The School of Nursing, founded in 1923, became the first school to prepare nurses under an educational rather than an apprenticeship program. Dean Annie Goodrich's insistence that her students came to Yale to learn a highly skilled profession rather than to provide extra hands to already trained nurses was truly revolutionary. The School has continued to spawn new ideas that have helped redefine nursing: the groundbreaking research of Virginia Henderson, the founding of the American hospice movement, and the first "graduate entry" system that enlivened nursing practice by attracting mature students with varied and rich life experiences.

Since its founding, the School routinely revises its curriculum to meet the profession's needs. Because of an increasing realization that a college education was essential in the profession of nursing, the School of Nursing admitted only college graduates after 1934. Fifteen years later an advanced program in mental health nursing was added to the basic program. In 1952 the School became coeducational when the first male student was admitted.

A study of nursing education at Yale was undertaken in 1952. The Yale Corporation decided that the University could contribute to nursing most effectively through a graduate program for nurses who had both basic professional preparation and a baccalaureate degree. The basic program was discontinued in 1956, and the curriculum of the advanced program was expanded to prepare nurses in psychiatric–mental health, maternal-newborn health, and community health nursing. Nurse-midwifery was an option in the Maternal-Newborn Health Program until 1972, when it became the total clinical component of the program. A Master of Science in Nursing degree was awarded to those who had successfully completed a minimum of one year's study, coupled with a summer field experience. A Certificate in Nurse-Midwifery was also awarded by Yale University until 1972, when national certification by the American College of Nurse-Midwives was instituted.

In 1959–60 a revised curriculum of two years of study leading to the master's degree was inaugurated. The curriculum was further expanded in 1969 to include pediatric nursing and in 1974 to include medical-surgical nursing. In September 1992 a specialty was added in nursing systems and policy, then renamed nursing management and policy; that specialty was discontinued in 2003. From 2006 to 2015 the curriculum included a specialty in nursing management, policy, and leadership to prepare leaders in the management of delivery systems that promote patient safety and quality of care. In April 1997 the Yale Corporation approved the Post-Master’s Certificate for advanced practice nurses seeking additional specialty preparation. The first certificates were awarded at the May 1997 commencement exercises.

In April 1970 the Corporation approved development of a three-year curriculum for college graduates from other fields, a program of study now known as the Graduate Entry Prespecialty in Nursing. The first class of twelve enrolled in the fall of 1974.

In November 1992 the Corporation approved the development of a Doctor of Nursing Science program. The first class was admitted and enrolled in September 1994; and the first graduates were awarded the D.N.Sc. in June 1998. In 2006 the Corporation approved the program's conversion from the Doctor of Nursing Science to a Doctor of Philosophy, awarded by the Graduate School of Arts and Sciences. The first Ph.D. class was admitted and enrolled in September 2006. In April 2011 the Corporation approved the development of a Doctor in Nursing Practice program. The first class of D.N.P. students was admitted and enrolled in September 2012.

In spring 2020 the Board of Permanent Officers approved three new programs: a Clinical D.N.P. program, a Pediatric Nurse Practitioner – Acute Care specialty in the M.S.N. program, and a Post-Master’s Pediatric Nurse Practitioner – Acute Care Certificate option.