UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS MÉDICAS: ENDOCRINOLOGIA

TESE DE DOUTORADO

BARREIRAS CLÍNICAS E PSICOSSOCIAIS POTENCIALMENTE PREDITORAS DE CONTROLE GLICÊMICO EM CRIANÇAS E ADOLESCENTES COM DIABETES MELITO TIPO 1

GABRIELA HEIDEN TELÓ

Porto Alegre, março de 2016

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Esta tese é dedicada a todos os pacientes com diabetes melito tipo 1 e seus familiares.

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“A menos que modifiquemos a nossa maneira de pensar, não seremos capazes de resolver os problemas causados pela forma como nos acostumamos a ver o mundo”.

Albert Einstein

SUMÁRIO

ABREVIATURAS E SIGLAS

#	*Number*
ADA	*American Diabetes Association*
AMA	*American Medical Association*
BMI	*Body mass index*
CGM	*Continuous glucose monitoring*
CI	*Confidence intervals*
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico
CSII	*Continuous subcutaneous insulin infusion*
DAWN	*Diabetes Attitudes, Wishes and Needs*
DCCT	*Diabetes Control and Complications Trial*
DFCS	*Diabetes Family Conflict Scale*
DFRQ	*Diabetes Family Responsibility Questionnaire*
DKA	*Diabetic ketoacidosis*
DMQ	*Diabetes Management Questionnaire*
DSMP	*Diabetes Self Monitoring Profile*
ERICA	*Study of Cardiovascular Risk in Adolescents*
Fig.	*Figure*
FIPE	Fundo de Incentivo ao Pesquisador
GHQ	*General Health Questionnaire*
HbA1c	Hemoglobina glicada / *hemoglobin A1c*
JDRF	*Juvenile Diabetes Research Foundation*
OR	*Odds ratio*
Pedi	*Pediatric*
PedsQL	*Pediatric Quality of Life Inventory*
r	*Coefficient of correlation*
ref.	*Reference*
R^2	*Coefficient of determination*
SBD	Sociedade Brasileira de Diabetes
SCI-R	*Self-Care Inventory-Revised version*
SD	*Standard deviation*
SE	*Standard error*
T1D	*Type 1 diabetes*
U.S.	*United States of America*
Units/kg	*Daily insulin dose*
vs.	*Versus*
X^2	*Chi-square*
β	*Standardized estimate*

TABELAS E FIGURAS

RESUMO

O diabetes melito tipo 1 é uma doença crônica e progressiva, com elevado risco de morbidade e mortalidade relacionadas a complicações agudas e crônicas, as quais podem ser reduzidas através de controle glicêmico adequado. Novas tecnologias para otimizar o manejo do diabetes vêm sendo estudadas, mas podem adicionar ainda mais demandas a um cuidado já repleto de exigências específicas. A adolescência parece ser um período essencialmente crítico, onde alterações fisiológicas somam-se à má adesão e a questões psicossociais. Ampla compreensão, por parte da equipe de saúde responsável pelo cuidado destes pacientes, é fundamental para um bom controle da doença.

Com o objetivo de identificar fatores associados à deterioração glicêmica, foi desenvolvida uma coorte, de 20 anos de seguimento, com 635 crianças, adolescentes e adultos jovens com diabetes tipo 1. Observou-se piora do controle glicêmico no sexo feminino ao final da puberdade. Os pacientes em uso de maiores doses de insulina apresentaram pior controle do diabetes, sugerindo que, além de resistência insulínica, má adesão poderia estar contribuindo para estes resultados. O uso de bomba de insulina associou-se a melhor controle glicêmico durante todo o período de observação da coorte.

Considerando os potenciais benefícios de tecnologias no manejo do diabetes, estudo transversal avaliou características de 120 crianças e adolescentes interessados no uso de monitores contínuos de glicemia (*continuous glucose monitoring,* CGM), em comparação a amostra geral de 238 crianças e adolescentes com diabetes tipo 1. O grupo motivado a iniciar CGM apresentou melhor adesão ao tratamento, melhor controle glicêmico, mais frequente verificação da glicemia capilar, menor conflito familiar e maior qualidade de vida. A baixa aceitação do uso de CGM neste estudo (28%) sugere que demandas adicionais podem ser um fator limitante para o uso de tecnologias em diabetes.

Dada a importância de adequadamente avaliar a adesão ao tratamento do diabetes, estudo comparativo avaliou métodos diretos e indiretos de verificação da adesão em

relação à sua capacidade de predizer o controle glicêmico em 82 pacientes com diabetes tipo 1. Autorrelato, questionários, diário de glicemia capilar e *download* de glicosímetros foram avaliados. Frequência de verificação da glicemia capilar por *download* de glicosímetro mostrou-se como o mais forte preditor de controle glicêmico. Questionário administrado por entrevistadores (*Diabetes Self Monitoring Profile*) também mostrou-se adequado, fornecendo informações adicionais sobre dieta, exercícios e insulinoterapia.

Baseado na associação de depressão e piora da adesão, avaliou-se a presença de transtornos de saúde mental em 116 adolescentes com diabetes tipo 1 em amostra de base populacional que incluía 73.624 adolescentes no Brasil. Em comparação ao restante desta população, diabetes tipo 1 não se associou a transtornos mentais. Entretanto, adolescentes com diabetes tipo 1 mais frequentemente relataram insatisfação com atividades diárias, dificuldade em superar dificuldades e sensação de inutilidade. Estes achados sugerem que as equipes de saúde devam estar preparadas para identificar sintomas subclínicos de transtornos mentais a fim de evitar possível deterioração no controle glicêmico.

Para avaliar as principais dificuldades encontradas por profissionais de saúde cuidando de adolescentes com diabetes tipo 1, questionário eletrônico foi enviado a 418 endocrinologistas de todas as regiões dos Estados Unidos da América. A maioria dos respondedores (58%) relatou não ter acesso a profissionais capacitados para o manejo de transtornos de saúde mental. Mesmo após controlar para experiência profissional e atuação em centros não acadêmicos, estes profissionais mais frequentemente relataram, em seus pacientes, barreiras como depressão, abuso de substâncias e distúrbios alimentares. Estes achados reforçam a necessidade de capacitação das equipes de saúde para um melhor cuidado de pacientes com diabetes tipo 1.

A identificação de barreiras clínicas e psicossociais potencialmente modificáveis e preditoras de deterioração glicêmica fornece oportunidades para otimização dos cuidados de saúde voltados a crianças e adolescentes com diabetes tipo 1.

APRESENTAÇÃO

Este trabalho consiste na tese de doutorado "**Barreiras clínicas e psicossociais potencialmente preditoras de controle glicêmico em crianças e adolescentes com diabetes melito tipo 1**", apresentada ao Programa de Pós-graduação em Ciências Médicas: Endocrinologia da Universidade Federal do Rio Grande do Sul em 29 de março de 2016. O trabalho será apresentado em 3 partes, descritas a seguir:

1. Introdução
2. Desenvolvimento
    a. Artigo 1: *Predictors of Changing Insulin Requirements and Glycemic Control in Children, Adolescents, and Young Adults with Type 1 Diabetes*
    b. Artigo 2: *Salient Characteristics of Youth with Type 1 Diabetes Initiating Continuous Glucose Monitoring*
    c. Artigo 3: *Comparison between Adherence Assessments and Blood Glucose Monitoring Measures to Predict Glycemic Control in Patients with Type 1 Diabetes*
    d. Artigo 4: *Mental Health Symptoms in Adolescents with and without Type 1 Diabetes: Reported Occurrence in a National Survey in Brazil*
    e. Artigo 5: *Health Care Transition in Young Adults with Type 1 Diabetes: Perspectives of Adult Endocrinologists in the U.S.*
3. Conclusões

INTRODUÇÃO

O diabetes melito tipo 1 é uma doença crônica, progressiva, causada por deficiência insulínica secundária à destruição das células beta produtoras de insulina no pâncreas, caracterizando-se por inabilidade em manter as condições normais de homeostase da glicose (1). Representa 90% dos casos de diabetes durante a infância e a adolescência (2). Ao diagnóstico, apresenta distribuição bimodal, com um primeiro pico entre quatro e seis anos e um segundo no início da puberdade (10 a 14 anos) (3). No Brasil, embora os dados tenham sido coletados em uma única região, observa-se um crescente número de casos novos da doença, com incidência estimada de 27,2/100.000 habitantes/ano (4). Apesar de fatores genéticos, infecções virais, imunizações, obesidade, deficiência de vitamina D, exposição precoce ao leite de vaca, fatores perinatais e determinadas características socioeconômicas serem associadas ao diagnóstico de diabetes tipo 1, as causas diretamente relacionadas ao aumento dos casos no Brasil e ao redor do mundo ainda permanecem incertas (3, 5, 6).

O diagnóstico de diabetes tipo 1 pode ser feito por três diferentes formas (7):

- sintomas clássicos, como poliúria, polidipsia e perda de peso, com posterior confirmação laboratorial;
- alteração laboratorial em pacientes assintomáticos (duas medidas de glicemia ≥126 mg/dL em jejum, glicemia ≥200 mg/dL pós-prandial ou hemoglobina glicada (HbA1c) ≥6,5% ou uma única medida pós-prandial ≥200 mg/dL com sintomas);
- cetoacidose diabética, caracterizada por hiperglicemia e cetoacidose.

A frequência de cetoacidose diabética no momento do diagnóstico varia entre 15 e 67%, sendo mais comum em crianças pequenas e de baixo nível socioeconômico (8). A cetoacidose é a mais séria complicação relacionada ao diabetes, sendo potencialmente ameaçadora à vida. Sua ocorrência em pacientes já diagnosticados associa-se principalmente a infecções e má adesão ao tratamento, seja por omissão de dose de insulina ou transgressão da dieta (9). Em estudo observacional realizado em pacientes com diabetes tipo 1 do Hospital de Clínicas de Porto Alegre, a taxa de má adesão à dieta e ao tratamento com insulina como causa precipitante da cetoacidose foi de 49% (10).

O diabetes tipo 1 carrega elevado risco de morbidade e mortalidade devido ao desenvolvimento de complicações agudas (hipoglicemia e cetoacidose) e crônicas microvasculares (retinopatia, nefropatia e neuropatia) e macrovasculares (doença cerebrovascular, doença arterial coronariana e doença arterial periférica), as quais resultam em níveis mais baixos de qualidade e expectativa de vida (11-13). O *Diabetes Control and Complications Trial* (DCCT) mostrou que o controle intensivo da hiperglicemia no diabetes tipo 1 diminui o risco de desenvolvimento de complicações crônicas microvasculares (14) e macrovasculares (15). Apesar da conhecida dificuldade de se conseguir alcançar os níveis recomendados de controle glicêmico (2, 16), dados observacionais a longo prazo evidenciaram que pacientes com diabetes tipo 1 por 30 anos que tenham recebido, inicialmente, tratamento intensivo tiveram uma menor incidência cumulativa de retinopatia proliferativa (21 vs. 50%), nefropatia (9 vs. 25%) e doença cardiovascular (9 vs. 14%) em comparação a pacientes submetidos a tratamento convencional, respectivamente (17).

O tratamento adequado do diabetes tipo 1, evitando-se hiperglicemias e hipoglicemias, requer monitorização do controle glicêmico através de duas modalidades: automonitorização da glicemia capilar e avaliação da exposição prolongada à glicose através da medida da HbA1c. A HbA1c estima a exposição de hemoglobina à glicose em um período de 8 a 12 semanas (1). Os valores recomendados para prevenção de complicações crônicas relacionadas ao diabetes em adultos é de <7% (7, 18). Entretanto, recente posicionamento da *American Diabetes Association* (ADA) traz alvos mais flexíveis para pacientes acima de 60-65 anos (7,5 a 8,5%, na dependência das condições de saúde), objetivando-se controle glicêmico adequado sem causar dano ao paciente, especialmente hipoglicemia (7). Para crianças e adolescentes, conforme as diretrizes da ADA (7) e da

International Society for Pediatric and Adolescent Diabetes (19), um alvo de HbA1c <7,5% é almejado. A monitorização frequente da glicemia capilar, por sua vez, tem sido associada a melhor controle glicêmico em crianças e adultos com diabetes tipo 1 (20, 21). Em crianças, o aumento da verificação da glicose, mesmo que intencionalmente antes do período de reavaliação médica, correlacionou-se com um melhor controle glicêmico (22). O uso de dispositivos de monitorização contínua da glicose, apesar de melhorar o controle glicêmico e o manejo do diabetes tipo 1 em adultos com motivação e habilidade para o uso (23), não apresentou os mesmos resultados em crianças (24). Novos estudos ainda são necessários para compreender a falta de efetividade encontrada em crianças e adolescentes e identificar o perfil de pacientes que potencialmente teriam benefício com o uso desta tecnologia.

A terapia insulínica como parte do tratamento do diabetes tipo 1, para ser efetiva, inclui quatro fases críticas de execução: iniciação, complacência, persistência e intensificação (25). Cada uma destas fases requer envolvimento de pacientes e seus familiares com profissionais da saúde, objetivando-se máxima compreensão sobre a prescrição, adequação do regime terapêutico à realidade do paciente, renovação de doses conforme reavaliação clínica e intensificação do regime quando apropriado. O objetivo da terapia insulínica no diabetes tipo 1 é replicar a secreção de insulina de um pâncreas normofuncionante, com liberação de insulina basal e *bolus* de correção e de cobertura pós-refeição (26). As atuais opções terapêuticas de reposição de insulina ainda não são capazes de simular com precisão o perfil de liberação endógena de insulina pelas células beta pancreáticas (27). As doses de insulina precisam ser individualizadas e podem variar de acordo com a idade de cada paciente. De maneira geral, doses diárias de 0,50-0,75 UI/kg são selecionadas para terapia inicial, ajustando-as, conforme necessidade, para obtenção de um controle glicêmico adequado (19). Algumas condições modificam a necessidade diária de insulina; obesidade e idade puberal, por exemplo, tipicamente requerem doses mais elevadas por induzirem e/ou exacerbarem resistência insulínica (28).

Formas mais avançadas de dispensação de insulina, como as bombas de insulina, são de crescente interesse para crianças e adolescentes por eliminarem a necessidade de injeções frequentes, mimetizarem a liberação fisiológica de insulina basal e garantirem maior flexibilidade ao tratamento (29). Em comparação a múltiplas injeções diárias, a bomba de insulina vem sendo associada a maior satisfação com o tratamento e melhor qualidade de vida (30). O benefício sobre o controle glicêmico, apesar de presente em inúmeros estudos, é pequeno e parece associado aos primeiros anos de uso desta tecnologia (29, 31, 32).

Inúmeros estudos vêm sendo realizados com foco em tecnologias relacionadas ao cuidado do diabetes, objetivando melhorar o controle glicêmico e reduzir, simultaneamente, as demandas usuais do tratamento do diabetes (33). Tecnologias têm sido utilizadas de três diferentes maneiras: tecnologias que afetam diretamente o tratamento diário do diabetes, como bombas de insulina e monitores contínuos da glicose; tecnologias voltadas à autoinformação em diabetes; e tecnologias voltadas à interação entre pacientes e profissionais de saúde, como plataformas interativas e programas de telessaúde (34). As novas tecnologias de efeito direto no cuidado diário com o diabetes parecem aumentar a flexibilidade do tratamento, mas podem, concomitantemente, adicionar ainda mais tarefas a um cuidado já repleto de informações e demandas específicas. Identificar o perfil de paciente com potencial benefício em relação ao uso destas tecnologias torna-se um desafio e parece ser o ponto-chave para um melhor controle glicêmico e para o adequado uso de tecnologias, as quais deveriam tornar mais simples o tratamento do diabetes (30).

O manejo do diabetes tipo 1 estabelece contínuas demandas tanto sobre o paciente quanto seus familiares (35). A identificação do perfil de adesão é fundamental, especialmente em populações de maior risco para piora do controle glicêmico (2, 36). Apesar do surgimento e amplo uso de tecnologias potencialmente benéficas no tratamento do diabetes em países desenvolvidos, o controle glicêmico médio da população manteve-se estável ao longo das últimas décadas (37), sugerindo que outros fatores, não só os relacionados a drogas e tecnologias, afetam o controle glicêmico de pacientes com diabetes tipo 1 (38). Em estudo multicêntrico, o Grupo Brasileiro de Estudos em Diabetes tipo 1 analisou dados demográficos, clínicos e socioeconômicos de pacientes com diabetes tipo 1 recebendo tratamento em centros públicos do Brasil. Embora a maioria dos pacientes estivesse em regime terapêutico complexo com acompanhamento por endocrinologistas em serviços de nível de atendimento secundário ou terciário, os resultados identificaram que aproximadamente 80% dos pacientes não apresentavam controle glicêmico satisfatório (16). Salienta-se, entretanto, que o tratamento do diabetes no Brasil é guiado pelas recomendações da Sociedade Brasileira de Diabetes (SBD) (18), a qual segue essencialmente as mesmas orientações da ADA (7). Esses dados sugerem que, além das orientações de tratamento e saúde, outros fatores possam interferir no cuidado dos pacientes com diabetes no Brasil. Dentre os fatores potencialmente relacionados, destaca-se o fator socioeconômico. No estudo acima mencionado (16), 61,7% dos pacientes com diabetes tipo 1 apresentavam-se em níveis socioeconômicos considerados baixo ou muito baixo. Entretanto, não foram identificadas, entre os diferentes níveis socioeconômicos, diferenças no percentual de pacientes que atingiram as metas de HbA1c recomendadas pela ADA/SBD (16). Outro fator potencialmente causal para o elevado percentual de pacientes com controle glicêmico inadequado no Brasil inclui a má adesão ao tratamento. A má adesão pode relacionar-se com pouca compreensão sobre a doença e dificuldade, por parte da equipe de saúde, de conscientizar e adequadamente orientar os pacientes sobre a importância de manter um tratamento adequado (36).

A Organização Mundial da Saúde define adesão como o grau em que o comportamento de um paciente corresponde às recomendações da equipe de saúde (39). Adesão é um termo amplo que engloba os conceitos de complacência e persistência. Complacência define o quão fiel um paciente é ao tratamento sugerido pela equipe de saúde, e persistência define a duração de tempo em que este tratamento é seguido (2). Em indivíduos com diabetes tipo 1, para se obter um bom controle glicêmico e prevenir complicações, recomenda-se adesão adequada a inúmeras medidas de cuidados com a saúde, as quais incluem coordenar quantidade e tempo corretos de aplicação de insulina, frequentes verificações da glicemia capilar, prevenção e manejo adequado de hipoglicemias, plano alimentar e atividade física (7). Há uma tendência, na literatura, de considerar adesão e controle glicêmico como construtos comuns, quando, na verdade, ambos devem ser avaliados simultaneamente, mas independentemente (40, 41).

Existem, na literatura, inúmeros métodos de avaliação de adesão ao tratamento de doenças crônicas, como autorrelato (42), contagem de pílulas (43), extração de dados advindos da farmácia de distribuição das medicações (44), medida dos metabólitos ativos no sangue (45), uso de dispositivos de monitorização eletrônica (46) e questionários (47). Alguns destes, devido às características relacionadas ao manejo e à monitorização do diabetes tipo 1, apresentam limitação quanto ao seu uso. Embora haja um consenso quanto à definição de adesão, há discordância em relação a como operacionalmente medir esse fenômeno (48). Sugere-se que um método para avaliação de adesão deva ser contínuo, dinâmico e capaz de capturar os regimes específicos de comportamento relevantes para a doença a ser avaliada (48). Recentemente, validou-se, para a língua portuguesa, dois instrumentos de medida de adesão voltados para pacientes com diabetes tipo 1 (49), ambos incluindo os principais domínios de avaliação de adesão (dieta, atividade física, insulinoterapia, monitorização da glicemia capilar e manejo de hipoglicemias) e estando disponíveis para uso em cenários clínicos e de pesquisa. Com base nas características relacionadas à adesão ao tratamento do diabetes tipo 1, os seguintes métodos poderiam potencialmente avaliar adesão ao tratamento: autorrelato, entrevistas estruturadas, diário de glicemia capilar e avaliação da frequência de verificação da glicemia capilar (50). Para auxiliar na decisão de qual ferramenta escolher, estudos comparativos avaliando estes diferentes métodos ainda precisam ser desenvolvidos.

Embora o manejo do diabetes seja difícil e repleto de demandas em qualquer idade, a adolescência mostra-se como um período essencialmente crítico para pacientes com diabetes tipo 1 devido a questões psicológicas e psicossociais (51, 52). Nesta fase, as tarefas relacionadas ao diabetes somam-se às novas demandas relacionadas à idade (53). Além das mudanças fisiológicas associadas ao período da puberdade, com aumento da resistência insulínica (27), muitos adolescentes modificam o tratamento sem orientação da equipe de saúde, alterando o perfil de adesão, o autocuidado e, consequentemente, o controle glicêmico (54). A transição de cuidados dos pais para o próprio paciente, a qual frequentemente ocorre durante a adolescência, pode comprometer ainda mais a adesão ao tratamento (38). Alguns estudos têm documentado que as mudanças psicológicas e comportamentais desta fase têm o potencial de piorar o controle glicêmico mesmo em pacientes em tratamento de longa data (55, 56), e que adolescentes com problemas de comportamento possuem probabilidade duas vezes maior de apresentar níveis de HbA1c >9% (57).

Enquanto alterações comportamentais podem levar a uma piora do controle glicêmico em pacientes com diabetes tipo 1 (57), a busca por um alvo de HbA1c, através da realização de múltiplas complexas tarefas relacionadas aos cuidados com o diabetes, pode favorecer o surgimento de determinadas barreiras psicossociais, as quais podem ser preditoras de futuros transtornos de saúde mental (53). Evidências sugerem, ainda, a possibilidade de uma ligação biológica entre diabetes tipo 1 e transtornos mentais, através de citocinas relacionadas ao processo autoimune, impacto direto da deficiência insulínica no metabolismo de neurotransmissores, estado hiperglicêmico crônico e hipoglicemias iatrogênicas (58). As evidências sobre a prevalência de psicopatologias entre adolescentes com diabetes tipo 1 são, ainda, controversas na literatura. Enquanto alguns estudos documentam maior prevalência de depressão e transtornos de saúde mental em pacientes com diabetes tipo 1 (59, 60), outros estudos mais bem delineados mostram-se negativos (61, 62). Mais recentemente, evidenciou-se que sintomas de depressão são mais frequentes do que diagnóstico de depressão em adolescentes com diabetes tipo 1 (63). Apesar das controversas na literatura, recente publicação da *Mental Health Issues of Diabetes Conference* (64) sugere que o rastreamento para transtornos de saúde mental deva ser parte da avaliação anual de pacientes com diabetes tipo 1 e seus familiares.

Com o objetivo de melhorar os cuidados do diabetes, a equipe de saúde responsável pelo cuidado de crianças e adolescentes com diabetes tipo 1 requer ampla compreensão de todas as possíveis barreiras relacionadas à doença e ao seu tratamento (65). Dentre elas, destacam-se as barreiras relacionadas ao desenvolvimento fisiológico, as psicológicas, as familiares, as culturais e as associadas aos cuidados da equipe de saúde (38, 66, 67). Todas estas barreiras deveriam ser avaliadas e acompanhadas por equipe preparada para manejo adequado do diabetes e de possíveis transtornos de saúde mental (64). Em comparação a tratamentos usuais, cuidados colaborativos voltados para o diabetes e para os transtornos de saúde mental parecem associar-se à melhora significativa nos desfechos relacionados à depressão e na adesão ao tratamento do diabetes (68). Alguns ensaios clínicos randomizados mostraram que o manejo combinado de depressão e diabetes significativamente melhorou o controle de ambos (69-71), e que determinadas intervenções preventivas, durante o período da adolescência, poderiam evitar o surgimento e diminuir o impacto de transtornos mentais relacionados direta ou indiretamente com o diabetes (64). Sugere-se um preparo adequado da equipe de saúde para reconhecer e apropriadamente tratar possíveis barreiras que venham a dificultar o manejo do diabetes e a otimização do controle glicêmico (7, 64). Apesar de estudo prévio sugerir que a falta de experiência e de tempo, além de dificuldades no referenciamento de pacientes para outros profissionais, possam ser barreiras para um melhor cuidado com o diabetes (72), a literatura ainda é falha na avaliação das equipes de saúde quanto às principais dificuldades e limitações de cuidado encontradas.

Baseado no aqui disposto, o objetivo desta tese é (1) avaliar as trajetórias de controle glicêmico e de necessidade de insulina ao longo das diferentes fases do desenvolvimento de crianças, adolescentes e adultos jovens com diabetes tipo 1; (2) identificar o impacto de determinadas tecnologias avançadas no manejo do diabetes tipo 1 e o perfil de pacientes que potencialmente se beneficiaria deste uso; (3) avaliar adesão e a melhor forma de acessá-la em pacientes com diabetes tipo 1; (4) avaliar a prevalência de barreiras psicossociais possivelmente presentes nos adolescentes com diabetes tipo 1 e compará-la à da população geral; (5) avaliar as dificuldades dos profissionais de saúde responsáveis pelos cuidados dos pacientes com diabetes tipo 1 em identificar e adequadamente manejar algumas destas barreiras relacionadas ao diabetes e ao seu tratamento.

Referências bibliográficas

1. Melmed SM, Polonsky KS, Larsen RM, Kronenberg HM. Williams Textbook of Endocrinology. 13th Edition ed2016. 1888 p.
2. Asche C, LaFleur J, Conner C. A review of diabetes treatment adherence and the association with clinical and economic outcomes. Clinical Therapeutics. 2011;33(1):74-109.
3. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA. 2014;311(17):1778-86.
4. Negrato CA, Dias JP, Teixeira MF, Dias A, Salgado MH, Lauris JR, et al. Temporal trends in incidence of Type 1 diabetes between 1986 and 2006 in Brazil. Journal of Endocrinological Investigation. 2010;33(6):373-7.
5. Redondo MJ, Rewers M, Yu L, Garg S, Pilcher CC, Elliott RB, et al. Genetic determination of islet cell autoimmunity in monozygotic twin, dizygotic twin, and non-twin siblings of patients with type 1 diabetes: prospective twin study. BMJ. 1999;318(7185):698-702.
6. Gale EA. The rise of childhood type 1 diabetes in the 20th century. Diabetes. 2002;51(12):3353-61.
7. Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. 2016;39 Suppl 1:S4-5.

8. Negrato CA, Cobas RA, Gomes MB, Brazilian Type 1 Diabetes Study G. Temporal changes in the diagnosis of type 1 diabetes by diabetic ketoacidosis in Brazil: a nationwide survey. Diabetic Medicine. 2012;29(9):1142-7.

9. Dabelea D, Rewers A, Stafford JM, Standiford DA, Lawrence JM, Saydah S, et al. Trends in the prevalence of ketoacidosis at diabetes diagnosis: the SEARCH for diabetes in youth study. Pediatrics. 2014;133(4):e938-45.

10. Weinert LS, Scheffel RS, Severo MD, Cioffi AP, Telo GH, Boschi A, et al. Precipitating factors of diabetic ketoacidosis at a public hospital in a middle-income country. Diabetes Research and Clinical Practice. 2012;96(1):29-34.

11. Lind M, Svensson AM, Kosiborod M, Gudbjornsdottir S, Pivodic A, Wedel H, et al. Glycemic control and excess mortality in type 1 diabetes. The New England Journal of Medicine. 2014;371(21):1972-82.

12. Lung TW, Petrie D, Herman WH, Palmer AJ, Svensson AM, Eliasson B, et al. Severe hypoglycemia and mortality after cardiovascular events for type 1 diabetic patients in Sweden. Diabetes Care. 2014;37(11):2974-81.

13. Cooper MN, de Klerk NH, Jones TW, Davis EA. Clinical and demographic risk factors associated with mortality during early adulthood in a population-based cohort of childhood-onset type 1 diabetes. Diabetic Medicine. 2014;31(12):1550-8.

14. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. The New England Journal of Medicine. 1993;329(14):977-86.

15. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. The New England Journal of Medicine. 2005;353(25):2643-53.

16. Gomes MB, Coral M, Cobas RA, Dib SA, Canani LH, Nery M, et al. Prevalence of adults with type 1 diabetes who meet the goals of care in daily clinical practice: a nationwide multicenter study in Brazil. Diabetes Research and Clinical Practice. 2012;97(1):63-70.

17. Diabetes C, Complications Trial/Epidemiology of Diabetes I, Complications Research G, Nathan DM, Zinman B, Cleary PA, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). Archives of Internal Medicine. 2009;169(14):1307-16.

18. Diretrizes da Sociedade Brasileira de Diabetes: 2014-2015/Sociedade Brasileira de Diabetes (organização José Egidio Paulo de Oliveira, Sérgio Vencio). São Paulo: AC Farmacêutica, 2015.

19. Rewers MJ, Pillay K, de Beaufort C, Craig ME, Hanas R, Acerini CL, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Assessment and monitoring of glycemic control in children and adolescents with diabetes. Pediatric Diabetes. 2014;15 Suppl 20:102-14.

20. Anderson B, Ho J, Brackett J, Finkelstein D, Laffel L. Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus. The Journal of Pediatrics. 1997;130(2):257-65.

21. Schutt M, Kern W, Krause U, Busch P, Dapp A, Grziwotz R, et al. Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. Experimental and Clinical Endocrinology & Diabetes. 2006;114(7):384-8.

22. Driscoll KA, Johnson SB, Tang Y, Yang F, Deeb LC, Silverstein JH. Does blood glucose monitoring increase prior to clinic visits in children with type 1 diabetes? Diabetes Care. 2011;34(10):2170-3.

23. Langendam M, Luijf YM, Hooft L, Devries JH, Mudde AH, Scholten RJ. Continuous glucose monitoring systems for type 1 diabetes mellitus. The Cochrane Database of Systematic Reviews. 2012;1:CD008101.

24. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study G, Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. The New England Journal of Medicine. 2008;359(14):1464-76.

25. Peyrot M, Rubin RR. Perceived medication benefits and their association with interest in using inhaled insulin in type 2 diabetes: a model of patients' cognitive framework. Patient Preference and Adherence. 2011;5:255-65.

26. Ferrannini E. Physiology of glucose homeostasis and insulin therapy in type 1 and type 2 diabetes. Endocrinology and metabolism clinics of North America. 2012;41(1):25-39.

27. Malik FS, Taplin CE. Insulin therapy in children and adolescents with type 1 diabetes. Paediatric Drugs. 2014;16(2):141-50.

28. Liu LL, Lawrence JM, Davis C, Liese AD, Pettitt DJ, Pihoker C, et al. Prevalence of overweight and obesity in youth with diabetes in USA: the SEARCH for Diabetes in Youth study. Pediatric Diabetes. 2010;11(1):4-11.

29. Pankowska E, Blazik M, Dziechciarz P, Szypowska A, Szajewska H. Continuous subcutaneous insulin infusion vs. multiple daily injections in children with type 1 diabetes: a systematic review and meta-analysis of randomized control trials. Pediatric Diabetes. 2009;10(1):52-8.

30. Hirose M, Beverly EA, Weinger K. Quality of life and technology: impact on children and families with diabetes. Current Diabetes Reports. 2012;12(6):711-20.

31. Yeh HC, Brown TT, Maruthur N, Ranasinghe P, Berger Z, Suh YD, et al. Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: a systematic review and meta-analysis. Annals of Internal Medicine. 2012;157(5):336-47.

32. Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J. Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. The Cochrane Database of Systematic Reviews. 2010(1):CD005103.

33. Garvey K, Wolfsdorf JI. The Impact of Technology on Current Diabetes Management. Pediatric Clinics of North America. 2015;62(4):873-88.

34. Harris MA, Hood KK, Mulvaney SA. Pumpers, skypers, surfers and texters: technology to improve the management of diabetes in teenagers. Diabetes, Obesity & Metabolism. 2012;14(11):967-72.

35. Danne T, Mortensen HB, Hougaard P, Lynggaard H, Aanstoot HJ, Chiarelli F, et al. Persistent differences among centers over 3 years in glycemic control and hypoglycemia in a study of 3,805 children and adolescents with type 1 diabetes from the Hvidore Study Group. Diabetes Care. 2001;24(8):1342-7.

36. Hood KK, Peterson CM, Rohan JM, Drotar D. Association between adherence and glycemic control in pediatric type 1 diabetes: a meta-analysis. Pediatrics. 2009;124(6):e1171-9.

37. McWilliams JM, Meara E, Zaslavsky AM, Ayanian JZ. Differences in control of cardiovascular disease and diabetes by race, ethnicity, and education: U.S. trends from 1999 to 2006 and effects of medicare coverage. Annals of Internal Medicine. 2009;150(8):505-15.

38. Anderson BJ, McKay SV. Barriers to glycemic control in youth with type 1 diabetes and type 2 diabetes. Pediatric Diabetes. 2011;12(3 Pt 1):197-205.

39. Yach D (2003) Adherence to long-term therapies - Evidence for action. World Health Organization.

40. Johnson SB. Methodological issues in diabetes research. Measuring adherence. Diabetes Care. 1992;15(11):1658-67.

41. Levine BS, Anderson BJ, Butler DA, Antisdel JE, Brackett J, Laffel LM. Predictors of glycemic control and short-term adverse outcomes in youth with type 1 diabetes. The Journal of Pediatrics. 2001;139(2):197-203.

42. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care. 1986;24(1):67-74.

43. Vitolins MZ, Rand CS, Rapp SR, Ribisl PM, Sevick MA. Measuring adherence to behavioral and medical interventions. Controlled Clinical Trials. 2000;21(5 Suppl):188S-94S.

44. Pladevall M, Williams LK, Potts LA, Divine G, Xi H, Lafata JE. Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. Diabetes Care. 2004;27(12):2800-5.

45. Donahoo WT, Bessesen DH, Higbee DR, Lei S, Grunwald GK, Higgins JA. Serum lithium concentration can be used to assess dietary compliance in adults. The Journal of Nutrition. 2004;134(11):3133-6.

46. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. Clinical Therapeutics. 1999;21(6):1074-90; discussion 3.

47. Norell SE. Accuracy of patient interviews and estimates by clinical staff in determining medication compliance. Social Science & Medicine Part E, Medical Psychology. 1981;15(1):57-61.

48. Johnson SB, & Carlson, D. N. (2004). Medical regimen adherence: Concepts, assessment, and interventions. In J. M. Raczynski & L. C. Leviton (Eds.), Handbook of Clinical Health Psychology, Vol. 2: Disorders of Behavior and Health (pp. 329–354). Washington, DC: American Psychological Association Press.

49. Telo GH, de Souza MS, Schaan BD. Cross-cultural adaptation and validation to Brazilian Portuguese of two measuring adherence instruments for patients with type 1 diabetes. Diabetology & Metabolic Syndrome. 2014;6:141.

50. Quittner AL, Modi AC, Lemanek KL, Ievers-Landis CE, Rapoff MA. Evidence-based assessment of adherence to medical treatments in pediatric psychology. Journal of Pediatric Psychology. 2008;33(9):916-36; discussion 37-8.

51. Mortensen HB, Hougaard P. Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidore Study Group on Childhood Diabetes. Diabetes Care. 1997;20(5):714-20.

52. Svoren BM, Volkening LK, Butler DA, Moreland EC, Anderson BJ, Laffel LM. Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes. The Journal of Pediatrics. 2007;150(3):279-85.

53. Duke DC, Harris MA. Executive function, adherence, and glycemic control in adolescents with type 1 diabetes: a literature review. Current Diabetes Reports. 2014;14(10):532.

54. Johnson SB, Kelly M, Henretta JC, Cunningham WR, Tomer A, Silverstein JH. A longitudinal analysis of adherence and health status in childhood diabetes. Journal of Pediatric Psychology. 1992;17(5):537-53.

55. Hassan K, Loar R, Anderson BJ, Heptulla RA. The role of socioeconomic status, depression, quality of life, and glycemic control in type 1 diabetes mellitus. The Journal of Pediatrics. 2006;149(4):526-31.

56. Lernmark B, Persson B, Fisher L, Rydelius PA. Symptoms of depression are important to psychological adaptation and metabolic control in children with diabetes mellitus. Diabetic Medicine. 1999;16(1):14-22.

57. Leonard BJ, Jang YP, Savik K, Plumbo PM, Christensen R. Psychosocial factors associated with levels of metabolic control in youth with type 1 diabetes. Journal of Pediatric Nursing. 2002;17(1):28-37.

58. Korczak DJ, Pereira S, Koulajian K, Matejcek A, Giacca A. Type 1 diabetes mellitus and major depressive disorder: evidence for a biological link. Diabetologia. 2011;54(10):2483-93.

59. Northam EA, Matthews LK, Anderson PJ, Cameron FJ, Werther GA. Psychiatric morbidity and health outcome in Type 1 diabetes--perspectives from a prospective longitudinal study. Diabetic Medicine. 2005;22(2):152-7.

60. Kongkaew C, Jampachaisri K, Chaturongkul CA, Scholfield CN. Depression and adherence to treatment in diabetic children and adolescents: a systematic review and meta-analysis of observational studies. European Journal of Pediatrics. 2014;173(2):203-12.

61. Sivertsen B, Petrie KJ, Wilhelmsen-Langeland A, Hysing M. Mental health in adolescents with Type 1 diabetes: results from a large population-based study. BMC Endocrine Disorders. 2014;14:83.

62. Johnson B, Eiser C, Young V, Brierley S, Heller S. Prevalence of depression among young people with Type 1 diabetes: a systematic review. Diabetic Medicine. 2013;30(2):199-208.

63. Silverstein J, Cheng P, Ruedy KJ, Kollman C, Beck RW, Klingensmith GJ, et al. Depressive Symptoms in Youth With Type 1 or Type 2 Diabetes: Results of the Pediatric Diabetes Consortium Screening Assessment of Depression in Diabetes Study. Diabetes Care. 2015;38(12):2341-3.

64. Ducat L, Rubenstein A, Philipson LH, Anderson BJ. A review of the mental health issues of diabetes conference. Diabetes Care. 2015;38(2):333-8.

65. Garvey KC, Markowitz JT, Laffel LM. Transition to adult care for youth with type 1 diabetes. Current Diabetes Reports. 2012;12(5):533-41.

66. Wysocki T, Nansel TR, Holmbeck GN, Chen R, Laffel L, Anderson BJ, et al. Collaborative involvement of primary and secondary caregivers: associations with youths' diabetes outcomes. Journal of Pediatric Psychology. 2009;34(8):869-81.

67. Weissberg-Benchell J, Antisdel-Lomaglio J. Diabetes-specific emotional distress among adolescents: feasibility, reliability, and validity of the problem areas in diabetes-teen version. Pediatric Diabetes. 2011;12(4 Pt 1):341-4.

68. Huang Y, Wei X, Wu T, Chen R, Guo A. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. BMC Psychiatry. 2013;13:260.

69. Katon WJ, Lin EH, Von Korff M, Ciechanowski P, Ludman EJ, Young B, et al. Collaborative care for patients with depression and chronic illnesses. The New England Journal of Medicine. 2010;363(27):2611-20.

70. Bogner HR, de Vries HF. Integrating type 2 diabetes mellitus and depression treatment among African Americans: a randomized controlled pilot trial. The Diabetes Educator. 2010;36(2):284-92.

71. Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Annals of Family Medicine. 2012;10(1):15-22.

72. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE. Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. Diabetic Medicine. 2005;22(10):1379-85.

ARTIGO 1

Predictors of Changing Insulin Requirements and Glycemic Control in Children, Adolescents, and Young Adults with Type 1 Diabetes

Insulin dose and HbA1c trajectories in T1D

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Abstract

Objective: This study aimed to investigate trajectories of daily insulin requirements and glycemic control in youth with type 1 diabetes, as well as to identify factors associated with changing insulin needs and deterioration in glycemic control.

Research Design and Methods: The study sample was a dynamic cohort of 635 youth with type 1 diabetes at a single pediatric diabetes center observed during 20 years of follow-up. Bivariate and multivariable analyses were performed to evaluate the impact of sex, insulin regimen, and weight status on glycemic control and daily insulin dose according to age, from age 7 to 24.

Results: At the first observation, participants had a mean age of 9.7±3.0 years and mean diabetes duration of 2.5±2.1 years. Participants provided a mean of 12.0±4.6 years of hemoglobin A1c (HbA1c) observation time. Females had higher daily insulin doses (units/kg) than males between the ages of 8-13 years ($P \leq 0.001$) whereas males had higher units/kg than females between the ages of 16-21 years ($P<0.05$). HbA1c levels were higher in females than males beginning at age 16 and persisting to age 24 ($P \leq 0.01$). Pump therapy was associated with lower units/kg and HbA1c levels than multiple daily injection therapy throughout childhood, adolescence, and emerging adulthood. Although HbA1c levels did not differ between overweight/obese and normal weight youth, overweight/obese youth had higher units/kg from age 8 to 13 ($P<0.04$).

Conclusions: This long-term longitudinal assessment provides an opportunity to identify factors predictive of insulin requirements and deteriorating glycemic control in type 1 diabetes, which allows providers to give added attention to youth with non-modifiable factors such as female sex and consideration to modifiable factors such as insulin delivery method.

Key words: type 1 diabetes; youth; daily insulin dose; glycemic control; trajectories

INTRODUCTION

Childhood, adolescence, and emerging adulthood are developmental stages that impact insulin requirements and glycemic control in patients with type 1 diabetes (1). Optimizing glycemic control substantially reduces the risk of microvascular and macrovascular complications (2, 3); however, achieving the recommended American Diabetes Association target levels of hemoglobin A1c (HbA1c) of <7.5% for patients <18 years old and <7% for young adults is still a challenge (4, 5). As noted in previous cohort studies involving youth with type 1 diabetes, poor glycemic control has been associated with older age, black race, and longer diabetes duration (6). However, many studies designed to analyze predictors of deterioration in glycemic control during childhood and adolescence have been limited by a short duration of follow-up (7-9), small sample size (10-14), and limited numbers of factors evaluated (10, 13, 14).

The interaction between insulin requirements and glycemic control needs to be further elucidated. Although several studies have addressed the mechanisms of insulin resistance in youth with type 1 diabetes (9, 15-17), the natural course of insulin requirements during childhood, adolescence, and emerging adulthood, as well as factors related to insulin dose requirements, is still not entirely understood. It is recognized that obesity impairs insulin action (18). Other reports have shown that females have higher insulin requirements than males during adolescence due to lower insulin sensitivity in girls, likely related to their increasing adiposity and decreasing physical activity during puberty (19, 20). Additionally, insulin pump has been associated with lower insulin requirements (16, 17, 19). However, the impact of weight, sex, and regimen on insulin requirements, as well as the trajectories of insulin dose and HbA1c according to age would benefit from further study.

In an effort to identify factors associated with insulin dose requirements and deterioration of glycemic control during childhood, adolescence, and young adulthood, we sought to investigate age trajectories of daily insulin dose and glycemic control in young persons with type 1 diabetes. We also sought to identify demographic and clinical characteristics associated with the trajectories of insulin dose and glycemic control. Understanding the impact of such characteristics on insulin requirements and HbA1c levels may inform approaches to improve glycemic control during childhood, adolescence, and young adulthood.

RESEARCH DESIGN AND METHODS

Subjects

We compiled a dynamic cohort of youth with type 1 diabetes identified by their enrollment in five short term non-interventional studies at a single pediatric diabetes center. These investigations provided an opportunity for rigorous data collection and careful ascertainment of clinical and demographic characteristics. All participants included in this analysis met the following inclusion criteria: duration of type 1 diabetes of ≥1 year and daily insulin dose ≥0.5 units/kg at first included observation; follow up for ≥1 year; and two or more observations including data on daily insulin dose and HbA1c. The local Institutional Review Board approved retrospective and prospective capture of data for the present study, and all youth/parents signed informed assent/consent, respectively, at the time of the short-term investigations.

Measures

Trained research staff reviewed paper and electronic medical records and extracted demographic and clinical data from participants' clinic visits that occurred during a period of 20 years from January 1993 until December 2013. Glycemic control was assessed by HbA1c, which was performed in a clinical laboratory using an assay standardized to the Diabetes Control and Complications Trial (ref. range 4.0-6.0%). Daily insulin dose was captured as units/day by clinicians report for youth under injection therapy and, for pump users, by pump downloads when available or clinicians report if pump data not available. Data were then converted to units/kg/day. Insulin regimen was classified as use of insulin pump or multiple daily injections. For youth <20 years of age, we calculated age- and sex-adjusted body mass index (BMI) percentiles using normative data from the U.S. Centers for Disease Control and Prevention (21). After age 20, BMI was calculated as weight in kg divided by height in m^2. Categories of weight status were defined as: underweight/normal weight (BMI <85^{th} percentile in youth <20 years of age; BMI <25 kg/m^2 for those ≥20 years of age) and overweight/obese (BMI ≥85^{th} percentile in youth <20 and BMI ≥25 kg/m^2 for those ≥20 years of age). Participants were also assessed in three age categories of 7 to 13, 14-18, and 19-24 in order to account for differences in developmental stages, with the first group representing pre-pubertal to early pubertal participants, 14 to 18 year olds representing pubertal and ending puberty participants, and 19 to 24 year olds representing post-pubertal participants and emerging adults (22). These age groupings also provided sufficient data for analyses.

Data analysis

Analyses were performed using SAS (version 9.2, SAS Institute, Inc., Cary, NC, USA). Descriptive data of the sample are presented at the initial and final daily insulin dose and/or HbA1c observation. Descriptive data are presented as mean ± standard deviation (SD) with ranges for continuous variables as percentages for categorical variables. Statistical analyses included unpaired t-test for continuous variables and Chi-square test for categorical variables. Daily insulin dose as units/kg and HbA1c results were captured within 6 months of each participant's birthday (birthday ±6 months). Annualized units/kg and HbA1c values were calculated for each participant as the mean of all available values within 6 months of the birthday from ages 7 to 24 years.

Bivariate analyses included the impact of sex, insulin regimen, and weight status on annual mean daily insulin dose and HbA1c according to age. In addition, we evaluated annual mean daily insulin dose and HbA1c as dependent variables in multivariable analyses. Longitudinal mixed modeling assessed the impact of different predictors of units/kg and HbA1c according to age, using unstructured covariance matrices for the repeated measure variables. In each of the models predicting daily insulin dose and HbA1c over time according to age, covariates included sex, age at diagnosis of type 1 diabetes, insulin regimen, weight status, and calendar year. The variable of calendar year was included to control for historical changes in diabetes treatment and glycemic control, given the changing availability of insulin analogs and technologies over time. In order to evaluate relationships between daily insulin dose and HbA1c, we created categorical variables for units/kg and HbA1c; in the model predicting daily insulin dose, we stratified HbA1c into two groups according to the overall mean HbA1c per person (<9 and ≥9%) and in the model predicting HbA1c, we stratified daily insulin dose into two groups based on the overall mean units/kg per person (<1 and ≥1 units/kg). An alpha level of <0.05 determined statistical significance.

RESULTS

Cohort characteristics

This study included a dynamic cohort of 635 youth with type 1 diabetes identified at a single diabetes center and who were followed over time. At the time of entry into the cohort, participants had a mean age of 9.7±3.0 years and mean duration of type 1 diabetes of 2.5±2.1 years. All were diagnosed in childhood with a mean age of onset of diabetes of 7.2±3.5 years; Approximately half of the cohort were female (54%) and the majority (91%) were Caucasian (see table 1). Insulin pump use increased from 4% at the time of entry into the cohort to 37% at last patient observation.

Mean duration of observations from first to last daily insulin dose was 10.7±4.3 years. The mean number of insulin dose observations per participant was 30.0±13.7, with an average of 4.4±3.7 months between insulin dose observations. At first observation, the mean daily insulin dose was 0.8±0.2 units/kg; at last observation, the mean daily insulin dose was 0.9±0.3 units/kg. Mean duration of observation from first to last HbA1c was 12.0±4.6 years. The mean number of HbA1c observations per participant was 34.9±15.4, with an average of 4.2±4.5 months between HbA1c observations. At first observation, the mean HbA1c was 9.0±1.7% (75±4 mmol/mol); at last observation, the mean HbA1c was 8.9±1.7% (74±4 mmol/mol). Due to sparse availability of data under age 7 and above age 24 years, bivariate and multivariable analyses only included participants between the ages of 7 and 24 years.

Insulin requirements trajectories

To evaluate insulin dose trajectories according to age, we assessed the daily insulin dose as units/kg by sex (female vs. male), insulin regimen (pump vs. injection therapy), and weight status (under/normal weight vs. overweight/obese). The mean daily insulin dose analysis over time by sex revealed that females had significantly higher units/kg than males between the ages of 8-13 years ($P \leq 0.001$) whereas males had significantly higher units/kg than females between the ages of 16-21 years ($P < 0.05$) (see figure 1A). In the analysis of daily insulin dose by regimen, those receiving insulin pump therapy had significantly lower units/kg than those receiving multiple daily injection therapy throughout childhood, adolescence, and emerging adulthood ($P \leq 0.01$) (Figure 1B). In the daily insulin dose trajectory analysis by weight status, those who were overweight/obese youth had significantly greater units/kg than those who were normal weight youth at ages 8-13 years ($P < 0.04$) (Figure 1C).

Glycemic control trajectories

To evaluate glycemic control trajectories according to age, we assessed HbA1c by sex, insulin regimen, and weight status, as above. The mean HbA1c over time by sex revealed that females had significantly higher HbA1c levels than males from ages 16 to 24

($P \leq 0.01$) (see figure 2A). In the HbA1c analysis by regimen, those receiving pump therapy compared with multiple daily injections had significantly lower HbA1c values throughout childhood, adolescence, and emerging adulthood ($P \leq 0.02$) (Figure 2B). In contrast, the HbA1c trajectory analysis comparing overweight/obese with normal weight youth yielded no differences over time except for a modestly higher HbA1c in overweight/obese youth at age 10 ($P=0.03$) (Figure 2C).

Multivariable analyses

Given that the shapes of the daily insulin dose trajectories were not linear in the bivariate analyses, with the trajectories resembling quadratic-cubic patterns, we performed separate longitudinal multivariable analyses in three age groups: 7-13, 14-18, and 19-24 years of age (see table 2A). The generalized mixed models predicting daily insulin dose confirmed differences in the impact of sex on daily insulin doses according to age with females having significantly higher daily insulin doses than males at ages 7-13 while males had higher daily insulin doses than females at ages 19-24. Similar to the bivariate analyses for insulin regimen, insulin pump therapy predicted lower HbA1c levels in the longitudinal models for all three age groups. Overweight and obesity was only predictive of higher units/kg in the youngest age group, those 7-13 years old. Attained age, age at diagnosis of type 1 diabetes, and calendar year had variable effects on daily insulin dose across the three age groups. As age increased, daily insulin dose increased in the youngest age group, the 7-13 year olds, while as age increased, daily insulin dose decreased in the 14-18 year olds and the 19-24 year olds. Similarly, as age at onset of type 1 diabetes increased, daily insulin dose decreased in the two younger age groups. Finally, daily insulin dose was lower for youth with HbA1c values <9% in the two older age groups. Similarly, given the variable HbA1c trajectories according to sex, insulin regimen, and weight status across the age span of 7 to 24 years, we performed separate longitudinal multivariable analyses in the same three age groups as above: 7-13, 14-18, and 19-24 years of age (see table 2B). Generalized linear mixed models indicated that female sex predicted significantly higher HbA1c in emerging adults, ages 19-24. Insulin pump therapy predicted significantly lower HbA1c in all three age groups. Surprisingly, overweight/obesity predicted lower HbA1c in the 14-18 year olds. Attained age was only predictive of HbA1c in the two older groups, where ages closer to the latter adolescent years were related to higher HbA1c. Notably, daily insulin dose <1 unit/kg was significantly predictive of lower HbA1c in all 3 age groups. Age at diagnosis and calendar year had modest effects on HbA1c.

CONCLUSIONS

Suboptimal glycemic control is a common problem in youth with type 1 diabetes (23). In this long-term dynamic cohort, age trajectories of insulin dose differed according to sex, insulin regimen, and weight status while age trajectories of glycemic control differed according to sex and insulin regimen. Insulin doses were higher during the pubertal years, as expected. HbA1c levels were higher in females in late adolescence and emerging adulthood and lower in insulin pump users over time, while overweight/obesity did not seem to negatively impact the HbA1c levels across ages. As age at diagnosis increased during childhood and adolescence, insulin dose requirement decreased as might be expected, given more aggressive beta cell destruction at younger ages (6). Insulin pump users and normal weight youth also required lower doses of insulin. Our results also showed that suboptimal glycemic control persisted over time. This study provides opportunities to identify characteristics to predict insulin requirements and deterioration in glycemic control in children, adolescents, and young adults with type 1 diabetes.

Adolescence is a period of cognitive, psychosocial, and physical maturation. The complex series of physical changes known as puberty may impact glycemic control in youth with type 1 diabetes (24). With the onset of puberty, glycemic control usually deteriorates despite concomitant increases in insulin doses (23, 25). Reaching adulthood is then associated with decreases in insulin requirement and, hopefully, improved glycemic control, although recent data from the Type 1 Diabetes Exchange indicates that glycemic control does not appear to improve until the latter half of the third decade of life (4). Adolescents in this registry averaged a 9.0 percent HbA1c compared with the 9.5 percent registered by the same age group during the Diabetes Control and Complications Trial (2). Similarly to this finding, in our study, calendar year also did not have an impact on glycemic control during adolescence, and suboptimal glycemic control persisted over time, indicating that advances in diabetes management over the past two decades have been less successful in overcoming the special challenges in managing adolescents with type 1 diabetes.

The rising insulin requirement during the early adolescent years, over the period of pubertal growth and development (23), corresponds to the physiological insulin resistance observed during puberty. Considering that puberty happens earlier in females than males (26), it is reasonable to expect insulin requirements to increase in females at a younger age than in males (19). Indeed, in our study, higher insulin doses were observed in females at younger ages than males. Of note, glycemic control did not differ by sex in childhood or early adolescence but only deteriorated in females in comparison to males in emerging adulthood (27). The observation that glycemic control deteriorates in the latter part of adolescence and during emerging adulthood suggests that puberty-associated insulin resistance is likely well managed with increased insulin dosing. Other factors, such as adherence and psychosocial issues, likely contribute to the deterioration in glycemic control that follows the period of pubertal growth and development, when family involvement in diabetes management is waning. Also, greater self-care on the part of the older teen and young adult is expected but may not materialize due to many competing social, emotional, and academic demands (27, 28).

Several studies have assessed the impact of insulin pump therapy on glycemic control in children with type 1 diabetes (29-31), and most of them have reported modest improvements in glycemic control with pump therapy, especially in the period immediately following pump initiation (31). Considering this potential benefit, insulin pump may be considered a modifiable factor that could positively impact glycemic control, particularly during adolescence when insulin needs are increasing due to the insulin resistance related to puberty (23). In our study, we found that insulin pump therapy was associated with better glycemic control and lower insulin doses across all ages. Although insulin pump use considerably increased from first to last observation, glycemic control did not improve over time. Insulin pump may be helping to prevent the expected glycemic control deterioration among adolescents in this study (4); however, our findings likely represent a better adherence profile associated with youth who were previously selected for advanced technology use. The lack of information regarding adherence, as well demographics such as socioeconomic status, limits interpretation of possible insulin pump benefit among adolescents. Moreover, with regard to insulin dose, in agreement with previous studies, age seems to be an important determinant of daily insulin dose in youth with type 1 diabetes, but differences in insulin doses between pump and injection therapy seemed to be maintained in childhood, adolescence, and young adulthood. It might be explained by the observation that insulin pump could deliver fasting and prandial insulin in a more physiological fashion than injection therapy (19).

Historically, overweight and obesity were not frequently seen in youth with type 1 diabetes. However, due to the recent epidemic of pediatric obesity (32), overweight and obesity in youth with type 1 diabetes are now more common, occurring in approximately one third of youth with type 1 diabetes, and can contribute to substantial health consequences (33). Data indicate that rates of overweight and obesity are similar to the rates seen in the general pediatric population (34). In our study, from first to last observation, overweight/obesity increased from 31 to 50%. It is well known that obesity increases insulin resistance, and our findings highlight the observation that overweight/obese youth require higher insulin doses, especially during adolescence when insulin resistance is present due to pubertal needs; however, the association of BMI, HbA1c, daily insulin dose, and insulin resistance is complex and still not completely understood. In contrast to some literature, in which increased BMI has been associated with higher HbA1c levels (35), there was no clear difference in glycemic control between normal weight and overweight/obese youth in our study. However, the lack of information regarding demographics, physical activity, adherence, and psychosocial issues limit the interpretations of this result.

It is important that we do not overstate our findings. First, this study was based on longitudinal follow-up data, mainly collected retrospectively, from a single center with many measurements obtained as part of routine clinical care rather than as part of a rigorous research study. Lack of information with regard to demographics, adherence, and clinical characteristics limits the interpretation of glycemic control trajectories over time according to modifiable factors such as weight and insulin pump, especially as considering pump to have a positive impact on glycemic control. Also, insulin dose was captured mostly electronically for pump users and by self-report for youth under injection therapy. Although reported insulin doses are the basis for suggested dose adjustments during outpatient visits in youth under injection therapy (19), reported insulin dose may systematically differ from actually administered insulin dose. Finally, weight status assumptions were limited by the lack of information regarding diet and exercises. Tanner stage was also not documented systematically in all patients and puberty assumptions were based on age associations. However, to our knowledge, this is one of the largest cohort studies of youth with type 1 diabetes with extensive data collectively longitudinally; thus, these findings provide important information regarding trajectories of insulin dosing and glycemic control across childhood, adolescence, and emerging adulthood. Our findings should be confirmed in future studies aimed to assess the impact of demographics, clinical characteristics, and psychosocial issues on glycemic control over time.

In conclusions, the knowledge from this study adds to the literature and highlights predictors of changing insulin dose requirements and glycemic control deterioration according to age in youth with type 1 diabetes. Female sex, later adolescence and young adulthood, and injection therapy seemed to have a negative impact on glycemic control. Our findings provide opportunities to identify modifiable and non-modifiable factors associated with glycemic control deterioration in order to improve glycemic control in youth with type 1 diabetes. Further studies are needed to investigate the impact of demographics and features such as adherence on glycemic control and insulin dose in adolescents.

Author Contributions: G.H.T. researched data, analyzed data, and wrote the manuscript. C.E.D. and M.L.K. researched data, analyzed data, and reviewed the manuscript. L.K.V. researched data and edited the manuscript. L.M.L. researched data, analyzed data, and edited the manuscript. L.M.L. is the guarantor of this work. All authors have approved the final version of this manuscript.

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The authors have no relevant conflict of interest to disclose related to this research.

References

1. Petitti DB, Klingensmith GJ, Bell RA, Andrews JS, Dabelea D, Imperatore G, et al. Glycemic control in youth with diabetes: the SEARCH for diabetes in Youth Study. The Journal of Pediatrics. 2009;155(5):668-72 e1-3.

2. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. The New England Journal of Medicine. 1993;329(14):977-86.

3. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. The New England Journal of Medicine. 2005;353(25):2643-53.

4. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, et al. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. Diabetes Care. 2015;38(6):971-8.

5. Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. 2016;39 Suppl 1:S4-5.

6. Levine BS, Anderson BJ, Butler DA, Antisdel JE, Brackett J, Laffel LM. Predictors of glycemic control and short-term adverse outcomes in youth with type 1 diabetes. The Journal of Pediatrics. 2001;139(2):197-203.

7. Rohan JM, Rausch JR, Pendley JS, Delamater AM, Dolan L, Reeves G, et al. Identification and prediction of group-based glycemic control trajectories during the transition to adolescence. Health Psychology. 2014;33(10):1143-52.

8. Hilliard ME, Holmes CS, Chen R, Maher K, Robinson E, Streisand R. Disentangling the roles of parental monitoring and family conflict in adolescents' management of type 1 diabetes. Health Psychology. 2013;32(4):388-96.

9. King PS, Berg CA, Butner J, Butler JM, Wiebe DJ. Longitudinal trajectories of parental involvement in Type 1 diabetes and adolescents' adherence. Health Psychology. 2014;33(5):424-32.

10. Luyckx K, Seiffge-Krenke I. Continuity and change in glycemic control trajectories from adolescence to emerging adulthood: relationships with family climate and self-concept in type 1 diabetes. Diabetes Care. 2009;32(5):797-801.

11. Lawes T, Franklin V, Farmer G. HbA1c tracking and bio-psychosocial determinants of glycaemic control in children and adolescents with type 1 diabetes: retrospective cohort study and multilevel analysis. Pediatric Diabetes. 2014;15(5):372-83.

12. Frey MA, Templin T, Ellis D, Gutai J, Podolski CL. Predicting metabolic control in the first 5 yr after diagnosis for youths with type 1 diabetes: the role of ethnicity and family structure. Pediatric Diabetes. 2007;8(4):220-7.

13. Helgeson VS, Siminerio L, Escobar O, Becker D. Predictors of metabolic control among adolescents with diabetes: a 4-year longitudinal study. Journal of Pediatric Psychology. 2009;34(3):254-70.

14. Helgeson VS, Snyder PR, Seltman H, Escobar O, Becker D, Siminerio L. Brief report: trajectories of glycemic control over early to middle adolescence. Journal of Pediatric Psychology. 2010;35(10):1161-7.

15. Yki-Jarvinen H, Koivisto VA. Insulin sensitivity in newly diagnosed type 1 diabetics after ketoacidosis and after three months of insulin therapy. The Journal of Clinical Endocrinology and Metabolism. 1984;59(3):371-8.

16. Lager I, Lonnroth P, von Schenck H, Smith U. Reversal of insulin resistance in type I diabetes after treatment with continuous subcutaneous insulin infusion. British Medical Journal. 1983;287(6406):1661-4.

17. Yki-Jarvinen H, Koivisto VA. Continuous subcutaneous insulin infusion therapy decreases insulin resistance in type 1 diabetes. The Journal of Clinical Endocrinology and Metabolism. 1984;58(4):659-66.

18. Kolterman OG, Insel J, Saekow M, Olefsky JM. Mechanisms of insulin resistance in human obesity: evidence for receptor and postreceptor defects. The Journal of Clinical Investigation. 1980;65(6):1272-84.

19. Wiegand S, Raile K, Reinehr T, Hofer S, Nake A, Rabl W, et al. Daily insulin requirement of children and adolescents with type 1 diabetes: effect of age, gender, body mass index and mode of therapy. European Journal of Endocrinology. 2008;158(4):543-9.

20. Chowdhury S. Puberty and type 1 diabetes. Indian Journal of Endocrinology and Metabolism. 2015;19(Suppl 1):S51-4.

21. Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, et al. 2000 CDC Growth Charts for the United States: methods and development. Vital and Health Statistics Series 11, Data from the national health survey. 2002(246):1-190.

22. Kelly A, Winer KK, Kalkwarf H, Oberfield SE, Lappe J, Gilsanz V, et al. Age-based reference ranges for annual height velocity in US children. The Journal of Clinical Endocrinology and Metabolism. 2014;99(6):2104-12.

23. Amiel SA, Sherwin RS, Simonson DC, Lauritano AA, Tamborlane WV. Impaired insulin action in puberty. A contributing factor to poor glycemic control in adolescents with diabetes. The New England Journal of Medicine. 1986;315(4):215-9.

24. Hofer SE, Raile K, Frohlich-Reiterer E, Kapellen T, Dost A, Rosenbauer J, et al. Tracking of metabolic control from childhood to young adulthood in type 1 diabetes. The Journal of Pediatrics. 2014;165(5):956-61 e1-2.

25. Swan KL, Weinzimer SA, Dziura JD, Steil GM, Voskanyan GR, Steffen AT, et al. Effect of puberty on the pharmacodynamic and pharmacokinetic properties of insulin pump therapy in youth with type 1 diabetes. Diabetes Care. 2008;31(1):44-6.

26. Sun SS, Schubert CM, Chumlea WC, Roche AF, Kulin HE, Lee PA, et al. National estimates of the timing of sexual maturation and racial differences among US children. Pediatrics. 2002;110(5):911-9.

27. Moreland EC, Tovar A, Zuehlke JB, Butler DA, Milaszewski K, Laffel LM. The impact of physiological, therapeutic and psychosocial variables on glycemic control in youth with type 1 diabetes mellitus. Journal of Pediatric Endocrinology & Metabolism. 2004;17(11):1533-44.

28. Chiang JL, Kirkman MS, Laffel LM, Peters AL, Type 1 Diabetes Sourcebook A. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. Diabetes Care. 2014;37(7):2034-54.

29. Kaufman FR, Halvorson M, Miller D, Mackenzie M, Fisher LK, Pitukcheewanont P. Insulin pump therapy in type 1 pediatric patients: now and into the year 2000. Diabetes/Metabolism Research and Reviews. 1999;15(5):338-52.

30. Tamborlane WV, Bonfig W, Boland E. Recent advances in treatment of youth with Type 1 diabetes: better care through technology. Diabetic Medicine. 2001;18(11):864-70.

31. Shashaj B, Sulli N. Difference in insulin usage patterns with pubertal development in children with type 1 diabetes during transition from multiple daily injections to continuous subcutaneous insulin infusion (CSII) and through the CSII treatment. Diabetes Technology & Therapeutics. 2009;11(12):767-74.

32. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014;311(8):806-14.

33. Minges KE, Whittemore R, Grey M. Overweight and obesity in youth with type 1 diabetes. Annual Review of Nursing Research. 2013;31:47-69.

34. Liu LL, Lawrence JM, Davis C, Liese AD, Pettitt DJ, Pihoker C, et al. Prevalence of overweight and obesity in youth with diabetes in USA: the SEARCH for Diabetes in Youth study. Pediatric Diabetes. 2010;11(1):4-11.

35. DuBose SN, Hermann JM, Tamborlane WV, Beck RW, Dost A, DiMeglio LA, et al. Obesity in Youth with Type 1 Diabetes in Germany, Austria, and the United States. The Journal of Pediatrics. 2015;167(3):627-32 e1-4.

Table 1 – ***Demographic and clinical characteristics of study participants***

	First observation (*N*=635)	**Last observation (*N*=635)**
Age (years)	9.7±3.0 (1.7-19.1)	21.8±4.3 (8.7-32.1)
Sex (% female)	54	-
Race/ethnicity (% Caucasian)	91	-
Age at type 1 diagnosis (years)	7.2±3.5	-
Diabetes duration (years)	2.5±2.1 (1.0-12.6)	14.6±5.0 (2.2-29.0)
HbA1c (%)	9.0±1.7 (5.5-20.6)	8.9±1.7 (5.8-15.8)
HbA1c (mmol/mol)	75±4 (37-201)	74±4 (40-149)
Daily insulin dose (units/kg)	0.8±0.2 (0.5-1.7)	0.9±0.3 (0.3-2.0)
Regimen (% pump use)	4	37
Weight status (% overweight/obese)	31	50
Calendar year (years range)	1993-2007	1997-2013

Data are mean ± SD (range) or %.

Table 2 – *Longitudinal multivariable model predicting annual daily insulin dose (units/kg) (A) and HbA1c (%) (B)*

(A) Daily insulin dose (units/kg)	**Effect estimate stratified by age**					
	7-13 years	***P* value**	**14-18 years**	***P* value**	**19-24 years**	***P* value**
Age (per 1 year increase)	0.06	<0.0001	-0.02	<0.0001	-0.02	<0.0001
Sex (female vs. male)	0.07	<0.0001	-0.03	0.07	-0.05	0.005
Age at diagnosis (per 1 year increase)	-0.01	<0.0001	-0.01	<0.0001	-0.01	0.09
HbA1c (<9% vs. ≥9%)	-0.01	0.39	-0.05	<0.001	-0.10	<0.0001
Regimen (pump vs. multiple daily injections)	-0.06	<0.0001	-0.13	<0.0001	-0.12	<0.0001
Weight status (overweight/obese vs. normal weight)	0.03	<0.001	0.01	0.31	-0.01	0.59
Calendar year (per year increase)	0.001	0.74	0.01	<0.001	0.01	0.02

(B) HbA1c (%)	**Effect estimate stratified by age**					
	7-13 years	***P* value**	**14-18 years**	***P* value**	**19-24 years**	***P* value**
Age (per 1 year increase)	-0.006	0.65	0.13	<0.0001	-0.05	0.01
Sex (female vs. male)	0.12	0.16	0.20	0.04	0.52	<0.0001
Age at diagnosis (per 1 year increase)	0.04	0.03	-0.03	0.11	-0.03	0.12
Daily insulin dose (<1 units/kg vs. ≥1 units/kg)	-0.53	<0.0001	-0.81	<0.0001	-0.63	<0.0001
Regimen (pump vs. multiple daily injections)	-0.26	<0.001	-0.44	<0.0001	-0.38	<0.0001
Weight status (overweight/obese vs. normal weight)	-0.04	0.41	-0.24	<0.0001	-0.14	0.03
Calendar year (per year increase)	-0.10	<0.0001	-0.009	0.47	0.01	0.56

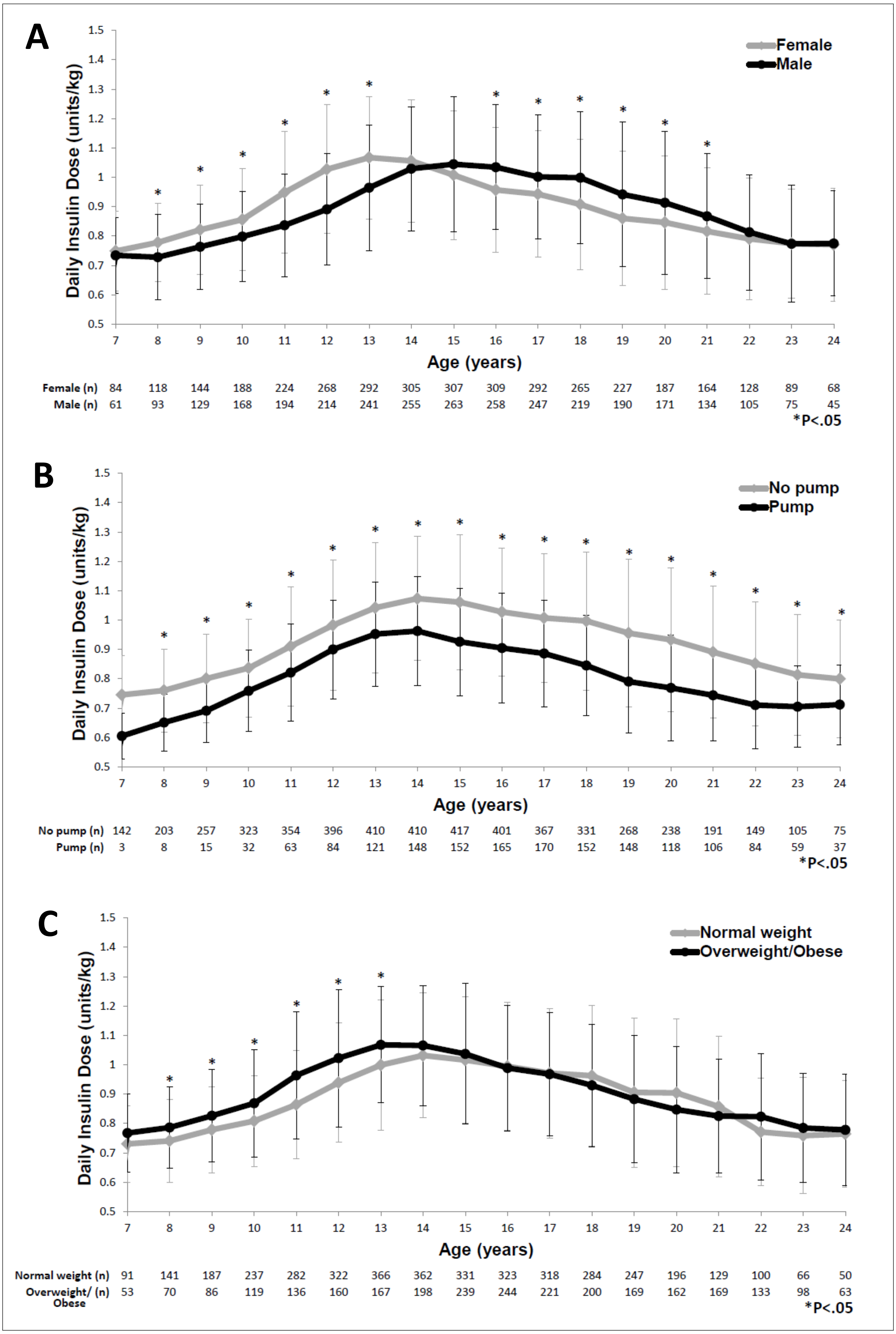

Figure 1 – ***Daily insulin dose trajectories by sex (A), regimen (B), and weight status (C)***

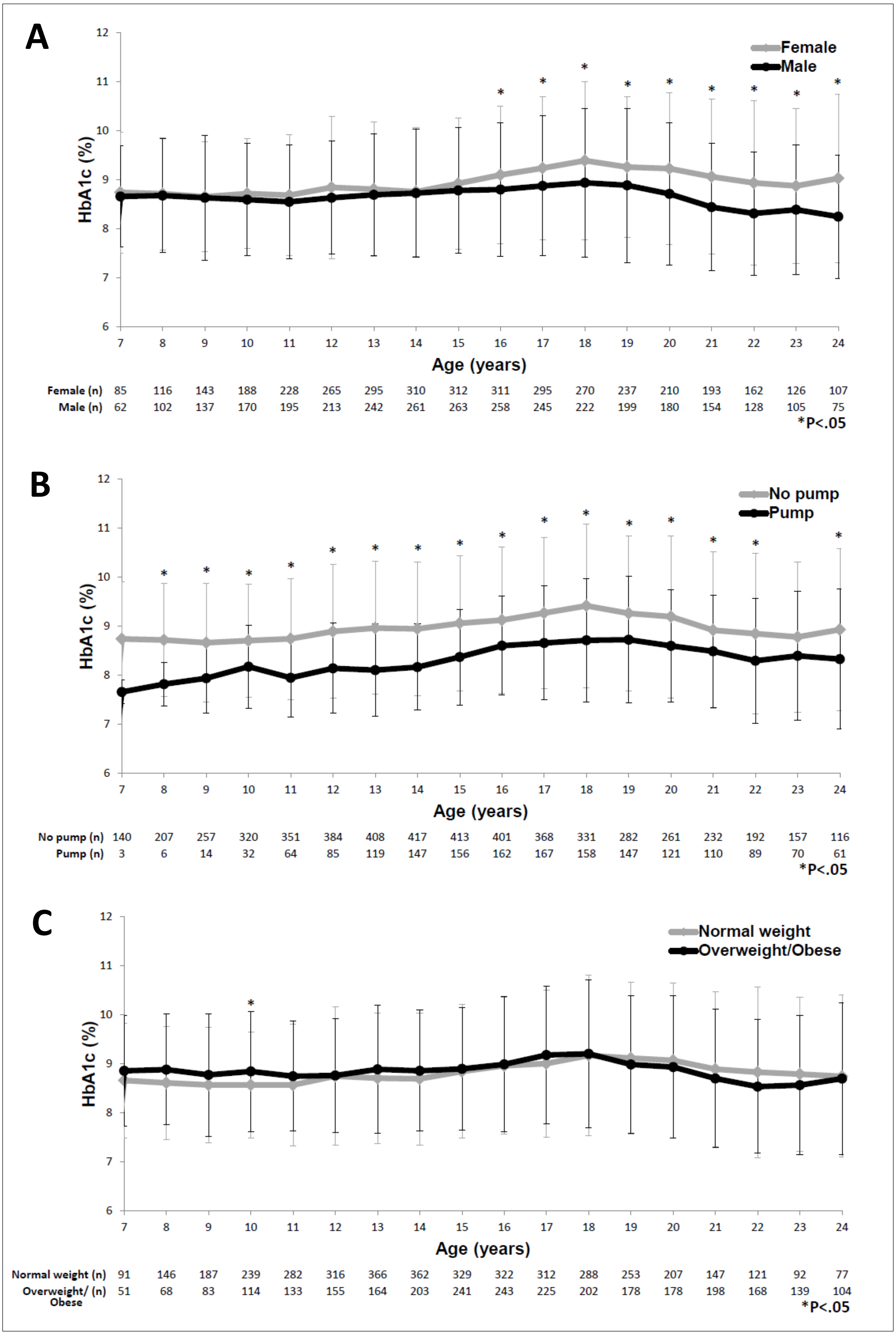

Figure 2 – ***HbA1c trajectories by sex (A), regimen (B), and weight status (C)***

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ARTIGO 2

Salient Characteristics of Youth with Type 1 Diabetes Initiating Continuous Glucose Monitoring

Youth with type 1 diabetes initiating CGM

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Abstract

Objective: Consistent continuous glucose monitoring (CGM) use is a challenge in youth with type 1 diabetes. This study aimed to investigate patient and family behavioral and clinical characteristics associated with interest in implementing CGM.

Research Design and Methods: In a cross-sectional study, we compared 120 youth interested in starting CGM (the CGM group) with a general sample of 238 youth with type 1 diabetes (the Standard group). Youth and their parents completed validated surveys assessing adherence to diabetes management, diabetes-specific family conflict, parent involvement in diabetes management, and youth quality of life. Demographic and clinical data were obtained from chart review and interview.

Results: Youth participants had a mean age of 13.0–2.8 years, diabetes duration of 6.3–3.4 years, and hemoglobin A1c (HbA1c) level of 8.2–1.0% (66–11 mmol/mol). Youth in the CGM group performed more frequent blood glucose monitoring, had lower HbA1c levels, and were more likely to be treated by continuous subcutaneous insulin infusion (CSII) and to be living in two-parent homes than youth in the Standard group. Compared with the Standard group, youth interested in wearing a CGM device and their parents reported greater adherence to diabetes management, less diabetes-specific family conflict, and higher youth quality of life. No differences were found between groups with respect to parent involvement in diabetes management by both youth and parent reports.

Conclusions: In efforts to enhance CGM uptake, it is important to address factors such as blood glucose monitoring frequency, CSII use, adherence, and diabetes-specific family conflict when considering youth with type 1 diabetes for CGM implementation.

Key words: Diabetes Mellitus, Type 1; Pediatrics; Continuous Glucose Monitoring; Patient Compliance; Medication Adherence; Quality of Life; Insulin Infusion Systems

INTRODUCTION

The management of type 1 diabetes places substantial physical demands on both patients and family members. The burdens are heightened owing to emotional demands such as fear of hypoglycemia and hyperglycemia. There are opportunities for potentially reducing these burdens with the use of new technologies, such as continuous glucose monitoring (CGM), which can assist in optimizing blood glucose levels (1). The advancements achieved in recent years with CGM provide substantial potential benefits for diabetes outcomes (2). Studies have identified that use of CGM improves glycemic control in patients with type 1 diabetes when the device is worn consistently (3-5); however, sustained CGM use has been shown to be difficult in pediatric patients (6,7). The recently published American Diabetes Association position statement on type 1 diabetes noted that CGM can reduce glycemic excursions in children; however, glycemic improvements are correlated with frequency of CGM use across all ages (8).

Despite opportunities afforded by CGM use, only 6–9% of youth appear to use CGM (9,10). There is a need to identify factors associated with successful CGM implementation as well as barriers to CGM use. Sustained use of technologies for diabetes management remains dependent on the patient’s active engagement and adherence to a complex management plan (11). One might expect that children versed in insulin pump therapy who perform frequent blood glucose monitoring may be ideal candidates for CGM use, as shown in one cross-sectional study (12). Diabetes-specific family stress and conflict may also be both potential drivers for and consequences of increasingly complex and demanding therapies such as CGM (13,14). However, there are likely many other factors that may be associated with CGM adoption by pediatric patients and families related to quality of life (2,15), fear of hypoglycemia (12), diabetes-related distress (6,16), and other behavioral barriers (11,14). Before exploring youth and family factors associated with sustained CGM use, it is important to gain improved greater understanding of the characteristics of youth and families preparing to begin CGM. Such knowledge may enhance opportunities to implement CGM in greater numbers of youth with type 1 diabetes (2).

In this study, we sought to investigate additional patient and family characteristics associated with interest in implementing CGM. We designed a cross-sectional study to explore differences between youth interested in using CGM and a general sample of youth with type 1 diabetes at the same diabetes clinic. We hypothesized that the percentage of youth and their families who are already engaged in intensive insulin therapy such as continuous subcutaneous insulin infusion (CSII) would be higher in the group preparing to begin CGM than in the general sample of youth with type 1 diabetes. We also hypothesized that youth interested in starting CGM would be more adherent and would report more parent involvement in diabetes management tasks than the general sample of youth with type 1 diabetes.

RESEARCH DESIGN AND METHODS

We compared characteristics of youth with type 1 diabetes beginning CGM (the CGM group) with a separate general sample of youth with type 1 diabetes (the Standard group) from the same pediatric diabetes clinic. In the CGM group, youth with type 1 diabetes and their caregivers were recruited to participate in a CGM family-focused teamwork intervention study designed to optimize CGM use. In the Standard group, youth with type 1 diabetes and their caregivers were recruited from the general clinic population at the same center to complete questionnaires at a single visit and did not receive intervention. In both groups, the data from only one parent were included in this analysis.

All participants included in these analyses met the following inclusion criteria: 8–17.9 years of age; type 1 diabetes duration of ≥1 year at enrollment; and documentation of daily insulin dose of ≥0.5 units/kg and hemoglobin A1c (HbA1c) level of 6.5–10% at a screening visit prior to enrollment. In addition, if a family enrolled multiple siblings with type 1 diabetes, data from the child with the longer diabetes duration were used. Entry criteria were harmonized between the two study samples. The electronic medical record and a parent–youth interview provided demographic and clinical data, all obtained by trained research staff. Glycemic control was assessed by HbA1c, which was performed in a clinical laboratory using a Diabetes Control and Complications Trial standardized assay (reference range, 4.0–6.0%). Uniform study procedures were used for collection of data regarding insulin regimen and daily insulin dose using pump downloads when available; if not available, both participant and clinician reported data were used. Blood glucose monitoring data were self-reported from parent–youth interviews.

The local Institutional Review Board approved the study protocols, and all youth/parents signed informed assent/ consent forms before beginning any study procedures. CGM group participants needed to complete a 1-week run-in period for inclusion in this analysis; however, all the data reported here were obtained during baseline assessment, prior to intervention group assignment and CGM implementation.

Measures

Youth and their caregivers independently completed the following previously validated assessment instruments. For all of the surveys, the total scores were adjusted to account for any missing responses.

Diabetes Management Questionnaire. The 20-item Diabetes Management Questionnaire (DMQ) (17) measures adherence to different diabetes management tasks on a 5-point response scale, with responses ranging from 1=almost never to 5=almost always. Scores range from 0 to 100. Higher scores indicate greater adherence.

Diabetes Family Conflict Scale. The 19-item Diabetes Family Conflict Scale (DFCS) (18) assesses diabetes-specific family conflict on a 3-point response scale, ranging from 1=almost never to 3=almost always. Previously published scoring methods for this survey result in total scores ranging from 19 to 57; however, in order to better calibrate the score to the other surveys used in this study, we normalized the total scores to a 0 to 100 scale. Higher scores indicate more diabetes-specific family conflict.

Diabetes Family Responsibility Questionnaire. The 17-item Diabetes Family Responsibility Questionnaire (DFRQ) (19) measures parent involvement in different diabetes management tasks. This questionnaire assesses who has primary responsibility for each task (1=child, 2=equal, or 3=parent). Previously published scoring methods for this survey result in total scores ranging from 17 to 51; however, we normalized the total scores to a 0–100 scale in order to better calibrate the results against the other measures. Higher scores indicate more parent involvement in diabetes management tasks.

Pediatric Quality of Life Inventory Generic Core Scales. The 23-item Pediatric Quality of Life Inventory (PedsQL) (20,21) measures youth self-report of generic quality of life and the caregiver's perception of the youth's quality of life in four domains: physical, emotional, social, and school functioning. The 5-point response scale ranges from 0=never a problem to 4=almost always a problem. Responses were linearly transformed and reverse-scored according to published scoring methods (20,21). Scores range from 0 to 100; higher scores indicate higher youth quality of life.

Data analysis

Analyses were performed using SAS software (version 9.2; SAS Institute, Inc., Cary, NC). Descriptive data are presented as mean ± SD values or percentages. Statistical analyses included an unpaired *t* test for continuous variables and Fisher's exact test for categorical variables. Youth and parent survey scores were compared using Spearman correlations and paired *t* tests. The survey scores were evaluated according to study group (CGM group vs. Standard group). An alpha level of ≤ 0.05 was used to determine statistical significance.

RESULTS

Participant characteristics

In total, 457 eligible youth were approached to participate in the CGM study, and 130 (28%) agreed to participate and provided written informed consent. Those who agreed were younger (0.7 years; P=0.01) and had shorter diabetes duration (1.2 years; P=0.01) than youth who declined to participate. HbA1c did not differ by enrollment status. Alternately, in a separate sample, 455 youth with type 1 diabetes were approached as the Standard group, and 302 (66%) agreed to participate and provided written informed consent. Those youth who declined participation in the Standard group had similar age, diabetes duration, and HbA1c as the youth who agreed. Four patients in the CGM group and 64 patients in the Standard group were excluded because they did not meet the harmonized inclusion criteria required for this current analysis. Six patients in the CGM group declined ongoing CGM use during the run-in period and were also excluded from this analysis, yielding a final sample of 120 youth in the CGM group and 238 youth in the Standard group.

Overall, participants in both groups (n=358) had a mean age of 13.0±2.8 years, a mean diabetes duration of 6.3±3.4 years, and a mean HbA1c level of 8.2±1.0% (66±11 mmol/mol); 51% were female, and 93% were white. The CGM and Standard groups were comparable with respect to age, diabetes duration, sex, and race/ethnicity distributions (Table 1). There were differences between the CGM group and the Standard group in the frequency of daily blood glucose monitoring (7.4±2.2 vs. 5.6±2.1; P<0.0001), CSII use (84% vs. 70%; P=0.004), and percentage of participants living in two-parent homes (92% vs. 84%; P=0.05). In addition, HbA1c was lower in the CGM group (8.0±0.8% [64±9 mmol/mol]) compared with the Standard group (8.3±1.0% [67±11mmol/mol]; P<0.001). There were no statistically significant differences between groups with respect to parental education (percentage of families with at least one parent with a college degree).

Survey results

Across the entire sample, youth and parent survey scores were significantly correlated for each of the four measures (DMQ, r=0.48; DFCS, r=0.35; DFRQ, r=0.75; PedsQL, r=0.42; all P<0.0001). Youth consistently reported lower adherence to diabetes treatment (P<0.0001), less parent involvement in diabetes management tasks (P<0.0001), and more diabetes-specific family conflict than their parents (P<0.001). It is interesting that the youths' report of quality of life was higher than their parents' proxy report of youth quality of life (P<0.0001).

The CGM and Standard groups had substantial differences in both child (Fig. 1) and parent (Fig. 2) scores regarding adherence to diabetes treatment, diabetes-specific family conflict, and youth quality of life assessments. Youth interested in wearing CGM and their parents, compared with the Standard group, reported greater adherence to diabetes care (youth, 75±10 vs. 72±12 [P=0.02]; parent, 79±11 vs. 75±12 [P=0.02]) and higher youth quality of life (youth, 86±14 vs. 83±12 [P=0.02]; parent, 83±12 vs. 79±13 [P<0.001]). Similarly, youth and their parents in the CGM group reported less diabetes-specific family conflict than those in the Standard group (youth, 13±17 vs. 20±23 [P=0.002]; parent, 11±11 vs. 15±12 [P=0.003]). However, as opposed to the other surveys, there were no differences between the CGM and Standard groups with respect to parent involvement in diabetes management, as reported by both children and their parents.

DISCUSSION AND CONCLUSIONS

Consistent use of CGM may improve HbA1c levels in the absence of severe hypoglycemia (4,22,23). Pediatric patients and families may have misconceptions and unrealistic expectations of CGM. In order to promote greater CGM uptake and consistent use for these patients, we sought to evaluate characteristics of pediatric patients and families interested in initiating CGM compared with a general pediatric sample.

In this study, youth interested in wearing a CGM device performed more frequent blood glucose monitoring and had lower HbA1c levels compared with a general sample of youth with type 1 diabetes. Those interested in CGM were also more likely to be treated by CSII than the general sample, even though the CGM device planned for use by the youth was not one that would be integrated into the pump. In addition, youth interested in starting CGM, along with their parents, reported greater adherence to diabetes management, less diabetes-specific family conflict, and higher youth quality of life. It is not surprising that we uncovered salient differences between the two groups because only 28% of eligible youth who were approached for the CGM study agreed to wear a CGM device compared with 66% of the eligible general pediatric population who were approached and agreed to participate in a nonintervention questionnaire study. The low rate of agreement to participate in the CGM study speaks to the recognized potential burdens related to current CGM technology. Adherence to CGM use appears to be particularly challenging for youth with type 1 diabetes. With the substantial financial and personnel demands required to use CGM technology, it may be opportune to focus efforts on those youth with type 1 diabetes and their families who possess the characteristics associated with CGM uptake. This analysis aimed to identify potentially modifiable diabetes-specific behavioral and clinical characteristics likely to predict uptake of CGM use.

Our findings highlight the observation that technology-assisted diabetes management, such as CGM, that requires user input is dependent on the patient's engagement in diabetes self-care. Indeed, the higher rate of CSII use among those interested in CGM supports the likely comfort of such youth to wear and interface with a diabetes management device. In this study, the percentage of CSII use was high in both CGM and Standard groups; however, it was significantly higher in the CGM group, as hypothesized. Patients who are already wearing CSII may be less reluctant to wear an additional device as they are already familiar with skin care and insertion techniques (24).

The value of managing youth with type 1 diabetes from diagnosis using a combination of CSII and CGM, in comparison with CSII and blood glucose monitoring, was previously evaluated, and no differences were found between the two groups in 1 year with respect to HbA1c (25). More studies, however, are needed to better understand the impact of multiple diabetes technologies on diabetes care. In fact, there is an ongoing study aimed at comparing durability of CGM use when implemented at the time of initiating CSII compared with a delay of 6 months for the CGM start (26).

It is well documented that lower levels of youth adherence to diabetes treatment correlate with higher levels of diabetes-specific family stress and conflict (13,27). In addition, there is growing consensus that youth whose parents are more engaged in diabetes management are more adherent than youth whose parents are less involved in diabetes tasks (13,28). These associations, however, have not previously been assessed in patients initiating CGM. In this study, we found lower diabetes-specific family conflict reported by patients and parents interested in starting CGM in comparison with a general population of youth with type 1 diabetes. Contrary to our hypothesis related to family support, although youth interested in starting CGM were more likely to be living in two-parent homes, parent involvement in diabetes management was not associated with motivation to start CGM. This lack of association is possibly due to the observation that youth must wear the CGM sensors and respond to CGM alarms and alerts, independently of their family support.

Perceived youth quality of life may also be associated with adherence to CGM use (15,29). In our sample, youth interested in wearing a CGM device reported a higher quality of life in comparison with the general sample. The parents of youth initiating CGM also endorsed higher quality of life for their children than did the parents of the general sample. The higher reported quality of life may be a marker of unmeasured family variables, such as family cohesion, that may aid in the uptake of advanced and complicated diabetes technologies such as CGM.

It is important that we do not overstate our findings. This study involved a cross-sectional research design, and our results represent associations, not causal relationships, between diabetes-specific behavioral characteristics and interest in CGM. Moreover, as occurs frequently in behavioral research, we were reliant on self-report of behaviors and related factors that were not confirmed objectively. Fear of hypoglycemia was also not assessed in this study and could also be an important determinant of CGM uptake. However, previous studies have not consistently found reductions in fear of hypoglycemia with CGM use in the pediatric population (6,14). Although we do not have follow-up data to determine if these patients sustained their use of CGM, to our knowledge, this is the first study to assess behavioral characteristics associated with CGM initiation in youth with type 1 diabetes. Longer-term studies will determine the factors that are predictive of sustained CGM use and subsequent benefits on glycemic control.

In summary, the knowledge from this study provides opportunities to identify youth with type 1 diabetes likely to be candidates for CGM technologies based on clinical and behavioral characteristics. Our findings support the International Society for Pediatric and Adolescent Diabetes statement, which recommends that the decision to wear CGM should be made jointly by the youth, who must have a personal interest in using CGM, their parents, and the diabetes team (30). Identifying modifiable factors related to CGM adoption, such as insulin regimen, blood glucose monitoring frequency, adherence to diabetes management, and avoidance of diabetes-specific family conflict, may aid providers as they consider CGM implementation in youth with type 1 diabetes. Further longitudinal studies are necessary to determine if the factors associated with initiation of CGM also predict sustained use of this advanced diabetes technology for youth with type 1 diabetes.

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Author Disclosure Statement

L.M.L. reports participation as a consultant or advisory board member for Sanofi, Roche, Lilly, Novo Nordisk, Oshadi, Animas/LifeScan, Johnson & Johnson, Boehringer Ingelheim, AstraZeneca, DexCom, Bayer, and Menarini, as well as participation in commercially sponsored research for DexCom and Boehringer Ingelheim. G.H.T., L.KV., and D.A.B. declare no competing financial interests exist.

G.H.T. researched data, analyzed data, and wrote the manuscript. L.K.V. researched data, analyzed data, and reviewed and edited the manuscript. D.A.B. researched data and reviewed and edited the manuscript. L.M.L. researched data, analyzed data, and wrote and edited the manuscript. L.M.L. is the guarantor of this work.

References

1. Markowitz JT, Harrington KR, Laffel LM: Technology to optimize pediatric diabetes management and outcomes. Curr Diab Rep 2013;13:877–885.

2. Liberman A, Buckingham B, Phillip M: Diabetes technology and the human factor. Diabetes Technol Ther 2014;16(Suppl 1):S110–S118.

3. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group: Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. Diabetes Care 2009;32:1947–1953.

4. Battelino T, Conget I, Olsen B, Schutz-Fuhrmann I, Hommel E, Hoogma R, Schierloh U, Sulli N, Bolinder J: The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. Diabetologia 2012;55:3155–3162.

5. Sacks DB, Bergenstal RM, McLaughlin S: Point: The reporting of estimated glucose with hemoglobin A1c. Clin Chem 2010;56:545–546.

6. Mauras N, Beck R, Xing D, Ruedy K, Buckingham B, Tansey M, White NH, Weinzimer SA, Tamborlane W, Kollman C: A randomized clinical trial to assess the efficacy and safety of real-time continuous glucose monitoring in the management of type 1 diabetes in young children aged 4 to < 10 years. Diabetes Care 2012;35:204–210.

7. Tsalikian E, Fox L, Weinzimer S, Buckingham B, White NH, Beck R, Kollman C, Xing D, Ruedy K: Feasibility of prolonged continuous glucose monitoring in toddlers with type 1 diabetes. Pediatr Diabetes 2012;13:301–307.

8. Chiang JL, Kirkman MS, Laffel LM, Peters AL: Type 1 diabetes through the life span: a position statement of the American Diabetes Association. Diabetes Care 2014;37:2034–2054.

9. Beck RW, Tamborlane WV, Bergenstal RM, Miller KM, Dubose SN, Hall CA: The T1D Exchange Clinic Registry. J Clin Endocrinol Metab 2012;97:4383–4389.

10. Wong JC, Foster NC, Maahs DM, Raghinaru D, Bergenstal RM, Ahmann AJ, Peters AL, Bode BW, Aleppo G, Hirsch IB, Kleis L, Chase HP, Dubose SN, Miller KM, Beck RW, Adi S: Real-time continuous glucose monitoring among participants in the T1D Exchange Clinic Registry. Diabetes Care 2014;37:2702–2709.

11. Rodriguez H: New technologies and old challenges in type 1 diabetes. Diabetes Technol Ther 2012;14:1082–1083.

12. Kashmer L, Clarke W, Gurka M, Elchuri S, Nyer M, Gonder-Frederick L: Predictors of parental interest in continuous glucose monitoring for children with type 1 diabetes. Diabetes Technol Ther 2009;11:373–378.

13. Anderson BJ, Vangsness L, Connell A, Butler D, Goebel-Fabbri A, Laffel LM: Family conflict, adherence, and glycaemic control in youth with short duration type 1 diabetes. Diabet Med 2002;19:635–642.

14. Markowitz JT, Pratt K, Aggarwal J, Volkening LK, Laffel LM: Psychosocial correlates of continuous glucose monitoring use in youth and adults with type 1 diabetes and parents of youth. Diabetes Technol Ther 2012;14:523–526.

15. Polonsky WH, Hessler D: What are the quality of life-related benefits and losses associated with real-time continuous glucose monitoring? A survey of current users. Diabetes Technol Ther 2013;15:295–301.

16. Juvenile Diabetes Research Foundation, Beck RW, Lawrence JM, Laffel L, Wysocki T, Xing D, Huang ES, Ives B, Kollman C, Lee J, Ruedy KJ, Tamborlane WV: Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial. Diabetes Care 2010;33:2175–2177.

17. Mehta SN, Nansel TR, Volkening LK, Butler DA, Haynie DL, Laffel LM: Validation of a contemporary adherence measure for youth with type 1 diabetes: the Diabetes Management Questionnaire. Diabet Medicine 2015, 32(9):1232–1238.

18. Hood KK, Butler DA, Anderson BJ, Laffel LMB: Updated and revised Diabetes Family Conflict Scale. Diabetes Care 2007;30:1764–1769.

19. Anderson BJ, Auslander WF, Jung KC, Miller JP, Santiago JV: Assessing family sharing of diabetes responsibilities. J Pediatr Psychol 1990;15:477–492.

20. Varni JW, Seid M, Knight TS, Uzark K, Szer IS: The PedsQL 4.0 Generic Core Scales: sensitivity, responsiveness, and impact on clinical decision-making. J Behav Med 2002;25:175–193.

21. Varni JW, Seid M, Kurtin PS: PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 Generic Core Scales in healthy and patient populations. Med Care 2001;39:800–812.

22. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group: Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008;359:1464–1476.

23. Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, Joyce C, Peoples T, Perkins BA, Welsh JB, Willi SM, Wood MA, STAR 3 Study Group: Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. N Engl J Med 2010;363:311–320.

24. Kruger D, Marcus AO: Psychological motivation and patient education: a role for continuous glucose monitoring. Diabetes Technol Ther 2000;2(Suppl 1):S93–S97.

25. Kordonouri O, Pankowska E, Rami B, Kapellen T, Coutant R, Hartmann R, Lange K, Knip M, Danne T: Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. Diabetologia 2010;53:2487–2495.

26. Lawson ML, Bradley B, McAssey K, Clarson C, Kirsch SE, Mahmud FH, Curtis JR, Richardson C, Courtney J, Cooper T, Downie CJ, Rajamannar G, Barrowman N: The JDRF CCTN CGM TIME Trial: Timing of Initiation of continuous glucose Monitoring in Established pediatric type 1 diabetes: study protocol, recruitment and baseline characteristics. BMC Pediatr 2014;14:183.

27. Schafer LC, McCaul KD, Glasgow RE: Supportive and nonsupportive family behaviors: relationships to adherence and metabolic control in persons with type I diabetes. Diabetes Care 1986;9:179–185.

28. Wysocki T, Taylor A, Hough BS, Linscheid TR, Yeates KO, Naglieri JA: Deviation from developmentally appropriate self-care autonomy. Association with diabetes outcomes. Diabetes Care 1996;19:119–125.

29. Langendam M, Luijf YM, Hooft L, DeVries JH, Mudde AH, Scholten RJ: Continuous glucose monitoring systems for type 1 diabetes mellitus. Cochrane Database Syst Rev 2012;(1):CD008101.

30. Phillip M, Danne T, Shalitin S, Buckingham B, Laffel L, Tamborlane W, Battelino T: Use of continuous glucose monitoring in children and adolescents. Pediatr Diabetes 2012;13:215–228.

Table 1-*Demographic and clinical characteristics of study participants*

	CGM group (*N*=120)	**Standard group (*N*=238)**	***P* value**
Age (years)	12.7±2.7	13.1±2.8	0.23
Sex (% female)	49	51	0.74
Race/ethnicity (% Caucasian)	95	92	0.50
Age at diagnosis (years)	6.6±3.6	6.7±3.2	0.93
Diabetes duration (years)	6.1±3.6	6.4±3.4	0.38
HbA1c (%)	8.0±0.8	8.3±1.0	**<0.001**
HbA1c (mmol/mol)	64±9	67±11	**<0.001**
Blood glucose monitoring (frequency/day)	7.4±2.2	5.6±2.1	**<0.0001**
Daily insulin dose (units/kg)	0.9±0.3	0.9±0.3	0.95
Insulin regimen (% CSII use)	84	70	**0.004**
Family structure (% 2-parent family)	92	84	**0.05**
Parental education (% college graduate)	73	76	0.52

Data are mean ± SD or %.

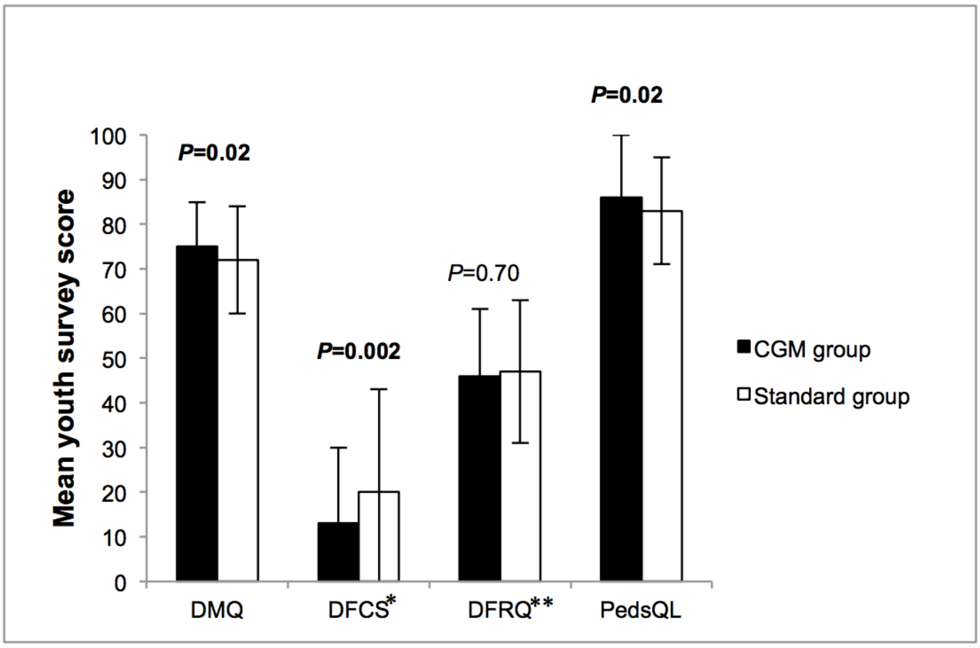

Figure 1-*Youth survey scores by study group*.
Youth interested in using CGM (CGM group), in comparison to a general sample of youth with type 1 diabetes (Standard group), reported, respectively, greater adherence to diabetes care (DMQ: 75±10 vs. 72±12), less diabetes-specific family conflict (DFCS: 13±17 vs. 20±23), and higher youth quality of life (PedsQL: 86±14 vs. 83±12). There were no differences between the CGM and Standard groups regarding parent involvement in diabetes management (DFRQ: 46±15 vs. 47±16, respectively).
*DFCS original scores, prior to normalization: 24.0±6.6 (CGM group) vs. 26.6±8.9 (Standard group).
**DFRQ original scores, prior to normalization: 32.7±5.0 (CGM group) vs. 32.9±5.4 (Standard group).

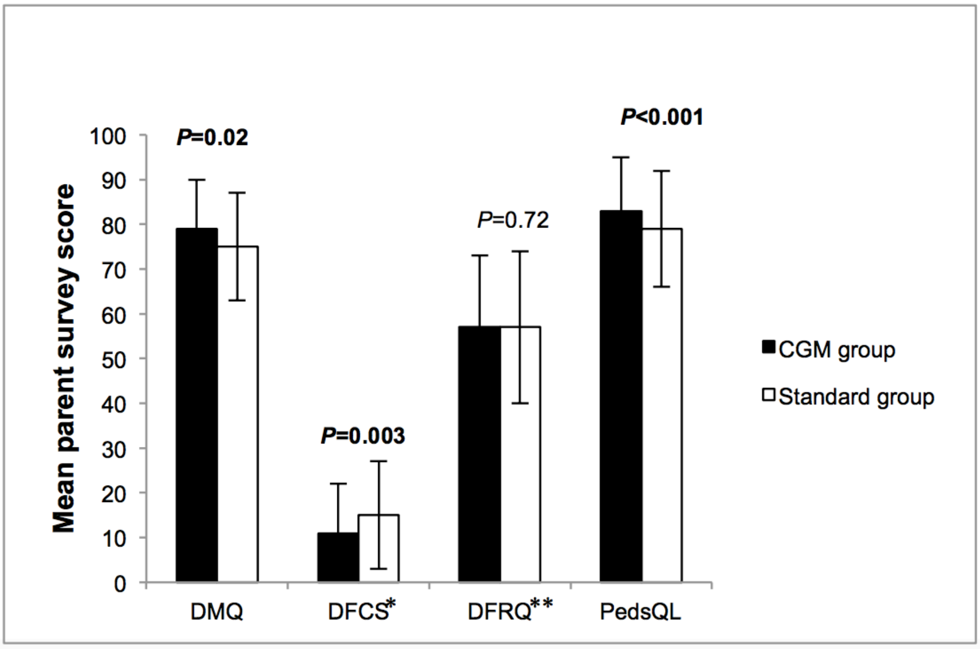

Figure 2-*Parent survey scores by study group*.
Parents of youth interested in using CGM (CGM group), in comparison to parents of youth in a general sample of youth with type 1 diabetes (Standard group), reported, respectively, greater adherence to diabetes care (DMQ: 79±11 vs. 75±12), less diabetes-specific family conflict (DFCS: 11±11 vs. 15±12), and higher youth quality of life (PedsQL: 83±12 vs. 79±13). There were no differences between the CGM and Standard groups regarding parent involvement in diabetes management (DFRQ: 57±16 vs. 57±17, respectively).
*DFCS original scores, prior to normalization: 23.1±4.3 (CGM group) vs. 24.6±4.7 (Standard group).
**DFRQ original scores, prior to normalization: 36.5±5.5 (CGM group) vs. 36.3±5.6 (Standard group).

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ARTIGO 3

Comparison between Adherence Assessments and Blood Glucose Monitoring Measures to Predict Glycemic Control in Patients with Type 1 Diabetes

Adherence measures in type 1 diabetes

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Abstract

Objective: We conducted analyses to compare adherence assessments and blood glucose monitoring measures with regard to their ability to predict glycemic control in adults with type 1 diabetes.

Research Design and Methods: We analyzed four instruments to evaluate adherence: Self-Care Inventory-Revised, a self-administered survey; Diabetes Self Monitoring Profile (DSMP), administered by trained researchers; a categorical (yes/no/sometimes) adherence self-evaluation; and a continuous (0-100) adherence self-evaluation. Blood glucose monitoring frequency was evaluated by self-report, diary, and meter download.

Results: Participants (N=82) were aged 39.0±13.1 years with a mean diabetes duration of 21.2±11.1 years; 27% monitored blood glucose >4 times/day. The DSMP score was the strongest predictor of glycemic control (*r*=-0.32, P=0.004) among adherence assessments, while blood glucose monitoring frequency assessed by meter download was the strongest predictor among blood glucose monitoring measures (*r*=-40, P<0.001). All the self-report assessments had a significant but weak correlation with glycemic control (*r*≤0.28, P≤0.02). The final adjusted model identified the assessment of blood glucose monitoring frequency by meter download as the most robust predictor of hemoglobin A1c (estimate effect size=-0.58, P=0.003).

Conclusions: In efforts to evaluate adherence, blood glucose monitoring frequency assessed by meter download has the strongest relationship with glycemic control in adults with type 1 diabetes.

Key words: Diabetes Mellitus, Type 1; Medication Adherence; Blood glucose monitoring

INTRODUCTION

Adherence to treatment has been defined as the degree to which a patient's behavior corresponds to medical or health advice (1). Despite all evidence that achieving good glycemic control helps prevent microvascular and macrovascular complications of diabetes, many patients do not achieve such control, mostly because treatment adherence is poor (2, 3). Sustained glycemic control has been shown to be difficult in adults of all ages, as the management of diabetes places substantial demands on patients (4). Challenges to adherence and active patient engagement in diabetes care include, but are not limited to, physical and emotional barriers, complex treatment regimens, and financial burdens (5). There is a tendency in the literature to treat adherence and glycemic control as interchangeable constructs (6), while, in fact, patient adherence and metabolic control need to be assessed both independently and concomitantly (6, 7). Patients in good glycemic control cannot be presumed to be adherent.

In the literature and in clinical practice, there are various methods of assessing adherence to diabetes care, such as structured interviews, self-report, diaries, and electronic monitoring (8). Many of these methods have been shown to correlate well with glycemic control (9). Surveys have been validated and widely used as measures to evaluate adherence (10, 11). Their domains usually capture behavioral characteristics related to diabetes management, such as insulin administration, meal plans, frequency/intensity of exercises, frequency of blood glucose monitoring, and hypoglycemia (6). The appropriate execution of all these tasks was shown to promote optimal glycemic control (2, 3), which solidified the association between adherence and metabolic results in diabetes treatment. In contrast, several studies have demonstrated the importance of focusing on specific adherence behaviors, such as frequency of blood glucose monitoring (12, 13). These studies demonstrated strong association between a higher frequency of blood glucose monitoring and lower hemoglobin A1c (HbA1c) levels. However, the most appropriate method to evaluate adherence to diabetes care in adults with type 1 diabetes has yet to be identified.

In this study, we sought to investigate different methods of assessing adherence and glycemic control. To accurately predict HbA1c in adults with type 1 diabetes, we designed a cross-sectional study to evaluate and compare adherence assessments by structured surveys and self-report, as well as blood glucose monitoring measures by self-report, diary, and electronic devices. Such knowledge may enhance opportunities to better understand this important barrier and assist in development of strategies to improve adherence to diabetes care and glycemic control in patients with type 1 diabetes.

RESEARCH DESIGN AND METHODS

Participants

We conducted exploratory multivariable analyses to compare adherence assessments and blood glucose monitoring measures with regard to their ability to predict HbA1c in adults with type 1 diabetes. All participants included in this analysis met the following inclusion criteria: ≥18 years of age and type 1 diabetes duration ≥1 year. Exclusion criteria included a developmental disability or a psychiatric disorder that would interfere with reliable completion of the structured instruments. We selected patients from the outpatient electronic medical record database of a single tertiary public hospital in Southern Brazil. The Institutional Review Board approved the study protocols, and all participants signed informed consent forms prior to beginning any study procedure.

Measures

Adherence assessments

We analyzed four different instruments to evaluate adherence to diabetes management. First, participants were asked to respond to a three-level (no/sometimes/yes) categorical self-evaluation question ("In the past month, have you managed your diabetes as recommended by your doctor?"). Patients were also asked to characterize themselves according to their adherence to diabetes care on a continuous self-evaluation scale, ranging from 0-100. Additionally, all participants completed the two following previously validated adherence surveys:

- Self-Care Inventory-Revised version (SCI-R) (11, 14): The 14-item SCI-R (14) is a self-administered survey, which measures adherence to different diabetes management tasks on a 5-point Likert scale. Responses range from 1=never to 5=always, and scores range from 14 to 70. Higher scores indicate greater adherence to type 1 diabetes treatment.

- Diabetes Self-Monitoring Profile (DSMP) (10, 14): The DSMP (14) is a 24-item survey administered by trained researchers, which measures adherence to five different domains: exercises, hypoglycemia, diet, blood glucose tests, and insulin dose. Scores range from 0 to 96. Higher scores indicate greater adherence to type 1 diabetes treatment.

Blood glucose monitoring measures

We evaluated blood glucose monitoring frequency by three different ways: self-report, diary, and meter download. Participants were asked to take their blood glucose meters and blood glucose diary to the study visit. An average frequency of blood glucose monitoring per day was calculated for the last 14 days, not including the visit day.

After collecting responses to the adherence assessments and blood glucose monitoring data, trained researchers interviewed participants to obtain demographics and diabetes clinical data. Glycemic control was assessed by HbA1c, which was performed in a clinical laboratory using a Diabetes Control and Complications Trial standardized assay (high-performance liquid chromatography, ref. range 4.0-6.0%).

Data analysis

Analyses were performed using SAS (version 9.3; Institute, Inc., Cary, NC). Descriptive data are presented as mean ± standard deviation (SD) or percentage. Statistical analyses included Pearson correlation to determine associations between adherence assessments and blood glucose monitoring measures. Exploratory multivariable analyses were conducted using stepwise regression to identify, among all adherence assessments and blood glucose monitoring measures, the best predictor of HbA1c. Three different steps were performed in the stepwise analyses: first, all three blood glucose monitoring assessments were included in the HbA1c model; second, all four adherence assessments were included in the HbA1c model; and, finally, after selecting the best HbA1c predictors among the adherence assessments and blood glucose monitoring measures based on the two first steps, a final step evaluated the two selected measures in order to elucidate which one could better predict HbA1c. Generalized linear model was then performed, including mean HbA1c as the dependent variable and the best adherence measure based on the final exploratory step as the independent variable. Multivariable analyses were performed to evaluate the impact of demographics and clinical characteristics on the adherence-glycemic control relationship. An alpha level of <0.05 was used to determine statistical significance. The Cohen's index was used to determine correlation coefficients and effect size (15). A sample size of 82 was calculated as sufficient to detect a moderate effect size between HbA1c and adherence measures considering an alpha of 0.05 and power of 80%.

RESULTS

Participant characteristics

In total, 103 eligible patients were approached to participate in this study (from March 2014 to September 2014), of those 82 (80%) agreed to participate. All participants provided written informed consent. Those who declined participation had similar age, diabetes duration, and HbA1c as those who agreed to participate ($P>0.05$). All participants provided data regarding blood glucose meter and diary and responded to the study visit interview and surveys. Participants had a mean age of 39.0 ± 13.1 years and mean diabetes duration of 21.2 ± 11.1 years; 39% were overweight/obese, and 27% had a frequency of blood glucose monitoring >4 times/day according to the study visit interview (see table 1). All participants in this study were using daily multiple injections for diabetes treatment and only 11% met the ADA HbA1c target of <7% (16).

Measures results

All adherence assessments appeared to be interrelated ($P<0.01$), as did the blood glucose monitoring measures ($P<0.001$). The correlations between DSMP score and blood glucose monitoring frequency assessed by self-report ($r=0.69$, $P<0.001$) and meter download ($r=0.52$, $P<0.001$) were identified as the two strongest correlations between the adherence and blood glucose monitoring measures (see table 2).

Exploratory analyses using stepwise multivariable regression were conducted to identify the best predictor of HbA1c based on all the adherence and blood glucose monitoring measures. In the first step, among all the blood glucose monitoring measures, frequency of blood glucose monitoring assessed by meter download was the strongest predictor of HbA1c (r=-40, $P<0.001$) (see table 3A). In the second step, among all the adherence assessments, DSMP score was the strongest predictor of glycemic control ($r=-0.32$, $P=0.004$) (see table 3B). During the two first steps, all adherence and blood glucose assessments were significantly correlated with HbA1c ($P<0.05$), except for frequency of blood glucose monitoring by diary ($r=-0.20$, $P=0.07$). All self-report assessments, which included the blood glucose monitoring frequency self-report, categorical adherence self-evaluation question, and continuous adherence self-evaluation question, had a weak, although significant, correlation with glycemic control. In the final step, which included the best adherence and blood glucose monitoring assessments based on the two first steps, frequency of blood glucose monitoring by meter download emerged as the most robust predictor of glycemic control (r=-33, P<0.001). The DSMP score, in this final model, was no longer significant (r=-15, P=0.22).

Generalized linear model was initially performed to evaluate the interaction between HbA1c and blood glucose monitoring frequency assessed by meter download. This analysis showed that as frequency of blood glucose monitoring increased 1 time/day, HbA1c decreased 0.63% (P<0.001). The final adjusted model (P<0.001), which controlled for age, diabetes duration, insulin dose, and socioeconomic status, slightly decreased the adherence-glycemic control association (estimate effect=-0.59, P=0.003). Demographics and clinical characteristics were not significant in this model (P>0.05). As DSMP may also be an alternative while assessing adherence in clinical settings, we also performed univariate analysis to evaluate the interaction between HbA1c and DSMP scores. In this analysis, as DSMP score increased by 10 points, HbA1c decreased by 0.74% (P=0.004).

DISCUSSION AND CONCLUSIONS

The conceptual and methodological issues related to adherence assessments are important for research but also have widespread clinical application. How healthcare providers conceptualize adherence impacts on diabetes management recommendations (6). In order to better understand the different instruments available to assess adherence in adults with type 1 diabetes, we sought to evaluate and compare adherence assessments and blood glucose monitoring measures to predict glycemic control. In this study, among the four instruments to assess adherence (DSMP, SCI-R, and categorical and continuous self-evaluations), DSMP score was the strongest predictor of glycemic control, while blood glucose monitoring frequency assessed by meter download was the most robust predictor of HbA1c among the blood glucose monitoring measures and all the studied assessments.

Our findings highlight the observation that there is a strong association between frequency of blood glucose monitoring and glycemic control patients with type 1 diabetes. Indeed, the T1D Exchange Clinic Network (13) clearly demonstrated that for all ages, increased frequency of blood glucose monitoring is associated with lower HbA1c. Previous studies also identified that capillary glucose information was valuable for making appropriate decisions with regard to insulin doses (17). This is true even after adjusting for demographics and socioeconomic confounders (13). In this study, demographics and clinical characteristics did not appear to have an impact on the adherence-glycemic control relationship. However, we know that frequent blood glucose monitoring by itself does not directly impact HbA1c; the capillary blood glucose information must be used effectively in diabetes management in order for the frequency of monitoring to impact glycemic control (5, 18). Thus, frequency of blood glucose monitoring seems to be a behavior strongly representative of adherence and very well associated with glycemic control.

Besides frequency of blood glucose monitoring, many other domains seem to be related to adherence and have been assessed by different surveys (10, 11). However, despite the well-known importance of adherence in achieving good glycemic control and preventing diabetes complications (3, 19), there are only a few questionnaires with established psychometric properties to assess it (10, 11, 20, 21). In this study, we evaluated the two instruments validated to Brazilian Portuguese population to assess adherence in patients with type 1 diabetes (14). Both surveys, as well as the self-evaluation questions, demonstrated significant correlation with glycemic control and seem to be appropriate to evaluate adherence in adults with type 1 diabetes. The DSMP, which includes domains regarding diet, exercises, insulin, blood glucose monitoring frequency, and hypoglycemia, showed to have the most powerful questions to predict glycemic control when compared to self-evaluations. Although the five DSMP domains were not validated to be assessed separately, the lack of association between HbA1c and DSMP after controlling for frequency of blood glucose monitoring suggests that this domain is likely to be the responsible for the HbA1c-DSMP association. It is essential to state that, although surveys are an easy-to-use instrument to assess adherence, frequency of blood glucose measures assessed by meter download appear to have the strongest relationship with HbA1c in adults with type 1 diabetes. Surveys may have utility for periodic use with patients in clinical and research settings (9); however, although surveys can predict glycemic control and health outcomes, they cannot be interpreted as substitutes of HbA1c and must be analyzed with consideration of the clinical setting (9). Interestingly, in this study, all the self-report assessments, including the SCI-R, which is a self-administered survey to assess adherence, had a significant but weak correlation with glycemic control. Consistent with previous studies (6, 13), adherence assessments by self-evaluation may over-report engagement in diabetes tasks and frequency of blood glucose self-monitoring.

It is important that we do not overestimate our findings. This study involved a cross-sectional design, and our results represent associations, not direct causal relationships, between glycemic control and adherence measures. Moreover, as occurs frequently in behavioral studies, we were reliant on self-reports that were not confirmed objectively. Further studies may want to confirm our findings in longitudinal research designs, while controlling for the timeframe of assessing adherence behaviors. Moreover, future studies need to be designed to better evaluate the impact of demographics and clinical characteristics on adherence in order to best predict glycemic control.

To our knowledge, this is the first study designed to compare different methods to assess adherence and blood glucose monitoring frequency in adults with type 1 diabetes. Our findings highlight blood glucose monitoring frequency by meter download as the best method to assess adherence and glycemic control. The knowledge from this study stresses the importance of downloading blood glucose monitoring devices and provides opportunities to better understand and assess adherence to diabetes management. Appropriately identifying modifiable characteristics associated with glycemic control may aid providers as they consider a diabetes prescription or management plan. Further studies are necessary to determine the role of each adherence assessment in diabetes care longitudinally.

Competing interests

The authors declare that they have no competing interests.

Author's contributions

G.H.T researched data, analyzed data, and wrote the manuscript. M.S.S. researched data, analyzed data, and reviewed the manuscript. T.S.A. researched data and reviewed the manuscript; B.D.S. researched data, analyzed data, and reviewed and edited the manuscript. All authors approved the final version of this manuscript. B.D.S. is the guarantor of this work.

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References

1. Haynes RB. Introduction. In: Haynes RB T-ID, Sackett DC, eds. Compliance in Health Care. Baltimore, MD: Johns Hopkins University Press; 1979:1–7

2. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. The New England Journal of Medicine 1993, 329(14):977-986.

3. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B, Diabetes C, Complications Trial/Epidemiology of Diabetes I et al: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. The New England Journal of Medicine 2005, 353(25):2643-2653.

4. Broadbent E, Donkin L, Stroh JC: Illness and treatment perceptions are associated with adherence to medications, diet, and exercise in diabetic patients. Diabetes Care 2011, 34(2):338-340.

5. Davies MJ, Gagliardino JJ, Gray LJ, Khunti K, Mohan V, Hughes R: Real-world factors affecting adherence to insulin therapy in patients with Type 1 or Type 2 diabetes mellitus: a systematic review. Diabetic Medicine 2013, 30(5):512-524.

6. Johnson SB: Methodological issues in diabetes research. Measuring adherence. Diabetes Care 1992, 15(11):1658-1667.

7. Levine BS, Anderson BJ, Butler DA, Antisdel JE, Brackett J, Laffel LM: Predictors of glycemic control and short-term adverse outcomes in youth with type 1 diabetes. The Journal of Pediatrics 2001, 139(2):197-203.

8. Kichler JC, Kaugars AS, Maglio K, Alemzadeh R: Exploratory analysis of the relationships among different methods of assessing adherence and glycemic control in youth with type 1 diabetes mellitus. Health Psychology 2012, 31(1):35-42.

9. Hood KK, Peterson CM, Rohan JM, Drotar D: Association between adherence and glycemic control in pediatric type 1 diabetes: a meta-analysis. Pediatrics 2009, 124(6):e1171-1179.

10. Harris MA, Wysocki T, Sadler M, Wilkinson K, Harvey LM, Buckloh LM, Mauras N, White NH: Validation of a structured interview for the assessment of diabetes self-management. Diabetes Care 2000, 23(9):1301-1304.

11. Weinger K, Butler HA, Welch GW, La Greca AM: Measuring diabetes self-care: a psychometric analysis of the Self-Care Inventory-Revised with adults. Diabetes Care 2005, 28(6):1346-1352.

12. Ziegler R, Heidtmann B, Hilgard D, Hofer S, Rosenbauer J, Holl R, Initiative DPVW: Frequency of SMBG correlates with HbA1c and acute complications in children and adolescents with type 1 diabetes. Pediatric Diabetes 2011, 12(1):11-17.

13. Miller KM, Beck RW, Bergenstal RM, Goland RS, Haller MJ, McGill JB, Rodriguez H, Simmons JH, Hirsch IB, Network TDEC: Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. Diabetes Care 2013, 36(7):2009-2014.

14. Telo GH, Souza MS, Schaan BD: Cross-cultural adaptation and validation to Brazilian Portuguese of two measuring adherence instruments for patients with type 1 diabetes. Diabetology and Metabolic Syndrome 2014, 6(1):141-146.

15. Cohen J: A power primer. Psychological Bulletin 1992, 112(1):155-159.

16. Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. 2016;39 Suppl 1:S4-5.

17. Schiffrin A, Belmonte M: Multiple daily self-glucose monitoring: its essential role in long-term glucose control in insulin-dependent diabetic patients treated with pump and multiple subcutaneous injections. Diabetes Care 1982, 5(5):479-484.

18. Peyrot M, Barnett AH, Meneghini LF, Schumm-Draeger PM: Insulin adherence behaviours and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. Diabetic Medicine 2012, 29(5):682-689.

19. Kuo YF, Raji MA, Markides KS, Ray LA, Espino DV, Goodwin JS: Inconsistent use of diabetes medications, diabetes complications, and mortality in older mexican americans over a 7-year period: data from the Hispanic established population for the epidemiologic study of the elderly. Diabetes Care 2003, 26(11):3054-3060.

20. Markowitz JT, Volkening LK, Butler DA, Antisdel-Lomaglio J, Anderson BJ, Laffel LM: Re-examining a measure of diabetes-related burden in parents of young people with Type 1

diabetes: the Problem Areas in Diabetes Survey - Parent Revised version (PAID-PR). Diabetic Medicine 2012, 29(4):526-530.

21. Mehta SNN, T. R.; Volkening, V. K.; Butler, D. A.; Haynie, D. L.; Laffel, L. M. : Validation of a contemporary adherence measure for youth with type 1 diabetes: the Diabetes Management Questionnaire. Diabetic Medicine 2015, 32(9):1232-1238.

Table 1 – *Demographic and clinical characteristics of study participants*

	N = 82
Age (years)	39.0 ± 13.1
Sex (% male)	63
Race/ethnicity (% Caucasian)	98
Socioeconomic class* (%)	
High	13
Medium	70
Low	15
Very low	2
Diabetes duration (years)	21.2 ± 11.1
Blood glucose monitoring (% ≥4 times/day)	27
HbA1c (%)	8.9 ± 2.2
HbA1c (mmol/mol)	74 ± 24
Daily insulin dose (units/kg)	0.74 ± 0.30
Weight status (% overweight/obese)	39

Data are mean ± SD or n (%).

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Table 2 – *Correlation between adherence and blood glucose monitoring assessments*

Assessments	Blood glucose monitoring frequency (self-report) (*r*)	Blood glucose monitoring frequency (diary) (*r*)	Blood glucose monitoring frequency (meter collection/ downloading) (*r*)
Self-administered survey (SCI-R)	**0.50**	**0.46**	**0.40**
P value	<0.0001	<0.0001	0.0002
Structured interview/survey (DSMP)	**0.69**	**0.32**	**0.52**
P value	<0.0001	0.004	<0.0001
Self-evaluation (categorical)	**0.31**	**0.28**	**0.41**
P value	0.005	0.01	0.0001
Self-evaluation (continuous)	**0.34**	**0.25**	**0.33**
P value	0.002	0.02	0.003

SCI-R = Self Care Inventory-Revised; DSMP = Diabetes Self-Monitoring Profile.

Table 3 – ***Stepwise regression for HbA1c and adherence assessments***

Assessments			
(A) Blood glucose monitoring assessments	**R^2**	**P value**	***β***
Blood glucose monitoring frequency (self-report)	0.08	0.01	-0.28
Blood glucose monitoring frequency (diary)	0.04	0.07	-0.20
Blood glucose monitoring frequency (meter collection/downloading)	0.16	0.0002	-0.40
Blood glucose monitoring frequency (meter collection/downloading)	**0.16**	**0.0002**	**-0.40**
(B) Adherence-specific assessments	**R^2**	**P value**	***β***
Self-evaluation (categorical)	0.06	0.02	-0.27
Self-evaluation (continuous)	0.07	0.01	-0.27
Self-administered survey (SCI-R)	0.05	0.04	-0.23
Structured interview/survey (DSMP)	0.10	0.004	-0.32
Structured interview/survey (DSMP)	**0.10**	**0.004**	**-0.32**
(C) Final model	**R^2**	**P value**	***β***
Structured interview/survey (DSMP)	0.18	0.22	-0.15
Blood glucose meter collection/downloading		0.007	-0.33
Blood glucose meter collection/downloading	**0.16**	**0.0002**	**-0.40**

SCI-R = Self Care Inventory-Revised; DSMP = Diabetes Self-Monitoring Profile; *β* = standardized estimate.

ARTIGO 4

Mental Health Symptoms in Adolescents with and without Type 1 Diabetes: Reported Occurrence in a National Survey in Brazil

Mental health in youth with type 1 diabetes

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Abstract

Objective: Current evidence is inconclusive about whether there is increased prevalence of mental health disorders among youth with type 1 diabetes. The aim of this study was to evaluate the frequency of mental health symptoms in adolescents with type 1 diabetes in comparison to a population-based sample of adolescents in Brazil.

Research Design and Methods: We compared demographics and clinical characteristics of 116 youth with and 73,508 youth without type 1 diabetes from the same population-based sample of adolescents aged 12 to 17 years, which were taken from the national Study of Cardiovascular Risk in Adolescents (ERICA). We evaluated the 12-item General Health Questionnaire (GHQ) score, which is a self-administered screening survey for detecting mental health symptoms. Scores ≥3 were used to determine mental health disorder.

Results: Adolescents with and without type 1 diabetes were comparable with respect to age and race/ethnicity distributions, although female sex was less frequently seen in the type 1 diabetes group. Youth with type 1 diabetes did not report higher scores on the weighted GHQ analyses in comparison to youth without type 1 diabetes (3.16, SE 0.76 *vs.* 2.10, SE 0.03, respectively; P=0.167). Also, no differences were found with regard to the odds of having a score ≥3 (OR 1.48, 95% CI 0.72-3.08). However, analyses of mental health symptoms separately consistently showed that youth with type 1 diabetes more frequently endorsed mental health barriers in comparison to youth without type 1 diabetes.

Conclusions: Mental health symptoms seem to be more frequent than diagnosis of mental health disorders in adolescents with type 1 diabetes, which may also interfere in glycemic control. Our findings highlight the need for appropriate mental health assessment in diabetes care in order to prevent glycemic control deterioration.

Keywords: type 1 diabetes; adolescents; mental health

INTRODUCTION

Mental health disorders have been associated with poor adherence to treatment and poor glycemic control in patients with type 1 diabetes (1), which increase the risk of chronic complications and hospital admissions (2, 3). Although effective therapies are available for adequate diabetes care, adherence to such a complex and demanding therapy is, by itself, an ongoing challenge that increases the burden of diabetes (4, 5). While the management of diabetes is difficult at any age, adolescents experience it in addition to increasing social and emotional demands of new regular daily tasks (6). A previous meta-analysis showed that youth with type 1 diabetes were more likely to experience different psychological difficulties in comparison to their peers (7). As a consequence of having difficulties in appropriately adhere to diabetes treatment (8), besides all the metabolic changes that happen in adolescents, such as insulin resistance (9), glycemic control is typically suboptimal during the adolescence years (10), with implications in later life (11).

Adolescents with diabetes seem to be at higher risk for psychological distress (8). During adolescence, mental health issues are possibly exacerbated by glycemic excursions in youth with type 1 diabetes (12). There are increasing evidences suggesting that the prevalence of mental health disorders may be not just higher in, but also partially caused by type 1 diabetes (13). Immuno-inflammatory factors, glucose dysregulation, and neurobiological findings that happen in individuals with diabetes may have a role in the plausible biological link between type 1 diabetes and mental health disorders (14). Data suggest a potential bidirectional relationship between depression and type 1 diabetes, which still requires further confirmation (13).

Type 1 diabetes in youth has previously been associated with depression (7), impaired executive function (6), and reduced quality of life (15). However, the majority of studies evaluating mental health disorders in adolescents with type 1 diabetes were based on small sample sizes and/or poor study design (16). One of the first population-based studies designed to evaluate mental health in adolescents with type 1 diabetes found no evidence of increased disorders (17), suggesting that conclusions with regard to mental health may need to be reconsidered.

Although current evidence is inconclusive about whether there is increased prevalence of mental health disorders among youth with type 1 diabetes, a systematic review with meta-analysis of 8 observational studies showed that those who are more depressed have poorer glycemic control and higher risk of hospitalization for diabetes-related issues (16). Also, the prevalence of subclinical depressive symptomatology appears to be greater in individuals with type 1 diabetes (17). In some studies, depressive symptoms at any time during young adult life, regardless of diagnosis of depression, presented as a predictor of continued or recurring depression (17, 18). As subclinical symptomatology of mental health disorders may be associated with poor clinical outcomes in youth with type 1 diabetes (17), the aim of this study was to evaluate the frequency of mental health disorders and their symptoms in adolescents with and without type 1 diabetes from a population-based sample of adolescents.

RESEARCH DESIGN AND METHODS

Design and procedures

In this study, we compared demographics and clinical characteristics of youth with type 1 diabetes from a population-based sample of adolescents with youth without type 1 diabetes from the same sample. Data were taken from the Brazilian Study of Cardiovascular Risks in Adolescents (ERICA), which is a national, cross-sectional study designed to determine the magnitude of cardiovascular risk factors in adolescents from cities with over 100,000 inhabitants in Brazil. The ERICA sample, which was planned to be representative of the national and macro-regional levels, as well as all state capitals, employed stratification and clustering for selection stages (19).

Uniform study procedures were used for data collection (20). The Institutional Review Board of each Federative Unit of Brazil approved the study protocols, and all adolescents/parents who agreed to participate in this study signed informed assent/consent forms before beginning any study procedures.

Participants

The ERICA sample consists on adolescents aged 12 to 17 years who were attending high school or one of the final three years of elementary school at public or private schools in urban or rural areas (19). In this analysis, participants were classified as having type 1 diabetes if they reported to take insulin for diabetes. Based on this classification, 116 adolescents with type 1 diabetes were compared with 73,508 adolescents without type 1 diabetes.

Measures

Sociodemographic features and clinical data were obtained through patient self-administered questionnaires and standardized anthropometric measurements (20). We used weight (kg) and height (m) to calculate body mass index according to the World Health Organization classification (21). Tanner stage, based on self-assessment, was used to classify pubertal development (22). To determine the level of physical activity, we used an adaptation of the Self-Administered Physical Activity Checklist (23, 24), which allows youth to report frequency (days) and time (minutes) of different activities in the past week. Adolescents who did not accumulated 300 min/week of physical activity were considered inactive (25). Socioeconomic status was characterized using the *Associação Brasileira de Empresas de Pesquisa* criteria (26), which includes data regarding costumer goods and parental education. The scores range from 0 to 46 and higher scores indicate higher socioeconomic status. Parental education was defined as the education level of the parent who was living with the youth at the time of the study. In case of adolescents living with two parents, the highest education level was used for analyses. Recent alcohol consumption was defined according to the ingestion of alcohol over the past month. Tobacco use was defined as cigarettes smoking for at least a day over the past month.

For mental health assessment, adolescents completed the previously validated 12-item General Health Questionnaire (GHQ) (27, 28). The GHQ is one of the most frequently assessed self-administered screening survey for detecting non-psychotic mental health symptoms in community settings. This survey asks whether respondents have experienced a particular symptom or behavior recently in a 4-point Likert scale ranging from 0-12. Higher scores indicate higher mental health symptoms. A GHQ score ≥3 was used to determine mental health disorder (29).

Data analysis

Analyses were performed using Stata statistical software (version 14; College Station, TX: StataCorp LP). The ERICA sample was based on stratification and clustering for all selection stages. Sample weight was previously calculated by the product of the inverse of inclusion probabilities and calibrated according to projections of the number of adolescents enrolled in schools for each geographic area (19). We used post-stratification estimative to modify the natural design weight. Twelve domains were defined based on the six different ages and two sexes studied.

Descriptive data are presented as mean and standard error (SE) values or percentages and 95% confidence interval (CI). Statistical analyses included *t* test for continuous variables and X^2 for categorical variables. The survey scores and all analyses were evaluated according to the two groups (type 1 diabetes and non-type 1 diabetes). Adjustments were performed according to sex, age, physical activity status, alcohol and tobacco use, weight status, socioeconomic status (tertiles), and macro-region (North, Northeast, Midwest, Southeast, and South). For GHQ score calculation, for each question, the first two Likert response categories were combined as “no” in a yes=1/no=0 symptoms category, and the last two Likert response categories were combined as “yes” in this same yes=1/no=0 symptoms category. Odds ratio was used to evaluate the odds of having a GHQ score ≥3 (30). Multivariable logistic regression analyses were used to determine the association of mental health symptoms with demographics and clinical characteristics of study participants. An alpha level of <0.05 was used to determine statistical significance.

RESULTS

Participants’ characteristics

Schools were selected from 124 cities, corresponding to a total of 3,734 classes in 1,251 schools. In total, 73,624 adolescents were included in this analysis. Details of the ERICA sample size were previously described elsewhere (19). Overall, participants had a mean age of 14.4 years old, SE 0.01; 55.4% (95% CI 55.1-55.8) were female (non-weighted value) and 40.1% (95% CI 38.5-41.7) were Caucasians. The two groups (adolescents with and without type 1 diabetes) were comparable with respect to age and race/ethnicity distributions, although female sex was less frequently seen in the type 1 diabetes group (Table 1). No significant differences between the two groups were found with regard to parental education. However, youth with type 1 diabetes were more likely to be from higher socioeconomic status families. Most adolescents with type 1 diabetes responding to the survey, as well as adolescents without type 1 diabetes, were studying in public schools (81.1 *vs.* 82.3%) and living in urban areas (99.0 *vs.* 96.1%) and in two-parent homes (63.7 *vs.* 57.3%), respectively.

The proportion of youth with type 1 diabetes who were physically active did not differ from youth without type 1 diabetes. Clinical differences were also not found between the two groups with regard to tobacco use, alcohol consumption, obesity and overweight, hypertension, and dyslipidemia.

The prevalence of type 1 diabetes in this sample was 0.18%. A clear North-South variation was not found, but the prevalence appears to slightly rise as the geographical latitude increases. Due to the way ERICA participants were selected, sample weights should always be used to produce an unbiased national estimate (19). However, although ERICA was designed to have a representative sample of the national level, macro-regional levels, and all state capitals, this study identified two states and its capitals with no cases of type 1 diabetes. While weighting scheme allows estimates to increase reliability when evaluating a subgroup of patients, this finding may be a limitation while interpreting our results. Based on this, we decided to report weighted and non-weighted analyses for mental health disorder scores (GHQ) and their respective multivariable logistic regression analyses (Table 2).

Mental health disorders

Analyses of mental health symptoms consistently showed that youth with type 1 diabetes more frequently endorsed barriers and mental health symptoms in comparison to youth without type 1 diabetes (Figure 1). Youth with type 1 diabetes more frequently reported not enjoying normal activities (27.4 *vs.* 13.7%, P=0.025), struggling to overcome difficulties (39.1 *vs.* 23.0, P=0.013), not feeling useful (26.5 *vs.* 13.2, P=0.032), and losing confidence (26.6 *vs.* 16.0, P=0.086) in comparison to youth without type 1 diabetes. Analyses also identified feeling depressed or under stress as two common endorsed barriers by youth with and without type 1 diabetes, although no statistical differences were seen between the two groups with regard to these barriers.

Weighted analyses

In terms of mental health disorders, youth with type 1 diabetes did not report higher scores on the GHQ in comparison to youth without type 1 diabetes (3.16, SE 0.76 *vs.* 2.10, SE 0.03, respectively; P=0.167). Also, no differences were found with regard to the odds of having a score ≥3 (OR 1.48, 95% CI 0.72-3.08) between the two groups. Logistic regression analyses calculated the odds of having a GHQ score ≥3 while controlling for demographics and clinical characteristics (Table 2A). Model P value was <0.0001. Male sex, Southern and Southeast regions, as well as tobacco use, were associated with lower odds of having a GHQ score ≥3, while older ages, overweight/obesity, and alcohol consumption were associated with higher odds of having a GHQ score ≥3. Demographics and clinical characteristics of participants did not have a significant impact on the odds of having a GHQ score ≥3 among adolescents with type 1 diabetes.

Non-weighted analyses

When evaluating non-weighted analyses, youth with type 1 diabetes reported higher GHQ scores in comparison to youth without type 1 diabetes (3.07±3.36 *vs.* 2.21±2.86, respectively; P=0.001). Also, type 1 diabetes was associated with higher odds of having a GHQ score ≥3 (OR 1.80, 95% CI 1.25-2.60). Logistic regression non-weighted analyses also calculated the odds of having a GHQ score ≥3 while controlling for demographics and clinical characteristics. A comparison between weighted and non-weighted multivariable logistic regression analyses is available at table 2. Model P value was <0.0001. Male sex, Southern and Southeast regions, Caucasians, physical activity, and tobacco use were associated with lower odds of having a GHQ score ≥3, while older ages, higher socioeconomic status, overweight/obesity, and alcohol consumption were associated with higher odds of having a GHQ score ≥3 (Table 2B). Demographics and clinical characteristics increased the impact of type 1 diabetes on the odds of having a GHQ score ≥3 according to the non-weighted analyses.

CONCLUSIONS

In order to highlight the need for increased mental health support in patients with type 1 diabetes, we sought to evaluate adolescents with type 1 diabetes in Brazil and compare mental health symptoms in youth with and without type 1 diabetes. To our knowledge, this is one of the largest and first population-based studies to evaluate mental health in adolescents with type 1 diabetes, providing, additionally, comparisons between weighted and non-weighted analyses. Based on the population-based sample, although the GHQ score did not differ between the two groups, youth with type 1 diabetes more frequently endorsed some mental health symptoms in comparison to youth without type 1 diabetes.

Type 1 diabetes in adolescence has been previously associated with mental health disorders (31, 32). Data suggest plausible mechanisms whereby a biological association between type 1 diabetes and mental health disorders may exist (13). These findings, however, were small in magnitude and limited by methodological problems and small sample sizes. Also, these effects have become weaker in most recent studies especially when well-matched comparison groups were evaluated (7, 14, 17). Some studies suggest that youth with type 1 diabetes are not restricted by their illness, having similar mental health in comparison to their peers (17). In a recently published study aimed to evaluate mental health in adolescents with type 1 diabetes, there was no evidence of increased psychopathology across a wide range of mental health measures evaluating depression, anxiety, sleep problems, and eating behavior (17). Current evidence is inconclusive about whether there is increased prevalence of mental health issues among adolescents with type 1 diabetes (16). In this large and well designed population-based study, weighted analyses, which have the power of not overestimating effect size, found no differences in mental health disorders using a frequently assessed self-administered screening survey for detecting mental health disorders in community settings. Moreover, tobacco use and alcohol consumption were also not more frequently seen in youth with type 1 diabetes in comparison to youth without type 1 diabetes based on weighted analyses.

Positive associations were found, however, when non-weighted analyses were performed. Besides more frequent mental health disorders in youth with type 1 diabetes, non-weighted analyses increased the impact of type 1 diabetes on the GHQ score after controlling for demographics and clinical data, such as physical activity, weight status, tobacco use, and alcohol consumption. This finding has to be carefully interpreted in order to not overstate associations. Although ERICA complex sample was not designed based on mental health disorders and we may have some limitations to interpret our results, the weighted sample is well representative of the national population of adolescents attending schools, which allows analyses to adequately estimate comparisons to achieve consistent estimates (33, 34). One of the reasons for considering weighted analyses to be more adequate is because this possible oversampling generated by complex samples creates opportunities to obtain more precise information on a subpopulation of particular interest, such as type 1 diabetes (33, 35). The positive associations found in the non-weighted analyses in this study, as well as previously published studies (32, 36), may be related to upward-biased estimate, which overrepresents associations (33). This may explain why mental health disorder association with type 1 diabetes becomes weaker or even negative in well-designed studies (14, 17).

Recent data suggested that subclinical depressive symptoms were more frequent than diagnosed depression in youth with type 1 diabetes (37). In our study, although no differences were found between the two groups in the population-based sample with regard to mental health disorders, analyses showed that youth with type 1 diabetes more frequently endorsed barriers and mental health symptoms in comparison to youth without type 1 diabetes. In previous studies, depressive symptoms predicted later depression diagnosis, suggesting that occurrence of depression at any time during adolescence is a risk factor for continued or recurring depression (16, 18, 38). Also, there is consistent evidence that more mental health symptoms were associated with poor glycemic control (16), which underscores the need for mental health assessment. This finding adds to the literature and suggests that, once considering our population-based assumptions, we may have instead of more frequent mental health disorders, more frequent subclinical mental health symptoms in adolescents with type 1 diabetes, which should be considered when evaluating patients in clinical settings.

In the literature, demographics, socioeconomic features, and clinical characteristics seem to have an impact on type 1 diabetes distribution (39) and may impact glycemic control and mental health issues (1). In this study, although not clear, the incidence of type 1 diabetes appears to slightly rise as the geographical latitude increases. While a clear North-South variation was also not found in the U.S. even after adjusting for ethnic groups (39), in Europe and China, this different distribution pattern was found (40-42). Wide variations in incidence among areas of similar latitude suggest the presence of other environmental features (43). Socioeconomic status seems to be one of these factors (39). In our study, as well as previously published research (39), measures of higher socioeconomic status were more frequently seen in adolescents with type 1 diabetes. Further studies are needed to understand all mechanisms underlying the neighborhood influence. Also, although most autoimmune diseases are more common in females, some studies suggest that type 1 diabetes has no gender differences (44). In contrast, and similarly to other studies in select population (45), our study showed type 1 diabetes to be more prevalent among males. With regard to mental health, based on this population-based sample, demographics and clinical characteristics of participants did not have an impact on the type 1 diabetes-mental health disorders association.

It is important that we do not overstate our findings. Although ERICA is a population-based study, the mental health instrument GHQ is only a screening instrument, which may overestimate the prevalence of mental health issues (46). Moreover, ERICA was not primarily designed to evaluate mental health disorders. Our findings should be confirmed using diagnosis tools for mental health disorders in population-based studies aimed to evaluate mental health. Nevertheless, this is the first Brazilian population-based study and one of the largest ones in the world to assess mental health in adolescents with and without type 1 diabetes, and our results should be addressed while considering mental health evaluation in diabetes care.

In conclusion, mental health symptoms seem to be more frequent than diagnosis of mental health disorders in adolescents with type 1 diabetes. Considering that mental health issues may be underlying risks that compromise glycemic control (8), our findings have practical implications for providers taking care of adolescents with type 1 diabetes, where mental health assessment may identify those at high risk of mental health disorders in order to prevent glycemic control deterioration.

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Author's Contribution

G.H.T researched data, analyzed data, and wrote the manuscript. F.V.C. researched data, analyzed data, and reviewed the manuscript. D.F.S. researched data and reviewed the manuscript. C.S.L. and B.D.S. researched data and reviewed and edited the manuscript. All authors have approved the final version of this manuscript.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Ducat L, Rubenstein A, Philipson LH, Anderson BJ. A review of the mental health issues of diabetes conference. Diabetes Care. 2015;38(2):333-8.

2. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. The New England Journal of Medicine. 1993;329(14):977-86.

3. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. The New England Journal of Medicine. 2005;353(25):2643-53.

4. Rodriguez H. New technologies and old challenges in type 1 diabetes. Diabetes Technology & Therapeutics. 2012;14(12):1082-3.

5. Borus JS, Laffel L. Adherence challenges in the management of type 1 diabetes in adolescents: prevention and intervention. Current opinion in pediatrics. 2010;22(4):405-11.

6. Duke DC, Harris MA. Executive function, adherence, and glycemic control in adolescents with type 1 diabetes: a literature review. Current Diabetes Reports. 2014;14(10):532.

7. Reynolds KA, Helgeson VS. Children with diabetes compared to peers: depressed? Distressed? A meta-analytic review. Annals of Behavioral Medicine. 2011;42(1):29-41.

8. Kongkaew C, Jampachaisri K, Chaturongkul CA, Scholfield CN. Depression and adherence to treatment in diabetic children and adolescents: a systematic review and meta-analysis of observational studies. European Journal of Pediatrics. 2014;173(2):203-12.

9. Melmed SM, Polonsky KS, Larsen R, Kronenberg HM. Williams Textbook of Endocrinology. 13th Edition ed2016. 1888 p.

10. Anderson B, Ho J, Brackett J, Finkelstein D, Laffel L. Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus. The Journal of Pediatrics. 1997;130(2):257-65.

11. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group. The Journal of Pediatrics. 1994;125(2):177-88.

12. Perantie DC, Lim A, Wu J, Weaver P, Warren SL, Sadler M, et al. Effects of prior hypoglycemia and hyperglycemia on cognition in children with type 1 diabetes mellitus. Pediatric Diabetes. 2008;9(2):87-95.

13. Korczak DJ, Pereira S, Koulajian K, Matejcek A, Giacca A. Type 1 diabetes mellitus and major depressive disorder: evidence for a biological link. Diabetologia. 2011;54(10):2483-93.

14. Lawrence JM, Standiford DA, Loots B, Klingensmith GJ, Williams DE, Ruggiero A, et al. Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. Pediatrics. 2006;117(4):1348-58.

15. Laffel LM, Connell A, Vangsness L, Goebel-Fabbri A, Mansfield A, Anderson BJ. General quality of life in youth with type 1 diabetes: relationship to patient management and diabetes-specific family conflict. Diabetes Care. 2003;26(11):3067-73.

16. Johnson B, Eiser C, Young V, Brierley S, Heller S. Prevalence of depression among young people with Type 1 diabetes: a systematic review. Diabetic Medicine. 2013;30(2):199-208.

17. Sivertsen B, Petrie KJ, Wilhelmsen-Langeland A, Hysing M. Mental health in adolescents with Type 1 diabetes: results from a large population-based study. BMC Endocrine Disorders. 2014;14:83.

18. Whittemore R, Kanner S, Singleton S, Hamrin V, Chiu J, Grey M. Correlates of depressive symptoms in adolescents with type 1 diabetes. Pediatric Diabetes. 2002;3(3):135-43.

19. Vasconcellos MT, Silva PL, Szklo M, Kuschnir MC, Klein CH, Abreu Gde A, et al. Sampling design for the Study of Cardiovascular Risks in Adolescents (ERICA). Cadernos de Saúde Pública. 2015;31(5):921-30.

20. Bloch KV, Szklo M, Kuschnir MC, Abreu GA, Barufaldi LA, Klein CH, et al. The Study of Cardiovascular Risk in Adolescents-ERICA: rationale, design and sample characteristics of a national survey examining cardiovascular risk factor profile in Brazilian adolescents. BMC Public Health. 2015;15:94.

21. Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bulletin of the World Health Organization. 2007;85(9):660-7.

22. Tanner JM. Growth at adolescence. 2nd ed. Oxford: Blackwell Scientific; 1962.

23. Farias Júnior JC LA, Mota J, Santos MP, Ribeiro JC, Hallal PC. Validade e reprodutibilidade de um questionário para medida de atividade física em adolescentes: uma adaptação do Self-Administered Physical Activity Checklist. Rev Bras Epidemiol. 2012;15(1):198-210.

24. Cureau FV, Silva TL, Bloch KV, Fujimori E, Belfort DR, Carvalho KM, et al. ERICA: Leisure-time physical inactivity in Brazilian adolescents. Revista de Saúde Pública. 2016;50 Suppl 1.

25. Organization WH. Global recommendations on physical activity for health. Geneva. 2010.

26. Associação Brasileira de Empresas de Pesquisa. Critério Brasil de avaliação econômica 2013. São Paulo: ABEP; 2013. Available in: http://www.abep.org/criterio-brasil.

27. Gouveia VV, Barbosa GA, Oliveira Andrade E, Carneiro MB. Factorial validity and reliability of the General Health Questionnaire (GHQ-12) in the Brazilian physician population. Cadernos de Saúde Pública. 2010;26(7):1439-45.

28. Lopes CS, Abreu GA, Santos DF, Menezes PR, Carvalho KM, Cunha Cde F, et al. ERICA: Prevalence of common mental disorders in Brazilian adolescents. Revista de Saúde Pública. 2016;50 Suppl 1.

29. Cano A, Sprafkin RP, Scaturo DJ, Lantinga LJ, Fiese BH, Brand F. Mental health screening in primary care: a Comparison of 3 brief measures of psychological distress. Journal of Clinical Psychiatry. 2001;3(5):206-10.

30. May S. Patient satisfaction and the detection of psychiatric morbidity in general practice. Family Practice. 1992;9(1):76-81.

31. Bernstein CM, Stockwell MS, Gallagher MP, Rosenthal SL, Soren K. Mental health issues in adolescents and young adults with type 1 diabetes: prevalence and impact on glycemic control. Clinical Pediatrics. 2013;52(1):10-5.

32. Kovacs M, Obrosky DS, Goldston D, Drash A. Major depressive disorder in youths with IDDM. A controlled prospective study of course and outcome. Diabetes Care. 1997;20(1):45-51.

33. White, H. A Heteroskedasticity-Consistent Covariance Matrix Estimator and a Direct Test for Heteroskedasticity. Econometrica. 1980;48(4): 817-38.

34. Caudill SP. Confidence interval estimation for pooled-sample biomonitoring from a complex survey design. Environment International. 2015;85:40-5.

35. Rader KA, Lipsitz SR, Fitzmaurice GM, Harrington DP, Parzen M, Sinha D. Bias-corrected estimates for logistic regression models for complex surveys with application to the United States' Nationwide Inpatient Sample. Statistical Methods in Medical Research. 2015.

36. Kakleas K, Kandyla B, Karayianni C, Karavanaki K. Psychosocial problems in adolescents with type 1 diabetes mellitus. Diabetes & Metabolism. 2009;35(5):339-50.

37. Silverstein J, Cheng P, Ruedy KJ, Kollman C, Beck RW, Klingensmith GJ, et al. Depressive symptoms in youth with type 1 or type 2 diabetes: results of the Pediatric Diabetes Consortium Screening Assessment of Depression in Diabetes Study. Diabetes Care. 2015;38(12):2341-3.

38. Insabella G, Grey M, Knafl G, Tamborlane W. The transition to young adulthood in youth with type 1 diabetes on intensive treatment. Pediatric Diabetes. 2007;8(4):228-34.

39. Liese AD, Puett RC, Lamichhane AP, Nichols MD, Dabelea D, Lawson AB, et al. Neighborhood level risk factors for type 1 diabetes in youth: the SEARCH case-control study. International Journal of Health Geographics. 2012;11:1.

40. Rosenbauer J, Herzig P, von Kries R, Neu A, Giani G. Temporal, seasonal, and geographical incidence patterns of type I diabetes mellitus in children under 5 years of age in Germany. Diabetologia. 1999;42(9):1055-9.

41. Waldhor T, Schober E, Karimian-Teherani D, Rami B, Austrian Diabetes Incidence Study G. Regional differences and temporal incidence trend of Type I diabetes mellitus in Austria from 1989 to 1999: a nationwide study. Diabetologia. 2000;43(11):1449-50.

42. Yang Z, Wang K, Li T, Sun W, Li Y, Chang YF, et al. Childhood diabetes in China. Enormous variation by place and ethnic group. Diabetes Care. 1998;21(4):525-9.

43. Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J. Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. Diabetes Care. 2000;23(10):1516-26.

44. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA. 2014;311(17):1778-86.

45. Gale EA, Gillespie KM. Diabetes and gender. Diabetologia. 2001;44(1):3-15.

46. O'Connor DW, Parslow RA. Mental health scales and psychiatric diagnoses: responses to GHQ-12, K-10 and CIDI across the lifespan. Journal of Affective Disorders. 2010;121(3):263-7.

Table 1. Population-weighted demographics and clinical characteristics

	Non-type 1 diabetes (n=73,508)	**Type 1 diabetes (n=116)**
Age (years)	14.4 ± 0.01	14.2 ± 0.23
Sex (% female)*	**55.4 (55.1-55.8)**	**41.4 (32.8-50.6)**
Race/ethnicity (% white)	40.1 (38.4-41.7)	50.5 (36.2-64.7)
Macro-region		
North	8.4 (8.4-8.4)	10.3 (5.7-18.0)
Northeast	21.3 (21.3-21.4)	12.9 (5.5-27.2)
Midwest	7.7 (7.7-7.7)	4.7 (1.8-11.6)
Southeast	50.8 (50.7-50.8)	53.8 (36.0-70.6)
South	11.8 (11.7-11.8)	18.3 (8.0-36.5)
Area (% urban)	96.1 (88.1-98.8)	99.0 (96.8-99.7)
School (% public)	82.6 (78.0-86.4)	81.1 (64.8-90.9)
Family structure (% two-parent home)	57.3 (55.8-58.7)	63.7 (47.7-77.1)
Parental education (% high school graduate)	54.8 (51.7-57.8)	56.2 (41.9-69.6)
Socioeconomic status (% tertiles)		
First (low)	34.9 (32.9-36.9)	22.4 (10.5-41.4)
Second (medium)	32.8 (31.5-34.2)	24.1 (10.4-46.5)
Third (high)	**32.3 (29.7-34.9)**	**53.5 (37.0-69.3)**
Puberty stage (% complete)	34.5 (33.8-35.2)	31.4 (19.0-47.1)
Physical activity (% ≥300 min/week)	45.7 (44.8-46.6)	41.8 (27.3-57.8)
Overweight (%)	17.1 (16.3-18.0)	14.1 (6.7-27.3)
Obesity (%)	8.4 (7.9-8.9)	6.0 (2.3-15.0)
Alcohol consumption (%)	7.5 (7.4-7.6)	7.0 (5.3-8.2)
Tobacco use (%)	2.5 (2.2-2.8)	3.6 (1.5-8.2)
Hypertension (%)	3.8 (3.4-4.2)	6.0 (2.2-15.0)
Dyslipidemias (%)	8.9 (8.3-9.6)	16.6 (8.0-31.2)
Asthma (%)	9.1 (8.6-9.6)	7.0 (3.3-14.1)

Data are mean ± SE or % (95% CI)

*Non-weighted value

Table 2. Weighted and non-weighted multivariable logistic regression of mental health disorders

GHQ ≥3	**(A) Weighted analyses**	**(B) Non-weighted analyses**
Age (years)	1.08 (1.04-1.13)*	1.11 (1.10-1.13)*
Sex (male)	0.44 (0.40-0.48)*	0.44 (0.42-0.46)*
Race/ethnicity (Caucasians)	1.05 (0.91-1.22)	0.94 (0.90-0.98)*
Macro-region		
Northeast	0.98 (0.89-1.10)	0.89 (0.84-0.94)*
Southeast	0.88 (0.79-0.99)*	0.85 (0.80-0.90)*
South	0.83 (0.73-0.94)*	0.82 (0.76-0.88)*
Midwest	1.00 (0.89-1.11)	0.93 (0.87-0.99)*
Socioeconomic status		
Medium	0.98 (0.85-1.14)	0.99 (0.94-1.03)
High	1.09 (0.96-1.24)	1.10 (1.05-1.16)*
Physical activity (≥300 min/week)	0.91 (0.82-1.02)	0.92 (0.88-0.96)*
Obesity/overweight	1.13 (1.02-1.26)*	1.07 (1.02-1.12)*
Alcohol consumption	1.78 (1.62-1.98)*	1.64 (1.57-1.71)*
Tobacco use	0.67 (0.50-0.90)*	0.70 (0.61-0.80)*
Type 1 diabetes	**1.02 (0.41-2.54)**	**2.08 (1.28-3.38)***

*P<0.05. Data are OR (95% CI).

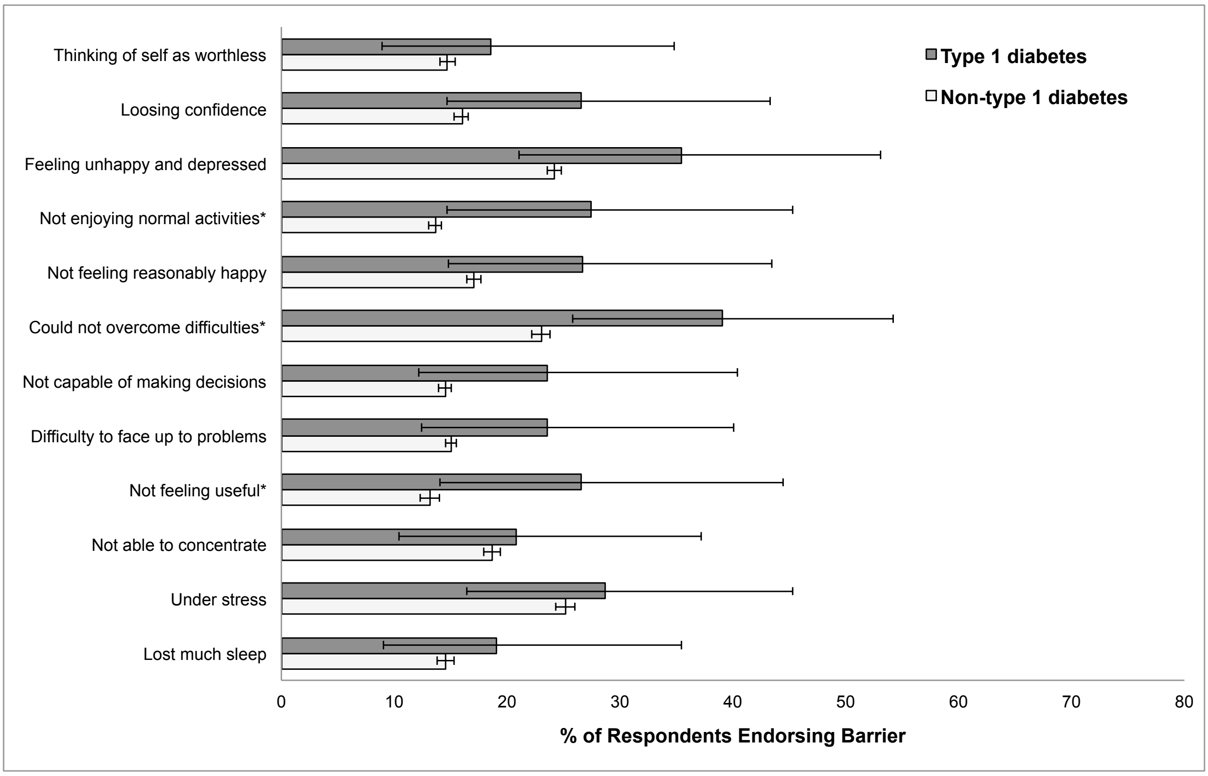

Figure 1. Mental health symptoms: reported occurrence in adolescents with and without type 1 diabetes
*P<0.05

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ARTIGO 5

Health Care Transition in Young Adults with Type 1 Diabetes: Perspectives of Adult Endocrinologists in the U.S.

Diabetes care in young adults with type 1 diabetes

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Abstract

Objective: Young adults with type 1 diabetes transitioning from pediatric to adult care are at risk for adverse outcomes. Our objective was to describe experiences, resources, and barriers reported by a national sample of adult endocrinologists receiving and caring for young adults with type 1 diabetes.

Research Design and Methods: We fielded an electronic survey to adult endocrinologists with a valid e-mail address identified through the American Medical Association Physician Masterfile.

Results: We received responses from 536 of 4,214 endocrinologists (response rate 13%); 418 surveys met the eligibility criteria. Respondents (57% male, 79% Caucasian) represented 47 states; 64% had been practicing >10 years and 42% worked at an academic center. Only 36% of respondents reported often/always reviewing pediatric records and 11% reported receiving summaries for transitioning young adults with type 1 diabetes, although >70% felt that these activities were important for patient care. While most respondents reported easy access to diabetes educators (94%) and dietitians (95%), fewer (42%) reported access to mental health professionals, especially in nonacademic settings. Controlling for practice setting and experience, endocrinologists without easy access to mental health professionals were more likely to report barriers to diabetes management for young adults with depression (odds ratio [OR] 5.3; 95% CI 3.4, 8.2), substance abuse (OR 3.5; 95% CI 2.2, 5.6), and eating disorders (OR 2.5; 95% CI 1.6, 3.8).

Conclusions: Our findings underscore the need for enhanced information transfer between pediatric and adult providers and increased mental health referral access for young adults with diabetes post-transition.

Key words: Diabetes Mellitus, Type 1; Pediatrics; Continuous Glucose Monitoring; Patient Compliance; Medication Adherence; Quality of Life; Insulin Infusion Systems

INTRODUCTION

The young adult period presents special challenges for patients with type 1 diabetes, a chronic illness that requires intensive daily self-management and close medical follow-up (1,2). As young adults with type 1 diabetes experience competing life priorities and decreasing parental involvement in diabetes care, treatment adherence and glycemic control may decline. Young adults with type 1 diabetes, like adolescents (3), have been shown to be at risk for poor glycemic control and adverse health outcomes, including acute diabetes complications such as ketoacidosis and severe hypoglycemia, chronic microvascular complications, and early mortality (4–10).

Health care transition has been defined as “the planned, purposeful movement of young adults from child-centered to adult-oriented health-care systems” (11). There is broad consensus that a lack of effective transition from pediatric to adult diabetes care may contribute to fragmentation of health care, decreased frequency of clinical follow-up, and increased risk for adverse outcomes in young adults with type 1 diabetes (2,12).

Empiric data are limited on best practices in transition care, especially in the U.S. (10,13–16). Prior research, largely from the patient perspective, has highlighted challenges in the transition process, including gaps in care (13,17–19); suboptimal pediatric transition preparation (13,20); increased post-transition hospitalizations (21); and patient dissatisfaction with the transition experience (13,17–19). Previous studies (22–24) have also identified differences between pediatric and adult diabetes care environments as perceived by patients, including, for example, an increased focus on the family in the pediatric setting and an increased focus on diabetes complications in the adult setting.

To advance improvements in care, the national landscape of health care transition and post-transition care for young adults with type 1 diabetes requires greater understanding of the barriers, especially with respect to receiving physician perspectives. Available data suggest that adult endocrinologists care for many young adults with type 1 diabetes following their transfer from pediatric endocrinologists. Among a cohort of participants ≥18 years old in the SEARCH for Diabetes in Youth Quality-of-Care Survey sample, 45% received care from an adult endocrinology care provider, compared with 17% from a generalist (25). However, in order to identify the best practices to enhance the transition process, it is critically important to evaluate the experiences of the adult endocrinologists accepting these transitioning young adult patients with type 1 diabetes.

The objectives of this study were to describe experiences reported by a national sample of adult endocrinologists caring for young adults with type 1 diabetes transferring from pediatric to adult diabetes care and to assess the clinical resources and barriers to care for young adults with type 1 diabetes reported by adult endocrinologists.

RESEARCH DESIGN AND METHODS

Survey Development

We developed a structured survey to characterize the clinical experiences, resources, and barriers reported by adult endocrinologists caring for young adults with type 1 diabetes. Academic literature review, patient survey results, and pediatric and adult provider interviews guided survey development. Initial revisions were made following individual and group feedback from pediatric and adult diabetes providers. The survey was then administered to a small convenience sample of eight endocrinologists for cognitive testing prior to final revisions.

The final survey included 60 items and required approximately 10 min for completion. The survey was divided into the following domains: 1) practice characteristics, 2) physician demographics, 3) health care transition components and their perceived importance, and 4) description of diabetes care provided for young adults, including resources, barriers, and recommendations for improvement. The survey ended with an optional open-ended question asking whether respondents wanted to share anything else regarding experiences caring for young adults with diabetes. A secure electronic version of the survey was created using Research Data Electronic Capture, or REDCap (26), hosted by the Joslin Diabetes Center in conjunction with user support from Harvard Catalyst. A copy of the survey is available upon reader request to the corresponding author. This study was approved by the Committee on Human Studies at the Joslin Diabetes Center, Boston, MA.

Description of Key Survey Variables

For assessment of components of transition care, the survey asked: "In your experience, how often do the following occur when patients with type 1 diabetes are transitioning to you from pediatric care?" Components included receipt of patient summary, review of pediatric records, communication with pediatric providers, parent involvement in first adult visit, combined pediatric/adult diabetes visit, and participation in a transition program. Response options included the following: never, rarely, sometimes, often, or always. Respondents then indicated the perceived importance of each component, with the following response options: not at all important, somewhat important, important, or very important.

To evaluate clinical resources, the survey asked respondents to first indicate resources to which they had easy access (diabetes educator, dietitian, mental health provider, exercise physiologist, care coordinator, and interpreter) and then to specify resources to which they still needed additional access to care effectively for young adults with diabetes.

For the assessment of barriers, the survey presented a series of clinical scenarios involving a 22-year-old patient with type 1 diabetes. Several scenarios focused on mental health topics (e.g., clinical depression, eating disorder, alcohol/drug abuse, severe fear of hypoglycemia, and developmental disability), while others focused on medical management (continuous glucose monitoring, elite athlete, obesity, and poor glycemic control with recurrent ketoacidosis). For each scenario, we asked respondents to describe the barriers to clinical diabetes management; response options included the following: 1) requires too much additional time, 2) inadequate clinical resources, 3) lack clinical expertise in this, 4) other, 5) none.

Survey Administration

Eligible subjects included physicians with a valid e-mail address with specialty listed as “Endocrinology” or “Diabetes” in the American Medical Association (AMA) Physician Masterfile, excluding trainees or physicians with pediatrics or pediatric endocrinology listed as the primary specialty. The AMA Physician Masterfile is a record of current and past data from physicians in the U.S. A physician’s profile is created upon entrance to medical school and is updated with information collected from board certification and state licensure programs, annual AMA census surveys, and an annual online profile update.

We sent an electronic survey to eligible physicians in four waves between July and September 2012. Responses were anonymous. For respondents to proceed with the survey, they had to report caring for five or more young adults with type 1 diabetes, and for inclusion in analyses, respondents had to complete all items related to health care transition. Subjects were offered a choice of a $10 donation to either the American Diabetes Association or JDRF upon survey completion.

Statistical Analysis

All statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC). Descriptive statistics were presented as the mean and SD or proportions. X^2 tests evaluated associations of practice (academic setting, yes/no) and physician (>10 years of experience, yes/no) characteristics with reported components of transition and clinical resources. Because of multiple comparisons across survey questions, a P value of <0.01 was used as the threshold for statistical significance. Following the recognition that mental health services were the only desired clinical resource that was unavailable to >50% of respondents, additional analyses explored factors associated with the absence of mental health services. For the clinical scenarios created to assess barriers, multivariable logistic regression (controlling for years of physician experience and practice setting) provided the odds (with 95% CI) of endorsing barriers in each specific scenario (e.g., depression) according to reported lack of mental health resources.

Open-Ended Response Analysis

Thematic analysis was undertaken of the responses to the open-ended question inviting further input from respondents about their experiences caring for young adults with type 1 diabetes. This analysis was iteratively conducted by three members of the research team (K.C.G., G.H.T., and L.M.L.). The team members independently read all free-text comments and marked and categorized key words and phrases to generate initial codes. Codes were organized using Microsoft Excel. Initial codes were discussed by the group, and discrepancies were resolved through consensus on each comment, ultimately generating a list of second-cycle codes. Each team member then applied the revised coding framework to all free-text comments, and the team met to reach consensus on six final themes.

RESULTS

Survey Response

A total of 6,398 physicians in the non-territorial U.S. were listed in the AMA Physician Masterfile in July 2012 with Endocrinology or Diabetes as the primary specialty (excluding trainees or pediatric physicians). For comparison, the American Board of Internal Medicine recorded 6,384 valid nonterritorial certifications in Endocrinology, Diabetes, and Metabolism as of February 2013 (www.abim.org). We sent the electronic survey to the 4,275 eligible physicians with an available e-mail address. Of these, 4,215 surveys were successfully delivered.

We received 536 responses (13% response rate). Of these, 29 surveys were minimally complete (according to predetermined criteria), 64 physicians sent messages to report their ineligibility (e.g., geriatric providers or working in industry), and 25 physicians cared for fewer than five young adults with diabetes. In sum, 418 surveys were analyzed.

Sample Characteristics

Table 1 displays respondent and practice characteristics. The majority of endocrinologists responding to the survey were male (57%), Caucasian (79%), >45 years old (59%) and had been practicing adult endocrinology/diabetes for >10 years (64%). Sex and age comparison data are available from a recent Endocrine Society analysis (27) of data from the 2011 AMA Physician Masterfile, in which 62% of endocrinologists were male and the mean age was 51 years. Half of the respondents worked in an urban setting, and 42% worked at an academic medical center. A total of 46 states plus the District of Columbia were represented in the sample; only Idaho, Nebraska, South Dakota, and Wyoming were not represented. Examining responses by U.S. Census region, 30% of respondents practiced in the Northeast, 30% in the South, 23% in the Midwest, and 17% in the West. On the basis of the regional breakdown of American Board of Internal Medicine endocrinology certifications as of February 2013, the sample represented between 5.5% and 7.5% of endocrinologists for each of the four census regions (www.abim.org).

Transition Referral Practices

Endocrinologists reported multiple referral sources for young adults with type 1 diabetes entering their practice. Referral sources often/always generating new patients in this population included referral by pediatric providers (43%), referral by family or friend (40%), self-referred (28%), referred by health insurance (11%) or student health (9%), or other (10%).

Components of Transition Care

Figure 1 shows the proportion of respondents reporting an occurrence of health care transition components (often/always) for young adults with type 1 diabetes entering their practices. None of these components was endorsed as often/always occurring by more than half of respondents. Having the patient's parent at the first adult visit was most commonly endorsed (47%), and approximately one-third of respondents endorsed having the opportunity to review pediatric records (36%). Very few endocrinologists reported receiving patient summaries, direct communication with pediatric providers, joint pediatric-adult provider visits, or patient participation in a transition program (all ≤12%). While occurring infrequently, half of the transition components were nonetheless rated as important/very important by the majority of respondents, including patient summary (73%), pediatric record review (72%), and parent presence at the first visit (56%). One-third of respondents rated direct communication with pediatric providers and transition programs as important/very important, while only 10% endorsed the importance of a joint pediatric-adult provider visit.

X^2 comparisons showed no significant differences in occurrence of transition care components for endocrinologists with >10 years of experience or those practicing in academic settings.

Clinical Resources for Young Adult Diabetes Care

Figure 2 depicts the availability of clinical resources for young adult diabetes care and reports the need for additional access; availability of and need for additional access were not mutually exclusive. Most endocrinologists reported easy access to diabetes educators (94%), dietitians (95%), and interpreter services (61%). Fewer (42%) reported access to mental health providers (e.g., social worker, psychologist, or psychiatrist). Endocrinologists who reported easy access to mental health referrals for young adults with type 1 diabetes were more likely to practice at academic medical centers (52% vs. 35%, P=0.0006). Very few endocrinologists reported easy access to care coordinators (15%) or exercise physiologists (16%). Regarding the need for additional resources, mental health (54%) was the only need endorsed by the majority of respondents.

Barriers to Clinical Management of Young Adults With Diabetes

In nine patient scenarios focusing on barriers to clinical diabetes management, specific barrier options included inadequate clinical resources, lack of clinical expertise, and too much additional time required. Of these, the resource barriers were the most highly endorsed, especially for the scenarios involving mental health issues, including substance abuse (47% endorsed the lack of resources barrier), eating disorder (39%), depression (38%), and developmental disability (31%). Resource barriers were less frequently endorsed (10–16%) for scenarios focused on medical management or technology. Similarly, for the mental health scenarios, 30% of endocrinologists endorsed lack of expertise as a barrier for substance and eating disorder cases (both 30%), followed by developmental disability (24%) and depression (15%), in contrast to minimal expertise barriers (1–3%) for recurrent ketoacidosis, obesity, and continuous glucose monitoring. Figure 3 summarizes the report of resource and expertise barriers.

In general, time barriers were less frequently selected. Time barriers were endorsed by 24% of respondents for developmental disability; by 11–13% of respondents for substance abuse, eating disorders, depression, continuous glucose monitoring, recurrent ketoacidosis, and elite athlete; by 9% for fear of hypoglycemia; and by 7% for obesity.

Logistic regression models calculated the odds of endorsing barriers for each specific scenario according to reported lack of mental health resources, controlling for physician experience and practice setting. All model P values (likelihood ratio test) were <0.0001. Endocrinologists without easy access to mental health referrals were most likely to report barriers to diabetes management for young adults with depression (odds ratio [OR] 5.3; 95% CI 3.4, 8.2), substance abuse (OR 3.5; 95% CI 2.2, 5.6), and eating disorders (OR 2.5; 95%

CI 1.6, 3.8). In addition, endocrinologists without easy access to mental health referrals were also more likely to report barriers to management for fear of hypoglycemia (OR 2.5; 95% CI 1.4, 4.4) and developmental disability (OR 2.3; 95% CI 1.5, 3.6). Barriers to management for all other scenarios were not significantly increased in endocrinologists without easy access to mental health referrals.

Overall Perceptions and Suggestions for Improvement in Young Adult Diabetes Care

Overall, 75% of endocrinologists reported that they enjoyed seeing young adults with type 1 diabetes (agree/ strongly agree), and 56% endorsed wanting to see more young adults with type 1 diabetes in their practice. About half felt that treating young adults with type 1 diabetes required more time (45%) and more resources (45%) compared with older adults with type 1 diabetes. To foster improvements in young adult diabetes care, respondents recommended patient support groups (82% helpful/very helpful), improved reimbursement rates (76%), online provider resources about young adult diabetes management (60%), and continuing medical education about young adult behavioral issues (57%).

Open-Ended Response Analysis Results

A total of 153 of 418 of the respondents (37%) provided comments to the open-ended question inviting further input regarding their experiences caring for young adults with type 1 diabetes. During the coding process, the team reached consensus on six final themes. More than 80% of narrative comment codes were encompassed by the following three themes: 1) intensive time and care coordination requirements of young adults with type 1 diabetes (36%): adult endocrinologists endorsed a need for increased time to spend with young adults as well as a need for increased resources to address young adult social, emotional, and family issues; 2) challenges with nonadherence among young adults with type 1 diabetes (30%): adult endocrinologists frequently cited competing priorities of young adults and their lack of acceptance of the potential severity of type 1 diabetes as major barriers to adherence; and 3) divergent approaches to care by pediatric and adult diabetes providers (18%): adult endocrinologists perceived “coddling” and “excessive” focus by pediatric endocrinologists on avoidance of hypoglycemia at the expense of glycemic control. Table 2 includes representative quotations from each of these three central themes, encompassing 84% of the comments.

The remaining narrative comment thematic categories included financial aspects of young adult diabetes care (7%), the role of family and social support in young adult diabetes care (6%), and (6) other/miscellaneous comments (3%).

CONCLUSIONS

To our knowledge, this is the largest study to date examining the experiences of adult endocrinologists caring for transitioning young adults with type 1 diabetes in the U.S.

Results from our sample, representing 418 adult endocrinologists practicing in 47 states, underscore a number of major challenges in the health care transition process.

Only one-third of adult endocrinologists reported the opportunity to review pediatric records of young adults entering their practice, although three-quarters felt that it was important to do so. A minority (<15%) described direct communication (e.g., e-mail or phone) with pediatric diabetes providers or the receipt of a formal transition medical summary. Further, adult endocrinologists in our sample noted that a majority of young adult patients with type 1 diabetes appeared without any physician referral.

These findings of deficiencies in transition care coordination reinforce results from young adult patient (13,20) and pediatric provider (28) surveys showing suboptimal transition planning. Joint expert consensus guidelines from the American Academy of Pediatrics, American Academy of Family Physicians, and the American College of Physicians state the importance of medical record review by the receiving adult provider as well as direct communication between pediatric and adult providers (29). A position statement of the American Diabetes Association, in collaboration with many professional societies, emphasizes the value of a pediatric care summary document, with recommended components including assessment of diabetes self-care skills, summary of past glycemic control and diabetes-related comorbidities, and summary of mental health issues (2). The Endocrine Society has created materials to help ease this transition process, including a comprehensive care summary template (30). Nonetheless, the gaps between national consensus recommendations and current physician practices, as demonstrated in our study, support the need for additional collaborative efforts at individual, practice, and systems levels to enhance provider hand-offs for transitioning young adults with type 1 diabetes.

A number of studies document deficiencies in provider hand-offs across other chronic conditions and point to the broader relevance of our findings. For example, in two studies of inflammatory bowel disease, adult gastroenterologists reported inadequacies in young adult transition preparation (31) and infrequent receipt of medical histories from pediatric providers (32). In a study of adult specialists caring for young adults with a variety of chronic diseases (33), more than half reported that they had no contact with the pediatric specialists.

Importantly, more than half of the endocrinologists in our study reported a need for increased access to mental health referrals for young adult patients with type 1 diabetes, particularly in non-academic settings. Report of barriers to care was highest for patient scenarios involving mental health issues, and endocrinologists without easy access to mental health referrals were significantly more likely to report barriers to diabetes management for young adults with psychiatric comorbidities such as depression, substance abuse, and eating disorders.

Prior research (34,35) has uncovered the lack of mental health resources in diabetes care. In the large cross-national Diabetes Attitudes, Wishes and Needs (DAWN) study (36), which was not specific to type 1 diabetes or young adults, diabetes providers often reported not having the resources to manage mental health problems; half of specialist diabetes physicians felt unable to provide psychiatric support for patients and one-third did not have ready access to outside expertise in emotional or psychiatric matters. Our results, which resonate with the DAWN findings, are particularly concerning in light of the vulnerability of young adults with type 1 diabetes for adverse medical and mental health outcomes (4,34,37,38).

In a recent report from the Mental Health Issues of Diabetes conference (35), which focused on type 1 diabetes, a major observation included the lack of trained mental health professionals, both in academic centers and the community, who are knowledgeable about the mental health issues germane to diabetes. Our results support a need for increased clinical training programs for mental health providers focusing on the mental health needs of young adults with diabetes, including depression, substance abuse, and eating disorders. In addition, continuing medical education programs for adult endocrinologists on mental health topics may foster an integration of mental and physical health care for young adults with type 1 diabetes.

Our thematic analysis also highlighted provider perceptions of the intensive psychosocial needs of young adults with type 1 diabetes, along with concerns about time constraints in clinical care. Challenges regarding the psychosocial needs of young adult patients have similarly been reported in qualitative work with general internists (39). The third most common theme in our study of adult endocrinologists related to perceived divergent approaches to care by pediatric and adult diabetes providers. This observation calls for future study and an open dialogue between pediatric and adult providers. Qualitative research (24,40) has suggested that pediatric and adult care systems represent two different medical "subcultures" and that the young adult's lack of preparation for successful independent participation in the adult health care culture may contribute to transition challenges. Pediatric diabetes providers may consider discussing with transitioning patients that adult providers may address glycemic control and diabetes complications in a different manner than experienced in pediatrics.

There are several limitations to this study. The study was limited to physicians with valid e-mail addresses listed in the AMA Physician Masterfile. Nonresponse bias is a concern, though the response rate is comparable with other studies using electronic physician surveys (28,41). Moreover, data were not available regarding demographic characteristics of the nonrespondents. Given the low proportion of respondents (9%) practicing in rural areas, future study is needed to capture the unique needs of transitioning young adults in rural areas. In addition, the results may be biased toward physicians who are interested in thinking about young adults with type 1 diabetes and thus may represent a "best case" scenario of transition care practices. Self-reported survey data are subject to recall bias and, perhaps, to a desire to provide socially desirable answers (though the anonymity of the survey should mitigate this). The survey was conducted in 2012, and the results may not reflect the latest advances in care following publication of expert consensus guidelines in recent years. Finally, this study focused solely on endocrinologists and did not evaluate the experiences of primary care physicians or nurse professionals, who may provide diabetes care for transitioning young adults with type 1 diabetes. Perceptions of young adult diabetes care from different types of adult diabetes care providers, including primary care physicians as well as certified diabetes educators and advanced practice registered nurses, require further study.

In conclusion, our results provide important information about the experiences of adult endocrinologists caring for young adults with type 1 diabetes in the U.S. Our findings support the high importance of enhanced information transfer and direct communication between pediatric and adult diabetes providers, along with efforts to increase mental health provider training and access and to implement educational opportunities for adult endocrinologists on behavioral health topics specific to young adults with type 1 diabetes.

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Duality of Interest

No potential conflicts of interest relevant to this article were reported. Author Contributions. K.C.G. researched the data and wrote the article. G.H.T. and P.F. analyzed the data and reviewed and edited the article. J.S.N. and L.M.L. researched the data and reviewed and edited the article. J.A.F. contributed to the discussion and reviewed and edited the article. K.C.G. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. American Diabetes Association. Standards of medical care in diabetes 2013. Diabetes Care 2013;36(Suppl. 1):S11–S66

2. Peters A, Laffel L; American Diabetes Association Transitions Working Group. Diabetes care for emerging adults: recommendations for transition from pediatric to adult diabetes care systems: a position statement of the American Diabetes Association, with representation by the American College of Osteopathic Family Physicians, the American

Academy of Pediatrics, the American Association of Clinical Endocrinologists, the American Osteopathic Association, the Centers for Disease Control and Prevention, Children with Diabetes, The Endocrine Society, the International Society for Pediatric and Adolescent Diabetes, Juvenile Diabetes Research Foundation International, the National Diabetes Education Program, and the Pediatric Endocrine Society (formerly Lawson Wilkins Pediatric Endocrine Society). Diabetes Care 2011;34: 2477–2485

3. Clements MA, Foster NC, Maahs DM, et al.; T1D Exchange Clinic Network. Hemoglobin A1c (HbA1c) changes over time among adolescent and young adult participants in the T1D Exchange Clinic Registry. Pediatr Diabetes. 8 July 2015 [Epub ahead of print]. DOI: 10.1111/ pedi.12295

4. Bryden KS, Dunger DB, Mayou RA, Peveler RC, Neil HA. Poor prognosis of young adults with type 1 diabetes: a longitudinal study. Diabetes Care 2003;26:1052–1057

5. Laing SP, Swerdlow AJ, Slater SD, et al. The British Diabetic Association Cohort Study, I: all-cause mortality in patients with insulin-treated diabetes mellitus. Diabet Med 1999;16:459– 465

6. Jacobson AM, Hauser ST, Willett J, Wolfsdorf JI, Herman L. Consequences of irregular versus continuous medical follow-up in children and adolescents with insulin-dependent diabetes mellitus. J Pediatr 1997; 131:727–733

7. Wills CJ, Scott A, Swift PG, Davies MJ, Mackie AD, Mansell P. Retrospective review of care and outcomes in young adults with type 1 diabetes. BMJ 2003;327:260–261

8. Bryden KS, Peveler RC, Stein A, Neil A, Mayou RA, Dunger DB. Clinical and psychological course of diabetes from adolescence to young adulthood: a longitudinal cohort study. Diabetes Care 2001;24:1536–1540

9. Laing SP, Jones ME, Swerdlow AJ, Burden AC, Gatling W. Psychosocial and socioeconomic risk factors for premature death in young people with type 1 diabetes. Diabetes Care 2005;28: 1618–1623

10. Lotstein DS, Seid M, Klingensmith G, et al.; SEARCH for Diabetes in Youth Study Group. Transition from pediatric to adult care for youth diagnosed with type 1 diabetes in adolescence. Pediatrics 2013;131:e1062–e1070

11. Blum RW, Garell D, Hodgman CH, et al. Transition from child-centered to adult health-care systems for adolescents with chronic conditions. A position paper of the Society for Adolescent Medicine. J Adolesc Health 1993; 14:570–576

12. Weissberg-Benchell J, Wolpert H, Anderson BJ. Transitioning from pediatric to adult care: a new approach to the post-adolescent young person with type 1 diabetes. Diabetes Care 2007;30:2441–2446

13. Garvey KC, Wolpert HA, Rhodes ET, et al. Health care transition in patients with type 1 diabetes: young adult experiences and relationship to glycemic control. Diabetes Care 2012;35: 1716–1722

14. Hanna KM, Weaver MT, Stump TE, et al. Initial findings: primary diabetes care responsibility among emerging adults with type 1 diabetes post high school and move out of parental home. Child Care Health Dev 2013;39:61–68 15. Helgeson VS, Reynolds KA, Snyder PR, et al. Characterizing the transition from pediatric to adult care among emerging adults with type 1 diabetes. Diabet Med 2013;30:610–615

16. Insabella G, Grey M, Knafl G, Tamborlane W. The transition to young adulthood in youth with type 1 diabetes on intensive treatment. Pediatr Diabetes 2007;8:228–234

17. Busse FP, Hiermann P, Galler A, et al. Evaluation of patients' opinion and metabolic control after transfer of young adults with type 1 diabetes from a pediatric diabetes clinic to adult care. Horm Res 2007;67:132–138

18. Kipps S, Bahu T, Ong K, et al. Current methods of transfer of young people with Type 1 diabetes to adult services. Diabet Med 2002;19: 649–654

19. Pacaud D, Stephure D, Dele-Davies H. Problems in transition from pediatric to adult care in individuals with diabetes. Can J Diabetes 2005; 40:29–35

20. Raymond JK, Duke DC, Shimomaeda L, Harris MA. Looking forward to transition: perspectives on transition from pediatric to adult diabetes care. Diabetes Manag (Lond) 2013;3 21. Nakhla M, Daneman D, To T, Paradis G, Guttmann A. Transition to adult care for youths with diabetes mellitus: findings from a Universal Health Care System. Pediatrics 2009;124: e1134–e1141

22. Dovey-Pearce G, Hurrell R, May C, Walker C, Doherty Y. Young adults' (16-25 years) suggestions for providing developmentally appropriate diabetes services: a qualitative study. Health Soc Care Community 2005;13:409–419 23. Visentin K, Koch T, Kralik D. Adolescents with type 1 diabetes: transition between diabetes services. J Clin Nurs 2006;15:761–769

24. Garvey KC, Beste MG, Luff D, Atakov-Castillo A, Wolpert HA, Ritholz MD. Experiences of health care transition voiced by young adults with type 1 diabetes: a qualitative study. Adolesc Health Med Ther 2014;5:191–198

25. Waitzfelder B, Pihoker C, Klingensmith G, et al.; SEARCH for Diabetes in Youth Study Group. Adherence to guidelines for youths with diabetes mellitus. Pediatrics 2011;128:531–538

26. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–381

27. Vigersky RA, Fish L, Hogan P, et al. The clinical endocrinology workforce: current status and future projections of supply and demand. J Clin Endocrinol Metab 2014;99:3112–3121 28. de Beaufort C, Jarosz-Chobot P, Frank M, de Bart J, Deja G. Transition from pediatric to adult diabetes care: smooth or slippery? Pediatr Diabetes 2010;11:24–27

29. Cooley WC, Sagerman PJ; American Academy of Pediatrics; American Academy of Family Physicians; American College of Physicians; Transitions Clinical Report Authoring Group. Supporting the health care transition from adolescence to adulthood in the medical home. Pediatrics 2011;128:182–200

30. Endocrine Society. Managing the transition of care for patients with type 1 diabetes [article online], 2012. Available from https://www.endocrine.org/education-and-practice-management/quality-improvement-resources/clinical-practice-resources/transition-of-care. Accessed 19 November 2015

31. Sebastian S, Jenkins H, McCartney S, et al. The requirements and barriers to successful transition of adolescents with inflammatory bowel disease: differing perceptions from a survey of adult and pediatric gastroenterologists. J Crohn’s Colitis 2012;6:830–844

32. Hait EJ, Barendse RM, Arnold JH, et al. Transition of adolescents with inflammatory bowel disease from pediatric to adult care: a survey of adult gastroenterologists. J Pediatr Gastroenterol Nutr 2009;48:61–65

33. Suris JC, Akre´ C, Rutishauser C. How adult specialists deal with the principles of a successful transition. J Adolesc Health 2009;45:551–555

34. Ducat L, Philipson LH, Anderson BJ. The mental health comorbidities of diabetes. JAMA 2014;312:691–692

35. Ducat L, Rubenstein A, Philipson LH, Anderson BJ. A review of the mental health issues of diabetes conference. Diabetes Care 2015;38:333–338

36. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE. Psychosocial problems and barriers to improved diabetes management: results of the cross-national Diabetes Attitudes, Wishes and Needs (DAWN) Study. Diabet Med 2005;22:1379–1385

37. Hislop AL, Fegan PG, Schlaeppi MJ, Duck M, Yeap BB. Prevalence and associations of psychological distress in young adults with Type 1 diabetes. Diabet Med 2008;25:91–96

38. Lawrence JM, Standiford DA, Loots B, et al.; SEARCH for Diabetes in Youth Study. Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. Pediatrics 2006;117: 1348–1358

39. Peter NG, Forke CM, Ginsburg KR, Schwarz DF. Transition from pediatric to adult care:

internists' perspectives. Pediatrics 2009;123: 417–423

40. Reiss JG, Gibson RW, Walker LR. Health care transition: youth, family, and provider perspectives. Pediatrics 2005;115:112–120 41. Nicholls K, Chapman K, Shaw T, et al. Enhancing response rates in physician surveys: the limited utility of electronic options. Health Serv Res 2011;46:1675–1682

Table 1. Sample Characteristics (n = 418)

CHARACTERISTIC	ITEM N	MEAN ± SD OR %
Male	400	57%
Race	403	
Black/African-American		1%
White/Caucasian		79%
Asian/Pacific Islander		17%
Other		3%
Age	405	
≤45 years		41%
46-64 years		48%
≥65 years		11%
Years in practice	404	
≤10 years		37%
11-20 years		28%
≥21 years		35%
United States census region of practice	403	
Northeast		30%
South		30%
Midwest		23%
West		17%
Practice setting	416	
Urban		51%
Suburban		40%
Rural		9%
Practice type	415	
Academic medical center		42%
Community hospital		9%
Large group practice		27%
Small group practice		12%
Solo practice		10%
Percent of patient panel with type 1 diabetes	413	22 ± 17
Percent of patient panel with type 2 diabetes	393	54 ± 22
Number of type 1 diabetes patients 18-30 years in physician panel	415	
5-25		40%
26-50		29%
51-100		17%
>100		14%
Report of typical diabetes return visit length	404	39%
Report of typical diabetes return visit length	415	
≤15 minutes		22%
20 minutes		39%
25-30 minutes		36%
>30 minutes		3%

Table 2. Representative Quotations from Thematic Analysis of Narrative Comments

Intensive time and care coordination requirements of young adults with type 1 diabetes	"I always plan on running behind with this group."
	"I often spend more time on social issues than actual medical decision-making."
	"It takes a great deal of time…I wish I had more resources to deal with the transition of adolescents/young adults to the adult endo clinic."
	"Very time-consuming and intense, requires coordination of care, family interaction and involvement, utilizes many resources."
Challenges with non-adherence among young adults with type 1 diabetes	"I find it frustrating at times because they do not yet realize the potential severity of their disease. They no-show for appointments at much higher rate than other adult patients."
	"Young adults are generally noncompliant and don't take their diagnoses seriously. There are very few young adults I see that are motivated to care about their disease. This is the biggest challenge."
	"They fall in two camps....very committed to their care, in which taking care of them is easy, and very negligent/irresponsible when it comes to managing diabetes...in which case I don't know how to help them."
	"Young adults with type 1 diabetes have many competing demands which puts their diabetes care last on their priorities…many are unprepared about the differences between pediatric and adult care or even how to function as an independent young adult with type 1 diabetes."
Divergent approaches to care by pediatric and adult diabetes providers	"Almost none of these young adults arrive in my office with the ability to care for their diabetes on their own. I have a sense that they learned nothing from their pediatric endocrinologists or they were taught nothing."
	"Generally ill-prepared to face responsibilities as adult diabetic patient. Are coddled too long by parents and pediatric practices. Adult practices in non-academic environments cannot 'hold hands'. These young adults are not trained to be accountable for their actions and have difficulty transitioning to adult care."
	"Overall I've been underwhelmed by pediatric endocrinologists from what the patients transitioning to me tell me. It seems that A1c's are not stressed and avoidance of hypoglycemia is stressed excessively…I then get patients that are developing complications in their mid-20's."
	"Patients transitioning from peds have been conditioned to think an A1c of 8 is OK. Then the adult endo becomes the bad news doctor, making the transition worse."

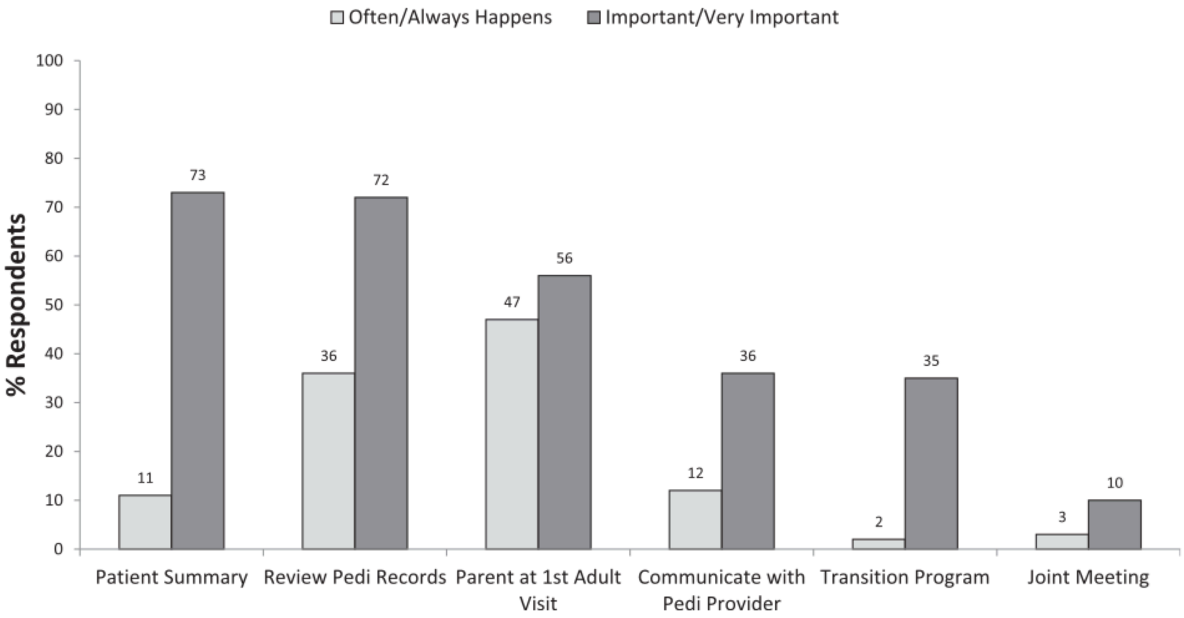

Figure 1—Health care transition components: reported occurrence in practice and perceived importance. Pedi, pediatric.

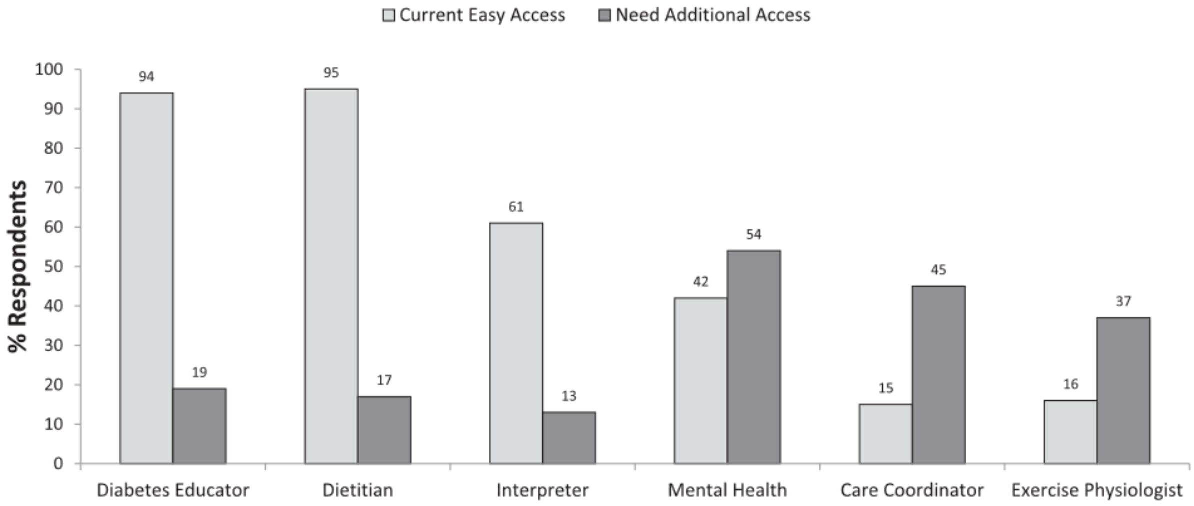

Figure 2—Clinical resources for young adult type 1 diabetes care: reported availability and recognition of need.

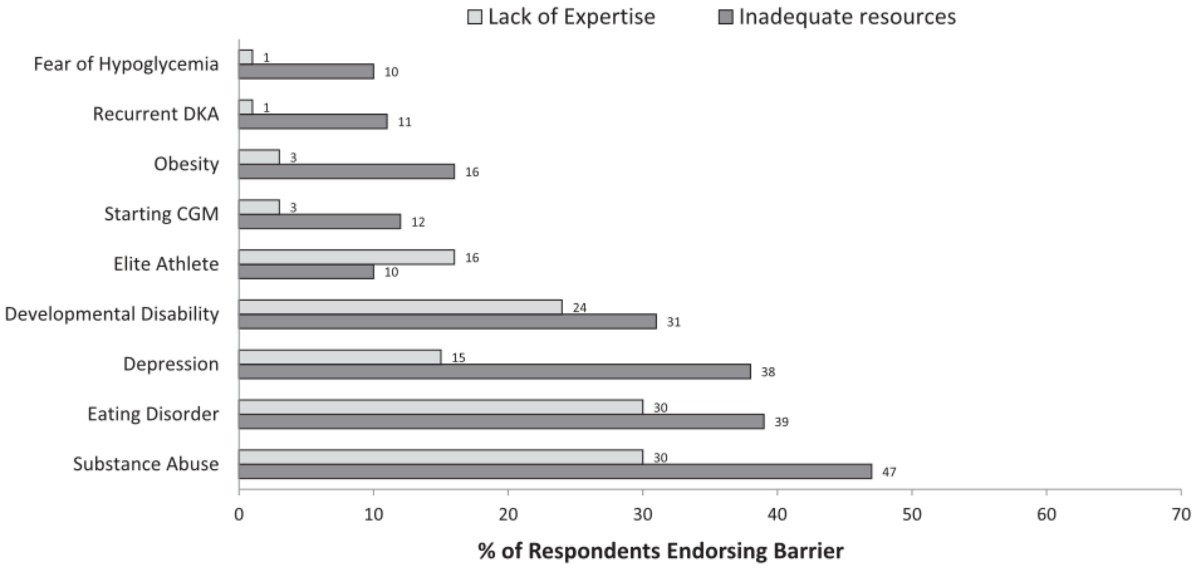

Figure 3—Common clinical challenges facing endocrinologists caring for young adults with type 1 diabetes: perceived lack of expertise and need for more resources. CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis.

CONCLUSÕES

O diabetes tipo 1 é uma doença crônica e progressiva, cujo tratamento estabelece contínuas demandas tanto para o paciente quanto para seus familiares, e a adolescência parece ser um período especialmente crítico para o controle glicêmico. A partir de dados deste trabalho, identificou-se que este controle tende a deteriorar especialmente no sexo feminino ao final da puberdade. De acordo com nossas análises, o uso de tecnologia em saúde, como bomba de insulina, associou-se a melhor controle glicêmico durante a infância, adolescência e idade adulta. Ressalta-se, entretanto, a importância de identificar adequadamente os pacientes que potencialmente se beneficiarão do uso de tecnologia para o manejo do diabetes. Nossos resultados identificaram, a partir de um grupo selecionado de pacientes, que aqueles motivados ao uso de monitores contínuos de glicemia (*continuous glucose monitoring,* CGM) já mostravam-se diferentes da população geral antes do início do uso de CGM, com melhor adesão ao tratamento, melhor controle glicêmico, maior frequência de verificação da glicemia capilar, menor conflito familiar relacionado ao diabetes e maior qualidade de vida. Avaliar adequadamente a adesão ao tratamento parece ser um ponto fundamental antes de considerar o uso de tecnologias na prática clínica. Para avaliação de adesão, nossos resultados identificaram a verificação da glicemia capilar por *download* de glicosímetro como o mais forte método preditor de controle glicêmico. O uso de um questionário administrado por entrevistadores também mostrou-se como método adequado, podendo fornecer informações adicionais à equipe de saúde relacionadas aos seus domínios (dieta, exercícios, insulinoterapia, monitorização da glicemia capilar e hipoglicemia). Para garantir adequada adesão, torna-se importante a identificação de potenciais transtornos de saúde mental capazes de modificar o controle glicêmico. Nossos resultados evidenciaram que, em comparação ao grupo controle de adolescentes sem diabetes tipo 1, os adolescentes com diabetes tipo 1 consistentemente apresentaram maior frequência de sintomas de transtornos de saúde mental. Estes achados têm implicações práticas para a equipe de saúde que deve estar preparada para identificar estes sintomas, a fim de evitar uma possível deterioração do controle glicêmico. Conforme dados de nossas análises, na população estudada, a maioria dos médicos endocrinologistas descreveu não ter acesso a profissionais capacitados para manejo de transtornos de saúde mental. Este despreparo da equipe pode predispor, ainda mais, ao surgimento de barreiras psicossociais potencialmente preditoras de deterioração do controle glicêmico. Nossos achados reforçam a necessidade de capacitação das equipes de saúde para um melhor cuidado de adolescentes com diabetes tipo 1.

ANEXO

OUTRAS PRODUÇÕES CIENTÍFICAS

Além dos artigos apresentados nesta tese, as seguintes produções científicas foram realizadas durante os dois anos e oito meses deste doutorado, tendo, como participação, autoria ou coautoria em estudos de diferentes desenhos (estudo de farmacocinética e farmacodinâmica - dados ainda não apresentados, estudos transversais, estudo de coorte, estudo qualitativo, estudo de protocolo, estudo epidemiológico de base populacional, ensaio clínico randomizado - dados ainda não apresentados, estudo de análise molecular, revisão sistemática e revisão sistemática com meta-análise):

Artigos completos

- Programmed Death Ligand-1 expression in adrenocortical carcinoma: an exploratory biomarker study. Journal for ImmunoTherapy of Cancer, BMC 2015;3. DOI10.1186/s40425-015-0047-3.
- Adrenocortical carcinoma: the management of metastatic disease. Critical Reviews in Oncology/Hematology 2014;92:123-132. IF 4.03.
- Prevalence of diabetes mellitus in Brazil over time: a systematic review with meta-analysis. Submetido para publicação, em revisão.
- Logistics of blood collection and biochemical analysis in the Study of Cardiovascular Risk in Adolescents – ERICA. Submetido para publicação, em revisão.
- Prevalence of elevated levels of HbA1c in schoolchildren from the Study of Cardiovascular Risk in Adolescents (ERICA). Pronto para submissão.
- Weight status of youth with type 1 diabetes: impact of childhood weight and glycemic control. Pronto para submissão.

Resumos em congressos

- Health care transition in young adults with type 1 diabetes: comparison of adult endocrinologist and adult diabetes educator perspectives. ADA 2015, Boston, U.S. (poster).
- Impact of A1c and zBMI on blood pressure over time in pediatric type 1 diabetes. ADA 2015, Boston, U.S. (poster).
- Biomedical predictors of consistent continuous glucose monitoring in youth with type 1 diabetes. ADA 2015, Boston, U.S. (poster).
- Contrasting reports of BG monitoring frequency in youth with type 1 diabetes: meter download, clinician report, and self report. ADA 2015, Boston, U.S. (poster).
- Under-management of hyperlipidemia in young persons with type 1 diabetes. ENDO 2015, San Diego, U.S. (oral).
- Predictors of visits with a registered dietitian for youth and young adults with type 1 diabetes. ENDO 2015, San Diego, U.S. (poster).
- Prevalence of diabetes mellitus in Brazil: a systematic review with meta-analysis. WDC 2015, Vancouver, Canada. (poster). SBD 2015, Porto Alegre, Brasil (oral).
- Comparison between Adherence Assessments and Blood Glucose Monitoring Measures to Predict Glycemic Control in Patients with Type 1 Diabetes. WDC 2015, Vancouver, Canada. (poster). SBD 2015, Porto Alegre, Brasil (oral).
- Perfil de adesão ao regime de insulina prescrito dos pacientes com diabetes melito tipo 1 em acompanhamento no ambulatório do Hospital de Clinicas de Porto Alegre. SBD 2015, Porto Alegre, Brasil (pôster).
- Weight status of youth with type 1 diabetes over time: impact of childhood weight and glycemic control. ADA 2014, San Francisco, U.S. (oral).
- Impact of zBMI on LDL and HDL cholesterol in childhood type 1 diabetes. ADA 2014, San Francisco, U.S. (poster).

- A1c trajectories from childhood to young adulthood in type 1 diabetes: impact of age and sex. ADA 2014, San Francisco, U.S. (poster)
- Salient features of youth with type 1 diabetes initiating continuous glucose monitoring. ADA 2014, San Francisco, U.S. (poster). ISPAD 2014, Boston, U.S. (oral).
- Dynamic changes in total daily insulin dose during childhood and adolescence in youth with type 1 diabetes: impact of age, sex, regimen and weight status. ENDO 2014, Chicago, U.S. (poster).