National Institutes of Health

Fact Sheet — *Research Into What Works Best*

Research into what works best is called "comparative effectiveness" research. Through such work, the National Institutes of Health (NIH) provides doctors, patients, and policy makers with information they need to choose among possible treatment options available in real-world settings.

Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)

- Compare the effectiveness, side-effects, and cost-effectiveness of older and newer antipsychotic medication to treat schizophrenia in real world settings.
- An older medication perphenazine tested against newer "atypical" antipsychotics, including olanzapine, quetiapine, risperidone, and ziprasidone.
- This National Institute of Mental Health (NIMH) clinical trial cost $42.6 million, with 1,460 participants enrolled.
- Findings suggested that as a whole, the newer medications have no substantial advantage over the older medication used in this study.
- The older medication was as effective as 3 of the 4 newer drugs.
- The fourth compound, olanzapine, was slightly better in terms of discontinuation and hospitalization rates, but was associated with higher rates of weight gain and metabolic side effects.

Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

- Tested whether the occurrence of heart attacks and strokes was lower for high-risk hypertensive patients treated with newer classes of drugs compared with long-established, inexpensive diuretics.
- The National Heart, Lung, and Blood Institute (NHLBI) funding for Fiscal Years (FY) 1993-2004 was $83,170,059 and 42,418 participants enrolled.
- Findings suggested that the diuretic was at least as effective as newer medications.
- At five-year follow-up blood pressure control had been achieved in 66 percent of participants (compared with 27.4 percent at entry) demonstrating that blood pressure levels can be improved in many patients.
- The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure updated its clinical practice guidelines in response to study findings.

Sudden Cardiac Death in Heart Failure Trial (SCD- HEFT)

- Tested whether an implantable cardiac defibrillator (ICD) or an antiarrhythmic drug would better prevent sudden death in heart failure patients.
- NHLBI funding for FY 1997-2003 was nearly $12 million and 2,521 participants enrolled.
- Findings revealed that the ICD significantly reduced deaths; an antiarrhythmic drug was no better than a placebo.
- The Centers for Medicare and Medicaid Services (CMS) agreed to cover ICDs. A condition of coverage will be participation in a CMS registry to establish which patients are most likely to benefit. Medicare pays an estimated $30,000 per ICD.
- Empirical analysis supports the cost-effectiveness of ICDs in heart failure.

National Emphysema Treatment Trial (NETT)

- This study tested the role, safety, and effectiveness of bilateral lung volume reduction surgery (LVRS) compared with standard medical care in the treatment of emphysema. A secondary objective was to develop criteria for identifying patients likely to benefit from LVRS. The study was cosponsored by CMS and the Agency for Healthcare Research and Quality (AHRQ).
- NHLBI funding for FY 1997-2004 was $35 million and 1,218 patients enrolled.
- The study demonstrated that LVRS benefits certain patients but is harmful to others.
- Prospective cost-effectiveness analysis found that though LVRS is costly relative to medical therapy over three years of follow-up, the procedure may be cost effective if benefits can be maintained over time.

Diabetes Prevention Program (DPP) Clinical Trial

- The program tested effectiveness of two approaches to slowing development of type 2 diabetes in high-risk patients with impaired glucose tolerance.
- Interventions included intensive lifestyle change (goal of 7% weight loss, 150 minutes physical activity/week) or treatment with metformin.
- Funding: FY 1994-2002 was $176 million and 3,234 participants enrolled (45% were minorities).
- Lifestyle intervention reduced development of diabetes by 58% over 3 years (and metformin by 31%) compared to placebo group (placebo and standard advice on diet and exercise).
- Follow-up studies also demonstrated advantages of lifestyle intervention over drug treatment.
- The American Diabetes Association (ADA) revised clinical practice guidelines; however third party coverage was not optimal.
- A cost-effectiveness model estimates that the DPP life-style intervention would cost society about $8,800 per person; and metformin would cost about $29,900 per quality-adjusted life-year saved over the lifetime of a patient.

Diabetes Control and Complication Trial (DCCT) and Epidemiology of Diabetes Intervention and Complications (EDIC)

- Tested whether sustained tight control of blood glucose could prevent or delay onset or progression of symptoms in type 1 diabetes.
- Compared “intensive” therapy (more frequent glucose self-monitoring and increased insulin dosing) with conventional monitoring and control.
- The DCCT funding for FY 1982-1995 was $169 million; EDIC 1966-ongoing funding is $58.4 million “intensive” therapy group demonstrated reduced risk of heart (76 %), and of kidney disease (50 %) and of nerve disease (60 %) compared to conventional treatment.
- National Diabetes Education Program was launched to disseminate findings and the ADA updated its clinical practice guidelines in response.
- EDIC shows sustained long-term benefit from “intensive” therapy for 8 years following DCCT completion.

Perinatal HIV Prevention Trial II

- Compared effectiveness of adding the drug nevirapine to standard zidovudine (AZT) therapy to lower risk of mother-to-child HIV transmission rate (Thailand).
- Interventions included: 1) administration of standard AZT therapy and formula-feeding, plus a combination with a single dose of nevirapine administered to mother at onset of labor, and to infant following birth; and 2) a single dose of nevirapine administered to mother at onset of labor.
- The NIH support for FY 2000-2003 was $3.7 million.
- Findings revealed that adding a single dose of nevirapine to AZT treatment and formula feeding regimen reduced mother-to-child HIV transmission rate from 6% to 1.1 % – similar to rates achieved with the drug treatment program delivered in the United States.
- In response, the Ministry of Public Health in Thailand modified its care practice recommendations for preventing mother-to-child HIV transmission; the World Health Organization adopted this regimen for all HIV-infected pregnant women in developing countries.

- Disseminated in peer-reviewed journal, updated WHO guidelines.
- Cost effectiveness: Nevirapine costs $4 and is often available in developing countries for free or for <$1. By adding this low cost intervention, transmission rates are further reduced by 80%. The WHO estimates 700,000 children are newly infected with HIV. If all countries implemented the effective combination regimen, approximately 560,000 children could be spared HIV transmission.
- References: NEJM (2004) 351:217-228; WHO (2004) Guidelines on Care, Treatment and Support for Women Living with HIV/AIDS and their Children in Resources-Constrained Settings: 34.

Medical Therapy for Prostatic Symptoms (MTOPS)

- Tested whether the combination of two drugs, doxazosin and finasteride, was more effective than either drug alone, in preventing progression of benign prostatic hyperplasia (BPH).
- Three thousand and forty-seven men (18 % minority) were treated and followed for 4.5 years at 17 recruiting sites.
- NIH support from 1992-2002 was $57 million, plus private sector support.
- Funding revealed combination therapy to be almost twice as effective as either drug individually—reducing progression of disease and reducing the need for more invasive treatments by two-thirds.
- Particularly for men with a high risk of progression, combination therapy is life-enhancing and cost-effective.
- The American Urological Association has revised its Guidelines on Management of Benign Prostatic Hyperplasia to incorporate these findings, recommending combined therapy for men at high risk of progression.

Timing of Cochlear Implants

- About 36,000 Americans, half of them children, have received cochlear implants, which convert vibrations into electrical impulses and thus can cure deafness. This study evaluated the most effective timing of treatment and provided third party payers evidence that the device was cost-effective.
- Two hundred child participants received cochlear implants at different ages.
- The earlier in life the device was implanted, the better speech perception and language outcomes were. Normal speech and language skills were documented in 80 % of children who lost hearing after birth who underwent implantation within a year of onset of deafness.
- A cost-utility analysis, comparing cost of therapy to money saved through reduction in need for special education, and increased projected future earning potential for an individual with hearing, revealed each implant resulted in a net saving to society of over $53,000 over the lifetime of the child.
- Now considered standard treatment, cochlear implants are covered by most insurance companies.