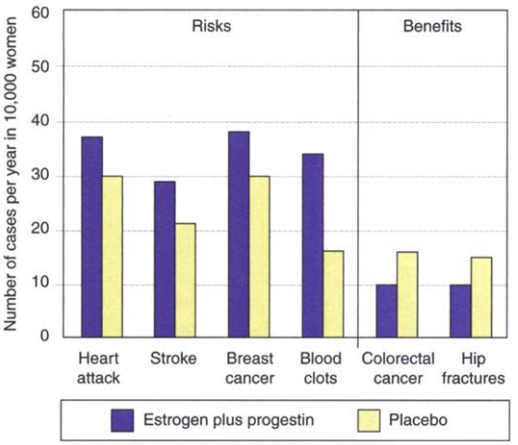


Bottom line. Risks of HRT outweighed benefits, according to a U.S. government study.

are planning to look into the discrepancy.

Other analysts, unwilling to discard long-term HRT, say there are different ways to explain the data. Clarkson, for instance, argues that studies in cynomolgus monkeys indicate that a real benefit occurs only if HRT is started as soon as natural hormone levels begin to drop (for most women, in their 40s) and is sustained from then on. A benefit in the WHI study was unlikely, he says, because most women started taking pills too late. Stanley Birge, a geriatrist at Washington University in St. Louis, argues that a reduction in Alzheimer's might not have shown up because the women were followed up for an average of only 5.2 years. He says it's "tragic" that the trial was ended "prematurely."

So what's the future of HRT? Most agree that Prempro will no longer be widely prescribed for long-term prevention. But some epidemiologists believe that doctors, nudged by skilled marketing, will continue prescribing other HRT combinations, lower doses, or therapies that use progestin intermittently. Birge, for one, thinks the study results say little about these alternatives, and he is advising women who consult him to keep taking their pills.

Ideally, says Birge, each alternative should be tested in a rigorous WHI-style trial. In the meantime, "I just don't think it's fair to withhold the potential benefits" of HRT, he says. But Barrett-Connor says this view is upside down: "When you're giving drugs to healthy people to prevent disease, there has to be evidence that they work," she says. "You shouldn't just start giving them until they're shown to be harmful."

The problem is that final answer might never come, because most agree that a study as large and costly as WHI is unlikely to be repeated. Currently, one other trial of Prempro is under way: the Women's International Study of long Duration Oestrogen after Menopause (WISDOM), a huge study that started 18 months ago. So far, the study has enrolled about 5000 out of the 22,000 women scheduled to participate in the United Kingdom, Australia, and New Zealand, says Madge Vickers of the U.K.'s Medical Research Council, one of the study's leaders.

Although many epidemiologists would love to see the trial completed, some wonder if that will happen: It could be difficult or even unethical to enroll more volunteers, now that U.S. women have been warned against taking HRT therapy. WISDOM's data-monitoring panel was scheduled to meet this week after *Science*'s deadline to recommend what should happen next. **–MARTIN ENSERINK**

MARINE SCIENCE

Researchers Plunge Into Debate Over New Sub

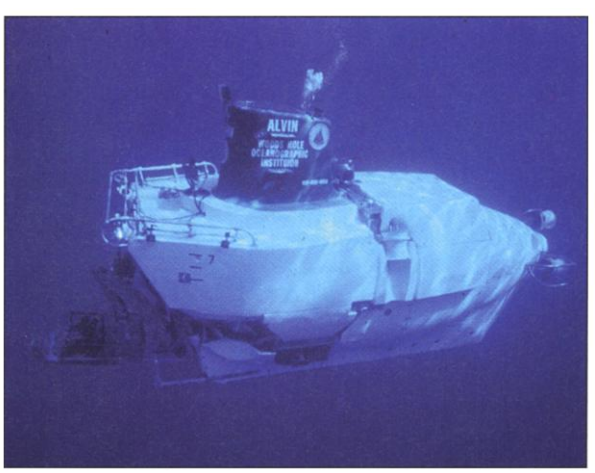
With its mainstay deep-sea submarine aging, U.S. marine scientists are talking about a replacement. There are lots of ideas but no consensus

U.S. marine scientists are thinking deep thoughts about a new research submarine. But there is fierce debate about how deep it should go—and whether humans should go along for the ride. "The idea of building a new human-operated vehicle is a polarizing issue; you hear strong views from all sides," says Marcia McNutt, head of the Monterey Bay Aquarium Research Institute in Moss Landing, California.

Competition for a slice of the nation's $400 million ocean research budget is always heated. But the contest has been sharpened by the aging of the 35-year-old *Alvin*, one of the world's few deep-water piloted submersibles (see table) and a mainstay of U.S. researchers. Although *Alvin* could last another decade, maintenance costs are mounting. So the National Science Foundation (NSF) and other agencies have asked the sub's operator, the Woods Hole Oceanographic Institution (WHOI) in Massachusetts, to design a more capable model by early next year.

Some researchers say a new *Alvin*, estimated to cost at least $20 million, doesn't need to go as deep as the current model, whereas others are pushing to go even deeper than planned. Another faction, to which McNutt belongs, argues that the money might be better spent on building some new, improved robotic craft. Meanwhile, members of Congress, a White House oceans panel, and a National Academy of Sciences group studying ocean exploration are preparing to wade in with their own ideas. "It's going to be a very energetic discussion," predicts James Yoder, director of NSF's ocean sciences division.

The sparring comes amid growing interest in exploring Earth's watery inner frontier. NSF and some international partners, for instance, are already pushing plans to build automated sea-floor observatories that would need tending from submarines. Other nations, such as Japan, are considering new deep-water submarines. And Congress has asked the academy panel to study ideas for an international ocean-exploration program that would take scientists into uncharted waters (*Science*, 24 May, p. 1386).



Sunken treasure. Scientists hope that a successor to *Alvin* would be more capable than existing piloted submersibles.

CREDITS: (TO TO BOTTOM) SOURCE: NIH; ROD CATANACH/WHOI

Such trailblazing has been *Alvin*'s forte since 1967. The stubby craft—which carries two scientists and a pilot—has made more than 3700 dives, giving researchers a glimpse of everything from historic shipwrecks to the evolving edges of continental plates. Among its greatest hits: retrieving a hydrogen bomb accidentally dropped into the Mediterranean Sea in 1966, discovering chemical-fed tubeworms and other chemosynthetic creatures huddled around deep-sea hydrothermal vents in 1977, and surveying the

sunken *Titanic*. "*Alvin* has been central to some great discoveries," says WHOI's Daniel Fornari, an *Alvin* manager.

But the wear and tear is beginning to show. Although most of the craft has been retooled or replaced over the years—"the name is the only original thing left," jokes WHOI engineer Barrie Walden—one expensive component is slowly degrading after heavy use. That is *Alvin*'s special buoyancy foam, designed to withstand the crushing pressure at the sub's maximum operating depth of 4500 meters. The foam is made from tiny glass spheres—the size of large sand grains—encased in hardened epoxy. At roughly $350,000 per cubic meter, *Alvin*'s load of foam costs about $1 million, Walden says, more than the titanium pressure sphere that protects the crew.

A proposal to use a cast-off Navy submarine as a replacement proved too expensive and too bulky for the *Atlantis*, *Alvin*'s nearly new tender. NSF and the National Oceanic and Atmospheric Administration (NOAA) then asked WHOI officials to start from scratch and to ask deep-sea researchers to help them envision an ideal replacement. There are some constraints: Any new model must fit on the *Atlantis*, and its annual operating budget should be close to *Alvin*'s current $5 million.

Topping the scientists' wish list was better visibility. Researchers have long complained that *Alvin*'s three view ports, which look to the sides and down, render it impossible to look over the pilot's shoulder to direct the sub's two manipulator arms or see exactly how a sample was taken. In addition, "you need to be a borderline contortionist" to look out the sub's windows, says Walden. So the new sub would have more forward-facing glass.

Scientists would also like to stay longer on the bottom. Up to half of a typical 8-hour dive is consumed by descending and ascending, and a more streamlined design would reduce transit times. "Getting even 10% more bottom time would be fantastic," says Fornari.

Many researchers also want to go deeper. *Alvin*'s 4500-meter depth range allows researchers to visit about 60% of the sea floor. But planners want to increase that to 6500 meters, giving the new sub access to an estimated 99% of the ocean bottom. Some researchers, however, question the need to go to 6500 meters when the vast majority of marine research is done in shallower waters. Even *Alvin* rarely operates at its limit.

Conversely, others say that even 6500 meters isn't deep enough. They want to return to the ocean's deepest trenches, 11,000 or even 12,000 meters down, which haven't been visited since the early 1960s. "If we're going to make a splash, we need to go all the way down," says deep-sea ecologist Richard Lutz of Rutgers University in New Brunswick, New Jersey. He and prominent marine biologist Sylvia Earle have been seeking converts in Congress and the media, and their allies are floating ideas on what research could be done in the abyss.

Then there are those—including McNutt and noted ocean explorer Bob Ballard—who have questioned the cost-effectiveness of sending scientists to the sea floor at all. They argue that the future belongs to unpiloted submersibles—either tethered remotely operated vehicles (ROVs), which are steered by a "video jockey" sitting aboard a ship, or their newer cousins, the independent autonomous underwater vehicles. These vehicles are particularly adept at mapping the sea floor, finding wrecks, and sampling hard-to-reach environments. Besides being cheaper to build, maintain, and operate than piloted submersibles, McNutt says ROVs can make longer, faster dives and collect more data. Comfort is a factor—"you're not cramped, damp, and cold," she says—and so is capability. "ROVs never get hungry, never run out of power—and nature never calls," she says.

Alvin's advocates say that the sub's critics downplay some important limitations of unpiloted vehicles. ROVs are indeed becoming more capable, they agree, but tethers still restrict range, movement, and payloads. Video cameras can never replace the human eye, they add, and ROVs are less agile in tight quarters. "It's hard to control something at the other end of a 3-mile-long [5-km-long] piece of spaghetti," says Fornari. And *Alvin*'s record for reliability and performance, they say, is unequaled. "We do things the others can't," he says.

Fornari and McNutt agree on one point, however. "What we really need to be discussing is the [vehicle] mix that will best serve the scientific community's needs" within available budgets, he says. There's also an incentive to minimize the number of craft, because operating costs eat into the funds available for science.

In Congress, *Alvin*'s future is drawing some attention, notably from Senator Ernest Hollings (D–SC) and Representative James Greenwood (R–PA), who helped create the Congressional Oceans Commission, which is preparing a report for release next year. The topic is also being discussed by the academy's ocean exploration panel, but it's not clear if the report, also due next year, will contain any recommendations.

Any consensus will be futile, of course, without money. Submarine backers are hoping that NSF, NOAA, and the Navy—which built and still owns and certifies the original *Alvin*—will pick up the tab. But the Navy is more interested in shallower water and unpiloted craft and has declined to join NSF and NOAA in funding the planning study. And any sub will face stiff competition within the ocean sciences budgets of the two agencies.

Such concerns, however, haven't stopped WHOI staff from eyeing the world's other deep-sea divers in a quest for possible improvements, from easier instrument installation and greater sample-carrying capacity to more agile manipulators and longer lived batteries. "We intend to steal plenty of good ideas from the competition," says Walden, part of a WHOI team that expects to produce an engineering design later this year that companies can use to fine-tune the price of the new craft.

In the meantime, *Alvin* continues its underwater dives. "It's old, it's tired," says McNutt, who despite her criticism of piloted vehicles remains a fan. "But it's been a phenomenal workhorse, and we'll miss it when it's gone."

–DAVID MALAKOFF

THE WORLD'S DEEP-SEA RESEARCH FLEET

	Proposed sub (U.S.)	*Alvin* (U.S.)	*MIR I & II* (Russia)	*Nautile* (France)	*Shinkai 6500* (Japan)
Depth (meters)	6500	4500	6000	6000	6500
% ocean coverage	99%	62%	98%	98%	99%
Dives/year	–	180	variable (low)	100–115	60
Scientists/dive	2	2	1 or 2	1	1
Battery operating costs per dive	–	$40	Unknown	$210	$35,000
Time on bottom (hours)	Longer	4–5	10–15	4–5	4
Payload (kg)	Heavier	680	290	200	150
Interior sphere volume (m^3)	Bigger	4.07	4.84	4.84	4.19
Observer visibility	Better	Side/down	Forward/ central	Forward/ central	Side/down

SOURCE: WHOI