Economic Evaluation of Quality Improvement Interventions Designed to Improve Glycemic Control in Diabetes: A Systematic Review and Weighted Regression Analysis

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OBJECTIVE

Quality improvement (QI) interventions can improve glycemic control, but little is known about their value. We systematically reviewed economic evaluations of QI interventions for glycemic control among adults with type 1 or type 2 diabetes.

RESEARCH DESIGN AND METHODS

We used English-language studies from high-income countries that evaluated organizational changes and reported program and utilization-related costs, chosen from PubMed, EconLit, Centre for Reviews and Dissemination, New York Academy of Medicine's Grey Literature Report, and WorldCat (January 2004 to August 2016). We extracted data regarding intervention, study design, change in HbA_{1c}, time horizon, perspective, incremental net cost (studies lasting ≤3 years), incremental cost-effectiveness ratio (ICER) (studies lasting ≥20 years), and study quality. Weighted least-squares regression analysis was used to estimate mean changes in HbA_{1c} and incremental net cost.

RESULTS

Of 3,646 records, 46 unique studies were eligible. Across 19 randomized controlled trials (RCTs), HbA_{1c} declined by 0.26% (95% CI 0.17–0.35) or 3 mmol/mol (2 to 4) relative to usual care. In 8 RCTs lasting ≤3 years, incremental net costs were $116 (95% CI −$612 to $843) per patient annually. Long-term ICERs were $100,000–$115,000/quality-adjusted life year (QALY) in 3 RCTs, $50,000–$99,999/QALY in 1 RCT, $0–$49,999/QALY in 4 RCTs, and dominant in 1 RCT. Results were more favorable in non-RCTs. Our limitations include the fact that the studies had diverse designs and involved moderate risk of bias.

CONCLUSIONS

Diverse multifaceted QI interventions that lower HbA_{1c} appear to be a fair-to-good value relative to usual care, depending on society's willingness to pay for improvements in health.

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Improving the value of health care has become a priority, and optimizing glycemic control among patients with diabetes may represent a promising opportunity. In the short term, poor control can affect clinic visits, emergency department visits, and hospitalizations related to hyper- and hypoglycemia. Over the long term, poor control leads to disabling and costly complications including cardiovascular disease, blindness, kidney disease, and neuropathy (1–3). Yet suboptimal control remains common, with HbA_{1c} levels exceeding individualized targets in 16%–72% of patients, particularly younger adults with complications (4). Thus, quality improvement (QI) interventions related to glycemic control may increase value by improving health outcomes and reducing costs (5). If net costs decline substantially, there may be a "business case" for improving quality.

QI interventions represent systematic and continuous efforts to achieve measurable improvements in the structure, processes, or outcomes of care, particularly the health of targeted patient populations, by means of an organizational or structural change (6–9). QI interventions frequently emphasize teamwork and can involve the combined efforts of health care organizations, clinicians, and patients and their families (8). Interventions related to glycemic control can involve three basic types of QI strategies: changing care systems, optimizing practitioner behavior, and supporting behavior change by patients (10). Systems of care can be restructured by instituting disease/case management, creating multidisciplinary teams, establishing electronic patient registries, and relaying information to clinicians, among others. Desired actions by practitioners can be fostered through audit and feedback, education, reminders, and financial incentives. Behavior change by patients can be supported through tailored care, education, self-management training, reminders, and financial incentives (11).

Although QI interventions can be effective at lowering HbA_{1c} (11), their economic value does not appear to have been evaluated systematically (5). It remains unclear whether QI interventions tend to produce net savings or losses in the short and long term and how costs compare with health gains. We sought to systematically review economic evaluations of QI interventions designed to improve glycemic control among adults with diabetes. Accordingly, we examined changes in HbA_{1c} and incremental net costs in the short term (within up to 3 years) and incremental cost-effectiveness in the long term (over 20 years or more). To estimate mean changes in HbA_{1c} and net costs in the short term, we performed weighted regression analyses that combined study results statistically.

RESEARCH DESIGN AND METHODS

We report this review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (12), including posting the study protocol on the Prospero registry (CRD42015014950) (13). A technical expert panel offered guidance during key stages of the project.

Data Sources and Searches

A reference librarian developed search terms related to diabetes and expanded on published terms related to economic evaluation (Supplementary Data 1) (14). Databases included MEDLINE, EconLit, and the Centre for Reviews and Dissemination. To identify grey literature, we searched New York Academy of Medicine's Grey Literature Report and WorldCat and invited expert panelists to suggest studies. Searches were restricted to English-language documents from January 2004 to August 2016, as clinical practices and cost structures have evolved over time. We hand-searched citations from previous systematic reviews (15–17) and other sources (11,18).

Study Selection

English-language studies were eligible if they represented original investigations, addressed QI interventions designed to improve glycemic control among adult outpatients with diabetes (type 1, type 2, or unspecified), measured or modeled the cost of the QI intervention, and compared alternatives (e.g., QI intervention vs. status quo). Studies needed to report both program costs (costs of implementation) and costs related to health care utilization for diabetes. We excluded studies from low- to middle-income countries due to differences in care practices and cost structures (19). We included all time horizons, clinical study designs, economic evaluation approaches, and analytical perspectives. Interventions that sought to influence only patient behavior without involving changes to systems of care (e.g., diet or exercise programs) or that tested new equipment or medications were not considered QI. Two trained reviewers determined eligibility by independently examining titles, abstracts, and full-text publications; discrepancies were resolved by consensus or, if needed, discussion with the research team.

Data Extraction and Quality Assessment

We obtained any additional publications related to the eligible analyses (such as study designs or clinical results published separately from economic analyses), and then pairs of experienced investigators with training in quality of care, population health, and economic evaluation extracted data from the articles. Discrepancies were resolved by consensus or, if needed, through discussion with the research team.

QI Strategies

Reviewers applied 16 categories of strategies for improving glycemic control, including 7 system-oriented strategies, 4 practitioner-oriented strategies, and 5 patient-oriented strategies (Supplementary Data 2) (11,20). System-oriented strategies included disease management, changes to the health care team, use of electronic registries, facilitated relay of information, continuous QI, enhancing efficiency, and standardizing care. Practitioner-oriented strategies included audit and feedback, provider education, provider decision support, and incentives for practitioners. Patient-oriented strategies included tailoring care for subgroups of patients, patient education, patient self-management, patient reminders, and incentives for patients.

Population, Context, and Study Design

Contextual variables included country, academic status (major, minor, nonteaching), setting (e.g., clinic, pharmacy, etc.), and location (urban, suburban/small city, rural). Clinical study designs included randomized controlled trial (RCT), controlled before-after analysis, uncontrolled before-after analysis, interrupted time series and repeated-measures studies, and modeling studies (21). Following a best evidence approach, we emphasize findings based on RCTs but include studies with nonrandomized designs because many QI interventions use such designs (22).

To assess risk of bias, we used the Cochrane Risk of Bias Tool for randomized

trials and the Newcastle-Ottawa Scale for nonrandomized studies (23,24). To assess whether authors reported key information about QI interventions, we applied items (3–5,10,11,14,15,17) from the Quality Intervention Minimum Quality Criteria Set (QI-MQCS) (25). Funding sources included government, nonprofit, commercial, and none.

Clinical Effectiveness

The primary clinical outcome was the change in HbA_{1c}. When studies used controlled designs, the change in HbA_{1c} represented differences between the control and intervention groups in changes from baseline to follow-up (i.e., difference in differences). When studies used uncontrolled designs, the change in HbA_{1c} represented changes from baseline to follow-up for the intervention group. Studies generally reported follow-up HbA_{1c} tests at 1 to 3 years, irrespective of the time horizon for the economic analysis. For each study, we extracted numbers of individuals in intervention and any comparison groups, duration of the intervention, baseline HbA_{1c}, change in HbA_{1c} with the intervention, and timing of follow-up HbA_{1c} tests. For long-term analyses, we also extracted quality-adjusted life years (QALYs) and years of life gained.

Economic Evaluation

Reviewers extracted the evaluation approach (cost analyses including cost, cost consequences, and business case analyses and cost-effectiveness analyses including cost utility, cost-benefit, and related analyses), perspective (clinic/provider, health system, payer, society), discount rate (when applicable), and year and currency of costs.

Reviewers classified studies by the time horizon of the economic analysis, including short term (up to 3 years), intermediate term, and long term (20 or more years). For short-term analyses, the primary economic outcome was the incremental net cost per patient per year, calculated as the sum of program and health care utilization–related costs. For long-term analyses, the primary economic outcome was the incremental cost-effectiveness ratio (ICER), calculated as the incremental net cost divided by the incremental QALYs per patient over the study time horizon. Few studies used intermediate time horizons.

We used the Quality-Cost Framework, which defines structure-, process-, and outcome-related costs, building on the Donabedian model of quality (26). Structure-related costs were the fixed costs associated with start-up and maintenance, such as labor costs associated creating new protocols and training providers. Process-related costs were variable, recurring costs resulting from the care of individual patients, such as physician visits and medications. Outcome-related costs included health care related to diabetes-related hospitalization, cardiovascular disease, blindness, nephropathy, etc. For this analysis, studies reported structure-related costs as program costs and health care utilization–related costs that included process- and outcome-related costs. When studies reported results for more than one discount rate, we extracted results based on a 3% rate (27).

We applied currency conversion and inflation factors to standardize costs per patient to 2015 U.S. dollars and the health system perspective. For short-term analyses, we graphed the relationship between the change in HbA_{1c} and standardized incremental net costs. For long-term analyses, we graphed the relationship between QALYs and standardized incremental net costs.

To assess whether economic evaluations met basic standards, reviewers applied a modified version of the Quality of Health Economics Studies Checklist (mQHES), as reported previously (28–30).

Data Synthesis and Analysis

Short-term Effectiveness

We conducted weighted regression analyses to identify factors potentially associated with changes in HbA_{1c}. We identified these factors a priori. Analyses were prespecified, unadjusted, and stratified by study design (RCT, controlled before-after analysis, and uncontrolled before-after analysis or other design). Independent variables examined for each study design included the baseline HbA_{1c} (continuous); study timing (year for cost data, continuous); numbers of system-oriented, practitioner-oriented, and patient-oriented strategies, respectively (continuous); and each of the 15 different individual QI strategies (dichotomous).

Weighted regression is similar to meta-regression in that studies are the unit of analysis in the model. The difference is the way studies are weighted. In the former, studies are weighted by the number of participants. In the latter, studies are usually weighted by the inverse of the study variance. We performed weighted regression because very few primary studies in our data set reported variance for cost estimates. The two approaches yield equivalent results, and weighted regression performs better when there may be concerns about publication bias or small sample sizes (31). When studies reported data separately for multiple subpopulations, we treated each subpopulation as a separate observation. Studies did not report enough data on variance to formally assess publication bias.

Short-term Costs

For analyses with short-term horizons, we used weighted least-squares regression to calculate mean incremental net costs along with 95% CIs, stratifying by study design. We could not examine predictors of net costs due to insufficient numbers of studies.

RESULTS

Study Selection

We identified 3,646 records, selecting 222 for full-text review; 45 articles met all eligibility criteria. Three articles reported results separately for different subpopulations, stratifying by baseline HbA_{1c} (32), sex (33), and payer (34). One article reported results for two different interventions (35), bringing the total number of unique studies to 46. Searches of grey literature did not identify eligible articles. Supplementary Data 3 includes the PRISMA flow diagram, and Supplementary Data 4 includes tables listing extracted data.

Study Characteristics and Quality Assessment

QI Strategies

Interventions involved a median of 4.5 different QI strategies. Thirty-one studies included disease/case management, 35 studies involved patient education, 29 studies promoted patient self-management, and 22 studies involved changes to the clinical team. Other strategies were used less frequently (Table 1 and Supplementary Data 4).

Population, Context, and Study Design

Thirty-one studies focused on type 2 diabetes, 4 included type 1 and 2 diabetes, and 11 did not specify type. Three studies examined populations with diabetes or cardiovascular disease risk factors. The median baseline HbA_{1c} was 8.1%

Table 1—QI interventions designed to improve glycemic control: targets, specific strategies, and study designs

Targets of QI and specific strategies	RCT (n = 19)	Controlled before-after analyses (n = 11)	Uncontrolled before-after analyses and other designs (n = 16)	Total (n = 46)
System				
Disease management	10 (52.6)	10 (90.9)	11 (68.8)	31 (67.4)
Team changes	8 (42.1)	7 (36.6)	7 (43.8)	22 (47.8)
Electronic registry	3 (15.8)	2 (18.2)	3 (18.8)	8 (17.4)
Facilitated relay	6 (31.6)	1 (9.1)	2 (12.5)	9 (19.6)
Continuous QI	0 (0)	1 (9.1)	3 (18.8)	4 (8.7)
Enhancing efficiency	3 (15.8)	0 (0)	0 (0)	0 (0)
Standardizing care	6 (31.6)	2 (18.2)	5 (31.3)	13 (28.3)
Practitioner				
Audit and feedback	6 (31.6)	0 (0)	4 (25.0)	10 (21.7)
Provider education	3 (15.8)	1 (9.1)	2 (12.5)	6 (13.0)
Provider decision support	4 (21.1)	3 (27.3)	4 (25.0)	11 (23.9)
Incentives for providers	2 (10.5)	0 (0)	1 (6.3)	3 (6.5)
Patient				
Tailoring care for group	7 (36.8)	0 (0)	4 (25.0)	11 (23.9)
Patient education	14 (73.7)	8 (72.7)	13 (81.3)	35 (76.1)
Patient self-management	9 (47.4)	9 (81.8)	11 (68.8)	29 (60.3)
Patient reminders	6 (31.6)	2 (18.2)	3 (18.8)	11 (23.9)
Incentives for patients	3 (15.8)	2 (18.2)	2 (12.5)	4 (8.7)

Data are n (%).

(65 mmol/mol) among 42 studies (including subpopulations); baseline HbA_{1c} was missing for 4 studies. Twenty-five studies were based in the U.S., and 33 were implemented in clinics. Nineteen studies were based on RCTs, including 9 cluster RCTs. Eleven studies were based on controlled before-after designs. Thirteen studies were based on uncontrolled before-after designs and 2 on serial cross-sectional analyses. One was a modeling analysis based on published literature (excluded from regression analyses).

Overall, the RCTs were at moderate risk of bias because the authors did not document random sequence generation and could not conceal allocation. Observational studies were also at moderate risk of bias because of concerns about the representativeness of study cohorts, selection of comparison groups, and adequacy of follow-up. Supplementary Data 4 includes items in the QI-MQCS and funding sources.

Economic Evaluation

There were 17 cost analyses and 29 cost-effectiveness analyses. Twenty studies took the health system perspective and 1 study reported results for both integrated health care system and societal perspectives. Eighteen studies considered the health care payer perspective, 7 other studies took the societal perspective, and 1 took the perspective of a hospital/clinic.

Twenty-three unique studies used short-term horizons, 4 studies used intermediate-term horizons, and 19 studies used long-term horizons. In the 23 studies with short-term economic evaluations, QI interventions were implemented and clinical outcomes and costs were examined over similar time frames, including 18 studies lasting up to 1 year, and 5 studies lasting 1.5–3 years.

The 19 studies with long-term economic evaluations involved modeling long-term effectiveness and costs based on shorter-term data. In 12 studies, authors assumed that both the intervention and any associated decline in HbA_{1c} were sustained over the full time horizon of the economic analysis; 7 of these studies measured HbA_{1c} at 1 year, 1 study at 1.5 years, 1 study at 3 years, 1 study at 4 years, and 1 study at 5 years; 1 study reported a short-term change in HbA_{1c} without specifying the timing of measurements. In 7 studies, the authors did not assume that the intervention or change in HbA_{1c} was sustained long term; these studies measured HbA_{1c} at 1 to 4 years. This assumption did not appear to affect results.

Overall, economic evaluation methods met basic standards, with a median mQHES score of 105 across the 46 unique studies.

Data Synthesis and Analysis

Clinical Effectiveness

On the basis of weighted regression analyses, the QI interventions were associated with significant improvements in HbA_{1c} across all three types of study designs. Findings were generally more favorable in studies based on nonrandomized designs, although differences did not reach statistical significance (P = 0.87). Among the 19 RCTs that reported changes in HbA_{1c} for intervention and control groups, the weighted mean improvement in HbA_{1c} was 0.26% (95% CI 0.17–0.35), or 3 mmol/mol (2–4), based on the difference in differences. Among 9 controlled before-after studies that reported changes in HbA_{1c} for intervention and control groups, the weighted mean improvement was 0.62% (0.37–0.88), or 7 mmol/mol (4–10), based on the difference in differences. Among 15 studies that used uncontrolled before-after or other designs, the weighted mean improvement in HbA_{1c} from baseline to follow-up was 0.41% (0.08–0.73), or 4 mmol/mol (1–8).

In unadjusted weighted regression analyses limited to RCTs, baseline HbA_{1c} was the only significant predictor of the change in HbA_{1c} (P = 0.010). With an increase in baseline HbA_{1c} from 7.5–8.5% (58–69 mmol/mol), for example, the improvement in HbA_{1c} relative to the control group increased from 0.22% (95% CI 0.14–0.29), or 2 mmol/mol (2–3), to 0.40% (0.29–0.52), or 4 mmol/mol (3–6). Study timing; numbers of system-, practitioner-, and patient-oriented strategies; and the specific QI strategies used

were not significant predictors in unadjusted analyses ($P < 0.05$) (Supplementary Data 5). Excluding an RCT that differed from the others in terms of target population, intervention, and results did not alter findings (36). Results were generally similar for studies that used nonrandomized designs, except that among uncontrolled before-after analyses, larger declines in HbA_{1c} were observed among earlier studies ($P < 0.001$) and among interventions that used fewer system-oriented QI strategies ($P < 0.001$), more practitioner-oriented strategies ($P < 0.001$), and more patient-oriented strategies ($P < 0.001$). We did not include supplementary data for these data due to the lower quality of the studies (data are available from authors upon request).

Fifteen long-term studies reported years of life saved, which ranged from 0.0245 to 1.100 years (Supplementary Data 4).

Short-term Costs

Figure 1 shows standardized program, health care utilization–related, and net costs per patient per year across 23 short-term analyses, where negative costs reflect savings (see Supplementary Data 6 for calculations). Across these studies, the median cost of implementing a QI intervention was $525 per patient per year, which was offset by a median change in health care expenditures of −$302 per patient per year.

Including both program costs and changes in health care expenditures, the mean incremental net cost per patient per year was not significantly different from zero, based on weighted regression analyses. This was true across all three study designs. The net cost was $116 (95% CI −612 to 843) among eight RCTs, −$831 (−1,527 to −134) among seven studies using controlled before-after designs, and −$401 (−1,255 to 453) in eight studies with uncontrolled before-after or other designs. The weighted mean net costs per patient per year was significantly higher for RCTs than for controlled before-after studies ($P = 0.02$).

Figure 2 shows the net cost per patient per year in relation to the change in HbA_{1c}, where each data point represents a unique study that reported both measures. We were unable to formally test whether larger improvements in HbA_{1c} were associated with greater net savings due to the small number of studies with each type of design.

Long-term Cost-effectiveness

Figure 3 shows the cost-effectiveness plane with willingness-to-pay thresholds of $50,000 and $100,000 per QALY. Lower costs and better health are toward the lower right, and each data point reflects a unique study or subpopulation, with RCTs represented by circles. All analyses

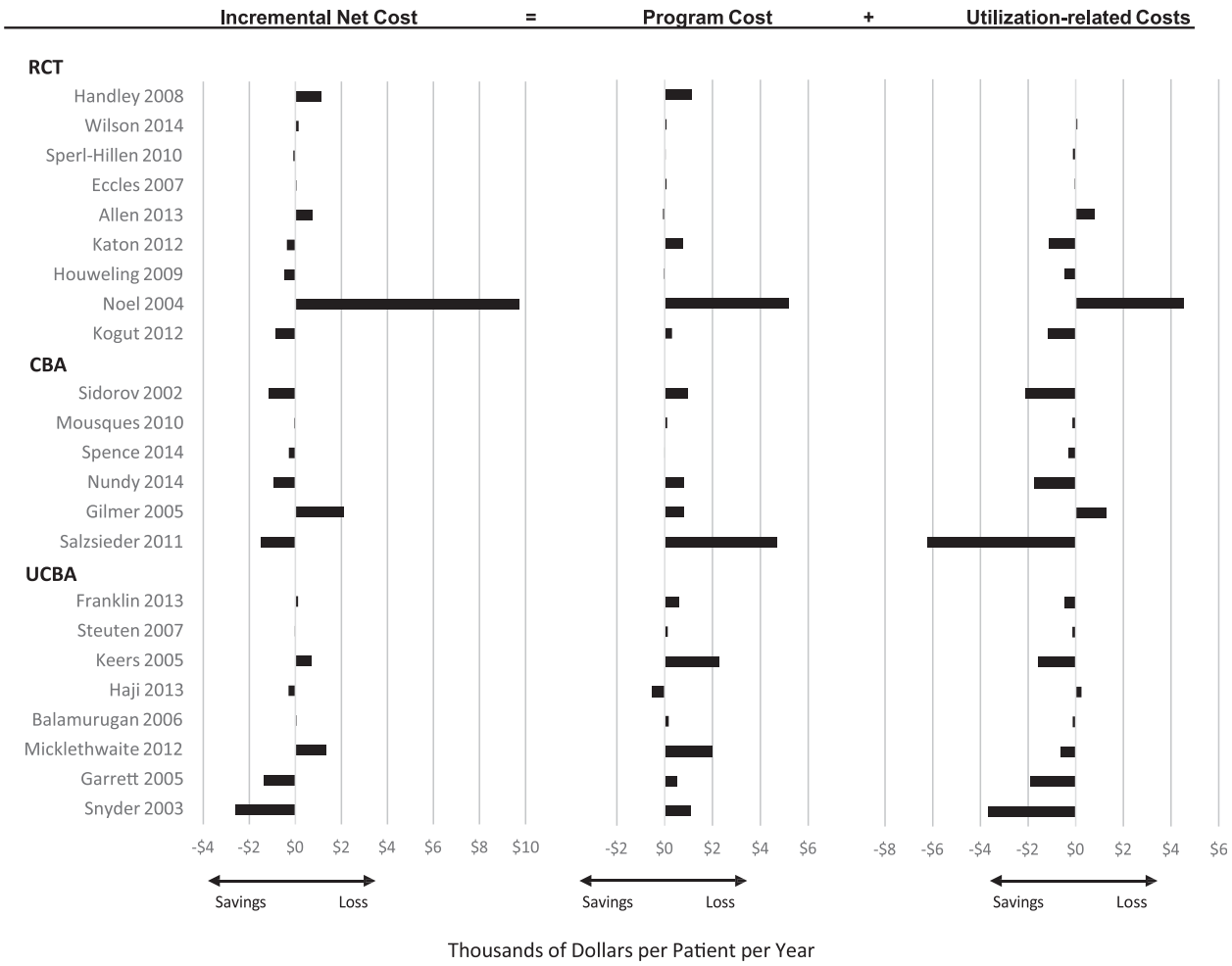

Figure 1—Incremental net cost per patient per year from the health system perspective in 2015 U.S. dollars. Study details are available in the Supplementary Data. CBA, controlled before-after design; UCBA, uncontrolled CBA.

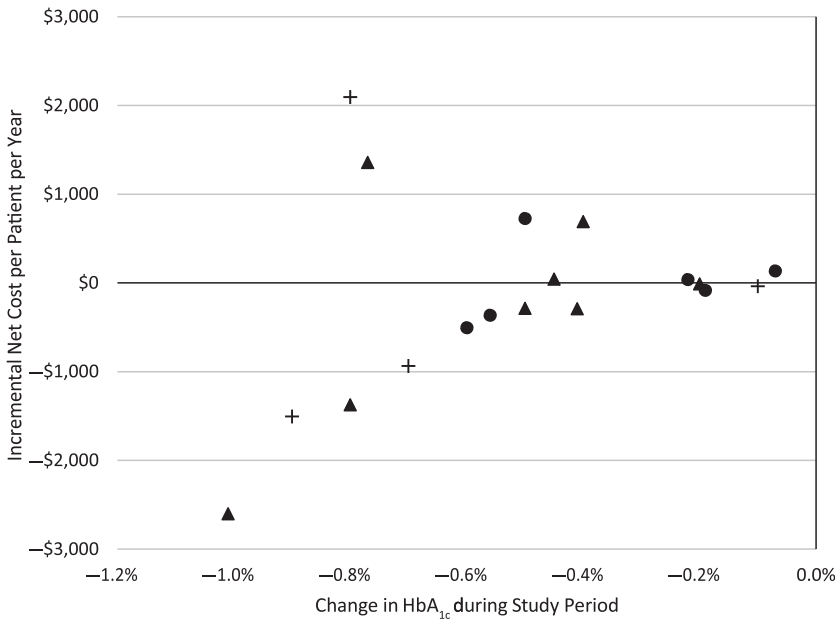

Figure 2—Change in HbA_{1c} during study period and incremental net cost per patient per year in 2015 U.S. dollars. Results not shown for Noel et al. (37), an RCT that included patients with diabetes, heart failure, or chronic obstructive pulmonary disease: change in HbA_{1c} was −1.8% (−20 mmol/mol) and incremental net cost was +$9,714 per patient per year. Circle, RCT; plus sign, controlled before-after design; triangle, uncontrolled before-after design.

yielded ICERs below $115,000 per QALY over 20 or more years. The ICER was $100,000–$115,000 per QALY in three RCTs (36,38,39), $50,000–$99,999 per QALY in one RCT (36), $0–$49,999 per QALY in four RCTs (including one with two study subpopulations) (32,39–41), and dominant (more effective and less costly than the status quo) in one RCT (42).

Results were somewhat more favorable in analyses based on nonrandomized designs. In seven studies based on controlled before-after designs, the ICER was $104,132 per QALY in one subpopulation (34), $50,000–$99,999 per QALY in one subpopulation (35), and $0–$49,999 per QALY in five studies or study subpopulations (33,34,43). In seven studies based on uncontrolled before-after and other designs, the ICER was $50,000–$99,999 per QALY in one study (44), $0–$49,999 per QALY in four studies (45–48), and dominant with more than $5,000 in net savings in two studies due to avoiding complications including renal disease (49,50).

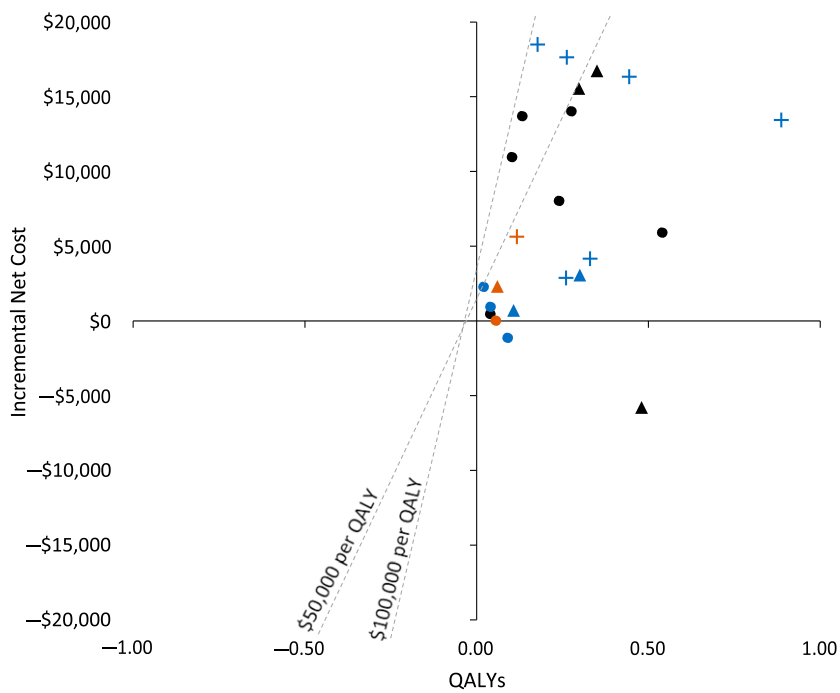

Figure 3—QALYs and incremental net cost per patient over long term in 2015 U.S. dollars. Each observation represents an individual study or results that were reported separately for a particular subgroup in an individual study. Circles, RCT; plus sign, controlled before-after analysis; triangle, uncontrolled before-after analysis. Black, lifetime economic horizon; blue, 40-year economic horizon; orange, 20-year economic horizon.

CONCLUSIONS

This systematic review examined economic evaluations of 46 multifaceted QI interventions designed to improve glycemic control among adults with diabetes, including 19 RCTs that included over 33,000 patients. There are three key findings. First, the studied QI interventions were effective, leading to average declines in HbA_{1c} of 0.26%, or 3 mmol/mol, based on RCT data. Second, the cost of implementing QI interventions was generally offset by reductions in health care expenditures in the short term, such that net costs to the health system were not significantly different from zero. Third, over 20 years or longer, costs rose along with survival, but the ICER was under $115,000 per QALY in all studies and populations. Declines in HbA_{1c}, short-term costs, and long-term cost-effectiveness were more favorable in studies based on nonrandomized designs.

The interventions that we examined emphasized QI strategies that have been recommended by the American Diabetes Association and found to be effective in prior systematic reviews, including patient self-management support, changes to the health care team, disease management, patient education, use of electronic registries, and clinical decision support (10,11). In a prior meta-analysis of 120 RCTs on QI strategies for glycemic control, HbA_{1c} declined by an average of 0.37% (95% CI 0.28–0.45), or 4 mmol/mol (3–5), overall, including declines of 0.57% (0.31–0.83), or 6 mmol/mol (3–9), for patient self-management support; 0.57%

(0.42–0.71), or 6 mmol/mol (5–8), for team changes; 0.50% (0.36–0.65), or 5 mmol/mol (4–7), for disease/case management; and 0.48% (0.34–0.61), or 5 mmol/mol (4–7), for patient education (11). In a systematic review of QI interventions that included components of the Chronic Care Model (CCM), the mean decline in HbA_{1c} was 0.5% (0.3–0.6), or 5 mmol/mol (3–7), across 48 primary studies (10,51). The CCM includes patient self-management support, delivery system redesign through team changes and clinical information systems such as patient registries, and clinical decision support (52).

Our work adds to this literature by demonstrating that QI interventions designed to improve glycemic control increased value from the health system perspective. However, these increases in value were entirely attributable to improvements in health outcomes as costs did not fall. In the short term, improving HbA_{1c} at no net cost is clearly a good value. In the long term, the interpretation of ICERs requires consideration of a society's willingness to pay for improvements in health. In the U.K., the National Institute for Health and Care Excellence currently considers health interventions that cost under £20,000–£30,000 ($23,815–$35,723) per QALY to be cost-effective. In the U.S., the Office of Management and Budget recommends that analyses supporting government regulations use a value of a statistical life of $9.6 million, which equates to a value of per discounted QALY of over $300,000 (53). Interventions that cost under $50,000 per QALY have been considered cost-effective since the 1970s. Accounting for inflation in prices, this equates to about $300,000 per QALY today. Some authors have suggested that, based on temporal trends in health and health care spending, society appears willing to pay at least $200,000 per QALY (54).

Yet, the fact that we found net cost savings to be unlikely in the short or long term is noteworthy. Glucose control in diabetes would seem to be the archetypal situation in which improving quality might lead to financial savings because underuse of evidence-based care may increase visits related to hyper- and hypoglycemia in the short term and contribute to costly complications in the long term. Prior studies indicate that improvements in HbA_{1c} can be associated with declines in health care utilization and expenditures in the short and long term—but these studies overlook costs associated with implementing interventions to change clinical practice (15,55–59). Furthermore, total lifetime health care expenditures rise with increases in survival. Our findings imply that investing in efforts to improve glycemic control are not likely to yield direct financial benefits to health systems and physician practices, which incur implementation costs and lose revenue when utilization declines. Accordingly, public reporting and value-based payment programs, such as the U.S. National Committee for Quality Assurance's Healthcare Effectiveness Data and Information Set (HEDIS) program and Centers for Medicare & Medicaid Services Quality Payment Program (60–62) or the U.K. National Health Service's Quality and Outcomes Framework, are designed to create external incentives for investing in QI (63–65).

This analysis has several limitations. Although we focused on HbA_{1c}, some eligible studies estimated the combined clinical benefits and costs of controlling HbA_{1c} and managing other cardiovascular disease risk factors (46). For example, intensive blood pressure control can be cost saving in patients with diabetes, excluding the cost of any QI interventions that might be implemented to attain such control. For the weighted regression analyses, stratifying by clinical study design reduced statistical power and, thus, the ability to detect factors associated with effectiveness and net costs, increasing the possibility of type II error (false negatives). A larger number of high-quality RCTs would be needed to conclude which types of QI strategies work best or are most cost efficient in which settings. We emphasize RCTs because the nonrandomized studies had more favorable findings and higher risks of bias. Measurement error may have occurred when assigning categories of QI studies to individual articles because this depended on clear and complete reporting by the original authors. QI interventions are context dependent, but we examined studies in diverse populations and settings in developed nations; lower cost interventions are likely to be emphasized in low- and middle-income countries. Studies were generally at moderate risk of bias related to study design. We were unable to formally assess publication bias or heterogeneity in costs because data on variance were limited to absent. Authors may not perform economic analyses until clinical effectiveness has been demonstrated; however, we found that changes in HbA_{1c} were somewhat smaller than in prior systematic reviews (11).

In conclusion, diverse multifaceted QI interventions designed to improve glycemic control improve health outcomes and appear to be a fair-to-good value relative to usual care, depending on society's willingness to pay for improvements in health. Given that the QI interventions do not yield net cost savings to the health system, a business case based solely on reducing costs appears unlikely.

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References

1. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352: 837–853
2. Clarke PM, Gray AM, Briggs A, Stevens RJ, Matthews DR, Holman RR; UKPDS 72 United Kingdom Prospective Diabetes Study. Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72). Diabetologia 2005;48:868–877
3. Gray A, Raikou M, McGuire A, et al.; United Kingdom Prospective Diabetes Study Group. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). BMJ 2000;320:1373–1378
4. Ali MK, Bullard KM, Saaddine JB, Cowie CC, Imperatore G, Gregg EW. Achievement of goals in U.S. diabetes care, 1999-2010. N Engl J Med 2013;368:1613–1624
5. Porter ME. What is value in health care? N Engl J Med 2010;363:2477–2481
6. Danz MS, Rubenstein LV, Hempel S, et al. Identifying quality improvement intervention evaluations: is consensus achievable? Qual Saf Health Care 2010;19:279–283
7. Batalden PB, Davidoff F. What is "quality improvement" and how can it transform healthcare? Qual Saf Health Care 2007;16:2–3
8. Agency for Healthcare Research and Quality. Practice Facilitation Handbook, Module 4. Approaches to Quality Improvement [Internet], c2013. Available from https://www.ahrq.gov/professionals/prevention-chronic-care/improve/system/pfhandbook/mod4.html. Accessed 7 February 2018
9. U.S. Department of Health and Human Services, Health Resources and Services Administration. Quality Improvement, April 2011. Available from https://www.hrsa.gov/sites/default/files/quality/toolbox/508pdfs/qualityimprovement.pdf. Accessed 7 February 2018
10. American Diabetes Association. Strategies for improving care. *Sec. 1. In Standards of Medical Care in Diabetes—2016*. Diabetes Care 2016;39 (Suppl. 1):S6–S12
11. Tricco AC, Ivers NM, Grimshaw JM, et al. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. Lancet 2012;379: 2252–2261
12. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. PLoS Med 2009;6:e1000097
13. National Institute for Health Research. Systematic review of cost outcomes of quality improvement. In: PROSPERO, http://www.crd.york.ac.uk [Internet]. London, U.K., National Institute for Health Research, 2015. Available from http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42015014950. PROSPERO Identifier: CRD42015014950. Accessed 7 February 2018
14. Glanville J, Kaunelis D, Mensinkai S. How well do search filters perform in identifying economic evaluations in MEDLINE and EMBASE. Int J Technol Assess Health Care 2009;25:522–529
15. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: a systematic review. Diabetes Care 2010;33:1872–1894
16. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. Pharmacotherapy 2008;28:421–436
17. Jackson CL, Bolen S, Brancati FL, Batts-Turner ML, Gary TL. A systematic review of interactive computer-assisted technology in diabetes care. Interactive information technology in diabetes care. J Gen Intern Med 2006;21:105–110
18. Shojania KG, Ranji SR, McDonald KM, et al. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression-analysis. JAMA 2006;296:427–440
19. Goeree R, Burke N, O'Reilly D, Manca A, Blackhouse G, Tarride JE. Transferability of economic evaluations: approaches and factors to consider when using results from one geographic area for another. Curr Med Res Opin 2007;23: 671–682
20. Ivers N, Tricco AC, Trikalinos TA, et al. Seeing the forests and the trees–innovative approaches to exploring heterogeneity in systematic reviews of complex interventions to enhance health system decision-making: a protocol. Syst Rev 2014;3:88
21. The Cochrane Collaboration. Consumers and Communication Group resources for authors [Internet], 2013. Available from http://cccrg.cochrane.org/author-resources. Accessed 26 November 2016
22. Treadwell JR, Singh S, Talati R, McPheeters ML, Reston JT. *A Framework for "Best Evidence" Approaches in Systematic Reviews*. Rockville, MD, Agency for Healthcare Research and Quality, 2011
23. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. Available from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 7 February 2018
24. The Cochrane Collaboration. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. Higgins JPT, Green S, eds. Available from http://handbook.cochrane.org/. Accessed 7 February 2018
25. Hempel S, Shekelle PG, Liu JL, et al. Development of the Quality Improvement Minimum Quality Criteria Set (QI-MQCS): a tool for critical appraisal of quality improvement intervention publications. BMJ Qual Saf 2015;24:796–804
26. Nuckols TK, Escarce JJ, Asch SM. The effects of quality of care on costs: a conceptual framework. Milbank Q 2013;91:316–353
27. Gold MR, Siegel JE, Russell LB, Weinstein MC (Eds). *Cost-Effectiveness in Health and Medicine*. New York City, Oxford University Press, 1996
28. Nuckols TK, Keeler E, Morton SC, et al. Economic evaluation of quality improvement interventions for bloodstream infections related to central catheters: a systematic review. JAMA Intern Med 2016;176:1843–1854
29. Walker DG, Wilson RF, Sharma R, et al. *Best Practices for Conducting Economic Evaluations in Health Care: A Systematic Review of Quality Assessment Tools.* Rockville, MD, Agency for Healthcare Research and Quality, 2012
30. Chiou CF, Hay JW, Wallace JF, et al. Development and validation of a grading system for the quality of cost-effectiveness studies. Med Care 2003;41:32–44
31. Stanley TD, Doucouliagos H. Neither fixed nor random: weighted least squares meta-analysis. Stat Med 2015;34:2116–2127
32. Slingerland AS, Herman WH, Redekop WK, Dijkstra RF, Jukema JW, Niessen LW. Stratified patient-centered care in type 2 diabetes: a cluster-randomized, controlled clinical trial of effectiveness and cost-effectiveness. Diabetes Care 2013;36: 3054–3061
33. Schouten LM, Niessen LW, van de Pas JW, Grol RP, Hulscher ME. Cost-effectiveness of a quality improvement collaborative focusing on patients with diabetes. Med Care 2010;48:884–891
34. Gilmer TP, Roze S, Valentine WJ, et al. Cost-effectiveness of diabetes case management for low-income populations. Health Serv Res 2007; 42:1943–1959
35. Dijkstra RF, Niessen LW, Braspenning JC, Adang E, Grol RT. Patient-centred and professional-directed implementation strategies for diabetes guidelines: a cluster-randomized trial-based cost-effectiveness analysis. Diabet Med 2006;23:164–170
36. Noel HC, Vogel DC, Erdos JJ, Cornwall D, Levin F. Home telehealth reduces healthcare costs. Telemed J E Health 2004;10:170–183
37. O'Reilly D, Holbrook A, Blackhouse G, Troyan S, Goeree R. Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records. J Am Med Inform Assoc 2012;19:341–345
38. Mason JM, Young RJ, New JP, et al. Economic analysis of a telemedicine intervention to improve glycemic control in patients with diabetes mellitus: illustration of a novel analytic method. Dis Manag Health Outcomes 2006;14:377–385
39. Gillett M, Dallosso HM, Dixon S, et al. Delivering the Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cost effectiveness analysis. BMJ 2010;341:c4093
40. Gilmer TP, O'Connor PJ, Sperl-Hillen JM, et al. Cost-effectiveness of an electronic medical record based clinical decision support system. Health Serv Res 2012;47:2137–2158
41. Prezio EA, Pagán JA, Shuval K, Culica D. The Community Diabetes Education (CoDE) program: cost-effectiveness and health outcomes. Am J Prev Med 2014;47:771–779
42. Gillespie P, O'Shea E, Paul G, O'Dowd T, Smith SM. Cost effectiveness of peer support for type 2 diabetes. Int J Technol Assess Health Care 2012; 28:3–11
43. Kuo S, Bryce CL, Zgibor JC, Wolf DL, Roberts MS, Smith KJ. Cost-effectiveness of implementing the Chronic Care Model for diabetes care in a military population. J Diabetes Sci Technol 2011; 5:501–513
44. Brownson CA, Hoerger TJ, Fisher EB, Kilpatrick KE. Cost-effectiveness of diabetes self-management programs in community primary care settings. Diabetes Educ 2009;35:761–769
45. McRae IS, Butler JR, Sibthorpe BM, et al. A cost effectiveness study of integrated care in health services delivery: a diabetes program in Australia. BMC Health Serv Res 2008;8:205
46. Huang ES, Zhang Q, Brown SE, Drum ML, Meltzer DO, Chin MH. The cost-effectiveness of

improving diabetes care in U.S. federally qualified community health centers. Health Serv Res 2007; 42:2174–2193; discussion 2294–2323
47. O'Reilly D, Hopkins R, Blackhouse G, et al. Long-term cost-utility analysis of a multidisciplinary primary care diabetes management program in Ontario. Can J Diabetes 2007;31:205–214
48. Brown HS 3rd, Wilson KJ, Pagán JA, et al. Cost-effectiveness analysis of a community health worker intervention for low-income Hispanic adults with diabetes. Prev Chronic Dis 2012;9:E140
49. Giorda CB, Nicolucci A, Pellegrini F, et al. Improving quality of care in people with type 2 diabetes through the Associazione Medici Diabetologi-annals initiative: a long-term cost-effectiveness analysis. Diabet Med 2014;31:615–623
50. Gozzoli V, Palmer AJ, Brandt A, Spinas GA. Economic and clinical impact of alternative disease management strategies for secondary prevention in type 2 diabetes in the Swiss setting. Swiss Med Wkly 2001;131:303–310
51. Elissen AM, Steuten LM, Lemmens LC, et al. Meta-analysis of the effectiveness of chronic care management for diabetes: investigating heterogeneity in outcomes. J Eval Clin Pract 2013;19: 753–762
52. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness: the Chronic Care Model, part 2. JAMA 2002;288:1909–1914
53. U.S. Department of Transportation. *Revised Departmental Guidance on Valuation of a Statistical Life in Economic Analysis*. Washington, DC, U.S. Department of Transportation, 2016
54. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness–the curious resilience of the $50,000-per-QALY threshold. N Engl J Med 2014;371:796–797
55. McAdam-Marx C, Dahal A, Jennings B, Singhal M, Gunning K. The effect of a diabetes collaborative care management program on clinical and economic outcomes in patients with type 2 diabetes. J Manag Care Spec Pharm 2015;21:452–468
56. Rosenthal MB, Alidina S, Friedberg MW, et al. A difference-in-difference analysis of changes in quality, utilization and cost following the colorado multi-payer patient-centered medical home pilot. J Gen Intern Med 2016;31:289–296
57. Carter BL, Malone DC, Billups SJ, et al. Interpreting the findings of the IMPROVE study. Am J Health Syst Pharm 2001;58:1330–1337
58. Wagner EH, Sandhu N, Newton KM, McCulloch DK, Ramsey SD, Grothaus LC. Effect of improved glycemic control on health care costs and utilization. JAMA 2001;285:182–189
59. Sidorov J, Shull R, Tomcavage J, Girolami S, Lawton N, Harris R. Does diabetes disease management save money and improve outcomes? A report of simultaneous short-term savings and quality improvement associated with a health maintenance organization-sponsored disease management program among patients fulfilling health employer data and information set criteria. Diabetes Care 2002;25:684–689
60. National Committee for Quality Assurance. HEDIS & performance measurement [Internet], 2016. Available from http://www.ncqa.org/hedis-quality-measurement. Accessed 22 November 2016
61. Centers for Medicare and Medicaid Services. Accountable care organizations [Internet], 2016. Available from https://www.medicare.gov/manage-your-health/coordinating-your-care/accountable-care-organizations.html. Accessed 22 November 2016
62. Centers for Medicare & Medicaid Services. MACRA - delivery system reform, Medicare payment reform [Internet], 2016. Available from https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/MACRA-MIPS-and-APMs/MACRA-MIPS-and-APMs.html. Accessed 22 November 2016
63. Totten AM, Wagner J, Tiwari A, O'Haire C, Griffin J, Walker M. Closing the quality gap: revisiting the state of the science (vol. 5: public reporting as a quality improvement strategy). Evid Rep Technol Assess (Full Rep) 2012;(208.5):1–645
64. Damberg CL, Sorbero ME, Lovejoy SL, Martsolf G, Raaen L, Mandel D. *Measuring Success in Health Care Value-Based Purchasing Programs Findings from an Environmental Scan, Literature Review, and Expert Panel Discussions*. Santa Monica, CA, RAND Corporation, 2014
65. Roland M, Campbell S. Successes and failures of pay for performance in the United Kingdom. N Engl J Med 2014;370:1944–1949