examine 200 to 400 genetic samples from four populations in Africa, Asia, and the United States. (Previous studies have shown that haplotype patterns differ in part based on migratory histories.)

Enthusiastic about the HapMap's potential to provide medical answers that the full human genome sequence has yet to offer, NIH paved the way, planning a $40 million commitment early this year. Since then, the Canadian government kicked in a little under $10 million and, more recently, the Wellcome Trust Sanger Institute in Hinxton, U.K., about $25 million. Japan, China, and the SNP Consortium, a public-private group seeking single-base differences among genomes, are also adding to the pot.

Work is expected to begin as soon as participants at genome centers in the United States and abroad agree on some ground rules for the project, perhaps the most unwieldy collaboration since the sequencing of the human genome. They have yet to determine, for instance, how data collection will be standardized. Also uncertain is precisely how the map will be structured and how the work will be divvied up.

"We've learned how to find good ways to work together," says David Bentley, head of human genetics at the Sanger Institute. But he notes that unlike the 3 billion bases biologists knew they'd uncover in the genome project, here no one knows quite what to expect.

–JENNIFER COUZIN

WOMEN'S HEALTH

More Questions About Hormone Replacement

Three months after a review panel abruptly stopped a 16,600-woman study of hormone replacement therapy (HRT), a stunned medical community is trying to resolve questions raised by the trial. Last week, several hundred experts and observers gathered at the National Institutes of Health (NIH) in Bethesda, Maryland, to weigh the implications. Most agreed that hormone therapy should not be used to prevent disease. But HRT might still have valid, short-term uses in treating the symptoms of menopause. The risks are not clear, however, nor will they be easy to study, for many acknowledge that large-scale hormone trials might no longer be feasible or ethical.

That point was underscored when the U.K.'s Medical Research Council announced in London at the same time that it was abandoning a similarly ambitious hormone study. The British trial, Women's International Study of Long Duration Oestrogen After Menopause (WISDOM), had planned to enroll up to 22,000 women. It was already struggling to recruit volunteers when the U.S. study of Prempro, a drug combining estrogen and progestin, was halted in July. An interim analysis of the U.S. research, part of NIH's Women's Health Initiative (WHI), had shown that the hormones increased the risk of heart disease, breast cancer, and stroke more than they reduced chances of osteoporosis, bone fractures, and colorectal cancer (*Science*, 19 July, p. 325).

WISDOM's leaders, fighting to keep their trial alive, argued that the benefits might still outweigh the risks for many women. But the Medical Research Council overruled them. Results from the $32 million study, not expected until 2016, were unlikely to differ enough from those of WHI to alter clinical practice, says Oxford University's Ray Fitzpatrick, chair of an international panel that recommended terminating the study.

> **"The dilemma now is [how do we decide] who's at too much risk to take hormone replacement therapy?"**
>
> **—Deborah Grady, UCSF**

WHI's outcome, meanwhile, has sown confusion among women and their doctors. NIH organized the workshop in an attempt to clear it up. The befuddlement was due in part to the fact that most women take hormones to counter symptoms of menopause such as hot flashes, which the trial was not designed to evaluate. It examined other health endpoints among women whose average age was 63. Many doctors questioned whether the WHI results applied to women typical of those in their waiting rooms—in their early 50s and just entering menopause. Could the risk of disease attributed to hormone use be lower in a younger cohort?

Shutting down the trial raised broad questions like these, said Deborah Grady of the University of California, San Francisco: "The dilemma now is [how do we decide] who's at too much risk to take hormone replacement therapy?" WHI investigators are poring over 5 years of data to try to identify risk factors. Grady and others cautioned against making assumptions that are not backed up by WHI's data.

The study was halted when 38 per 10,000 women receiving Prempro for a year were diagnosed with invasive breast cancer, compared to 30 in the placebo group. Although this 26% increase is substantial, the risk for an individual woman remains small.

In the future, researchers should "focus on 50 to 59 [year-olds]," was the message from the audience, says Marian Limacher, a WHI investigator at the University of Florida College of Medicine in Gainesville. But she thinks it would be next to impossible to run such a trial: "Who's going to be willing to stay on long-term hormones now?" she asks. Not many, if the aborted WISDOM trial is any indication. Although closely watched trials of HRT to prevent Alzheimer's disease will continue, others—including one on lupus patients—have been abandoned, according to NIH officials.

One of the most vexing questions is whether the risks linked to Prempro use apply to the four other combination HRT products on the market. The National Heart, Lung, and Blood Institute (NHLBI), which funded the WHI study, hopes to find out, although NHLBI's Jacques Rossouw agrees that "women might be a little leery" about enrolling in another hormone trial. Although the Food and Drug Administration is considering relabeling combination hormones to reflect the risks, Janet Woodcock, director of the agency's Center for Drug Evaluation and Research, says differences among product recipes make it "not possible to extrapolate" from Prempro to other medications.

While efforts to sift the results continue, investigators are watching for the next step by Wyeth, Prempro's manufacturer. In July, Wyeth requested access to the study data; NIH agreed to hand the information over. "Once it's released we can't control what they do with it," explained Limacher, who's unhappy that Wyeth will access the data before investigators publish all the findings. But Wyeth vice president Ginger Constantine argued, as Prempro sales plummeted, that "nobody needs science more than us."

–JENNIFER COUZIN AND MARTIN ENSERINK

ANTHROPOLOGY

Going Head-to-Head Over Boas's Data

Studying skull dimensions is commonplace in forensics and paleoanthropology. But two new papers offering diametrically opposed analyses of a classic study by Franz Boas suggest that the technique is still controversial for many anthropologists entwined in the ongoing debate over the relation among genes, environment, and race.

Boas, the father of American anthropology, published a study in 1912 challenging the prevailing belief that ironclad genetic rules govern cranial shapes. He took measurements from 13,000 European immigrants and their offspring living in New York comprising seven ethnic groups, the