients died from GI than from breast cancers. These disparities in funding seriously affect science and solutions. We seek to rebalance our national (and global) cancer research investment toward GI cancers in keeping with the relative magnitude of the problem. Our national prioritization on breast cancer research has yielded major success for our breast cancer patients but has unintentionally left other major cancers, most notably GI cancers, far behind.

Unlike lung cancer, prostate cancer, and breast cancer, we have few insights into why GI cancers occur and how to prevent them. Among GI cancers, only colon cancer has an official screening recommendation in the US, and even this test, the colonoscopy, has sub-optimal compliance and high cost. Most significantly, due to lack of research investment, we have failed to realize major progress in treating these cancers, making them among the most feared cancers of all.

ROLE OF THE GI CANCER ALLIANCE

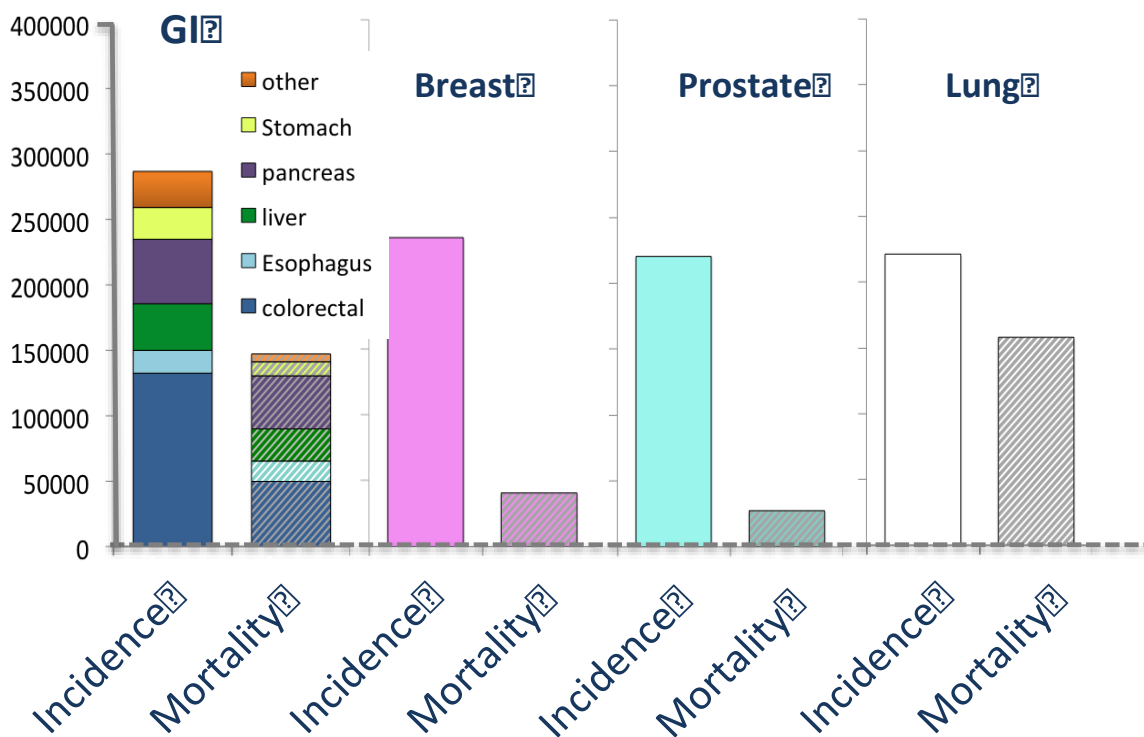
A newly formed GI Cancer Alliance of 20 individual GI cancer advocacy organizations has the *vision* of creating a stronger, more unified voice to fight GI cancers—which collectively make up the most common and deadly cancer group.

The mission of the GI Cancer Alliance is to raise awareness; provide education; and advocate for the prevention, treatment, and cure of gastrointestinal cancers. This will occur through the

collaboration of advocacy groups with patients, government leaders, industry, and institutional partners.

Figure 1. "Top" cancers - incidence & mortality: ACS, Cancer Facts and Figures (www.cancer.org)

2015



Other = cancers of the anus, small intestine, gallbladder & bile ducts (other than liver)

The members of the Alliance include: Beat Liver Tumors, The Bili Project Foundation, Cholangiocarcinoma Foundation, Colon Cancer Alliance, Colon Cancer Challenge, Debbie's Dream Foundation: Curing Stomach Cancer, Esophageal Cancer Action Network, Fibrolamellar Cancer Foundation, Fight Colorectal Cancer, Gastric Cancer Foundation, Global Liver Institute, Hope for Stomach Cancer, Michael's Mission, National Pancreas Foundation, No Stomach for Cancer, Pancreatic Cancer Action Network, Prevent Cancer Foundation, The Raymond Foundation, The Ruesch Center for the Cure of GI Cancers and TargetCancer Foundation.

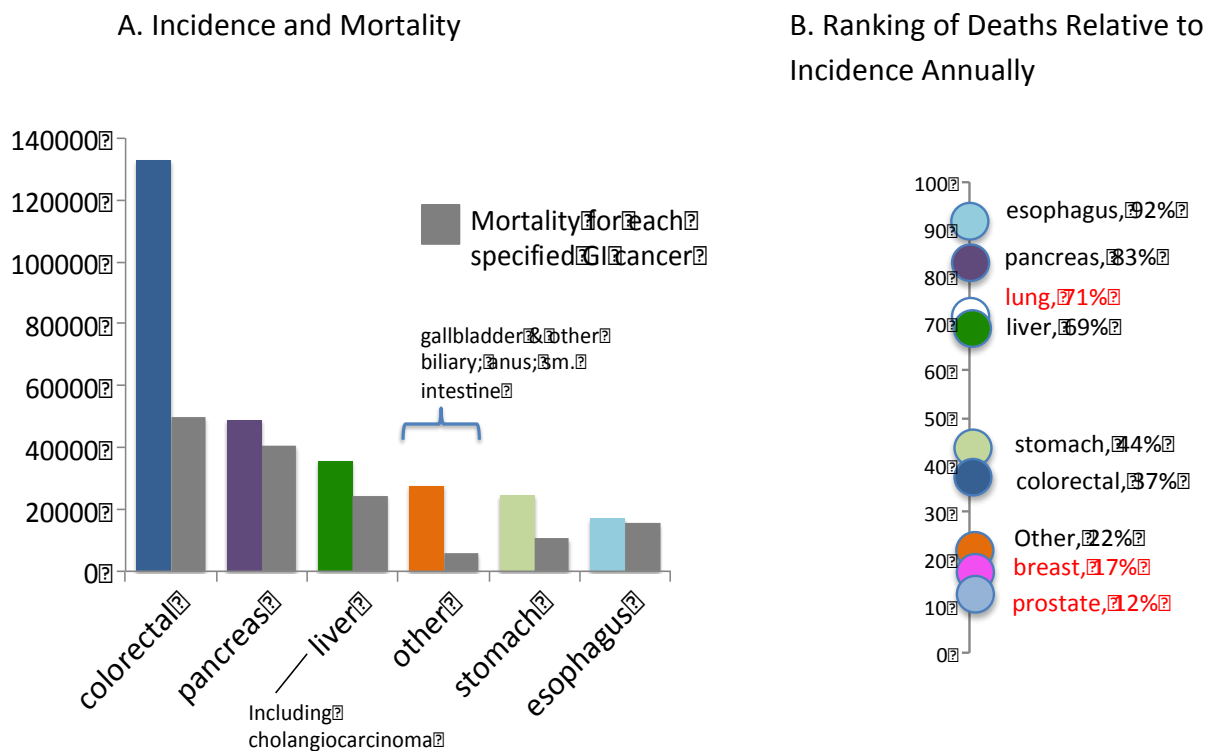
GROUPING GI CANCERS TOGETHER; why are we stronger together?

You might ask why the different alliance groups are joining forces—what is the rationale for collaborating?

There is more than one answer to this question:

1. The death rate for all GI cancers is extremely high.

Figure 2: GI cancers in the US



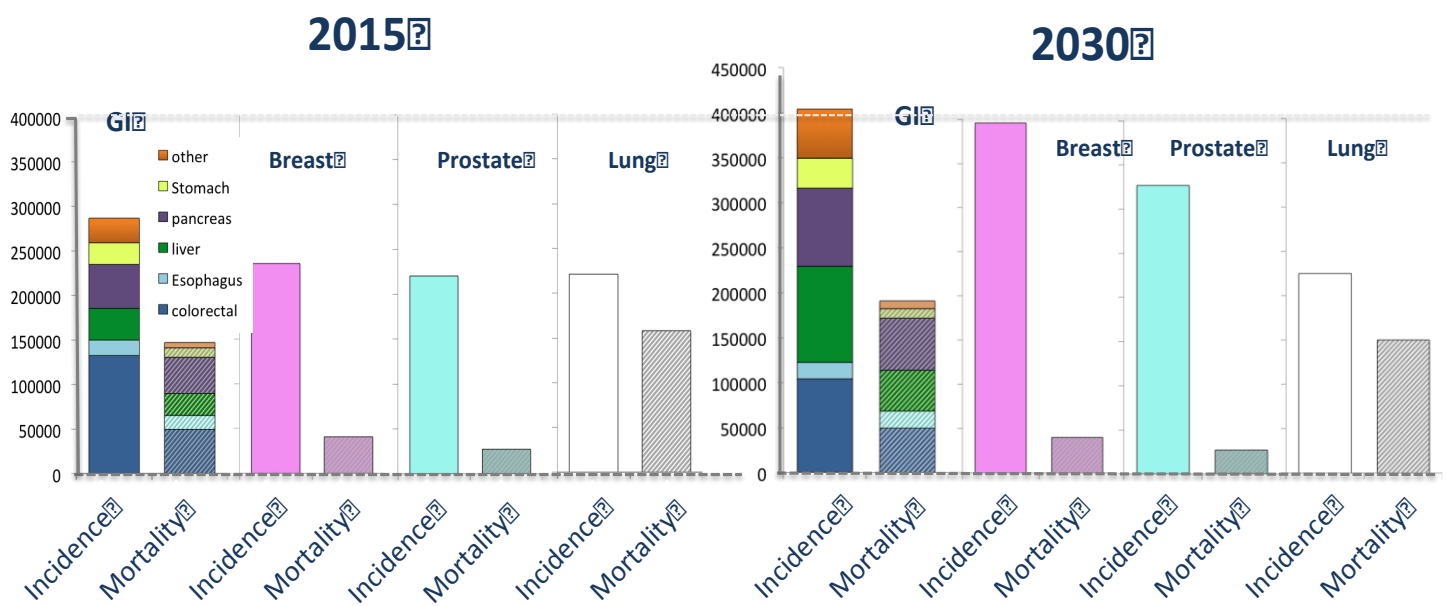
Survival rates are particularly bad for pancreas, liver (including cholangiocarcinoma), and esophageal cancers.

2. Their impact on patients and their families (symptoms, financial burden, death rates) is dramatic. They strike the young and old, men and women. They are treated with major life altering surgery, intensive chemotherapy, and radiation, all of which result in a major deterioration in productivity and quality of life.
3. Research investment in GI cancers does not match the magnitude of the problem.
4. GI cancers are related biologically and have similar, overlapping molecular characteristics

5. GI cancers share healthcare teams; the healthcare system and professional societies (ASCO, AACR, ACS) see them as one group
6. Other “groups” of cancers are treated as a groups (e.g. leukemia/lymphoma)
7. The problem is not going away:

Figure 3 shows the 2015 impact compared with the estimated 2030 impact, extrapolated from 2015 using a continuation of annual % incidence and mortality trends from 2008 to 2015.

Figure 3:



GI CANCER IMPACT

On a National level, GI cancers have a huge impact on both men and women.

It was estimated that 286,480 people were living with a GI cancer diagnosis in 2015 and more than half this number—147,090—died from this set of diseases that same year. These numbers are growing annually (Figure 2).

A GI cancer diagnosis leads not only to a physical health impact but also an emotional, financial, and logistical one. Social isolation is a common result.

The financial and logistical burdens relate not only to cancer treatment costs, but extend to the indirect and often unanticipated costs of cancer care: e.g., transportation, childcare, and lost wages.

The emotional impact applies not only to the patient but also their loved ones.

RECOMMENDATIONS

As a group, the GI Cancer Alliance makes the following recommendations:

We increase GI cancer awareness, including the number of people's lives it affects, both nationally and globally; the measures that can be taken to prevent this deadly group of diseases, including diet, exercise, and, in some cases, screening; the number of trials that are available to patients with GI cancers in the US; and the impact that increased funding will make on implementation of national screening programs, discovery and testing of more effective GI cancer-fighting agents, raising awareness to trial availability, and helping patients and their families out with the unexpected and logistical indirect costs of a GI cancer diagnosis.

We suggest an increase in the amount of funding allocated annually to the following GI cancer-related research areas:

1) Screening.

We recommend development and implementation of screening methods for all GI cancers. By traditional definitions, screening for a disease should be non-invasive, effective and inexpensive. Very few tests actually meet this standard. GI cancers have different incidences depending on geographic location, genetics, and environment. To put forward one global standard will be challenging. However increased research in this area will have a major impact on lives and healthcare costs of the future.

There is a limited role for GI cancer screening and prevention in the United States. The impact of effective screening methods is exemplified by breast and prostate cancer mortality rates. Both disease groups have fully implemented and approved national screening programs, dramatically improving patient survival rates.

In the US, colonoscopy is recommended and fully implemented for patients over 50 years of age or at high risk of the disease. The reality is that compliance is low and payers do not always support this screening. Additionally, individuals are developing colorectal cancers at an increasingly younger age, suggesting that screening should be mandated at age 40 or earlier. Thus, we need novel techniques for early detection that move beyond invasive, expensive procedures; this can only become reality through focused research and development.

2) Understanding the interface with our environment

Increasing recognition is being given to the "microbiome", defined by the National Human Genome Research Institute (NHGRI) as "the collective genomes of the microbes (composed of

bacteria, bacteriophage, fungi, protozoa, and viruses) that live inside and on the human body.” The NHGRI says, “we have about 10 times as many microbial cells as human cells.” The institute recommends studying humans as “supraorganisms,” composed of both human and non-human cells.

During childhood, microbial colonization of mucosal tissues has major impact on the development of our immune systems and how our bodies deal with environmental exposures and development of diseases later in life. Components of our microbiome digest the food we eat and seem to influence our risk of obesity, bowel diseases, and other health problems.

Research of people indigenous to the Amazon rainforest (on the Brazilian/Venezuelan border) who have not come into contact with outsiders and the ways of the Western world has shown us the impact of the environment on the human microbiome. The guts and skins of these people are found to have double the microbial diversity of an average American—many microbial species harbored by these Amazonian people are completely undetectable in samples from Westerners.

These people may hold the key to our future health and their immediate study is paramount before the developed world infiltrates further into their lives.

For now, we should question our overuse of antibiotics and antibacterial hand wipes, as well as excessive hand washing. We may be denying our children’s bodies a vital education.

3) Focusing on developing novel molecular and immune therapies. “Catching a ride on the moonshot”

We have to acknowledge the heterogeneity of cancer, and the current failure of our empirical standard of care, which comprises a one-size fits all strategy. We must increase funding for biomarker development in humans, acknowledging that preclinical models have fallen short of giving us the answers we need.

We believe that molecular (gene, protein, and phosphoprotein) testing of patients’ tumors is key to successful cancer treatment. The development of agents that target mutated genes and aberrant proteins pave the way to successful personalized cancer therapy.

Cancer immunotherapy has been the surprise scientific breakthrough of the decade, having startling results in a number of patients. We need to promote ongoing investigations and development of agents that can activate our immune systems against tumor cells and maintain that activity.

4) Raising clinical trial awareness

Only 5% of the current US population is enrolled into any clinical trial. In order to speed up the cancer drug development and approval process we need to invest in methods to raise physician and patient clinical trial awareness. We need to develop patient-friendly Websites that give individuals with GI cancers, and their loved one, access to clinical trial information that is easy to understand. A much higher proportion of pediatric cancer patients and breast cancer patients enroll onto trials, one of the keys to their success. We need to create tools and support to enable a similar trend in GI cancers.

5) Focusing on patient and family impact.

GI cancer patients and their families endure unique burdens that have a major negative impact on their work, quality of life, and sexuality—often robbing them of normal social existence. Few tools exist to support patients and their families, nor are we aware as a society of their burdens. These gaps must be filled.

6) Incentivize the collection and sharing of appropriately protected patient health information

Data sharing and analysis will uncover many hidden secrets of cancer. Over 95% of cancer patients are eager to offer their medical information, tumor samples, and genetic data in the hopes that it will contribute to new answers. While protecting privacy is critical, HIPAA must be modified, and electronic health data collection must be simplified and standardized. There is power in numbers; and GI cancer patients are lined up to be the army. Finally, we must incentivize patient partnerships instead of viewing patients as consumers. As patients are provided with more transparency regarding our use of their healthcare investment, they will become better consumers, and demand better outcomes and better value from their therapy.