

**UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM EPIDEMIOLOGIA**



**Controle Individual e Combinado dos Fatores de Risco para
Complicações em Diabetes e Associação com Mortalidade – ELSA-
Brasil**

Bruna Cristine Chwal

Orientador: Prof. Dr. Bruce Bartholow Duncan

Co-orientador: Prof Dr. Rodrigo Citton Padilha dos Reis

Porto Alegre
2023

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TESE DE DOUTORADO

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ABREVIATURAS E SIGLAS

ABC - A: A1C (hemoglobina glicada); B: Blood Pressure (pressão arterial); C: Cholesterol (low density lipoprotein-cholesterol)

ADA - American Diabetes Association

BRAs - Bloqueadores dos Receptores da Angiotensina II

DALYs - Anos de vida ajustados para incapacidade (Disability Adjust Life Years)

DCNT - Doenças Crônicas Não Transmissíveis

DCV - Doença Cardiovascular

ELSA - Estudo Longitudinal da Saúde do Adulto

ECA - Inibidor da Enzima Conversora de Angiotensina

GBD - Global Burden of Disease

IAM - Infarto Agudo do Miocárdio

IDF - International Diabetes Federation

LDL-c - Low Density Lipoprotein-Cholesterol

MS - Ministério da Saúde

NHANES - National Health and Nutrition Examination Survey

PIB - Produto Interno Bruto

PNS - Pesquisa Nacional de Saúde

RNDS - Rede Nacional de Dados em Saúde

RAS - Rede de Atenção à Saúde

SGTLT2 - Inibidor do Cotransportador sódio-glicose 2

SUS - Sistema Único de Saúde

VEGF - Agentes Inibidores do Fator de Crescimento Endotelial Vascular

VIGITEL - Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico

YLDs - Anos vividos com incapacidade (years of health life lost due disability)

WHO - World Health Organization

RESUMO

Introdução: O diabetes mellitus tipo 2 é um importante problema de saúde global. O controle da glicemia, pressão arterial e tabagismo melhora o prognóstico de indivíduos com diabetes mellitus e reduz a chance de morte.

Objetivo: Avaliar o controle individual e combinado dos fatores de risco (glicemia, pressão arterial, colesterol LDL-c e não tabagismo) para complicações em adultos brasileiros com diabetes conhecido na coorte ELSA-Brasil (primeiro artigo) e caracterizar o risco de morte conforme esses fatores (segundo artigo).

Métodos: Foram realizados análises transversais (primeiro artigo) e longitudinais (segundo artigo) de dados de participantes do Estudo Longitudinal Brasileiro de Saúde do Adulto, composto por aqueles que relataram diagnóstico prévio de diabetes ou uso de medicação antidiabética. No primeiro artigo, baseado nos dados da onda 3 (visita de 2017 a 2019), consideramos hemoglobina glicada (HbA1c) <7% como controle glicêmico (alvo A); pressão arterial <140/90 mmHg (ou <130/80 mmHg em alto risco cardiovascular) como controle da pressão arterial (alvo B) e LDL-c <100 mg/dl (ou <70 mg/dl em alto risco) como controle de LDL-c (alvo C), de acordo com as diretrizes da American Diabetes Association (ADA) de 2022. Realizamos modelos de regressão de Poisson com variância robusta para ajustar associações para fatores sociodemográficos e clínicos. No segundo artigo, acompanhamos os participantes do Estudo Longitudinal Brasileiro de Saúde do Adulto com diabetes autorreferido, apurado por diagnóstico médico autorreferido ou uso de medicamentos, no período de 2008 a 2019. Definimos o controle de glicose, pressão arterial e colesterol (LDL-c) de acordo com as diretrizes da ADA de 2022. Nossa vigilância telefônica anual identificou óbitos que foram confirmados por registros hospitalares e atestados de óbito. Em seguida, aplicamos modelos de riscos proporcionais de mortalidade de Cox para ajustar associações com controle para idade, sexo e outras covariáveis relevantes.

Resultados: No primeiro artigo, dos 2.062 participantes com diabetes conhecido, 1.000 (48,5%) eram homens, 1.217 (59,0%) tinham idade entre 45 e 64 anos, 961 (46,6%) eram autodeclarados brancos e 1.068 (51,8%) tinham ensino superior completo. Além

disso, 1.380 (66,9%) relataram possuir plano de saúde privado. HbA1c foi igual ou abaixo do alvo em 1.364 (66,1%), pressão arterial em 1.596 (77,4%) e LDL-c em 1.086 (52,7%). No entanto, apenas 590 (28,6%) participantes estavam dentro ou abaixo da meta para todos os ABCs. As mulheres (RP=1,05; IC95% 1,00-1,11) e com plano de saúde privado (RP=1,15; IC95% 1,07-1,23) ou maior renda per capita (RP=1,19; IC95% 1,06-1,34) foram mais propensos a atingir duas ou mais metas ABC em análises ajustadas. No segundo artigo, dos 2.492 indivíduos com diabetes conhecido, 272 morreram. Em análises ajustadas por modelos de riscos proporcionais, o nível de HbA1c dentro do alvo conferiu maior proteção (HR=0.62; 95% IC 0.47-0,81) contra todas as causas de mortalidade, seguido por pressão arterial sistólica dentro do alvo (HR=0.77; 95% IC 0.59 -0.99). O LDL-c dentro do alvo, no entanto, não (HR=1.38; 95% IC 1.03-1.84). Alcançar duas ou mais metas do ABC reduziu o risco de mortalidade em 43% (HR = 0.57 a 0.63; 95% IC 0.38-0.99). Não fumar também reduziu este risco (HR=0.60; 95% CI 0.43-0.83).

Conclusão: Há muito espaço para melhorias no controle desses fatores prognósticos modificáveis. Fatores sociais desempenham um papel importante na determinação do controle ABC do diabetes. Em termos de mortalidade, o controle inadequado da glicose foi o mais forte preditor de morte, e o controle de glicose e pressão arterial sistólica reduziu as mortes por diabetes, entretando o LDL-c não. Não fumar também foi fator de notável importância. O maior risco associado à manutenção do LDL-c dentro da meta merece uma investigação mais aprofundada.

Palavras-chave: Diabetes Mellitus, Fatores de Risco Cardiometabólicos, Mortalidade, Hemoglobina A Glicada, Hipertensão, Hipercolesterolemia, Tabagismo

ABSTRACT

Introduction: Type 2 diabetes mellitus is an important global health problem. The control of blood glucose, blood pressure and smoking improves the prognosis of individuals with diabetes mellitus and reduces the chance of death.

Objective: To evaluate the individual and combined control of risk factors (blood glucose, blood pressure, cholesterol and non-smoking) for complications in Brazilian adults with known diabetes in the ELSA-Brasil cohort (first article) and to characterize the risk of death according to these factors (second article).

Methods: Cross-sectional (first article) and longitudinal (second article) analyzes were performed on data from participants in the Brazilian Longitudinal Study of Adult Health, comprising those who reported a previous diagnosis of diabetes or use of antidiabetic medication. In the first article, based on wave 3 data (visit from 2017 to 2019), we considered glycated hemoglobin (HbA1c) <7% as glycemic control (target A); blood pressure <140/90 mmHg (or <130/80 mmHg at high cardiovascular risk) as a blood pressure control (target B) and LDL-c <100 mg/dl (or <70 mg/dl at high risk) as a control of LDL-c (target C) according to the 2022 American Diabetes Association (ADA) guidelines. We performed Poisson regression models with robust variance to adjust for associations for sociodemographic and clinical factors. In the second article, we followed the participants of the Brazilian Longitudinal Study of Adult Health with self-reported diabetes, verified by self-reported medical diagnosis or use of medication, from 2008 to 2019. We defined glucose control, blood pressure and cholesterol (LDL-c) per 2022 ADA guidelines. Our annual telephone surveillance identified deaths that were confirmed by hospital records and death certificates. We then applied Cox proportional hazards mortality models to adjust associations with controls for age, gender, and other relevant covariates.

Results: In the first article, of the 2062 participants with known diabetes, 1000 (48.5%) were men, 1217 (59.0%) were aged between 45 and 64 years, 961 (46.6%) were self-declared white and 1068 (51.8%) had completed higher education. In addition, 1,380 (66.9%) reported having a private health plan. HbA1c was at or below target in 1364 (66.1%), blood pressure in 1596 (77.4%) and LDL-c in 1086 (52.7%). However, only 590 (28.6%) participants were at or below the target for all ABCs. Women (PR=1.05; 95%CI

1.00-1.11) with private health insurance (PR=1.15; 95%CI 1.07-1.23) or higher per capita income (PR=1.19; 95%CI 1.06-1.34) were more likely to achieve two or more ABC goals in adjusted analyses. In the second article, of the 2,492 individuals with known diabetes, 272 died. In analyzes adjusted by proportional hazards models, within-target HbA1c level conferred the greatest protection (HR=0.62; 95% CI 0.47-0.81) against all-cause mortality, followed by within-target systolic blood pressure (HR =0.77; 95% CI 0.59 -0.99). On-target LDL-c, however, was not (HR=1.38; 95% CI 1.03-1.84). Achieving two or more ABC goals reduced the risk of mortality by 43% (HR = 0.57 to 0.63; 95% CI 0.38 to 0.99). Not smoking also reduced this risk (HR=0.60; 95% CI 0.43-0.83).

Conclusion: There is much room for improvement in controlling these modifiable prognostic factors. Social factors play an important role in determining the ABC control of diabetes. In terms of mortality, poor glucose control was the strongest predictor of death, and controlling both glucose and systolic blood pressure reduced deaths from diabetes, whereas LDL-c did not. Not smoking was also a factor of notable importance. The greater risk associated with maintaining LDL-c within the target range deserves further investigation.

Keywords: Diabetes Mellitus, Cardiometabolic Risk Factors, Mortality, Glycated Hemoglobin A, Hypertension, Hypercholesterolemia, Smoking

APRESENTAÇÃO

Esse trabalho consiste na tese de doutorado intitulada “**Controle Individual e Combinado dos Fatores de Risco para Complicações em Diabetes e Associação com Mortalidade – ELSA-Brasil**” que será apresentada ao Programa de Pós-Graduação em Epidemiologia da Universidade Federal do Rio Grande do Sul, no dia 30/03/2023. O trabalho é apresentado em quatro partes, na ordem que segue:

1. Introdução, Justificativa, Revisão da Literatura, Objetivos
2. Artigo 1: Levels and Correlates of Risk Factor Control in Diabetes Mellitus –ELSA Brasil
3. Artigo 2: Mortality in patients with type 2 diabetes according to achievement of treatment goals: ELSA-Brasil Study
4. Considerações Finais

INTRODUÇÃO

O diabetes mellitus é uma doença crônica e complexa decorrente da falta de insulina e/ou da incapacidade de insulina exercer adequadamente seus efeitos, levando à hiperglicemia permanente e conseqüentemente múltiplos danos ao organismo. O diabetes é um problema de saúde global e importante causa de mortalidade e de morbidade (Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration, 2014; Seuring et al., 2015). Nas Américas, em 2019, a taxa de mortalidade padronizada por idade para diabetes mellitus tipo 2 foi 25% maior que a média mundial (46,8 por 100.000) e os anos de vida ajustados para incapacidade (DALYs) foram 29% maior do que a carga observada globalmente (1.875 DALYs por 100.000). No Brasil a diabetes que já é uma importante causa de morte (sexta principal causa de morte em 2019) possui perspectivas de piorar, tornando-se a 3ª principal causa até 2040 (Global Burden of Disease: GBD cause and risk summaries, 2019) (GBD Compare | IHME Viz Hub, 2022). Os custos também são altos, estimados em média 29.2 bilhões de dólares internacionais com indivíduos com diabetes em nosso país (Sun et al., 2022).

Para reduzir a carga de doença relacionada ao diabetes e prevenir a progressão de complicações, indica-se além do controle glicêmico, a redução multifatorial de risco (pressão arterial, colesterol, não tabagismo) (American Diabetes Association Professional Practice Committee, 2022a). Intervenções para controlar a hiperglicemia, hipertensão e hipercolesterolemia, bem como para parar de fumar, demonstraram produzir benefícios sustentados nas complicações vasculares, com reduções nos desfechos cardiovasculares, mortalidade cardiovascular e geral (Gaede et al., 2003a, 2008a). Em termos de mortalidade, pacientes com diabetes tipo 2 que possuem cinco fatores de risco para complicações dentro as faixas-alvo parecem ter pouco ou nenhum risco excessivo de morte por todas as causas (o risco de morrer foi de 6% maior naqueles indivíduos com diabetes que alcançaram todos as metas de controle do que em indivíduos sem diabetes) (Rawshani et al., 2018a).

Diretrizes, entre elas a American Diabetes Association (ADA) 2022, embora recomendando individualizar o tratamento do paciente com diabetes, estabeleceu alvos terapêuticos para os principais fatores de risco para complicações, também chamados de alvos ABC, que no geral incluem (A) hemoglobina glicada (HbA1c) inferior a 7%, (B)

pressão arterial <140/90 mmHg e (C) LDL-colesterol (LDL-c) < 100 mg/dl. O controle mais rígido também foi sugerido para aqueles com doença cardiovascular ou com alto risco de desenvolvê-la (American Diabetes Association Professional Practice Committee et al., 2022b). Dados populacionais, entretanto, vem demonstrando que bem menos que 50% de indivíduos com diabetes alcançam estas metas (dos Reis et al., 2021a),(Fang, M.; Wang, D.; Coresh, J.; Selvin, E., 2021), (Ji et al., 2013). No Brasil, uma recente subamostra de uma pesquisa nacional probabilística brasileira (PNS) demonstrou que o controle de hiperglicemia, hipertensão e hipercolesterolemia em diabetes foi de apenas 12,5% (dos Reis et al., 2021a). No entanto, essa subamostra carecia de poder estatístico para caracterizar os fatores associados a este controle, que poderiam apontar caminhos para melhorar este quadro.

Tendo em vista a relevância do controle multifatorial para prevenção de complicações e incerteza sobre fatores associados ao controle, buscamos analisar o controle individual e combinado dos fatores de risco para complicações em diabetes (alvos ABC) e sua influência na mortalidade de participantes com diabetes do Estudo Longitudinal da Saúde do Adulto (ELSA-Brasil).

REVISÃO DA LITERATURA

Diabetes Mellitus

O termo diabetes descreve um grupo de distúrbios metabólicos caracterizados e identificados pela presença de hiperglicemia na ausência de tratamento. A fisiopatologia é heterogênea e inclui defeitos na secreção de insulina, ação da insulina, e distúrbios do metabolismo de carboidratos, gorduras e proteínas (American Diabetes Association, 2010) (Geneva: WHO;, 2006).

Classificação do diabetes

A classificação do diabetes, em geral, é feita de acordo com os grupos etiológicos, embora tentativas de classificação prognóstica para o desenvolvimento de complicações estejam sendo desenvolvidas. (Geneva: WHO;, 2006) (Geneva: WHO;, 2011). O WHO Diagnosis and Classification of Diabetes inclui novos tipos de diabetes (tipos híbridos de diabetes e diabetes não classificável) na sua classificação e aponta que existe um conflito entre classificação clínica e etiológica porque ainda existem lacunas no conhecimento da etiologia e fisiopatologia da doença (WHO About Diabetes, 2019). Abaixo, seguem as classificações adaptadas conforme as recomendações atuais da WHO:

Diabetes Tipo 1: o diabetes tipo 1 é devido à destruição autoimune das células β , geralmente levando à deficiência absoluta de insulina, incluindo diabetes autoimune latente da idade adulta.

Diabetes tipo 2: é devido a uma perda progressiva da secreção adequada de insulina das células β frequentemente no contexto da resistência à insulina. O diabetes tipo 2 é o tipo mais prevalente e é o foco do nosso estudo. Além de fatores genéticos, a obesidade, baixos níveis de atividade física, entre outros hábitos de vida, tais como tabagismo e alimentação desequilibrada, são fatores de risco conhecidos para o desenvolvimento de diabetes tipo 2 (Bellou et al., 2018; Sun et al., 2022). Os sintomas são mais brandos que o tipo 1 e o início da doença é muitas vezes insidioso.

Formas Híbridas: o WHO incluiu nessa categoria dois tipos de diabetes, o diabetes autoimune com início tardio (LADA) e o diabetes tipo 2 com propensão à

cetose, sendo a LADA frequentemente confundida com o diabetes tipo 2 em decorrência de seu aparecimento em adultos e de sua progressão mais lenta, porém apresenta autoanticorpos pancreáticos caracterizando sua etiologia autoimune.

Diabetes não-classificado: classificação transitória que ocorre especialmente em jovens com obesidade em que a distinção entre tipo 1 e 2 pode ser mais difícil no início.

Outros tipos: à medida que um determinado processo patogênico é estabelecido, os casos identificados passam a ser classificados nessa categoria (diabetes monogênico, doenças do pâncreas exócrino, induzido por fármacos, entre outros).

Hiperglicemia detectada na gravidez: inclui o diabetes gestacional e o diabetes detectada na gravidez.

Diagnóstico do diabetes

O diabetes pode ser diagnosticado laboratorialmente por três exames: glicose de jejum ≥ 126 mg/dL, glicemia pós 2h sobrecarga ≥ 200 mg/dL e hemoglobina glicada $\geq 6.5\%$ ou em pacientes com sintomas clássicos de hiperglicemia (poliúria, polidipsia e polifagia) ou crise hiperglicêmica com uma glicose plasmática aleatória ≥ 200 mg/dL. Se os valores elevados forem detectados em pessoas assintomáticas, a repetição do teste, de preferência com o mesmo teste, é recomendada assim que possível em um dia subsequente para confirmar o diagnóstico. (Geneva: WHO;, 2006) (Geneva: WHO;, 2011)

Complicações do diabetes

A hiperglicemia crônica do diabetes pode levar a danos em múltiplos órgãos resultando em diversas complicações. As complicações causadas pelo diabetes podem ser agudas (cetoacidose diabética, estado hiperglicêmico hiperosmolar e hipoglicemia, todas com grande potencial de gravidade) ou crônicas (micro e macrovasculares). Nas complicações microvasculares está a retinopatia, a qual é uma das principais causas de cegueira e incapacidade visual; a nefropatia, que pode levar a falência renal, e a neuropatia que pode levar a dor neuropática, tontura por sintomas vasovagais (neuropatia autonômica) e/ou perda de sensibilidade gerando o pé diabético que muitas vezes evolui para amputações. Já nas complicações macrovasculares, está a doença

cardiovascular aterosclerótica, infarto agudo do miocárdio, acidente vascular cerebral, entre outros (Geneva: WHO;, 2006). Outras complicações também vêm sendo relacionadas ao diabetes como cânceres (especialmente hepático, de pâncreas, de ovário, colo retal, pulmonar, de bexiga e de mama), doenças infecciosas como a tuberculose, transtornos do sistema nervoso, suicídio e transtornos degenerativos (Gregg et al., 2018; Rao Kondapally Seshasai et al., 2011).(Tomic et al., 2022)

A prevenção das complicações crônicas é um dos objetivos principais do tratamento do diabetes tanto na identificação quanto no controle de fatores de risco para o desenvolvimento da doença (através dos alvos ABC - A1c, pressão arterial e colesterol LDL). O controle glicêmico, especialmente associado ao controle dos demais fatores de risco pode minimizar os riscos de retinopatia, nefropatia e neuropatia tanto no diabetes tipo 1 quanto no tipo 2, além de diminuir o risco de doenças cardiovasculares (DCV), podendo estar associado a reduções de até 50-76% nas taxas de desenvolvimento e progressão de complicações microvasculares (Gaede et al., 2008a).

Epidemiologia do Diabetes

Globalmente, a prevalência de diabetes aumentou nas últimas quatro décadas, e é provável que continue aumentando na maioria dos países (NCD Risk Factor Collaboration (NCD-RisC), 2016). O aumento da prevalência resultou predominantemente de um aumento da incidência da doença, porém é difícil precisar exatamente quais os fatores teriam causado o aumento da incidência. Contudo, é consensual o entendimento de que mudanças estruturais que ocorreram na sociedade produziram um ambiente com novos comportamentos e exposições que, por sua vez, propiciaram ganho de peso/obesidade e, em decorrência, aumento na incidência de diabetes tipo 2 (Popkin, 2015).

De acordo com a International Diabetes Federation (IDF), a prevalência global do diabetes em pessoas de 20 a 79 anos em 2021 foi estimada em 10,5% (536,6 milhões de pessoas), com projeções de aumentar para 12,2% (783,2 milhões de pessoas) em 2045. Em 2021, a prevalência foi semelhante em homens e mulheres, maior nas faixas etárias mais velhas, maior nas áreas urbanas (12,1%) do que nas rurais (8,3%), e maior nos países de alta renda (11,1%) em comparação com os países de baixa renda (5,5%)

(Sun et al., 2022). O Brasil ocupou a sexta posição no ranking de número de casos do diabetes, com 15.7 milhões de pessoas acometidas pela doença (Sun et al., 2022) na faixa etária de 20 a 79 anos com projeção de aumentar para 23.2 milhões em 2045 (Sun et al., 2022). A Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico (VIGITEL) em 2021 obteve estimativas semelhantes com 9,1% de prevalência da doença. Pessoas em desvantagens sociais, provavelmente em função das condições desfavoráveis de vida, também frequentemente apresentaram maior prevalência (Schmidt et al., 2014) além de menor cobertura de tratamentos propostos, como demonstrado recentemente por um estudo abrangente de países de média e baixa renda que mostrou que menos de uma em cada dez pessoas com diabetes em países de menores condições socioeconômicas recebeu cobertura de tratamento para diabetes baseado em diretrizes (Flood et al., 2021).

Morbidade e Mortalidade em Diabetes

A morbidade relacionada ao diabetes é alta, principalmente em decorrência das suas complicações (doença arterial coronariana, doença arterial periférica e doença cerebrovascular, pé diabético, retino e nefropatia). O diabetes também aumenta o risco de desenvolver problemas de saúde como demência, apneia do sono, cirrose, infecções crônicas (tuberculose e HIV) e, mais recentemente, descobriu-se que piora o prognóstico da Covid-19 (Lv et al., 2022). No diabetes tipo 2, o início da doença é muitas vezes insidioso e, por isto o diagnóstico tende a ser tardio. Como resultado, as complicações do diabetes podem estar presentes no momento do diagnóstico (Harris et al., 1992), e sua frequência aumenta ao longo do tempo. A multimorbidade do diabetes é onerosa e contribui para um pior prognóstico de eventos específicos (pneumonia, trauma, entre outros).

Em termos de morbidade, a incapacidade gerada pelo diabetes resultou em 66,3 milhões (95% UI 55,5–79,0) de anos de vida ajustados por incapacidade (DALYs – disability-adjusted life years) globais em 2019 e foi responsável por 2,6% (2,3–2,9) do total de DALYs globais, correspondendo a mais de 35.2 milhões de anos vividos com incapacidade (YLDs), um aumento de 41.3% desde 2010 (Diabetes mellitus type 2 — Level 4 cause, 2020; Vos et al., 2020). O Brasil apresenta taxas de DALYs mais altas do que as mundiais (Duncan et al., 2017; GBD Compare | IHME Viz Hub, 2022),

correspondendo a 3.92% (3.6-4.27) de DALYs em 2019 e 4.64% (4.0 – 5.4) de YLDs (GBD Compare | IHME Viz Hub, 2022).

Em 2019, o diabetes ocupou o terceiro lugar entre as causas de mortalidade no Brasil em ambos os sexos na faixa etária de 60 a 90 anos (GBD Compare | IHME Viz Hub, 2022). A maior parte das estatísticas de mortalidade em diabetes no Brasil se baseia nas informações das declarações de óbito, que não capta toda a carga causada pela doença (Schmidt et al., 2015). Estima-se, a partir de cálculos de fração atribuível, que cerca de 9% de todas as mortes ocorridas no Brasil em 2013 possam ser atribuídas ao diabetes, sendo a proporção maior em homens (10.5%) do que em mulheres (7.2%) (Bracco et al., 2020). A principal causa de morte é por doença cardiovascular (34%) seguida de câncer (20%), sendo o restante (46%) atribuído a doenças renais, hepáticas, infecciosas e neurológicas, muitas vezes diretamente associadas à hiperglicemia (Gregg et al., 2018).

Custos em Saúde

Os gastos em saúde são altos. Gastos diretos relacionados à doença no mundo foram estimados em 1,3 trilhão de dólares, 1,8% do produto interno bruto (PIB) mundial com projeções de aumento até 2030 (Bommer et al., 2018). Em nosso país não é diferente, um estudo conduzido com dados do Sistema Único de Saúde (SUS) no Brasil entre 2008 e 2010 inferiu que de 8.1% a 12.2% das hospitalizações nos serviços de saúde público eram devido ao diabetes sendo que o custo de cada hospitalização variou de 1.302 a 1.315 reais. Dessas hospitalizações, 10.3% eram devido diretamente ao diabetes, 36.6% devido às complicações crônicas associadas aos diabetes e 53.1% ao excesso de internação em pacientes com diabetes devido a condições médicas gerais (Rosa et al., 2014). Dados indicam custos da doença em nosso país de aproximadamente 0,52% do PIB brasileiro e em 5,9% de todo o orçamento em saúde (Bahia et al., 2019; Rosa et al., 2018).

Prevenção da Morbimortalidade

A prevenção da morbidade cardiovascular é uma prioridade importante para pacientes com diabetes, especialmente o tipo 2. Dados de Framingham Heart Study mostraram que indivíduos com diabetes têm risco aumentado de desenvolver e morrer de doença cardiovascular aterosclerótica; em comparação com aqueles sem diabetes,

as pessoas com diabetes diminuíram a expectativa de vida (seis a oito anos a menos) (Franco et al., 2007). No momento do diagnóstico do diabetes tipo 2, muitos pacientes já apresentam um ou mais fatores de risco para doença macrovascular (obesidade, hipertensão, dislipidemia, tabagismo) e muitos apresentam evidências de aterosclerose (infarto do miocárdio passado), alterações isquêmicas no eletrocardiograma, ou doença vascular periférica) (Tancredi et al., 2015).

Devido à relevância do diabetes mellitus tipo 2 como problema de saúde pública, ações destinadas à prevenção da doença e do surgimento ou retardo das complicações crônicas vem sendo discutidas (Costa et al., 2017). No Brasil, o Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas Não Transmissíveis 2011-2022, do Ministério da Saúde (MS), teve como objetivo preparar o Brasil para deter o crescimento e enfrentar as DCNT, abordando os quatro principais grupos de doenças (circulatórias, câncer, respiratórias crônicas e diabetes).

Alvos ABC - A1c, Pressão Arterial e Colesterol

O desenvolvimento de complicações pode ser retardado com o manejo da hiperglicemia, hipertensão e dislipidemia (American Diabetes Association Professional Practice Committee et al., 2022a). Da mesma forma, uma vez presentes, a progressão dessas complicações pode ser retardada com as mesmas estratégias de manejo. Os alvos terapêuticos recomendados pela ADA em 2022, também chamados de metas ABC, para auxiliar nesse controle de fatores de risco, incluem (A) hemoglobina glicada (HbA1c) inferior a 7%, (B) pressão arterial <140/90 mmHg e (C) LDL-colesterol (LDL-c) < 100 mg/dl. Um controle mais rígido também é sugerido para aqueles com doença cardiovascular ou com alto risco de desenvolvê-la (American Diabetes Association Professional Practice Committee et al., 2022b). A cessação do tabagismo é fortemente recomendada para os pacientes que fumam à medida que fumantes com diabetes (e pessoas com diabetes expostas ao fumo) têm risco aumentado de DCV, morte prematura, complicações microvasculares e pior controle glicêmico quando comparados com não fumantes (Kar et al., 2016; Śliwińska-Mossoń and Milnerowicz, 2017).

Apesar dessa considerável heterogeneidade de benefícios na base de evidências, as principais autoridades na Europa e nos Estados Unidos atualmente recomendam tratamento cada vez mais intensivo. No entanto, eles sugerem que o controle glicêmico deve ser personalizado e recentemente têm focado mais na seleção

da classe de medicamentos antidiabéticos prescritos (EISayed et al., 2023a). A European Society of Cardiology (ESC) e a European Association for the Study of Diabetes (EASD) recomendam HbA1c <7% com exceções individualizadas, pressão arterial <130mmHg e LDL-c <100mg/dl, <70mg/dL e <55mg/dL para risco moderado, alto e muito alto de DCV (Cosentino et al., 2020). O Instituto Nacional de Excelência em Saúde e Cuidados do Reino Unido (NICE) recomenda HbA1c <7% com exceções individualizadas (Type 2 diabetes in adults, 2015), pressão arterial <135/85 mmHg para adultos com menos de 80 anos e <145/85 mmHg para adultos com 80 anos ou mais (Hypertension in adults, 2022), e atorvastatina 20 mg para aqueles que têm 10% ou mais de risco em 10 anos de desenvolver DCV (Cardiovascular disease, 2016).

Uma minoria de adultos com diabetes atinge todos os objetivos recomendados para A1C, controle da pressão arterial e controle da dislipidemia (Ji et al., 2013). Em estudos em diversos países, o alcance de todas as metas do ABC sempre foi baixo. Nos EUA, segundo a Pesquisa Nacional de Exames de Saúde e Nutrição (NHANES), 22,2% dos indivíduos atingiram simultaneamente todas as três metas (HbA1c <7%, pressão arterial <140/90 mmHg e LDL-c <130 mg/dl) (Fang, M.; Wang, D.; Coresh, J.; Selvin, E., 2021). No NHANES coreano, com uma meta mais rigorosa para controle glicêmico (HbA1c <6,5%), e com metas de pressão arterial <140/85 mmHg e LDL-c abaixo de 100 mg/dl, apenas 8,4% dos indivíduos atingiram os três alvos (Kim, B.-Y.; Won, J.C.; Lee, J.H.; Kim, H.-S.; Park, J.H.; Ha, K.H.; Won, K.C.; Kim, D.J.; Park, K.S., 2019), sendo necessários esforços renovados para implementar estratégias de redução de fatores de risco multifatoriais e aumentar a adesão ao tratamento no curso do diabetes tipo 2.

No Brasil, o alcance de todas as metas ABC também é baixo. Um estudo da Pesquisa Nacional de Saúde (PNS) 2013 (dos Reis et al., 2021a) mostrou que 46% dos participantes alcançou a meta glicêmica, 90,3% era não fumante (provavelmente devido à implementação em longo prazo de múltiplas e fortes políticas públicas contra o tabaco no Brasil (Portes et al., 2018) e apenas 12,5% alcançou as três metas recomendadas para glicose, pressão arterial e colesterol.

Em 2023, as novas diretrizes da ADA publicadas forneceram limites mais rígidos para pressão arterial (<130/80mmHg para todos) e LDL-c (<70mg/dl e, para aqueles

com alto risco ou doença cardiovascular clínica, <55md/dl) o que agrava ainda mais o cenário de baixo alcance de metas terapêuticas, especialmente no Brasil (EISayed et al., 2023b).

Alvos ABC e Mortalidade em Diabetes

A magnitude do benefício de mortalidade conferido pelo bom controle metabólico integral no diabetes não é suficientemente conhecida, especialmente entre os pacientes de países de baixa e média renda (Mendivil et al., 2023). O controle intensivo de múltiplos fatores de risco de DCV foi demonstrado pelo Steno-2, que mostrou que o tratamento intensivo produziu uma redução relativa de 46% na mortes e redução de 57% nas de causa cardiovascular (Gaede et al., 2008b). Em 2018, em um estudo sueco, pacientes com diabetes tipo 2 que tinham cinco fatores de risco para complicações dentro as faixas-alvo pareciam ter pouco ou nenhum risco excessivo de morte por todas as causas. Neste estudo como no nosso, um nível de hemoglobina glicada fora da faixa-alvo foi o preditor mais forte de risco (Rawshani et al., 2018b).

No entanto, a meta-análise de ensaios semelhantes ao Steno-2 mostrou apenas 18% de redução relativa na mortalidade por todas as causas e uma redução de 28% nas mortes cardiovasculares (Seidu et al., 2016). Além disso, o benefício é menos certo em pacientes mais idosos. Um julgamento japonês visando HbA1c <6,9%, pressão arterial sistólica <130 mmHg, LDL-c <100 mg/dl, entre outros alvos, em 1.173 pacientes com idade média de 72 anos, não encontrou benefício do tratamento intensificador (Araki et al., 2012). Mais recentemente um estudo de coorte colombiano mostrou que o controle sustentado de pressão arterial, hemoglobina glicada e LDL-c teve fortes associações protetoras contra a mortalidade geral em diabetes (Pressão Arterial Sistólica OR=0,42 [0,41-0,43]; HbA1c OR=0,25 [0,24-0,26]; LDLc OR=0,28 [0,27-0,29]) teve fortes associações negativas com a morte (Mendivil et al., 2023).

LDL-c e Mortalidade em Diabetes

Não há dúvida de que a redução do LDL-c em indivíduos com diabetes e DCV conhecida como prevenção secundária é benéfica. No entanto, ensaios clínicos de redução de LDL-c para prevenção primária de DCV em diabetes, embora geralmente incluíssem pacientes com maior risco de DCV do que aqueles com diabetes em geral (Colhoun et al., 2004) (Gazi and Mikhailidis, 2006) (Gupta et al., 2018) demonstraram

apenas um pequeno benefício, ou uma redução não estatisticamente significativa na mortalidade por todas as causas (de Vries et al., 2012) ou ainda ausência de benefício (Chen et al., 2012) Além disso, estudos observacionais do mundo real, menos focados em pacientes com risco cardiovascular mais alto, demonstram que os níveis de LDL-c de menor mortalidade são acima de 100 mg/dl., tanto no diabetes (Chiang et al., 2014) (McEwen et al., 2007), quanto na população em geral (Liu et al., 2021), especialmente em indivíduos mais velhos (Ravnskov et al., 2016). Estes achados colocam que as recomendações de colocar LDL-c em níveis abaixo e frequentemente bem abaixo de 100 mg/dl precisam de maior esclarecimento. Níveis baixo de LDL-c nesses estudos identificam pessoas com uma pior saúde na linha de base dos estudos ou são um verdadeiro fator de risco para complicações e morte? (Chiang et al., 2014; Johannesen et al., 2020; Ranieri et al., 1998)

Cuidado em diabetes

O diabetes acarreta um estresse enorme ao paciente e a sua família e essa carga se eleva quando são consideradas as margens de mudanças necessárias na rotina diária, situação financeira e social (Hood et al., 2016). Muitos pacientes com diabetes não recebem os níveis recomendados de cuidados de saúde, incluindo pacientes idosos, dificuldades com o idioma, dificuldades financeiras ou comorbidades complexas, e aqueles de países com menos recursos para controlar o diabetes (Fernandez et al., 2011). A compreensão dos fatores sociais envolvidos no processo saúde-doença do diabetes é fundamental para elaborarmos uma linha de cuidados adequada. De acordo com a American Heart Association (AHA), os cuidados clínicos e o tratamento são responsáveis por 10% a 20% dos contribuintes modificáveis para os resultados de saúde. Os outros 80% a 90% são os determinantes sociais da saúde, que incluem comportamentos relacionados à saúde, fatores socioeconômicos (educação, emprego, renda, segurança na comunidade e suporte social/familiar), fatores ambientais (poluição atmosférica, trânsito) e racismo, todos reconhecidos por terem um impacto profundo nas doenças cardiovasculares e diabetes (Hood et al., 2016; Joseph et al., 2022).

No Brasil, a fim de padronizar e integrar ações para o tratamento de pessoas com diabetes mellitus no Sistema Único de Saúde (SUS), o governo criou a Linhas de

Cuidado, projeto do Ministério da Saúde que orienta o caminho que o paciente deve percorrer e os cuidados e encaminhamentos que as equipes devem prescrever no atendimento. Além disso, as Linhas de Cuidado trazem informações relativas às ações e atividades de promoção, prevenção, tratamento e reabilitação a serem desenvolvidas por equipe multidisciplinar em cada serviço de saúde (Ministério da Saúde., 2021).

Sendo assim, a implementação de ações destinadas a obter maior controle no nível do sistema de saúde, apoiadas por maior rastreamento e feedback dos cuidados, é viável no nosso sistema único de saúde devido aos avanços da tecnologia da informação e já foi feito em outros ambientes. A implantação e expansão de um registro de diabetes orientando o atendimento ao paciente em vários países asiáticos produziu melhora no controle de todos os ABCs. Em Hong Kong, a implementação de um registro de diabetes com feedback para o paciente e seus cuidadores a cerca de seu estado de saúde e plano de cuidados, foi acompanhada por uma redução de 40% nas complicações cardiovasculares ou microvasculares e uma redução de 66% na mortalidade por todas as causas, (Ng et al., 2018a). Foi adicionalmente estimado de ter gerado economia de custos (Jiao et al., 2018a).

OBJETIVOS

Objetivo Geral

- Avaliar o controle individual e combinado dos fatores de risco para complicações em diabetes (alvos ABC) e sua associação com a mortalidade em participantes do ELSA-Brasil com diabetes mellitus tipo 2.

Objetivos Específicos

- Caracterizar o controle de glicemia, pressão arterial, colesterol e tabagismo nos participantes com diabetes mellitus no estudo ELSA – Brasil, de acordo com seu risco cardiovascular.
- Avaliar associações entre os níveis de controle de glicêmico, pressão arterial, colesterol e tabagismo com variáveis sócio demográficas e clínicas.
- Contrastar os resultados de nossa amostra com as recomendações da Associação Americana de Diabetes (ADA, 2022) e com estudos populacionais brasileiros e latinoamericanos que por ventura já tenham sido publicados.
- Estimar o risco de morte por todas as causas de acordo com o controle desses fatores em participantes com diabetes mellitus tipo 2 no estudo ELSA-Brasil.

RESUMO ARTIGO 1

Introdução: O controle da glicemia, pressão arterial e tabagismo é reconhecido como fundamental para melhorar o prognóstico de indivíduos com diabetes mellitus. Nosso objetivo foi avaliar o nível de controle desses fatores de risco em adultos brasileiros com diabetes conhecido e avaliar correlações com variáveis sociodemográficas e clínicas.

Métodos: Amostra transversal do Estudo Longitudinal Brasileiro de Saúde do Adulto, composta por participantes que referiram diagnóstico prévio de diabetes ou uso de medicação antidiabética. Medimos a hemoglobina glicada (HbA1c) e o LDL-colesterol em um laboratório central e a pressão arterial seguindo protocolos padronizados. Definimos HbA1c <7% como controle de glicose (alvo A); pressão arterial <140/90 mmHg (ou <130/80 mmHg em alto risco cardiovascular) como controle da pressão arterial (alvo B) e LDL-c <100 mg/dl (ou <70 mg/dl em alto risco) como alvo de colesterol (alvo C), de acordo com as diretrizes de 2022 da American Diabetes Association.

Resultados: Entre 2.062 indivíduos com diabetes, 1.364 (66,1%) atingiram a meta A, 1.596 (77,4%) a meta B e 1.086 (52,7%) a meta C; apenas 590 (28,6%) alcançaram todas as três metas. Ao considerar também a meta de não fumar, aqueles que atingiram todas as metas caíram para 555 (26,9%). Mulheres (PR=1,13; IC95% 1,07-1,20), com idade >74 (PR=1,20; IC95% 1,08-1,34) e com maior renda per capita (por exemplo, maior renda PR=1,26; IC95% 1,10-1,45) tiveram maior probabilidade de atingir o controle da glicose. Aqueles negros (PR = 0,91; IC 95% 0,83-1,00) ou com diabetes de longa duração (por exemplo, > 10 anos PR = 0,43; IC 95% 0,39-0,47) eram menos prováveis. As mulheres (RP=1,05; IC95% 1,00-1,11) e aquelas com plano de saúde privado (RP=1,15; IC95% 1,07-1,23) tiveram maior chance de atingir duas ou mais metas do ABC; e os negros (PR=0,86; IC 95% 0,79-0,94) e com diabetes de longa duração (por exemplo, >10 anos desde o diagnóstico de diabetes, PR=0,68; IC 95% 0,63-0,73) tiveram menor chances de alcançar duas ou mais metas do ABC.

Conclusão: O controle das metas do ABC foi ruim, notadamente para o LDL-c e principalmente quando se considera o controle combinado. Indicadores de situação social desfavorecida associaram-se a controle menos frequente.

ARTIGO 1

Levels and Correlates of Risk Factor Control in Diabetes Mellitus –ELSA-Brasil

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Abstract

BACKGROUND: Control of glucose, blood pressure, cholesterol, and smoking improves the prognosis of individuals with diabetes mellitus. Our objective was to assess the level of control of these risk factors in Brazilian adults with known diabetes and evaluate correlates of target achievement.

METHODS: Cross-sectional sample of the Brazilian Longitudinal Study of Adult Health, composed of participants reporting a previous diagnosis of diabetes or the use of antidiabetic medication. We measured glycated hemoglobin (HbA1c) and LDL-cholesterol at a central laboratory and blood pressure following standardized protocols. We defined HbA1c <7% as glucose control (target A); blood pressure <140/90 mmHg (or <130/80 mmHg in high cardiovascular risk) as blood pressure control (target B), and LDL-c <100 mg/dl (or <70 mg/dl in high risk) as lipid control (target C), according to the 2022 American Diabetes Association guidelines.

RESULTS: Among 2062 individuals with diabetes, 1364 (66.1%) reached target A, 1596 (77.4%) target B, and 1086 (52.7%) target C; only 590 (28.6%) achieved all three targets. When also considering a non-smoking target, those achieving all targets dropped to 555 (26.9%). Women (PR=1.13; 95%CI 1.07-1.20), those aged ≥ 74 (PR=1.20; 95%CI 1.08-1.34), and those with greater per capita income (e.g., greatest income PR=1.26; 95%CI 1.10-1.45) were more likely to reach glucose control. Those black (PR=0.91; 95%CI 0.83-1.00) or with a longer duration of diabetes (e.g., ≥ 10 years PR=0.43; 95%CI 0.39-0.47) were less likely. Women (PR=1.05; 95%CI 1.00-1.11) and those with private health insurance (PR=1.15; 95%CI 1.07-1.23) were more likely to achieve two or more ABC targets; and those black (PR=0.86; 95%CI 0.79-0.94) and with a longer duration of diabetes (e.g., >10 years since diabetes diagnosis, PR=0.68; 95%CI 0.63-0.73) less likely.

CONCLUSION: Control of ABC targets was poor, notably for LDL-c and especially when considering combined control. Indicators of a disadvantaged social situation were associated with less frequent control.

KEYWORDS: Diabetes Mellitus, Cardiometabolic Risk Factors, Glycated Hemoglobina A, Hypertension, Hypercholesterolemia, Tobacco Smoking

Introduction

Diabetes mellitus is a chronic and complex disease that requires continuous medical care. In addition to adequate glycemic control, multifactorial risk reduction is indicated (American Diabetes Association Professional Practice Committee, 2022b). In clinical trial settings, interventions to control hyperglycemia, hypertension, and hypercholesterolemia, as well as to stop smoking, have been shown to produce sustained benefits in vascular complications, with major reductions in cardiovascular outcomes (2,3). Additionally, the risk of dying is only 6% greater in those at or below targets than in individuals without diabetes (Rawshani et al., 2018c).

Recommended therapeutic targets, also called the ABC goals, usually include (A) glycated hemoglobin (HbA1c) less than 7%, (B) a blood pressure <140/90 mmHg, and (C) LDL-cholesterol (LDL-c) <100 mg/dl. Tighter control has also been suggested for those with cardiovascular disease or at high risk of developing it (American Diabetes Association Professional Practice Committee et al., 2022b). Additionally, non-smoking is an important goal to be achieved.

Studies demonstrating the control of multiple risk factors in diabetes are scarce in low- and middle-income countries. Based on a small subsample of a probabilistic national Brazilian survey, we demonstrated that target achievement is usually poor, except for non-smoking (dos Reis et al., 2021b). However, that study lacked statistical power to assess the factors related to ABC control. Therefore, we sought to analyze the Longitudinal Study of Adult Health (ELSA-Brasil) to explore these associations. This large ongoing occupational cohort study enrolled 15105 adults in 6 capital cities from 2008 to 2010. We aimed to assess the level of control of blood glucose, blood pressure, lipids, and smoking habits of ELSA-Brasil participants with known diabetes mellitus and to evaluate correlates of target achievement.

Methods

Study population and ethics

We conducted a cross-sectional study based on the third clinic visit (2017-2019) of ELSA-Brasil. The study was approved by the research ethics committees of participating institutions, and all participants gave their written informed consent. The ELSA-Brasil cohort enrolled 15,105 in-service or retired civil servants aged 35 to 74 at six public institutions of higher education located in capital cities of the states of Bahia, Espírito Santo, Minas Gerais, Rio de Janeiro, São Paulo, and Rio Grande do Sul (Aquino et al., 2012). We included all participants returning for the 2017-2019 clinic visit with self-report of and/or pharmacologic treatment for diabetes. We excluded those who did not have all measures necessary to assess whether targets were achieved.

Measurements

Centrally trained and certified teams conducted standardized interviews and clinical assessments and collected samples for biochemical tests (Bensenor et al., 2013a). We obtained data on age, sex, self-declared race, history of a medical diagnosis of diabetes, duration of diabetes, and depressive episodes by questionnaire. Physical activity was obtained by leisure-time physical activity and categorized as (1) high ≥ 1500 MET-minutes/week, (2) moderate (600-1499 MET-minutes/week, and (3) low (< 600 MET-minutes/week).

Medication use was confirmed by packaging or prescriptions brought to the clinic. Blood pressure was measured three times, and systolic and diastolic blood pressure each was ascertained as the mean of the last two measurements. We assessed weight and height using a standardized protocol and calculated body mass index (BMI) as weight/height^2 (kg/m^2).

We obtained blood samples after an overnight ($> 8\text{h}$) fast and froze and shipped them to a central laboratory for determination. Plasma glucose was measured using the hexokinase method (Cobas c501[□], Roche Diagnostics), HbA1c by high-pressure chromatography (HPLC - Bio-Rad Laboratories, Hercules, CA, USA), total cholesterol by enzymatic colorimetric method, and triglycerides by glycerol-phosphate peroxidase (Cobas c501[□], Roche Diagnostics). Low-

density cholesterol (LDL-c) was estimated by the Friedewald equation when total triglycerides were <400mg/dl and measured directly when they were \geq 400 mg/dl.

Ten-year risk of a major cardiovascular event (myocardial infarction, stroke, or cardiovascular death) was estimated based on age, sex, diabetes, smoking, systolic blood pressure, and total cholesterol according to the WHO Risk Chart Working Group chart for the Tropical Latin America region (WHO CVD Risk Chart Working Group, 2019a). We categorized this estimated risk as high (\geq 20%) or low.

In line with the 2022 American Diabetes Association (ADA) guidelines for therapeutic targets (American Diabetes Association Professional Practice Committee, 2022c), we considered glucose control to be adequate when HbA1c was less than 7%. For those without high cardiovascular risk, we considered blood pressure <140/90 mmHg and LDL-c <100 mg/dl as meeting targets (American Diabetes Association Professional Practice Committee et al., 2022b); and for those with high risk or clinical cardiovascular disease, <130/80 mmHg and <70 mg/dl, respectively (American Diabetes Association Professional Practice Committee, 2022c).

Statistical analyses

We described categorical variables as frequencies and percentages, and continuous ones as means and standard deviations (SD). We performed unadjusted statistical testing with the chi-square test for categorical and ANOVA for continuous variables. We analyzed the adjusted associations of socio-demographic and clinical factors with the level of control using Poisson regression with robust variance. We undertook all analyses with R software (RStudio, version 1.3. 1056, © 2009-2020 RStudio Inc.).

Results

Of the 15,105 participants at baseline, 550 had died, 123 had moved away, 217 were not localized, 39 were too ill to attend clinic at visit 3 and 1540 did not attend this visit for other reasons. Of the remaining 12,636 (83.7%) participants at visit 3, 2385 (18.9%) had a known

diagnosis of diabetes. After excluding 323 participants with missing data on risk factor control or covariates, 2062 remained.

Among these 2062 participants, 1000 (48.5%) were men, 1217 (59.0%) aged 45-64, 961 (46.6%) with self-declared white race/skin color, and 1068 (51.8%) with a complete university education. Additionally, 1380 (66.9%) reported having private health insurance. Mean BMI was 29.6 (4.97) kg/m², and 1812 (87.9%) individuals related use of an antidiabetic drug. (Table 1)

Figure 1, which presents the overlap in achieving goals, shows greater success in achieving that of blood pressure and lesser success in achieving that of LDL-c, as well as no particular pattern of clustering in the success of achieving more than one goal. Only 589 (28.6%) achieved all three goals (center of the figure). As shown in Figures 1 and 2, HbA1c was at or below target in 1364 (66.1%), blood pressure in 1596 (77.4%), and LDL-c in 1086 (52.7%). Control was more frequent in those without high risk for CVD, reflecting the more rigorous targets for those at high risk. Non-smokers comprised 1904 (92.3%) of the sample. However, all ABCs were at or below target in only 590 (28.6%) participants and, when also considering non-smoking as a target, in 555 (26.9%).

As further seen in Table 1, in crude comparisons, being a woman, older, white, and having greater educational attainment, greater income, and private health insurance, as well as having a shorter duration of diabetes were all associated with better glucose control.

As seen in crude comparisons in Table 2, several sociodemographic and clinical characteristics, mostly the same as those seen in Table 1, were associated with a greater number of ABC goals being reached – being white, having greater educational attainment, greater income, and private health insurance, pursuing greater physical activity, having a lower BMI and using antidiabetic medications.

As seen in Table 3, after adjustment for multiple potential confounders, women (PR=1.13; 95%CI 1.07-1.20), those ≥ 74 years old (RR=1.20; 95%CI 1.08-1.34), and those with greater income (e.g. for those with the highest income (PR 1.26. 95%CI 1.10-1.45) were more likely to achieve the HbA1c goal, while those black (PR= 0.91; 95%CI 0.83-1.00) and with

diabetes of longer duration (e.g. ≥ 10 years PR= 0.43; 95%CI 0.39-0.47) less likely. In terms of ABC goals, women (PR=1.05; 95%CI 1.00-1.11) and those with private health insurance (PR=1.15; 95%CI 1.07-1.23) and with higher per capita income (e.g. for those with highest income PR=1.19; 95%CI 1.06-1.34) had a greater probability of meeting two or more ABC goals. On the other hand, those black (PR=0.86; 95%CI 0.79-0.94), with greater body mass index (PR=0.96; 95%CI 0.94-0.99), and with a longer duration of diabetes (e.g. ≥ 10 years PR=0.68; 95%CI 0.63-0.73) were less likely to achieve two or more of the goals.

Discussion

In this free-living sample of 2063 Brazilian adults with known diabetes, HbA1c was controlled in more than half of the sample (66.1%), as were blood pressure (77.4%) and LDL-c (52.6%). However, only 28.6% of participants had all three factors controlled. Some indicators of greater social privilege (white ethnicity, higher income, and access to private health insurance) are associated with meeting targets.

The fraction of individuals reaching glycemic, blood pressure, and LDL-c goals in the ELSA-Brasil cohort was greater than that seen in the 2013 Brazilian National Health Survey (6): 66.1% in ELSA-Brasil vs 46% in the national survey when using identical control cutoffs for targets. Attainment of all three ABC goals in ELSA-Brasil participants was also greater than in this Brazilian National Health Survey (28.6% vs 12.5%). Consonant with the high estimates of non-smoking in Brazilian adults in general, achievement of the non-smoking target was similar in both studies (92.3% vs 90.3%) and higher than that found in other surveys (25) (Fang et al., 2021). This achievement results from the long-term implementation of multiple, strong public policies against tobacco (Portes et al., 2018) in Brazil.

In studies in diverse countries, attainment of all ABC goals was always low. In the US NHANES, 22.2% of individuals simultaneously achieved all three targets (HbA1c <7%, blood pressure <140/90 mmHg, and non-high-density lipoprotein cholesterol <130 mg/dl) (Kim, B.-Y.; Won, J.C.; Lee, J.H.; Kim, H.-S.; Park, J.H.; Ha, K.H.; Won, K.C.; Kim, D.J.; Park, K.S., n.d.). In

the Korean NHANES, with a more stringent target for glycemic control (HbA1c <6.5%), and with targets of blood pressure <140/85 mmHg, and LDL-C below 100 mg/dl, only 8.4% of subjects reached all three targets (Kim et al., 2019). In a study in nine Latin American countries, glycemic control was also lower (43.5%) than that described here (Control of Type 2 Diabetes Mellitus among General Practitioners in Private Practice in Nine Countries of Latin America. *Rev. Panam. Salud Pública* 2007, 22, 12–20., n.d.). Our findings thus complement those already present in the literature, showing the current difficulty faced by diabetic patients in achieving desired levels of the principal factors affecting their prognosis which are modifiable at the individual level.

We found several characteristics that identified those not reaching targets for hyperglycemia and the ABC goals. As expected, a greater duration of diabetes was one. A higher BMI was marginally associated with a lesser frequency of control. Women were more frequently in glycemic control and achieved greater ABC control. The additional factors associated with worse control – being non-white, with lower income, and not having private health insurance, all point to better control being in part the result of social privilege.

Similarly, a representative survey of adults with diabetes showed that private health insurance led to their receiving better quality primary care, as measured by the cardinal attributes of quality primary care, especially access. Greater access to care provides a logical pathway linking this insurance to better control (Silva et al., 2016). A multicenter Brazilian study of hospital outpatients showed that multi-professional care and having had diabetes education as well as disease of lesser duration significantly associated with improved glycemic control (Prevalence and Correlates of Inadequate Glycaemic Control: Results from a Nationwide Survey in 6,671 Adults with Diabetes in Brazil. *Acta Diabetol.* 2010, 47, 137–145., n.d.). Morães et al., evaluating only glycemic control at the baseline ELSA-Brasil visit, demonstrated similar associations with socioeconomic factors (Moraes et al., 2020) as those we found here for overall ABC target achievement.

Our study has limitations, principally that our sample is composed of active or retired civil

servants, a socially privileged sample when compared to the general Brazilian population in terms of educational achievement, income, and job stability among other factors. That we found major socioeconomic determinants of control in this more privileged population only emphasizes the likelihood of greater health disparities in achieving ABC targets in the general diabetic population.

Strengths of our study include its free-living sample of participants obtained in multiple cities across Brazil, different from many other studies which investigated less representative inpatient or outpatient samples which will have both more comorbidities and, by their entry criteria, better access to care. Additional strengths include ELSA's careful and extensive collection of factors examined, its standardized and centralized laboratory measurements, and its sample size permitting adequate investigation of epidemiologically relevant associations.

As has been shown for health outcomes in general (Hood et al., 2016), the correlates of control we found demonstrate the major role of social determinants of health in the ABCs of diabetes control. As put forth by the American Heart Association, clinical care and treatment account for 10% to 20% of the modifiable contributors to health outcomes. The other 80% to 90% are the social determinants of health, which include health-related behaviors, socioeconomic factors, environmental factors, and racism, all recognized to have a profound impact on cardiovascular disease and diabetes and their outcomes (Joseph et al., 2022). The ADA also recently summarized what is known about the importance of social determinants (Hill-Briggs et al., 2020). One implication from these findings is clear: though better control across the board is necessary, improvement and greater resources for the care for people with diabetes in the SUS, Brazil's national health system should be a major goal if the aim is to improve control in the overall population of those with diabetes in Brazil. The SUS covers the bulk of the population and the majority of its underprivileged citizens. It also presents the advantage of providing cost-effective, evidence-based protocols to achieve treatment goals.

These findings are particularly relevant now, as actions aimed to achieve greater control at the health system level, supported by greater tracking and feedback of care, are now feasible

given advances in information technology. The implementation and expansion of a diabetes registry orienting patient care in several Asian countries produced improvement in control of all the ABCs. In Hong Kong, a setting for which longer follow-up is available, the implementation of the registry was accompanied by a 40% decrease in CVD or microvascular complications and a 66% decrease in all-cause mortality, (Ng et al., 2018b) and was additionally estimated to be cost-saving. (Jiao et al., 2018b) In Brazil, advances in the integration of databases within the national health system, which favors primary care and focuses resources on underprivileged communities, offer great hope in this regard. In this scenario, our study, by expanding knowledge of control of diabetes in Brazil and demonstrating the major role of socioeconomic factors, contributes to future strategies for better control and health promotion of Brazilians with diabetes. Future research can refine questions related to the relative benefit of greater control across the board as opposed to focus on better control among those with worst baseline levels.

Additionally, issues of relaxed control, especially of HbA1c, in older patients and those with greater morbidity and thus greater difficulty in managing multiple medications, are also important (6. Glycemic Targets: Standards of Medical Care in Diabetes—2021 | Diabetes Care, n.d.). The American Heart Association currently emphasizes a comprehensive approach to the management of all cardiovascular risk factors in patients with diabetes, including glycemic, blood pressure, lipid abnormalities, thrombotic risk, obesity, and smoking through applying lifestyle and pharmacological approaches with proven benefit using a patient-centered approach. This latter implies reframing clinical encounters to approach patients as people who live in families, communities, and societies that must be considered in their cardiovascular risk management. (American Diabetes Association Professional Practice Committee et al., 2022b) While the ideal fraction of the diabetes population in control of all the ABCs, given these issues, is a question that remains open for debate, certainly it is much greater than the current fraction.

In conclusion, control of ABC targets was poor, notably for LDL-c and especially when considering combined control. Our findings reinforce that much room exists for improvement in controlling these modifiable prognostic factors, notably LDL-c and especially when considering

combined control. Less frequent control among those black, with lower income, and without health insurance reinforces the role of social factors in the multicausal context of control of risk factors for complications in diabetes. With due attention to social determinants and focusing on better integration of health system data to evaluate and orient patient care, health systems and clinicians can and should strive to implement better care for people with diabetes.

Declarations

Ethical approval and consent to participate: ELSA-Brasil study was approved by the research ethics committees of participating institutions, and all participants gave their written informed consent.

Competing interests: none

Author's contributions: BCC, BBD and MIS conceived the study and drafted the manuscript. BCC and RCPR conducted the analyses. BBD, MIS, SMB and RG are principal investigators of ELSA-Brasil and contributed to study design and data collection. All authors reviewed and approved the manuscript.

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approved by the ethics committee of each institution (Universidade Federal da Bahia, Universidade Federal de Minas Gerais, Universidade Federal do Espírito Santo, Fundação Oswaldo Cruz, Universidade de São Paulo, Universidade Federal do Rio Grande do Sul) and by the Publications Committee of ELSA-Brasil (publiELSA), the data used in this study can be made available for research proposals by a request to ELSA's Datacenter (estatisticaelsa@gmail.com) and to the ELSA's Publications Committee.

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Table 1 - Sociodemographic and clinical characteristics of individuals with known diabetes according to levels of glycated hemoglobin (HbA1c) – ELSA-Brasil, 2017-2019. N=2062

	Overall	HbA1c				p*
		<7%	7% to <8%	8% to <9%	≥9%	
All	2062 (100)	1364 (66.1)	275 (13.3)	172 (8.34)	251 (12.1)	
Sex						<0.001
Men	1000 (48.5)	616 (45.2)	157 (57.1)	94 (54.7)	133 (53.0)	
Women	1062 (51.5)	748 (54.8)	118 (42.9)	78 (45.3)	118 (47.0)	
Age (years), M(SD)						0.003
> 44 to ≤ 54	377 (18.3)	256 (18.8)	37 (13.5)	25 (14.5)	59 (23.5)	
> 54 to ≤ 64	840 (40.7)	549 (40.2)	104 (37.8)	77 (44.8)	110 (43.8)	
> 64 to ≤ 74	659 (32.0)	422 (30.9)	108 (39.3)	58 (33.7)	71 (28.3)	
≥ 74	186 (9.02)	137 (10.0)	26 (9.45)	12 (6.98)	11 (4.38)	
Race						<0.001
Black	423 (20.5)	235 (17.2)	74 (26.9)	33 (19.2)	81 (32.3)	
Pardo	583 (28.3)	378 (27.7)	71 (25.8)	59 (34.3)	75 (29.9)	
White	961 (46.6)	682 (50.0)	117 (42.5)	73 (42.4)	89 (35.5)	
Yellow/Indigenous	95 (4.61)	69 (5.06)	13 (4.73)	7 (4.07)	6 (2.39)	
Education						<0.001
Less than University	994 (48.2)	562 (41.2)	156 (56.7)	109 (63.4)	167 (66.5)	
University	1068 (51.8)	802 (58.8)	119 (43.3)	63 (36.6)	84 (33.5)	
Private health insurance						<0.001
Yes	1380 (66.9)	972 (71.3)	172 (62.5)	112 (65.1)	124 (49.4)	
Per capita income (minimum wages/month) ¹						<0.001
Less than 4	356 (17.3)	174 (12.8)	71 (25.8)	36 (20.9)	75 (29.9)	
From 4 to less than 8	760 (36.9)	489 (35.9)	89 (32.4)	72 (41.9)	110 (43.8)	
From 8 to less than 12	375 (18.2)	250 (18.3)	55 (20.0)	33 (19.2)	37 (14.7)	
From 12 to less than 16	214 (10.4)	171 (12.5)	21 (7.64)	11 (6.40)	11 (4.38)	
16 or more	357 (17.3)	280 (20.5)	39 (14.2)	20 (11.6)	18 (7.17)	
BMI (kg/m ²), M (SD)	29.6 (4.97)	29.5 (4.97)	29.8 (5.23)	29.5 (4.37)	29.8 (5.09)	0.671
Diabetes medication						0.521
Yes	1812 (87.9)	1201 (88.0)	238 (86.5)	156 (90.7)	217 (86.5)	
WHO CVD risk						
High CVD risk	53 (2.57)	28 (2.05)	7 (2.55)	8 (4.65)	10 (3.98)	0.084
Years since diabetes diagnosis						<0.001
0-1	352 (17.1)	346 (25.4)	1 (0.36)	2 (1.16)	3 (1.20)	
1-10	1062 (51.5)	755 (55.4)	133 (48.4)	64 (37.2)	110 (43.8)	
10+	648 (31.4)	263 (19.3)	141 (51.3)	106 (61.6)	138 (55.0)	

n (%) unless otherwise indicated; M (SD)=Mean (Standard Deviation);
 Except for the row "All", percentages are for column totals.

Yellow skin color refers to Asian ancestry.

* Chi-square test for categorical variables and ANOVA for continuous ones of statistical significance of the difference in variable level or frequency across categories of HbA1c.

¹SM=The monthly minimum wage was BRL 986.00 at the time of the study.

Table 2 - Socio-demographics and clinical characteristics of individuals with type 2 diabetes according to the number of ABC goals reached. ELSA-Brasil, 2017-2019. N=2062

	Overall	Goals Reached			p*
		0	1 or 2	3	
All	2062(100)	111 (5.4)	1360 (66.0)	589(28.6)	
Sex					0.483
Men	1000 (48.5)	60 (54.1)	655 (48.1)	285 (48.3)	
Women	1062 (51.5)	51 (45.9)	706 (51.9)	305 (51.7)	
Age (years), M (SD)					0.002
> 44 to ≤ 54	377 (18.3)	13 (11.7)	273 (20.1)	91 (15.4)	
> 54 to ≤ 64	840 (40.7)	44 (39.6)	568 (41.7)	228 (38.6)	
> 64 to ≤ 74	659 (32.0)	47 (42.3)	407 (29.9)	205 (34.7)	
≥ 74	186 (9.02)	7 (6.31)	113 (8.30)	66 (11.2)	
Race					<0.001
Black	423 (20.5)	38 (34.2)	303 (22.3)	82 (13.9)	
Pardo (mixed)	583 (28.3)	36 (32.4)	389 (28.6)	158 (26.8)	
White	961 (46.6)	33 (29.7)	604 (44.4)	324 (54.9)	
Yellow/Indigenous	95 (4.61)	4 (3.60)	65 (4.78)	26 (4.41)	
Education					<0.001
Less than University	994 (48.2)	81 (73.0)	701 (51.5)	212 (35.9)	
University	1068 (51.8)	30 (27.0)	660 (48.5)	378 (64.1)	
Private health insurance					<0.001
Yes	1380 (66.9)	48 (43.2)	876 (64.4)	456 (77.3)	
Per capita income (minimum wages/month) ¹					<0.001
Less than 4	356 (17.3)	37 (33.3)	260 (19.1)	59 (10.0)	
From 4 to less than 8	760 (36.9)	43 (38.7)	518 (38.1)	199 (33.7)	
From 8 to less than 12	375 (18.2)	17 (15.3)	247 (18.1)	111 (18.8)	
From 12 to less than 16	214 (10.4)	9 (8.11)	127 (9.33)	78 (13.2)	
16 or more	357 (17.3)	5 (4.50)	209 (15.4)	143 (24.2)	
BMI (kg/m ²), M (SD)	29.6 (4.97)	30.3 (5.48)	29.5 (4.89)	29.6 (5.05)	0.245
Physical activity (MET-minutes/week) ²					0.046
Low	1490 (72.3)	89 (80.2)	995 (73.1)	406 (68.8)	
Moderate	453 (22.0)	20 (18.0)	292 (21.5)	141 (23.9)	
High	119 (5.77)	2 (1.80)	74 (5.44)	43 (7.29)	

	Overall	Goals Reached			p*
		0	1 or 2	3	
Depressive episodes	107 (5.19)	6 (5.41)	74 (5.44)	27 (4.58)	0.729
Yes					
Diabetes medication					<0.001
Yes	1805 (87.5)	91 (82.0)	1172 (86.1)	541 (91.7)	
Years since diabetes diagnosis					<0.001
0-1	352 (17.1)	2 (1.80)	199 (14.6)	151 (25.6)	
1-10	1062 (51.5)	54 (48.6)	699 (51.4)	309 (52.4)	
10+	648 (31.4)	55 (49.5)	463 (34.0)	130 (22.0)	

n (%) unless otherwise indicated; M (SD)=Mean (Standard Deviation);

Except for the row "All", percentages are for column totals.

Yellow skin color refers to Asian ancestry, physical activity refers to physical activity during leisure time;

* Chi-square test for categorical variables and ANOVA for continuous ones of statistical significance of the difference in variable level or frequency across categories of HbA1c.

¹SM=The monthly minimum wage was BRL 986.00 at the time of the study.

²High 1500 MET-minutes/week; moderate 600 MET-minutes/week; low less than 600 MET minutes/week

Table 3 – Adjusted* associations of selected population and clinical characteristics among individuals with known type 2 diabetes. ELSA-Brasil, 2017-2019. N=2062

Characteristic	HbA1C < 7%		Achieving ≥ 2 treatment goals**	
	PR (95% CI)	P	PR (95% CI)	P
Sex (reference: Men)				
Women	1.13(1.07-1.20)	<0.001	1.05(1.00-1.11)	0.050
Age (years, reference: ≤ 54)				
> 54 to ≤ 64	1.03(0.95-1.11)	0.453	1.01(0.94-1.08)	0.836
> 64 to ≤ 74	1.08(0.99-1.17)	0.080	1.03(0.96-1.11)	0.415
≥ 74	1.20(1.08-1.34)	<0.001	1.02(0.91-1.04)	0.646
Race (reference: White)				
Black	0.91(0.83-1.00)	0.041	0.86(0.79-0.94)	<0.001
Pardo (mixed)	1.01(0.95-1.08)	0.701	0.95(0.90-1.02)	0.139
Yellow/Indigenous	1.05(0.93-1.19)	0.433	0.94(0.83-1.06)	0.307
Education (reference: University)				
Less than University	0.94(0.86-1.01)	0.101	0.97(0.91-1.04)	0.419
Private health insurance (reference: No)				
Yes	1.07(0.99-1.15)	0.083	1.15(1.07-1.23)	<0.001
Per capita income (minimum wages/mo. Reference: less than 4) ¹				
4 to < 8	1.20(1.07-1.34)	0.002	1.12(1.01-1.23)	0.031
8 to < 12	1.16(1.02-1.32)	0.023	1.11(1.00-1.25)	0.061
12 to <16	1.27(1.11-1.45)	0.001	1.18(1.05-1.33)	0.007
≥ 16	1.26(1.10-1.45)	0.001	1.19(1.06-1.34)	0.004
Body mass index (increase of 5 kg/m ²)	0.97(0.95-1.00)	0.087	0.96(0.94-0.99)	0.012
Diabetes medication				
Yes	1.03(0.94-1.12)	0.535	1.03(0.95-1.12)	0.507
Years since diabetes diagnosis (reference: 0-1)				

Characteristic	HbA1C < 7%		Achieving ≥ 2 treatment goals**	
	PR (95% CI)	P	PR (95% CI)	P
1-10	0.74(0.71-0.77)	<0.001	0.87(0.82-0.91)	0.001
10+	0.43(0.39-0.47)	<0.001	0.68(0.63-0.73)	<0.001

*through Poisson regression with robust variance for age, sex, educational achievement, race/skin color, private health insurance, per capita income, diabetes medication, body mass index, and years since diagnosis.

**Treatment goals: glucose, blood pressure and LDL-c

†Minimum wage: The monthly minimum wage was BRL 986.00 at the time of the study.

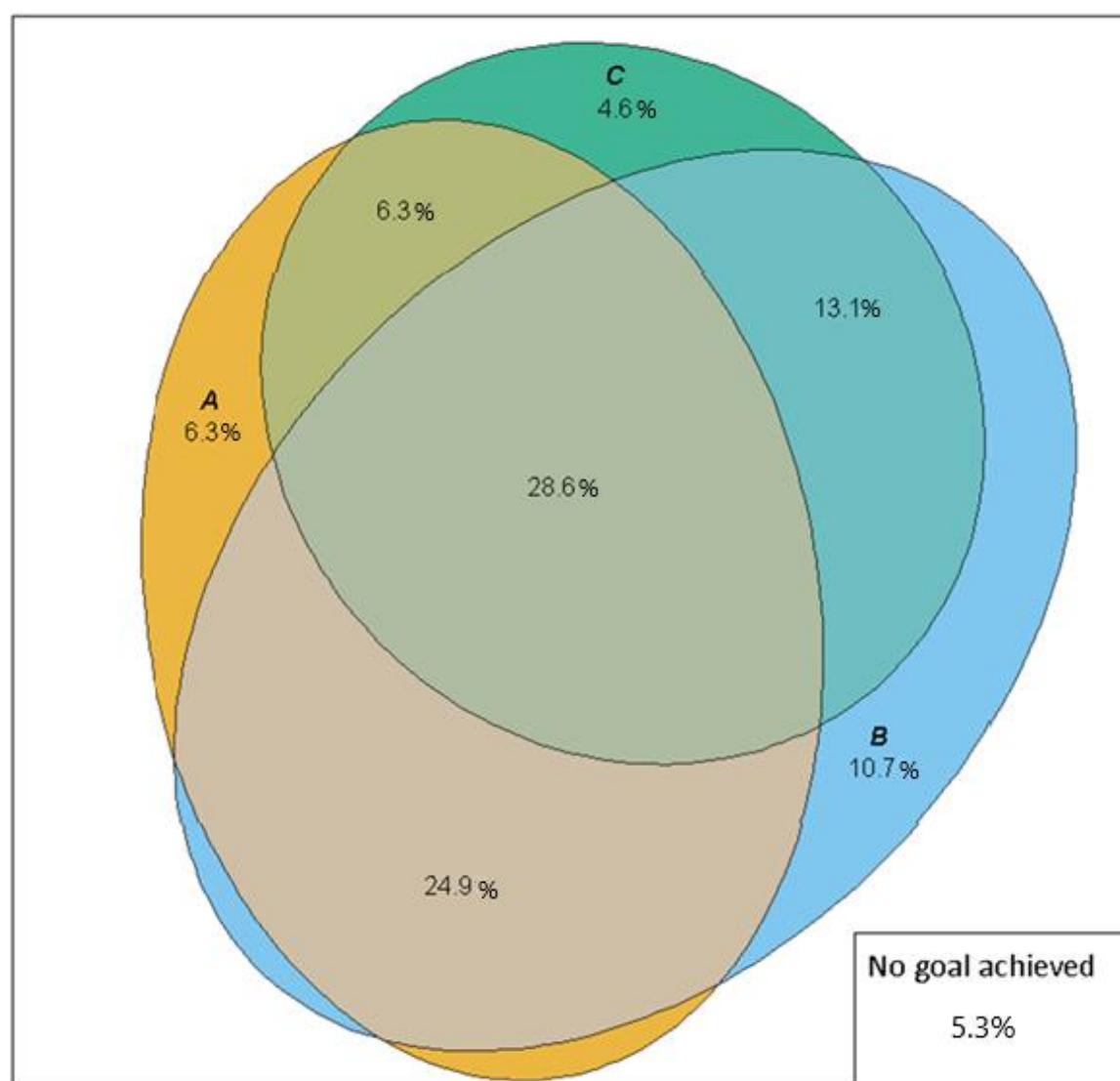


Figure 1 - Venn diagram showing the overlap in the attainment of treatment goals in individuals with self-reported diabetes: HbA1c (A), blood pressure (B), and LDL-c (C). ELSA-Brasil, 2017-2019. N=2062

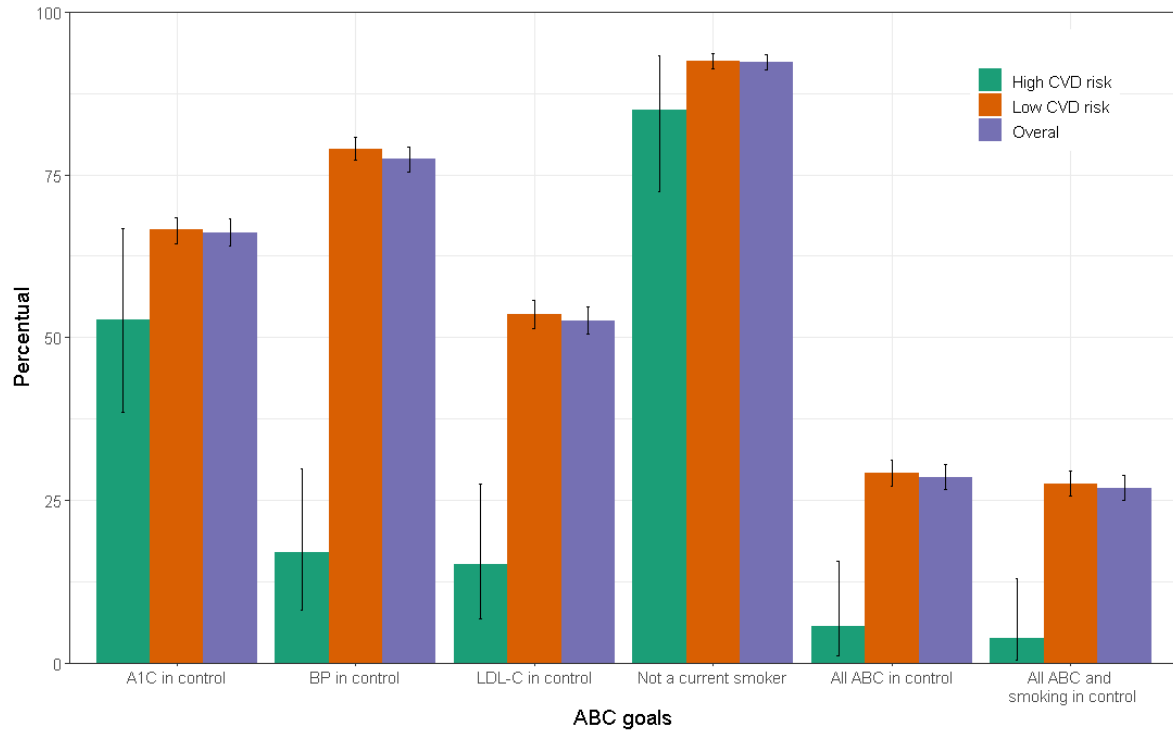


Figure 2 - Percentual of attainment of each of the three treatment goals, with 95% confidence interval, of non-smoking and of combinations of the goals among individuals with self-reported diabetes in Elsa-Brasil, 2017-2019. N=2062

RESUMO ARTIGO 2

Introdução: O diabetes mellitus tipo 2 é um importante problema de saúde global. No Brasil, o diabetes foi a sexta causa de morte em 2019 e deve se tornar a 3ª causa até 2040.

Objetivos: Caracterizar o risco de morte em participantes com diabetes tipo 2 em uma grande coorte de adultos e idosos brasileiros de acordo com o alcance das metas da American Diabetes Association para o controle da glicemia, hipertensão e lipídios.

Métodos: Acompanhamos os participantes da coorte do Estudo Longitudinal Brasileiro de Saúde do Adulto com diabetes tipo 2 de 2008 a 2019. Verificamos o diabetes por autorrelato e confirmamos pelo uso de medicamentos ou laboratório alterado em qualquer visita clínica ou na vigilância telefônica anual do estudo. Medimos a pressão arterial e determinamos a hemoglobina glicada (HbA1c) e o colesterol LDL em um laboratório central. Definimos controle para glicose como HbA1c < 7% e para pressão arterial como <140/90 mmHg (ou <130/80 mmHg em alto risco cardiovascular), e para LDL-c como <100 mg/dl (ou <70 mg/dl em alto risco), de acordo com as diretrizes da American Diabetes Association de 2022 na linha de base do estudo. Realizamos vigilância telefônica anual para averiguar as mortes incidentes por qualquer causa, confirmando-as por registros hospitalares e certidões de óbito.

Resultados: Dos 2.492 indivíduos com diabetes conhecido, 272 morreram. Em análises ajustadas por modelos de riscos proporcionais, o nível de HbA1c dentro do alvo conferiu maior proteção (HR=0.62; 95% IC 0.47-0,81) contra todas as causas de mortalidade, seguido por pressão arterial sistólica dentro do alvo (HR=0.77; 95% IC 0.59 -0.99). O LDL-c dentro do alvo, no entanto, não (HR=1.38; 95% IC 1.03-1.84). Alcançar duas ou mais metas do ABC reduziu o risco de mortalidade em 43% (HR = 0.57 a 0.63; 95% IC 0.38-0.99).

Conclusão: O controle de glicose e pressão arterial, mas não o controle de LDL-c, reduziu as mortes. Glicose e a pressão sanguínea dentro do alvo conferem proteção amplificada. O maior risco associado à manutenção do LDL-c dentro da meta merece uma investigação mais aprofundada.

CONSIDERAÇÕES FINAIS

O diabetes vem crescendo como epidemia e avançou silenciosamente durante a pandemia do Covid-19. O Brasil vem se tornando destaque no ranking mundial do diabetes, atrás dos Estados Unidos, China, Índia e Paquistão (Sun et al., 2022). O diabetes é responsável por reduzir a expectativa de vida de pessoas de meia idade e é um dos principais fatores de risco para morte por doenças cardíacas, renais ou câncer bem como uma das principais causas de cegueira e amputações (Tancredi et al., 2015). A morbidade do diabetes e seus custos elevados sobrecarregam o custo de vida das pessoas e famílias, principalmente as menos favorecidas economicamente, para quem o acesso ao sistema de saúde e a medicamentos é mais dificultoso (Bommer et al., 2018). Na maioria das vezes a doença também é silenciosa e quando se descobre o indivíduo já pode possuir complicações no momento do diagnóstico (Franco et al., 2007).

De acordo com os principais resultados do primeiro artigo, dos 2.062 participantes com diabetes conhecido nos anos de 2017 a 2019, HbA1c foi igual ou abaixo do alvo (HbA1c <7%) em 1.364 (66,1%), pressão arterial (<140/90 mmHg ou <130/80 mmHg em alto risco cardiovascular) em 1.596 (77,4%) e LDL-c (LDL-c <100 mg/dl ou <70 mg/dl em alto risco) em 1.086 (52,7%) e apenas 590 (28,6%) participantes estavam dentro ou abaixo da meta para todos os ABCs. Mulheres (RP=1,05; IC95% 1,00-1,11) e indivíduos com plano de saúde privado (RP=1,15; IC95% 1,07-1,23) ou maior renda per capita (por exemplo, RP=1,19; IC95% 1,06-1,34) foram mais propensos a atingir duas ou mais metas ABC em análises ajustadas.

Em nosso segundo artigo, dos 2492 participantes com diabetes conhecido selecionados desde a linha de base até a onda 3, 272 (10.9%) foram a óbito. Após ajustar as associações de fatores prognósticos modificáveis para covariáveis, menor risco de óbito estava presente naqueles com HbA1c ≤ 7 (HR = 0,62; IC 95% 0,47-0,81), que atingiram meta de pressão arterial sistólica menor que 140 mmHg (entre os de baixo risco) e inferior a 130 mmHg (entre os de alto risco) (HR = 0,77; IC 95% 0,59-0,99) e entre aqueles com 2 metas ABC alcançadas (HR = 0,57 a 0,63; IC 95% 0,38-0,98). Em contraste, o maior risco estava presente principalmente quando HbA1c $\geq 9\%$ (HR = 2,05; IC 95% 1,41-2,98) e a pressão arterial sistólica ≥ 160 mmHg (HR = 1,50; IC 95% 1,05-2,14). No entanto, contrario ao esperado, aqueles que atingiram a meta lipídica apresentaram risco aumentado nas análises bruta (HR=1,55; IC 95% 1,20-2,00)

e ajustada (HR = 1,61; IC 95% 1,20-2,16). O risco foi especialmente alto naqueles com valores de LDL-c <70 mg/dl (FC ajustada = 2,14; IC 95% 1,44-3,18).

Os pontos fortes de nosso estudo incluem sua amostra contemporânea de participantes residentes em vários locais do Brasil, sua coleta cuidadosa e extensa de dados sobre esses fatores examinados, sua ampla caracterização de covariáveis e suas medições laboratoriais padronizadas e centralizadas. Já as limitações residem principalmente no fato de nossa amostra ser composta por servidores públicos ativos ou aposentados, uma amostra socialmente privilegiada quando comparada à população brasileira em geral.

Nossos achados reforçam a necessidade de melhorias no controle dos fatores de risco modificáveis, principalmente de glicemia e pressão arterial (metas ABC) em termos de controle, demonstrando sua importância na mortalidade geral em diabetes. Estudos adicionais em diabetes são necessários para entender a causa da associação inesperada de baixos níveis de LDL-c com a maior mortalidade geral em diabetes. Estes achados colocam em questão as recomendações de colocar os níveis de LDL-c frequentemente bem abaixo de 100 mg/dl inclusive em indivíduos com diabetes de baixo risco cardiovascular. Esperamos investigar essa relação com mais detalhes em um futuro breve a fim de explicar se os baixos níveis de LDL-c relacionados com maior risco de mortalidade geral representam um risco real ou seriam resultantes de doenças subjacentes no início do estudo (Ranieri et al., 1998) (Poplawski et al., 2018) ou uma pior saúde na linha de base (Chiang et al., 2014; Johannesen et al., 2020). O ELSA-Brasil tem informações adicionais sobre participantes com níveis baixos de LDL-c e representa uma excelente oportunidade de investigar a questão de nível ideal de LDL-c e pontos de corte para iniciar terapia para baixar o nível de LDL-c.

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ANEXOS

- a. Publicação “Levels and Correlates of Risk Factor Control in Diabetes Mellitus –ELSA Brasil”

RESEARCH

Open Access



Levels and correlates of risk factor control in diabetes mellitus –ELSA-Brasil

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Abstract

Background Control of glucose, blood pressure, cholesterol, and smoking improves the prognosis of individuals with diabetes mellitus. Our objective was to assess the level of control of these risk factors in Brazilian adults with known diabetes and evaluate correlates of target achievement.

Methods Cross-sectional sample of the Brazilian Longitudinal Study of Adult Health, composed of participants reporting a previous diagnosis of diabetes or the use of antidiabetic medication. We measured glycated hemoglobin (HbA1c) and LDL-cholesterol at a central laboratory and blood pressure following standardized protocols. We defined HbA1c < 7% as glucose control (target A); blood pressure < 140/90 mmHg (or < 130/80 mmHg in high cardiovascular risk) as blood pressure control (target B), and LDL-c < 100 mg/dl (or < 70 mg/dl in high risk) as lipid control (target C), according to the 2022 American Diabetes Association guidelines.

Results Among 2062 individuals with diabetes, 1364 (66.1%) reached target A, 1596 (77.4%) target B, and 1086 (52.7%) target C; only 590 (28.6%) achieved all three targets. When also considering a non-smoking target, those achieving all targets dropped to 555 (26.9%). Women (PR = 1.13; 95%CI 1.07–1.20), those aged ≥ 74 (PR = 1.20; 95%CI 1.08–1.34), and those with greater per capita income (e.g., greatest income PR = 1.26; 95%CI 1.10–1.45) were more likely to reach glucose control. Those black (PR = 0.91; 95%CI 0.83–1.00) or with a longer duration of diabetes (e.g., ≥ 10 years PR = 0.43; 95%CI 0.39–0.47) were less likely. Women (PR = 1.05; 95%CI 1.00–1.11) and those with private health insurance (PR = 1.15; 95%CI 1.07–1.23) were more likely to achieve two or more ABC targets; and those black (PR = 0.86; 95%CI 0.79–0.94) and with a longer duration of diabetes (e.g., > 10 years since diabetes diagnosis, PR = 0.68; 95%CI 0.63–0.73) less likely.

Conclusion Control of ABC targets was poor, notably for LDL-c and especially when considering combined control. Indicators of a disadvantaged social situation were associated with less frequent control.

Keywords Diabetes mellitus, Cardiometabolic risk factors, Glycated hemoglobina A, Hypertension, Hypercholesterolemia, Tobacco smoking

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Introduction

Diabetes mellitus is a chronic and complex disease that requires continuous medical care. In addition to adequate glycemic control, multifactorial risk reduction is indicated [1]. In clinical trial settings, interventions to control hyperglycemia, hypertension, and hypercholesterolemia, as well as to stop smoking, have been shown to produce sustained benefits in vascular complications, with major reductions in cardiovascular outcomes [2, 3]. Additionally, the risk of dying is only 6% greater in those



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at or below targets than in individuals without diabetes [4].

Recommended therapeutic targets, also called the ABC goals, usually include (A) glycated hemoglobin (HbA1c) less than 7%, (B) a blood pressure <140/90 mmHg, and (C) LDL-cholesterol (LDL-c) <100 mg/dl. Tighter control has also been suggested for those with cardiovascular disease or at high risk of developing it [5]. Additionally, non-smoking is an important goal to be achieved.

Studies demonstrating the control of multiple risk factors in diabetes are scarce in low- and middle-income countries. Based on a small subsample of a probabilistic national Brazilian survey, we demonstrated that target achievement is usually poor, except for non-smoking [6]. However, that study lacked statistical power to assess the factors related to ABC control. Therefore, we sought to analyze the Longitudinal Study of Adult Health (ELSA-Brasil) to explore these associations. This large ongoing occupational cohort study enrolled 15,105 adults in 6 capital cities from 2008 to 2010. We aimed to assess the level of control of blood glucose, blood pressure, lipids, and smoking habits of ELSA-Brasil participants with known diabetes mellitus and to evaluate correlates of target achievement.

Methods

Study population and ethics

We conducted a cross-sectional study based on the third clinic visit (2017–2019) of ELSA-Brasil. The study was approved by the research ethics committees of participating institutions, and all participants gave their written informed consent. The ELSA-Brasil cohort enrolled 15,105 in-service or retired civil servants aged 35 to 74 at six public institutions of higher education located in capital cities of the states of Bahia, Espírito Santo, Minas Gerais, Rio de Janeiro, São Paulo, and Rio Grande do Sul [7]. We included all participants returning for the 2017–2019 clinic visit with self-report of and/or pharmacologic treatment for diabetes. We excluded those who did not have all measures necessary to assess whether targets were achieved.

Measurements

Centrally trained and certified teams conducted standardized interviews and clinical assessments and collected samples for biochemical tests [8]. We obtained data on age, sex, self-declared race, history of a medical diagnosis of diabetes, duration of diabetes, and depressive episodes by questionnaire. Physical activity was obtained by leisure-time physical activity and categorized as [1] high ≥ 1500 MET-minutes/week, [2]

moderate (600–1499 MET-minutes/week, and [3] low (<600 MET-minutes/week).

Medication use was confirmed by packaging or prescriptions brought to the clinic. Blood pressure was measured three times, and systolic and diastolic blood pressure each was ascertained as the mean of the last two measurements. We assessed weight and height using a standardized protocol and calculated body mass index (BMI) as weight/height² (kg/m²).

We obtained blood samples after an overnight (>8 h) fast and froze and shipped them to a central laboratory for determination. Plasma glucose was measured using the hexokinase method (Cobas c501[®], Roche Diagnostics), HbA1c by high-pressure chromatography (HPLC—Bio-Rad Laboratories, Hercules, CA, USA), total cholesterol by enzymatic colorimetric method, and triglycerides by glycerol-phosphate peroxidase (Cobas c501[®], Roche Diagnostics). Low-density cholesterol (LDL-c) was estimated by the Friedewald equation when total triglycerides were <400 mg/dl and measured directly when they were ≥ 400 mg/dl.

Ten-year risk of a major cardiovascular event (myocardial infarction, stroke, or cardiovascular death) was estimated based on age, sex, diabetes, smoking, systolic blood pressure, and total cholesterol according to the WHO Risk Chart Working Group chart for the Tropical Latin America region [9]. We categorized this estimated risk as high ($\geq 20\%$) or low.

In line with the 2022 American Diabetes Association (ADA) guidelines for therapeutic targets [10], we considered glucose control to be adequate when HbA1c was less than 7%. For those without high cardiovascular risk, we considered blood pressure <140/90 mmHg and LDL-c <100 mg/dl as meeting targets [5]; and for those with high risk or clinical cardiovascular disease, <130/80 mmHg and <70 mg/dl, respectively [10].

Statistical analyses

We described categorical variables as frequencies and percentages, and continuous ones as means and standard deviations (SD). We performed unadjusted statistical testing with the chi-square test for categorical and ANOVA for continuous variables. We analyzed the adjusted associations of socio-demographic and clinical factors with the level of control using Poisson regression with robust variance. We undertook all analyses with R software (RStudio, version 1.3. 1056, ©2009–2020 RStudio Inc.).

Results

Of the 15,105 participants at baseline, 550 had died, 123 had moved away, 217 were not localized, 39 were too ill to attend clinic at visit 3 and 1540 did not attend this visit

for other reasons. Of the remaining 12,636 (83.7%) participants at visit 3, 2385 (18.9%) had a known diagnosis of diabetes. After excluding 323 participants with missing data on risk factor control or covariates, 2062 remained.

Among these 2062 participants, 1000 (48.5%) were men, 1217 (59.0%) aged 45–64, 961 (46.6%) with self-declared white race/skin color, and 1068 (51.8%) with a

complete university education. Additionally, 1380 (66.9%) reported having private health insurance. Mean BMI was 29.6 (4.97) kg/m², and 1812 (87.9%) individuals related use of an antidiabetic drug. (Table 1).

Figure 1, which presents the overlap in achieving goals, shows greater success in achieving that of blood pressure and lesser success in achieving that of LDL-c, as well

Table 1 Sociodemographic and clinical characteristics of individuals with known diabetes according to levels of glycated hemoglobin (HbA1c)—ELSA-Brasil, 2017–2019. N = 2062

	HbA1c					P*
	Overall	< 7%	7% to < 8%	8% to < 9%	≥ 9%	
All	2062 (100)	1364 (66.1)	275 (13.3)	172 (8.34)	251 (12.1)	
Sex						< 0.001
Men	1000 (48.5)	616 (45.2)	157 (57.1)	94 (54.7)	133 (53.0)	
Women	1062 (51.5)	748 (54.8)	118 (42.9)	78 (45.3)	118 (47.0)	
Age (years), M(SD)						0.003
> 44 to ≤ 54	377 (18.3)	256 (18.8)	37 (13.5)	25 (14.5)	59 (23.5)	
> 54 to ≤ 64	840 (40.7)	549 (40.2)	104 (37.8)	77 (44.8)	110 (43.8)	
> 64 to ≤ 74	659 (32.0)	422 (30.9)	108 (39.3)	58 (33.7)	71 (28.3)	
≥ 74	186 (9.02)	137 (10.0)	26 (9.45)	12 (6.98)	11 (4.38)	
Race						< 0.001
Black	423 (20.5)	235 (17.2)	74 (26.9)	33 (19.2)	81 (32.3)	
Pardo	583 (28.3)	378 (27.7)	71 (25.8)	59 (34.3)	75 (29.9)	
White	961 (46.6)	682 (50.0)	117 (42.5)	73 (42.4)	89 (35.5)	
Yellow/Indigenous	95 (4.61)	69 (5.06)	13 (4.73)	7 (4.07)	6 (2.39)	
Education						< 0.001
Less than University	994 (48.2)	562 (41.2)	156 (56.7)	109 (63.4)	167 (66.5)	
University	1068 (51.8)	802 (58.8)	119 (43.3)	63 (36.6)	84 (33.5)	
Private health insurance						< 0.001
Yes	1380 (66.9)	972 (71.3)	172 (62.5)	112 (65.1)	124 (49.4)	
Per capita income (minimum wages/month) ¹						< 0.001
Less than 4	356 (17.3)	174 (12.8)	71 (25.8)	36 (20.9)	75 (29.9)	
From 4 to less than 8	760 (36.9)	489 (35.9)	89 (32.4)	72 (41.9)	110 (43.8)	
From 8 to less than 12	375 (18.2)	250 (18.3)	55 (20.0)	33 (19.2)	37 (14.7)	
From 12 to less than 16	214 (10.4)	171 (12.5)	21 (7.64)	11 (6.40)	11 (4.38)	
16 or more	357 (17.3)	280 (20.5)	39 (14.2)	20 (11.6)	18 (7.17)	
BMI (kg/m ²), M (SD)	29.6 (4.97)	29.5 (4.97)	29.8 (5.23)	29.5 (4.37)	29.8 (5.09)	0.671
Diabetes medication						0.521
Yes	1812 (87.9)	1201 (88.0)	238 (86.5)	156 (90.7)	217 (86.5)	
WHO CVD risk						
High CVD risk	53 (2.57)	28 (2.05)	7 (2.55)	8 (4.65)	10 (3.98)	0.084
Years since diabetes diagnosis						< 0.001
0–1	352 (17.1)	346 (25.4)	1 (0.36)	2 (1.16)	3 (1.20)	
1–10	1062 (51.5)	755 (55.4)	133 (48.4)	64 (37.2)	110 (43.8)	
10+	648 (31.4)	263 (19.3)	141 (51.3)	106 (61.6)	138 (55.0)	

n (%) unless otherwise indicated. Except for the row "All", percentages are for column totals. Yellow skin color refers to Asian ancestry

M (SD) mean (standard deviation)

* Chi-square test for categorical variables and ANOVA for continuous ones of statistical significance of the difference in variable level or frequency across categories of HbA1c.

¹SM = The monthly minimum wage was BRL 986.00 at the time of the study

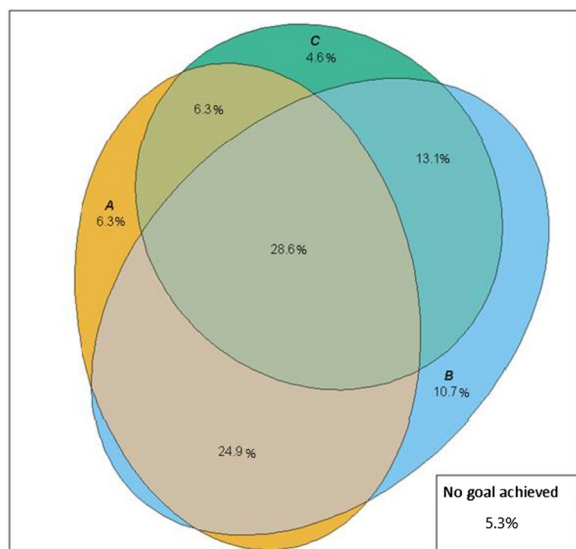


Fig. 1 Venn diagram showing the overlap in the attainment of treatment goals in individuals with self-reported diabetes: HbA1c (A), blood pressure (B), and LDL-c (C). ELSA-Brasil, 2017–2019. N = 2062

as no particular pattern of clustering in the success of achieving more than one goal. Only 589 (28.6%) achieved all three goals (center of the figure). As shown in Figs. 1, 2, HbA1c was at or below target in 1364 (66.1%), blood pressure in 1596 (77.4%), and LDL-c in 1086 (52.7%). Control was more frequent in those without high risk for CVD, reflecting the more rigorous targets for those at high risk. Non-smokers comprised 1904 (92.3%) of the sample. However, all ABCs were at or below target in only 590 (28.6%) participants and, when also considering non-smoking as a target, in 555 (26.9%).

As further seen in Table 1, in crude comparisons, being a woman, older, white, and having greater educational attainment, greater income, and private health insurance, as well as having a shorter duration of diabetes were all associated with better glucose control.

As seen in crude comparisons in Table 2, several sociodemographic and clinical characteristics, mostly the same as those seen in Table 1, were associated with a greater number of ABC goals being reached—being white, having greater educational attainment, greater income, and private health insurance, pursuing greater

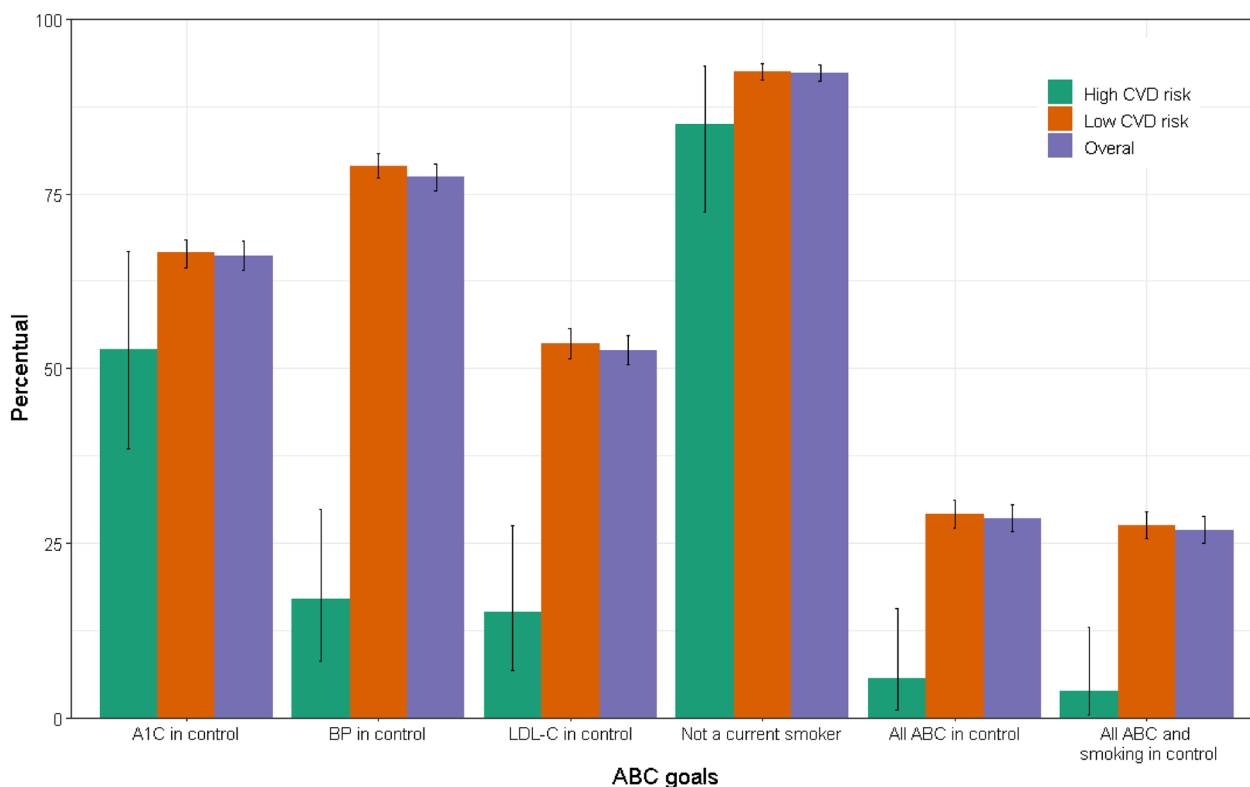


Fig. 2 Percentual of attainment of each of the three treatment goals, with 95% confidence interval, of non-smoking and of combinations of the goals among individuals with self-reported diabetes in Elsa-Brasil, 2017–2019. N = 2062

Table 2 Socio-demographics and clinical characteristics of individuals with type 2 diabetes according to the number of ABC goals reached. ELSA-Brasil, 2017–2019. N = 2062

	Overall	Goals reached			p*
		0	1 or 2	3	
All	2062(100)	111 (5.4)	1360 (66.0)	589(28.6)	
Sex					
Men	1000 (48.5)	60 (54.1)	655 (48.1)	285 (48.3)	0.483
Women	1062 (51.5)	51 (45.9)	706 (51.9)	305 (51.7)	
Age (years), M (SD)					0.002
> 44 to ≤ 54	377 (18.3)	13 (11.7)	273 (20.1)	91 (15.4)	
> 54 to ≤ 64	840 (40.7)	44 (39.6)	568 (41.7)	228 (38.6)	
> 64 to ≤ 74	659 (32.0)	47 (42.3)	407 (29.9)	205 (34.7)	
≥ 74	186 (9.02)	7 (6.31)	113 (8.30)	66 (11.2)	
Race					< 0.001
Black	423 (20.5)	38 (34.2)	303 (22.3)	82 (13.9)	
Pardo (mixed)	583 (28.3)	36 (32.4)	389 (28.6)	158 (26.8)	
White	961 (46.6)	33 (29.7)	604 (44.4)	324 (54.9)	
Yellow/Indigenous	95 (4.61)	4 (3.60)	65 (4.78)	26 (4.41)	
Education					< 0.001
Less than University	994 (48.2)	81 (73.0)	701 (51.5)	212 (35.9)	
University	1068 (51.8)	30 (27.0)	660 (48.5)	378 (64.1)	
Private health insurance	1380 (66.9)	48 (43.2)	876 (64.4)	456 (77.3)	< 0.001
Yes					
Per capita income (minimum wages/month) ¹					< 0.001
Less than 4	356 (17.3)	37 (33.3)	260 (19.1)	59 (10.0)	
From 4 to less than 8	760 (36.9)	43 (38.7)	518 (38.1)	199 (33.7)	
From 8 to less than 12	375 (18.2)	17 (15.3)	247 (18.1)	111 (18.8)	
From 12 to less than 16	214 (10.4)	9 (8.11)	127 (9.33)	78 (13.2)	
16 or more	357 (17.3)	5 (4.50)	209 (15.4)	143 (24.2)	
BMI (kg/m ²), M (SD)	29.6 (4.97)	30.3 (5.48)	29.5 (4.89)	29.6 (5.05)	0.245
Physical activity (MET-minutes/week) ²					0.046
Low	1490 (72.3)	89 (80.2)	995 (73.1)	406 (68.8)	
Moderate	453 (22.0)	20 (18.0)	292 (21.5)	141 (23.9)	
High	119 (5.77)	2 (1.80)	74 (5.44)	43 (7.29)	
Depressive episodes					
Yes	107 (5.19)	6 (5.41)	74 (5.44)	27 (4.58)	0.729
Diabetes medication					< 0.001
Yes	1805 (87.5)	91 (82.0)	1172 (86.1)	541 (91.7)	
Years since diabetes diagnosis					< 0.001
0–1	352 (17.1)	2 (1.80)	199 (14.6)	151 (25.6)	
1–10	1062 (51.5)	54 (48.6)	699 (51.4)	309 (52.4)	
10+	648 (31.4)	55 (49.5)	463 (34.0)	130 (22.0)	

n (%) unless otherwise indicated. Except for the row "All", percentages are for column totals. Yellow skin color refers to Asian ancestry, physical activity refers to physical activity during leisure time.

M (SD) mean (standard deviation)

* Chi-square test for categorical variables and ANOVA for continuous ones of statistical significance of the difference in variable level or frequency across categories of HbA1c

¹ SM = The monthly minimum wage was BRL 986.00 at the time of the study

² High 1500 MET-minutes/week; moderate 600 MET-minutes/week; low less than 600 MET minutes/week

Table 3 Adjusted* associations of selected population and clinical characteristics among individuals with known type 2 diabetes. ELSA-Brasil, 2017–2019. N = 2062

Characteristic	HbA1c < 7%		Achieving ≥ 2 treatment goals**	
	PR (95% CI)	P	PR (95% CI)	P
Sex (reference: men)				
Women	1.13 (1.07–1.20)	< 0.001	1.05 (1.00–1.11)	0.050
Age (years, reference: ≤ 54)				
> 54 to ≤ 64	1.03 (0.95–1.11)	0.453	1.01 (0.94–1.08)	0.836
> 64 to ≤ 74	1.08 (0.99–1.17)	0.080	1.03 (0.96–1.11)	0.415
≥ 74	1.20 (1.08–1.34)	< 0.001	1.02 (0.91–1.04)	0.646
Race (reference: white)				
Black	0.91 (0.83–1.00)	0.041	0.86 (0.79–0.94)	< 0.001
Pardo (mixed)	1.01 (0.95–1.08)	0.701	0.95 (0.90–1.02)	0.139
Yellow/indigenous	1.05 (0.93–1.19)	0.433	0.94 (0.83–1.06)	0.307
Education (reference: university)				
Less than uni- versity	0.94 (0.86–1.01)	0.101	0.97 (0.91–1.04)	0.419
Private health insurance (reference: no)				
Yes	1.07 (0.99–1.15)	0.083	1.15 (1.07–1.23)	< 0.001
Per capita income (minimum wages/mo. Reference: less than 4) ¹				
4 to < 8	1.20 (1.07–1.34)	0.002	1.12 (1.01–1.23)	0.031
8 to < 12	1.16 (1.02–1.32)	0.023	1.11 (1.00–1.25)	0.061
12 to < 16	1.27 (1.11–1.45)	0.001	1.18 (1.05–1.33)	0.007
≥ 16	1.26 (1.10–1.45)	0.001	1.19 (1.06–1.34)	0.004
Body mass index (increase of 5 kg/ m ²)	0.97 (0.95–1.00)	0.087	0.96 (0.94–0.99)	0.012
Diabetes medication				
Yes	1.03 (0.94–1.12)	0.535	1.03 (0.95–1.12)	0.507
Years since diabetes diagnosis (reference: 0–1)				
1–10	0.74 (0.71–0.77)	< 0.001	0.87 (0.82–0.91)	0.001
10+	0.43 (0.39–0.47)	< 0.001	0.68 (0.63–0.73)	< 0.001

* through Poisson regression with robust variance for age, sex, educational achievement, race/skin color, private health insurance, per capita income, diabetes medication, body mass index, and years since diagnosis

** Treatment goals: glucose, blood pressure and LDL-c

¹ Minimum wage: the monthly minimum wage was BRL 986.00 at the time of the study

physical activity, having a lower BMI and using antidiabetic medications.

As seen in Table 3, after adjustment for multiple potential confounders, women (PR = 1.13; 95%CI 1.07–1.20), those ≥ 74 years old (RR = 1.20; 95%CI 1.08–1.34), and those with greater income (e.g. for those with the highest income (PR 1.26. 95%CI 1.10–1.45) were more likely to achieve the HbA1c goal, while those black (PR = 0.91; 95%CI 0.83–1.00) and with diabetes of longer duration (e.g. ≥ 10 years PR = 0.43; 95%CI 0.39–0.47) less likely. In terms of ABC goals, women (PR = 1.05; 95%CI

1.00–1.11) and those with private health insurance (PR = 1.15; 95%CI 1.07–1.23) and with higher per capita income (e.g. for those with highest income PR = 1.19; 95%CI 1.06–1.34) had a greater probability of meeting two or more ABC goals. On the other hand, those black (PR = 0.86; 95%CI 0.79–0.94), with greater body mass index (PR = 0.96; 95%CI 0.94–0.99), and with a longer duration of diabetes (e.g. ≥ 10 years PR = 0.68; 95%CI 0.63–0.73) were less likely to achieve two or more of the goals.

Discussion

In this free-living sample of 2063 Brazilian adults with known diabetes, HbA1c was controlled in more than half of the sample (66.1%), as were blood pressure (77.4%) and LDL-c (52.6%). However, only 28.6% of participants had all three factors controlled. Some indicators of greater social privilege (white ethnicity, higher income, and access to private health insurance) are associated with meeting targets.

The fraction of individuals reaching glycemic, blood pressure, and LDL-c goals in the ELSA-Brasil cohort was greater than that seen in the 2013 Brazilian National Health Survey [6]: 66.1% in ELSA-Brasil vs 46% in the national survey when using identical control cutoffs for targets. Attainment of all three ABC goals in ELSA-Brasil participants was also greater than in this Brazilian National Health Survey (28.6% vs 12.5%). Consonant with the high estimates of non-smoking in Brazilian adults in general, achievement of the non-smoking target was similar in both studies (92.3% vs 90.3%) and higher than those found in other surveys [11, 12]. This achievement results from the long-term implementation of multiple, strong public policies against tobacco [13] in Brazil.

In studies in diverse countries, attainment of all ABC goals was always low. In the US NHANES, 22.2% of individuals simultaneously achieved all three targets (HbA1c < 7%, blood pressure < 140/90 mmHg, and non-high-density lipoprotein cholesterol < 130 mg/dl) [14]. In the Korean NHANES, with a more stringent target for glycemic control (HbA1c < 6.5%), and with targets of blood pressure < 140/85 mmHg, and LDL-C below 100 mg/dl, only 8.4% of subjects reached all three targets [15]. In a study in nine Latin American countries, glycemic control was also lower (43.5%) than that described here [16]. Our findings thus complement those already present in the literature, showing the current difficulty faced by diabetic patients in achieving desired levels of the principal factors affecting their prognosis which are modifiable at the individual level.

We found several characteristics that identified those not reaching targets for hyperglycemia and the ABC

goals. As expected, a greater duration of diabetes was one. A higher BMI was marginally associated with a lesser frequency of control. Women were more frequently in glycemic control and achieved greater ABC control. The additional factors associated with worse control—being non-white, with lower income, and not having private health insurance, all point to better control being in part the result of social privilege.

Similarly, a representative survey of adults with diabetes showed that private health insurance led to their receiving better quality primary care, as measured by the cardinal attributes of quality primary care, especially access. Greater access to care provides a logical pathway linking this insurance to better control [17]. A multi-center Brazilian study of hospital outpatients showed that multi-professional care and having had diabetes education as well as disease of lesser duration significantly associated with improved glycemic control [18]. Morães et al., evaluating only glycemic control at the baseline ELSA-Brasil visit, demonstrated similar associations with socioeconomic factors [19] as those we found here for overall ABC target achievement.

Our study has limitations, principally that our sample is composed of active or retired civil servants, a socially privileged sample when compared to the general Brazilian population in terms of educational achievement, income, and job stability among other factors. That we found major socioeconomic determinants of control in this more privileged population only emphasizes the likelihood of greater health disparities in achieving ABC targets in the general diabetic population.

Strengths of our study include its free-living sample of participants obtained in multiple cities across Brazil, different from many other studies which investigated less representative inpatient or outpatient samples which will have both more comorbidities and, by their entry criteria, better access to care. Additional strengths include ELSA's careful and extensive collection of factors examined, its standardized and centralized laboratory measurements, and its sample size permitting adequate investigation of epidemiologically relevant associations.

As has been shown for health outcomes in general [20], the correlates of control we found demonstrate the major role of social determinants of health in the ABCs of diabetes control. As put forth by the American Heart Association, clinical care and treatment account for 10% to 20% of the modifiable contributors to health outcomes. The other 80% to 90% are the social determinants of health, which include health-related behaviors, socioeconomic factors, environmental factors, and racism, all recognized to have a profound impact on cardiovascular disease and diabetes and their outcomes [21]. The ADA also recently summarized what is known about

the importance of social determinants [22]. One implication from these findings is clear: though better control across the board is necessary, improvement and greater resources for the care for people with diabetes in the SUS, Brazil's national health system should be a major goal if the aim is to improve control in the overall population of those with diabetes in Brazil. The SUS covers the bulk of the population and the majority of its underprivileged citizens. It also presents the advantage of providing cost-effective, evidence-based protocols to achieve treatment goals.

These findings are particularly relevant now, as actions aimed to achieve greater control at the health system level, supported by greater tracking and feedback of care, are now feasible given advances in information technology. The implementation and expansion of a diabetes registry orienting patient care in several Asian countries produced improvement in control of all the ABCs. In Hong Kong, a setting for which longer follow-up is available, the implementation of the registry was accompanied by a 40% decrease in CVD or microvascular complications and a 66% decrease in all-cause mortality, [23] and was additionally estimated to be cost-saving. [24] In Brazil, advances in the integration of databases within the national health system, which favors primary care and focuses resources on underprivileged communities, offer great hope in this regard. In this scenario, our study, by expanding knowledge of control of diabetes in Brazil and demonstrating the major role of socioeconomic factors, contributes to future strategies for better control and health promotion of Brazilians with diabetes. Future research can refine questions related to the relative benefit of greater control across the board as opposed to focus on better control among those with worst baseline levels.

Additionally, issues of relaxed control, especially of HbA1c, in older patients and those with greater morbidity and thus greater difficulty in managing multiple medications, are also important [5]. The American Heart Association currently emphasizes a comprehensive approach to the management of all cardiovascular risk factors in patients with diabetes, including glycemic, blood pressure, lipid abnormalities, thrombotic risk, obesity, and smoking through applying lifestyle and pharmacological approaches with proven benefit using a patient-centered approach. This latter implies reframing clinical encounters to approach patients as people who live in families, communities, and societies that must be considered in their cardiovascular risk management. [5] While the ideal fraction of the diabetes population in control of all the ABCs, given these issues, is a question that remains open for debate, certainly it is much greater than the current fraction.

In conclusion, control of ABC targets was poor, notably for LDL-c and especially when considering combined control. Our findings reinforce that much room exists for improvement in controlling these modifiable prognostic factors, notably LDL-c and especially when considering combined control. Less frequent control among those black, with lower income, and without health insurance reinforces the role of social factors in the multicausal context of control of risk factors for complications in diabetes. With due attention to social determinants and focusing on better integration of health system data to evaluate and orient patient care, health systems and clinicians can and should strive to implement better care for people with diabetes.

Author contributions

BCC, BBD and MIS conceived the study and drafted the manuscript. BCC and RCP conducted the analyses. BBD, MIS, SMB and RG are principal investigators of ELSA-Brasil and contributed to study design and data collection. All authors reviewed and approved the manuscript.

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Availability of data and materials

Due to ethical restrictions approved by the ethics committee of each institution (Universidade Federal da Bahia, Universidade Federal de Minas Gerais, Universidade Federal do Espírito Santo, Fundação Oswaldo Cruz, Universidade de São Paulo, Universidade Federal do Rio Grande do Sul) and by the Publications Committee of ELSA-Brasil (publiELSA), the data used in this study can be made available for research proposals by a request to ELSA's Datacenter (estatisticaelsa@gmail.com) and to the ELSA's Publications Committee.

Declarations

Ethical approval and consent to participate

ELSA-Brasil study was approved by the research ethics committees of participating institutions, and all participants gave their written informed consent.

Competing interests

None.

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