Since publication of their article, the authors report no further potential conflict of interest.

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Medicare Health Support Pilot Program

TO THE EDITOR: McCall and Cromwell (Nov. 3 issue)[1] raise doubts about the ability of commercial disease-management programs to improve the quality of care and reduce utilization in the Medicare fee-for-service population. In contrast to the programs noted in the study, we have successfully approached disease support, admittedly in the Medicare Advantage population, with a different strategy supported by the medical literature (Table 1).[2,3] Key differences in our approach include risk stratification targeting those at highest risk, a boots-on-the-ground approach with clinician home visits allowing for identification and intervention on both social and health determinants of utilization, and communication with the primary care team through a personal health record. In response to the authors' concern regarding regression to the mean, we note that it accounted for less than half of the improvement in cost and utilization when assessed in control subjects who were matched with intervention subjects with respect to age, sex, and level of acuity. Commercial support programs, when executed with a targeted, intensive, and collaborative approach, can have a substantial positive impact on the health of elderly patients and on health care costs.

Table 1. Cost and Utilization of Health Services by Beneficiaries in the Medicare Advantage Plan with or without Disease-Management Support.

Variable	Intervention Group (N=94)	Control Group (N=94)
Total medical and pharmacy expenditures ($)		
12 Mo before analysis	4,453,782	3,458,996
12 Mo after analysis	2,873,388	2,766,417
Difference	1,580,394	692,579
No. of hospital admissions		
12 Mo before analysis	261	170
12 Mo after analysis	142	113
Difference	119	57
No. of hospital readmissions at 30 days		
12 Mo before analysis	23	12
12 Mo after analysis	4	11
Difference	19	1

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: In their study of the Medicare Health Support program's initial cohort, McCall and Cromwell report data from the program operated by Aetna. In the Aetna intervention group, the savings of $22 per beneficiary per month did not exceed the fee. The intervention and control groups, however, were not balanced at baseline, since the costs in the intervention group were 2% greater than those in the control group.[1] Sick beneficiaries become sicker, a baseline between-group inequality of 2% increases over 2 years, and this discrepancy is not resolved with the baseline adjustment. Therefore, the results from the initial cohort are not definitive. After the first year of the program, Aetna received a refresh cohort of 4587 beneficiaries with similar costs in the intervention group and the control group at the time of randomization. For 2 years, this cohort received care interventions that were identical to those in the initial cohort and that were provided by the same staff. The costs in the intervention group in the refresh cohort were reduced by $124 per beneficiary per month, as compared with the control group, an amount much greater than the savings in the initial cohort. The

results for the refresh cohort suggest successful reductions in hospital admissions and costs.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Learning from failure is much better than denial of failure.[1] The failure of the Medicare Health Support Pilot Program to find benefits or reduce costs will raise further consternation for advocates of nurse-led programs for the management of chronic disease. Explaining these failures away on the basis of selective past successes is wrong. Rather, advocates need to embrace negative findings and openness to debate rather than dismissing failure on the basis of anecdotal speculations about why success was masked. Failure, far from being rare, prevails in the vast majority of instances across biologic, social, and economic systems.[1] It occurs despite all manner of conscious and unconscious efforts targeted toward its very avoidance.[1] Indeed, for some years, these interventions have had inconsistent effects that were poorly understood[2,3] but consistently explained away.[2]

How can we be more open to the opportunities gifted by failure? To generate useful knowledge about why interventions work or do not, designs should collect data on which components influence outcomes and through which mechanisms this occurs.[4] Learning can then occur whether or not programs fail.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: McCall and Cromwell underreport design and analysis failures in their analysis of the Medicare Health Support Pilot Program. We evaluated their study for Healthways, one of the participating providers, and subsequently published our critique.[1] For example, the investigators violated the intention-to-treat protocol and induced post-treatment bias[2] by adding and removing subjects after randomization. The ad hoc adjustments for this design flaw (only some of which appear to be reported) compounded the bias. Consent was obtained only from members in the intervention group and only after randomization, leading to more bias. The use of an inefficient block-randomization approach (rather than a matched-pair approach) and a 7-month delay in instituting the intervention after randomization left the design underpowered, which was equivalent to discarding data from numerous subjects.[3] Their statistical procedures introduced unnecessary model dependence,[2] and published tables appear to be inconsistent with available data.

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Dr. King and Mr. Nielsen report receiving consulting fees from Healthways. No other potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: We used two estimation techniques to test for the combined effect of successfully engaging Medicare fee-for-service beneficiaries and improving health while saving money.

The difference-in-differences approach tested for changes in rates of growth between the intervention group and the control group, thereby adjusting for any minor differences in baseline costs. In addition, the analysis of covariance was adjusted for differences in beneficiary characteristics — including age, sex, race, Hierarchical Condition Category severity score, presence of heart failure or diabetes, and baseline costs — at the start of each pilot program. In the analysis of covariance, the statistically nonsignificant difference-in-differences effect on the growth in costs for Aetna was more than halved, not increased, implying that Aetna benefited from a healthier intervention population.

Average Medicare monthly care-management fees ranged from 5 to 11% of average payments per beneficiary per month. Hence, the concern over statistical power was unfounded, since we would have found savings rates of only 3 to 4% that were significant at the 95% confidence level, far less than paid fees. We observed improved performance with the refresh population for several companies; however, savings remained statistically nonsignificant and were less than required savings. Our results were consistent across all eight companies and for both the original and refresh populations.

Savings and health outcomes for beneficiaries with very short lengths of eligibility were substantially down-weighted by their fraction of eligible time during the intervention, thereby avoiding any bias from short spells. Substantial regression to the mean (≥50%) over short periods increases the estimated variance, thereby reducing statistical power. Even so, we still found a cost savings of 3 to 4%. We directly adjusted for regression to the mean by including baseline costs in our models.

Terry and Moisuk affirm what we believe to be major challenges with improving health outcomes in the commercial fee-for-service population in contrast to a managed-care environment in which payers play a role in patients' access to care. Our evaluation of care management for high-cost beneficiaries at Massachusetts General Hospital showed a statistically significant return on investment of 3:1, given a similar intention-to-treat study design and a substantially smaller sample size.[1] Case managers became integral members of each beneficiary's primary care team with access to real-time clinical information and face-to-face interactions with primary care physicians and beneficiaries. It may be that both elements are necessary in the fee-for-service population.

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The Human Plasma Lipidome

TO THE EDITOR: In their review, Quehenberger and Dennis (Nov. 10 issue)[1] describe plasma lipids implicated in Gaucher's disease. Although they could not possibly mention every lipid, we believe it is worth commenting on the cationic amphiphilic glycolipid globotriaosylsphingosine (lyso-Gb3) and its contribution to a better understanding of the pathogenesis and monitoring of Fabry's disease. High plasma concentrations of lyso-Gb3 were observed in patients with this disease,[2] and these levels correlated with several of its manifestations[3] and decreased in response to enzyme-replacement therapy.[4,5] Furthermore, lyso-Gb3 promoted vascular smooth-muscle cell proliferation[2] as well as transforming growth factor-β1–mediated synthesis of extracellular matrix components in cultured podocytes at concentrations found in the plasma.[6] In Fabry's disease, vascular smooth-muscle cells and podocytes are cell targets, whereas fibrosis is a key feature of organ injury. The novelty, from a pathogenetic point of view, resides in the fact that a soluble mediator promotes cell injury in a disease long thought to be the result of intracel-