basic scientific knowledge necessary to develop a device was available.

In the artificial heart program's early years, rapid growth in resources—from $500,000 in 1964 to $8 million in 1967—nurtured anticipation of early clinical results. Technical difficulties were greater than anticipated, however, and the basic knowledge necessary to design and produce the needed components was not available. There was no solution to two major technical problems: developing hemocompatible biomaterials and a power source. Researchers today are still attempting to perfect an inner surface material for the artificial heart that will not cause adverse chemical reactions when in constant contact with blood, yet is sufficiently durable to flex more than once a second over a decade without cracking or chipping (41,69). A compact, long-lived, and reliable power source has still not been developed; permanently implanted nuclear energy sources, popular in the 1960's, have been given a diminished priority, and greater emphasis is now placed on electrical engines that require a continuous energy supply or recharging.

In 1974, in response to these problems, the artificial heart program was moved into NHLBI's Division of Heart and Vascular Diseases. There it developed a more narrow focus, with an emphasis on the development of circulatory-assist devices that would augment the left ventricle of the heart by pumping blood from the left ventricle to the aorta. In 1975, authorization was given to begin clinical trials of a left-ventricular-assist device (LVAD) to be used temporarily in patients unable to resume cardiac function at the completion of open-heart surgery. Clinical trials for a 2-year implantable LVAD are expected to begin in an estimated 3 to 5 years. Targeted efforts beyond that include the development of a 5-year implantable LVAD and electrically energized engines. Researchers see the longer term implantable LVAD as a significant step, possibly a decade away. *

Parallel work on totally implantable artificial hearts is still continuing. Willem Kolff, at the University of Utah, has a number of calves in which his prototype heart has been successfully implanted. Nevertheless, the power source for a totally implantable artificial heart remains a continuing source of concern. Kolff's calves are on air-driven pumps, tethered to the wall; other prototypes require that an external battery-pack power an implanted motor. Estimates as to when a totally implantable artificial heart system capable of long-term support will be achieved are uncertain. The most common forecast is "many years away." Since the achievement of a totally implantable artificial heart depends on significant advances in basic knowledge and in bioengineering, it remains today a distant goal.

*LVAD research and clinical trials are discussed at greater length in a separate section of this case study.

POOL OF POTENTIAL RECIPIENTS IN THE UNITED STATES

Sources of Candidates

The authors of this case study assume that in order to be a candidate for heart replacement, a person must be in the hospital, with death imminent or highly probable, and must survive for 1 hour after the "replacement" decision is made (i.e., the amount of time needed to set up the operating room and get the patient on cardiopulmonary bypass).

The following three groups are sources of potential candidates:

1. survivors of recent myocardial infarction (heart attack) and/or cardiac arrest with worsening course,
2. persons with worsening chronic severe heart disease, and
3. persons having open-heart surgery whose heart after surgery is unable to reassume the hemodynamic load from the cardiopulmonary bypass pump.

In order to be candidates, persons in the first group would have to survive their attack or cardiac arrest through the following phases: home/

work (attack and replacement decision times), transportation to hospital, treatment in the emergency room, and initial stabilization in the coronary care unit. Candidates in the first and second groups would be primarily patients with ischemic heart disease (IHD), but would also include some patients with rheumatic heart disease (RHD).

The second group would include, in addition, persons with severe cardiomyopathy (heart muscle disease) which has rendered the heart incapable of supporting the body's needs at any level of exertion above absolute rest, and persons with severe electrical instability of the heart which has been refractory to treatment with medication. These individuals, we assume, would have to survive at least 1 hour of hospitalization in order to be candidates.

The third group would consist of persons whose heart is unable to reassume the body's hemodynamic load after the heart has been mechanically bypassed during open-heart surgery. Such surgery includes operations for coronary artery bypass, cardiac valve replacement, and cardiac muscle resection in hearts with severe mechanical or electrical dysfunction.

Our estimates of the number of potential recipients of an artificial heart are presented below. These estimates are based on information available from the Ad Hoc Task Force on Cardiac Replacement in 1969 (1) and recent literature regarding the following:

- the percentage of persons experiencing myocardial infarction or cardiac arrest who die:
  —at home or work,
  —during transportation by mobile coronary units,
  —in emergency rooms, or
  —during stabilization in coronary care units;
- the distribution of "mobile coronary units" (i.e., urban v. rural);
- the total number and distribution of cardiac deaths per year; and
- the prevalence of severe, irreversible, potentially lethal noncardiac diseases in candidates (we assume no change from the 1969 task force estimate of 262/1,000).

We differ from the 1969 task force as follows:

- We do not consider that a patient's prior knowledge of cardiac disease alters the pattern of patient delays in seeking medical assistance, nor that it alters the candidacy status once a patient has been hospitalized.
- We do not concur with the task force's category of "unexpected" deaths, neither with the numerical estimates of such deaths nor with the significance attributed to them. We believe that cardiac deaths can be considered "instantaneous" (occurring in less than 1 to 2 minutes) or "sudden" (occurring in less than 1 hour). The 1969 estimate of 42 percent (98/233) "unexpected" deaths seems unreasonably high for "instantaneous" deaths.

  Further, the 1969 report does not appear to exclude all persons who die within 1 hour after onset of symptoms. As noted earlier, at least 1 hour after the replacement decision is made will be required to prepare the operating room and the patient for heart replacement. We consider that if the patient survives for 1 hour or more in a hospital (avoids "sudden death"), he or she becomes a potential recipient, as reflected in our estimates below.

Finally, we assume that there will be no "elective" replacements, i.e., there will be no implantation in patents who are stable under medical management, regardless of the severity of such patients' disease. This consideration might change over time if the artificial heart proved highly successful.

Estimates of Potential Candidates in the United States, 1979

Group 1: Survivors of Recent Myocardial Infarction and/or Cardiac Arrest

Three separate sets of figures from the medical literature **(23,44,61)** are employed in our analysis of the number of potential candidates

among persons suffering acute myocardial infarction and/or cardiac arrest. Therefore, we present three separate estimates below and then use these to arrive at a pooled estimate.

Estimate A

1. Myocardial infarctions/year.	700,000
less those who survive uneventfully (50%).	–350,000
less those who die before hospitalization (25%)	–175,000
less those die "suddenly" in hospital (s%). . . .	–35,000
Subtotal	140,000
2. Cardiac arrests/year.	300,000
less those who die "at home".	–80,000
less those who die before hospitalization. . . .	–80,000
less those who die in hospital.	–80,000
less survivors (no mechanical damage to heart).	. . –60,000
Subtotal	. . 0
Total estimate A.	140,000

Estimate B

Seventy-five percent of all cardiac deaths are said to occur within 2 hours of symptom onset. Thus, 25 percent of deaths occur after 2 hours; one-sixth of these deaths occur "without warning. "

Cardiac deaths/year.	684,000
less 75% who die within 2 hours.	. –513,000
	171,000
less 1/6 who die "without warning".	. . –28,500
Total estimate B.	142,500

Estimate C

Fifty percent of all cardiac deaths are said to be "immediate" (time undefined). Of the rest, so percent die before hospitalization, and one-sixth die in the hospital "suddenly. "

Cardiac deaths/year.	684,000
less 50% whose deaths are "immediate". .	. –342,000
	342,000
less *5070* who die before hospitalization. .	...171,000
	171,000
less 1/6 who die in hospital "suddenly". . .	. . –28,500
Total estimate C.	142,500

Pooled Estimate

Thus, in group 1 we estimate 140,000 to 142,500 candidates for artificial hearts. The round figure of 140,000 will be used hereafter. *

Group 2: Persons With Worsening Chronic Severe Heart Disease

Patients with severe cardiomyopathy and patients with severe electrical instability of the heart are also prone to die instantaneously or "suddenly." The percentage of those persons who survive 2 or more hours in the hospital, yet have a worsening course, is estimated from figures at Stanford University Medical Center, which serves as a referral center for medical and surgical treatment of patients in both categories. We estimate 11,000 such patients per year.

Group 3: Persons Who Are Unable to Come Off the Cardiopulmonary Bypass Pump Following Open-Heart Surgery

Patients undergoing open-heart surgery occasionally survive the surgery but are "unable to come off the pump, " i.e., the patient's heart will not reassume the hemodynamic load when a transfer is attempted from the artificial cardiopulmonary bypass machinery.

Approximately 100,000 coronary bypass operations are performed yearly, as well as other open-heart surgery. Of the patients undergoing these procedures, we estimate that no more than 1,000 patients a year would be "unable to come off the pump. "

All Groups

By combining the estimates presented above, we estimate the total number of potential candidates for artificial hearts to be 140,000 +

*The figures used in the three estimates presented for this group of potential candidates are compatible with data recently collected in the area of Miami, Fla., which as of 1979 had not yet been published in manuscript form.