

THE **DRA** Accelerating Disparity  
Reducing Advances  
**PROJECT**  
THE **BFP Project**  
Biomonitoring Futures



## Current Best Biomonitoring Practices

Background Report (BFP 1) March 30, 2006

## Current Best Biomonitoring Practices

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# DIABETES

## Screening for Diabetes

### Prediabetes

- Criteria:
  - Fasting plasma glucose (FPG) of 100-125 mg/dl
  - Oral glucose tolerance test (OGTT) of 140-199 mg/dl at 2 hours

### Diabetes

- Criteria
  - Fasting plasma glucose (FPG) of 126 mg/dl or higher on 2 separate occasions
  - Oral glucose tolerance test (OGTT) of 200 mg/dl or higher at 2 hours
- Technique
  - Blood drawn for lab test associated with physician visit
  - Glucometer screening at health fair has been discouraged because it is too easy to lose patient to follow-up for appropriate intervention (do not know ADA's current policy)
- Effectiveness
  - Lab testing extremely accurate
  - Glucometers – several brands and styles – many accurate to within 5% of reference tests; other sources suggest there can be a 10-15% error rate under ideal conditions (probably not a serious problem for management, but not good for screening)
- Cost, ease of use
  - All require a blood sample drawn by a trained individual
  - Cost of lab test about \$8 and up
- Disparities issues
  - Have to get patient into clinic or health fair for screening – should do screen whenever patient shows up – electronic record would help to identify who needs test
- What's missing
  - Accurate noninvasive device that could be easily used in clinic, workplace, mall, health fair, home, etc.

## Managing Diabetes

### Blood Glucose – Glucometer

- Mainstay of therapy – suggest testing 3 times a day or more for severe cases, but many with type 2 diabetes get by with once a day (or less)
- Effectiveness – ADA recommends accuracy of  $\pm 5\%$ , but not all meter brands meet this standard
- Cost
  - Cost of glucometer – between \$42 and \$66 (including 100 test strips)
  - Cost of test strips – around 75¢ - \$1 a strip (purchased in 50 and 100 unit boxes)
- Disparities issues
  - Expensive for uninsured
  - For all – the pain and hassle reduce compliance
- What's missing – accurate noninvasive device

## Hemoglobin A1c

- Most effective way to measure compliance with therapy and whether diabetes is under good control
  - Ideal is HA1c <7% (ideal is less than 6.5%), but many accept level <9% as “adequate” or “fair control”
- Recommended testing every 6-12 months depending upon severity
- Cost, ease of use (HA1c)
  - A1c home tests cost about \$20 per kit, which includes the laboratory analysis (person must draw blood sample with test either done at home or mailed to reference lab)
  - Clinic labs can do it for ~\$8 per test, but outside lab may charge ~\$65
- Disparities issues
  - Should be available in CHC, but many do not have trained lab technicians and equipment so must send test out at greater expense (cost and hassle could limit number of tests done)
  - Moderate expense if patient has to pay for it
  - Would be ideal if patients could get results while still in clinic so action can be taken then if necessary
- What’s needed
  - Simple device with rapid result that can be used at point of care or at home
  - Ideally would be wirelessly downloaded to cell phone or computer with longitudinal tracking and transfer of data to health care providers

## Managing Dyslipidemia

Serum cholesterol, LDL cholesterol, HDL cholesterol, triglycerides

- Important for screening of all diabetics as between 70-97% have dyslipidemia; screening should be every 1-2 years with testing every 4-12 months if being treated (every 2-3 months while initiating therapy until under good control)
- Screening should include LDL cholesterol or total cholesterol, HDL cholesterol and triglycerides – more sophisticated tests also available
- Test costs
  - Very accurate lab test versions – actual cost probably ~\$5-10 per test, but cost to patient probably ~\$100 for the 3 tests
  - Point of service/home test kits are available for about \$20-55 depending upon which tests provided
- Disparities issues
  - Most CHCs must send tests out, getting results in 1-5 days electronically or via mail as they do not have the equipment or trained lab technicians. Simple CLIA-waived test kits are available
  - Moderate expense if patient has to pay for it
  - Would be ideal if patients could get results while still in clinic so action can be taken then if necessary
- What’s needed
  - Simple device with rapid result that can be used at point of care or at home ideally wirelessly downloaded to cell phone or computer with longitudinal tracking and transfer of data to health care providers

# CANCERS

- CHCs can do screening for common cancers, but almost always must refer the patient to specialists for definitive management
- Screening of breast and colon cancer is straight forward, but lung cancer is very difficult to discover early.
- What's needed
  - Genetic testing to forecast future risk
  - Simple screening tests that are easy to obtain without being unpleasant or embarrassing – could detect protein(s), genetic changes, metabolites or volatile organic compounds predictive of the presence of cancer
  - These are probably going to be far off and expensive – besides discovery and development, it will take large, long-term trials to confirm effectiveness and benefit

## BREAST CANCER

### Screening for Breast Cancer

#### *Breast Self Exam*

- Breast Self Exam (BSE) is an option for women starting at about 20 y/o. It may not be any more effective than finding a breast lump by chance and has not been shown to reduce cancer mortality. Some professional guidelines recommend not doing it, but the American Cancer Society web site still lists it as an option.
- Patient needs training – brochure or demonstration by health professional
- Most breast changes are not cancer and BSC leads to more breast biopsies and the diagnosis of more benign lesions
- Some patients are stressed about doing technique right to the point that it produces more harm than good

#### *Clinical Breast Examination*

- Done by a professional as part of health exam every 3 years in 20s and 30s and annually after 40 y/o – often done by gynecologist along with pelvic exam and pap smear

#### *Screening Mammogram*

- Recommended annually after 40 y/o
- Uncomfortable, expensive, must be done at center with special mammogram machine, technician and radiologist (also there is a shortage of capacity and radiologists to read studies in some areas)
- Can miss early cancers, many false positives requiring biopsies
  - Only 1-2 of 1,000 studies are found to have cancer; about 80% of biopsies resulting from suspicious area turn out to be negative
- It is important to get results of study, not assume that if you don't hear the study was negative
- A screening mammogram costs between \$100 and \$150.
- Computer-Aided Detection CAD mammogram may raise the cost per test between \$15 to \$20  
<http://imaginis.com/breasthealth/cad.asp>

- It is possible that a digital mammogram is better than a conventional study and the technology is likely to shift this way as part of digital radiology departments
- Disparities issues:
  - The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) provides financial assistance for those without insurance and attempts to reach underserved communities
  - Need to see patient, schedule study, make sure patient can get to center and get study, make sure results tracked and patient contacted, follow through with any additional procedures if suspicious result
  - Expense for clinic or patient

### *Genetic Testing of BRCA1 & BRCA2 Mutations*

- If BRCA1 or BRCA2 positive there is up to an 80% chance of developing cancer during lifetime; also increased risk of developing ovarian cancer
- Testing is recommended only for those with a strong family history of breast cancer and those of Eastern and Central European (Ashkenazi) Jewish ancestry
- Cost of full sequencing is \$2975 in one center – if positive also need counseling

### **Diagnosis of Breast Cancer**

Diagnostic mammogram – more views to analyze suspected area

- If suspicious area appears to be a cyst can do ultrasound or needle aspiration
- Suspicious lump should still be biopsied even if mammogram is normal

MRI – Some studies suggest this finds more cancers in high risk patients

### *Biopsy*

- Fine needle biopsy or surgical excision biopsy
- Sometimes hard to locate the suspicious area for biopsy – new MRI guided vacuum-assisted biopsies being studied for more difficult cases

### *Tests to Determine Cancer Spread*

- CT scan, MRI, PET scan, bone scan, blood tests
- Costs for typical scans:
  - PET scan costs \$2,000
  - MRI scan costs between \$700 and \$900
  - CAT scan costs \$500 and \$700 - <http://www.post-gazette.com/pg/05030/449686.stm>

### *Tests to Characterize Tumor for Therapeutic Options*

- HER2/neu Testing
  - 1/3 of cancers produce too much growth-promoting protein (HER2/neu) and tend to grow and spread more aggressively
  - They are treated with Herceptin and special combinations of chemotherapy
  - Cost of the Oncotype DX test from Genomic Health is about \$3,500
  - Herceptin therapy was \$27,000 to \$81,000 annually a couple years ago
- Other tests are being studied – changes in p53 tumor suppressor gene, epithelial growth factor receptor, microvessel density, etc.

# COLON CANCER

## Screening

- Believe 50% of deaths could be prevented through use of screening tests
- Only 40% of adults over 50 y/o had colonoscopy in past 5 yrs and only 22% had fecal occult blood test in past 12 months. Those without insurance get screened much less often. Part of the problem is because the health system doesn't reach the patient and push for testing or patient doesn't follow through with tests. The other problem involves culture and embarrassment – some cultures don't allow rectal exam or expect a female physician to do it.
- Disparities issues
  - Fecal occult blood test is inexpensive and easy, but need to be seen and instructed in how to do test, must return samples and must be seen or called in follow-up
  - Flexible Sigmoidoscopy could be performed in CHC inexpensively, but probably rarely done because need trained staff, takes time and need equipment
  - Barium enema, colonoscopy and virtual colonoscopy need referral and are expensive
- What's missing
  - Simple screening test with high sensitivity and specificity such as DNA, messenger RNA or specific protein stool test or a protein blood test [all in various stages of R&D]
  - Predictive test, i.e. SNP pattern highly correlated with specific cancers [probably in early development]

## Stool Testing

- Fecal occult blood test (FOBT) – looks for hidden blood in feces
  - Can lower mortality 15%-33% with biennial screening
  - Effectiveness:
    - Sensitivity about 24% for 3 home FOBTs; as high as 81% with serial testing
    - Specificity up to 88%-98% (of some pathology), but only 10% of positives found to have cancer
  - Challenges
    - Need to stop some medicines and avoid some foods for few days before test
    - Many patients resist the hassle – collecting 2 stool samples on 3 separate days
    - Many false positives and negatives
- Immunochemical FOBT
  - Use antibodies that detect partial sequences of antigenic sites on globin portion of hemoglobin making dietary restrictions unnecessary
    - Probably work slightly better than FOBT, but as it is more expensive the cost-effectiveness may be less
- Stool DNA
  - Look for mutations of DNA (K-ras, p53, BAT-26, etc.) in exfoliated neoplastic cells in the stool (DNA is quite stable in the stool, but have to differentiate cancer DNA from normal cells and bacteria)
  - Effectiveness: study of 4,404 patients undergoing colonoscopy with 31 cancers found – Fecal DNA detected 52%
  - In 2003 the first commercially available stool DNA test was \$795
  - Still awaiting larger study results and more refined tests before establishing when it is appropriate

- Stool Proteins, Mucus and Messenger RNA Tests – still experimental
- Relative cost of fecal screening tests:
  - FOBT ranges from \$3 to \$40.
  - Fecal DNA ranges from \$400 to \$800 - [http://www.medscape.com/viewarticle/512276\\_print](http://www.medscape.com/viewarticle/512276_print)

### Double-Contrast Barium Enema

- 90% sensitivity for polyps 1 cm, but misses 20%-50% of small polyps
- Usually skipped in favor of colonoscopy (as can also do biopsies), unless patient refuses colonoscopy
- Cost \$250-500

### Flexible Sigmoidoscopy

- 59%-79% of cancers within reach of scope
- Cost \$150-300

### Colonoscopy

- “Gold standard,” but still misses 10%-20% of small polyps (especially in right colon) [entire colon “visualized” in 98% of patients]
- Advantage is that biopsy (remove) small lesions that could later turn into cancer
- Cost \$800-\$1600 and up
- Requires uncomfortable bowel prep, sedation during procedure
- Mortality rate due to perforation of about 1/5000 procedures
- It is 3 times as expensive as barium enema, but has the advantage of greater accuracy and biopsy can be done of any suspicious area

### Virtual Colonoscopy

- Uses high-resolution CT scanning to image inside of colon
  - The advantage is that it avoids a colonoscopy (if biopsy not needed), but the patient still has to go through the same uncomfortable bowel prep as colonoscopy
    - There is an experimental process that avoids the bowel prep by ingesting contrast media a day before the study and then digitally subtracting the visualized stool to see the empty bowel lumen
  - A major disadvantage is that if a polyp biopsy is required the patient must go through a second bowel cleanout and then a colonoscopy
- Still debating its effectiveness compared to colonoscopy
  - Results of one trial: 89% sensitivity and 80% specificity for polyps larger than 6 mm (~ equivalent to colonoscopy)
  - Another trial: only sensitivity of 39% for 6 mm polyps
- The cost of a virtual colonoscopy is \$1,200.00. This is 1/3 the cost of a traditional optical colonoscopy - <http://www.theplc.net/MD-VC-FAQ.shtml#COst>

### ACS screening recommendations for average risk patient beginning at 50 y/o:

- FOBT every year or
- Flexible sigmoidoscopy every 5 years or
- FOBT every year plus flex sig every 5 yrs or
- Double-contrast barium enema every 5 years or
- Colonoscopy every 10 years

## Diagnosis of Colon Cancer

### *Biopsy*

- Usually done by colonoscopy
- CT guided needle biopsy for suspected metastases

### *Staging for Therapy and Prognosis*

- CT scan, MRI, PET scan, angiography as appropriate

## LUNG CANCER

### Screening

- So far screening tests have not detected cancer early enough to prevent people from dying; so there is no standard for routine screening and most early diagnoses are fortuitously spotted on X-rays for other purposes

### *Chest X-ray*

- Criteria
  - Routine physical exams with chest X-rays are becoming uncommon
  - Physicians may order chest X-rays on older smokers, especially if they have suggestive symptoms (late in the disease)
- Effectiveness - cancer has to be big enough to be seen which often means advanced disease [not cost effective for routine screening of smokers]
- Cost - \$50-150 dollars, need equipment, technician and access to radiologist to read study – often must be sent off site for the study
- Disparities issues – have to be seen and have test ordered, often go offsite for study, and be reached for follow-up
- What's missing – does not provide early diagnosis, expensive, not effective screening tool
- On the web, the cost of the x-ray is listed everywhere from \$60 to \$790. My best guess is around \$120 (for the patient).

### *Sputum Cytology*

- Must give specimen and it must be analyzed under the microscope by lab experts looking for cancer cells – don't find many cancers early and usually used as a diagnostic test in symptomatic patient

### *Spiral or Helical Low Dose CT Scanning*

- Large ongoing study (National Lung Screening Trial – NLST) to see if it is warranted as a screening test
- Effectiveness – can pick up smaller cancers than chest X-rays [but still often advanced cancer]
- Cost - \$250 - \$750 – need sophisticated expensive equipment, technicians and radiologists found in hospitals and imaging centers
- Disparity issues – expensive, must be ordered and done offsite, need to reach patient in follow-up

Experimental Tests – looking for DNA changes in bronchial cells and breath analysis of volatile organic compounds

### Diagnosis of Lung Cancer

- Need a tissue sample studied under the microscope to confirm cancer cells and determine type and other characteristics. The tissue is obtained by bronchoscopy, mediastinoscopy, thoracentesis, fine needle biopsy, sputum cytology or other surgery. Staging can involve CT scan, MRI, PET scan, bone scan, blood tests, bone marrow biopsy, etc. All these things are sophisticated and usually are done by referral to cancer specialists.

## GENERAL SCREENING GUIDELINES – ADA, ACS, AHA

Joint recommendations from the American Diabetes Association, the American Cancer Society and the American Heart Association.

### Men & Women

- Blood pressure measurement:  
Starting at age 20, each regular healthcare visit, at least every two years
- Body Mass Index (BMI) measurement:  
Starting at age 20, each regular healthcare visit
- Blood cholesterol test:  
Starting at age 20, at least every five years
- Blood glucose (sugar) test:  
Starting at age 45, every three years
- Colorectal screening:  
Starting at age 50, every 1-10 years depending on the test your doctor uses

### Women

- Clinical breast exam (CBE):  
Starting at age 20, every three years; yearly after age 40
- Mammography:  
Starting at age 40, yearly
- Pap test:  
Starting at age 20, yearly. After age 30, every one to three years, depending on the test your doctor uses and past results

### Men

- Prostate specific antigen test and digital rectal exam:  
Starting at age 50 ask your doctor about the pros and cons of testing