THE **DRA** Accelerating Disparity
PROJECT Reducing Advances

THE **BFP Project**
Biomonitoring Futures

**The Biomonitoring Futures Project:
Final Report and Recommendations**

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THE BFP Project
Biomonitoring Futures

Final Report

Executive Summary

Introduction

Health disparities in the United States are a real and unfair burden on underserved populations. There are a number of opportunities for reducing health disparities and the Disparity Reducing Advances (DRA) Project is exploring these opportunities. Biomonitoring is one of the most exciting opportunities for future prevention of disparities. The Robert Wood Johnson Foundation provided funding to the Institute for Alternative Futures (IAF) to explore this opportunity through the Biomonitoring Futures Project. The Biomonitoring Futures Project was designed to forecast advances in disease knowledge, biomonitoring approaches and health information systems. This Final Report and all of the BFP Reports summarized here are available at www.altfutures.com/bfp.

The opportunities and learning presented in this report will be continued through the larger Disparity Reducing Advances (DRA) Project. The DRA Project is a multi-year, multi-stakeholder project developed by the Institute for Alternative Futures (IAF) to identify the most promising advances for bringing health gains to the poor and underserved. Working groups have been developed around a number of these opportunities.

Developing a Network of Stakeholders

The Biomonitoring Futures Project has developed a network of stakeholders, including patients, care providers, funders, and technology developers, to review the advances and determine how best to apply them. As part of this process, IAF reviewed current best practices in biomonitoring for cancer and diabetes, developments in biomonitoring using various platforms or approaches (e.g., blood, breath, physiology monitoring), and forecasts for diabetes and cancer care over the next decade.

IAF assembled an Advisory Committee of experts in healthcare and biomonitoring technology and conducted focus groups with patients and care providers. The learning from the Project has also been shared and disseminated with the sponsors and partners of the larger DRA Project. A list of the Advisory Committee as well as a list of DRA Project Sponsors and Partners can be found in Appendix A. The BFP Advisory Committee gathered on April 5th, 2006 in Alexandria, Virginia. They identified key opportunities and recommendations for advancing the field of biomonitoring and for using

biomonitoring to reduce health disparities. These key opportunities will be pursued through the larger DRA Project and the DRA network of partners.

Assessment of Emerging Platforms for Biomonitoring

This project reviewed current and anticipated developments in various forms of testing. Given the right cost and usability for consumers and community health centers, these tests could lead to dramatically better early detection of disease and pre-disease states, and support better treatment for diabetes, cancer and many other diseases.

Blood & Serum Tests: There are a number of biomarker tests using blood and serum under development that could dramatically change the screening, diagnosis and treatment of disease, especially cancer. It is difficult to tell which tests in development will pass the hurdles of FDA approval, prove effective, and gain market acceptance. However, based on the pace and activity of research, it is likely that there will be a number of changes in the healthcare system based on these tests. Within in the next ten years, most patients will have a pharmacogenomic profile that indicates the likelihood of benefit and side effects from medicines. These profiles will be routinely checked when prescribing drugs. Biomarker tests that determine an increased risk of disease and tests that can identify predisease states as well as sub-types of disease will also become much more common over the next ten years.

Saliva & Oral Testing: An oral test for oral cancer is likely to be available in 2008. Saliva tests for other cancers, including breast and ovarian cancer, will likely take longer. In 2008, it is likely that researchers will have completed the saliva roadmap. This will help researchers to identify molecular signatures for non-cancer diseases such as diabetes and rheumatoid arthritis. Their goal is to identify genetic signatures for at least 10 common diseases by 2007. From there, it will take time to perfect the tests, get them through clinical trials, secure regulatory approval and get the tests to market. This could take at least 3 to 7 years.

Breath Testing: A prototype diabetes testing device is in development and will need to prove acceptable levels of specificity and sensitivity as well as passing FDA certification before it could be used as a screening test. Breath tests for cancer could reach the market soon, with lung cancer as the first

candidate. But there must be clear indications of when they are most beneficial and cost-effective in screening or for monitoring therapy.

Stool Testing: Two very good stool tests for colorectal cancer already exist. One is very affordable and widely available. The other is newer, more expensive and better at detecting early colorectal cancer. Unfortunately, only 22% of those over 50 years old received fecal tests in the past 12 months due to low consumer acceptability with collecting the samples.

Skin Testing: A new test for cholesterol that can be performed on bare skin can be used at community outreach programs and has potential as a home testing device. A novel skin test for prostate cancer is under development. However, the evidence is mixed or inconclusive that early detection of prostate cancer improves health outcomes. A skin test for detecting prostate cancer could be a great advance for reducing health disparities if the test can determine that treatment is beneficial for the individual. Skin tests for glucose monitoring are also in development.

Urine Testing: Current research is looking for specific protein and genetic biomarkers in urine that could be useful in diagnosing cancers and other conditions. Urine testing is relatively inexpensive compared to other forms of testing, but sophisticated gene and protein tests could be quite expensive for the foreseeable future. Qualitative accuracy is good, but variable urine dilution depending upon hydration and other factors make quantitative measurement difficult. This could limit urine testing to screening tests.

Behavioral & Lifestyle Monitoring: A number of new devices have been developed for monitoring the home and for individual use. These devices can gather useful data on motion, body position, body heat dissipation, galvanic skin response, heart rate, breath rate and brain-wave activity. Algorithms can convert the data into measures such as duration of physical activity, calories burned at rest or during activity, times of sleeping and awakening, heart rate, or the effects of anesthesia and sedatives on the brain. Behavioral and lifestyle monitoring, combined with advances in health coaching software, have the potential for encouraging healthy living, and disease management, preventing diseases such as diabetes, and allowing elderly or chronically ill patients to avoid hospitalization.

Imaging Tests: In the future, imaging devices will increasingly be relied upon for early diagnosis, extent of disease and rapidly verifying the benefit of specific expensive therapies. Routine use in community health clinics (CHCs) of the newer and more expensive imaging technologies will likely be a long way off unless the cost effectiveness of treating common severe diseases such as lung or breast cancer is so great as to justify the expense of doing imaging studies.

Health Information Systems 2016

Advances in health information systems by 2016 will change how healthcare is delivered. A national health information system will allow providers to transfer electronic medical records and will improve the coordination of care. Patients are also likely to have access to a personal health record with their health information that they can access through a computer or cell phone. These systems will be interoperable, so that the patient or health care provider can transfer the results of biomonitoring tests from the patient's personal health record and the provider's electronic medical record.

Biomonitoring devices in 2016 will be wirelessly linked to the patient's personal health record. The patient can choose to send this information to their healthcare providers prior to meeting them. The personal health record will also have knowledge technology incorporated in it. This will help patients to use their health data by presenting the data in a format that is easily understandable (i.e. graphs, charts and health warnings), and by searching their health care provider's systems and the internet for health information that is relevant to their unique risk profile and current conditions.

By 2016, the combination of biomonitoring technology with knowledge technology will give patients the tools needed to improve their own health and become more proactive consumers of healthcare. This empowerment of patients through access to their own medical information and information technology can reduce health disparities, if underserved communities have access to these technologies in forms that are linguistically and culturally appropriate.

Diabetes 2016

By 2016, people with risk factors for diabetes will be screened routinely. This will be accomplished using blood glucose tests currently available in 2006, but there may also be less invasive screening tests available using other platforms. Early identification of the disease will be followed with effective health/behavior change interventions. Health care payors will routinely pay for effective health/behavior intervention from a range of health care providers, including CHCs.

Body monitors are commonly used by patients to manage diabetes and other chronic diseases and improve health by 2016. A small wearable body monitor keeps track of motion, heart rate, breath rate and other measures of general health. The body monitor can keep track of a patient's caloric expenditure and stress levels, and automatically uploads that information into the patient's personal health and medical records. This information is combined with other biomonitoring devices such as a glucometer, blood pressure cuff, weight scale and cholesterol tests to identify patterns that contribute to ill health. Health coaching software works with the patient and her healthcare provider to set personal health goals for weight loss, diabetes and cancer prevention and stress reduction.

In 2016, those with diabetes have access to biomonitoring devices linked to insulin delivery systems. These systems will take the form of an external closed-loop insulin pump and monitoring device. The complexity and expense of the system limit closed-loop systems to a smaller category of diabetics with severe cases of the disease.

Cancer 2016

By 2016, advances in biomonitoring and biotechnology have improved the prevention, early detection and screening of cancer. Newer blood tests that identify genes and proteins allow providers to predict the risk of future cancers, and diagnose early, asymptomatic (even precancerous) disease for a variety of cancers. Combined with better health information systems, and lifestyle biomonitoring, doctors and patients have better tools for preventing cancer. Blood based and imaging biomarker tests also help doctors to identify subtypes of cancer and for personalizing therapy.

By 2016, molecular imaging will allow doctors to visualize early cancer changes years before symptoms appear. The identification of asymptomatic or precancerous disease opens up new, less aggressive therapies for cancer. Imaging will also be used to determine within a couple days whether a new therapy is working. The imaging agent can also be combined with a therapy to specifically target cancer cells without harming normal tissue. While this will be much more expensive, it will dramatically improve quality of life and reduce the need for more aggressive chemotherapy and more expensive personalized therapy for many cancer subtypes. It is likely that these interventions will be used for difficult to detect and manage cancers, and will mostly be performed at cancer centers rather than local hospitals and clinics.

Key Opportunities for Reducing Health Disparities

The Biomonitoring Futures Project identified four key opportunities for biomonitoring based on the input from the BFP Advisory Committee. These key opportunities have the potential to reduce disparities in health if they can be effectively developed and deployed in underserved communities. These key opportunities as well as the use of cell phones to reduce health disparities were further explored by committees developed by the DRA Project. These opportunities will be further pursued by the DRA Project in 2007 and 2008.

Continuous, Passive Biomonitoring for Health and Prevention: A number of new technologies are available for personal and home use that can monitor mobility, sleep patterns and general activity. In the home, these technologies are already being used to monitor elderly patients and patients with chronic conditions. Personal, continuous, passive monitors can monitor physiological parameters such as motion, body heat, heart rate, and breath rate. Using sophisticated algorithms, these parameters can provide useful information such as energy expenditure and physical activity. Combined with software for health coaching, these monitors can improve health and help manage diseases such as diabetes. Their continuous information gathering is likely to yield new insights into disease and general health enable new, appropriate definitions of "norms" or "normal ranges" both for individuals and populations groups (e.g. by age and disease conditions).

The DRA Project has formed a working group to explore opportunities for continuous, passive biomonitoring. This working group will develop pilot tests with local health care providers using biomonitoring systems from BodyMedia and the Medical Automation Research Center (MARC). BodyMedia provides continuous body monitoring solutions for individuals and healthcare practitioners. MARC, at the University of Virginia Health Sciences Center, is a research, development and consulting organization focusing on monitoring and automation.

Automated Control of Insulin Levels: A committee was developed to pursue this opportunity. On further evaluation, the committee considering this topic did not find automated control of insulin levels a good candidate for reducing disparities. The challenges for engineering a closed-loop system are considerable. Such monitors have to be robust enough to withstand continuous use while accurate enough to monitor changes in blood sugar from activities such as exercise. Due to these challenges, it is unlikely that an internal closed loop biomonitoring and insulin pump system will be available for widespread use by 2016. It is likely that current systems will evolve to create an external closed-loop system. However, the cost and complexity of the system will likely limit its use to diabetics with severe forms of the disease.

Early Detection of Cancer Using Blood Screening: A large component of health disparities in cancer are due to cancers that are not identified early. New and more accurate tests for screening and early diagnosis could dramatically reduce disparities through the early detection of cancer in underserved populations. Some of the tests under development will be easier to use and more accurate than existing tests. Other tests will screen for cancers for which there are currently no appropriate tests. While saliva, breath and other platforms may advance, blood tests for pre-cancer and cancer markers are further along in development and are likely to be used by health care providers. However the costs of some of these tests are likely to be significant. Reducing health disparities will require not only improvements in cancer screening tests, but also a commitment to making these tests available to everyone who needs them.

Community and National Biomonitoring to Support Upstream Change: A major opportunity to reduce both health disparities and the cost of care will be to target at risk populations at the community

and national level. Biomonitoring and environmental monitoring data collected at the individual level and the community level can be used to better understand the causes of ill health and of disparities in health. This information can be used to move upstream, targeting root causes, and support changes in individual behavior, public policies, market practices, and health care. Protections of privacy and security, and protection against discrimination will need to be in place for these biomonitoring advances and their benefits to communities to be effective.

Using Cell Phones to Reduce Health Disparities: The use of cellphones as a platform for biomonitoring is another promising opportunity. Cellphones can record information or convey biomonitoring data from an individual to data storehouses or to their health care provider. By 2016, it is possible that current cell phone service will be replaced by a mix of WiMax, and other wireless access to the internet that includes telephone services. These options need to be monitored for their impact on reducing disparities. However cell phones and biomonitoring, by themselves, will not reduce health disparities. But, if they help to provide better management of disease by patients and their doctors, and if they reinforce healthy behavior, their impact could be significant.

Recommendations for the Field

The Advisory Committee also developed a number of recommendations for effectively advancing and using biomonitoring to reduce health disparities. These recommendations will be pursued through the larger DRA Project, where a number of the key organizations listed are partners in the DRA Network. The recommendations developed are below:

- Health Resources and Services Administration (HRSA) and the Centers for Medicare and Medicaid Services (CMS) should enhance partnerships for evaluating the intersection of biomonitoring platforms, specific disease biomarkers, and Community Health Centers (CHCs).
- The Clinical Director's Network and other appropriate groups should help design and implement controlled studies of effectiveness of biomonitoring systems in CHCs as well as diffusing best practices.
- Major federal agencies involved in funding research, such as the Department of Defense (DoD), the National Institutes of Health (NIH), and the Department of Veteran's Affairs (VA), should

develop more coherent early stage funding programs based around biomonitoring for disparity reduction.

- The DRA Project should work with industry associations, such as the Pharmaceutical Research and Manufacturers of America (PhRMA) and the National Electrical Manufacture's Association (NEMA), on their member's biomonitoring activities and opportunities for reducing health disparities.

- The Food and Drug Administration (FDA) should encourage testing and evaluation of biomonitoring devices among populations with less access and resources.

- Forecasts or estimates of platforms under development or in consideration as well as potential disruptive innovations should be publicly available and shared with key stakeholders.

- Efforts should be made to enhance the ability of CHCs and others to design, deploy and evaluate experiments/tests of potential biomonitoring advances.

- Work with organizations to support the development of interoperability standards for biomonitoring devices.

- Review and encourage reimbursement strategies for effective biomonitoring, especially around prevention.

- Identify specific forums and support a web based directory for biomonitoring technology, drug and device companies as well as early stage researchers, payors and healthcare providers to network around biomonitoring for disparity reduction (similar to Medical Automation.org).

Introduction

Health disparities in the United States are real and they are an unfair burden on underserved populations. However, health disparities are avoidable through improvements in prevention and care. Awareness of health disparities is growing as is the support for preventing and reversing disparities. There are a number of opportunities for reducing health disparities and the Disparity Reducing Advances (DRA) Project is exploring these opportunities. Biomonitoring is one of the most exciting opportunities for future prevention of disparities. The Robert Wood Johnson Foundation provided funding to the Institute for Alternative Futures (IAF) to explore this opportunity through the Biomonitoring Futures Project.

The Biomonitoring Futures Project was designed to forecast advances in disease knowledge, biomonitoring approaches and health information systems. The Project focuses on the ability of these advances to reduce health disparities for cancer and diabetes as well as improving health promotion. Supported with a grant from the Pioneer Portfolio of the Robert Wood Johnson Foundation, the Biomonitoring Futures Project is a component of the Disparity Reducing Advances (DRA) Project, a multi-year, multi-stakeholder project developed by the Institute for Alternative Futures (IAF) to identify the most promising advances for bringing health gains to the poor and underserved. This Final Report and all of the BFP Reports summarized here are available at www.altfutures.com/bfp.

The Biomonitoring Futures Project looked at biomonitoring technologies for prevention, screening and treatment of cancer and diabetes. Cancer and diabetes are two diseases with high incidence of disparities. The project also looked at the use of biomonitoring for health and prevention as well as the information infrastructure needed to link the data from biomonitoring devices to the larger care system. These biomonitors will in most cases not reduce health disparities by themselves. They can complement ongoing prevention and treatment efforts and require other factors such as appropriate access to care, compliance with treatment regimes and environmental changes to be effective.

A number of biomonitoring advances will be available over the next ten years to prevent and reverse health disparities. New technologies for the detection of cancer will create opportunities for early stage cancer detection. Continuous, passive biomonitoring will provide new ways to assist patients and

providers in the prevention and management of diabetes. Information systems will be linked together to transfer health information from biomonitoring devices to healthcare systems to improve treatment. In ten years, the cell phone will be increasingly used as a platform for biomonitoring and health coaching.

The opportunities and learning presented in this report will be continued through the larger DRA Project. Working groups have been developed around a number of these opportunities. They will look to develop pilot projects to identify and accelerate the use of biomonitoring in underserved populations.

Developing a Network of Stakeholders

The Biomonitoring Futures Project has developed a network of stakeholders, including patients, care providers, funders, and technology developers, to review the advances and determine how best to apply them. As part of this process, IAF assembled an Advisory Committee of experts in healthcare and biomonitoring technology. It has also conducted focus groups with patients and care providers. The learning from the project will also be shared and disseminated with the sponsors and partners of the larger DRA Project. A list of DRA Project Sponsors and Partners can be found in Appendix A.

Background

The next decade will see dramatic advances in biomonitoring, including early indicators for cancer, diabetes and other chronic diseases. In addition to advanced biomarkers, there will be new and simpler ways of testing. The results from these biomonitoring devices and biomarker tests will be integrated into the electronic health record accessible by individuals and their health care providers.

This report looks at current best practices in biomonitoring for diabetes and cancer and current research and development in biomonitoring. It forecasts the development of different biomonitoring approaches and their impact on the two important diseases with high incidents of disparities: cancer and diabetes. This report also looks at the potential of biomonitoring to encourage healthy living and preventing disease before it occurs.

As part of the project, IAF gathered a group of experts in healthcare and biomonitoring technologies to identify key opportunities and make recommendations for using emerging biomonitoring technologies

for reducing disparities in healthcare. The BFP Advisory Committee met on April 5th, 2006 in Alexandria, Virginia. They identified key opportunities and recommendations to advance the field of biomonitoring and to use biomonitoring advances to reduce health disparities. Through the summer of 2006, these key opportunities were further explored through the DRA Project.

This report will present current best practices, assess an intriguing range of biomonitoring platforms under development, and then provide general forecasts to 2016 about developments in health information systems and biomonitoring specifically for diabetes and cancer. Forecasts prepared by the BFP project will be shown in italics. This report ends with the results of the Advisory Committee Meeting providing criteria for biomarkers as disparity reducing advances, the results of the DRA Committees for key opportunities in biomonitoring, and recommendations for key players for promoting the development of biomarkers as disparity reducing advances.

Key Current Conditions and Best Biomonitoring Practices: Diabetes and Cancer

Two high disparity diseases that offer particular promise for biomonitoring were chosen as the focus for the project: diabetes and cancer. For the Biomonitoring Futures Project, IAF focused on these two conditions in order to dig deeper into current best practices for biomonitoring and how future biomonitoring technologies will change those practices in 2016. Diabetes and cancer were chosen for two reasons. Both have significant health disparities in screening, treatment and prevalence.[1] They are also diseases which are characterized by extensive use of biomonitoring and biomarker detection.

Current Conditions - Diabetes

There is a looming diabetes crisis in the United States. The prevalence of diabetes increased 5% annually over the past five years with an estimated 1,500,000 new cases in 2005 for a total of 20.8 million patients with the disease (14.6 million diagnosed and 6.2 million undiagnosed).[2] If this trend continues there will be at least 30 million[3] and possibly even 35 million[4] people with diabetes in 2015. The risk of an American male getting diabetes in his life time is 1 in 3 whereas females have a 2 in 5

chance.[5] Minorities have an even higher lifetime risk: 53% for a Mexican American female and 49% for a Black female.[6]

The primary factor accelerating the incidence of diabetes appears to be the epidemic of obesity. Currently, two-thirds of American adults are overweight with almost one-third reaching the obese level (greater than 30% body fat).[7] A new Framingham heart study concludes that 80% of White Americans will become overweight during their lifetimes with 40-50% going on to obesity.[8] This is likely to be higher in minorities. Obesity is becoming a disease of the young with 15% of 6-19 year old being overweight (23% for Blacks and Hispanics).[9] Type 2 (adult onset) diabetes was until recently unheard of in children, but now it makes up 40-50% of cases with the rest being type 1 diabetes. Children as young as four have been found with abnormally high insulin levels and 13% of all children have elevated cholesterol levels.[10] These trends portend rising numbers of young adults with diabetes and cardiovascular disease.

The most effective way to prevent this coming epidemic of obesity and its negative effects on health is to change the communities in which we live. We live in an obesogenic environment where exercise has been engineered out of our daily lives and high calorie food is ever present. Changing the obesogenic environment will require large changes in how we build our communities, how we structure our lives and our values as a society. It also requires a change in how society addresses the social determinants of health, such as the elimination of poverty.[11] Until there is a value shift in our nation that addresses these societal factors, the health care system will be faced with ever rising numbers of diabetic patients, especially from underserved communities.

Apart from a value shift in the way we structure our communities, there are proactive steps the health care system can take to deal with both the epidemic of diabetes and its disparities in health. The medical professions are becoming aware of the need for action using as a model the effective campaigns against smoking and encouraging seat belt usage. The most comprehensive approach for reducing the potential disease burden would be to address the major risk factors simultaneously – obesity, physical inactivity,

smoking, hypertension, hyperglycemia, hyperlipidemia – that predict the development of several major chronic diseases – diabetes, cardiovascular disease, cancer and dementia.[12]

Routine screening of those with risk factors for diabetes and aggressive primary intervention for those with pre-diabetes would dramatically lower the numbers of patients with diabetes. It would also lower the disparities in the prevalence of diabetes since poor nutrition and a lack of physical activity are risk factors that lead to disparities in diabetes.[13]

Current Best Practices for Biomonitoring - Diabetes

The use of biomonitoring to screen, diagnose and manage diabetes is well established. Community Health Centers also deal with diabetes on a daily basis, both in diagnosis and management. Glucose testing is used to diagnosis diabetes and pre-diabetes. Glucose testing requires drawing blood for a lab test and is extremely accurate. The test requires a trained individual to draw the blood and the cost of the lab test ranges from $8 and up. Using a glucometer for screening at health fairs has been successful, but is currently discouraged because it is too easy to lose patients for follow-up. This type of screening would require less training, is easier to use outside the clinic and costs about $1 for the test strip. Many glucometers are accurate to within 5% of reference tests, but other sources suggest 10-15% error rate in real conditions. This makes glucometer testing less than ideal for screening. What is missing is an accurate noninvasive device for screening that could be easily used in clinic, workplace, mall, health fair, home, etc.

Blood glucose readings and Hemoglobin A1c are the mainstays of diabetes management. Glucose monitoring ranges from 3 or more times a day for severe cases to 1 time a day (or less) for other cases. The average glucometer costs between $42 and $66 and comes with 100 test strips. Additional test strips cost between $.75 and $1, and this cost is a significant barrier to effective diabetes management for the uninsured. What is needed is an accurate, inexpensive, non-invasive device to monitor blood sugar.

Researchers have been trying for years to create effective noninvasive methods for determining blood glucose using infrared spectroscopy, iontophoresis and sonophoresis as ways to measure serum through the skin. The Glucowatch was such a device, but it was expensive and of limited clinical usefulness. It is

realistic to expect that technical obstacles will be overcome with a suitable device likely available by 2016. Effective noninvasive testing devices with high accuracy will also dramatically improve screening for diabetes and hyperlipidemia.

Hemoglobin A1c is the most effective test for measuring compliance with therapy as it tells whether the diabetes is under good control. Recommended testing is once every six to twelve months depending on the severity of the case. An in- house lab can do the test for as low as $6 dollars. Outside lab cost can be as low as $3 dollars or as high as $65 per test. A home test kit is available for $20. This home testing kit for HA1c could improve a patient's ability to monitor his diabetes provided the information comes to him in a format he can use and if the test is affordable.

Inexpensive home test kits are now available for hemoglobin A1c, LDL and HDL cholesterol and triglycerides. It is important for patients to receive periodic feedback about how well they are managing glucose, blood pressure or lipids. Patients tend to stop taking medicines after a few months because they have no symptoms and can't tell that the drugs are making any difference.

A Korean company makes a cell phone that has an internal glucometer and a motion sensor for monitoring daily exercise. The results are stored and can be sent to health providers. The cell phone (or personal computer or PDA) can be used to give the patient reminders about care, to provide information from the Web and to easily consult electronically with a nurse. Healthpia introduced this cell phone glucometer with diabetes management services in the US in the Fall of 2006. With increasing artificial intelligence capabilities the glucometer, cell phone or computer will assess lab trends and give the patient recommendations for better management of glucose or lipids. The "Glucoboy" was an early example of a game that promotes effective management. It is a Gameboy attached to a glucometer. The patient gets access to higher levels of a game if her blood sugar is under better control from appropriate testing and insulin usage.

Current Conditions - Cancer

Cancer has become the leading cause of death for those less than 85 years of age. One half of men and one third of women will develop a cancer during their lifetimes. While the death rate has dropped by 60% (age-adjusted per 100,000) for heart disease and 70% for stroke between 1950 and 2002, cancer rates are essentially unchanged.[14] Since 1993 the death rates from the four most common cancers – breast, colon, lung and prostate – have been declining about 1% per year, but for other cancers the decline has been minimal.[15] Overall, cancer incidence rates have been dropping about 0.5% per year for the past 15 years, but still 1,373,000 new cases of cancer will be diagnosed in 2005.

Lifestyle choices have a clear correlation with many types of cancers. Cigarette smoking alone is directly responsible for 30% of all cancer deaths. Cigarette smoking is the cause of 87% of lung cancer deaths and is responsible for most cancers of the larynx, oral cavity and pharynx, esophagus and bladder.[16] Obesity and physical inactivity may account for 25% to 30% of some major cancers including cancers of the colon, breast (post-menopause), uterine lining, kidney and esophagus.[17]

There are clear health disparities in cancer detection and treatment. Underserved populations are more likely than the overall population to develop and die from preventable cancers, miss regular screening and be diagnosed with late-stage cancers, receive no or sub-standard treatment, die from cancers that are generally curable and suffer from pain due to inadequate treatment.[18]

Disparities differ by cancer type, but overall, African Americans are affected disproportionately. They are more likely to die of cancer than people of any other racial or ethnic group. From 1997 through 2001, the average annual death rate per 100,000 people for all cancers combined was 253 for African Americans, 200 for white Americans, 137 for Hispanic Americans, 135 for American Indians/Alaska Natives, and 122 for Asians/Pacific Islanders.[19]

However, much of the disparities among racial and ethnic groups may be due to factors associated with socioeconomic status rather than ethnicity. Studies have found that socioeconomic status predicts the likelihood of a group's access to education, certain occupations, and health insurance, as well as income

level and living conditions -- all of which are associated with someone's chance of developing and surviving cancer.[20]

Ensuring that all populations have access to appropriate cancer screening services is a core element of reducing cancer health disparities. Screening for colorectal, breast and cervical cancer can reduce the chance of illness and death through early treatment. These three cancers account for close to a fifth of all cancer deaths in the United States.[21] Current and best practices for two of these cancers, breast and colorectal cancer, are highlighted below. The third, lung cancer, does not have an effective screening test, although there is significant biomarker research dedicated to this end.

The use of biomarkers for cancer screening and management varies significantly by the type of cancer. Community Health Centers can do screening for common types of cancers, but almost always must refer patients to specialists for definitive management. Across all types of cancers, there is a need for genetic tests for risk identification and simple screening tests that can be used in Community Health Centers.

Best Practices for Biomonitoring - Cancer

Breast Cancer

Breast cancer is the most common type in women representing 32% of all cancers (excluding skin cancers). About 211,000 new cases of invasive breast cancer will be diagnosed in 2006 with the incidence increasing 0.3% per year. With an estimated 40,400 deaths in 2006, breast cancer is the second leading cause of cancer deaths in women (behind lung cancer), representing 15% of all cancer deaths. The death rate has been declining about 2.3% per year since 1990 due to earlier diagnosis and more effective treatment.[22]

Breast cancer can be prevented with physical activity and diet. Physically active women can reduce their risk by up to 40 percent. Most evidence suggests that physical activity reduces breast cancer risk in both pre-menopausal and postmenopausal women. Obesity increases the risk of breast cancer in post-menopausal women. Obese women have 1.5 times the risk of women of a healthy weight and are also at increased risk of dying from breast cancer after menopause compared with lean women.[23] Scientists

estimate that about 11,000 to 18,000 deaths per year from breast cancer in U.S. women over age 50 might be avoided if women could maintain a BMI under 25 throughout their adult lives.[24]

Regular screening is vital for reducing mortality, but there are clear disparities in screening rates. The disparities in screening are clearly linked with disparities in income, education and insurance coverage.[25] A mammogram every 1–2 years can reduce the risk of dying of breast cancer by approximately 20%–25% over 10 years for women aged 40 years or older.[26]

Screening mammograms are uncomfortable, expensive ($100-$150 a test), can miss early cancers and have a high rate of false positives. About 80% of biopsies of suspicious areas turn out negative. A computer aided detection (CAD) mammogram can raise the cost by $15-$20 dollars. But CAD mammograms may be more accurate than regular mammograms, and there will likely be a shift over the next few years to CAD mammograms in radiology departments. BRCA 1 and BRCA 2 testing can identify those with high (80%) risk of breast cancer. The cost of the sequencing test for BRCA 1 and 2 can run up to $3,000 dollars and is recommended only for those with a strong family history of breast cancer or those of Eastern and Central European (Ashkenazi) Jewish ancestry.

Imaging tests are often used along with a biopsy to diagnose and assess breast cancer. Imaging tests can range from $500 to $700 for a CAT scan to $2,000 for a PET scan. Imaging tests are important for identifying the spread of the cancer. Tests to characterize the tumor for therapeutic options are also available. HER2/neu testing is used to identify a particularly aggressive subtype of breast cancer that occurs in 1/3 of breast cancers. This subtype of cancer can be treated more effectively with a combination of Herceptin and chemotherapy. Other tests such as p53 tumor suppressor gene, epithelial growth factor receptor, and micro-vessel density are being studied.

Colon Cancer

Colorectal cancer is the third most common cancer with about 145,300 new cases per year, and the second most common cause of cancer death with 56,300 expected to die in 2006. Seventy-two percent of the cases arise in the colon with the rest originating in the rectum. The incidence has been declining since 1998, probably due to better detection and removal of precancerous polyps. The death rate has

been steadily declining for many years (from 35 per 100,000 men in 1975 down to 24 in 2000). This likewise has been due to earlier and more effective treatment.[27] Both incidence and mortality for colorectal cancer is higher among African Americans than any other racial or ethnic group.[28]

Like breast cancer, colon cancer can be prevented through lifestyle choices and regular screening. Individuals who are physically active can reduce their risk of developing colon cancer by 40 percent to 50 percent.[29] Colon cancer is also more common among those who are obese than those of a healthy weight. The links between physical activity, weight and risk for colon cancer are stronger for men than women.[30]

There are good screening tests for colon cancer but unfortunately they are often not used. It is believed that 50% of colon cancer deaths could be prevented by screening. There are a few factors for the low screening rate. One is a lack of insurance. Another part of the problem is the health care system doesn't push for testing, and the patient doesn't follow through with tests. Another problem involves culture or embarrassment with the tests.

There are two common types of tests for colon cancer: fecal testing and colonoscopy. Testing for blood in the stool (fecal occult blood test) can lower mortality 15-33% with screening and ranges from $8 to $40 dollars a test. Fecal DNA tests are currently under study and cost from $400 to $800 a test. Colonoscopy is the "gold standard" of testing for colon cancer, but still misses 10-20% of small polyps in the colon. It is uncomfortable, requires sedation and costs between $800 and $1,600. Virtual colonoscopy, which uses high resolution CT scanning, allows the patient to avoid the colonoscopy, although he would still have to undergo an uncomfortable bowl preparation. The cost is $1,200, but the effectiveness of a virtual colonoscopy vs. a traditional colonoscopy has yet to be determined. What is needed is a simple screening test with high specificity and sensitivity such as DNA, mRNA or protein blood test (all of which are in various stages of R&D –see below). A predictive test that would identify genetic patterns highly correlated with specific cancers is also needed and is probably in the early stages of development.

Lung Cancer

Lung cancer is the biggest cancer killer with 163,500 deaths expected in 2006. The incidence has been declining since the early 1990s in men and is just coming off its peak in women due to the decline in smoking several years earlier. However, because most diagnoses are made late, the five year survival is still only 15% overall. Lung cancer is the second leading type of cancer (behind prostate in men and breast in women) with 172,500 new cases being diagnosed this year. Advances in targeted therapy are just becoming available for lung cancer.[31]

Lung cancer is characterized by a striking disparity in incidence and mortality among African-American men compared to all other ethnic groups. The incidence and mortality for African-American men are 113.9 and 101.3 per 100,000 men compared to 77.8 and 76.3 per 100,000 men in the larger population.[32] Cigarette smoking or passive exposure to cigarette smoke are believed to be the cause of 87% of lung cancer deaths.[33] Smoking rates among African-Americans have historically been higher than the general population. However, effective anti-smoking campaigns have lowered the percentage of current African-American adults who smoke to a lower percentage than whites.[34] These gains might be in jeopardy as cigarette companies become more aggressive in targeting African-American and Hispanic communities with advertising.[35]

A screening test that provides early diagnosis for lung cancer is needed. Chest x-rays are becoming uncommon for lung cancer screening. By the time the tumor is large enough to appear on an X-ray, it is often in an advanced stage. Results of a recent study found that CT scans are able to detect lung cancer at its earliest and most curable stage in 85% of patients. When followed by prompt surgical removal, those patients had a 10-year survival rate of 91%. This is a remarkable survival rate since most lung cancer patients die within two years of diagnosis. Critics of the study point to the lack of a control group, high false positive rates and the high cost of CT scans.[36] The cost of CT scans ranges from $250-$750 and requires expensive equipment, trained technicians and radiologists. Experimental tests looking at the DNA changes in bronchial cells and the breath analysis of volatile organic compounds are ongoing.

Assessment of Emerging Platforms for Biomonitoring

This section reviews current and anticipated developments in various forms of biomonitoring using blood, breath, saliva, urine and other platforms for identifying, diagnosing and managing prediabetes and precancer conditions. This report describes current test development and the potential these advances may offer. Where outcomes data is available, this paper reports on the degree of success or failure for these tests.

Developers of these tests are enthusiastic. Yet realities often fall short of the promise. For example, a saliva test for HER2/neu in women with breast cancer was being tested in clinical trials in 2002 with hope of FDA approval in 2003. There was a flurry of articles at that time. But there has been no further publication on these trials, and the test developer's website is no longer available. The promise, particularly if companies are seeking more investment capital or buyers, often far exceeds ultimate success.

However, at least some of the tests identified here will likely prove successful. Given the right cost and usability for consumers and community health centers, these could lead to dramatically better early detection of disease and pre-disease states and support better treatment for diabetes, cancer and many other diseases.

The following sections deal with blood and serum testing, saliva and oral testing, breath testing, stool testing, skin testing, urine testing, behavioral and lifestyle monitoring, and imaging tests. Each section is preceded by a summary forecast for 2016. These forecasts will be provided in italics. There is great uncertainty in each of these areas – the summary forecasts are conservative estimates of what is likely to be available in a decade. Each section ends with a "bottom line" summary of the potential for disparity reduction using that platform for biomonitoring. These sections abstract from the full BFP Paper on this topic (BFP Paper #4). That paper with its more complete description of these platforms and some other emerging approaches (e.g. dog sniffing) are available at www.altfutures.com/BFP.

Blood and Serum Tests

Forecast: *By 2016, the developments of gene and protein biomarker tests have changed the healthcare system. Personalized therapies based on biomarker tests have become much more common. Personalized assessments of risk tied to strategies for prevention have also become more common.*

Blood is the ideal medium for monitoring health and detecting disease. It is the body's transport system hauling nutrients, wastes, disease causing pathogens and hormones everywhere. Rapid circulation and mixing means plasma is representative of the body's chemical balance. A sample from a vein or finger stick is likely to contain a few molecules of an abnormal protein or other substance created by a disease state somewhere in the body. Sampling is easy, but the slight pain of blood drawing keeps some people away from appropriate testing. Only those with the motivation of a serious disease typically draw blood samples at home for monitoring on a routine basis. New testing technologies can detect incredibly small amounts of a substance and many devices run autonomously with high accuracy making them ideal for point-of-care and home use.

Rapid advances are being made in analyzing proteins and gene markers, often discerning unique patterns of hundreds of elements looking for characteristics consistent with disease states, especially cancers. This research is very complex and it is unknown how long it will take for effective tests to reach the market. The big challenges for clinical application are specificity for a particular disease, (proportion of people without the disease who have a negative result) and sensitivity (proportion of people with the disease who have a positive result), complexity of doing the test and the cost. A good example of the problem is the PSA test for prostate cancer where a low value does not rule out cancer. Benign conditions can cause an elevated value and an abnormal value doesn't tell if the cancer is indolent or aggressively growing. The result is a lot of negative biopsies (finding no cancers) and conflict over appropriate management. There will be announcements of many promising biomonitoring tests over the coming years. The challenge for clinicians, administrators and payors will be to put these tests into proper context and selecting those that are truly valuable and cost effective.

Mechanism of Action

There are many technologies for evaluation depending upon the substance to be measured. Anything circulating in the blood – electrolytes, plasma proteins, sugars and fats, blood elements such as neutrophils, pathogens such as HIV, toxins, abnormal genetic or protein products of disease, and other

substances can all be measured. Standard tests are automatically done in self contained units, and many are suitable for point-of-care or home use. Sampling usually requires blood drawn from a vein or a finger stick. With micro-technologies, sample sizes are often a drop or even much less. Blood spot testing uses a finger prick to place a couple drops of blood on filter paper where it is dried and sent to a lab. In some cases a series of tests can be done on the sample. This is a simple, inexpensive, highly accurate way to get selected blood tests that should have wide acceptance for empowered patient self-management. Noninvasive testing technologies are also being researched for blood glucose testing.

Potential Applications

Blood testing has a wide variety of applications for multiple diseases. Blood testing is currently being used for screening for disease, determining diagnosis and sub-diagnoses, identifying specific etiologies, assessing risk of developing future diseases, managing disease, estimating prognosis and for all aspects of biomedical research. Two areas of particular interest are in noninvasive testing and new protein and gene biomarker tests.

Noninvasive testing methodologies have long been needed for people with diabetes who must do multiple daily blood glucose tests. A number of different methods are under development including using micro-needles, transdermal serum technologies, implanted probes and even fiberoptic nanowires for sampling. There is even a device that shines infrared light into the sclera of the eye to record the changes in light frequencies reflecting off hemoglobin molecules in the blood (similar to the pulse oximeter). A number of these non-invasive or semi-invasive tests have reached market in recent years, but have not proved practical for everyday use. They have required regular checks by traditional blood glucometers to ensure their readings are accurate. A practical commercial product suitable for routine daily use is likely within the next few years, although it is not clear which technology, or combination of technologies will be successful.

Researchers are aggressively looking for ways to assess proteins and genes in the blood to forecast the risk for serious diseases, make early diagnoses before symptoms develop and help guide therapy. This is a very complex undertaking and most tests are still experimental. While the goal has been to find effective early screening tests for cancer, there usually are not enough abnormal proteins circulating in

the blood to be detected until the tumor is large enough to be detected in other ways. Tests that look at genes to characterize cancers require analysis of biopsies of the cancer cells themselves. Effective screening tests may still be a few years off.

Genetics

Genetic variations, mostly consisting of scattered changes to single letters of the DNA code (called single nucleotide polymorphisms or SNPs), might be responsible for a disease or make a person more susceptible to getting a disease. Genetic testing is already available. Anyone can go online to labs of questionable standing for DNA tests ranging from paternity testing ($125) to genetic tests for increased risk of breast and ovarian cancer ($3,311).[37] Below are areas of interest and recent examples of research.

Gene Variations That Increase Risk – Tests looking for specific mutations can identify higher risk individuals for close monitoring or preventive interventions. For example, DeCode Genetics has identified a gene carried by 1/3 of Americans that might indicate added risk of type 2 diabetes. Of several variations, one appears to partially protect patients against diabetes whereas two variations increase risk. About 21% of diabetes cases could be attributed to the risky variations. The gene appears to play a role in the regulation of other genes involved in hormone secretion, but it is not an all-or-none predictor of diabetes risk.

Gene Patterns Associated with Increased Risk – "Genomic fingerprints" look at variations in dozens to hundreds of genes to find predictive patterns associated with characteristics of specific diseases for identifying high risk patients or to detect early disease. Patterns differentiating disease subsets could also help determine the most effective therapeutic option. Examples of ongoing work are genetic profiles related to predisposition to diabetes, genetic susceptibility to kidney disease in type 2 diabetes, and proinflammatory genetic profiles that may contribute to the development and progression of cardiovascular diseases.

Abnormal Genes in Established Disease – Diagnostic biomarker tests for specific abnormal genes can be used to identify subtypes of disease and help guide therapeutic decisions. Cancer is a major focus of research efforts. There are tests available that detect mutations in specific cancer genes that make them

susceptible to new targeted therapies. To assess the genes in cancer cells these tests must be done on tumor tissue samples. An example of a single gene test is Genzyme's EGFR Mutation Assay. It looks for the presence of epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer patients that correlate with a successful clinical response to Tarceva (erlotinib) or IRESSA (gefitinib). The test costs about $975. Examples of gene pattern tests that look at a profile of 21 or 70 genes are Oncotype DX and MammaPrint. These blood micro-array cancer diagnostics analyze the DNA expression profile of an individual's breast cancer to predict likelihood of recurrence and whether chemotherapy in addition to tamoxifen would be beneficial. Both tests cost over $3,000.

DNA Methylation – DNA methylation results when a carbon atom surrounded by three hydrogen atoms attaches to cytosine within the DNA sequence, silencing the gene without changing its actual sequence. Abnormal methylation occurs early in disease, especially in cancer where several alterations are necessary for cells to evolve into cancerous ones. So far about 50 genes have been identified where methylation plays a role in cancer development. Researchers are looking for methylation patterns in biopsy specimens, serum, saliva, sputum, urine and stool to detect precancerous changes and established cancer before symptoms develop. Someday these biomarkers could be used for risk assessment, screening, confirming diagnosis, staging disease and determining the most likely beneficial therapies based upon specific cancer mutations. These biomarkers could also determine that a patient is unlikely to have cancer, avoiding invasive procedures, and if a cancer is likely to be slow growing so that radical surgery isn't necessary. Researchers are particularly interested in bladder, breast, colon, lung, ovarian, and prostate cancers. Current testing equipment used in research is very sensitive in detecting just a few cancer cells in a specimen.

Mitochondrial Genetics – The metabolic syndrome with risk factors for diabetes, hypertension, hyperlipidemia, obesity and cardiovascular disease might be triggered by genetic changes in mitochondria. Mitochondria have their own DNA (mtDNA), and as they are the power house of the cell, there is a close correlation between mitochondrial dysfunction and beta-cell dysfunction. The 16189 gene variant is found slightly more commonly in type 2 diabetes than in controls. A team at the Center for Molecular and Mitochondrial Medicine and Genetics at UC Irvine is studying the genetic variations of mtDNA associated with various metabolic diseases. It is also developing biomarkers, including

exploring rapid non-invasive methods potentially using infrared laser or breath analysis technologies. It is too early to tell if this research will lead to a test for screening or therapeutic decision making in metabolic disorders.

Pharmacogenomics – Variations in specific genes determine how well certain drugs are metabolized and excreted by an individual. Testing guides therapeutic decisions by identifying when a drug's standard dose should be altered or if a particular drug should not be given to that patient. This information is important for expensive or high risk medications and determining the right drug at the optimum dose immediately in a life threatening disease. Examples of recently approved pharmacogenomic tests are (1) Invader UGT1A1 Molecular Assay that detects variation in a gene affecting the metabolism of irinotecan, a colon cancer treatment, (2) the Roche AmpliChip that is used to individualize dosage of beta-blockers, antipsychotics, antidepressants and some chemotherapy drugs, and (3) the TRUGENE HIV-1 Genotyping Kit that detects variations in the genes of human immunodeficiency virus making it resistant to some drugs.

Proteins

Researchers have come to the realization that understanding genes and their function alone are not enough to develop new diagnostic tests. Recent developments in protein sequencers have allowed a hundred fold improvement in identification of proteins and the development of proteomics as a research field.

Single Protein Markers – Prostate specific antigen (PSA) is a widely used but controversial screening test for prostate cancer. Other protein markers such as carcinoembryonic antigen (CEA) for colon cancer and CA 125 for ovarian cancer are not specific enough for screening, but are somewhat helpful in monitoring the management of extensive disease. Researchers continue to look for the ideal, highly predictive biomarker for serious diseases.

A blood test monitoring for an increase of proteins that regulate angiogenesis (development of new blood vessels) in platelets could provide an early indication that a cancer is developing or that a metastasis is occurring. Clinical trials are testing the predictive value of this methodology.

Protein Profiling – This methodology analyzes hundreds of proteins from blood or tissues with mass spectrometry and protein micro-arrays to identify significant changes occurring when cells progress from normal to disease. Cancer cells overproduce many proteins so a pattern of peaks and troughs, each representing the blood level of a specific protein, will hopefully detect a cancer with a high degree of accuracy. Large numbers of blood protein levels are compared between cancer patients and normal controls using sophisticated pattern recognition algorithms to discover unique "fingerprints" associated with specific early cancers. These must then be tested in large groups of cancer and non-cancer patients to determine predictive value. OvaCheck, a test for early detection of epithelial ovarian cancer, is an example of work in this area. Similar research is being undertaken by several biotech firms looking for predictive biomarker patterns for breast, lung, pancreatic and other types of cancer and a wide variety of other serious diseases. For example, researchers are seeing if protein profiling can distinguish between aggressive and indolent prostate cancers for selecting the right course of therapy.

Metabolites

A new area of investigation, called metabolomics, is using advances in biotechnology to detect and interpret the small molecules (metabolites) present in the body, particularly unique molecules that can distinguish the onset of a disease like cancer from normal body functions.

Sugars

Sugar chains, like DNA and proteins, also play an important role in the cellular network. Sugars are involved in everything from embryonic development to regulation of the immune system. Sugars also help to transmit the signals that prompt unchecked cell growth. Like genomics, and proteomics, developing a better understanding of the interaction of sugar molecules could lead to new diagnostics or therapies for diseases such as cancer.

The Bottom Line

There are a number of biomarker tests using blood and serum under development that could dramatically change the screening, diagnosis and treatment of disease, especially cancer. It is difficult to tell which tests in development will pass the hurdles of FDA approval and gain market acceptance. However, based on the pace and activity of research, it is likely that the following will occur:

1) Within in the next ten years, most patients will have a pharmacogenomic profile (like knowing their blood type today) that will be routinely checked when prescribing drugs.

2) Biomarker tests that identify sub-types of disease will become much more common over the next ten years.

3) Biomarker tests for determining increased risk of disease will become much more common over the next ten years.

4) Within the next few years there is likely to be an effective non-invasive blood sugar monitor.

These tests are likely to have two very large effects on the healthcare system:

1) The personalization of therapy based on biomarker tests. Pharmacogenetic tests, such as the Roche AmpliChip, will help determine which therapies will suit a patient's genetic makeup. Other biomarker tests will help determine sub-types of disease that will guide therapies. This is already occurring for some sub-types of cancer.

2) A shift to prevention based on a personalized risk assessment. Tests that identify gene variations or patterns for increased risk of diseases such as cancer, diabetes and cardiovascular disease will help individuals prevent disease before they occur. In the long run, this will be less costly than waiting for disease to develop. However, for this to be effective, it requires commitment on the patient's part for behavior change and effective tools in the healthcare system to change behavior.

Both these shifts in the healthcare system are likely to be expensive. New biomarker tests based on genes and proteins are orders of magnitude more expensive than previous blood/serum tests. Personalizing therapy based on these tests is also an expensive option. Prevention based on personalized risk assessments is likely to be cheaper in the long run, but effective prevention will require changes in the healthcare system that is by almost any measure, resistant to change.

The challenge for the healthcare system and us as a society it to identify those tests that are truly valuable and cost effective and making sure they are available to all populations and communities. As the tests become more common and more personnel are trained in their use, the costs will come down slightly. However, there is the possibility that these expensive tests will further widen the divide between those with access and those without. Without universal health coverage there is likely to be a tiering of care between those who have access to these tests and those that do not. Prevention based on personalized risk assessments also opens the possibilities for further health disparities. The first is the possibility of insurance discrimination based on a person's genetic susceptibility to disease. The other is that a shift to prevention favors those with a high level of health literacy, the resources to invest in health (better food, exercise coaches, health coaching software, etc.) and environments supportive of healthier behavior (e.g. safe neighborhoods for physical activity, good quality affordable food).

Saliva and Oral Testing

Forecast: *By 2016, there are screening tests for molecules in saliva for a variety of conditions including early stage diabetes and some types of cancer. There are also testing kits that can screen for multiple conditions, which are ideal for community outreach programs.*

Active research is uncovering ways to use saliva testing to diagnose and monitor health and disease states, predict progression, detect exposure to infectious, environmental and biological substances and detect microbial biomarkers. Diagnostic devices using MEMS/NEMS (microelectromechanical systems and nanoelectromechanical systems) chips, micro-fluidics, and multiple detection methodologies are in active development with impressive prototypes being tested. Saliva as a testing platform offers promise for real-time, painless, cost-effective disease screening that can be performed at the point of care. Tests are already available to detect alcohol, illegal drugs, various hormonal levels, HIV, failed pregnancy and other things. Researchers are looking at patterns of DNA, RNA, proteins, fatty acids, bacteria, viruses and other molecules to try to discover specific patterns that will accurately detect common diseases such as cancers, diabetes, rheumatoid arthritis, and cardiovascular disease. It may take a few years before reliable patterns for saliva testing can be confirmed through clinical trials and regulatory approval secured. The first role of new modalities will be screening. Over time as accuracy improves it could shift into definitive diagnosis and management.

The dental community is very involved in this approach and will likely be the first group of medical professionals to use these new saliva tests to screen for common diseases during oral exams. It may be a harder sell to get physicians to accept the value of this new paradigm in diagnostic screening, but the attributes of low cost and ease of use at the point of care or in the home should be a compelling motivator – if the technology proves reliable for common serious diseases. The platform could become extremely valuable for community health centers.

Mechanism of Action

The 1.5 liters of saliva a person produces daily comes from blood filtered through the salivary glands so it mirrors the blood. However, saliva concentrations of molecules are often 0.1 – 1% of that in the blood requiring more sensitive assays. Some of the molecules that can be measured include DNA, RNA, proteins, bacteria, viruses, and fatty acids. Oral swab tests, such as the oral HIV test, can measure the same molecules and are included in this section.

Potential Applications

Saliva testing is already used for measuring hormones (i.e., cortisol, estrogen, testosterone, DHEA), illegal drug testing, screening for antibodies against HIV, measuring the rate of bone loss, screening for periodontal disease, checking identity, and paternity testing. Under development are tests for:

- Oral cancer using messenger RNA
- Messenger RNA patterns predictive of breast cancer and diabetes
- Bacteria populations indicative of oral cancer and early diabetes
- A test that can simultaneously diagnose several childhood respiratory infections within minutes in the clinic
- Oral microbes can predict infection elsewhere in the body
- Patterns of salivatory glycoproteins that can predict the life-time risk of developing cavities
- Ovarian cancer marker CA-125
- C-reactive protein, an inflammation marker linked to high risk of heart attack, stroke and type 2 diabetes

- Saliva DNA that may be used for accurately assessing how well the brain is controlling levels of serotonin

The Bottom Line

Alcohol, drug, hormone, HIV and other saliva tests are already on the market. Almost all of them, excluding the HIV saliva test, are available as home tests. An oral test for oral cancer is likely to be available in 2 years (2008). Saliva tests for other cancers, including breast and ovarian cancer, will likely take longer. In 2008, it is likely that researchers will have completed the saliva roadmap. This will help researchers to identify molecular signatures for non-cancer diseases such as diabetes and rheumatoid arthritis. Their goal is to identify genetic signatures for at least 10 common diseases by 2007. From there, it will take time to perfect the test, get it through clinical trials, secure regulatory approval and get the test to market. This will take at least 3 to 5 years.

It is probable that by the time these tests do reach market, micro-assay technology will have progressed enough to allow assays of multiple markers. This means that saliva tests might be quickly combined to test for multiple diseases in one testing kit.

Saliva testing is a promising platform for reducing health disparities. Saliva testing requires little training to conduct and is therefore a good candidate for home testing and community outreach programs. It is minimally invasive and painless, which makes it ideal for screening. Saliva testing is also cheap relative to other platforms for biomonitoring. Most existing saliva/oral tests (e.g. alcohol and drug) cost only a few dollars per test. Newer hormone and HIV tests cost more (about $30-$50 a test).

The greatest potential for reducing health disparities would be point of care or home saliva screening tests for cancer and diabetes. Both of these conditions have high health disparities characterized by underserved populations with lower screening rates. The use of saliva C-reactive protein test linked to effective health promotion activities could also lower health disparities for cardiovascular disease. Saliva testing for infectious diseases, particularly for HIV testing and childhood respiratory diseases, can also be very useful for combating high disparity diseases.

Breath Testing

Forecast: *By 2016, a portable screening test for lung and breast cancer using breath is available. The device is common in community health centers and health fairs. The results are relatively quick allowing for follow-up with additional diagnostic tests and counseling by trained professionals.*

Police use simple breathalyzers to confirm drunk drivers, but now technological advances permit analysis of volatile organic compounds (VOCs) that are a billion times more sensitive. Researchers have done several studies using patterns of specific VOCs to screen for diabetes, lung and breast cancer and other diseases. Early results are promising as first line screening tests. The breath collection procedures often require trained personnel and the analyzer technology is still complex, but if further testing in a wide range of patients shows clear benefit these problems will be overcome in commercial versions of the machines. The proper role in screening and therapy would need to be proven. The technology is clearly noninvasive and painless, but its cost-effectiveness must be shown before it is useful in community health centers.

Mechanism of Action

New technologies, such as cavity ring-down spectroscopy, can perform precise assessment of very small amounts of volatile organic compounds (VOCs) in breath. These assessments are combined with analysis of patterns of compound concentration and compared to unique patterns associated with disease states. Researchers are currently looking at about 400 VOCs as markers for various diseases. Diabetics, for example, have increased levels of acetone in the breath. Breath tests are noninvasive, but the collection of breath and simultaneous ambient room air samples for some tests requires technical exactness. Monitoring technology is simple and fast for commercially available tests, but could be complex and time consuming for diseases under investigation. Once the technology and validity are worked out simple versions are likely to be developed.

Potential Applications

The most common breath test is for alcohol. The FDA has also approved a breath test for heart transplant rejection that tests oxidative stress by analyzing 200 VOCs in the breath. There are no other breath tests on the market. A number of devices are in the basic or advanced research stages that test for VOCs in the breath.

Diabetes

A prototype device exists that analyses the acetone in a single breath to rapidly determine if a person is diabetes-free or in an early or severe stage of the disease. The developers envision a device that costs $5-15,000 by about 2010 that could be used for rapid screening in a clinic or at the mall. The device could also monitor effectiveness of therapy and even be used for home monitoring with results also sent to care providers.

Breast Cancer

A pilot study measured changes of VOCs in the breath related to breast cancer and could distinguish between women with and without breast cancer with a sensitivity of 94% and specificity of 73.8%. The negative predictive value using this breath test was better than screening mammograms, but screening mammograms had better positive predictive value (more accurately identifying the presence of breast cancer). If large group studies confirm the results, the test could be used as a primary screen for breast cancer. **Tuberculosis** and **Pre-eclampsia** are also being studied using a similar approach.

Lung Cancer

Multiple researchers are developing methods to screen for lung cancer based on VOCs in the breath. For example, the Cleveland Clinic Lerner Research Institute used a hand-sized "electronic nose" originally designed to measure the safety and quality of food based on a "smell-print" of VOCs. The device showed differences in the exhaled breath of lung cancer patients compared to those without cancer. These differences could be used for early diagnosis and to monitor effectiveness of treatment. The study included 14 with lung cancer compared with 62 normal patients and yielded a positive predictive value of 66% and negative predictive value of 92%.

The Bottom Line

Breath tests have a long way to go before they can have an impact on disparities. The diabetes testing device needs to prove acceptable levels of specificity and sensitivity as well as passing FDA certification before it could be used as a screening test. Even then, the use of blood testing for blood glucose or H1Ac is still likely to be both more accurate and cheaper.

Breath tests for cancer could reach the market soon, but there must be clear indications for when they are most beneficial and cost-effective in screening or for monitoring therapy. They would also require FDA approval. The heart transplant rejection test is the only test using oxidative stress that has been approved by the FDA. Research on both the breast and lung cancer breath tests is promising and there is a real need for a screening test for lung cancer. A test that is less uncomfortable and expensive than current screening tests for breast cancer would also be a welcome addition. Further studies, especially with larger populations, are needed.

Breath screening tests for lung and breast cancer could dramatically lower disparities. A breath testing device, similar to the prototype developed for diabetes testing, could lower disparities by allowing rapid non-invasive screening at community health centers. Another potential application of a breath test machine would be to set up screening booths at health fairs and community locations. Feasibility and cost benefit will depend on the size, complexity of the device and the amount of training or preparation required by staff operating the machine.

Lung cancer, in particular, lacks an effective screening test for early diagnosis and has clear disparities in incidence. For example, African-American men are at least 50% more likely to develop lung cancer than white men.[38] A breath test for these conditions that could be placed in community health centers, health fairs and other community locations could help reduce disparities through early detection and treatment. Any such device would also need a support system that follows up with counseling and treatment.

Stool Testing

Forecast: *In 2016, stool testing remains the best test for colorectal cancer. Wider use of fecal DNA testing leads to higher survival rates for colorectal cancer due to earlier detection.*

Testing stool for occult blood, typically called fecal occult blood testing (FOBT), has long been the standard for screening for colorectal cancer. The newer immunochemical fecal occult blood test makes dietary restrictions unnecessary and eliminates false positives, but it is more expensive and less effective in detecting cancer. The traditional FOBT is very inexpensive with the patient typically paying $10-25.

The latest method is fecal DNA testing which detects mutations in sloughed neoplastic cells. All these stool screening tests can make a big difference by often detecting colorectal cancer at an early stage. This test is much more expensive than the FOBT at close to $800 for the first commercially available test.

The Bottom Line

Two very good biomonitoring tests for colorectal cancer already exist. One is very affordable and widely available. The other is newer, more expensive and better at detecting early colorectal cancer. The price of fecal DNA tests should drop substantially over the next 10 years, hopefully making it practical for community health centers. Unfortunately, only 22% of those over 50 years old received fecal tests in the past 12 months due to low consumer acceptability with collecting the samples.

Skin Testing

Forecast: *By 2016, a skin test for early stage prostate cancer is available. While this makes screening for prostate cancer easier, the patient still has to make the hard choice of between further monitoring or aggressive therapy.*

Skin is actually a large organ comprising about 17% of body weight, but it is not often considered for testing except for dermatologic conditions and allergen skin tests. Skin tests have the advantage of being non-invasive and simple to obtain. Below are two skin tests, one is available and the other is in early research.

PREVU is an FDA approved non-invasive 3 minute point-of-care skin test for measuring skin sterol (cholesterol). Two drops of liquid on the palm result in a color change reaction which is read by a hand-held spectrophotometer (color reader). It is a screening test useful for stratification of primary care patients according to cardiovascular risk and could potentially be used for monitoring response to therapy. This test is available for use, but it is not clear if it is a better screening test than traditional serum cholesterol.

A novel skin test for prostate cancer is under development. The test analyzes genes on the skin's surface looking for alterations in gene expression due to the cancer. A specially designed adhesive tape harvests

surface skin cells. Cell DNA or mRNA is then analyzed. Prostate cancer cells produce substances that influence growth of other tissues, including skin. An ongoing study of patients at UC San Diego will analyze at least 47,000 genes and hopefully narrow that down to about 25 genes that are statistically predictive of the cancer. If successful, the next step will be to see if the test can determine whether the prostate cancer is likely to be slow growing requiring only monitoring or more aggressive requiring therapy.

The Bottom Line

The prostate cancer death rate is higher for African-American men than for any other racial or ethnic group. However, the evidence is mixed or inconclusive that early detection of prostate cancer improves health outcomes. In addition, treating prostate cancer can have a very negative impact on a patient's quality of life.[39] A skin test for detecting prostate cancer could be a great advance for reducing health disparities *if* the test can determine if treatment is beneficial for the individual.

Urine Testing

Forecast: *By 2016, urinalysis tests that can screen for a select group of cancers are available.*

Urine testing was first used in ancient times for diagnosing disease. Urinalysis is useful for evaluating the urinary system and can help diagnose diabetes, hepatitis and other conditions. An example of urine chemical testing is specific hormone levels for evaluating endocrine function. Current research is looking for specific protein and genetic biomarkers in urine that could be useful in diagnosing cancers and other conditions. Urine is easily and painlessly obtainable, making it an excellent specimen source. Anything that passes through the kidneys into the urine, including many large proteins, is available for analysis. Also tumor cells sloughed from the urinary tract can be detected.

Potential Applications

- **Urinary track cancer** – tumor cells, or their gene and protein biomarkers, from the kidney, ureter and bladder can be detected in urine.

- **Breast cancer** – a small study at Boston Children's Hospital detected a protein biomarker called ADAM 12 in the urine of 94% of breast cancer patients, but only low concentrations in 15% of controls. It is highest in advanced, metastatic breast cancer. ADAM 12 may be detectable before

the mammogram is positive or it may help determine whether a lesion seen on mammogram is likely malignant or benign.

- **Multiple cancers (bladder, breast, colon, lung) –** protein biomarkers such as matrix metalloproteinases (MMPs) increase once a tumor is ready to grow. MMPs break down the extra-cellular matrix surrounding cells so angiogenesis can develop new blood vessels in the tumor. In theory, protein biomarkers in the urine could determine a tumor's aggressiveness, track effectiveness of therapy and determine when a tumor reaches certain milestones such as developing a blood supply and spreading to distant sites.

- **Ovarian Cancer –** other researchers are looking for unique serum and urine biomarkers for detecting early stage ovarian cancer to use as screening tests.

- **Toilet for Diabetes –** Toto, Ltd., a Japanese manufacturer has a" smart toilet" that checks for glucosuria. This might be used as an initial screening test for diabetes. However, urine glucose does not correlate well enough with blood glucose for precise control of diabetes.

The Bottom Line

Urine is easily and painlessly collected and biomonitoring tests can be developed for home use. An example is the urine dipstick rapidly performing several tests that can be easily read by comparing color changes. Urine testing is relatively inexpensive compared to other forms of testing, but sophisticated gene and protein tests could be quite expensive for the foreseeable future. Qualitative accuracy is good, but variable urine dilution depending upon hydration and other factors make quantitative measurement difficult.

Urine could be a promising platform for reducing health disparities as it is non-invasive. Gene and protein tests are likely to be expensive, but if cancer can be detected, the cost may be justified for CHCs. Problems with quantitative measurement are likely to limit many urine tests to a screening role.

Behavioral and Lifestyle Monitoring

Forecast: *By 2016, body monitors are commonly used by patients to manage diabetes and other chronic diseases and improve health.*

Although many diseases are caused by genetic makeup, about 40-50% of our disease burden is due to poor lifestyle choices – people not taking care of themselves. Yet only 2% of the $1.9 trillion U.S. health care expenditure is spent on helping people better manage their own health. Helping people change their

behavior is extremely difficult. Part of the problem is not being able to manage what you can't measure. New wearable devices permit monitoring of physiological parameters that are then translated through algorithms into useful health information, such as daily energy (calorie) expenditure, amount of physical activity and duration of sleep. This information is collated over time and made available electronically to the individual and health providers in several useful formats. The net result is that people learn more about themselves, providing a feedback loop for actions taken to improve their health. This concept is an elegant integrated system designed to provide medically accurate data through unobtrusive, noninvasive wearable sensors that are simple enough for consumer use while being relatively inexpensive to produce.

Many companies are now developing biomonitoring and assistive devices, primarily for permitting elders to safely live at home. But these technologies can also be used to measure compliance in taking medications and even as part of systems to coach healthy behavior. There are ways to continuously monitor a patient for level of depression. Devices can be designed to assist patients in self-managing their health or to provide useful data for controlled clinical trials for drug regulatory approval. It is reaching the point that biomedical engineers can create a monitoring device for any activity that is important to measure. For instance a "smart bed" can assess amount and quality of sleep, vital signs and body weight. Motion sensors in a house can measure activity, assess gait and detect a fall. Devices in the kitchen can tell if a person is eating properly and whether food preparation is sanitary. Smart devices, maybe using radio frequency identification tags and other technologies, can monitor whether the subject is taking pills properly and can remind him if he forgets.

These technologies can be useful in assisting patients play a major role in self-management of chronic diseases such as diabetes, asthma and congestive heart failure. This approach requires moderate to significant up front costs, depending upon the sophistication of devices used, but can save money in the long run by preventing expensive complications and hospitalization.

Principle or Mechanism of Action

Physiologic data is measured non-invasively and assessed by sophisticated algorithms to interpret and derive meaningful health information about the individual. The monitoring system may be a wearable

device like a wrist watch, attached to the body as an adhesive patch or embedded in clothing. Sensors might include a two-axis accelerometer (detect motion and body position), heat-flux (body heat dissipation), galvanic skin response (varies with sweating and emotional stimuli), single lead EKG (heart rate), impedance pneumography (breath rate) or electroencephalogram (brain-wave activity). Algorithms convert data into measures such as duration of physical activity, calories burned at rest or during activity, times of sleeping and awakening, heart rate, or the effects of anesthesia and sedatives on the brain. Data from additional stand-alone biomonitoring devices such as a glucometer can be wirelessly uploaded into the monitoring system computer to enhance the picture of a patient's health status. Many of these monitors can also be incorporated in personal electronic devices such as cell phones. Wearable devices that include most of the monitors mentioned above, such as the BodyMedia armband device, cost about $300. With increased volume and mass marketing, the devices could drop to $100 or less.

Many home and work monitoring devices incorporate sensors already in use in industry, such as motion sensors and RFID tags, into monitoring devices. These sensors are low cost and non-invasive. Most home monitoring devices do not involve cameras or microphones, in order to preserve a patient's privacy. The devices monitor general health and activity levels. Home monitoring can help spot problems before they occur, assist informal caregivers (family & friends) and help formal caregivers in making decisions.

Potential Applications

- **Weight loss and controlling weight** – monitor exercise, total calories burned a day, calorie intake (computerized food diary), real-time daily calorie deficit or excess to provide an accurate picture of activity and impact on calorie balance for the patient. This can reinforce healthy patient behavior and provide valuable information to a professional providing health coaching.

- **Diabetes management** – lifestyle changes to increase activity and lose weight have been shown to prevent pre-diabetes from progressing in 58% of patients, adequately manage early disease without medications and improve outcomes in more advanced cases. Sensors can keep track of activity and calories burned (as noted above). Additional information such as blood glucose, blood pressure, EKG readings and weight can be captured by other monitoring devices and wirelessly added to the monitoring system for a comprehensive computerized picture of ongoing health status. The system provides feedback to reinforce patient behavior and assist providers in disease management.

- **Level of anesthesia** – monitoring of brain-waves can directly tell whether anesthesia is deep enough for the patient to be unconscious and free of pain during surgery.

- **Effectiveness of a central nervous system drug** – normally it takes 4-6 weeks of trial and error to determine if a newly administrated anti-depressant drug is effective and select the optimal dose. A simple brain-wave reader with sensors periodically strapped to the forehead can determine efficacy in about a week.

- **Monitoring Living or Working Environment** – monitoring of vital signs can track progress for patients rehabilitating from an injury. Home monitoring can also be used to allow elderly or chronically ill patients to remain in their homes longer. Workplace monitoring can be used to monitor and respond to accidents faster, identify stressful work environments or identify high risk activities.

- **Identifying Pollution** – Monitoring devices for work and home can identify potentially toxic materials thereby preventing exposure.

- **Research projects** where continuous "free-living" physiologic data is needed to correlate with other experimental parameters.

- **Mental state, health status, other conditions** where information derived from physiologic parameters assists management. For instance, researchers are investigating whether brain wave patterns can detect Alzheimer's disease before clinical symptoms are apparent.

The Bottom Line

Behavioral and lifestyle monitoring have potential for encouraging healthy living, allowing elderly or chronically ill patients to avoid hospitalization and preventing diseases such as diabetes. Advances in these monitors are closely tied to related developments in software for managing and correlating data from the devices and displaying this data in a format that is usable by patients and care providers. Advances in health coaching software combined with physiologic and lifestyle monitoring could be a very effective way to motivate behavior change.

Imaging Tests

Forecast: *By 2016, imaging technologies are much more capable, with ease of use in the clinic and dramatically reduced in price. They are relied upon for early diagnosis, extent of disease and rapidly verifying the benefit of specific expensive therapies.*

Imaging technologies have improved. In 2006 there are digital imaging tools for easy transfer of images and hand-held portable devices exist for ultrasound and even CT scans for use in clinics. Progressive advances are constantly changing the cutting edge of screening and diagnostic tests for breast, colon and lung cancer, but standard tests (chest X-ray for lung cancer; mammogram for breast cancer which are increasingly digital with automatic reading; colonoscopy for colon cancer) usually remain the most cost effective for patients of community health clinics. The big breakthrough though is noninvasive molecular imaging that visualizes and measures normal as well as abnormal cellular processes at molecular or genetic levels of function. This provides the ability to detect the presence of a disease such as a specific cancer, earlier and more accurately, rapidly shows whether a therapy is working, and detects asymptomatic recurrences.

Potential Applications

Imaging devices rely on a variety of technologies. These technologies all have different applications and costs. All are currently in use, but some have been in use a long time in comparison to others. The use of these imaging tests for cancer diagnosis is also discussed in greater detail under the best practices for biomonitoring section.

- **X-Ray Imaging:** Advances in information technology combined with methods of layering images digitally have created breakthroughs in x-ray imaging. New advances, such as spiral computerized axial tomography (CT) scans, are not only less invasive and less expensive, but also improve our diagnostic capability in diseases such as cancers, cardiovascular disease, infectious disease, trauma and musculoskeletal disorders. A large study recently released found that CT scans are able to detect lung cancer at its earliest and most curable stage in 85% of patients. When followed by prompt surgical removal, those patients had a 10-year survival rate of 91%. Lung cancer kills most patients within a year or two of diagnosis.[40] CT scans cost between $450 and $750. CT scans are becoming more common in smaller hospitals as prices decline.

- **Magnetic Resonance Imaging:** Magnetic Resonance Imaging (MRI) provides better contrast resolution than CT scans and does not use ionizing radiation. This has made MRI imaging the preferred method of distinguishing pathological tissue, particularly cancer, from normal tissue. Advances in functional MRI (fMRI) have opened up new areas of research for understanding the brain and pin pointing areas of cerebral activity following external and internal stimuli. MRI scans can cost between $700 and $900 dollars and are located in large medical centers.

- **Radionuclide Imaging:** Positron emission tomography (PET) and single positron emission computed tomography (SPECT) are powerful technologies capable of imaging biochemical processes in-vivo and in real time by visualizing very low concentrations of radionuclide probes. PET imaging has opened up areas of study in epilepsy, dementia, stroke, and coronary heart disease. PET can also be used for the early assessment of the efficacy of various cancer therapies or even to predict which type of cancer therapy is most likely to be successful. PET scans cost between $2,000 and $6,000 dollars and are only available in major medical and research centers.

- **Ultrasound Imaging:** Ultrasound imaging, also called ultrasonography, is an often used clinical diagnostic modality in cardiology, obstetrics, gynecology and other clinical areas. However, there are many exciting new clinical applications for ultrasound currently under development. Acoustic Radiation Force Impulse (ARFI) ultrasound, for example, uses two different sound pulses to help physicians diagnose abnormalities such as tumors. One pulse is a high energy beam that pushes the tissue while the other monitors the resulting motion in the tissue. Ultrasound is cheaper than the other imaging modalities, with traditional ultrasound costing $200 and $300 dollars for the patient.

- **Optical Imaging:** Optical imaging uses fluorescent and bioluminescent probes that emit radiation in the visible or near-infrared wavelengths, which can be scanned by optical cameras. Optical imaging is currently being used in research to follow cells and proteins in the body, but may have clinical uses in the future.

- **New Probes & Diagnostic Pharmaceuticals:** A lot of imaging research is dedicated to creating new probes. These probes are improving image resolution and contrast. They are also allowing researchers to follow individual cells and molecules in the body (molecular imaging) using different imaging modalities.

- **Molecular Imaging:** Molecular imaging is progressively being used in clinical medicine, particularly for the diagnosis and management of cancer. However, the expense of equipment and staff limit its use to larger medical centers and imaging centers. Its use will grow exponentially as new indications are verified, equipment costs decline and more medical centers adopt molecular imaging technologies.

The Bottom Line

In the future, imaging technologies will be much more capable, portable with ease of use in the clinic and dramatically reduced in price. For example, the price of ultrasound is likely to come down as simple ultrasound devices that can be plugged into a laptop computer are developed. Imaging devices will increasingly be relied upon for early diagnosis, extent of disease and rapidly verifying the benefit of specific expensive therapies. Routine use in community health clinics of the newer and more expensive imaging technologies will likely be a long way off.

Health Information Systems 2016

The development of health information systems will play a large role in the effectiveness of future biomonitoring technologies in reducing health disparities. It is important to focus on health information systems of individuals, health care providers and communities since there is likely to be growth in all, and the lines among them are likely to blur. For the purposes of this report, health information systems will refer to a variety of information technologies that can improve patient care including:

- Health Coaching and Monitoring Software

- Electronic Personal Health Records (PHRs) for Patients

- Electronic Medical Records (EMRs) for Providers

- Communication Technologies

- Knowledge Technologies

- Web based clinical care activities

- Access to healthcare information sources

Since the 1990s, advances in computer power and connectivity have created new ways to manage health data and disease. The price of computing power both in relative and absolute terms has also dropped, making computing power, once only available to government agencies, research laboratories and large companies, available to small healthcare clinics and average citizens. This same computing power is also available in smaller, mobile platforms such as the cell phone. Improved user interfaces have made interacting with and using information systems easier and more intuitive.

The ability of community health centers, small healthcare clinics and average citizens to access this technology is changing how healthcare is delivered and the relationship of the patient to her health providers. Many of the biomonitoring technologies discussed previously are available or will be available for home use. The ability of biomonitoring data to be transferred between healthcare institutions and patients through interoperable electronic medical and personal health records have the potential to dramatically improve care. Combined with improved programs for tracking health

information, providing information therapy and health coaching, there is a large potential for patients to improve their own health and become more proactive consumers of healthcare. This empowerment of patients through access to their own medical information and information technology can reduce health disparities if underserved communities have access to these technologies in forms that are linguistically and culturally appropriate.

Access to the Internet and Cell Phones

Forecast: *By 2016, 95% of households have home access to a computer and the internet or their functional equivalent. It will be commonplace for cell phones to link to medical or personal biomonitoring devices and relay the information to the individual's personal health record or to his doctor's system. Health coaching software is advanced and works with the patient and healthcare provider to set personal health goals for weight loss and disease prevention.*

Access to information technology is growing rapidly regardless of family income, age or ethnicity. However, the benefits of the information age have not been shared equitably. There is a considerable gap in access and use of information technology. This divide is largely a function of income and education level. Those earning less than $30,000 a year and those with no college education have significantly lower rates of computer use at home to access health information.[41] Access to information technologies, especially broadband internet access, is also lower in rural areas where private companies are less likely to invest in infrastructure.[42]

New technologies and the policies of leading American cities have the potential to dramatically reduce the digital divide. Cities such as Philadelphia are already developing citywide wireless access using the current Wireless Fidelity (WiFi) technologies to help narrow the digital divide.[43] Cities and rural areas interested in providing wireless access and broadband will have a new technology to assist them in 2008. Worldwide Interoperability for Microwave Access (WiMAX) is often mentioned as the next stage in both broadband and wireless. WiMAX broadcast towers will have a radius of three to ten kilometers that proponents claim will be capable of supporting hundreds of businesses and thousands of residences at broadband speeds. WiMAX has the potential for transforming broadband, wireless internet access into a public utility since it can cover wider areas than current wireless technologies and is able to penetrate

buildings.[44] Cities continue to grow in their development of free wireless access and WiMAX will make this easier.

New third generation cell phones have the potential for reducing the digital divide and could be an excellent platform for biomonitoring technologies. Third generation cell phones are able to download information from the internet at speeds in between dial-up and broadband. Costs for third generation service will initially be high as the service is rolled out, but is likely to be lowered in price or included as part of a basic wireless package as the technology becomes widespread. Wireless phone companies have already set standards for faster 3.5 generation cell phones and WiMax has been mentioned as a possible fourth generation cell phone technology, but no standards have been set yet.[45] Improved software capability and broadband connections on third and fourth generation phones make them capable of storing personal health data from biomonitoring devices. Biomonitors, especially lifestyle biomonitors, could also be built into the phone for monitoring that is available throughout the day.

The digital divide for cell phones is much less pronounced than other communication modes. A 2002 study by knowledge networks showed that a higher proportion of African-Americans owned a cell phone (65%) than whites (62%).[46]

Electronic Medical Records & Personal Health Records

Forecast: *By 2016, most primary care providers and all Community Health Centers will have Electronic Medical Records tied into advanced clinical management systems. Patients will have access to a personal health record that is linked to the electronic medical records of their healthcare providers and to biomonitoring devices. The personal health record is automatically updated with information from the electronic medical record and biomonitoring devices. Knowledge management software combined with the personal health record help patients to analyze their health records. Health coaching software combined with biomonitoring devices help patients use that information to improve their health.*

The data relevant to doctors and healthcare providers is growing rapidly. Advances in biotechnology are expanding the number and range of treatments for disease. At the same time, evidence-based medicine is expanding the amount of data through post-market studies on efficacy and safety. As medicine becomes more personalized to the genetic proclivities and specific health conditions of individual patients, and as

our definitions of disease broaden to sub-disease and to pre-disease states, the amount of relevant data available to the clinician will rise.

The Electronic Medical Record (EMR) is a platform on which a more efficient healthcare system with better outcomes for patients can be built, but the EMR alone is not sufficient. Rather a collection of advances need to be combined with the EMR to improve the healthcare system with:

- Interoperable Data
- Knowledge Management Software
- Patient Access
- Digitally Linked Biomonitoring Platforms
- Regional and National Information Infrastructure
- Protections to Ensure Privacy and Security and Prevent Discrimination

Currently, the information in EMRs is a combination of older paper records scanned into an electronic format and data stored in an interoperable format. The second type of data is more useful in improving clinical care because it improves the interoperability of the health information system[47] and can be interpreted by knowledge management software. Knowledge management software is a specialized kind of software that supports tasks and decision making.

Today, patients have little access to the information and knowledge they need to manage their own care. The Personal Health Record (PHR) is designed to address the needs of the patient by bridging the gap between providers and patients. A number of different electronic PHRs are available online. Currently, these PHRs are stand-alone systems with limited interoperability with the EMRs of most providers. Recent trends in healthcare, such as consumer directed health care, will increase the need for patients to have access to and use of their health data. They will be more responsible for choosing plans based on their risk profiles, for choosing treatments, and for navigating the healthcare system.

Patients may have a number of options on how their personal health record is stored. One option mentioned previously is the cell phone. Also, the data might be saved at a central location and accessed online through a cell phone or other device through a username and password. It might also be stored in

a physical device like a flash memory drive designed to look like a necklace or bracelet. Another possibility is a combination of both with important information stored in a physical device accessible by emergency personnel and larger, harder to store items, such as medical images stored in a database accessible to those with the appropriate authorization. It is also possible that implantable microchips with this information will be used, especially for highly mobile populations like military personnel. These also become relevant for some populations, such as homeless or mentally impaired.

Like EMRs, the addition of knowledge management software can help patients use their own health data to improve their health care. This can take the form of tracking software that can integrate the readings of digitally linked biomonitoring devices or the results of lab tests into easy to read charts showing trends in patients' health. Other applications of knowledge management software to PHRs are actively linking new healthcare research so patients know the latest developments in their disease areas, health coaching software that helps patients set healthcare goals and helps them monitor their progress, and software that uses patients' medical and family history to develop risk profiles for disease.

These advances in knowledge management software will be enabled by new IT tools that change the way people access data and turn it into usable knowledge and wisdom. As more knowledge from research is placed directly into machine readable formats, opportunities will expand for "automated learning" in which software programs generate hypotheses and, where possible, test them against appropriate data.[48]

The ability of IT tools to manipulate data to create knowledge for doctors and patients is vital as new biomonitoring devices create loads of data for analysis. As these tools develop, less and less time will be needed by doctors and patients to analyze the data from biomonitoring devices and more time can be spent on using the knowledge gained from biomonitoring to improve health. Knowledge management software in 2016 will be able to sift through vast amounts of biomedical data to highlight and analyze the data that is important to specific patients. Better biomonitors, biomarkers and genomic information will enable these systems to apply the data to the patient's unique circumstances. This kind of tailored healthcare is likely to be much more efficacious and cost-effective than many current treatments.

Moving to a National Health Information Infrastructure

Forecast: *By 2016, there is a national health information network in the United States for the electronic transfer of health information. The system will largely be comprised of regional networks linked by open standards. Interoperability problems will remain, as will gaps in coverage. However, most patients at CHCs will be able to have their health information travel with them.*

A number of important trends are driving the healthcare industry to embrace health information systems. These include:

- The growth of market-driven healthcare

- The increasing digitization of information

- The restructuring of the healthcare industry to be more efficient

- The demands of evidence-based medicine

- The need to improve quality and reduce preventable errors

- And the continuing advances in information technology.

Health information systems are being rolled out in healthcare provider networks and regions across the United States. Regional Health Information Organizations (RHIOs) are being developed to share EMRs and other information among providers in a region.[49] RHIOs are a key part of President Bush's push to have EMRs accessible to every American within 10 years. RHIOs would then be linked together to form a National Health Information Network (NHIN).[50] However, interoperability between different RHIOs remains a major challenge for a NHIN. Currently, each individual RHIO is being developed using different systems and therefore many different standards.

The Department of Health and Human Services (HHS) understands the need for common standards for RHIOs.[51] Without a common set of standards, it is likely that the nation's health infrastructure will remain fragmented. Poor and rural regions might be worse off since they would be less able to afford upgrades to their system. This would leave them with antiquated systems based on standards that are not supported by the NHIN. A better solution might well be open standards and open source software for electronic medical records and health information systems.

Whichever approach ultimately develops by 2016, the US is likely to have a national information network. Such a network linked to a patient's electronic medical and personal health record would be an important tool for reducing health disparities. It would allow mobile populations to transfer medical records and would keep records safe and accessible for emergency health providers. This could be very important during a natural disaster or terrorist attack; and a national health information network that allowed researchers access to large amounts of current biomonitoring data (with appropriate privacy and other personal protections) could greatly improve rapid targeting of public health interventions. However, consideration should be given now to the development of open standards and low cost health information systems for community health centers and other providers of care to the underserved so that everyone is fully integrated into the national health information network.

Forecasts

Throughout the report we have compiled forecasts for cancer and diabetes, different biomonitoring platforms and health information systems. In this section we provide forecasts that combine these forecasts to look at how biomonitoring will be integrated into diabetes and cancer prevention, screening and treatment. These forecasts provide a vision of what is possible if we are able to harness the power of biomonitoring to reduce health disparities.

Forecasts for Diabetes Biomonitoring & Therapy in 2016

By 2016, unless current trends change, the twin epidemics of obesity and diabetes will be the biggest challenge in public health and for the healthcare system. Minorities and the underserved will be impacted the most. Health care providers, particularly community health centers, will devote a major portion of their resources and efforts in addressing the multiple co-morbidities of these twin problems.

By 2016, people with risk factors for diabetes are screened routinely. This is accomplished using existing blood glucose tests, but there are also less invasive screening tests available using other platforms. Early identification of the disease is followed with effective health/behavior change interventions. Health care payors routinely pay for effective health/behavior intervention starting with predisease from a range of health care providers, including CHCs.

Body monitors are commonly used by patients to manage diabetes and other chronic diseases and improve health by 2016. A small wearable body monitor keeps track of motion, heart rate, breath rate and other measures of general health. The body monitor keeps track of a patient's caloric expenditure and stress levels, and automatically uploads that information into the patient's personal health and medical records. This information is combined with other biomonitoring devices such as a glucometer, blood pressure cuff, weight scale and cholesterol tests to identify patterns that contribute to ill health. Health coaching software works with the patient and his healthcare provider to set personal health goals for weight loss, diabetes prevention and stress reduction.

In 2016, those with diabetes have access to biomonitoring devices linked to insulin delivery systems. These systems will take the form of an external closed-loop insulin pump and monitoring device. The complexity and expense of the system limit closed-loop systems to a smaller category of diabetics with severe cases of the disease.

Forecasts for Cancer Biomonitoring & Therapy in 2016

By 2016, advances in biomonitoring and biotechnology improve the prevention, early detection and screening of cancer. Newer blood tests that identify genes and proteins allow providers to predict the risk of future cancers, and diagnose early, asymptomatic (even precancerous) disease for a variety of cancers. Combined with better health information systems, and lifestyle biomonitoring, doctors and patients have better tools for preventing cancer. Blood based and imaging biomarker tests also help doctors to identify subtypes of cancer and personalize therapy.

These advances are not cheap, but a societal commitment to health equity helps to ensure that tests that are truly valuable and cost effective are available to all populations and communities. The most valuable cost effective option is risk identification and prevention. More resources are devoted to tests for identifying risks, regular screening and encouraging behavior change.

By 2016, molecular imaging allows doctors to visualize early cancer changes years before symptoms appear. The identification of asymptomatic or precancerous disease opens up new, less aggressive

therapies for cancer. Molecular imaging can tell if a new therapy is effective in a couple of days, where it can take weeks to detect clinical improvement. The imaging agent can also be combined with a chemotherapeutic agent to directly target cancer cells without harming normal tissue. While these interventions will be much more expensive, they will dramatically improve quality of life and reduce the need for more aggressive chemotherapy.

By 2016, protocols evolve for determining the optimal combinations and time sequences of chemotherapy and targeted agents to use in specific cancers. Advances in biomarkers lead to more precise selection based upon unique characteristics of the individual's cancer cells at that point in time. These new therapies dramatically increase survival, but they are very expensive ($10,000 - $30,000 per course of medication plus drug administration, laboratory and other associated costs). Health plans struggle to determine under which circumstances to cover a prolonged course of multiple drugs. It takes sustained political will to make sure these advances are available to the uninsured, underinsured and underserved.

On the other hand, better screening technologies pre-empt the use of more expensive combinations of chemotherapy and targeted agents in two ways. The first is by identifying high risk individuals and lowering their risk through lifestyle changes. The second is by more effective screening so cancers are detected in early, asymptomatic or precancerous states. By identifying the cancer early, while it is localized, it opens up less aggressive options for treatment such as image guided therapy or targeted drug delivery.

Key Advances in Cancer Therapy in 2016 Using Biomarker Tests and Biomonitoring:

1) **Predicting Future Risk:** *By 2016, genetic tests that can identify gene variations, specifically single nucleotide polymorphisms (SNPs), are able to identify individuals at increased risk for cancer.* Almost all of the tests will be blood based and cost a few hundred dollars. The results are incorporated into the patient's personal health record so they receive regular reminders for screening tests and any lifestyle modifications (quitting smoking, exercise and better nutrition) that would reduce their risk. The results are also tied to the patient's electronic medical record so that healthcare providers can quickly identify patients that have missed regular screenings when they come in to a health center for other reasons.

2) **Early Diagnosis:** *By 2016, better identification of individuals at high risk and electronic reminders for regular screening reduces disparities in the early diagnosis of cancer.* Prices for these tests range from older, inexpensive tests to much more expensive gene and protein tests. Better technologies for early diagnosis allow doctors to identify and treat asymptomatic or precancerous disease earlier, with less aggressive therapies.

3) **Targeted Drug Delivery:** *In 2016, many cancer therapies are designed on the molecular level to target cancerous tissue.* These therapies will greatly improve the quality of life of cancer patients. A number of different delivery mechanisms are available for targeting drug delivery. Toxic drugs can be encapsulated in liposomes, dentrimers or other nano-structures. Tumor-specific antibodies are associated with drug molecules which cause them to seek out and attach to cancer cells. Genetically-modified viruses preferentially infect cancer cells and destroy them. Photodynamic therapy uses laser light focused on a tumor to activate a photosensitizing drug which is preferentially absorbed by fast-growing cancer cells. Also, a prodrug enzyme can be administered to tumor cells by gene therapy or stem cells to activate a later administered prodrug into a cytotoxin killing the cells.

4) **Image Guided Therapy:** *Advances in imaging technologies will also enable more precise therapies in 2016.* Many targeted drugs will be combined with an imaging probe so doctors can visualize the therapy's effects on a molecular level in real time. Activation therapies will allow clinicians to visualize a cancer and then target an energy source directly to the cancerous tissue to destroy it or activate a targeted therapy (such as photodynamic therapy). Nanostructures are also used to improve imaging resolution by injecting them into the site of the cancer. There they can then be heated with an outside energy source to destroy the cancer. Also, automated, image guided surgery reduces the side-effects of surgical options.

5) **Targeted Therapies:** *By 2016, dozens of targeted therapies specifically designed to interfere with a molecular or gene targets known to have an important role in cancer growth, progression or destruction are available.* These targeted therapies are often paired with biomarker tests to determine if the therapy is likely to be successful before treatment. This leads to the personalization of therapy based on an individual's sub-type of cancer and other factors.

Breast Cancer

By 2016, there is at least a 23% reduction in breast cancer mortality rates from 2005. Women with a family history of breast cancer routinely undergo genetic testing to identify their risk. Lifestyle monitoring and health coaching software are effective at changing behaviors and reducing their risk of developing breast cancer. High risk women and women over forty routinely undergo screening tests. Screening tests using platforms other than imaging (i.e. blood, breath, saliva and urine) allow more screening tests to be done at home or at health fairs. Routine reminders for screening linked to a patient's electronic medical and personal health record improve screening rates, meaning more breast cancers are

discovered in early asymptotic states. Targeted drug delivery and image guided therapy reduce the need for mastectomies in most cases.

For patients with advanced breast cancer, targeted therapy is more common. Besides the test for HER2/neu positive breast cancer, there are tests for subtypes of cancer based on unique signaling pathways and other characteristics. Doctors use these tests in combination with advanced disease management protocols to select a combination of chemotherapy and targeted therapy that is unique to the patient's subtype of cancer. While this dramatically improves survival rates for advanced breast cancer, it is extremely expensive.

Colon Cancer

By 2016, there is at least an 18% reduction in colorectal cancer mortality rates from 2005. Lifestyle monitoring and health coaching software are effective at increasing rates of physical activity and improving diet, which lower the risk of colorectal cancer. Colonoscopies remain the gold standard for screening and diagnosis. Improvements in contrast agents and imaging technology make virtual colonoscopies more effective tests for screening and diagnosis. New contrast media allows patients to do a colonoscopy without a bowl prep and improvements in imaging processing technology makes virtual colonoscopies more effective at identifying small polyps. The improved convenience of virtual colonoscopies improves screening rates and dramatically lowers the number of deaths due to colorectal cancer.

Lung Cancer

By 2016, there is at least an 18% reduction in lung cancer mortality rates from 2005. The reduction in lung cancer mortality comes from three main areas.

- A continual decline in smoking rates, especially in public places and among racial and ethnic minorities.
- A breakthrough screening technology for early lung cancers based on changes in VOCs in the breath

- Advances in the identification and treatment for a variety of lung cancer subtypes based on gene and protein biomarkers and targeted therapies

Due to a decrease in smoking, the incidence of lung cancer continues to decline from its peak in the 1990s for men and its peak in the early part of the century in women. The largest decline occurs in African-American men as the disparity in lung cancer incidence drops dramatically.

A breakthrough screening technology for lung cancer based on detecting VOCs in the breath is available on the market in 2016. This and other advances in the identification and treatment of lung cancer based on gene and protein biomarkers improve the five year survival rate of lung cancers by enabling early identification and treatment. These advances come at a price as the cost of treatment for lung cancer rises dramatically.

Consumer and Provider Reflections on the Forecasts

The DRA Project took some of the forecasts listed above and presented them at a series of focus groups with patients and providers at community health centers and a free clinic. Patients were presented with forecasts on advances screening, prevention and treatment of cancer and diabetes using biomonitoring. These forecasts also explored the future uses of personal biomonitoring data for long-term care management and prevention activities. Providers were presented with similar forecasts with more detailed information on how these advances might be used in a clinical care environment. Both patients and providers were asked for their opinions on the forecasts.

Patients were generally enthusiastic about the biomonitoring advances related to diabetes that were presented, often wanting them to be available sooner than the forecasts suggested. Clinicians likewise were encouraged by the forecasts, but raised a broader range of questions about their impact and integration into care protocols. The cost of the advance, the ease of use, portability and the availability of the advance in multiple languages were all important considerations for both patients and providers. Ongoing costs for screening, such as diabetes test strips, were a reoccurring concern for both patients

and providers. Some patients wanted the biomonitoring devices to be more fashionable than in their current form.

Patients were positive about forecasted advances in biomonitoring for cancer prevention, screening and treatment. Both patients and providers were intrigued with using biomonitoring to determine cancer risk. Most patients were concerned with ensuring the privacy of the biomonitoring data. Providers were concerned with the integration of this new data into ongoing care activities. Many felt that integrating this information into care would require a large amount of training and upgrades in technology. Some providers raised concern about liability in these systems, while others saw them as a more intelligent extension of current aids to interacting with patients. The forecasts presented in the focus groups as well as comments from the focus groups are included in Appendix B.

Criteria for Biomonitoring

Individual Biomonitoring Advances

As part of the BFP process, the Institute for Alternative Futures developed a series of criteria for supporting a biomarker test or biomonitoring device in the context of its potential for reducing health disparities. These criteria were reviewed by experts and organizations and then by the advisory committee at its meeting. The criteria – initially focused on biomonitoring advances, were then merged with the DRA Project's longer list of criteria for disparity reducing advances. The first list below presents the initial criteria focused on biomonitoring advances. The second list below incorporates those into the larger set of criteria from the DRA Project.

Biomonitoring Criteria:

- Biomonitoring device that is proven to:
    - Be reliable
    - Be effective in changing behavior
    - Improve health at the population level
    - Compatible with IT infrastructure (digital output)

- Biomarker that is proven in controlled clinical trials to:
  - Yield high index of suspicion for further evaluation
  - Provide accurate diagnosis or forecast
- Compatible with clinical practices:
  - Administratively feasible; compatible with IT systems & infrastructure; has digital output or is easily recorded
  - Addresses a disease that is important to the clinic/provider and patient population
  - Easy to use for patients and providers
  - Clear guidelines for action or follow-up activities
- Where appropriate: passive, continuous, communicates results automatically
- Provides clear results, so further action can be taken
- Provides rapid results, so can take action during that encounter
- Provides a Clear Cost Benefit
  - Better cost/benefit ratio than current test
  - Low cost enough on a per/person basis for screening
  - Permits clinic to provide a test previously unobtainable
- Culturally, linguistically, age, and gender appropriate
  - For core client populations
  - For all client populations
  - For elderly populations

Criteria for Priority Setting Among Biomonitoring Advances

These initial criteria were added to the DRA Project's longer list of criteria for judging and prioritizing disparity reducing advances. The resulting criteria are as follows:

The biomonitoring advance:

- Can make a very large, measurable difference in reducing health disparities
  - Across multiple diseases/conditions
    - Stimulates prevention by identifying pre-disease conditions or risks

- - Enables earlier detection of the disease
  - Enables better, higher cost/benefit treatment
  - Lowers morbidity and mortality
  - o Within single high disparity diseases
    - Stimulates prevention by identifying pre-disease conditions or risks
    - Enables earlier detection of the disease
    - Enables better, higher cost/benefit treatment
    - Lowers morbidity and mortality
- Assists providers of care to the underserved
  - o Adds functionality
  - o Adds value to their services
- Practical for use
  - o In the home
  - o In the community
  - o At the point of care
- Cost effective enough to be applied and reapplied as necessary
  - o For the health care provider
  - o For the consumer/patient
  - o For the insurer/third party payor
  - o For society
- Appropriate for multiple poor and marginalized populations
  - o Culturally, linguistically, age and gender appropriate
  - o Large scale applicability across populations
    - Applicable and Easy to Use
    - Accepted by providers and population
    - Compatible with forecasts for other relevant emerging advances and developments
- Interoperable with key systems, approaches
- Encourages participation of individuals and key stakeholders
- Can be communicated to decision-makers and to the public

Key Opportunities for Reducing Health Disparities

After considering a range of key possibilities for biomonitoring advances in diabetes, cancer and healthy living, the Advisory Committee members nominated their sense of the most important or most promising advances. The leading four are presented below. Others on the list with a lower priority included:

- Better interoperability standards,

- A continuous non-invasive glucose monitor,

- Smart home monitoring linked feedback to the individual, connecting genetic proclivity forecasts with environmental exposure monitoring,

- New reimbursement policies for biomonitoring aimed at prevention.

Continuous, Passive Biomonitoring for Health and Prevention

Continuous, passive biomonitoring that aids in prevention and healthy living was ranked highest as a promising advance for reducing health disparities. A committee comprised of partners from the DRA Project and from the BFP Advisory Committee was developed to explore this opportunity. Their report can be found online at www.altfutures.com/DRA.

Continuous, passive biomonitoring can occur in the home or as a personal portable device (see the *Behavioral & Lifestyle Monitoring* section above for more information). Both have the potential to reduce the burden of chronic disease and lower the cost of care by aiding in prevention and management. These reinforce healthy behaviors. Their continuous nature allows gathering data on each person's unique patterns of physiological biomarkers. The combined knowledge of many individuals will support advances in knowledge in effective population approaches to health, as well as personalizing the care of each individual.

A number of new technologies are available for home use that can monitor mobility, sleep patterns and general activity. These technologies are already being used to monitor elderly patients and patients with

chronic conditions. They allow patients to age in the home and can prevent catastrophic falls and other events that can lead to a sudden decline in health.

Continuous, passive monitors can also be worn in personal devices to monitor physiological parameters such as motion, body heat, heart rate, and breath rate. Using sophisticated algorithms, these parameters can be used to provide useful information such as energy expenditure and physical activity. Combined with software for health coaching, these monitors can improve health and help manage diseases such as diabetes.

Based on current technologies and adoption, the following are reasonable forecasts for the adoption and use of continuous, passive biomonitoring:

- *By 2008, software standards for continuous, passive biomonitoring will allow devices from different companies to wirelessly share data (see ongoing work and goals of the Continua Health Alliance for more detail).*
- *By 2012, reimbursement models change so insurance companies reimburse for electronic monitoring in the home or on the body.[52]*
- *By 2016, continuous passive home and body monitors are commonly used to monitor elderly patients, patients with chronic disease and those that are concerned with improving their health.*

Continuous, passive biomonitoring has the potential to reduce health disparities if the technology is widely adopted. A number of opportunities exist to speed up the development and deployment of continuous, passive biomonitoring for reducing health disparities:

- Development of interoperability standards.
- Development of evaluation frameworks to study the use of continuous, passive biomonitoring in underserved communities.
- Pilot projects using continuous, passive biomonitoring in underserved communities.
- Guidelines for implementation of continuous, passive biomonitoring in underserved communities and for diseases with high health disparities.

The DRA Project is assembling a working group of committee partners to develop pilot projects using continuous, passive biomonitoring for reducing disparities. This working group will work in partnership with BodyMedia and the Medical Automation Research Center (MARC). BodyMedia provides continuous body monitoring solutions for individuals and healthcare practitioners. MARC, at the University of Virginia Health Sciences Center, is a research, development and consulting organization focusing on monitoring and automation.

Automated Control of Insulin

For diabetes, an implanted, closed-loop insulin pump driven by a continuous blood glucose monitoring system was identified as one of the most promising technologies for reducing health disparities. Such a device, if available to underserved populations, would improve the management of diabetes and reduce complications. Complications from diabetes, such as heart disease, stroke, amputation, blindness and kidney failure are a significant source of health disparities. More on health disparities related to diabetes and its implications for the future are in the *Diabetes 2016* section of this report.

A committee was developed to pursue this opportunity. On further evaluation, the committee considering this topic did not find automated control of insulin levels a good candidate for reducing disparities. The challenges for engineering such a device have been considerable. Developing a robust, continuous blood sugar monitor has been a challenge biomedical engineers have struggled with for over fifty-years. Such monitors have to be robust enough to withstand continuous use while accurate enough to monitor changes in blood sugar from activities such as exercise. Due to these challenges, it is unlikely that an internal closed loop biomonitoring and insulin pump system will be available on the marketplace by 2016.

External, continuous blood sugar monitors are already available. Most patients are still required to regularly check the accuracy of these monitors with traditional blood sugar monitors. Three or four of these monitors are available on the market in 2006. Many researchers believe the accuracy of these monitors will improve over the next few years. Even so, the costs for these technologies are expected to be in the $500 to $2,000 range for the device plus close to $35 for the replaceable sensor patch. While

the costs for these systems will probably go down over the next ten years, they will likely remain high for our targeted populations.

More significant is the care and attention required to maintain the system. The sensor and catheter sites must be kept sterile and bandaged. Finger stick blood glucose must be drawn at the time of new sensor insertion and 2-4 times a day while it is in place to calibrate the readings. Federal Food and Drug Administration has approved the system with the recommendation that the patient check a finger stick blood sugar before pushing a button approving the pump to administer the amount of insulin recommended by the data manager. Therefore, this is an "advise you" open loop system, not a fully automated "closed-loop" system. It is probable that these systems will slowly improve to become external closed-loop systems. However, the complexity and cost of these systems makes them more suitable for a small segment of the diabetic population with more severe forms of diabetes.

Early Detection of Cancer Using Blood Screening

A significant part of the discussion at the advisor's meeting was dedicated to the incredible increase in research geared toward the development of cancer screening tests based on biomarkers in the blood. The majority of these tests look at molecules in the blood such as genes and proteins to detect cancer. This research is incredibly complex and at an early stage, but is extremely promising (see *Blood and Serum Tests* for more information).

A large component of health disparities in cancer are due to cancer that are not identified early. New and more accurate tests for screening and early diagnosis could dramatically reduce disparities by identifying cancer in underserved populations. Many of the tests under development could be easier to use, more accurate than existing tests and screen for cancers for which there are no good existing tests. However, the costs of these tests are likely to be significant. Reducing health disparities will require not only improvements in cancer screening tests, but also a commitment to making these tests available to everyone who needs them. More on the impact of biomonitoring on cancer is available in *Cancer 2016*.

The committee gathered to look at these opportunities and came to the conclusion that there is too much early stage R&D activity in this area to identify clear winners for reducing health disparities. However,

as this field develops, it is important to monitor developments for promising advances that can be accelerated. To help the DRA Project in monitoring these developments they developed three horizons for monitoring. A more detailed description of DRA Project activities in each of these horizons is available in the Report of the *Early Detection of Cancer Using Blood Testing Committee* at www.altfutures.com/DRA.

- Horizon 1 (1-3 years) – near term – Review Currently Available Approaches; Monitor and Shape Emerging Potentials
- Horizon 2 (4-6 years) – mid term – Position Strategy and Resources to Leverage Promising Advances
- Horizon 3 (7-10 years) – long term – Uncover Possibilities and Create Options

The DRA Project will monitor these developments in the cancer blood test area and related areas and stimulate readiness of health care providers, particularly community health centers, to use them and for funders to be clear on the standards for reimbursement. In the process, the DRA Project will work to compress the normal diffusion time of tests that can make important differences in cancer detection and survival. The DRA Project will also monitor parallel advances in other forms of monitoring for early stage cancer and precancer, e.g. breath, saliva and other forms of testing in addition to blood tests.

Community and National Biomonitoring to Support Upstream Change

A major opportunity to reduce both health disparities and the cost of care will be to target at risk populations at the community and national level. Biomonitoring and environmental monitoring data collected at the individual level and the community level can be used to better understand the causes of ill health and of disparities in health. This information can be used to move upstream, targeting root causes, and support changes in individual behavior, public policies, market practices, and health care. Protections of privacy and security, and protection against discrimination will need to be in place for these biomonitoring advances and their benefits to communities to be effective.

The Committee assigned to exploring this opportunity developed four recommendations for the DRA Project. A complete look at this area of opportunity is available in the Committee Report on

Biomonitoring Used to Change Behavior Upstream at the Community and National Level. Recommendations for the DRA Project to Pursue include:

- **Biomonitoring & Surveillance Confidentiality:** The DRA Project could develop confidentiality agreements that the public and public health agencies are comfortable with by looking to the agreements used in other arenas, such as AIDS and STDs.

- **Prevention Promotion Pathway:** The DRA Project could study and identify promising advances in social marketing for individual behavior change and community change to address the social determinants of health and disparity. Proven or promising practices could then be adapted and deployed through the DRA Project Network.

- **Community Health Clinic Experiments with Information Integration:** The DRA Project could organize a user's technical support group among community health clinics to accelerate the effective integration of the electronic medical record, the personal health record, biomonitoring and related communications devices for their patients.

- **Leveraging Social Determinants:** A critical part of moving upstream is being able to affect the social determinants of health. The DRA Project should address how information from individual and population level monitoring can be used to promote improvement in the social determinants of health.

Using Cell Phones to Reduce Health Disparities

Another promising opportunity for reducing health disparities is through the use of cell phones. Cell phones are likely to be an important platform for biomonitoring. They can record information or convey biomonitoring data from an individual to data storehouses or to their health care provider. Cell phones and biomonitoring, by themselves, will not reduce health disparities. But, if they help to provide better management of disease by patients and their doctors, and if they reinforce healthy behavior, their impact could be significant. Cell phones include the "hand set", the infrastructure for communications with the hand set, and the services. There will be revolutions in all three areas, with major uncertainties and opportunities for reducing disparities.

The DRA Committee looked at a number of opportunities and ideas for using cell phones for reducing health disparities. Potential opportunities that would support cell phones as a platform for biomonitoring include:

- Identifying critical junctures for supporting disparity reduction in equipment or system design, infrastructure and services package development, for self care and managing diseases, particularly for high disparity diseases.

- Increasing awareness across stakeholders of the disparity reducing opportunities of cell phone and internet access evolution.

- Gathering funders and health care providers to provide input on the requirements for effective use and for reimbursement of cell phone related health services.

- Work with guideline, standard setting, and interoperability groups to consider the disparity reducing implications of these systems as they develop.

- Encourage tests/applications using cell phones and related technologies for various health applications among poor and underserved populations.

- Looking forward, the DRA Project can work with associations such as the Continua Health Alliance to consider the disparity reducing implications of the interoperable standards.

- Encourage "bottom of the pyramid" business strategies for cell phone hand sets, infrastructure, and services.

- Encourage free or low cost municipal, and possibly national, access

- Work to ensure that these systems do not leave the poor in a technological backwater, experiencing disparities because of outdated equipment, services or infrastructure.

Recommendations for Developing Biomonitoring to Reduce Disparities

The Advisory Committee also developed a number of recommendations for effectively advancing the field and using biomonitoring to reduce health disparities. These recommendations will be pursued through the larger DRA Project, where a number of the key organizations listed are partners in the DRA Network. The recommendations developed are below:

- Health Resources and Services Administration (HRSA) and the Centers for Medicare and Medicaid Services (CMS) should enhance partnerships for evaluating the intersection of biomonitoring platforms, specific disease biomarkers, and Community Health Centers (CHCs).

- The Clinical Director's Network and other appropriate groups should help design and implement controlled studies of effectiveness of biomonitoring systems in CHCs as well as diffusing best practices.

- Major federal agencies involved in funding research, such as the Department of Defense (DoD), the National Institutes of Health (NIH), and the Department of Veteran's Affairs (VA), should develop more coherent early stage funding programs based around biomonitoring for disparity reduction.

- The DRA Project should work with industry associations, such as the Pharmaceutical Research and Manufacturers of America (PhRMA) and the National Electrical Manufacture's Association (NEMA), on their member's biomonitoring activities and opportunities for reducing health disparities.

- The Food and Drug Administration (FDA) should encourage testing and evaluation of biomonitoring devices among populations with less access and resources.

- Efforts should be made to enhance the ability of CHCs and others to design, deploy and evaluate experiments/tests of potential biomonitoring advances.

- Forecasts or estimates of platforms under development or in consideration as well as potential disruptive innovations should be publicly available and shared with key stakeholders.

- Identify specific forums to develop and share information on biomonitoring for disparity reduction.

- Work with organizations to support the development of interoperability standards for biomonitoring devices.

- Review and encourage reimbursement strategies for effective biomonitoring, especially around prevention.

- Support a web based directory for biomonitoring technology, drug and device companies as well as early stage researchers and healthcare provides to network around biomonitoring for disparity reduction (e.g. Medical Automation.org).

Appendix A: Acknowledgements

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Appendix B: Focus Group Input

Focus groups with low income and minority populations and their health care providers were hosted by DRA Project Partners in Orlando, Galveston and Detroit. On February 28, two focus groups on advances in diabetes biomonitoring were held in conjunction with the Central Florida Family Health Center (CFFHC) in Orlando. Focus groups with both patients and providers were held in partnership with the Detroit Medical Center at Wayne State University and the University of Texas Medical Branch in Galveston. These focus groups considered both cancer biomonitoring and the use of biomonitoring for health and prevention. The focus groups were designed to get honest feedback from patients and providers on possible advances in biomonitoring. The group size ranged from 10 to 15 patients or providers. The patient population was ethnically diverse and recruited from the patient population of the partnering health care providers (a community health center, a managed care organization and a free clinic). The discussions with providers generally included both clinicians and management staff.

Each group was given a description of the Biomonitoring Futures Project and a set of forecasts to react to. The forecasts are presented below as well as a summary of their reactions to the forecasts.

Highlights

Patients were generally enthusiastic about the biomonitoring advances related to diabetes that were presented, often wanting them to be available sooner than the forecasts suggested. Clinicians likewise were encouraged by the forecasts but raised a broader range of questions about their impact and integration into care protocols. The cost of the advance, the ease of use, portability and the availability of the advance in multiple languages were all important considerations for both patients and providers.

Some clinicians raised questions of medical or legal liability that would accompany the patient's use of systems that provide advice. For the biomonitoring devices that are worn, some patients raised the request for fashionable equipment, rather than clunky or more athletic looking equipment.

Digital Blood Sugar Management – the "Digital Doctor"

The forecasts used in the focus groups are presented in italics:

Computer tracking and guidance to help patients manage their diabetes is common. The software is located in the patient's cell phone or computer and helps her identify when her blood sugar is too high and too low. The software also helps guide the patient in managing her diet, physical activity and medication use. One of the most popular models is the Digital Doctor. In easy to read graphs and charts, the Digital Doctor shows patient's their blood sugar levels over time and ways to bring their blood sugar back under control. The Digital Doctor can help guide patients through their results in over fifty different languages. The results are also sent to the patient's doctor. The doctor can use this data to help patients manage their diabetes.

Patient Comments

- Patients thought this would be a great to have and that they would use it, though some thought they might disconnect the monitor if they were doing the wrong thin (i.e. eating a candy bar).
- Their concerns with the forecast were the need to either to keep paying for cell phone service or needing to have a computer. The threat of computer shut downs due to a virus was a concern.

Clinician/Administrator Comments

- Clinician/Administrators were enthusiastic about the self management capacity of the digital doctor, the provision of reliable data and the language translation capacity.
- Their concerns were that not all patients would use this; that it could be too complex; that it might not link effectively with patient's cell phone to transmit data; and that it might lead to the patient not keeping appointments. They thought that some patients would definitely use the digital doctor tool while others would not.

Cancer Screening in 2015

By 2015, cancer screening is done annually or more often for most people. Those with access to healthcare have a blood spot test panel that screens for several common cancers (particularly breast, lung and colon cancer). These very sensitive tests are based on molecular markers, DNA fragments or cancer cells in the blood, and they are even capable of detecting pre-cancer in some cases. Because of smart development and large volume use these tests are relatively inexpensive ($2 or $3 for the panel plus the cost of the machine) and are easily performed in a clinic setting. Results are fast enough so decisions can be made at the time the patient is being seen. For those who don't go to the doctor or clinic routinely, screenings are done at health fairs or special events at local pharmacies, malls, schools, churches and homeless shelters.

The testing device can wirelessly send results to the patient's personal health record and to his health care provider's electronic health record. If the test comes back positive, a health counselor (human or electronic) will contact the patient and set-up a follow-up visit with a doctor where he will receive tests to confirm the diagnosis, appropriate counseling and intervention as needed.

Patient Comments

- Patients generally liked the forecast, including the ability to be screened at establishments in their neighborhood. One patient likened it to the flu shots available at health fairs and supermarkets.

- Many patients had concerns with the wireless sharing of results. In general, they were concerned about the security of the information and the possibility of discrimination based on the results.

- Opinions were mixed about the automatic follow-up after a test. Many felt it was a good idea, especially if the test was positive. Others felt they were ambivalent, worrying about the cost of care and if care was really necessary.

Provider Comments

- Providers generally liked the forecast. Especially if the costs for the panel plus the machine were inexpensive. They were concerned about additional training costs.

- There were some general hurdles of durability and usability of the test at health fairs and other sites. The tests would need to be quick and easy to conduct and the machine would need to be able to withstand transport without re-calibration.

- Many providers felt follow-up was important, but felt some questions about access to care would need to be worked out for the follow-up interventions.

Health Monitoring – the "Digital Companion"

By 2015, in addition to blood glucose monitors, body monitors are available to track stress levels, calories expended and other measures of health. These monitors can be linked wirelessly with other monitors such as a glucometer, bathroom scale or home blood pressure monitor. The information is sent from a computer or cell phone, and can be linked to the local community health center.

The Digital Companion is one of the newest and most popular body monitors. The Digital Companion can measure heart rate, blood pressure, stress levels, and the amount of calories expended, among other information. It can also link wirelessly to bathroom scales, glucometers, home Hemoglobin A1c monitors, and other biomonitors. All this information can be used by the Digital Companion, which is linked to patients' cell phones or computers, to help them manage their health. The Digital Companion can also create exercise plans, healthy recipes and provide motivation for exercise. The Digital Companion can talk directly to patients through their cell phone, stereo, computer or television set in over fifty different languages. When the patient meets with his doctor, the doctor can use the information from the Digital Companion to help the patient set goals for healthy living and to prevent diabetes before it occurs.

Patient Comments:

- Patients liked the fact that the digital companion monitors several things at once, particularly stress levels, and that it deals with prevention. Patients foresaw a price difference depending on how fashionable it was (ultra fashionable, fashionable, clunky). They also felt it would be useful if it gave assistance with sleep apnea, specifically if it awakened the patient or his spouse when needed or tells the spouse to get the oxygen mask. Another feature, that would make the digital companion useful to them, is being internet enabled and useable in foreign countries, including the ability to transfer medical records.

- Some patients disliked having to use a computer for the Digital Companion. Their concerns were how often it would need to be replaced or upgraded (should last longer than 3 to 5 years) and whether they would need loss replacement insurance. They would use it if were covered by Medicare or Medicaid or it cost $100 or less.

Clinician/administrator Comments

- Clinicians/administrators liked the breadth of information captured; the different approaches to capturing that information, its relevance to patient and physician, and that it would allow creation of exercise plans and healthy recipes tailored to the individual patient.

- They were concerned about issues of privacy and confidentiality, how best practices would be revised, and whether it would be cost effective. They were also concerned that the system be:

    o Easy to use (minimal computer, keyboard and technical skills required for both patient and physician)

    o Integrated into the medical record; yet not generate increased 24/7 demands on the clinician, nor increase the clinician's liability.

- They saw a similar device as being able to enhance the health-coaching role and capacity of mid-level providers (nurse practitioners/physician assistants), but there would be a need to clarify the additional responsibilities and protocols that would arise with this expanded approach.

- Clinicians believed well versed diabetics may really run with this, especially if it offered hope of getting off of insulin.

Other Topics Covered in the Focus Groups

- Inhaled Insulin – patients and clinicians liked this option, especially if it was linked to a biomonitoring system like a glucose monitor for easy calibration.

- Breathalyzer for Pre-Diabetes Screening – patients and clinician/ administrators liked this.

- When presented with the option of biomonitoring, most would prefer devices that are passive and continuous.

- Clinicians generally saw biomonitoring as another tool useful in giving patients more options.

- Some groups were presented with the example of the bathroom scale problem (i.e. We have an effective biomonitor in bathroom scales that show weight – a good biomarker for pre-diabetes and diabetes management. But the bathroom scale is often unused).

- o When presented with this problem, patients thought that the ability to have continuous passive monitoring would make a difference.
- o Clinician/administrators thought the problem of the bathroom scale reflected the diversity of patients – in their willingness to know, their readiness to change.

- Patients expressed their concerns on the effects of multiple medications; the intensity of cravings "my mind says no, my body says go"; job and workforce discrimination, particularly related to the side effects of diabetes.

- Regarding physical activity, physicians felt that a minority of patients will actually sustain exercise. Yet, as one physician put it – he tells his patients that they can do more to control their blood sugar by walking than by medicines. They felt information on a patient's progress in burning calories will be helpful with some people. Others will want the easiest way out – e.g. a pill.

- Some clinician/administrators argued that the focus should be on preventing diabetes in high risk patients along with reducing disparities for Hispanics and African-Americans. Shaping healthy eating and physical activity in the schools and for the entire family are important.

Appendix C: Endnotes

[1] McDonough, J., Gibbs, B., Scott-Harris, J., Kronebusch, K., Navarro, A., and Taylor, K. A. State Policy Agenda to Eliminate Racial and Ethnic Health Disparities, *Commonwealth Fund* (June 2004). http://www.cmwf.org/programs/minority/mcdonough_statepolicyagenda_746.pdf

[2] CDC, National Diabetes Fact Sheet: United States, 2005. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf (accessed 10/26/05).

[3] Honeycutt, AA, et al. A Dynamic Markov Model for Forecasting Diabetes Prevalence in the United States through 2050. *Health Care Management Science* 2003; 6:155-164.

[4] Rowley, WR & Bezold, C. *Diabetes Forecasts to 2025 and Beyond: The Looming Crisis Demands Change*, Changing Diabetes Forum, Washington, DC, November 9, 2005, Novo Nordisk National Changing Diabetes Program.

[5] Narayan, KMV, et al. Lifetime Risk for Diabetes Mellitus in the United States, *JAMA* 2003;290:1884-1890.

[6] Narayan, Op.cit.

[7] Flegal, KM, et al. Prevalence and Trends in Obesity Among US Adults, 1999-2000. *JAMA* 2002;288:1723-1727.

[8] Vasan, RS, et al. Estimated Risks for Developing Obesity in the Framingham Heart Study. *Ann Intern Med* 2005;143:473-480.

[9] Narayan, Op. cit.

[10] Davis, JL. Childhood Obesity Seen Even in Preschool. *WebMD Medical News*, May 5, 2003. http://my.webmd.com/content/Article/64/72383.htm?printing=true (accessed 10/13/05).

[11] McGinnis, MJ, Williams-Russo, P, and Knickman, JR. The Case For More Active Policy Attention To Health Promotion. *Health Affairs* 2002: 78-93.

[12] Tuomilehto, J. Primary Prevention of Type 2 Diabetes: Lifestyle Intervention Works and Saves Money, but What Should be Done with Smokers? *Ann Intern Med* 2005;142:381-383.

[13] The Prevention Institute. Health for all: California's Strategic Approach to Eliminating Racial and Ethnic Health Disparities. (Nov. 2003) http://www.preventioninstitute.org/pdf/H4A_EXECSUMM_1Scites_021304.pdf

[14] American Cancer Society. Cancer Statistics 2005. http://www.cancer.org (accessed 2/7/06).

[15] American Cancer Society. Annual Report to the Nation Finds Cancer Incidence and Death Rates on the Decline: Survival Rates Show Significant Improvement. http://www.cancer.org (accessed 4/29/05).

[16] National Cancer Institute. Cigarette Smoking and Cancer: Questions and Answers. http://www.cancer.gov/cancertopics/factsheet/Tobacco/cancer

[17] Vainio H, Bianchini F. IARC handbooks of cancer prevention. Volume 6: Weight control and physical activity. Lyon, France: IARC Press, 2002

[18] National Cancer Institute. Cancer Health Disparities: Fact Sheet. http://www.cancer.gov/newscenter/healthdisparities

[19] Center for Disease Control and Prevention. Preventing and Controlling Cancer: The Nation's Second Leading Cause of Death, At a Glance 2005. http://www.cdc.gov/nccdphp/publications/aag/pdf/aag_dcpc2005.pdf

[20] Ward, E, Jemal, A, Cokkinides, V, Singh, GK, Cardinez, C, Ghafoor, A and Thun, M. Cancer Disparities by Race/Ethnicity and Socioeconomic Status. *CA Cancer J Clin* 2004; 54:78-93 http://caonline.amcancersoc.org/cgi/content/full/54/2/78

[21] U.S. Cancer Statistics Working Group. United States Cancer Statistics: 2002 Incidence and Mortality. Atlanta, Georgia: Department of Health and Human Services, the Centers for Disease Control and Prevention and the National Cancer Institute, 2005. http://www.cdc.gov/cancer/npcr/uscs/pdf/2002_USCS.pdf

[22] American Cancer Society. Breast Cancer Facts & Figures 2005-2006. http://www.cancer.org (accessed 2/7/06).

[23] National Cancer Institute. Obesity and Cancer: Questions and Answers. http://www.cancer.gov/cancertopics/energybalance

[24] Petrelli JM, Calle EE, Rodriguez C, Thun MJ. Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of U.S. women. Cancer Causes and Control 2002; 13(4):325-332.

[25] Agency for Healthcare Research and Quality. 2005 National Healthcare Disparities Report. Accessed online (March, 2006): http://www.ahrq.gov/qual/nhdr05/nhdr05.pdf

[26] U.S. Preventive Services Task Force. What's New? Screening for Breast Cancer. Rockville, Maryland: Agency for Healthcare Research and Quality, 2002. Available at http://www.ahrq.gov/clinic/3rduspstf/breastcancer/brcannew.pdf

[27] American Cancer Society. Colorectal Cancer Facts & Figures, Special Edition 2005. http://www.cancer.org (accessed 2/7/06).

[28] National Cancer Institute. Cancer of the Colon and Rectum. Surveillance Epidemiology and End Results (SEER) Fact Sheets. http://seer.cancer.gov/statfacts/html/colorect.html

[29] National Cancer Institute. Physical Activity and Cancer: Fact Sheet. http://www.cancer.gov/newscenter/pressreleases/PhysicalActivity

[30] Vainio H, Bianchini F. IARC handbooks of cancer prevention. Volume 6: Weight control and physical activity. Lyon, France: IARC Press, 2002.

[31] American Cancer Society. Lung Cancer. http://www.cancer.org (accessed 1/2/05).

[32] Center for Disease Control and Prevention. Preventing and Controlling Cancer: The Nation's Second Leading Cause of Death, At a Glance 2005. http://www.cdc.gov/nccdphp/publications/aag/pdf/aag_dcpc2005.pdf

[33] National Cancer Institute. Cigarette Smoking and Cancer: Questions and Answers. http://www.cancer.gov/cancertopics/factsheet/Tobacco/cancer

[34] Centers for Disease Control and Prevention. Cigarette Smoking Among Adults - U.S., 2004. Morbidity and Mortality Weekly Report 2004; 54 (44): 1121-1124, Nov. 2005.

[35] U.S. Department of Health and Human Services. Tobacco Use Among U.S. Racial/Ethnic Minority Groups - African Americans, American Indians and Alaska Natives, Asian Americans and Pacific Islanders, and Hispanics: A Report of the Surgeon General. 1998.

[36] Arnst, C. (Oct. 25, 2006). Lung Cancer for Early Detection. *BussinessWeek.com.* Retrieved 10/26/2006 at http://www.businessweek.com

[37] For examples, visit www.dnadirect.com

[38] American Lung Association. Lung Disease Data in Culturally Diverse Communities: 2006 Updated Fact Sheets. http://www.lungusa.org/site/pp.asp?c=dvLUK9O0E&b=326027

[39] National Center for Chronic Disease Prevention and Health Promotion. Prostate Cancer: The Public Health Perspective. 2003 Fact Sheet. http://www.cdc.gov/cancer/prostate/prostate.htm

[40] Arnst, C. (Oct. 25, 2006). Lung Cancer for Early Detection. *BussinessWeek.com.* Retrieved 10/26/2006 at http://www.businessweek.com

[41] Mollyann Brodie, M., Flournoy, R.E., Altman, D.E., Blendon, R.J., Benson, J.M. and Rosenbaum, M.D. Health Information, The Internet, And The Digital Divide. *Health Affairs* 2000; 256-265.

[42] Parker, E.B. Closing the Digital Divide in Rural America. Telecommunications Policy 2000; 281-290.

[43] Smith, T. Philadelphia Plans Citywide Wireless Internet. PBS Online News Hour, Nov. 22nd, 2005. http://www.pbs.org/newshour/bb/cyberspace/july-dec05/philadelphia_11-22.html accessed 12/13/2005.

[44] Griffith, E. Standard for Mobile WiMAX Official. Wi-Fi Planet, Dec. 8th, 2005. http://www.wi-fiplanet.com/news/article.php/3569511 accessed 12/13/2005.

[45] Paterson, B. CNet's Quick Guide to 3G Cell Phone Service. http://reviews.cnet.com/4520-3504_7-5664933-1.html accessed 12/6/2005.

[46] Fatah, H. America Untethered - nearly 29 mil Americans had cell phones as of end-2002. American Demographics, March 1st, 2003. http://www.upoc.com/corp/news/UpocAmDem.pdf accessed 12/6/2005

[47] Interoperability between electronic systems can be broken down into three levels. Basic interoperability allows messages from one system to be received by another but does not require the computers to interpret the data. Functional interoperability allows the receiving computer to interpret the data fields, but does not allow th(computer to interpret the data inside. Semantic interoperability allows information within the data fields to be used intelligently. The interoperability of an EMR system depends not only on the technology the system uses, but how the data in the system is entered.

[48] Institute for Alternative Futures. The 2029 Project: Achieving an Ethical Future in Biomedical R&D. Alexandria, Virginia, 2005. http://www.altfutures.com/2029/The%202029%20Report.pdf accessed 12/13/2005.

[49] A Regional Health Information Organization (RHIO) is a multi-stakeholder organization that enables the exchange and use of health information, in a secure manner, for the purpose of promoting the improvement of health quality, safety and efficiency.

[50] Featherly, K. RHIO Grand? Healthcare Informatics Online. http://www.healthcare-informatics.com/newsclips/newsclips03_4_05.htm accessed 12/13/2005.

[51] Office of the National Coordinator for Health Information Technology (ONC). Goals of Strategic Framework. Department of Health and Human Services. http://www.hhs.gov/healthit/goals.html accessed 12/13/2005.

[52] Joseph Kvedar cited in Wang, U. (2006, June 6) Intel: Better Health Inside? Red Herring: The Business of Technology. www.redherring.com