PANCREATIC CANCER ACTION NETWORK®
ADVANCE RESEARCH. SUPPORT PATIENTS. CREATE HOPE.

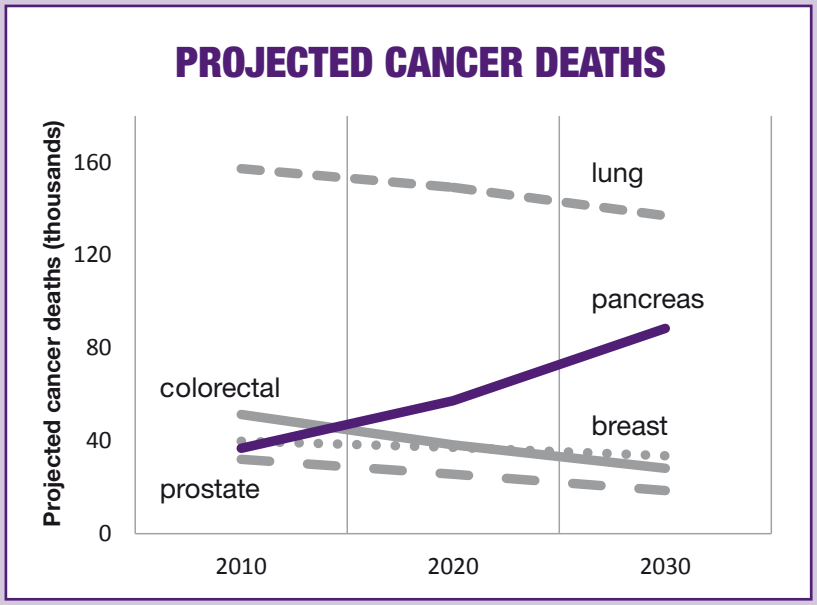
THE ALARMING RISE OF PANCREATIC CANCER DEATHS IN THE UNITED STATES:

WHY WE NEED TO STEM THE TIDE TODAY

EXECUTIVE SUMMARY

Pancreatic cancer is the fourth leading cause of cancer death in the U.S., and is the only one of the most commonly diagnosed cancers with a five-year relative survival rate in the single digits, at just six percent. Projections based on the changing demographics of the U.S. population and changes in incidence and death rates reveal the startling observation that **pancreatic cancer is anticipated to move from the fourth to the second leading cause of cancer death in the U.S. by 2020**. An increase in the number of older adults and minorities in the nation will raise the number of total cancer cases. However, this will be offset by decreases in death rates for most cancer types due to improvements in early detection and/or treatment so that the number of anticipated cancer deaths will remain largely unchanged.

Pancreatic cancer is one of a handful of cancer types for which an increase in the number of new cases due to demographic changes is unusually large. Even more striking is the realization that pancreatic cancer is unique among the top five cancer killers (currently lung, colorectal, breast, pancreas and prostate) in that both the incidence rate and death rate are increasing. The result of the combination of these factors is that both the projected number of new pancreatic cancer cases and pancreatic cancer deaths will more than double by 2030. By as early as 2015, the number of deaths from pancreatic cancer will exceed those from breast and colorectal cancer, and be surpassed only by the loss of life from lung cancer.



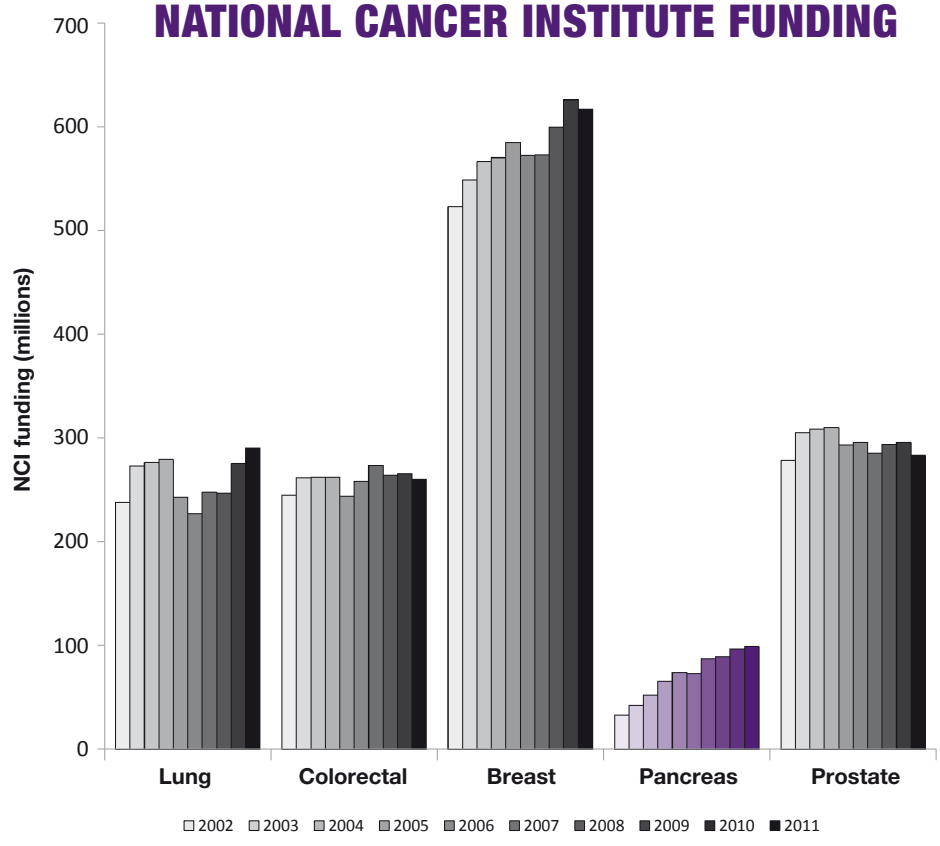
Projected cancer deaths for the major cancer killers. Projections of the number of deaths from the current top five cancer killers indicate that pancreatic cancer will become the second leading cause of cancer deaths as early as 2015. The estimated number of deaths in 2010 is from the 2010 American Cancer Society Facts & Figures. Projections were calculated by considering expected changes in the number of new cases for that cancer site and the average annual change expected in the death rate (number of deaths/100,000 population). Separate values were calculated for men and women and then combined to obtain the value for the total population. The projected number of new cases for 2020 and 2030 were calculated using age-, sex-, race-, and origin-specific incidence figures from Smith et al (*JCO* 27:2758, 2009, Table 1) and applying the delay-adjusted average annual percent changes in incidence rate calculated by Eheman et al (*Cancer* 118:2338, 2012, Table 1). These figures were further adjusted by the average annual percent changes in death rate calculated by Eheman et al (*Cancer* 118:2338, 2012, Table 2).

What is particularly alarming is that there are currently no early detection tools or effective treatments for pancreatic cancer. The research advances that have markedly changed the death rate for so many other cancers have not translated into clinical benefits for pancreatic cancer patients. Specific biological challenges have impeded efforts to reduce the mortality rate from pancreatic cancer, including the anatomical location of the pancreas, an unusually dense and impenetrable barrier that inhibits the delivery of therapeutic drugs to the tumor, and genetic alterations which elude targeted therapies. These challenges have been compounded by a historically small, fragmented and underfunded research community

dedicated to studying the disease. Funding for pancreatic cancer research lags significantly behind the other current top five cancer killers. The largest source of cancer research funding in the U.S. is the National Cancer Institute (NCI). NCI research investment towards pancreatic cancer is just two percent of the NCI's total budget, representing only one-third to one-sixth the amount dedicated to the other top cancer killers. The long lag time between laboratory research advances and clinical benefit for patients facing the disease, coupled with the alarming rise projected for pancreatic cancer deaths, indicates that never has it been more urgent that a national effort become focused on research that will lead to improvements in the outcomes from a pancreatic cancer diagnosis.

Real progress in changing the trajectory of the rise in deaths from pancreatic cancer will require not only increased funding, but a carefully considered, long-term and comprehensive strategic plan to ensure that our limited federal resources target the areas of greatest need and potential for patient benefit. Congress is currently debating the *Pancreatic Cancer Research & Education Act* (S. 362/H.R. 733), which asks the NCI to create a long-term, comprehensive strategic plan to bring the intellectual and infrastructural resources of the nation to bear on this urgent problem. It is critical that this country take steps to shine a light on this disease so that we can identify new pathways to success.

Pancreatic cancer does not need to be the death sentence that it is for most patients today. The Pancreatic Cancer Action Network set a bold goal in 2011 to double the pancreatic cancer survival rate by 2020 as an important step in stemming the rapidly rising threat of pancreatic cancer. This initiative, and the passage of legislation like the *Pancreatic Cancer Research & Education Act*, will help lead to a plan to develop new approaches for the early detection and treatment of pancreatic cancer and accelerate urgently needed improvements in patient outcomes. By understanding the findings outlined in this report and heeding the warnings they offer, we can change the statistics and the course of this disease.



Data from the NCI budget tool

CURRENT STATE OF AFFAIRS

In 2012, pancreatic cancer ranked as the fourth leading cause of cancer death in the U.S., and the 10th most commonly diagnosed tumor type in men and women.[1] Estimates of incidence and deaths caused by pancreatic cancer this year are approximately 44,000 and 37,000, respectively. The similarity of these figures underscores the severity of this disease: pancreatic cancer is the only one amongst the top ten cancer killers with a five-year relative survival rate in the single digits, at just six percent.

Progress made in the more than 40 years since the National Cancer Act was passed in 1971 has led to a significant increase in the five-year relative survival rate of all cancer types from under 50 to over 65 percent.[1] However, advances made in other solid tumors have not translated to clinical benefit for pancreatic cancer patients. Pancreatic tumors are extremely complex and exquisitely resistant to current treatment modalities. Even patients diagnosed in stage I, when the tumor is thought to be confined to the pancreas and surgically removable, have a five-year relative survival rate of only about 23 percent.[2]

The largest source of research funding for cancer biology studies in the U.S. is the NCI within the National Institutes of Health (NIH). According to the NCI, its investment in

DIANA SOKOL ROTH: THE PERSPECTIVE OF A PANCREATIC CANCER SURVIVOR

I knew my body well enough to realize that the severe abdominal pain I was experiencing was far worse than my normal acid reflux. I know now that seeking treatment for it quickly may be the only reason I am still alive to write this letter.

I saw my GI physician two weeks after that intense pain started. After my initial pancreatic cancer diagnosis, I sought a second opinion at a facility which is a six-hour drive from my home in Chicago. On a Thursday, I was diagnosed with stage II pancreatic cancer. The doctors said that my tumor was attached to the portal vein next to my pancreas and it meant my cancer could progress from stage II to stage IV in just a matter of weeks.

They strongly recommended that I schedule surgery for the next day but I chose to wait until the following Monday. I spent that weekend writing my will and getting my affairs in order to prepare for the worst.

When I had the Whipple procedure, the recommended and highly complex surgery used to treat pancreatic cancer, the surgeon removed two -thirds of my pancreas, part of my small intestine, my gall bladder and common bile duct. The operation was followed by months of grueling chemotherapy and radiation back in Chicago.

I was stunned when diagnosed. I have no family history of cancer. I'm also an extremely healthy and active person. As a newlywed at age 43, I had only been married to my husband Scott for six months at the time of my diagnosis.

Of course, this ordeal has been a tremendous struggle, but I am grateful and happy every day because I feel fortunate. I know I beat nearly insurmountable odds.

The doctors who treated me are some of the nation's best. Because of the medical knowledge gained from my occupation in the medical field, I knew to act quickly when my symptoms appeared. My disease was caught at an early stage. But my life will never be the same – I must now live as a person with diabetes. And I had to surrender a lifelong dream. Due to pancreatic cancer, becoming pregnant is no longer a viable option for me.

When I think about my life and those of many others I have met in the last three years who are living with pancreatic cancer or have passed, I have to wonder why research for it is still so underfunded. Pancreatic cancer is the fourth leading cause of cancer death. Why isn't there enough funding available to find a cure?

Congress can end a lot of suffering and loss of life by simply passing the *Pancreatic Cancer Research & Education Act.* They need to act. I don't want any other families in our nation to have to deal with this. This bill can make a difference for tens of thousands of people who desperately need help. Without the passage of this bill, pancreatic cancer patients will continue to hear, "I'm sorry, but there is no cure for your disease."

I'm happy to say I have been cancer free for two-and-a-half years now. But every six months, during my routine CT scan, I pray that my cancer does not return because I remain in fear that there will be nothing my doctors can do for me then.

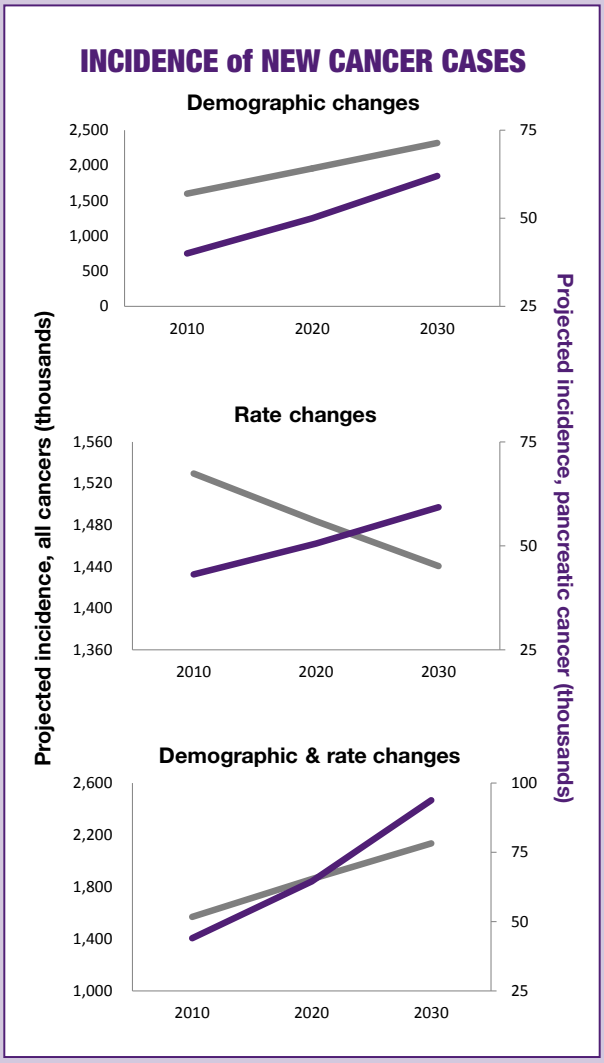
pancreatic cancer research accounts for only two percent of its total budget.[3] A critical need exists for more funding and a national strategic plan to address this deadly disease and the unacceptable burden it poses for society. This need is becoming more urgent given the rise that is projected in the incidence and the deaths for pancreatic cancer, causing it to become the second leading cause of cancer death in the U.S. in the very near future.

PROJECTING THE NUMBER OF NEW CANCER CASES IN 2030

In a report entitled *Future of Cancer Incidence in the United States: Burdens on an Aging, Changing Nation*, researchers used cancer incidence data from the Surveillance Epidemiology and End Results database (the same source from which the American Cancer Society gets its annual data) to analyze trends in cancer diagnoses in relation to projected demographic changes in the U.S. population.[4] The results demonstrate that overall cancer incidence will increase by 45 percent from the year 2010 to 2030. That translates to 2.3 million cases of cancer of all types in 2030, up from 1.6 million in 2010. The authors attribute this change to rising proportions of older adults and changing ratios of different racial groups with different propensities for cancer diagnoses.

For pancreatic cancer, the picture is even worse: the analyses reveal that pancreatic cancer incidence is projected to increase by 55 percent from 2010 to 2030. Pancreatic cancer is one of only eight cancers for which diagnosis is projected to increase by more than 50 percent. Based on these data alone, it is predicted that 62,000 individuals will be diagnosed with pancreatic cancer in 2030.

Another recent report illustrates the fact that changes in demographics alone are not sufficient to predict the incidence of pancreatic and other cancer types in the coming years. The *Annual Report to the Nation on the Status of Cancer, 1975-2008, Featuring Cancers Associated with Excess Weight and Lack of Sufficient Physical Activity* was published in early 2012.[5] This study analyzes changes in the trends of incidence and death rates and discusses the future impact of these diseases.



Projected new cancer cases

Top: The number of new cases of cancer (grey line) is projected to increase as a result of demographic changes, namely the growing number of older adults and minorities in the population. The number of new cases of pancreatic cancer (purple line) is growing at a slightly faster rate than cancer in general.

Middle: The average number of new cases of cancer/100,000 population is decreasing for men (0.6%/year) but not changing for women, resulting in a slight decline in the projected incidence of cancer overall (grey line). In contrast, the average number of new cases of pancreatic cancer/100,000 population (purple line) is increasing in both men and women, resulting in a steady increase in the projected incidence of pancreatic cancer.

Bottom: The combination of changing demographics and the increase in the average annual incidence rate for pancreatic cancer work together to result in a more rapid increase in the projected total number of new cases of pancreatic cancer (purple line) compared to cancer in general (grey line).

Sources and methodology are found in footnote.[10]

Why is the incidence rate of pancreatic cancer increasing?

The rise in obesity in the U.S. may contribute to the increased rates of several types of cancer, including pancreatic. While the incidence of pancreatic cancer has been previously shown to be slightly higher in individuals with elevated body mass indexes (BMI), this does not account for the entire difference. Among the six cancer types that were shown in the *Annual Report to the Nation on the Status of Cancer* to be related to obesity, pancreatic cancer is one of the least impacted. For example, an increase in BMI by five units is associated with a 14% increased risk of pancreatic cancer but as much as a 30 to 60% increase in endometrial, esophageal or kidney cancer. Moreover, while whites are the only racial group found to experience a statistically significant increase in the average annual incidence rate of pancreatic cancer during 1999 to 2008, the obesity epidemic has impacted all racial groups. This finding suggests that there are factors in addition to obesity that contribute to the rising incidence rate of pancreatic cancer.

This study shows that from 1999 to 2008, the overall cancer incidence rate remained stable. By rate, the authors are referring to the number of new cancer diagnoses per 100,000 Americans, and not the absolute number of cases. Of the current top five cancer killers in the U.S., rates of lung, colorectal and prostate cancer decreased, while breast cancer stayed about the same. However, pancreatic cancer rates were found to have steadily increased over this period of time, and this rise has accelerated in recent years (see sidebar). From 2004 to 2008, the incidence of pancreatic cancer increased an average of 1.8 percent in men and 1.4 percent in women each year. Six other types of cancer also showed average annual increases in incidence rate during this time period.

The *Future of Cancer Incidence* study predicts a 55 percent increase in the number of people

ELMER RIDLEY: A PANCREATIC CANCER SURVIVOR BEATING THE ODDS

When I was diagnosed with pancreatic cancer, I knew I was in for the fight of my life. I heard it was one of the most deadly of all cancers with a very low survival rate, although at that time, I didn't realize how low the survival rate actually was. I am fortunate to be one of the few people who have beaten the odds and still be here to tell my story.

Due to a severe back problem, I had to leave my job as a truck driver and go on disability in February of 2005. Pancreatic cancer invaded my body shortly thereafter, so I am now an almost seven-year survivor.

I first thought something might be wrong when I kept feeling a dull but persistent pain on my left side and a bloated feeling almost all of the time. My family members kept urging me to get it checked out. I found out through an ultrasound that I had pancreatic cancer.

A little over two weeks later, I was having surgery near my home in Richmond, Virginia. My surgeon informed me he would remove part of the tail of my pancreas, spleen and some other surrounding tissue. Most people who are eligible for surgery undergo the Whipple procedure; in my case the surgeon performed a distal pancreatectomy.

The operation was followed by 28 rounds of radiation treatments in the morning and chemotherapy in the afternoon. I did not tolerate the chemotherapy drug well at all. It took away my energy, appetite, and made me nauseous, and I ended up losing about 30 pounds. After recovering from surgery and treatments in the spring of 2006, my condition improved and I did very well for the next three years with no sign of cancer.

Cancer returned to my body in the fall of 2009, this time in my left lung. The prognosis wasn't good; they gave me three to six months to live. They said that I couldn't survive this because the cancer was metastatic. However, my faith and the prayers of my family members and many other special people helped me to persevere. Thankfully, I am still here to carry on this fight and help others facing pancreatic cancer.

In 2011, I attended the Pancreatic Cancer Action Network's Advocacy Day in Washington, D.C. for the first time. I was there again in 2012, when I served as the Pancreatic Cancer Action Network's state leader from Virginia. Since then, I have been doing what I can to convince my legislators that the *Pancreatic Cancer Research & Education Act* must be passed soon.

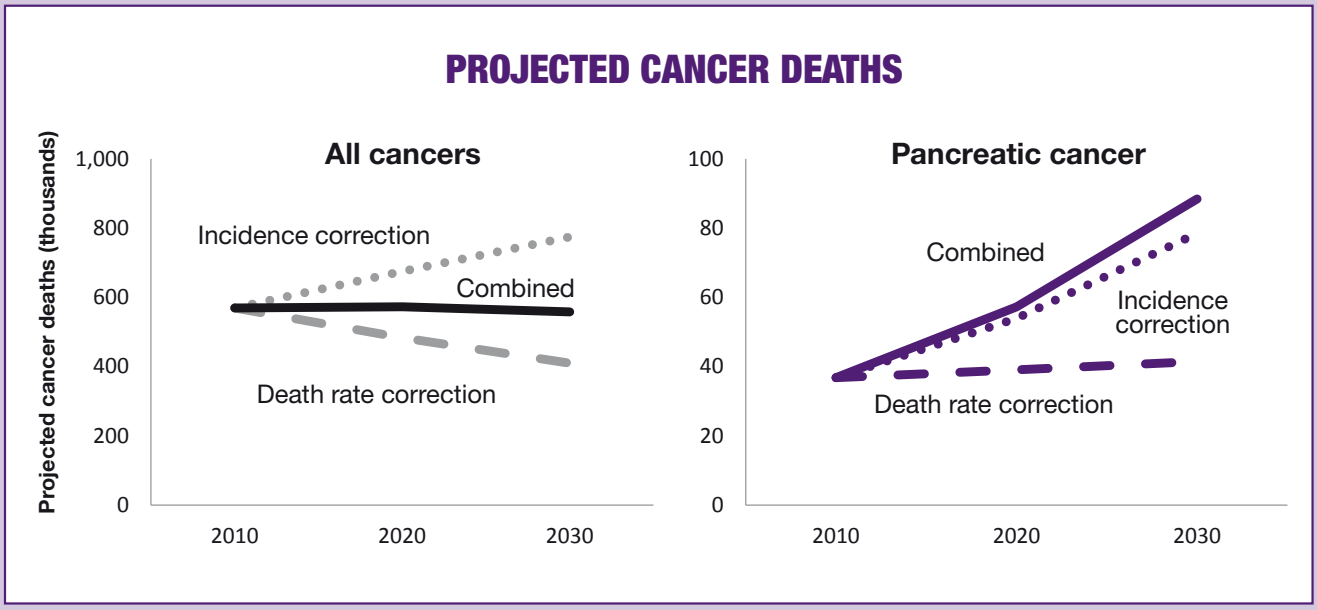
My own political beliefs are that this is a bill that both parties can come together and agree on. It now has a lot of bipartisan support. More politicians on both sides need to stop and think about all of the people who need what this legislation will bring: early diagnostic tools and the road to a cure. This cancer does not discriminate — it attacks both Democrats and Republicans.

diagnosed with pancreatic cancer from the years 2010 to 2030, due to overarching changes to the composition of the U.S. population. This analysis, however, is based on the assumption that the incidence rate of pancreatic cancer will remain constant. The *Annual Report to the Nation* demonstrates that the incidence rate of pancreatic cancer has been rising at an average rate of 1.4 to 1.8 percent each year. Combining the two analyses, we calculated that there could be 94,000 new cases of pancreatic cancer in 2030. ***This figure represents an over two-fold rise in new cases of the disease, making pancreatic cancer the eighth most commonly diagnosed cancer type in women and ninth in men, as compared to ranking 10th today.***

PROJECTING THE NUMBER OF CANCER DEATHS IN 2030

The *Annual Report to the Nation* shows that the death rate (the number of people per 100,000 in the population who die from cancer each year) for almost all cancer types has been decreasing.[5] This change is largely due to continual advancements in cancer treatments, as well as improved early detection, so that surgery or other highly effective approaches to treatment can be utilized. Pancreatic cancer is one of only four cancer types that shows a small but statistically significant increase in the rate at which patients are dying of the disease. Although the reasons for the slight increase in the death rate are not fully understood, what is clear is that the substantial medical advances that have occurred for other cancer types have not translated to clinical benefits for pancreatic cancer patients.

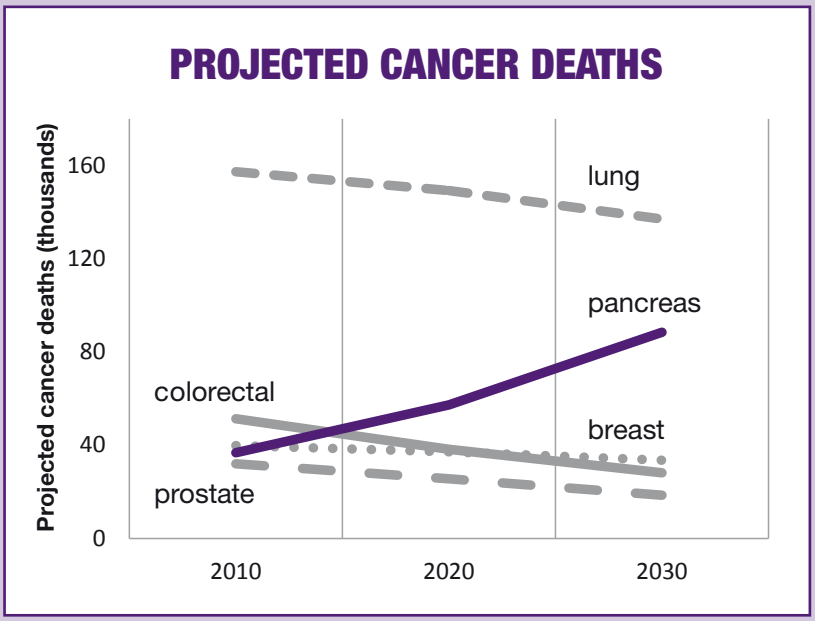
To calculate the projected deaths through 2030, we incorporated the projected increase in the number of



Projected cancer deaths. The number of deaths for cancer in general (solid line, left) is projected to remain relatively constant, whereas deaths from pancreatic cancer (solid line, right) are projected to increase steadily over time. The number of cancer deaths is projected by considering both the change in the number of new cases (incidence correction) and changes in the average annual number of cancer deaths per 100,000 population (death rate correction). Separate values were calculated for men and women and then combined to obtain the value for the total population. The number of projected cancer deaths is expected to rise as a result of the increase in the number of new cases (incidence correction, dotted lines) for both pancreatic cancer and cancer in general. The death rate for cancer in general is decreasing by 1.8% per year for men and 1.5% per year for women, resulting in a decrease in the projected number of deaths over time (dashed line, left). In contrast, the death rate for pancreatic cancer is increasing by 0.6% per year for both men and women, resulting in an increase in the projected number of pancreatic cancer deaths (dashed line, right). When both the increase in the number of new cases and the decrease in the death rate is considered, the projected number of deaths from cancer in general in 2030 is approximately the same as that in 2010 (combined, solid line, left). In contrast, the number of deaths from pancreatic cancer in 2030 is projected to be 2.4 times greater than in 2010 (combined, solid line, right). *Sources and methodology are found in footnote.*[11]

cancer cases described above with any changes in death rates presented in the *Annual Report to the Nation*. We found that the number of people who are expected to lose their lives to cancer in the year 2030 is approximately the same as in 2010. Although more people will be diagnosed with cancer, the death rate has been decreasing due to improvements in treatment and diagnostic tools. So, the numbers balance each other out, leading to about the same number of cancer deaths in 2030 as in 2010.

In stark contrast, we estimate that more than 88,000 people will die from pancreatic cancer in the year 2030, representing a 2.4-fold increase from the number dying in 2010. This trend is because the projected rise in the incidence of the disease is compounded by the projected increase in the death rate. When similar analyses were conducted to predict the number of deaths from the other current leading cancer killers (lung, colorectal, breast and prostate), the data suggest the startling conclusion that ***pancreatic cancer will leap to become the second leading cause of cancer death before 2020, and possibly as early as 2015, only three years from now.***



Projected cancer deaths for the leading cancer killers. Projections of the number of deaths from the current top five cancer killers indicate that pancreatic cancer will become the second leading cause of cancer deaths as early as 2015. The estimated number of deaths in 2010 is from the 2010 ACS Facts & Figures. Combined corrections for both the projected number of new cases and the death rate were made as described for the previous figure.[11] Note that 86,000 deaths from cancer of the liver and 36,000 deaths from cancer of the kidney are projected by 2030 and will exceed breast, colorectal and prostate cancer.

HOW WILL WE COMBAT THE DISPROPORTIONAL PROJECTED RISE IN DEATHS FROM PANCREATIC CANCER?

The alarming increase in the projected number of pancreatic cancer deaths is due to several factors: demographic changes in the U.S. population, a rising incidence rate of pancreatic cancer, and a death rate that continues to go up despite significant improvements for other types of cancer.

Changes to the demographics of the U.S. population cannot be easily altered in the coming years. The aging of our population is in fact cause for celebration – we have been highly effective in reducing mortality from many diseases. Advanced age is the number one risk factor for cancer in general, and pancreatic cancer is no exception.

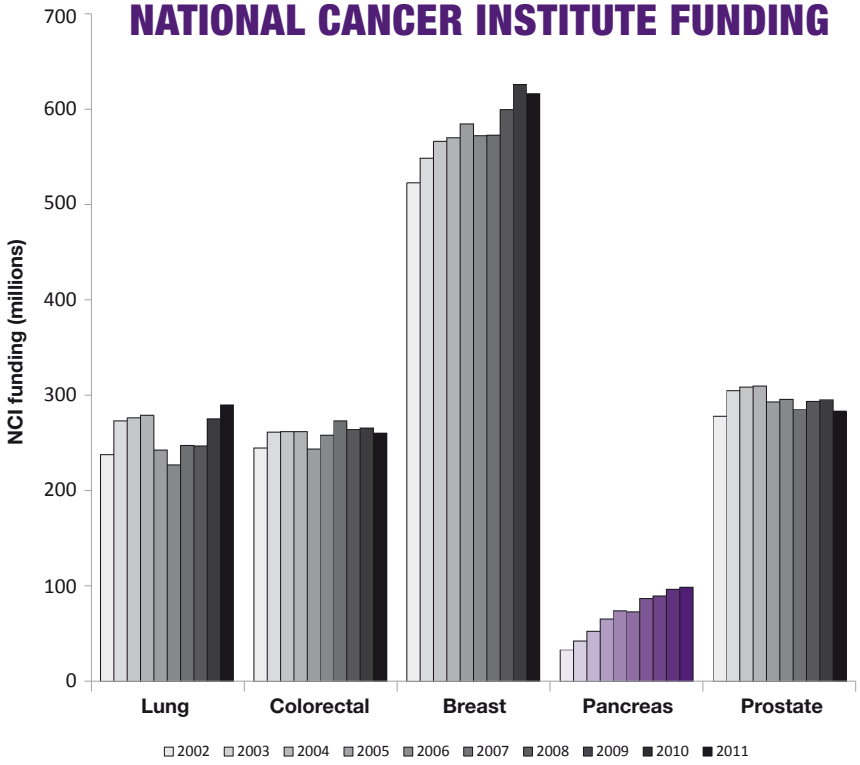
Continued national efforts to fight the obesity epidemic in the U.S. should improve the health of society as a whole, and should have some impact on pancreatic and other cancer types. However, the effect of obesity on pancreatic cancer incidence is relatively modest and obesity is not sufficient to explain the observed rise in pancreatic cancer. A decrease in obesity alone will not halt or reverse the staggering increases projected for pancreatic cancer diagnoses and deaths.

While the projected increase in the incidence of pancreatic cancer may be largely outside of our control, the rise that is expected in the number of deaths can be reversed. Particular scientific challenges have impeded efforts to reduce the mortality rate from pancreatic cancer. (See sidebar on page

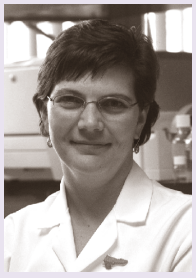
10.) These challenges have been compounded by a historically small, fragmented and underfunded research community dedicated to studying pancreatic cancer. Research advances take considerable time to develop and validate. For example, if laboratory research leads to a new drug that shows promising results in animal models of pancreatic cancer, it would take an average of almost eight years for the necessary clinical testing and regulatory approval to occur before it could be brought to market and have an impact on pancreatic cancer patients.[7] Tragically, the analyses described above show that deaths from pancreatic cancer are destined to rise quickly in the coming years. And as the only one of today's top five cancer killers showing an upward trend in mortality, the time has come to focus a national effort on improving the outcomes from a pancreatic cancer diagnosis.

Increased research attention and resources from the federal government urgently need to be directed towards pancreatic cancer in preparation for the anticipated future burden. Funding for pancreatic cancer research lags significantly behind the other current top five cancer killers. The largest source of cancer research funding in the U.S. is the NCI, which provided just under $100 million in pancreatic cancer research funding in 2011. Although this amount has grown over the past decade, the investment towards this devastating disease is only two percent of the NCI's total budget and is disproportionately low compared to the other top cancer killers.

An increase in funding, however, will not be sufficient in itself to address the rapidly rising need. Real progress in changing the trajectory of the rise in deaths from pancreatic cancer will require a carefully considered



NCI funding. 2002-2011. Data from the NCI budget tool[3]



DIANE SIMEONE, MD: A PANCREATIC CANCER RESEARCHER'S VIEWPOINT

As a gastrointestinal surgeon and pancreatic cancer researcher, I am all too familiar with the dismal outcomes for pancreatic cancer patients. Despite a growing field of scientists and clinicians, we remain deficient in our ability to diagnose and treat this deadly disease. In order to make progress, we'll need to continue to deepen our basic science understanding and increase access to appropriate model systems that replicate human disease in a laboratory setting. Improving patient outcomes can be achieved if we design effective and appropriate clinical trials stemming from rigorous data generated in the laboratory. These investigations require sufficient funding, resources and a multidisciplinary team approach. Pancreatic cancer presents a unique challenge in the laboratory and clinic and requires specialized attention and focus.

Diane Simeone, MD is the Lazar J. Greenfield Endowed Professor of Surgery and Physiology at the University of Michigan and the Director of its Pancreatic Tumor Program. Dr. Simeone has routinely been listed among the Best Doctors of America, Best Surgeons in America, and America's Top Doctors for Cancer. She is a member of the Institute of Medicine, Past President of the Society of University Surgeons and the American Pancreatic Association, and a member of the Pancreatic Cancer Action Network's Scientific Advisory Board.

strategic plan that optimizes any research investment. A long-term and comprehensive strategic plan would ensure that our limited federal resources are targeted to the areas of greatest need and potential for patient benefit, that any potential breakthrough is quickly and thoroughly tested for application in the clinic, and that collaborative efforts and careful combining of complementary expertise, capabilities and infrastructure accelerate progress.

The Pancreatic Cancer Action Network set a bold goal to double the pancreatic cancer survival rate by 2020 as a first step in stemming the rapidly rising threat of pancreatic cancer. The approach is comprehensive and far-reaching. We raise awareness nationwide through a network of Volunteer Affiliates that disseminate information in their local communities to increase the number of patients who see a specialist and get state-of-the-art care and treatment. We provide up-to-date information about the disease to patients and caregivers, including a comprehensive list of active clinical trials with the goal of increasing accrual to accelerate clinical advances. We help convene the scientific community to facilitate the exchange of information and encourage collaborative efforts. Not-for-profit organizations in the U.S., including the Pancreatic Cancer Action Network, provided approximately $13 million in research grant support in 2011.[8] This funding augments the NCI's investment by filling much-needed gaps to increase the number of investigators in the field and support exciting translational research opportunities. Finally, the Pancreatic Cancer Action Network is working at the national level to make sure private and taxpayers' investment in pancreatic cancer research through the NCI is used in the best and most efficient way. Congress is currently debating the *Pancreatic Cancer Research & Education Act* (S. 362/H.R. 733), which seeks to create a long-term and comprehensive strategic plan to accelerate research progress and the development of new tools for the early diagnosis and treatment of pancreatic cancer.

Why has pancreatic cancer been such a challenge?

Studies in the laboratory and clinic have repeatedly uncovered features of pancreatic tumors that make them particularly challenging to diagnose and treat.[9] Symptoms are quite nonspecific, contributing to late diagnoses in the majority of cases. The pancreas is located deep within the body and not routinely screened or imaged, allowing tumors to form and grow undetected for many years. No biomarkers or other novel imaging modalities have proven effective in improving the diagnosis of pancreatic cancer to date.

While other cancer types are thought to metastasize, or spread, late in the progression of the disease, increasing evidence has suggested that pancreatic tumors form small metastatic deposits, or micro-metastases, quite early in the disease progression. Generally, solid tumors are either curable or have a greatly enhanced survivability if the tumor can be caught early and successfully removed surgically, before metastases occur. In the case of pancreatic cancer, even tumors seemingly caught early and surgically resected tend to recur at an astounding frequency, leading to poor survival rates at all stages of disease.

Pancreatic cancer cells have also been found to be extremely resilient and able to grow under very harsh conditions. Unlike many other solid tumor types, pancreatic tumors generate a dense matrix that forms a barrier between them and the normal organ. They do not effectively form their own blood vessels, causing the tumor cells to survive with very little exposure to oxygen. This ability to adapt to a stressful environment contributes to the ability of pancreatic tumors to survive even after treatment with toxic chemotherapeutics or radiation. Moreover, the absence of blood vessels impedes the ability of intravenously administered drugs to reach the tumor, further rendering conventional treatment modalities largely useless.

Finally, the vast majority of pancreatic tumors express a mutant version of a protein called K-Ras. K-Ras mutation leads to an extremely active protein that stimulates constant growth, blocks normal cell death pathways, and allows the tumor cell to obtain fuel in ways that are unique and distinct from normal cells. K-Ras mutation happens early in the development of nearly 100% of pancreatic adenocarcinomas and continues to be a driving force throughout disease progression. While efforts to therapeutically target cancer-promoting proteins have been successful in the treatment of other cancer types, no drugs to date can effectively block the activity of K-Ras. Additionally, the subsets of other solid tumors that are shown to express mutant K-Ras have a significantly worse prognosis than the cases without mutant K-Ras expression.

All these features combine to make pancreatic cancer a formidable enemy in laboratory and clinical settings and underscore the urgent need for more research to speed scientific and medical breakthroughs.

This country must take steps to shine a light on this disease and enact legislation like the *Pancreatic Cancer Research & Education Act*, so that we can identify new paths forward that will finally lead to success. Pancreatic cancer does not need to be the death sentence that it is to most patients today. By understanding the findings outlined in this report and heeding the warnings they offer, we can change the statistics of this disease and prevent the tragedies that loom before us.

Prepared August 2012 by the Research and Scientific Affairs department of the Pancreatic Cancer Action Network: Lynn M. Matrisian, PhD, Rhonda Aizenberg, PhD, and Allison Rosenzweig, PhD.

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[2] http:/seer.cancer.gov/statfacts/html/pancreas.html, accessed July 2012.

[3] http://budgettool.cancer.gov/budget-spending/funding-by-cancer-type/fiscal-year-2011.aspx, accessed July 2012.

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[8] Internal analysis by the Pancreatic Cancer Action Network based on information provided by Lustgarten Foundation, American Cancer Society, American Pancreas Association, Hirshberg Foundation, and American Institute for Cancer Research. Data for the American Cancer Society and the American Institute for Cancer Research were contributed through the International Cancer Research Partnership database, accessed August 2012 (www.icrpartnership.org).

[9] Vincent A, Herman J, Schulick R, Hruban RH, Goggins M. Pancreatic Cancer. *Lancet* 378:607-620, 2011.

[10] Source and methodology for Projected Cancer Incidence: a) Projections due to demographic changes are based on the projections reported by Smith et al (Table1).[4] b) Projections due to changes in the incidence rate were made by applying the delay-adjusted average annual percent change (AAPC) in the incidence rate for 2004-2008 for men and women reported by Eheman et al (Table 1)[5] to the incidence data for men and women reported in the 2010 Cancer Facts & Figures.[6] The AAPC value was adjusted for 10 years for the 2020 projections, and 20 years for the 2030 projections. AAPC values that are not statistically significantly different from zero were considered to be zero. The figures for men and women were combined to derive a figure for the total population. c) Projections due to the combined changes in demographics and incidence rates were made by adjusting the projections for men and women reported by Smith et al (Table 1)[4], and correcting them for the AAPC in incidence rates for men and women that were reported in Eheman et al (Table 1).[5] To account for the fact that the Smith et al projections were based on 2003-2005 data, the adjustments were for 6 years for the 2010 projections, 16 years for the 2020 projections, and 26 years for the 2030 projections. Values for men and women were calculated separately and then added together for the total population value. We thank BD Smith, MD for methodological advice.

[11] Source and methodology for Projected Cancer Deaths: a) Projections for the death rate correction use the estimated number of deaths for men and women reported in the 2010 Cancer Facts and Figures[6] and adjust them by the average annual percent change (AAPC) in death rates from 2004-2008 for men and women reported by Eheman et al (Table 2).[5] The number of deaths was adjusted by the AAPC value for 10 years for the 2020 projections, and for 20 years for the 2030 projections. AAPC values that are not statistically significantly different from zero were considered to be zero. The separate calculations for men and women were combined to derive the projection for the total population. b) Projections for the incidence correction were derived by determining the percent increase in new cancer cases in 2020 and 2030 relative to 2010 from the previous figure, and adjusting the 2010 value for the estimated number of deaths as reported in 2010 Cancer Facts & Figures.[6] These calculations were completed for men and women separately and then combined to obtain a figure for the total population. c) Projections for combined cancer deaths were determined by adjusting the 2010 estimated number of deaths for both the incidence correction and the death rate correction. Values for men and women were calculated separately and added together to derive the value for the total population.

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