SUPPLEMENTARY DATA

conomic Evaluation of Quality Improvement Interventions Designed to Improve Glycemic Control in Diabetes Mellitus: A Systematic Review

Supplementary 1. Search Strategy

DATABASE SEARCHED & TIME PERIOD COVERED:
 PubMed – 1/1/2000-4/10/2014

LANGUAGE:
 English

SEARCH STRATEGY:
"HbA1c"[tiab] OR "glycemic"[tiab] OR glycosylated hemoglobin* OR glycosylated haemoglobin* OR "glucose control"[tiab] OR "euglycemia"[tiab] OR "hemoglobin A1c" OR A1C OR glycated hemoglobin* OR glycated haemoglobin* OR glycohemoglobin OR glycohaemoglobin OR "haemoglobin A1c" OR "Hb1c" OR "normoglycemia" OR "Hemoglobin A, Glycosylated"[MeSH]
AND
Economics[mh] OR "Costs and Cost Analysis"[mh] OR "Value of Life"[mh] OR Economics, Dental[mh] OR Economics, Hospital[mh] OR Economics, Medical[mh] OR Economics, Nursing[mh] OR Economics, Pharmaceutical[mh] OR economic*[tiab] OR cost[tiab] OR costs[tiab] OR costly[tiab] OR costing[tiab] OR price[tiab] OR prices[tiab] OR pricing[tiab] OR pharmacoeconomic*[tiab] OR (expenditure* NOT energy) OR value[ti] OR budget*[tiab] OR cost-benefit analysis[mh] OR cost savings[mh] OR investments[Majr] OR budgets[Majr] OR drug utilization/economics[Majr] OR costs and cost analysis[mh] OR models, economic[mh] OR iatrogenic disease/economics[Majr] OR health care costs[mh] OR health expenditures[Majr] OR capital expenditures OR "medical errors/economics" OR "Quality Improvement/economics" OR "Quality Indicators, Health Care/economics" OR "Quality Assurance, Health Care/economics" OR "quality of health care/economics" OR "total quality management/economics" OR net benefit[tiab] OR net-benefit[tiab] OR return on investment[tiab] OR Save money[tiab] OR Savings[tiab] OR profit[tiab] OR financial[tiab] OR investment*[tiab] OR invest[tiab] OR investing[tiab] OR fiscal[tiab] OR monetary[tiab] OR money[tiab] OR dollar*[tiab] OR "willingness to pay"[tiab] OR willingness-to-pay[tiab] OR "willing to pay"[tiab] OR business case[tiab] OR charges[tiab] OR charge[tiab] OR pay[tiab] OR pays[tiab] OR paying[tiab] OR payment[tiab] OR fee[tiab] OR fees[tiab] OR "market force"[tiab] OR "market forces" OR accounting[tiab] OR spending[tiab] OR health resource allocation OR unit-cost OR unit-costs OR valuation OR fees and charges[mh] OR saving[tiab] OR economics[sh] OR cost-effective[tiab] OR budget impact analys* OR roi[tiab] OR cost-minimiz* OR cost-consequence OR cost-utility OR net-cost OR net-costs
NOT
predictive value OR prognostic value

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DATABASE SEARCHED & TIME PERIOD COVERED:
 EconLit – 1/1/2000-3/6/2015

LANGUAGE:
 English

SEARCH STRATEGY:
HbA1c OR glycemic OR glycosylated hemoglobin* OR glycosylated haemoglobin* OR glucose control OR euglycemia OR hemoglobin A1c OR A1C OR glycated hemoglobin* OR glycated haemoglobin* OR glycohemoglobin OR glycohaemoglobin OR haemoglobin A1c OR Hb1c OR normoglycemia
 AND
 diabetes OR diabetic

VALUE OF QI – GLYCEMIC CONTROL (DIABETES) – 2016 UPDATE
SEARCH METHODOLOGY

DATABASE SEARCHED & TIME PERIOD COVERED:

SUPPLEMENTARY DATA

PubMed – 1/1/2014-8/1/2016

LANGUAGE:
English

SEARCH STRATEGY:
"HbA1c"[tiab] OR "glycemic"[tiab] OR glycosylated hemoglobin* OR glycosylated haemoglobin* OR "glucose control"[tiab] OR "euglycemia"[tiab] OR "hemoglobin A1c" OR A1C OR glycated hemoglobin* OR glycated haemoglobin* OR glycohemoglobin OR glycohaemoglobin OR "haemoglobin A1c" OR "Hb1c" OR "normoglycemia" OR "Hemoglobin A, Glycosylated"[MeSH] OR (glycemic index OR glycemic load[MH])
AND
Economics[mh] OR "Costs and Cost Analysis"[mh] OR "Value of Life"[mh] OR Economics, Dental[mh] OR Economics, Hospital[mh] OR Economics, Medical[mh] OR Economics, Nursing[mh] OR Economics, Pharmaceutical[mh] OR economic*[tiab] OR cost[tiab] OR costs[tiab] OR costly[tiab] OR costing[tiab] OR price[tiab] OR prices[tiab] OR pricing[tiab] OR pharmacoeconomic*[tiab] OR (expenditure* NOT energy) OR value[ti] OR budget*[tiab] OR cost-benefit analysis[mh] OR cost savings[mh] OR investments[Majr] OR budgets[Majr] OR drug utilization/economics[Majr] OR costs and cost analysis[mh] OR models, economic[mh] OR iatrogenic disease/economics[Majr] OR health care costs[mh] OR health expenditures[Majr] OR capital expenditures OR "medical errors/economics" OR "Quality Improvement/economics" OR "Quality Indicators, Health Care/economics" OR "Quality Assurance, Health Care/economics" OR "quality of health care/economics" OR "total quality management/economics" OR net benefit[tiab] OR net-benefit[tiab] OR return on investment[tiab] OR Save money[tiab] OR Savings[tiab] OR profit[tiab] OR financial[tiab] OR investment*[tiab] OR invest[tiab] OR investing[tiab] OR fiscal[tiab] OR monetary[tiab] OR money[tiab] OR dollar*[tiab] OR "willingness to pay"[tiab] OR willingness-to-pay[tiab] OR "willing to pay"[tiab] OR business case[tiab] OR charges[tiab] OR charge[tiab] OR pay[tiab] OR pays[tiab] OR paying[tiab] OR payment[tiab] OR fee[tiab] OR fees[tiab] OR "market force"[tiab] OR "market forces" OR accounting[tiab] OR spending[tiab] OR health resource allocation OR unit-cost OR unit-costs OR valuation OR fees and charges[mh] OR saving[tiab] OR economics[sh] OR cost-effective[tiab] OR budget impact analys* OR roi[tiab] OR cost-minimiz* OR cost-consequence OR cost-utility OR net-cost OR net-costs
NOT
predictive value* OR prognostic value*

==

DATABASE SEARCHED & TIME PERIOD COVERED:
EconLit – 1/1/2014-8/1/2016

LANGUAGE:
English

SEARCH STRATEGY:
HbA1c OR glycemic OR glycosylated hemoglobin* OR glycosylated haemoglobin* OR glucose control OR euglycemia OR hemoglobin A1c OR A1C OR glycated hemoglobin* OR glycated haemoglobin* OR glycohemoglobin OR glycohaemoglobin OR haemoglobin A1c OR Hb1c OR normoglycemia
AND
diabetes OR diabetic

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DATABASE SEARCHED & TIME PERIOD COVERED:
Grey Literature Report – 1/1/2014-8/1/2016

LANGUAGE:
English

SEARCH STRATEGY:
hemoglobin OR glycemic OR A1C OR glucose OR diabetes

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Supplementary 2. Classification of QI Strategies for Improving Glycemic Control

We used the following definitions for system-oriented, practitioner-oriented and patient-oriented strategies.

<u>System-oriented Strategies</u>

Disease Management: Any system for coordinating diagnosis, treatment, or ongoing patient management (e.g., arrangement for referrals, follow-up of test results) by a person or multidisciplinary team in collaboration with or supplementary to the primary care clinician. Often a nurse will be collecting data and act as a liaison between patient and others. Focuses on a specific disease.

Case Management: Any system for coordinating diagnosis, treatment, or ongoing patient management (eg, arrangement for referrals, follow-up of test results) by a person or multidisciplinary team in collaboration with or supplementary to the primary care clinician. The high cost patients and the very frail or geriatric patients go here. Focuses on the patient, not the disease. QII for people with a particular disease, such as diabetes goes into disease management. If the study calls it case management, so do we. Disease and case management were collapsed during analysis due to their inherent similarities and the fact that only one study addressed case management.

Team Changes: Changes to the structure or organization of the health care team, defined as present if any of the following applied. Of note, the professionals need to be part of the clinical team; individuals who act on behalf of payers or other external entities would not be included.
- Adding a team member or "shared care," e.g., routine visits with personnel other than the primary physician (including physician or nurse specialists in diabetic care, pharmacists, nutritionists, podiatrists).
- Use of multidisciplinary teams, i.e., active participation of professionals from more than one discipline (e.g., medicine, nursing, pharmacy, nutrition) in the primary, ongoing management of patients.
- Expansion or revision of professional roles (e.g., nurse or pharmacist plays more active role in patient monitoring or adjusting medication regimens).

Electronic Patient Registry: General electronic medical record system or electronic tracking system for patients with diabetes. Valuable QI tool, but only code it if it is new.

Facilitated Relay of Clinical Information: Clinical information collected from patients and transmitted to clinicians by means other than the existing medical record. Conventional means of correspondence between clinicians were excluded. For example, if the results of routine visits with a pharmacist were sent in a letter to the primary care physician, the use of routine visits with a pharmacist would count as a "team" change, but the intervention would not also be counted as "facilitated relay." Usually electronic or Web-based tools through which patients provide self-care data, but also structured diaries for patients to record self-monitored health data, which are brought in person to office visits to review with the primary physician. Includes point-of-care testing.

Continuous Quality Improvement: Interventions explicitly identified as using the techniques of continuous quality improvement, total quality management, or plan-do-study-act, or any iterative process for assessing quality problems, developing solutions to those problems, testing their impacts, and then reassessing the need for further action.

Enhancing Efficiency: These interventions focus on reducing the cost of care, generally while keeping clinical quality/ outcomes constant. This includes interventions designed to eliminate the use of discretionary or unnecessary services, or to reduce the costs involved in high priced or overpriced services. This includes eliminating services (laboratory tests, procedures, etc.), increasing the use of less costly substitutes (e.g., substituting generic for brand drugs, substituting group for individual visits). Generally, these analyses will involve equivalence trials (test of non-inferiority) or an assumption that outcomes will not worsen.

Standardizing Care: These interventions include checklists, protocols, care pathways and other ways of standardizing care such that the bundle of services received by patients in similar situations is more consistent. E.g., checklists and bundles to reduce ventilator-associated pneumonia, standardize the steps involved in a surgical procedure, etc.

<u>Practitioner-oriented Strategies</u>

SUPPLEMENTARY DATA

Audit and Feedback: Summary of clinical performance of health care delivered by an individual clinician or clinic over a specified period, which is then transmitted back to the clinician (e.g., the percentage of a clinician's patients who have achieved a target glycosylated hemoglobin [HbA1c] level, or patients who were readmitted within 30 days). Can include number of patients with missing data or dropouts.

Provider Education: Interventions designed to promote increased understanding of principles guiding clinical care or awareness of specific clinical recommendations for a target condition or patient population. Could be conferences or workshops, distribution of educational materials, and educational outreach visits. (Ivers call this clinician education) We exclude training for an intervention: e.g. how to use the website, educate patients etc. Judgment is required in how much provider education counts; it needs to be more than the minimum required to implement a different category of QI intervention (e.g., more than training providers how to use decision support, for example).

Provider Decision Support: Paper-based or electronic system intended to prompt a health professional to recall patient-specific information (e.g., most recent HbA1c value) or to perform a specific task (e.g., perform a foot examination). Usually includes a recommendation. (Ivers calls this QII clinical reminders)

Financial Incentives for Providers: These interventions offer providers financial incentives for improving quality or reducing costs (e.g., pay for performance) or structure reimbursement or payment systems to create implicit incentives for improving quality or reducing costs (value-based insurance design, prospective, capitated, or bundled payment). Improving quality or reducing costs may be a primary or secondary objective of the implementing the incentives, but the economic evaluation must consider effects on clinical outcomes and costs.

Patient-oriented Strategies

Tailoring Care for Unique Patient Subgroups: These interventions focus on specific subgroups that share certain non-clinical characteristics, such as culture, language, income, age, gender, social situation (e.g., homeless, immigrant, incarcerated), or sexual identity. They ALSO tailor clinical care (not just patient education or self-management) based on the needs of the subgroup._ For example, patients in certain immigrant populations share culture and language, but they may also share risk factors for certain diseases, such as TB, hepatitis C, etc. Interventions that group patients with similar clinical characteristics (e.g., diabetes, heart failure, etc.) will generally go into other categories depending on what the intervention entails, such as provider education, patient self-management, etc.

Patient Education: Interventions designed to promote increased understanding of a target condition or to teach specific prevention or treatment strategies, or specific in-person patient education (eg, individual or group sessions with diabetes nurse educator; distribution of printed or electronic educational materials). Judgment needed to say how much patient education counts (e.g. just giving them a pamphlet does not), needs to be more than the minimum required to implement a different category of QI intervention (e.g., more than training how to perform self-management).

Promotion of Patient Self-Management: Provision of equipment (eg, home glucometers) or access to resources (eg, system for electronically transmitting home glucose measurements and receiving insulin dose changes based on those data) to promote self-management. This includes increasing availability of provider advice, such as through nursing hot lines, email exchanges with providers, interpreter services, and other interventions designed to improve patient adherence to the care plan, including medications, diet, exercise, and other self-care modalities.

Patient Reminder Systems: Any effort (eg, postcards or telephone calls or Patient Portals like MyUCLA) that have useful information re appointments, results etc. to remind patients about upcoming appointments or important aspects of self-care.

Financial Incentives for Patients: These interventions offer patients financial incentives for improving self-care, medication adherence, or other behaviors that may improve outcomes or reduce costs; or structure reimbursement or payment systems to create implicit incentives for improving quality or reducing costs (e.g., value-based insurance design). Improving quality or reducing costs may be a primary or secondary objective of the implementing the incentives, but the economic evaluation must consider effects on clinical outcomes and costs.
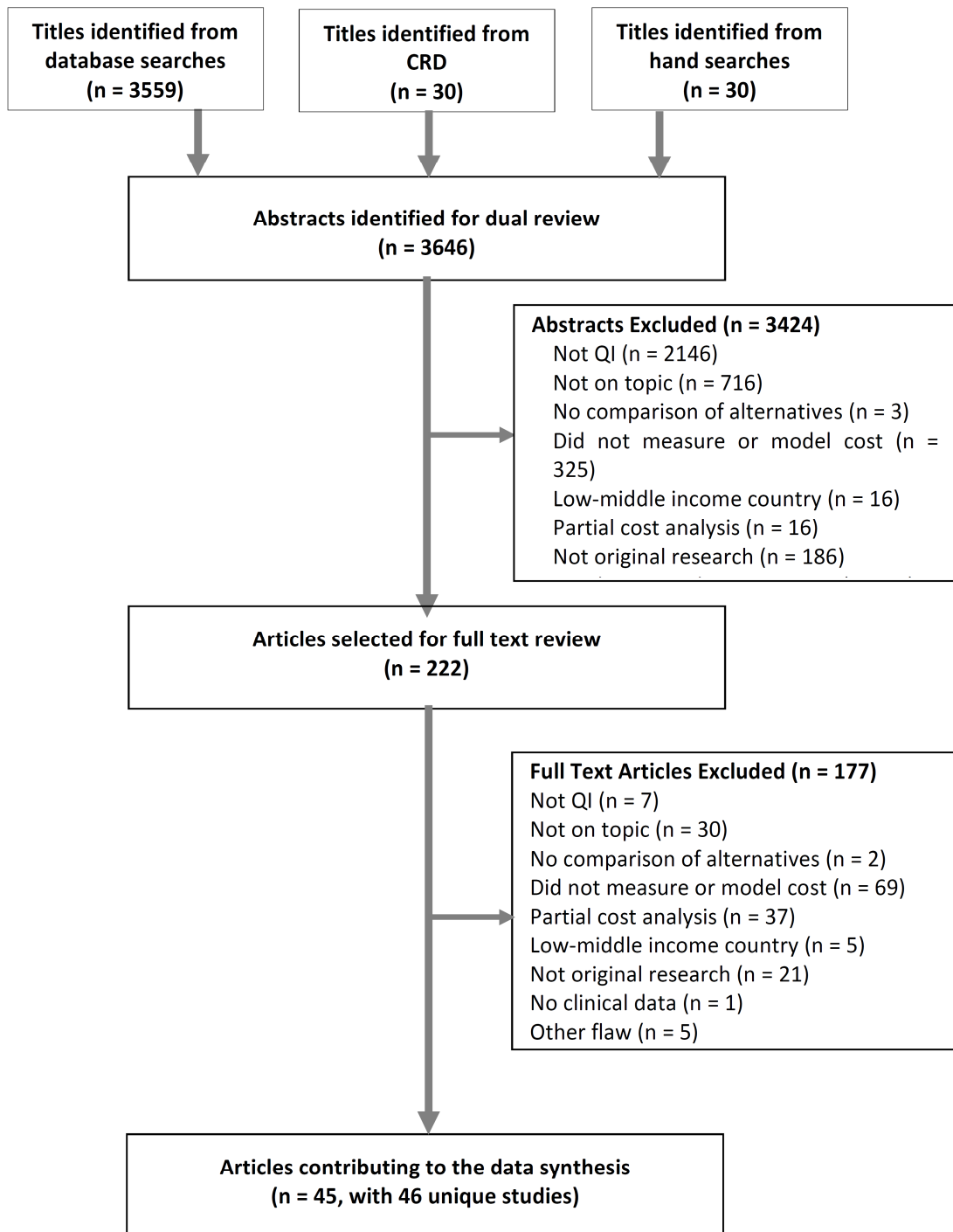
Sources:

SUPPLEMENTARY DATA

Andrea C Tricco, Noah M Ivers, Jeremy M Grimshaw, David Moher, Lucy Turner, James Galipeau, Ilana Halperin, Brigitte Vachon, Tim Ramsay, Braden Manns, Marcello Tonelli, Kaveh Shojania. Eff ectiveness of quality improvement strategies on the
management of diabetes: a systematic review and meta-analysis. Lancet 2012; 379: 2252–61.

Ivers N, Tricco AC, Trikalinos TA, Dahabreh IJ, Danko KJ, Moher D, Straus SE, Lavis JN, Yu CH, Shojania K, Manns B, Tonelli M, Ramsay T, Edwards A, Sargious P, Paprica A, Hillmer M, Grimshaw JM. 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 Aug 12;3:88. doi: 10.1186/2046-4053-3-88.

Shojania KG, Ranji SR, McDonald KM, Grimshaw JM, Sundaram V, Rushakoff RJ, Owens DK. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. JAMA. 2006 Jul 26;296(4):427-40.

SUPPLEMENTARY DATA

Supplementary 3. PRISMA Flow Diagram

Titles identified from database searches (n = 3559)	**Titles identified from CRD (n = 30)**	**Titles identified from hand searches (n = 30)**

Abstracts identified for dual review (n = 3646)

Abstracts Excluded (n = 3424)
Not QI (n = 2146)
Not on topic (n = 716)
No comparison of alternatives (n = 3)
Did not measure or model cost (n = 325)
Low-middle income country (n = 16)
Partial cost analysis (n = 16)
Not original research (n = 186)

Articles selected for full text review (n = 222)

Full Text Articles Excluded (n = 177)
Not QI (n = 7)
Not on topic (n = 30)
No comparison of alternatives (n = 2)
Did not measure or model cost (n = 69)
Partial cost analysis (n = 37)
Low-middle income country (n = 5)
Not original research (n = 21)
No clinical data (n = 1)
Other flaw (n = 5)

Articles contributing to the data synthesis (n = 45, with 46 unique studies)

Supplementary 4. Data Extracted for Each Eligible Study

Table 1. Quality Improvement Strategies Used in Each Eligible Study

Author and Year (Citations)	System-oriented Strategies								Practitioner-oriented Strategies				Patient-oriented Strategies				
	Case Management	Disease Management	Team Changes	Electronic Patient Registry	Facilitated Relay	Continuous QI	Enhancing Efficiency	Standardizing Care	Audit and Feedback	Provider Education	Provider Decision Support	Incentives for Providers	Tailoring Care	Patient Education	Patient Self-Management	Patient Reminders	Incentives for Patients
Short Term																	
Handley 2008 [1,2]		X	X										X	X	X	X	
Wilson 2014 [3,4]		X	X					X						X	X		
Sperl-Hillen 2010 [5]								X	X	X							
Eccles 2007 [6,7]									X		X			X		X	
Allen 2013 [8,9]		X	X					X						X	X	X	
Katon 2012 [10]		X	X								X			X	X		
Houweling 2009 [11]		X	X					X						X			
Noel 2004 [12]	X				X									X			
Kogut 2012 [13]		X						X						X	X		X
Sidorov 2002 [14,15]		X	X	X						X				X	X		X
Mousques 2010 [16]		X	X	X							X			X			
Spence 2014 [17]		X												X	X		
Nundy 2014 [18]		X			X									X	X	X	
Gilmer 2005 [19]		X	X										X	X	X		
Salzsieder 2011 [20]		X									X						
Franklin 2013 [21,22]		X	X											X			
Steuten 2007 [23,24]		X	X					X	X					X	X		
Keers 2005 [25]		X						X						X	X		
Haji 2013 [26]		X												X	X		
Balamurugan 2006 [27]					X								X	X	X	X	X
Micklethwaite 2012 [28]		X	X											X	X	X	
Garrett 2005 [29]		X	X											X	X		X
Snyder 2003 [30]		X		X							X			X	X	X	
Intermediate Term																	
Palmas 2010 [31-33]		X	X	X	X			X					X	X			
Gordon 2014 [34-36]		X	X	X										X	X	X	
Yu 2013 [37,38]		X	X												X		
Beaulieu 2006 [39]		X							X			X		X	X		
Long Term																	
Gillett 2010 [40,41]								X						X	X		
Gillespie 2012 [42-44]											X				X		
O'Reilly 2012 [45,46]				X	X						X					X	

Study															
Gilmer 2012 [47,48]							X		X	X					
Mason 2006 [49,50]	X												X	X	X
Dijkstra 2006, Provider [51,52]							X	X							
Dijkstra 2006, Provider and patient [51,10452]				X			X	X					X		
Slingerland 2013 [53]	X	X		X			X						X		
Prezio 2014 [54,55]				X								X	X	X	
Schouten 2010 [56]		X			X								X	X	
Gilmer 2007 [19,57]	X	X				X						X	X	X	X
Kuo 2011 [58]	X	X								X				X	
McRae 2008 [59]	X			X		X	X		X						
Giorda 2013 [60,61]	X				X	X	X								
Huang 2007 [62-64]			X	X	X				X			X		X	
Brownson 2009 [65]	X							X				X	X	X	
O'Reilly 2007 [66,67]	X	X	X					X					X		
Gozzoli 2002* [68]						X			X				X		
Brown 2012 [69]	X											X	X	X	

*Study included simulations for four scenarios; only the multifactorial one met the study definition of a QI intervention

SUPPLEMENTARY DATA

Table 2. Information Related to the Clinical Evaluation for Each Eligible Study*

Author and Year (Citations)	Intervention (Duration)	Location and Sites	Population	Study Design, Comparator	Intervention Group, N	Control Group, N	Baseline HbA1c in Intervention Group	Change in HbA1c † (Timing of Follow-up Test)	Change in HRQoL per Patient (Time Horizon)
Short Term									
Handley 2008 [1,2]	Interactive phone technology to provide surveillance, education, and counseling (9 mos)	United States, urban, 4 safety net clinics	T2DM, in diabetes registry	RCT, SQ	112	114	9.3%	NR	0.012 QALY (1 yr)
Wilson 2014 [3,4]	Intermediate care clinics for DM in which general practitioners work with community-based specialist teams (1.5 yr)	United Kingdom, urban, 3 primary care trusts with 49 general practices	T2DM	Cluster RCT, SQ	591	636	7.18%	-0.07% (1.5 yr)	n/a
Sperl-Hillen 2010 [5]	Physician education using cases to teach mastery of 25 essential practices (1 yr)	United States, 11 primary care clinics	T2DM	Cluster RCT, SQ	1,847 at 6 clinics	1,570 (5 clinics)	7.4%	-0.19% (1 yr)	n/a
Eccles 2007 [6,7]	Individualized patient management prompts added to computerized DM registry (1 yr)	United Kingdom, 58 general practices	T2DM, age ≥ 35	Cluster RCT, SQ	713 with 30 physicians	720 with 28 physicians	7.75%	-0.22% (1 yr)	n/a
Allen 2013 [8,9]	Comprehensive CVD risk reduction program administered by nurse practitioner-community health worker teams instead of physician visits (1 yr)	United States, urban, 2 federally qualified community health centers	T2DM, CVD, HTN, or hyperlipidemia	RCT, SQ	261	264	8.9%	-0.5% (1 yr)	n/a
Katon 2012 [10]	Physician-supervised nurses collaborated with physicians to provide treatment of multiple disease risk factors (1 yr)	United States, 14 primary care clinics in integrated system	Depression and poorly controlled DM or CHD	RCT, SQ	106	108	8.14%	-0.56% (1 yr), -0.14% (2 yrs)	0.335 QALY (2 yrs)
Houweling 2009 [11]	Diabetes specialist/nurse treated blood glucose, blood pressure, and hyperlipidemia per protocol (1 yr)	Netherlands, urban/ suburban, 2 outpatient clinics	T2DM, referred to program	RCT, SQ	46	38	8.9%	-0.6% (1 yr)	n/a
Noel 2004 [12]	Home telehealth systems integrated in an electronic medical record system (0.5 yr)	United States, urban, 1 Veterans Affairs health system	DM, COPD, or HF	RCT, SQ	23 with DM	28 with DM	8.3%	-1.8% (0.5 yr)	n/a
Kogut 2012 [13]	Disease management and medication copayment reduction (1 yr)	United States, 5 employers covered by one payer	DM	CBA, SQ	649 at participating employers	9049 declined or at other employers	NR	NR	n/a
Sidorov 2002 [14,15]	Disease management with patient and provider education, promotion of clinical guidelines and early specialist referral (1 yr)	United States, not-for-profit HMO covering 41 counties	T2DM	CBA, SQ	3,118 opted in	3,681 did not opt in	NR	NR	n/a

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Mousques 2010 [16]	Electronic patient registry and clinical reminder system; patient education and counseling (11 mos)	France, 18 general practices	T2DM	Matched CBA, SQ	588 from participating practices	202 from other practices	7.16%	-0.1% (1 yr)	n/a
Spence 2014 [3]	When patients presented to outpatient pharmacy for any reason, pharmacists performed spontaneous consults to help patients use DM medication more effectively (1 yr)	United States, California, integrated healthcare system	T2DM, low medication adherence, and HbA1C > 8%	CBA, SQ	359	428	9.79%	-0.50% (1 yr)	n/a
Nundy 2014 [18]	Mobile health, patient education (0.5 yr)	United States, urban, employee health plan at academic center	DM type 1 or 2	CBA, SQ	74 participated	274 declined	7.9%	-0.7% (0.5 yr)	n/a
Gilmer 2005 [19]	Disease management plus culturally oriented peer-led self-empowerment training (1 yr)	United States, urban, 17 County health centers	DM, indigent	CBA, SQ	188	160 historical controls	8.5%	-0.8% (1 yr)	n/a
Salzsieder 2011 [20]	Telemedicine with patient-focused personalized decision support (1 yr)	Germany, 1 health insurance payer	T1DM or T2DM, CVD	CBA, SQ	214 with participating MDs	75 with other MDs	7.1%	-0.9% (1 yr)	n/a
Franklin 2013 [21,22]	Collaborative care model with pharmacists and physicians (1 yr)	United States, 7 primary care practices at academic center	T2DM, CVD risk factors	UCBA, SQ	206	n/a	11% had HbA1c <7%	36% had HbA1c <7% (1 yr)	n/a
Steuten 2007 [23,24]	Multidisciplinary disease management program with central coordination, provider feedback, patient education (2 yrs)	Netherlands, urban, 63 academic general practices	T1DM or T2DM	UCBA, SQ	473	n/a	7.5%	-0.2% (2 yrs)	n/a
Keers 2005 [25]	12-d multidisciplinary intensive education program (1 yr)	Netherlands, small city, 1 University hospital	T1DM or T2DM, self-management difficulties	UCBA, SQ	56	n/a	8.5%	-0.4% (1 yr)	n/a
Haji 2013 [26]	Practices with high vs. low involvement of nurses in care for DM (3 yrs)	Australia, Urban, 10 general practices	T2DM, >3 visits in 2 yrs	UCBA, SQ	231 at 6 high-involvement practices	108 at 4 low-involvement practices	7.02%	-0.41% (3 yrs)	n/a
Balamu-rugan 2006 [27]	Self-management education with needs assessment followed by group education (1 yr)	United States, Arkansas Medicaid recipients	DM	UCBA, SQ	212	n/a	8.00%	-0.45% (1 yr)	n/a
Mickleth-waite 2012 [28]	Diabetes screening, self-management education, skills training, and case management (3 yr)	United States, 1 federally qualified health center	T2DM, recent hospital or ED use	UCBA, SQ	81	n/a	8.31%	-0.77% (0.5-3 yrs)	n/a
Garrett 2005 [29]	Pharmacist consultations, goal setting, monitoring, and collaborative management; referrals to DM educators (1 yr)	United States, 80 community pharmacy providers in 4 states	DM covered by self-insured employers	UCBA, SQ	256	n/a	7.9%	-0.8% (1 yr)	n/a
Snyder 2003 [30]	Disease management program with outreach telephone calls to pts (3 yrs)	United States, Nevada, benefits administrator for teachers	DM	UCBA, SQ	166	n/a	8.89%	-1.01% (3 yrs)	n/a

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Intermediate Term									
Palmas 2010 [31,32]	Telemedicine with nurse case management (5 yrs)	United States, multiple primary care practices	DM, age ≥55, living in under-served areas	RCT, SQ	844	821	7.43%	-0.29% (5 yrs)	n/a
Gordon 2014 [34,35]	Automated telephone-linked system promoting self-management, with clinical targets set by PCP (0.5 yr)	Australia, urban, 2 academic hospitals	T2DM, HbA1c ≥7.5%	Model based on RCT, SQ	60	60	8.7%	-0.6% (0.5 yr)	0.004 QALY (5 yrs)
Yu 2013 [37,38]	Clinical pharmacist/DM educator controlled DM, blood pressure, & cholesterol (1 → 10 yrs) ‡	United States, California, 2 clinics in integrated system	T2DM, HbA1c ≥7%, prior care by study pharmacist	Model based on matched CBA, SQ	147 at study clinics	147 at other clinics	9.5%	-1.7% (1 → 10 yrs)	0.49 QALY (10 yrs)
Beaulieu 2006 [39]	Diabetes disease management involving patient education and provider feedback and reminders (10 yrs)	United States, urban, health maintenance organization in Minnesota	DM	Serial cross-sectional analyses, SQ	26,545 in year 10	13,120 at baseline	8.7% at baseline	-1.9% (at 10 yrs)	n/a
Long Term									
Gillett 2010 [40,41]	Diabetes education and self-management program (1 yr)	United Kingdom, 13 primary care trusts (162 practices)	Newly diagnosed T2DM	Model based on cluster RCT, SQ	437	387	8.3%	-0.06% (1 → 3 yrs)	0.0392 QALY 0.0283 LY (80 yrs)
Gillespie 2012 [42,44]	Group-based peer support with standardized DM care (2 yrs)	Ireland, 20 general practices	T2DM	Model based on cluster RCT, SQ (with standardized care)	192	203	7.06%	-0.08% (2 yrs)	0.09 QALY (40 yrs)
O'Reilly 2012 [45,46]	Web-based DM tracker that interfaced with EMR, gave MD and pt access, and had automated telephone reminders (1 yr)	Canada, 47 primary care practices in 3 regions	T2DM	Model based on RCT, SQ	253	258	7.0%	-0.2% (1 yr)	0.0201 QALY 0.0245 LY (40 yrs)
Gilmer 2012 [47,48]	EMR-based clinical decision support with drug-specific advice plus reorganized clinic workflow (0.5 → 40 yrs)	United States, 11 clinics in a large medical group	DM, HbA1c ≥7.0%	Model based on cluster RCT, SQ	471	621	8.5%	-0.26% (1 → 40 yrs)	0.04 QALY 0.03 LY (40 yrs)
Mason 2006 [49,50]	Protocol-driven call center that supported patient education, self-care, and referrals (1 yr → lifetime)	United Kingdom, small city, population-based registry	T2DM	RCT, SQ	394	197	7.9%	-0.31% (1 yr → lifetime)	0.103 QALY 0.320 LY (lifetime)
Dijkstra 2006 [51,52]	Education, reminders and feedback for health professionals (1 yr)	Netherlands, clinics at 13 general hospitals	T2DM	Model based on cluster RCT, SQ	248	276	8.1%	-0.4% (1 yr)	0.29 QALY (0.133 QALY discounted at 3%) 0.34 LY (lifetime)
	Same plus education and "diabetes passports" for patients (1 yr)				240		8.0%	-0.5% (1 yr)	0.59 QALY (0.276 discounted at 3%)

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Study	Intervention	Location	Population	Model	N (intervention)	N (comparison)	Baseline HbA1c	HbA1c change	Outcome
									0.53 LY (lifetime)
Slingerland 2013 [53]	Patient-centered care, patient education, diabetes passports, feedback to physicians and nurses (1 yr → lifetime)	Netherlands, clinics at 13 hospitals	T2DM	Model based on cluster RCT, SQ with DM team	240	276	>8.5%: mean 9.5%	-0.83% (1 yr → lifetime)	0.54 QALY (lifetime)
							7-8.5%: mean 7.7%	-0.49% (1 yr → lifetime)	0.24 QALY (lifetime)
Prezio 2014 [54,55]	Diabetes education and self-management program tailored to low literacy Mexican American population (1 → 20 yrs)	United States, urban, 1 community clinic	T2DM, uninsured, Mexican-American	Model based on RCT, SQ	90	90	8.9%	-0.7% (1 → 20 yrs)	0.056 QALY 0.0354 LY (20 yrs)
Schouten 2010 [56]	QI collaboratives that developed multidisciplinary teams, introduced patient self-management, created registry of clinical parameters, and used plan-do-study-act cycles (1 yr)	Netherlands, 37 general practices and 13 outpatient clinics	T2DM	Model based on CBA, SQ	607 in 6 regions (54.8% male)	1,254 in 9 regions	7.5%	No change (2 yrs)	0.26 QALY 0.76 LY female, 0.33 QALY 0.97 LY male (lifetime, discounted at 1.5%)
Gilmer 2007 [19,57]	Culturally-specific self- management training by nurse/diabetes educator, dietician, medical assistant; education by peer educators (1 → 40 yrs)	United States, urban, 4 cohorts defined by insurance status	DM	Model based on CBA, SQ	Commercial 575		7.8%	-0.4% (1 → 40 yrs)	0.18 QALY 0.20 LY (40 yrs)
					Medicaid 1,213		8.2%	-0.5% (1 → 40 yrs)	0.26 QALY 0.30 LY (40 yrs)
					County 1,345		8.6%	-0.8% (1 → 40 yrs)	0.44 QALY 0.60 LY (40 yrs)
					Uninsured 760		9.4%	-1.3% (1 → 40 yrs)	0.89 QALY 1.1 LY (40 yrs)
Kuo 2011 [58,70]	Chronic Care Model with multidisciplinary DM-specific team (up to 3 → 20 yrs)	United States, diabetes clinic at an Air Force Medical Center	T2DM, age 50, no compli-cations	Model based on CBA, SQ	196 treated in study clinic	1,221 treated in other clinics	6.8%	-0.6% (up to 3 → 20 yrs)	0.117 QALY (20 yrs)
McRae 2008 [59]	Centralized database used to promote guideline implementation via reminders, feedback, and guidance to providers (5 → 40 yrs)	Australia, regional network with 16 general practices	T2DM, participated for 5 yrs, had all desired data	Model based on UCBA, SQ	74 in model; 1,087 in program	n/a	6.9%	0.3% (5 yrs)	0.30 QALE 0.36 LY (40 yrs)
Giorda 2013 [60,61]	Physician-led initiative related to glycemic control and CVD risk factors (5 → 50 yrs)	Italy, about 224 diabetes treatment centers with 1/6th of all patients with T2DM in the country	T2DM, participated for 5 yrs	Model based on UCBA, SQ	195,851	n/a	7.8%	-0.2% (1 → 50 yrs)	0.48 QALY 0.55 LY (50 yrs)
Huang	Collaborative conducted in	United States, 17 health	T2DM	Model based	80	n/a	8.53%	-0.45%	0.35 QALY

2007 [62,63]	community health centers (4 yrs)	centers		on serial cross-section, SQ				(4 yrs)	0.35 LY (lifetime)
Brownson 2009 [65]	Self-management training that included patient education, telephone follow-up, counseling, goal setting, support groups (1-4 yrs → lifetime)	United States, nonprofit community-based health care organization in 4 states	T2DM, Hispanic or African American, low-income	Model based on UCBA, SQ	2,920	n/a	NR	-0.5% (1-4 yrs → lifetime)	0.297 QALY 0.54 LY (lifetime)
O'Reilly 2007 [66,67]	Multidisciplinary primary care diabetes management program (1.5 yrs)	Canada, multidisciplinary health services organization	DM	Model based on UCBA, SQ	401	n/a	8.14%	-1.02% (1 yr)	0.1075 QALY 0.8400 LY (lifetime)
Gozzoli 2002 [68]	Educational program, screening for DM complications and CVD risk factors (sustained)	Switzerland, hypothetical cohort	T2DM	Model based on literature, SQ	NR	NR	7.4%	assumed -1.6% (short term)	n/a
Brown 2012 [69]	Lifestyle modification program led by community health workers via home-based counseling and education (1.5 → 20 yrs)	United States, 1 clinic for medically underserved	T2DM, HbA1c >7%, Hispanic, low income	Model based on UCBA, SQ	30	n/a	9.93%	-2.7% (1.5 → 20 yrs)	0.060 QALY 0.063 LY (20 yrs)

* Abbreviations

Medical Diagnoses: DM = diabetes mellitus (type unspecified), T1DM = type 1 diabetes mellitus, T2DM = type 2 diabetes mellitus, CVD = cardiovascular disease, CHD = coronary heart disease; HTN = hypertension

Units of Time: mo = month, yr = year

Study designs: RCT = randomized controlled trial, NRCT = non-randomized controlled trial, CBA = controlled before-after analysis, UCBA = uncontrolled before-after analysis

HbA1c = hemoglobin A1c

HRQoL = health-related quality of life

Pt   =   Patient

NR = Not reported

SQ = status quo

QALY = quality-adjusted life-years/life-expectancy

LY = life-years/life expectancy

n/a = not applicable

† In studies that used uncontrolled designs (UCBA, serial cross-sectional analysis), the change in HbA1c represents the change from the baseline test to the follow-up test. In studies that used controlled designs (RCT, NRCT, or CBA), the change in HbA1c represents the difference between the intervention and control groups in the change the baseline test to the follow-up test.

‡ In the notation used (e.g., 1 → 10 yrs), the first number indicates the actual duration of the intervention or timing of the follow-up HbA1c test (in this example, 1 yr). The arrow and second number indicate that the authors assumed the intervention or change in HbA1c was sustained over a longer period (in this example, over 10 yrs).

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Table 3. Information Related to Economic Evaluation for Each Eligible Study*

Author and Year (Citation)	Approach & Perspective	Time Horizon, Discount Rate	Year of Costs	Program Cost	Healthcare Utilization Costs	Types of Healthcare Utilization Included					Incremental Net Cost	Incremental Cost-Effectiveness Ratio	mQHES Score
						Clinic Visits	Medi-cations	Labor-atory Tests	Hospital-izations	Patient Costs			
Short Term													
Handley 2008 [1]	CEA, health system	1 yr, n/a	2004	$782 per pt	$0 (no difference)	NR	NR	NR	NR		NR	$65,167 per QALY	111
Wilson 2014 [3]	CEA, single-payer system	1.5 yrs, n/a	2010	$60.18 per pt	$52.98 per pt	X		X	X		$113.16 per pt	£7,778 per QALY	98
Sperl-Hillen 2010 [5]	Cost analysis, payer	1 yr, n/a	2009	$27 per pt	Included, not itemized	X	X				-$71 per pt	n/a	87
Eccles 2007 [6]	Cost analysis, society	1 yr, n/a	2003	£104,502 for 3,780 pts in average primary care trust	-£12.41 per pt	X	X	X		Productivity, travel, other out of pocket costs (£7.15 per pt per year)	NR	n/a	93
Allen 2013 [8]	CEA, health system	1 yr, n/a	2010	-$57 per pt	$688 per pt	(PC)†	X	X			$631 per pt	n/a	100
Katon 2012 [10]	CEA, health system	2 yrs, n/a	2008	$1224 per pt	Included, not itemized	X	X	X	X	Specialty & mental health care	-$594 per pt	n/a	113
Houweling 2009 [11]	Cost analysis, payer	1 yr, n/a	2003	-€23.75 per pt	-€273.80 per pt	(PC)	X	X			NR	n/a	92
Noel 2004 [12]	Cost analysis, integrated health system	0.5 yr, n/a	2002	$78,302 for 47 pts	$1,459 per pt	X#				Transport	$3,125 per pt	n/a	100
Kogut 2012 [13]	Cost analysis, payer	1 yr, n/a	2010	$285 per pt	-$1,102 per pt	X	(PC)	X	X		-$817 per pt	n/a	85
Sidorov 2002 [14]	CEA, integrated health system	1 yr, n/a	2001	$1.81 million for 3,118 pts	-$1,294.32 per pt	X	X	X	X		NR	n/a	95
Mousques 2010 [16]	Cost analysis, health system	1 yr, n/a	2005	€60 per pt	-€81.28 per pt	X			X		NR	n/a	76
Spence 2014 [3]	Cost analysis, integrated health system	1 yr, n/a	2010	$526,672 + $52,396 per 40,000 pts with DM or dyslipidemia	-$11,640,296 + $1,134,400 per 40,000 pts with DM or dyslipidemia		X		X		Return on investment 5.79	n/a	97
Nundy 2014	Cost analysis,	0.5 yr,	2012	$375 per pt	-$812 per pt	X	X	X	X		-$437 per pt	n/a	91

[18]	payer	n/a											
Gilmer 2005 [19]	Cost analysis, payer	1 yr, n/a	2002	$507 per pt	$839 per pt	X	X		X		$1,346 per pt	n/a	101
Salzsieder 2011 [20]	Cost analysis, payer	1 yr, n/a	2009	€2,850 per pt	-€3,760 per pt	X	X		X		-€910 per pt	n/a	82
Franklin 2013 [21]	Cost analysis, health system	1 yr, n/a	2011	$527.83 per pt	-$421 per pt	X	X	X	X		$106.81 per pt	n/a	108
Steuten 2007 [23]	CEA, society	2 yrs, n/a	2002	€21 per pt per 3 mo	(back calculated to account for productivity)	X#	X		X	Productivity (-€27 per pt per 3 mo)	-€29 per pt per 3 mo (including productivity)	n/a	108
Keers 2005 [25]	Cost analysis, society	1 yr, n/a	2003	€1,327 per pt	-€1,469 per pt including productivity, travel	X			X	Travel (-€7 per pt), productivity (-€543 per pt)	NR	n/a	103
Haji 2013 [26]	CEA, health system	3 yrs, n/a	2010	-AU$1,489 per pt	Included, not itemized	(PC)	X		(avail-able)		-AU$826 per pt	n/a	107
Balamurugan 2006 [27]	Cost analysis, health system	3 yrs, n/a	2003	$335 per pt	-$246 per pt	X	X	X	X		$89 per pt	n/a	79
Micklethwaite 2012 [28]	CEA, clinic/provider	1 yr, n/a	2010	$140,279 per 81 pts	-$551 per pt	X			X		NR	n/a	104
Garrett 2005 [29]	Cost analysis, payer	1 yr, n/a	2003	$351 per pt	-$1,269 per pt	X	X		X		-$918 per pt	n/a	91
Snyder 2003 [30]	Cost analysis, payer	3 yrs, n/a	2001	Included, not itemized	-$189.29 per pt per mo	X		X	X		-$986,538 over 7,407 pt-mo	n/a	75
Intermediate Term													
Palmas 2010 [31]	Cost analysis, health system	6 yrs, n/a	2006	$622 per pt per mo	$629 per pt per yr	X#	X	X	X		NR	n/a	101
Gordon 2014 [34]	CEA, health system	5 yrs, 5%	2011	£533 per pt	Included, not itemized	X	X		X		-£683 per pt	NR, intervention dominates	110
Yu 2013 [37]	CEA, health system	10 yrs, 3%	2011	Included, not itemized	Included, not itemized	X	X	X	X		-$8,788 per pt over 10 yrs	NR, intervention dominates	108
Beaulieu 2006 [39]	Cost analysis, integrated health system	10 yrs, 7%	2004	$233 per pt over 10 yrs	-$5,560 per pt at 10 yrs vs. at baseline	X	X	X	X		-$5,345 per pt at 10 yrs vs. at baseline	n/a	84
Long Term													
Gillett 2010 [40]	CEA, single-payer system	lifetime, 3.5%	2008	£219 per pt	-£10 per pt	X	X	X	X		£209 per pt	£5,387 per QALY	111

Study	Perspective	Time horizon, discount	Year	Intervention cost	Usual care					Other costs	Incremental cost	ICER	Ref
Gillespie 2012 [42]	CEA, society	40 yrs, 3.5%	2008	€246 per pt	Included	X	X	X	X	Travel, productivity	-€623 per pt	NR, intervention dominates	108
O'Reilly 2012 [45]	CEA, single-payer system	40 yrs, 3%‡	2010	C$1,912 per pt	Included, not itemized	X	X	X	X		C$2,048 per pt	C$102,053 per QALY	110
Gilmer 2012 [47]	CEA, single-payer system	40 yrs, 3%	2009	$81 per pt in first yr, $37 per pt per yr in later yrs	Included, not itemized	X#	X	X	X	Dental, equipment	$803 per pt over 40 yrs	$21,690 per QALY	108
Mason 2006 [49]	CEA, health system	lifetime, 5%	2003	£1,088 per pt over lifetime	Included, not itemized	X	X	X	X		NR	£43,500 per QALY	113
Dijkstra 2006 [51,71], Provider	CEA, payer	lifetime, 3%	2001	€2.00 per pt per yr	Included, not itemized	X	X	X	X		€9,389 per pt over lifetime	€70,630 per QALY	106
Dijkstra 2006 [51,71], Provider and patient	CEA, payer	lifetime, 3%	2001	€3.50 per pt per yr	Included, not itemized	X	X	X	X		€9,620 per pt over lifetime	€34,808 per QALY	106
Slingerland 2013 [53], HbA1c >8.5%	CEA, integrated health system	lifetime, 3% cost only‡	2000	$3.70 per pt per yr	Included, not itemized	X	X	X	X		$3,482 per pt over lifetime	$6,443 per QALY	108
Slingerland 2013 [53], HbA1c 7-8.5%	CEA, integrated health system	lifetime, 3% cost only‡	2000	$3.70 per pt per yr	Included, not itemized	X	X	X	X		$4,731 per pt over lifetime	$20,086 per QALY	108
Prezio 2014 [54]	CEA, society	20 yrs, 3%	2012	$4,958 per pt	Included, not itemized	X	X	X	X		Included, not itemized	$355 per QALY	105
Schouten 2010 [56], Women	CEA, payer in single-payer system	lifetime, 3% ‡	2006	€22.19 per pt	€643 per pt (discounted at 4.5%)	X	X	X	X		Included, not itemized	€6,672 per QALY (discounted at 3%)	111
Schouten 2010 [56], Men	CEA, single-payer system	lifetime, 3% ‡	2006	€22.19 per pt	€860 per pt (discounted at 4.5%)	X	X	X	X		Included, not itemized	€7,614 per QALY (discounted at 3%)	111
Gilmer 2007 [57], Commercial	CEA, payer	40 yrs, 3%	2003	$507 per pt per yr	Included, not itemized	X	X	X	X		$12,368 per pt over 40 yrs	$69,587 per QALY	104
Gilmer 2007 [57], Medicaid	CEA, payer	40 yrs, 3%	2003	$507 per pt per yr	Included, not itemized	X	X	X	X		$11,792 per pt over 40 yrs	$44,941 per QALY	104
Gilmer 2007	CEA,	40 yrs,	2003	$507 per pt	Included, not	X	X	X	X		$10,921 per	$24,584 per	104

Study	Type, perspective	Time, discount	Year	Intervention cost	Utilization cost					Other costs	Net cost	ICER	Ref
[57], County	payer	3%		per yr	itemized						pt over 40 yrs	QALY	
Gilmer 2007 [57], Uninsured	CEA, payer	40 yrs, 3%	2003	$507 per pt per yr	Included, not itemized	X	X	X	X		$8,991 per pt over 40 yrs	$10,141 per QALY	104
Kuo 2011 [58]	CEA, integrated health system and society	20 yrs, 3%	2010	Included, not itemized	Included, not itemized	X	X	X	X	Patient out-of-pocket costs, productivity	$4,909 per pt over 20 yrs (society)	$42,051 per QALY (society)	111
McRae 2008 [59]	CEA, health system	40 yrs, 5%	2005	+AU$196 per pt per yr	-AU$617 per pt	X	X	X	X		AU$2,919 per pt	AU$9,730 per QALE	109
Giorda 2013 [60]	CEA, single-payer system	50 yrs, 3%	2010	€871 per pt	Included, not itemized	X	(PC)	X	X		-€3,786 per pt	NR, intervention dominates	110
Huang 2007 [63]	CEA, society	lifetime, 3%	2004	$1,784 per pt per 3 yrs plus $378 per pt per yr for lifetime	Included, not itemized	X	X	X	X		$11,685 per pt over lifetime	$33,386 per QALY	115
Brownson 2009 [65]	CEA, health system	lifetime, 3%	2006	$15,031 per pt	-$3,385 per pt	X	X	X	X		$11,760 per pt	$39,563 per QALY	109
O'Reilly 2007 [66]	CEA, integrated health system	40 yrs, 3%	2004	C$664 per pt	Included, not itemized	X	X	X	X		C$644 per pt	C$5,992 per QALY	113
Gozzoli 2002 [68]	CEA, single-payer system	lifetime, 3%	1996	Included, not itemized	Included, not itemized	X	X	X	X		-CHF7,313 per pt	NR, intervention dominates	105
Brown 2012 [69]	CEA, society	20 yrs, 3%	2010	$1,176 per pt over 1.5 yrs plus $141 per pt per yr from 1.5 to 20 yrs	Included, not itemized	X	X	X	X	Travel, productivity	Included, not itemized	$33,319 per QALY	109

* Abbreviations:

Currencies: C$ = Canadian dollars, AU$ = Australian dollars, CHF = Swiss Francs

Units of Time: mo = month, yr = year

CEA = cost-effectiveness analyses and related designs

DM = diabetes mellitus

QALY = quality-adjusted life years

QALE = quality-adjusted life expectancy

Pt = patient

NR = not reported

n/a = not applicable

† (PC) Authors included this utilization costs as part of program costs

‡ Authors presented data for several discount rates; results for 3% reported for consistency with other studies. # = includes home care

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Table 4. Assessment of Bias in RCTs using Cochrane Collaboration Tool

Author and Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective reporting
Short Term						
Handley 2008	?	?	-	?	+	?
Wilson 2014	+	?	-	?	-	+
Sperl-Hillen 2010	?	?	-	?	-	+
Eccles 2007	+	?	-	-	-	+
Allen 2013	+	?	-	+	+	+
Katon 2012	?	?	-	+	+	+
Houweling 2009	-	?	-	+	+	+
Noel 2004	?	?	-	-	-	?
Intermediate Term						
Palmas 2010	?	?	-	+	-	+
Gordon 2014	+	?	-	-	+	+
Long Term						
Gillett 2010	?	?	-	?	+	?
Gillespie 2012	+	-	-	?	+	+
O'Reilly 2012	+	+	-	+	+	+
Gilmer 2012	?	?	-	?	+	+
Mason 2006	?	?	-	?	?	+
Dijkstra 2006	?	+	-	?	-	+
Slingerland 2013	?	+	-	-	+	+
Prezio 2014	+	?	-	?	+	?

Legend: +, present; - , absent, ?, uncertain if present or absent.

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Table 5. Assessment of Bias in Observational Studies Using the Newcastle-Ottawa Scale (NOS)

	Selection			Comparability			Outcome		
	1. Representativeness of exposed cohort	2. Selection of non-exposed cohort	3. Ascertainment of exposure	4. Demonstration that outcome of interest was not present at study start	1. Study control for most important confounder	2. Study controls for any additional factor	1. Assessment of outcome	2. Follow-up long enough to capture outcomes	3. Adequacy of follow-up cohorts
Short Term									
Kogut 2012	0	0	*	*	*	*	*	*	*
Sidorov 2002	0	0	*	*	0	0	*	*	0
Mousques 2010	*	*	*	*	*	*	*	*	*
Spence 2014	0	*	*	*	*	*	*	*	0
Nundy 2014	0	0	*	*	0	0	*	*	0
Gilmer 2005	*	0	*	*	*	*	*	*	0
Salzsieder 2011	0	0	*	*	0	0	*	*	0
Franklin 2013	*	0	*	*	0	0	*	*	0
Steuten 2007	*	0	*	*	0	0	*	*	*
Keers 2005	*	0	*	*	0	0	*	*	*
Haji 2013	*	*	*	*	*	*	*	*	*
Balamurugan 2006	*	*	*	*	*	*	*	*	0
Micklethwaite 2012	0	0	*	*	0	0	*	*	0
Garrett 2005	0	0	*	*	0	0	*	*	0
Snyder 2003	*	0	*	*	0	0	*	*	0
Intermediate Term									
Yu 2013	*	*	*	*	*	*	*	*	*
Beaulieu 2006	*	0	*	*	0	0	*	*	0
Long Term									
Schouten 2010	*	*	*	*	0	0	*	*	0
Gilmer 2007	*	0	*	*	0	0	*	*	0
Kuo 2011	0	*	*	*	*	*	*	*	0
McRae 2008	*	0	*	*	0	0	*	*	0
Giorda 2003	N/A								
Huang 2007	*	0	*	*	*	*	*	*	0

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Brownson 2009	*	0	*	*	0	0	*	*	0
O'Reilly 2007	*	0	*	*	0	0	*	*	0
Gozzoli 2002	N/A								
Brown 2012	*	0	*	*	0	0	*	*	0

Legend: *, criterion met; 0, criterion not met; N/A: Not applicable because cost analysis was based on data from multiple studies.

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Table 6. Funding Sources and MQCS Components

Author (Year)	Funding Source	MQCS Components Described in Article		
		Implementation	Adherence/Fidelity	Penetration/Reach
Handley 2008 [1]	Government, Non-profit	X		
Wilson 2014 [3]	Government	X	X	X
Sperl-Hillen 2010 [5]	Government	X		
Eccles 2007 [6]	Government	X	X	
Allen 2013 [8]	Government	X	X	X
Katon 2012 [10]	Government, Non-profit	X	X	X
Houweling 2009 [11]	Government, Non-profit			
Noel 2004 [12]	Government, Commercial	X	X	X
Kogut 2012 [13]	Commercial	X	X	X
Sidorov 2002 [14,15]	Not reported			
Mousques 2010 [16]	Not reported			
Spence 2014 [17]	Not reported	X		
Nundy 2014 [18]	Non-profit, Commercial	X		
Gilmer 2005 [19]	Non-profit		X	X
Salzsieder 2011 [20]	Government		X	
Franklin 2013 [21]	Government			X
Steuten 2007 [23,24]	Not reported	X	X	X
Keers 2005 [25]	Not reported	X		
Haji 2013 [26]	Government	X		X
Balamurugan 2006 [27]	Commercial		X	X
Micklethwaite 2012 [28]	Government, Non-profit	X	X	X
Garrett 2005 [29]	Commercial			X
Snyder 2003 [30]	Not reported	X	X	
Palmas 2010 [31]	Government			
Gordon 2014 [34]	Government	X		
Yu 2013 [37]	Non-profit	X		
Beaulieu 2006 [39]	Non-profit			
Gillett 2010 [40]	Government, Non-profit	X		X
Gillespie 2012 [42]	Government	X		
O'Reilly 2012 [45]	None	X		
Gilmer 2012 [47]	Government	X		
Mason 2006 [49]	Commercial	X		X
Dijkstra 2006 [51,52]	Government	X		
Slingerland 2013 [53]	Government	X	X	X
Prezio 2014 [54]	None	X		X
Schouten 2010 [56]	Government	X		X
Gilmer 2007, Uninsured [19,57]	Non-profit		X	X
Kuo 2011 [58]	Government			
McRae 2008 [59]	Government		X	

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Author (Year)	Funding Source	MQCS Components Described in Article		
		Implementation	Adherence/Fidelity	Penetration/Reach
Giorda 2013 [60]	Commercial	X		X
Huang 2007 [63]	Government	X		
Brownson 2009 [65]	Non-profit	X	X	X
O'Reilly 2007 [66]	Government	X	X	X
Gozzoli 2002 [68]	Not reported			
Brown 2012 [69]	Government, Non-profit		X	X

SUPPLEMENTARY DATA

Supplement 5. Results of Unadjusted Weighted Regression Analyses for Change in HbA1c in RCTs

Table. Randomized Controlled Trials of QI Interventions Designed to Improve Glycemic Control: Factors Predicting Change in Change in HbA1c, Weighted by Population Size in Intervention Group

Predictor	k	Change in HbA1c, Mean (95% CI)	p
Overall Change in HbA1c	19	-0.26% (-0.35%, -0.17%)	
Baseline HbA1c	19		**0.010**
7.5% (58 mmol/mol)		-0.22% (-0.29%,-0.14%)	
8.5% (69 mmol/mol)		-0.40% (-0.52%,-0.29%)	
Timing of Study	19		0.093
2004		-0.33% (-0.43%,-0.22%)	
2009		-0.22% (-0.31%,-0.12%)	
System-oriented Strategies	19		0.538
Mean No. of Strategies (1.63)		-0.26% (-0.34%,-0.18%)	
One More Strategy (2.63)		-0.28% (-0.38%,-0.18%)	
Disease Management	10	-0.33% (-0.46%,-0.19%)	0.241
No Disease Management	9	-0.22% (-0.32%,-0.12%)	
Team Changes	8	-0.31% (-0.46%,-0.16%)	0.414
No Team Changes	11	-0.24% (-0.34%,-0.14%)	
Electronic Registry	3	-0.29% (-0.49%,-0.08%)	0.793
No Electronic Registry	16	-0.26% (-0.35%,-0.16%)	
Facilitated Relay	7	-0.39% (-0.55%,-0.23%)	0.084
No Facilitated Relay	12	-0.22% (-0.31%,-0.13%)	
Standardizing Care	6	-0.20% (-0.31%,-0.10%)	0.113
No Standardizing Care	13	-0.34% (-0.46%,-0.22%)	
Provider-oriented Strategies	19		0.784
Mean No. of Strategies (1.11)		-0.26% (-0.34%,-0.18%)	
One More Strategy (2.11)		-0.25% (-0.37%,-0.13%)	
Audit and Feedback	7	-0.26% (-0.38%,-0.15%)	0.990

No Audit and Feedback	12	-0.26% (-0.38%,-0.14%)	
Provider Education	3	-0.24% (-0.39%,-0.10%)	0.784
No Provider Education	16	-0.27% (-0.37%,-0.17%)	
Provider Decision Support	4	-0.25% (-0.43%,-0.07%)	0.916
No Decision Support	15	-0.26% (-0.36%,-0.17%)	
Incentives for Providers	2	-0.21% (-0.48%,0.06%)	0.691
No Incentives	17	-0.27% (-0.35%,-0.18%)	
Patient-oriented Strategies	19		0.522
Mean No. of Strategies (0.29)		-0.26% (-0.34%,-0.18%)	
One More Strategy (1.29)		-0.29% (-0.40%,-0.17%)	
Tailoring Care for Group	7	-0.26% (-0.38%,-0.14%)	0.990
No Tailoring Care	12	-0.26% (-0.38%,-0.15%)	
Patient Education	14	-0.30% (-0.41%,-0.19%)	0.320
No Patient Education	5	-0.21% (-0.34%,-0.09%)	
Patient Self-Management	8	-0.23% (-0.38%,-0.08%)	0.656
No Self-Management	11	-0.27% (-0.37%,-0.17%)	
Patient Reminders	5	-0.30% (-0.46%,-0.13%)	0.656
No Patient Reminders	14	-0.25% (-0.35%,-0.15%)	

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Supplement 6. Information Used to Standardize Costs

We used information reported by study authors (in table above) to standardize costs for economic evaluations with short-term or long-term time horizons. Too few studies had intermediate time horizons and the intermediate time horizons were too variable to facilitate comparisons.

Short-term Studies

Conversion of costs to 2015 U.S. dollars per patient per year: We extracted information reported by authors, converted to U.S. dollars, inflated to August 2015,* and converted costs to an annual basis (e.g., for costs reported over 0.5 years, we multiplied by 2). When a category of costs was not reported, we used information from the other two categories to derive it (e.g., subtracting program costs from incremental net costs yields healthcare utilization and patient costs).

Author and Year	Currency	Year of Costs	Number of Years over Which Costs Are Reported	Program Cost	Healthcare Utilization and Patient Costs	Incremental Net Cost	Currency Conversion	Inflation Adjustment	Conversion to Annual Basis	Program Cost	Healthcare Utilization and Patient Costs	Incremental Net Cost
				Information Reported by Authors			**Conversion Factors ***			**Standardized Costs**		
Handley 2008 [1]	USD	2004	1.0	782	0	.	$1.00	1.43	1.00	$1,121	$0	$1,121
Wilson 2014 [3]	GBP	2010	1.5	60	53	113.16	$1.57	1.15	0.67	$72	$64	$136
Sperl-Hillen 2010 [5]	USD	2009	1.0	27	.	-71	$1.00	1.19	1.00	$32	-$116	-$84
Eccles 2007 [6]	GBP	2003	1.0	28	-12	.	$1.64	1.50	1.00	$68	-$30	$37
Allen 2013 [8]	USD	2010	1.0	-57	688	.	$1.00	1.15	1.00	-$66	$791	$725
Katon 2012 [10]	USD	2008	2.0	1224	.	-594	$1.00	1.23	0.50	$750	-$1,114	-$364
Houweling 2009 [11]	EUR	2003	1.0	-24	-274	.	$1.13	1.50	1.00	-$40	-$465	-$505
Noel 2004 [12]	USD	2002	0.5	1666	1459	3125	$1.00	1.55	2.00	$5,179	$4,535	$9,714
Kogut 2012 [13]	USD	2012	1.0	285	-1102	-817	$1.00	1.07	1.00	$305	-$1,180	-$875
Sidorov 2002 [14]	USD	2001	1.0	581	-1294	.	$1.00	1.63	1.00	$945	-$2,106	-$1,162
Mousques 2010 [16]	EUR	2005	1.0	60	-81	.	$1.25	1.38	1.00	$103	-$140	-$37
Spence 2014 [17]	USD	2010	1.0	14	-263	.	$1.00	1.15	1.00	$17	-$302	-$285
Nundy 2014 [18]	USD	2012	0.5	375	-812	-437	$1.00	1.07	2.00	$803	-$1,739	-$936
Gilmer 2005 [19]	USD	2002	1.0	507	839	1346	$1.00	1.55	1.00	$788	$1,304	$2,092
Salzsieder 2011 [20]	EUR	2009	1.0	2850	-3760	-910	$1.39	1.19	1.00	$4,713	-$6,218	-$1,505
Franklin 2013 [21]	USD	2011	1.0	528	-421	107	$1.00	1.11	1.00	$588	-$469	$119
Steuten 2007 [23]	EUR	2002	2.0	168	.	-16	$0.94	1.55	0.50	$123	-$135	-$12
Keers 2005 [25]	EUR	2003	1.0	1327	-919	.	$1.13	1.50	1.00	$2,252	-$1,560	$692
Haji 2013 [26]	AUD	2010	3.0	-1489	.	-826	$0.92	1.15	0.33	-$525	$234	-$291
Balamurugan 2006 [27]	USD	2003	3.0	335	-246	89	$1.00	1.50	0.33	$167	-$123	$44
Micklethwaite 2012 [28]	USD	2010	1.0	1732	-551	.	$1.00	1.15	1.00	$1,991	-$633	$1,357
Garrett 2005 [29]	USD	2003	1.0	351	-1269	-918	$1.00	1.50	1.00	$525	-$1,899	-$1,374
Snyder 2003 [30]	USD	2001	1.0	.	-2271	-1598	$1.00	1.63	1.00	$1,096	-$3,696	-$2,601

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Long-Term Studies

Conversion of costs to 2015 U.S. dollars per patient over study time horizon: We extracted information reported by authors, converted to U.S. dollars, and inflated to August 2015. These were the only changes applied to costs per QALY. To estimate the other cost components, we undertook additional steps.

1. As seen in Table 3 in the paper, several authors reported program costs on an annual basis. In this case, we discounted the recurring program costs over the long-term using a rate of 3%. For studies using a lifetime time horizon, we used 40 years.
2. If incremental net costs were not reported, we derived it by multiplying the cost per QALY by the number of QALYs per patient as listed in Table 2.
3. To derive healthcare utilization and patient costs for all but one study, we subtracted program costs from incremental net costs.
4.

Author and Year	Information Reported by Authors						Conversion Factors *		Standardized Estimates			
	Currency	Year of Costs	Time Horizon	Program Cost	Incremental Net Cost	Cost per QALY	Currency Conversion	Inflation Adjustment	Program Cost	Healthcare Utilization and Patient Costs	Incremental Net Cost	Cost per QALY
Gillett 2010 [40]	GBP	2008	lifetime	219	209	5387	$1.86	1.23	$498	-$23	$475	$12,246
Gillespie 2012 [42]	EUR	2008	40	246	-623	.	$1.47	1.23	$443	-$1,567	-$1,124	.
O'Reilly 2012 [45]	CAD	2010	40	1912	2,048	102,053	$0.97	1.15	$2,133	$152	$2,285	$113,871
Gilmer 2012 [47]	USD	2009	40	annual	803	21,690	$1.00	1.19	$3,862	-$2,910	$952	$25,722
Mason 2006 [49]	GBP	2003	1.0	1088	.	43,500	$1.64	1.50	$2,663	.	.	$106,463
Dijkstra 2006, Provider [51]	EUR	2001	lifetime	annual	9,398	70,630	$0.90	1.63	$67	$13,622	$13,689	$102,980
Dijkstra 2006, Provider and patient [51]	EUR	2001	lifetime	annual	9,620	34,808	$0.90	1.63	$118	$13,908	$14,026	$50,751
Slingerland 2013 [53]	USD	2000	lifetime	annual	3,482	6,443	$1.00	1.70	$145	$5,776	$5,921	$10,956
Slingerland 2013 [53]	USD	2000	lifetime	86	4,731	20,086	$1.00	1.70	$145	$7,899	$8,045	$34,155
Prezio 2014 [54]	USD	2012	20	4958	.	355	$1.00	1.07	$5,308	-$5,286	$21	$380
Schouten 2010 [56]	EUR	2006	40	22	.	7,614	$1.26	1.32	$37	$2,845	$2,882	$11,084
Schouten 2010 [56]	EUR	2006	40	22	.	6,672	$1.26	1.32	$37	$4,137	$4,174	$12,648
Gilmer 2007, Commercial [57]	USD	2003	40	annual	12,368	69,587	$1.00	1.50	$17,537	$971	$18,508	$104,132
Gilmer 2007, Medicaid [57]	USD	2003	40	annual	11,792	44,941	$1.00	1.50	$17,537	$109	$17,646	$67,251
Gilmer 2007, County [57]	USD	200	40	annual	10,921	24,584	$1.00	1.50	$17,537	-$1,194	$16,343	$36,788

		3											
Gilmer 2007, Uninsured [57]	USD	2003	40	annual	8,991	10,141		$1.00	1.50	$17,537	-$4,083	$13,454	$15,175
Kuo 2011 [58]	USD	2010	20	.	4,909	42,051		$1.00	1.15	.	.	$5,643	$48,337
McRae 2008 [59]	AUD	2005	40	annual	3,745	9,730		$0.76	1.38	$4,762	-$826	$3,936	$10,228
Giorda 2013 [60]	EUR	2010	50	871	-3,786	.		$1.33	1.15	$1,329	-$7,106	-$5,777	.
Huang 2007 [63]	USD	2004	lifetime	annual	11,685	33,386		$1.00	1.43	$6,316	$10,429	$16,745	$47,844
Brownson 2009 [65]	USD	2006	lifetime	15,031	11,760	39,563		$1.00	1.32	$19,875	-$4,325	$15,550	$52,314
O'Reilly 2007 [66]	CAD	2004	40	664	644	5,992		$0.77	1.43	$733	-$22	$711	$6,614
Gozzoli 2002 [68]	CHF	1996	lifetime	.	-7,313	.		$0.81	1.95	.	.	-$11,539	.
Brown 2012 [69]	USD	2010	20	annual	.	33,319		$1.00	1.15	$3,519	-$1,210	$2,309	$38,300

*Currency conversion: USForex Foreign Exchange Services, Historical Exchange Rates, available at: http://www.usforex.com/forex-tools/historical-rate-tools/historical-exchange-rates, last accessed August 31, 2016.

 Inflation: Bureau of Labor Statistics, Consumer Price Index, Medical Care, available at: http://www.bls.gov/cpi/home.htm#data, last accessed July 24, 2016.

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