was detected, most of their patients required prednisone treatment after thymectomy. In fact, they showed the remission rate to be 40% in younger patients, but 8% in older patients.[5] Considering these observations together, we emphasize that the prognosis after thymectomy in older patients is not as good as in younger patients, and that their clinical features constitute a particular challenge in treating older patients with MG.

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APOLIPOPROTEIN E AND LONGEVITY: THE ROTTERDAM STUDY

To the Editor: Certain mutations may double life span in *Caenorhabditis elegans*. In contrast to worms, little is known about genetic factors that determine survival in man. A candidate gene for longevity in humans is the apolipoprotein E polymorphism (apo E) because it is involved in several, crucial pathological pathways. As compared with the most frequent genotype, E3E3, carriers of the apo E E2 allele have lower levels of atherogenic lipoproteins, a lower risk of Alzheimer's disease and strongest protection from oxidative stress.[1] The apo E E4 allele has opposite effects.[1] However, the apo E genotype seems to play a limited role in the development of vascular and malignant diseases,[2] the most common causes of death in industrialized countries. Yet several previous publications on apo E and longevity suggest that apo E E2 lengthens and apo E E4 reduces life expectancy.[3,4] Most of these reports are cross-sectional studies in the oldest old, leaving unanswered whether apo E is related to survival in the common age categories. The aim of this cohort study was to investigate whether the apo E genotype predicts mortality in the general older population.

We used data from the Rotterdam Study, a population-based prospective cohort study of persons age 55 and older, for which the Ethics Committee of the Erasmus University gave approval. Out of 10,275 eligible residents, 7,983 subjects were included (response rate 78%), and apo E could be determined in 6,852 persons (86%), who were followed for 5.4 years (mean; standard deviation 1.5). Information on the vital status of all participants was obtained at regular intervals from the municipal health authorities. Apo E genotyping was performed on coded samples, using a polymerase chain reaction. With Kaplan-Meier analysis and the log rank test statistic, we studied survival for the various apo E genotypes. Cox proportional hazards models were used to assess the relative risk of death, using the E3E3 group as reference.

The distribution of the apo E polymorphism in our study population was in Hardy-Weinberg equilibrium (χ^2 = 0.53; df = 3; P = .452). During 36,993 person-years observation, 1,260 participants died (mortality rate 34.1/1,000 person-years). At baseline, E2E2 carriers were on average older (t-test; P = .089) and E4E4 carriers younger (P = .002) than persons with E3E3 (Table 1). During follow-up, the mortality rate was slightly higher in the E2E2 group and lower in subjects with E4E4, but this was not statistically significant (logrank = 1.75; df = 5; P = .879). When we adjusted for age at baseline, there was no evidence of a relationship between apo E and risk of death (Table 1). Similar findings were obtained after stratification according to age.

In a previous study on centenarians, the frequency of apo E E2 was higher and the frequency of apo E E4 lower compared with younger subjects.[3] However, these findings could not be replicated in a smaller case-control study on octo- and nonagerians.[5] In a population-based cohort study, apo E E4 was weakly related to mortality in a subgroup only.[4] Our population-based study is six times larger than that study, has a high response rate and complete follow-up, and is therefore not subject to bias or lack of power. In line with previous studies that suggested that the association of apo E with vascular diseases weakens with aging,[2] we found that apo E was related to baseline age but not to mortality in the elderly. These findings

Table 1. Apolipoprotein E Genotype and Mortality

	E2E2 (n = 51)	E2E3 (n=877)	E2E4 (n=185)	E3E3 (n=3,989)	E3E4 (n=1,588)	E4E4 (n=162)
Mean baseline age (years; SD)	72.2 (9.0)	69.7 (9.5)	69.6 (9.0)	69.9 (9.4)	69.6 (9.2)	67.9 (8.0)
Mean follow-up (years; SD)	5.5 (1.8)	5.5 (1.5)	5.3 (1.5)	5.4 (1.5)	5.4 (1.5)	5.4 (1.4)
Number of deaths	11 (22%)	156 (18%)	37 (20%)	738 (19%)	293 (19%)	25 (15%)
Mortality rate (× 1000 person-years)	39.2	32.6	37.8	34.4	33.9	28.8
Relative risk of death*	1.0 (0.5–1.8)	1.0 (0.8–1.2)	1.2 (0.9–1.7)	1 (reference)	1.1 (0.9–1.2)	1.2 (0.8–1.7)

*Adjusted for baseline age, with 95% confidence interval.
SD = standard deviation.

suggest that apo E exerts its effects on longevity before the age of 55 years.

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PHARMACY REVIEW OF CULTURE AND SENSITIVITY WITH PROMPTING OF PHYSICIANS TO REDUCE ANTIBIOTIC PRESSURE

To the Editor: Antibiotic resistance is a problem in nursing homes.[1] Infections are treated empirically with broad spectrum antibiotics that select resistant organisms, but do not provide coverage for the resistant organisms selected.[2,3] Whenever possible, antibiotic choices should be directed by culture and sensitivity to identify resistant organisms that would not respond to empiric antibiotics and to allow substitution of narrow spectrum for broad spectrum antibiotics. We report a pharmacy-based program that reviews culture results and makes suggestions to focus antibiotic therapy. The Wisconsin Veterans Home is a 721-bed skilled nursing facility (SNF). The point prevalence of antibiotic use is 6.3%. The home has an on-site bacteriology laboratory. Culture and sensitivity results and current antibiotic therapy were reviewed Monday through Friday. Pharmacists do not call if the resident is not on an antibiotic for fear of encouraging antibiotic treatment of "colonization." If the existing antibiotic does not provide coverage, the physician is contacted. In addition, the pharmacist looked for opportunities to reduce antibiotic pressure. Between May 1, 1999, and October 31, 2000, 372 reports were reviewed, with 43 calls to physicians. The antibiotic did not cover organisms such as *Enterococcus*, methicillin-resistant *Staphylococcus aureus* (MRSA), or *Pseudomonas*, and the call recommended a switch to an effective antibiotic. Table 1 presents the 23 cases currently treated with a quinolone or cephalosporin for a single organism also sensitive to an antibiotic with a narrower spectrum. The physician elected to make the switch 14 times, with four cases associated with late communication. In five, the physician declined to make the switch. The rationale was not recorded. A catheterized patient was treated for *Citrobacter freundii* urinary tract infection with ciprofloxacin. The culture and sensitivity returned 2 days later, revealing sensitivity to ciprofloxacin, trimethoprin (TMP)-sulfa, tetracycline, and nitrofurantoin. The physician declined to make a switch to TMP-sulfa. A follow-up culture 20 days later revealed a heavy growth of MRSA (for the first time in that individual) resistant to ciprofloxacin, but sensitive to TMP-sulfa, tetracycline, and nitrofurantoin.

Programs to reduce antibiotic resistance should include a diversity of antibiotics and emphasize prevention of resistance rather than cost savings.[4] We have had a modest initial impact and will improve timeliness. We will determine why physicians decline a suggested switch. Possible reasons include a need to calculate a dose reduction (TMP-sulfa, nitrofurantoin); desire to treat with an antibiotic that penetrates prostatic tissue (e.g., quinolones, TMP-sulfa); lack of confidence in sputum or wound cultures; concern about infection in a second, noncultured site; or a desire not to "rock the boat" when the initial antibiotic lead to a good result. We do not know how much impact a fully effective program may have on antibiotic resistance or cost of therapy. However, a switch to narrow spectrum antibiotics after the return of culture and sensitivity is universally recommended to decrease the emergence of resistance.

Quinolone resistance is common among MRSA strains.[5] It follows that quinolone pressure would favor the emergence of MRSA. In the catheterized resident with *Citrobacter* urinary tract infection, (Table 1) one might speculate that if the switch from ciprofloxacin to TMP-sulfa had been made, MRSA would not have emerged. Bjork et al. reported that 70% of 63 antibiotic courses in catheterized residents were followed by a resistant organism.[6]

Our recommendations to switch primarily involved quinolones in urinary tract infections. Quinolones are also suited for empiric treatment of lower respiratory tract infections.[7] A recent Society for Healthcare Epidemiology of America position paper stated, "These agents are used because they allow oral therapy with an agent with good bioavailability, are easily administered, . . . and have a