Population Health Screenings for the Prevention of Chronic Disease Progression

Maren S. Fragala, PhD; Dov Shiffman, PhD; and Charles E. Birse, PhD

The majority of employees in the United States have laboratory evidence of chronic disease, and 1 in 3 is likely to have unidentified disease.[1] Chronic diseases, including cardiovascular disease (CVD), diabetes, cancer, and chronic kidney disease (CKD), present a substantial and growing economic burden to large employers in that annual per capita expenditures for persons with chronic disease are 2.3-fold higher (for diabetes)[2] to 10-fold higher (for advanced CKD)[3] than for those without chronic disease. Early detection of and care for chronic diseases enabled by health screening can reduce morbidity and mortality[4,5] and avoid the higher costs of advanced disease.[3] For example, all-cause costs of a person with CKD increase dramatically as the disease advances in stage, from $26,843 per year for stage 3 to $76,969 per year for stages 4 and 5 and $121,948 per year for end-stage renal disease (ESRD),[3] with $88,000 per year for hemodialysis.[6]

In addition to incurring healthcare costs, employees experiencing poor health may experience absence, short-term disability, and lower productivity.[7] Without intervention, the chronic disease burden in the US workforce is expected to rise. Fortunately, chronic diseases can be prevented, delayed, or alleviated. The CDC estimates that as much as 80% of heart disease, stroke, and type 2 diabetes cases and 40% of cancer cases could be prevented through modification of lifestyle behaviors. Moreover, most employers (>90%) believe that their healthcare costs could be reduced by improvements in healthy behaviors.[8] Although most large employers (70%-85%) offer basic health screenings, less than 25% provide a comprehensive worksite population health program that includes comprehensive health screening, access to related health improvement programs, and an environment that supports health.[9]

Employer-sponsored annual health screenings offer an opportunity to facilitate the delivery of population health; the identification of health risk factors offers early opportunities for intervention and connection to care. However, general wellness programs have generated mixed evidence,[10,11] given the broad variation in program designs, organizational settings, and diverse populations in which they are implemented. Evidence-informed programs based on the identification of prediabetes, diabetes, CKD, or colorectal cancer

ABSTRACT

OBJECTIVES: Early detection of disease enables prompt treatment that can prevent disease progression and costly health outcomes. We report incidence of previously unrecognized disease and investigate the expected effect of early detection and care on health outcomes.

STUDY DESIGN: Population health study based on laboratory evidence.

METHODS: Laboratory evidence of prediabetes, diabetes, chronic kidney disease, and colorectal cancer was evaluated in an employee and spouse population (65% women; mean [SD] age = 46 [12] years). Expected disease progression was assessed.

RESULTS: Annual screening found laboratory evidence for 1185 previously unrecognized cases of prediabetes, 287 cases of diabetes, 73 cases of chronic kidney disease, and 669 positive colorectal screens per 10,000 people.

CONCLUSIONS: Early identification and appropriate medical care may delay 34 cases of end-stage kidney disease and prevent diabetes-related complications, 210 cases of diabetes, and 3 cases of late-stage colorectal cancer over 5 years per 1000 cases identified.

Am J Manag Care. **2019;25(11):548-553**

in their early stages may enable more targeted and successful programs that offer early treatment and care that can slow or prevent disease development and debilitating and costly health outcomes. Of all participants in a population health screening with evidence of diabetes, 28% were previously unrecognized, and of all participants with laboratory evidence of CKD, 89% were previously unrecognized.[1] In addition, colorectal cancer screening via stool testing for hemoglobin may increase detection of lesions due to higher acceptance of the test method[12] and a participation rate 40% higher than that of colonoscopy.[13] However, the longitudinal impact of annual health screenings on disease progression and health outcomes is largely unknown. Thus, the purpose of this analysis was to evaluate the projected value of annual health screenings in 35,258 employees and spouses who participated in annual health screenings in 2017 for early detection of prediabetes, diabetes, evidence of CKD, and hemoglobin in stool on disease outcomes and progression.

METHODS

Laboratory evidence of prediabetes incidence and diabetes incidence was assessed in 35,254 employees and spouses of a single employer who participated in annual health screenings in 2017. Prediabetes was defined as having a glycated hemoglobin (A1C) measurement between 5.7% and 6.4% or a fasting glucose (FG) measurement between 100 mg/dL and 125 mg/dL. Diabetes was defined having an A1C higher than 6.4% or FG higher than 125 mg/dL. Newly identified prediabetes was defined as prediabetes in 2017 without evidence of diabetes or prediabetes in the prior year. Newly identified diabetes was defined as diabetes in 2017 without evidence of diabetes in the prior year. Cases of diabetes prevented by intervention and care were projected based on results of the Diabetes Prevention Program.[14] Expected incidence of CVD and microvascular complications (retinopathy, neuropathy, and nephropathy) were projected based on previous reports.[15,16]

Laboratory evidence of new-onset CKD incidence was assessed in employees and spouses who participated in annual health screenings in 2017 (35,258 participants). Evidence of CKD was defined as a single estimated glomerular filtration rate (eGFR) measurement of less than 60 mL/min/1.73 m² without CKD in the prior year. Confirmed evidence of CKD and progression rate to stages 4 and 5 disease and ESRD were projected based on previous research.[17-20]

Colorectal cancer screening was offered to eligible employees and spouses aged 50 to 75 years who participated in annual health screenings between 2013 and 2017 (18,976 tests). A positive screening test was determined by the evidence of hemoglobin in the stool from a fecal immunological test (FIT), InSure FIT (Clinical Genomics; Bridgewater, New Jersey). Follow-up colonoscopy results[21] and stage distribution[22] were based on prior research.

TAKEAWAY POINTS

▸ Early identification and appropriate medical care may delay 34 cases of end-stage kidney disease and prevent diabetes-related complications, 210 cases of diabetes, and 3 cases of late-stage colorectal cancer over 5 years per 1000 cases identified.

▸ Avenues to detect previously unrecognized and early-stage disease may positively affect the health trajectories of many individuals within 1 to 5 years.

▸ Employers may serve as a conduit to health screening to benefit the health outcomes of employees and manage healthcare costs.

TABLE 1. Previously Unrecognized Cases of Prediabetes Identified by Annual Population Health Screening[2,14,23,24]

Prediabetes	Value
Definition	A1C of 5.7%-6.4% or FG of 100-125 mg/dL
Number (%) per 10,000 screened	1185 (11.9)
Number of expected diabetes events[14,23] per 1000 with confirmed prediabetes, untreated vs intensive lifestyle modification	
Within 1 year	104 vs 47
Within 5 years	423 vs 213
Average annual cost of diabetes[2,24]	~$10,000

A1C indicates glycated hemoglobin; FG, fasting glucose.

RESULTS

Screening for prediabetes (A1C of 5.7%-6.4% or FG of 100-125 mg/dL) identified 1185 (11.9%) cases not recognized in the previous year (previously unrecognized) per 10,000 individuals screened. Based on the Diabetes Prevention Program[14] results, we estimate that for every 1000 confirmed prediabetes cases, 210 diabetes cases can be prevented over 5 years (**Table 1**[2,14,23,24]).

Annual screening of employees and spouses found that for every 10,000 participants, 287 (2.9%) had previously unrecognized hyperglycemia (laboratory evidence of diabetes; A1C >6.4% or FG >125 mg/dL). Using previous reports of CVD incidence[16] and microvascular complications (retinopathy, neuropathy, and nephropathy),[15] we estimated that within 1 year, for every 1000 patients with confirmed diabetes, about 105 would experience complications (**Table 2**[15,16,25]): 10 patients would have CVD, 14 patients would have retinopathy, 36 patients would have neuropathy, and 45 patients would have nephropathy. Within 5 years, about 489 would experience complications, including 50 patients with CVD, 68 patients with retinopathy, 168 patients with neuropathy, and 203 patients with nephropathy.

Annual screening for laboratory evidence of CKD found that for every 10,000 participants, 146 (1.46%) had previously unrecognized

TABLE 2. Previously Unrecognized Diabetes Cases Identified by Annual Population Health Screening[15,16,25]

Diabetes	Value
Definition	A1C >6.4% or FG >125 mg/dL
Number (%) per 10,000 screened	287 (2.9)
Number of expected complications[a] per 1000 with confirmed diabetes	
Within 1 year	105
Within 5 years	489
Average annual cost of diabetes with complications[25]	~$30,000

A1C indicates glycated hemoglobin; FG, fasting glucose.

[a]Expected cardiovascular disease was assessed from estimated 10-year risk[16]; expected retinopathy, neuropathy, and nephropathy were estimated from published transition probabilities.[15]

TABLE 3. Previously Unrecognized CKD Cases Identified by Annual Population Health Screening[3,6,17,20]

CKD	Value
Definition	eGFR <60 mL/min/1.73 m²
Number (%) per 10,000 screened	146 (1.5)
Number (%) with confirmed low eGFR[17]	73 (0.75)
Number of expected ESRD cases[a] per 1000 with confirmed CKD	
Within 1 year	7
Within 5 years	34
Average annual cost of hemodialysis for ESRD[b]	~$88,000
Average annual all-cause cost for ESRD[3]	$121,948

CKD indicates chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease.

[a]Based on annual transition probabilities for those with and without diabetes, with or without proteinuria, in the Alberta Kidney Disease Network.[20]

[b]Cost of hemodialysis based on 2016 US Renal Data System annual data report.[6]

TABLE 4. Previously Unrecognized Colorectal Cancer Cases Identified by Annual Population Health Screening[21,22]

Colorectal Cancer	Value
Definition	InSure FIT positive
Number (%) per 10,000 screened	669 (6.7)
Number of expected outcomes[21]	
Colonoscopy	525
Adenoma	263
Colorectal cancer	14
Number of cases by stage distribution,[22] with screening vs without screening	
I	6 vs 3
II	4 vs 5
III	4 vs 4
IV	0 vs 2

FIT indicates fecal immunochemical test.

low eGFR (<60 mL/min/1.73 m²) (**Table 3**[3,6,17,20]). Similar rates have been observed in patients screened in primary care settings.[26] Prior research[17] suggests that approximately 50% of initial low eGFR findings are confirmed as CKD upon follow-up. Considering the progression rate from CKD to ESRD observed in the Alberta Kidney Disease Network,[20] we predicted that for every 1000 cases of confirmed CKD, about 7 patients would progress to ESRD within a year and about 34 within 5 years (Table 3[3,6,17,20]). In addition, based on previous research,[18,19] 136 would be expected to progress to stage 4 or stage 5 (of 5 stages) over 5 years.

Annual screening for colorectal cancer resulted in a positive screening test rate of 6.7% (**Table 4**[21,22]). For every 10,000 FIT tests evaluated, 669 had a positive result. Assuming that 78% of those with a positive test have a follow-up colonoscopy[21] (n = 525), we estimate subsequent diagnosis of 263 adenomas (some considered precancerous) and 14 colorectal cancers. Assuming a similar stage distribution to profiles observed in other FIT-based screening studies,[22] we estimate that the 14 colorectal cancers detected would be made up of 6 stage I , 4 stage II, and 4 stage III cases (of 4 stages). We also assume that the screen-dependent shift toward earlier-stage detection would result in 3 more stage I cancers and 1 fewer stage II cancer and 2 fewer stage IV cancers being diagnosed than would have been the case without screening.

DISCUSSION

Prediabetes

Early detection of prediabetes is important because type 2 diabetes can be present for 9 to 12 years before being diagnosed and, as a result, complications are often present at the time of diagnosis.[27] Without detection and early intervention, 4% to 19% of those with prediabetes develop diabetes each year, depending on the population and criteria.[28,29] A1C and FG are accepted methods for prediabetes screening and diagnosis of diabetes. We recently reported that elevated A1C in working-age individuals with normal FG in an employee wellness program was associated with 2- to 8-fold greater odds of incident diabetes within 4 years.[30]

Fortunately, lifestyle interventions are effective in reducing incidence of diabetes.[14,29] Lifestyle interventions may reduce incidence of diabetes by up to 58% over 3 years.[14,29] Prior research has similarly shown the effectiveness of employer-based health screening for diabetes and prediabetes,[31] but benefits depend on many factors. Benefits of diabetes prevention are greater when diabetes risk is detected early.[32] Thus, in addition to disease prevention, prompt screening and intervention is associated with reduced absolute and relative risk and all-cause mortality at 5 years compared with a 3-year delay in diagnosis.[32]

Medical costs of prediabetes and undiagnosed diabetes are approximately $510 and $4030 per year per person, respectively.[2] When prediabetes progresses to diabetes, people with diagnosed diabetes, on average, have medical expenditures approximately 2.3 times higher than they would be in the absence of diabetes.[24] In addition, indirect costs associated with absence, productivity, and disability further exacerbate the costs of chronic health conditions.[7,24] The American Diabetes Association quantified the estimated cost of diagnosed diabetes in the United States in 2017 as $327 billion, including $237 billion (72%) in direct medical costs and $90 billion (28%) in reduced productivity.[24]

Diabetes

Poor management of diabetes can be associated with disease-related complications such as CVD, nephropathy, retinopathy, and neuropathy, which can lead to chronic morbidities and mortality.[33,34] More than 20% of diabetes in the United States is undiagnosed,[35] and risk of complications is associated with diabetes duration.[36] Detection and treatment that is delayed by 3 years has been shown to translate into 40% higher 5-year CVD risk (11.2% vs 7.9%) and 20% higher incidence of all-cause mortality (7.2% vs 6.0%).[32] In addition, risk for cardiovascular events or vascular events is 11% to 16% higher with every 1% increase in A1C[37,38] or 18 mg/dL (1 mmol/L) increase in FG greater than 100 mg/dL.[39,40] Thus, detection and care may reduce CVD and microvascular complications, including retinopathy, neuropathy, and nephropathy. Average lifetime medical costs for an individual with diabetes have been estimated at $85,200, of which 53% is due to treating diabetic complications.[41] Per-year medical costs for a person with diabetes are approximately $16,750, and about $9600 to $10,970 of these costs are attributed to diabetes.[2,24]

CKD

Progression of CKD can be slowed when it is detected in the early stages.[42-44] Early identification, intervention, and referral to a nephrologist are essential to slow progression of CKD and avoid complications of ESRD.[5,42] Typically, a multifactorial treatment approach is advocated to treat the causes and consequences of CKD, slow CKD progression, and avoid ESRD.[43] As hypertension and type 2 diabetes are the major causes of CKD and are important treatment targets, it is possible to attenuate disease progression and slow reductions in eGFR with proactive treatment.[44] Progression rates of CKD vary with annual reductions in kidney function ranging from 2 mL/

min/1.73 m^2 to 12 mL/min/1.73 m^2 per year depending on the stage of CKD and comorbidities, such as diabetes.[44,45] Rates of decline may be as high as 10 mL/min/1.73 m^2 to 14 mL/min/1.73 m^2 in individuals with diabetes who are not receiving early antihypertensive treatment.[46] Although individuals in stage 3 typically do not have symptoms,[44] progression to stages 4 and 5 is associated with such complications as hypertension, anemia, bone disease, metabolic acidosis, and increased risk of CVD.[47] Prior research[44,48] has supported the value of screening for and initiating intervention at stage 3a with eGFR less than 60 mL/min/1.73 m^2 to generate the most quality-adjusted life-years.[48] The decline in renal function may be slowed from an annual eGFR decline of 12.0 mL/min/1.73 m^2 to a decline of 3.4 mL/min/1.73 m^2 with early detection and care.[48] With a baseline screening eGFR value of 58 mL/min/1.73 m^2, this may represent a difference of 9 years (12.6 years vs 3.6 years) until eGFR declines to less than 15 mL/min/1.73 m^2 (ESRD) with screening and nephrology care.

CKD is an increasingly prevalent healthcare burden, affecting approximately 13% of the US population.[49] From an economic perspective, costs attributable to the disease increase by $9200 per person per year from stage 3 ($3500) to stage 4 ($12,700).[50] Individuals with CKD incur medical costs due to comorbidities that are substantially greater in advanced stages of CKD (stages 4 and 5).[3] Considering all-cause costs, progression between stage 3a ($27,000/year) and stages 4 and 5 ($77,000/year) equates to a roughly $50,000 difference (vs $122,000 for ESRD without dialysis) in commercial health plans, mostly due to inpatient costs.[3] The estimated costs of hemodialysis (direct cost of treating CKD) for those who progress to ESRD among patients with newly identified CKD are expected to be greater than $300,000 in the first year and balloon to more than $7 million over 5 years based on the cost of hemodialysis treatment.[6]

Colorectal Cancer

Screening for colorectal cancer has been shown to reduce both incidence and mortality.[4,51,52] Earlier-stage detection of colorectal cancer toward localized disease, more commonly treated with surgery, results in substantial cost savings spanning the continuum of cancer care, from the year of diagnosis (stage I, $30,000; stage IV, $67,000) through continuing years (stage I, $2500; stage IV, $11,000) to the last year of life (stage I, $54,000; stage IV, $76,000).[53] Generally, adherence to colorectal cancer screening is more important than which strategy is used, with higher rates of screening being associated with a 25.5% reduction in annual colorectal cancer incidence.[54] Despite these findings, more than one-third of eligible adults remain nonadherent to current colorectal cancer screening recommendations.[55] Noninvasive stool testing improves compliance, with adherence nearly double that for colonoscopy.[56] In addition, 97% of patients refusing colonoscopy accept a noninvasive screening test.[12] Accordingly, the US Preventive Services Task Force recommends annual screening with a sensitive noninvasive stool test as part of a screening strategy for colorectal cancer.[57] Although other screening modalities are considered effective,[58] annual FIT screening for colorectal cancer is deemed more effective and

less costly compared with other options.[52] Moreover, newer FIT tests offer greater simplicity and sensitivity relative to historical fecal occult guaiac-based blood tests while remaining relatively inexpensive compared with other diagnostic screening modalities at $20 to $50 per kit.[59]

Limitations

A few limitations to the study should be considered when interpreting the study findings. First, although the study reflects data from a large workforce, the study population may not necessarily represent the demographics of all employers. Second, because participation in the annual health screening program was voluntary, participation reflected about 65% of the entire pool of employees and spouses eligible to participate and might include those more likely to be engaged in their healthcare; however, this population is likely to reflect other employee wellness program populations. Third, the study is based on laboratory evidence of chronic disease and self-reported physician diagnosis, but physician diagnoses from health records were not available for study; thus, definite diagnoses cannot be made. However, those identified based on laboratory evidence and self-reported diagnoses should provide a good indication of the fraction of participants who would benefit from additional follow-up. Despite these limitations, knowledge of previously unrecognized disease may enable health engagement and more positive health outcomes for individuals in a large population.

CONCLUSIONS

Population health screening identifies early evidence of unrecognized prediabetes, diabetes, CKD, and colorectal cancer in large populations to improve health trajectories. Early identification enables prompt treatment that can prevent disease progression and yield positive value on investment. This study provides quantification of unknown health risk for conditions that are not always screened for in employee populations[9] and extrapolates the health impact and opportunity for an employee population. Provided data and insights may facilitate the delivery of population health programs to targeted employee segments—a strategy required to drive results.[10] Driven by data, care pathways may narrow gaps in care and improve patient understanding, clinical outcomes, quality of life, and productivity, which may further benefit population health. As chronic diseases present a substantial and growing economic burden to large employers in regard to both healthcare costs and productivity, employer-sponsored annual health screenings may facilitate the delivery of population health. ∎

Address Correspondence to: Maren S. Fragala, PhD, Quest Diagnostics, 500 Plaza Dr, Secaucus, NJ 07094. Email: maren.s.fragala@questdiagnostics.com.

REFERENCES

1. Kaufman HW, Williams FR, Odeh MA. Value of laboratory tests in employer-sponsored health risk assessments for newly identifying health conditions: analysis of 52,270 participants. *PLoS One*. 2011;6(12):e28201. doi: 10.1371/journal.pone.0028201.
2. Dall TM, Yang W, Halder P, et al. The economic burden of elevated blood glucose levels in 2012: diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes Care*. 2014;37(12):3172-3179. doi: 10.2337/dc14-1036.
3. Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. *Am J Manag Care*. 2017;23(suppl 10):S163-S172.
4. Mandel JS, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. *J Natl Cancer Inst*. 1999;91(5):434-437. doi: 10.1093/jnci/91.5.434.
5. Chen SC, Hwang SJ, Tsai JC, et al. Early nephrology referral is associated with prolonged survival in hemodialysis patients even after exclusion of lead-time bias. *Am J Med Sci*. 2010;339(2):123-126. doi: 10.1097/MAJ.0b013e3181c0678a.
6. US Bureau of Labor Statistics. Consumer Price Index: medical care in U.S. city average, all urban consumers [CPIMEDSL]. Federal Reserve Bank of St. Louis website. fred.stlouisfed.org/series/CPIMEDSL. Accessed December 12, 2018.
7. Goetzel RZ, Long SR, Ozminkowski RJ, Hawkins K, Wang S, Lynch W. Health, absence, disability, and presenteeism cost estimates of certain physical and mental health conditions affecting U.S. employers. *J Occup Environ Med*. 2004;46(4):398-412. doi: 10.1097/01.jom.0000121151.40413.bd.
8. Mello MM, Rosenthal MB. Wellness programs and lifestyle discrimination—the legal limits. *N Engl J Med*. 2008;359(2):192-199. doi: 10.1056/NEJMhle0801929.
9. Linnan L, Bowling M, Childress J, et al. Results of the 2004 National Worksite Health Promotion Survey. *Am J Public Health*. 2008;98(8):1503-1509. doi: 10.2105/AJPH.2006.100313.
10. Abraham JM. Employer wellness programs—a work in progress. *JAMA*. 2019;321(15):1462-1463. doi: 10.1001/jama.2019.3376.
11. Song Z, Baicker K. Effect of a workplace wellness program on employee health and economic outcomes: a randomized clinical trial [erratum in *JAMA*. 2019;321(18):1830. doi: 10.1001/jama.2019.5197]. *JAMA*. 2019;321(15):1491-1501. doi: 10.1001/jama.2019.3307.
12. Adler A, Geiger S, Keil A, et al. Improving compliance to colorectal cancer screening using blood and stool based tests in patients refusing screening colonoscopy in Germany. *BMC Gastroenterol*. 2014;14:183. doi: 10.1186/1471-230X-14-183.
13. Quintero E, Castells A, Bujanda L, et al; COLONPREV Study Investigators. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. *N Engl J Med*. 2012;366(8):697-706. doi: 10.1056/NEJMoa1108895.
14. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403. doi: 10.1056/NEJMoa012512.
15. Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. *Ann Intern Med*. 2004;140(9):689-699. doi: 10.7326/0003-4819-140-9-200405040-00008.
16. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [erratum in *J Am Coll Cardiol*. 2014;63(25, pt B):3026. doi: 10.1016/j.jacc.2014.03.006]. *J Am Coll Cardiol*. 2014;63(25, pt B):2935-2959. doi: 10.1016/j.jacc.2013.11.005.
17. Sim JJ, Rutkowski MP, Selevan DC, et al. Kaiser Permanente creatinine safety program: a mechanism to ensure widespread detection and care for chronic kidney disease. *Am J Med*. 2015;128(11):1204-1211.e1. doi: 10.1016/j.amjmed.2015.05.037.
18. Khatami Z, Handley G, Narayanan K, Weaver JU. Applicability of estimated glomerular filtration rate in stratifying chronic kidney disease. *Scand J Clin Lab Invest*. 2007;67(3):297-305. doi: 10.1080/00365510601045070.
19. Orlando LA, Owen WF, Matchar DB. Relationship between nephrologist care and progression of chronic kidney disease. *N C Med J*. 2007;68(1):9-16.
20. Manns B, Hemmelgarn B, Tonelli M, et al; Alberta Kidney Disease Network. Population based screening for chronic kidney disease: cost effectiveness study. *BMJ*. 2010;341:c5869. doi: 10.1136/bmj.c5869.
21. Jensen CD, Corley DA, Quinn VP, et al. Fecal immunochemical test program performance over 4 rounds of annual screening: a retrospective cohort study. *Ann Intern Med*. 2016;164(7):456-463. doi: 10.7326/M15-0983.
22. Cole SR, Tucker GR, Osborne JM, et al. Shift to earlier stage at diagnosis as a consequence of the National Bowel Cancer Screening Program. *Med J Aust*. 2013;198(6):327-330. doi: 10.5694/mja12.11357.
23. Knowler WC, Fowler SE, Hamman RF, et al; Diabetes Prevention Program Research Group. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study [erratum in *Lancet*. 2009;374(9707):2054. doi: 10.1016/S0140-6736(09)62154-1]. *Lancet*. 2009;374(9702):1677-1686. doi: 10.1016/S0140-6736(09)61457-4.
24. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care*. 2018;41(5):917-928. doi: 10.2337/dci18-0007.
25. Li R, Bilik D, Brown MB, et al. Medical costs associated with type 2 diabetes complications and comorbidities. *Am J Manag Care*. 2013;19(5):421-430.
26. Sharma P, McCullough K, Scotland G, et al. Does stage-3 chronic kidney disease matter?: a systematic literature review. *Br J Gen Pract*. 2010;60(575):e266-e276. doi: 10.3399/bjgp10X502173.
27. Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. *Diabetes Care*. 1992;15(7):815-819. doi: 10.2337/diacare.15.7.815.
28. Gerstein HC, Santaguida P, Raina P, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. *Diabetes Res Clin Pract*. 2007;78(3):305-312. doi: 10.1016/j.diabres.2007.05.004.

29. Tuomilehto J, Lindström J, Eriksson JG, et al; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18):1343-1350. doi: 10.1056/NEJM200105033441801.

30. Shiffman D, Tong CH, Rowland CM, Devlin JJ, Meigs JB, McPhaul MJ. Elevated hemoglobin A1c is associated with incident diabetes within 4 years among normoglycemic, working-age individuals in an employee wellness program. *Diabetes Care*. 2018;41(6):e99-e100. doi: 10.2337/dc17-2500.

31. Adams SR, Wiley DM, Fargeix A, George V, Neugebauer RS, Schmittdiel JA. Employer-based screening for diabetes and prediabetes in an integrated health care delivery system: a Natural Experiment for Translation in Diabetes (NEXT-D) Study. *J Occup Environ Med*. 2015;57(11):1147-1153. doi: 10.1097/JOM.0000000000000548.

32. Herman WH, Ye W, Griffin SJ, et al. Early detection and treatment of type 2 diabetes reduce cardiovascular morbidity and mortality: a simulation of the results of the Anglo-Danish-Dutch study of intensive treatment in people with screen-detected diabetes in primary care (ADDITION-Europe). *Diabetes Care*. 2015;38(8):1449-1455. doi: 10.2337/dc14-2459.

33. Teliti M, Cogni G, Sacchi L, et al. Risk factors for the development of micro-vascular complications of type 2 diabetes in a single-centre cohort of patients. *Diab Vasc Dis Res*. 2018;15(5):424-432. doi: 10.1177/1479164118780808.

34. Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus: atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus—mechanisms, management, and clinical considerations. *Circulation*. 2016;133(24):2459-2502. doi: 10.1161/CIRCULATIONAHA.116.022194.

35. Prevalence of both diagnosed and undiagnosed diabetes. CDC website. cdc.gov/diabetes/data/statistics-report/diagnosed-undiagnosed.html. Updated February 2, 2018. Accessed December 7, 2018.

36. Maghbooli Z, Pasalar P, Keshtkar A, Farzadfar F, Larijani B. Predictive factors of diabetic complications: a possible link between family history of diabetes and diabetic retinopathy. *J Diabetes Metab Disord*. 2014;13:55. doi: 10.1186/2251-6581-13-55.

37. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med*. 2008;359(15):1577-1589. doi: 10.1056/NEJMoa0806470.

38. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405-412. doi: 10.1136/bmj.321.7258.405.

39. Sarwar N, Gao P, Seshasai SR, et al; Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies [erratum in *Lancet*. 2010;376(9745):958. doi: 10.1016/S0140-6736(10)61452-3]. *Lancet*. 2010;375(9733):2215-2222. doi: 10.1016/S0140-6736(10)60484-9.

40. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, et al; Emerging Risk Factors Collaboration. Diabetes mellitus, fasting glucose, and risk of cause-specific death [erratum in *N Engl J Med*. 2011;364(9):829-841. doi: 10.1056/NEJMx110023]. *N Engl J Med*. 2011;364(9):829-841. doi: 10.1056/NEJMoa1008862.

41. Zhuo X, Zhang P, Hoerger TJ. Lifetime direct medical costs of treating type 2 diabetes and diabetic complications. *Am J Prev Med*. 2013;45(3):253-261. doi: 10.1016/j.amepre.2013.04.017.

42. Menzin J, Lines LM, Weiner DE, et al. A review of the costs and cost effectiveness of interventions in chronic kidney disease: implications for policy. *Pharmacoeconomics*. 2011;29(10):839-861. doi: 10.2165/11588390-000000000-00000.

43. Turner JM, Bauer C, Abramowitz MK, Melamed ML, Hostetter TH. Treatment of chronic kidney disease. *Kidney Int*. 2012;81(4):351-362. doi: 10.1038/ki.2011.380.

44. Thomsen S. Delayed progression to dialysis with early and intensive management of predialysis chronic kidney disease: a case-based approach. *Case Rep Nephrol Urol*. 2013;3(1):74-86. doi: 10.1159/000353265.

45. Mitch WE, Walser M, Buffington GA, Lemann J Jr. A simple method of estimating progression of chronic renal failure. *Lancet*. 1976;2(7999):1326-1328. doi: 10.1016/s0140-6736(76)91974-7.

46. Murussi M, Gross JL, Silveiro SP. Glomerular filtration rate changes in normoalbuminuric and micro-albuminuric type 2 diabetic patients and normal individuals: a 10-year follow-up. *J Diabetes Complications*. 2006;20(4):210-215. doi: 10.1016/j.jdiacomp.2005.07.002

47. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. *Prim Care*. 2008;35(2):329-344. doi: 10.1016/j.pop.2008.01.008.

48. Black C, Sharma P, Scotland G, et al. Early referral strategies for management of people with markers of renal disease: a systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis. *Health Technol Assess*. 2010;14(21):1-184. doi: 10.3310/hta14210.

49. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298(17):2038-2047. doi: 10.1001/jama.298.17.2038.

50. Honeycutt AA, Segel JE, Zhuo X, Hoerger TJ, Imai K, Williams D. Medical costs of CKD in the Medicare population. *J Am Soc Nephrol*. 2013;24(9):1478-1483. doi: 10.1681/ASN.2012040392.

51. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. *N Engl J Med*. 2000;343(22):1603-1607. doi: 10.1056/NEJM200011303432203.

52. Heitman SJ, Hilsden RJ, Au F, Dowden S, Manns BJ. Colorectal cancer screening for average-risk North Americans: an economic evaluation [erratum in *PLoS Med*. 2012;9(11). doi: 10.1371/annotation/0fd49c83-2c6d-42b5-a8c1-45a0aaedaa77]. *PLoS Med*. 2010;7(11):e1000370. doi: 10.1371/journal.pmed.1000370.

53. Vanness DJ, Knudsen AB, Lansdorp-Vogelaar I, et al. Comparative economic evaluation of data from the ACRIN National CT Colonography Trial with three cancer intervention and surveillance modeling network microsimulations. *Radiology*. 2011;261(2):487-498. doi: 10.1148/radiol.11102411.

54. Levin TR, Corley DA, Jensen CD, et al. Effects of organized colorectal cancer screening on cancer incidence and mortality in a large community-based population. *Gastroenterology*. 2018;155(5):1383-1391.e5. doi: 10.1053/j.gastro.2018.07.017.

55. Cyhaniuk A, Coombes ME. Longitudinal adherence to colorectal cancer screening guidelines. *Am J Manag Care*. 2016;22(2):105-111.

56. Inadomi JM, Vijan S, Janz NK, et al. Adherence to colorectal cancer screening: a randomized clinical trial of competing strategies. *Arch Intern Med*. 2012;172(7):575-582. doi: 10.1001/archinternmed.2012.332.

57. Bibbins-Domingo K, Grossman DC, Curry SJ, et al; US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement [errata in *JAMA*. 2016;316(5):545. doi: 10.1001/jama.2016.9943; *JAMA*. 2017;317(21):2239. doi: 10.1001/jama.2017.5918]. *JAMA*. 2016;315(23):2564-2575. doi: 10.1001/jama.2016.5989.

58. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of benefits, burden, and harms of colorectal cancer screening strategies: modeling study for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2595-2609. doi: 10.1001/jama.2016.6828.

59. Issa IA, Noureddine M. Colorectal cancer screening: an updated review of the available options. *World J Gastroenterol*. 2017;23(28):5086-5096. doi: 10.3748/wjg.v23.i28.5086.

Visit **ajmc.com/link/4344** to download PDF