Journal of Nursing & Interprofessional Leadership in Quality & Safety

Volume 2 | Issue 1 Article 7

2018

Use of Best Practice Alerts to Improve Adherence to Evidence-Based Screening in Pediatric Diabetes Care

Daniel DeSalvo

Baylor College of Medicine/Texas Children's Hospital; Section of Pediatric Diabetes and Endocrinology, Daniel.DeSalvo@bcm.edu

Sara K. Bartz

Baylor College of Medicine/Texas Children's Hospital; Section of Pediatric Diabetes and Endocrinolog, klinepet@bcm.edu

Blair Mockler

Baylor College of Medicine, blair.mockler@bcm.edu

Rona Y. Sonabend

Baylor College of Medicine/Texas Children's Hospital; Section of Pediatric Diabetes and Endocrinology, rys1@bcm.edu

Follow this and additional works at: https://digitalcommons.library.tmc.edu/uthoustonjqualsafe

Part of the Endocrinology, Diabetes, and Metabolism Commons, Health and Medical Administration Commons, Industrial and Organizational Psychology Commons, Nursing Administration Commons, Pediatric Nursing Commons, and the Pediatrics Commons

Recommended Citation

DeSalvo, D., Bartz, S. K., Mockler, B., & Sonabend, R. Y. (2019). Use of Best Practice Alerts to Improve Adherence to Evidence-Based Screening in Pediatric Diabetes Care. *Journal of Nursing & Interprofessional Leadership in Quality & Safety*, 2 (1). Retrieved from https://digitalcommons.library.tmc.edu/uthoustonjqualsafe/vol2/iss1/7

Use of Best Practice Alerts to Improve Adherence to Evidence-Based Screening in Pediatric Diabetes Care

Abstract

Background: Youth with type 1 diabetes (T1D) are at increased risk for comorbid autoimmune conditions and long-term complications. To help with early identification of these complications, the American Diabetes Association (ADA) has published evidence-based screening guidelines. The aim of our quality improvement intervention was to improve and sustain adherence to the ADA recommended screening guidelines to >90% for youth with T1D in the Texas Children's Hospital (TCH) Diabetes Center by utilizing best practice alerts (BPA) within the electronic medical record (EMR).

Methods: In accordance with the ADA Standards of Care screening guidelines for youth with T1D, we analyzed the database of TCH patients to obtain the following baseline percentages: 1) urine microalbumin-to-creatinine ratio, 2) thyroid function screen, 3) lipid panel, and 4) retinopathy screen. In the TCH EMR, we developed BPAs to alert providers and provide decision support on ADA-based screening recommendations at each clinic encounter. Comparisons were made to screening rates for each category pre- and post-intervention.

Results: In the four years following the BPA build, the screening percentage for each category improved from a baseline of 90%, which has been maintained for three consecutive fiscal years.

Conclusions: The use of EMR-based BPAs to alert providers of the need for evidenced-based screening is effective in increasing adherence to standard of care guidelines. With this quality improvement intervention, we achieved our goal of >90% for each category. Similar tools for decision support may be effectively utilized for evidence-based screening in other disease states.

Keywords

 $quality\ improvement,\ best\ practice\ alerts,\ decision\ support,\ electronic\ medical\ record,\ evidence-based\ screening,\ type\ 1\ diabetes$

Introduction

Type 1 diabetes (T1D) is most commonly diagnosed in pediatric patients, with three-quarters of all cases diagnosed in patients less than 18 years old (Marcovecchio et al., 2014; Oram et al., 2016). The impact of T1D is broad, and has been associated with increased risk for other autoimmune conditions, most commonly thyroid and celiac disease (Craig et al., 2017; Hughes et al., 2016), as well as long term complications such as retinopathy, nephropathy, and cardiovascular disease (DCCT Research Group, 1993). Previous studies have demonstrated the importance of early diagnosis and treatment of these comorbidities (Daniels et al., 2013; Schwab et al., 2006; Triolo et al., 2011), and the American Diabetes Association (ADA) has published evidence based screening guidelines to facilitate their identification (American Diabetes, 2018).

Despite the recognized importance of early screening for diabetes comorbidities, our clinic and others have had challenges implementing the recommended guidelines (Dorsey, Songer, Zgibor, & Orchard, 2006; Molitch et al., 2003; Porta et al., 2014). The Texas Children's Hospital (TCH) Diabetes Center includes six clinics across the greater Houston, TX, USA metropolitan area and serves a diverse patient population including over 2,000 patients with T1D annually. Prior to the implementation of our quality improvement intervention, screening rates of pediatric T1D comorbidities including nephropathy, thyroid dysfunction, dyslipidemia, and retinopathy, were all below 75% at our center. This was due to inconsistency among providers on timing of screening tests, difficulty assessing the need for screening in the context of a busy clinic, and lack of a standardized protocol for ordering the screening tests.

Electronic medical records (EMR) have the potential to assist in improving health care quality by facilitating access to patient information, reducing medical errors and improving patient safety (Menachemi & Collum, 2011). Use of electronic clinical prompts, or best practice alerts (BPAs) in the EMR can assist in alerting clinicians when patient-specific interventions are indicated, particularly in the management of chronic conditions. Adopting strategies such as BPAs to aid the management of chronic conditions may help facilitate appropriate and timely screening for comorbidities and complications.

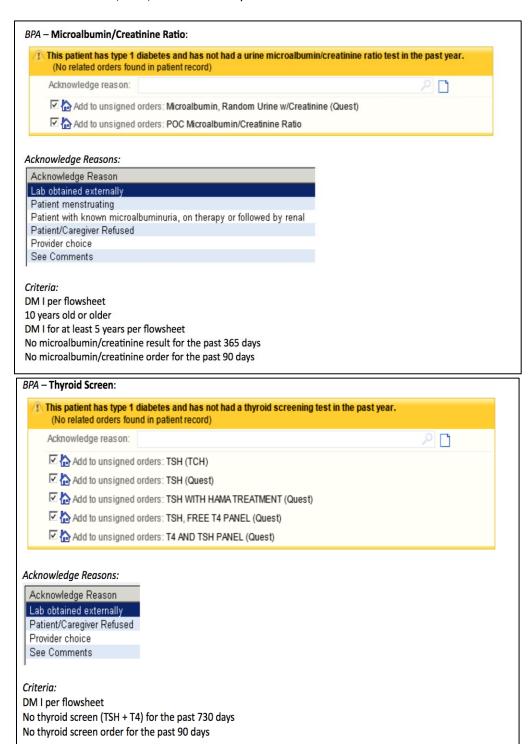
Aim Statement

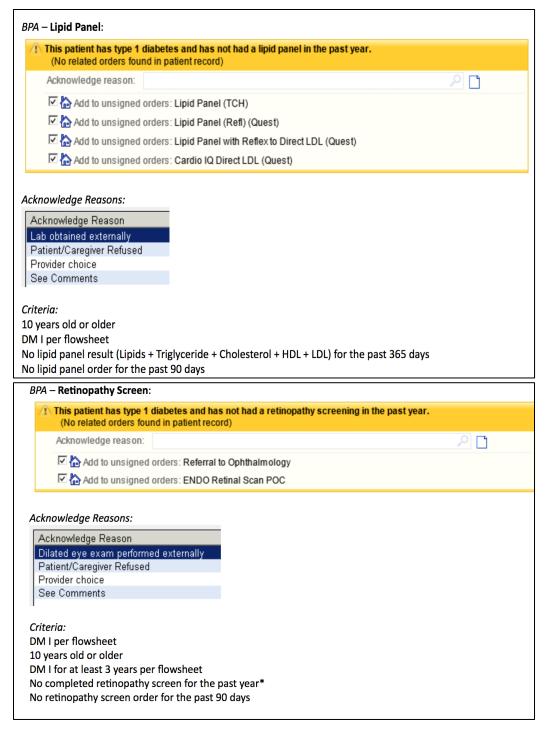
The aim of this quality improvement intervention was to improve and sustain adherence to the ADA recommended screening guidelines to greater than 90% for youth with T1D in the TCH Diabetes Center by utilizing BPAs within the EMR.

Design and Methods

In the TCH EMR, we developed decision support BPAs that automatically alert providers to the need for screening based on ADA recommendations at each clinic encounter. The BPA for nephropathy detection is activated yearly to order a urine microalbumin-to-creatinine ratio for T1D patients \geq 10 years old with diabetes duration greater than (>) 5 years. The thyroid function BPA is activated to order a yearly thyroid stimulating hormone (TSH) level for T1D patients of all ages and diabetes duration. To facilitate screening for dyslipidemia, the BPA fires annually for T1D patients \geq 10 years old to order a lipid panel. The retinopathy screen BPA fires annually for T1D patients \geq 10 years old with diabetes duration >5 years to obtain a point-of-care retinal photo in our clinic with automated digital non-mydriatic fundus camera, which is interpreted by a TCH Optometrist or to place a referral to TCH Ophthalmology for dilated fundoscopic exam. These BPAs (as displayed in Figure 1) were activated in the last quarter of the 2015 fiscal year (FY2015).

Figure 1: Best Practice Alerts (BPAs) for T1D clinic patients





In accordance with the ADA Standards of Care screening guidelines for youth with T1D (including age and T1D duration) (American Diabetes Association, 2018), we analyzed the database of TCH patients with T1D with at least two clinic visits per year (N=1,600) to obtain the following baseline percentages for FY2014 [October 1, 2013-September 30, 2014 (FY2014)]: 1) urine microalbumin-to-creatinine ratio for early detection of renal dysfunction, 2) TSH level for thyroid function screen, 3) lipid panel to screen for dyslipidemia, and 4) annual retinal exam for early detection of retinopathy. The baseline screening percentages were then compared to post-intervention screening rates in FY2015-FY2018.

Results

As demonstrated in **Figure 2**, the baseline percentages of screening for microalbuminuria, thyroid dysfunction, dyslipidemia, and retinopathy (in accordance with the ADA Standards of Care guidelines) for youth with T1D at TCH were below 75% in FY2014, prior to deployment of the BPAs. Screening rates increased in FY2015 after BPAs were deployed in the last quarter, and the subsequent screening percentages for three fiscal years following implementation of BPAs have been >90% for all four screening categories. Microalbuminuria screening rates increased from 66% at baseline to 91% in 2015, and have been maintained at >90%. Thyroid screening rates increased from 71% at baseline to 82% in 2015, and further increased and have been maintained at >90%. Screening for dyslipidemia increased from 74% at baseline to 84% in 2015, with further improvement to >90%, while screening for retinopathy increased from 61% at baseline to 92% in 2015, and has been maintained at >90% post-intervention.

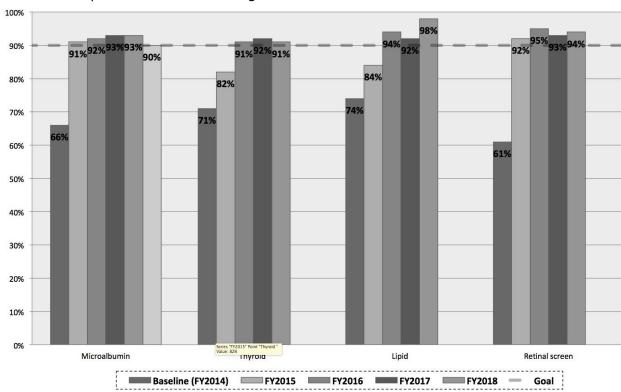


Figure 2: Pre- and post-intervention screening rates.

Discussion

T1D is an autoimmune disease that affects 1.25 million individuals in the US and is one of the most common chronic diseases of childhood (Chiang, Kirkman, Laffel, Peters, & Type 1 Diabetes Sourcebook, 2014). Individuals with T1D are at high risk of developing other autoimmune conditions, micro- and macro-vascular complications. These complications are largely responsible for the morbidity and mortality associated with T1D (Kadiyala, Peter, & Okosieme, 2010; Margeirsdottir et al., 2008; Mohn, Di Michele, Di Luzio, Tumini, & Chiarelli, 2002; Molitch et al., 2003). While the risk of developing diabetes-related complications increases with the duration and poor glycemic control, the onset of the most common complications experienced in T1D is often subclinical. The silent development of potentially debilitating complications highlights the importance of regular screening for the most common comorbidities, as recommended by the ADA (American Diabetes, 2018). This quality improvement initiative focused on improving screening rates for dyslipidemia, thyroid dysfunction, nephropathy, and retinopathy.

Despite recommendations encouraging improved screening for common complications of T1D, national screening rates are relatively unknown, especially among children. A 2006 study of adults with T1D reported screening rates of 73.3% for microalbuminuria, 68.7% for dyslipidemia, and 81.9% for retinopathy (Dorsey et al.,

2006), while a 2013 study of pediatric patients found that only 64% of patients were screened for diabetic retinopathy during a two year period, with lower screening rates among minority patients (Dumser, Ratcliffe, Langdon, Murphy, & Lipman, 2013). These rates are not dissimilar from pre-initiative screening rates at our institution, reflecting the importance of improving screening rates for common complications of T1D across all centers.

At our center, screening rates for diabetes complications and comorbidities were low (<75%) prior to our quality improvement intervention in which we implemented BPAs for real-time decision support in the context of a clinic visit. Screening rates increased immediately after BPAs were deployed, and have remained above the goal >90% in the three years following implementation of our QI intervention. We have monitored screening rates closely to assess for any potential decline in screening for microalbuminuria, thyroid dysfunction, dyslipidemia, and retinopathy in our center. Although there have been small fluctuations in screening rates, they have remained above 90%, which is substantially higher than pre-intervention rates of 61-74%.

Nephropathy

Diabetic nephropathy is the most common cause of end-stage renal disease in the US and Europe (Molitch et al., 2003), and may be an important risk factor for coronary artery disease (Maahs, Jalal, et al., 2013; Maahs & Rewers, 2006). Microalbuminuria, an early indicator for diabetic nephropathy, is strongly associated with increased diabetes duration and HBA1c levels (Daniels et al., 2013). Regular screening is necessary to ensure the early diagnosis of diabetic nephropathy, but following up with appropriate treatment is equally important, considering that only about one-third of individuals diagnosed with microalbuminuria receive appropriate treatment (Daniels et al., 2013). This is critical as effective treatments exist to limit the progression of diabetic nephropathy (American Diabetes, 2018). The most effective renal-protective treatments for adolescents with T1D likely differ from those for their adult counterparts, and additional research is needed to fully understand the impact of these drugs on an adolescent population (M. Loredana Marcovecchio et al., 2017). Prior to implementation of BPAs to screen for microalbuminuria, only 66% of eligible patients at our center were being screened. This improved to >90% post-intervention, and should lead to improved treatment with glucose control measures, lifestyle modifications and ACE-inhibitor or angiotensin receptor blocker therapy.

Thyroid disease

Autoimmune thyroid disease is the most common autoimmune disease among children with T1D, with prevalence rates ranging from 3.9% to 50% (Burek, Rose, Guire, & Hoffman, 1990; Landing, Pettit, Wiens, Knowles, & Guest, 1963). The peak incidence of thyroid autoimmunity occurs during early to mid-puberty (Kim, Shin, & Yang, 2003), and 50% of children with T1D who have elevated titers of anti-thyroperoxidase antibodies develop thyroid problems within 3-4 years of thyroid antibody detection (Kordonouri et al., 2002). Untreated hypothyroidism has been associated with poor glycemic control, dyslipidemia, and hypoglycemia (Jin et al., 2011; Mohn et al., 2002; Severinski, Banac, Severinski, Ahel, & Cvijovic, 2009), while hyperthyroidism has been associated with DKA (Dost et al., 2015) and increased cardiovascular risk (Kadiyala et al., 2010). This emphasizes the importance of performing regular screening for thyroid disease given the high prevalence and potential for complications if left untreated (Roberts & Ladenson, 2004). With our intervention deploying BPAs to obtain annual TSH levels in T1D patients, thyroid screening improved from 71% at baseline to >90% post-intervention; thereby, facilitating timely treatment of thyroid disease.

Dyslipidemia

Premature and extensive atherosclerosis is the major cause of morbidity and mortality in patients with T1D, and population based studies estimate that 14-45% of children with T1D have two or more cardiovascular disease risk factors, with the number of risk factors increasing with age (Margeirsdottir et al., 2008; Rodriguez et al., 2006; Schwab et al., 2006). Overall, cardiovascular events occur earlier and more frequently in patients with T1D than in non diabetic patients, underscoring the seriousness of CVD in this population (de Ferranti et al., 2014). Furthermore, observations measuring cardiovascular disease show that pediatric patients with T1D may have subclinical CVD within the first decade of diagnosis, demonstrating the importance of identifying and treating cardiovascular disease risk factors among pediatric patients (Haller et al., 2007; Singh, Groehn, & Kazmers, 2003; Urbina et al., 2010). Despite this, dyslipidemia is largely undiagnosed and under treated in the T1D pediatric population (Maahs, Dabelea, et al., 2013). This is concerning considering that trials of dietary counseling, lifestyle interventions, and treatment with statins have all been shown to be safe and effective

interventions that demonstrated improvements in lipid levels (Cadario et al., 2012; McCrindle, Ose, & Marais, 2003; Salem, AboElAsrar, Elbarbary, ElHilaly, & Refaat, 2010; Salo et al., 1999; Wiegman et al., 2004). The American Heart Association recommends both lifestyle and pharmacologic treatment for type 1 diabetic patients with elevated LDL cholesterol levels, however adhering to these guidelines would require more effective screening for and subsequent treatment of dyslipidemia (McCrindle et al., 2003). With our QI intervention, screening for dyslipidemia improved from a baseline of 74% to >90% post-intervention. This should aid timely treatment of dyslipidemia with lifestyle and/or pharmacologic therapy, thereby, decreasing future risk of cardiovascular events.

Retinopathy

Retinopathy most commonly occurs after the onset of puberty and after 5-10 years of diabetes duration (Cho et al., 2011). Although diabetic retinopathy is uncommon and typically mild in pediatric patients, evidence shows that pre-pubertal years with diabetes may be an independent predictor for the later development of eye complications, so proper diabetes management retinal screening is important during pediatric years to help prevent later disease (Porta et al., 2014). Recent data show that as few as 65% of youths with T1D had undergone an eye examination within six years following their initial diabetes diagnosis (Wang et al., 2017). Considering the relative infrequency of diabetic retinopathy and the sub-standard screening rates, screening practices may be optimized by utilizing in clinic non-mydriatic retinal scans. Adaptation of in-clinic retinal scans has been shown to increase rates of surveillance, decrease the economic disparities observed in screening rates, increase access to care, and prevent vision-threatening diabetic retinopathy (Jani et al., 2017). Our quality improvement intervention relied on BPAs to aid in retinopathy screening via retinal scanning in our clinic with automated digital non-mydriatic fundus camera or referrals for dilated exams by eye experts. This resulted in an improvement in retinopathy screening from 61% at baseline to >90% post-intervention for our population of youth with T1D who were eligible for screening based on ADA best-practice recommendations.

Interpretation

The aim of this quality improvement initiative was to improve and sustain adherence to the ADA recommended screening guidelines for youth with T1D in the TCH Diabetes Center. Prior to the implementation of our intervention, the screening rates according to ADA guidelines was 66% for renal dysfunction, 71% for thyroid dysfunction, 74% for dyslipidemia, and 61% for diabetic retinopathy. In the year following the implementation of our interventions, our proportion of patients receiving appropriate screening for diabetes-associated complications increased to and were sustained at >90% for each category. These improved screening rates will facilitate timely treatment of T1D comorbidities among our patient population.

It is important to note that use of BPAs for clinical decision support are not limited to T1D care, but could feasibly be implemented in any clinic for evidence-based screening. Given the nearly universal use of EMR systems, there is significant interest in methods incorporating BPAs, which may present an efficient and effective approach to increase screening rates. Our hospital uses an EPIC-based EMR, which is utilized by many other health centers in the US. Therefore, BPAs similar to those designed for our program could feasibly be implemented in other EPIC-based systems, or adapted for other EMR systems. Furthermore, the use of BPAs is a low cost, efficient and highly effective EMR based screening program that diminishes the burden of work on the physician, and may also serve to ameliorate screening disparities present in many cohorts.

Conclusion

Our quality improvement intervention utilizing BPAs within the EMR was successful in improving and sustaining adherence to the ADA recommended screening guidelines to greater than 90% for youth with T1D. Similar tools for decision support may be effectively utilized for evidence-based screening in other chronic disease states. Future QI initiatives in our diabetes center will include revising BPA timing based on whether previous screens are positive or negative, and developing a BPA for celiac disease screen.

References

- American Diabetes Association. (2018). 12. Children and Adolescents: Standards of Medical Care in Diabetes. *Diabetes Care*, 41(Supplement 1), S126-S136. https://doi.org/10.2337/dc18-S012
- Burek, C. L., Rose, N. R., Guire, K. E., & Hoffman, W. H. (1990). Thyroid autoantibodies in black and in white children and adolescents with type 1 diabetes mellitus and their first degree relatives. *Autoimmunity*, 7(2-3), 157-167. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/1983329
- Cadario, F., Prodam, F., Pasqualicchio, S., Bellone, S., Bonsignori, I., Demarchi, I., ... Bona, G. (2012). Lipid profile and nutritional intake in children and adolescents with Type 1 diabetes improve after a structured dietician training to a Mediterranean-style diet. *Journal of Endocrinology Investigation*, 35(2), 160-168. https://doi.org/10.3275/7755
- Chiang, J. L., Kirkman, M. S., Laffel, L. M., Peters, A. L., & Type 1 Diabetes Sourcebook, A. (2014). Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes Care*, 37(7), 2034-2054. https://doi.org/10.2337/dc14-1140
- Cho, Y. H., Craig, M. E., Hing, S., Gallego, P. H., Poon, M., Chan, A., & Donaghue, K. C. (2011). Microvascular complications assessment in adolescents with 2- to 5-yr duration of type 1 diabetes from 1990 to 2006. *Pediatric Diabetes*, 12(8), 682-689. https://doi.org/10.1111/j.1399-5448.2011.00762.x
- Craig, M. E., Prinz, N., Boyle, C. T., Campbell, F. M., Jones, T. W., Hofer, S. E., Simmons, J.H., Holman, N., Tham, E., Fröhlich-Reiterer, E. & DuBose, S. (2017). Prevalence of Celiac Disease in 52,721 Youth with Type 1 Diabetes: International Comparison Across Three Continents. *Diabetes Care*, 40(8), 1034-1040. https://doi.org/10.2337/dc16-2508
- Daniels, M., DuBose, S. N., Maahs, D. M., Beck, R. W., Fox, L. A., Gubitosi-Klug, R., ... T1D Exchange Clinic Network. (2013). Factors associated with microalbuminuria in 7,549 children and adolescents with type 1 diabetes in the T1D Exchange clinic registry. *Diabetes Care*, 36(9), 2639-2645. https://doi.org/10.2337/dc12-219
- DCCT Research Group. (1993). The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus. *New England Journal of Medicine*, 329(14), 977-986. https://doi.org/10.1056/NEJM199309303291401
- de Ferranti, S. D., de Boer, I. H., Fonseca, V., Fox, C. S., Golden, S. H., Lavie, C. J., ... Eckel, R. H. (2014). Type 1 diabetes mellitus and cardiovascular disease: a scientific statement from the American Heart Association and American Diabetes Association. *Circulation*, 130(13), 1110-1130. https://doi.org/10.1161/CIR.0000000000000000034
- Dorsey, R. R., Songer, T. J., Zgibor, J. C., & Orchard, T. J. (2006). Influences on screening for chronic diabetes complications in type 1 diabetes. *Disease Management: DM*, 9(2), 93-101. https://doi.org/10.1089/dis.2006.9.93
- Dost, A., Rohrer, T. R., Frohlich-Reiterer, E., Bollow, E., Karges, B., Bockmann, A., Hamann, J. & Holl, R.W. (2015). Hyperthyroidism in 276 Children and Adolescents with Type 1 Diabetes from Germany and Austria. *Hormone Research in Paediatrics*, 84(3), 190-198. https://doi.org/10.1159/000436964
- Dumser, S. M., Ratcliffe, S. J., Langdon, D. R., Murphy, K. M., & Lipman, T. H. (2013). Racial disparities in screening for diabetic retinopathy in youth with type 1 diabetes. *Diabetes Research and Clinical Practice*, 101(1), e3-5. https://doi.org/10.1016/j.diabres.2013.03.009
- Haller, M. J., Stein, J., Shuster, J., Theriaque, D., Silverstein, J., Schatz, D. A., ... Mahmud, F. H. (2007). Peripheral artery tonometry demonstrates altered endothelial function in children with type 1 diabetes. *Pediatric Diabetes*, 8(4), 193-198. https://doi.org/10.1111/j.1399-5448.2007.00246.x
- Hughes, J. W., Riddlesworth, T. D., DiMeglio, L. A., Miller, K. M., Rickels, M. R., McGill, J. B., & Network, T. D. E. C. (2016). Autoimmune Diseases in Children and Adults with Type 1 Diabetes From the T1D Exchange Clinic Registry. *The Journal of Clinical Endocrinology & Metabolism*, 101(12), 4931-4937. https://doi.org/10.1210/jc.2016-2478
- Jani, P. D., Forbes, L., Choudhury, A., Preisser, J. S., Viera, A. J., & Garg, S. (2017). Evaluation of Diabetic Retinal Screening and Factors for Ophthalmology Referral in a Telemedicine Network. *JAMA Ophthalmology*, 135(7), 706-714. https://doi.org/10.1001/jamaophthalmol.2017.1150
- Jin, P., Huang, G., Lin, J., Yang, L., Xiang, B., Zhou, W., & Zhou, Z. (2011). High titre of antiglutamic acid decarboxylase autoantibody is a strong predictor of the development of thyroid autoimmunity in patients

- with type 1 diabetes and latent autoimmune diabetes in adults. *Clinical Endocrinology (Oxf)*, 74(5), 587-592. https://doi.org/10.1111/j.1365-2265.2011.03976.x
- Kadiyala, R., Peter, R., & Okosieme, O. E. (2010). Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. *International Journal of Clinical Practice*, 64(8), 1130-1139. https://doi.org/10.1111/j.1742-1241.2010.02376.x
- Kim, E. Y., Shin, C. H., & Yang, S. W. (2003). Polymorphisms of HLA class II predispose children and adolescents with type 1 diabetes mellitus to autoimmune thyroid disease. *Autoimmunity*, *36*(3), 177-181. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12911285
- Kordonouri, O., Deiss, D., Danne, T., Dorow, A., Bassir, C., & Gruters-Kieslich, A. (2002). Predictivity of thyroid autoantibodies for the development of thyroid disorders in children and adolescents with Type 1 diabetes. *Diabetic Medicine*, 19(6), 518-521. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12060066
- Landing, B. H., Pettit, M. D., Wiens, R. L., Knowles, H., & Guest, G. M. (1963). Antithyroid antibody and chronic thyroiditis in diabetes. *The Journal of Clinical Endocrinology & Metabolism*, 23, 119-120. https://doi.org/10.1210/jcem-23-1-119
- Maahs, D. M., Dabelea, D., D'Agostino, R. B., Andrews, J. S., Shah, A. S., Crimmins, N., ... SEARCH for Diabetes in Youth Study. (2013). Glucose control predicts 2-year change in lipid profile in youth with type 1 diabetes. *The Journal of Pediatrics*, 162(1), 101-107.e1. https://doi.org/10.1016/j.jpeds.2012.06.006
- Maahs, D. M., Jalal, D., Chonchol, M., Johnson, R. J., Rewers, M., & Snell-Bergeon, J. K. (2013). Impaired renal function further increases odds of 6-year coronary artery calcification progression in adults with type 1 diabetes: the CACTI study. *Diabetes Care*, 36(9), 2607-2614. https://doi.org/10.2337/dc12-2538
- Maahs, D. M., & Rewers, M. (2006). Mortality and Renal Disease in Type 1 Diabetes Mellitus—Progress Made, More to Be Done. *The Journal of Clinical Endocrinology & Metabolism*, 91(10), 3757-3759. https://doi.org/10.1210/jc.2006-1730
- Marcovecchio, M. L., Woodside, J., Jones, T., Daneman, D., Neil, A., Prevost, T., Dalton, R.N., Deanfield, J., Dunger, D.B. and AdDIT Investigators. (2014). Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT): urinary screening and baseline biochemical and cardiovascular assessments. *Diabetes Care*, 37(3), 805-813. https://doi.org/10.2337/dc13-1634
- Marcovecchio, M. Loredana, Chiesa, S. T., Bond, S., Daneman, D., Dawson, S., Donaghue, K. C., Jones, T.W., Mahmud, F.H., Marshall, S.M., Neil, H.A.W. & Dalton, R.N. (2017). ACE Inhibitors and Statins in Adolescents with Type 1 Diabetes. *New England Journal of Medicine*, 377(18), 1733-1745. https://doi.org/10.1056/NEJMoa1703518
- Margeirsdottir, H. D., Larsen, J. R., Brunborg, C., Overby, N. C., Dahl-Jørgensen, K., & Norwegian Study Group for Childhood Diabetes. (2008). High prevalence of cardiovascular risk factors in children and adolescents with type 1 diabetes: a population-based study. *Diabetologia*, 51(4), 554-561. https://doi.org/10.1007/s00125-007-0921-8
- McCrindle, B. W., Ose, L., & Marais, A. D. (2003). Efficacy and safety of atorvastatin in children and adolescents with familial hypercholesterolemia or severe hyperlipidemia: a multicenter, randomized, placebocontrolled trial. *Journal of Pediatrics*, 143(1), 74-80. https://doi.org/10.1016/S0022-3476(03)00186-0
- Menachemi, N., & Collum, T. H. (2011). Benefits and drawbacks of electronic health record systems. *Risk Management and Health Policy*, 4, 47-55. https://doi.org/10.2147/RMHP.S12985
- Mohn, A., Di Michele, S., Di Luzio, R., Tumini, S., & Chiarelli, F. (2002). The effect of subclinical hypothyroidism on metabolic control in children and adolescents with Type 1 diabetes mellitus. *Diabetic Medicine*, 19(1), 70-73. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11869306
- Molitch, M. E., DeFronzo, R. A., Franz, M. J., Keane, W. F., Mogensen, C. E., Parving, H. H., & American Diabetes, A. (2003). Diabetic nephropathy. *Diabetes Care*, 26 Suppl 1, S94-8. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12502629
- Oram, R. A., Patel, K., Hill, A., Shields, B., McDonald, T. J., Jones, A., ... Weedon, M. N. (2016). A Type 1 Diabetes Genetic Risk Score Can Aid Discrimination Between Type 1 and Type 2 Diabetes in Young Adults. *Diabetes Care*, 39(3), 337-344. https://doi.org/10.2337/dc15-1111
- Porta, M., Schellino, F., Montanaro, M., Baltatescu, A., Borio, L., Lopatina, T., ... Cavallo, F. (2014). Prevalence of retinopathy in patients with type 1 diabetes diagnosed before and after puberty. *Acta Diabetologica*, 51(6), 1049-1054. https://doi.org/10.1007/s00592-014-0671-2

- Roberts, C. G., & Ladenson, P. W. (2004). Hypothyroidism. *Lancet*, *363*(9411), 793-803. https://doi.org/10.1016/S0140-6736(04)15696-1
- Rodriguez, B. L., Fujimoto, W. Y., Mayer-Davis, E. J., Imperatore, G., Williams, D. E., Bell, R. A., ... Linder, B. (2006). Prevalence of cardiovascular disease risk factors in U.S. children and adolescents with diabetes: the SEARCH for diabetes in youth study. *Diabetes Care*, 29(8), 1891-1896. https://doi.org/10.2337/dc06-0310
- Salem, M. A., AboElAsrar, M. A., Elbarbary, N. S., ElHilaly, R. A., & Refaat, Y. M. (2010). Is exercise a therapeutic tool for improvement of cardiovascular risk factors in adolescents with type 1 diabetes mellitus? A randomised controlled trial. *Diabetology & metabolic syndrome*, 2(1), 47. https://doi.org/10.1186/1758-5996-2-47
- Salo, P., Viikari, J., Hamalainen, M., Lapinleimu, H., Routi, T., Ronnemaa, T., ... Simell, O. (1999). Serum cholesterol ester fatty acids in 7- and 13-month-old children in a prospective randomized trial of a low-saturated fat, low-cholesterol diet: the STRIP baby project. Special Turku coronary Risk factor Intervention Project for children. *Acta Paediatrica*, 88(5), 505-512. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10426172
- Schwab, K. O., Doerfer, J., Hecker, W., Grulich-Henn, J., Wiemann, D., Kordonouri, O., ... Diabetology, D. P. V. I. of the G. W. G. for P. (2006). Spectrum and prevalence of atherogenic risk factors in 27,358 children, adolescents, and young adults with type 1 diabetes: cross-sectional data from the German diabetes documentation and quality management system (DPV). *Diabetes Care*, 29(2), 218-225. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16443863
- Severinski, S., Banac, S., Severinski, N. S., Ahel, V., & Cvijovic, K. (2009). Epidemiology and clinical characteristics of thyroid dysfunction in children and adolescents with type 1 diabetes. *Collegium Antropologicum*, 33(1), 273-279. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19408637
- Singh, T. P., Groehn, H., & Kazmers, A. (2003). Vascular function and carotid intimal-medial thickness in children with insulin-dependent diabetes mellitus. *Journal of the American College of Cardiology*, *41*(4), 661-665. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12598080
- Triolo, T. M., Armstrong, T. K., McFann, K., Yu, L., Rewers, M. J., Klingensmith, G. J., ... Barker, J. M. (2011). Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. *Diabetes Care*, 34(5), 1211-1213. https://doi.org/10.2337/dc10-1756
- Urbina, E. M., Wadwa, R. P., Davis, C., Snively, B. M., Dolan, L. M., Daniels, S. R., ... Dabelea, D. (2010). Prevalence of increased arterial stiffness in children with type 1 diabetes mellitus differs by measurement site and sex: the SEARCH for Diabetes in Youth Study. *Journal of Pediatrics*, 156(5), 731-737, 737 e1. https://doi.org/10.1016/j.jpeds.2009.11.011
- Wang, S. Y., Andrews, C. A., Gardner, T. W., Wood, M., Singer, K., & Stein, J. D. (2017). Ophthalmic Screening Patterns Among Youths With Diabetes Enrolled in a Large US Managed Care Network. *JAMA Ophthalmology*, 135(5), 432-438. https://doi.org/10.1001/jamaophthalmol.2017.0089
- Wiegman, A., Hutten, B. A., de Groot, E., Rodenburg, J., Bakker, H. D., Buller, H. R., ... Kastelein, J. J. (2004). Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized controlled trial. *Journal of the American Medical Association*, 292(3), 331-337. https://doi.org/10.1001/jama.292.3.331