

Universidade Federal do Rio Grande do Sul
Faculdade de Medicina
Programa de Pós-Graduação em Ciências Médicas: Endocrinologia
Área de Concentração: Nutrição e Metabolismo
Mestrado e Doutorado

**Questionário de Frequência Alimentar Quantitativo em pacientes com Diabetes Melito tipo 2:
desenvolvimento e validação de instrumento**

Roberta Aguiar Sarmento

Orientadoras:
Prof^a Dr^a Jussara Carnevale de Almeida
Prof^a Dr^a Mirela Jobim de Azevedo

Porto Alegre, julho de 2012.

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Se as coisas são inatingíveis... ora!

Não é motivo para não querê-las...

Que tristes os caminhos, se não fora

A presença distante das estrelas!

Mário Quintana

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Formato da dissertação

Esta dissertação de Mestrado segue o formato proposto pelo Programa de Pós-Graduação em Ciências Médicas: Endocrinologia da Universidade Federal do Rio Grande do Sul, sendo apresentada através de uma breve revisão da literatura e dois manuscritos referentes ao tema estudado:

Capítulo I. Referencial teórico

Capítulo II. Artigo original submetido para publicação no periódico *Public Health Nutrition*, redigido conforme as normas do periódico

Capítulo III. Artigo original a ser submetido para publicação no periódico *International Journal of Epidemiology*, redigido conforme as normas do periódico

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BMI – *body mass index*

CI – *confidence interval*

DM – Diabetes Melito

FFQ – *food frequency questionnaire*

GI – *glycemic index*

GL – *glycemic load*

GNE – *Group of Nutrition in Endocrinology*

HbA1C – hemoglobina glicada

HDL-cholesterol – *high density lipoprotein cholesterol*

IMC – índice de massa corporal

LDL-cholesterol – *low density lipoprotein cholesterol*

QFA – questionário de frequência alimentar

r – coeficiente de correlação

RA – registro alimentar

SD – *standard deviation*

T2DM – *type 2 diabetes mellitus*

WDR – *weighed diet Record*

p – validity coefficient

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Capítulo I

Referencial teórico

IMPORTÂNCIA DO PROBLEMA

Diabetes

O Diabetes Melito (DM) é uma doença crônica que acomete parte significativa da população mundial - cerca de 366 milhões de pessoas, 8,3% de prevalência global (1). No Brasil, a prevalência do diabetes no ano de 2011 foi de 12,4 milhões de pessoas e estima-se que para o ano de 2030 ocorra um aumento para 19,6 milhões de pessoas com a doença (1). O diabetes constitui um importante problema de saúde pública em razão da elevada prevalência e morbi-mortalidade (2), além dos custos envolvidos no seu tratamento (3).

O diabetes tipo 2 é a forma mais comum de diabetes e ocorre geralmente na vida adulta, estando associado à obesidade em cerca de 80% dos casos. A hiperglicemia sustentada, resultado da resistência à ação da insulina e da incapacidade pancreática em suplantar essa resistência, associada a fatores genéticos e ambientais é uma das principais responsáveis pelo desenvolvimento das complicações crônicas microvasculares, neuropáticas e, possivelmente, macrovasculares (3).

A redução das complicações crônicas do diabetes é usada como alvo terapêutico no tratamento da doença e as incidências de retinopatia, nefropatia e neuropatia estão diretamente associadas com o grau de hiperglicemia (3). Modificações no estilo de vida a partir de um plano alimentar saudável e individualizado com a prática regular de exercícios físicos associadas ao tratamento farmacológico (3) são recomendados para o manejo rigoroso da hiperglicemia, embora este controle intensivo possa aumentar em duas vezes o risco de episódios graves de hipoglicemia (4). Assim, a melhor estratégia farmacológica para reduzir a glicemia em pacientes com DM tipo 2 tem sido constantemente avaliada (5) e muitos pacientes não conseguem atingir os alvos terapêuticos estabelecidos (6) reforçando a importância de aspectos relacionados ao estilo de vida, em especial o manejo da dieta, no controle do diabetes. Entretanto, as relações entre componentes da dieta e complicações da doença ainda não estão completamente esclarecidas.

A epidemiologia nutricional tem como objetivo estabelecer a relação entre componentes da dieta e desfechos de saúde (7), como a determinação do seu papel na ocorrência das complicações crônicas do diabetes. Além disto, a avaliação do consumo alimentar dos pacientes pode fornecer subsídios para o desenvolvimento e a implantação de estratégias dietoterápicas mais focadas e avaliar a adesão às recomendações nutricionais (8). Independente da finalidade, é necessário mensurar a ingestão dos alimentos a partir de instrumentos que combinem facilidade na aplicação ou na coleta da informação, validade e precisão (7). Os inquéritos dietéticos mais utilizados para a obtenção de dados sobre consumo alimentar em epidemiologia são inquéritos recordatórios, registros alimentares (RA) e o questionário de frequência alimentar (QFA) (7) que serão descritos com maior detalhamento a seguir.

INQUÉRITOS RECORDATÓRIOS

O inquérito recordatório consiste de uma entrevista (pessoal ou por telefone) conduzida por um entrevistador treinado onde são definidos e quantificados todos os alimentos e bebidas consumidos nas 24, 48 ou 72 horas precedentes (7). A entrevista deve ser realizada preferencialmente a partir de técnica estruturada (9, 10) para reduzir o erro na obtenção dos dados de consumo alimentar. A técnica denominada “Múltiplos Passos” tem sido descrita como uma forma de estimular o entrevistado a recordar os alimentos consumidos no dia anterior mais facilmente. Esta técnica divide-se em três fases distintas, como descritas brevemente a seguir: a) listagem rápida de todos os alimentos consumidos no dia anterior; b) descrição detalhada retomando os alimentos citados anteriormente; c) revisão da lista de alimentos junto ao entrevistado (9). A partir deste método, o Departamento de Agricultura dos Estados Unidos (USDA) incluiu mais duas etapas para a realização de um recordatório de ingestão alimentar de 24 horas: o questionamento sobre alimentos usualmente omitidos através de uma lista pré-definida (etapa 2); e o detalhamento do horário, local e ocasião em que cada alimento citado foi consumido (etapa 3). As etapas 1, 4 e 5

são semelhantes ao método dos “Múltiplos Passos” e este método recordatório com cinco etapas é chamado de *USDA Multiple Pass Method* (10).

Entre as principais vantagens na utilização dos inquéritos recordatórios estão o baixo custo, o tempo reduzido de aplicação e o fato de que o procedimento não provoca alterações nos hábitos alimentares, além de não exigir muitas habilidades do respondente. Entretanto, as principais desvantagens estão relacionadas à memória e às dificuldades na estimativa das quantidades consumidas, além de investigar somente a ingestão pontual e não necessariamente o usual ou habitual se aplicada em um único momento (7). Para reduzir as dificuldades pelo entrevistado em relação ao relato de tamanho e volume da porção, podem ser utilizados álbuns fotográficos, utensílios domésticos (colheres, pratos, copos e xícaras) e/ou exemplos de alimentos em material não perecível (biscuit, isopor, papel ou plástico) para representar as porções alimentares mais comumente consumidas e auxiliar as respostas (11).

Ainda, em epidemiologia nutricional, a aplicação do recordatório de 24 horas em um único momento é pouco utilizada para avaliar ou estimar o consumo usual de uma determinada população, bem como relacionar o hábito alimentar ao surgimento de determinadas doenças. Desta forma, recomenda-se a aplicação de mais de um recordatório ao longo de um determinado período para a estimativa de ingestão usual e não somente pontual (7).

REGISTROS ALIMENTARES

Nos registros ou diários alimentares é feita a descrição prospectiva e detalhada dos tipos e quantidades de alimentos e bebidas consumidos ao longo do dia, discriminados por horários e/ou refeição, diminuindo o viés da memória e possibilitando uma relativa precisão nas quantidades ingeridas. Geralmente é repetido por alguns dias, que podem ser consecutivos ou não, conforme o objetivo do estudo (7). A forma como são mensuradas as porções alimentares é o que diferencia os tipos de RA e atribui maior custo ao método: os alimentos e bebidas podem ser estimados com o

auxílio de medidas caseiras, fotos de porções ou modelos de alimentos ou pesados em balanças e copos medidores (11). Mais recentemente, tem sido proposta a utilização de equipamentos fotográficos, filmadoras e/ou portáteis (*Personal Digital Assistants*) para o registro dos alimentos e bebidas consumidos ao longo do dia (12, 13). Se por um lado o uso destas tecnologias pode reduzir o tempo e o trabalho de registrar os alimentos, por outro lado requer cooperação, habilidade e treinamento do investigado (14), além de elevar os custos do projeto de pesquisa pela necessidade de fornecimento dos equipamentos aos participantes.

O número de dias de RA depende da população envolvida e de sua variabilidade de ingestão de acordo com o(s) nutriente(s) avaliado(s) (7). Estudo prospectivo com a finalidade de determinar o número de dias necessários para avaliar o consumo de calorias totais, macronutrientes e alguns micronutrientes foi realizado com 29 participantes que realizaram RA ao longo de um ano, totalizando 365 dias de RA (15). Os autores observaram que o número de dias necessários para avaliar o consumo deste grupo de indivíduos variou de acordo com o nutriente a ser avaliado: entre três (para calorias totais) e 44 dias (para estimativa de vitamina A).

Um importante viés observado nos estudos que utilizam RA é o sub-registro do consumo alimentar. Este fenômeno pode apresentar-se de duas formas: como subconsumo ou sub-relato. No primeiro, o indivíduo diminui o seu consumo alimentar e realiza um registro pouco compatível com o seu peso atual e hábito alimentar. Já o sub-relato retrata o indivíduo que deixou de registrar parte do seu consumo (16). Em estudo realizado no nosso meio com 205 pacientes com diabetes tipo 2, observou-se que o sub-registro da ingestão de proteínas em RA com pesagem de alimentos foi inversamente associado com valores de hemoglobina glicada menores do que 6,9% [Razão de chances (RC) = 0,40; IC 95% 0,16-0,99; P = 0,046], após ajuste para gênero, idade, IMC, vínculo empregatício e o fato do individuo morar sozinho (17). Por outro lado, o supra-registro também é fenômeno descrito (18). Entretanto, os fatores associados ao sub- e supra-registro alimentar ainda não estão totalmente esclarecidos (19).

Apesar da necessidade de maior envolvimento e colaboração do indivíduo e possibilidade de sub-relato de ingestão, o RA é descrito como o melhor instrumento para estimativa de consumo alimentar, pois é um método que não depende da memória e os alimentos consumidos são diretamente registrados, diminuindo os erros de percepção e interpretação (20). Assim, o uso de RA com pesagem dos alimentos de três dias, dois dias de semana e um dia de final de semana, foi validado para investigação do consumo alimentar de pacientes com diabetes tipo 2 em nosso meio (17, 21) e tem sido bastante utilizado pelo nosso grupo de pesquisa em estudos transversais (22-25) e ensaios clínicos randomizados (26-29). Entretanto, o método necessita de envolvimento e dedicação do paciente para a realização dos RAs de maneira plausível. Além disso, são necessárias pelo menos três visitas para treinamento, verificação do entendimento do procedimento a partir da realização de um dia de RA e entrega do material para a finalização do método, aumentando o tempo para a coleta da informação de ingestão alimentar.

QUESTIONÁRIOS DE FREQUÊNCIA ALIMENTAR

O QFA é um instrumento no qual o paciente é apresentado a uma lista de alimentos e solicitado a relatar com que frequência cada item é usualmente consumido em um determinado período - no último mês, semestre ou ano. O estabelecimento do período deve estar relacionado ao objetivo do estudo e amplitude dos hábitos que se pretende investigar. Além disto, em países de zona temperada, como o Brasil, é interessante que sejam utilizados questionários desenvolvidos que consideram o ano precedente, pois em um ano ocorre um ciclo completo de estações, permitindo considerar a influência da variabilidade sazonal no consumo alimentar (20).

Os QFAs podem ser classificados de acordo com a informação dietética que eles obtêm em qualitativos, quantitativos ou semi-quantitativos. A partir de um QFA qualitativo são obtidas informações sobre os alimentos consumidos sem especificação das quantidades consumidas, enquanto que em um QFA quantitativo é solicitado ao paciente que ele descreva a porção usual de

consumo de cada item da lista. Esta descrição pode ser a partir de uma questão aberta (em que o paciente apresenta a sua porção consumida) ou de uma porção média apresentada e o paciente estima se a sua porção consumida é menor, semelhante ou maior do que a porção média apresentada. Já em um QFA semi-quantitativo, uma porção média de referência para cada item alimentar é apresentada e o consumo deve ser estimado como um múltiplo dessa porção (7).

Assim como os inquéritos recordatórios, o QFA também depende da memória do entrevistado (30). Além disso, o supra-relato da ingestão pelo QFA também deve ser considerado. Estudos de validação conduzidos na população brasileira demonstraram que o QFA tende a superestimar a ingestão de calorias totais e nutrientes quando comparado com inquéritos recordatórios (31, 32) ou RA (33). Porém, o princípio do QFA é estimar a dieta habitual praticada ao longo de semanas, meses ou anos, pois esse hábito é um fator de exposição mais importante do que a estimativa da dieta pontual. Essa premissa justifica a utilização de informações menos precisas, mas relacionadas ao consumo habitual, em detrimento da precisão de dados relativos à ingestão pontual de alimentos obtida a partir de RA (7).

A lista de alimentos de um QFA deve refletir o hábito regional (34) e características da população como idade, etnia/origem, gênero, escolaridade e estado de saúde podem afetar o seu desempenho (35). Portanto, a avaliação de sua validade e reproduzibilidade precisa ser testada na população de interesse antes de relacionarmos as informações da dieta obtidas no QFA com desfechos de saúde ou doença da população investigada (7).

Nos estudos de validação de QFA, as estimativas de consumo do instrumento que está sendo testado são comparadas às médias de informações do consumo obtidas a partir da aplicação de vários RA e/ou inquéritos recordatório realizados ou aplicados no mesmo período de abrangência da informação do QFA ou pela comparação com a informação obtida por biomarcadores de ingestão. O instrumento de consumo alimentar (RA ou recordatório) escolhido para validar um QFA corresponde ao um método de referência relativa. Nesta escolha, o RA com pesagem de alimentos

tem sido considerado como o melhor método para validação de QFA, pois apresenta erros de coleta da informação da dieta independentes (20).

Neste tipo de estudo de validação, um aspecto importante na estimativa da ingestão habitual que deve ser considerado é a variabilidade da dieta, uma vez que os indivíduos não consomem todos os dias os mesmos alimentos, e consequentemente, as mesmas quantidades de nutrientes. São vários os componentes de variabilidade da dieta, e maior destaque têm sido dado às variâncias intra-individual, inter-individual e aquelas geradas pela quantidade de calorias diárias ingeridas. O componente intra-individual representa a variação no consumo de um mesmo indivíduo ao longo dos dias enquanto que o componente inter-individual representa a variação no consumo de um indivíduo para o outro (34). Neste sentido, deve-se considerar que os estudos de validação de QFA comumente utilizam três ou mais medidas do método de referência relativa e o efeito da variância intra-pessoal pode subestimar o desempenho do QFA. Uma alternativa para os pesquisadores é aplicar técnicas estatísticas descritas como deatenuação dos coeficientes de correlação que buscam remover ou controlar esta variabilidade intra-pessoal (34). Ainda, a influência na estimativa de ingestão de nutrientes devido à quantidade de alimentos ingeridos e não somente pela qualidade da dieta também deve ser considerada e a aplicação do método estatístico de ajuste para o total de calorias tem sido fortemente recomendada há algumas décadas. Este ajuste para o total de calorias é feito a partir da determinação de um valor residual, calculado por modelo de regressão considerando a ingestão calórica como variável independente e que deve considerado na estimativa de ingestão do nutriente avaliado do grupo de indivíduos investigado (34).

Outra maneira de avaliar a confiabilidade das informações obtidas a partir de inquéritos dietéticos é compará-las a medidas objetivas, como o uso de marcadores biológicos da ingestão de nutrientes que, na sua maioria, fornecem uma medida mais acurada e fatores de confusão independentes quando comparados aos inquéritos dietéticos (30). Resumidamente, os biomarcadores podem ser classificados em três tipos (36): a) de recuperação: são aqueles que apresentam um equilíbrio entre a ingestão e a excreção de determinado nutriente como água

duplamente marcada, excreções urinárias de nitrogênio, sódio e potássio; b) preditivos: são aqueles que apresentam uma relação dose-resposta com a ingestão de determinado nutriente como, por exemplo, as excreções urinárias de frutose e sacarose; c) de concentração ou substituição: não podem ser traduzidos para níveis absolutos de ingestão por apresentarem valores menores de correlação com a estimativa de ingestão, como vitaminas séricas, lipídeos sanguíneos, eletrólitos urinários.

De uma maneira geral, existem biomarcadores para a maioria dos nutrientes e seus metabólitos, medidos em diferentes amostras biológicas (37). A excreção urinária de nitrogênio tem sido bastante utilizada como biomarcador de ingestão de proteínas (38). Em nosso grupo de pesquisa, a plausibilidade da realização de RA com pesagem de alimentos é verificada a partir da comparação da informação registrada com a estimativa de ingestão de proteínas obtida pela medida de nitrogênio urinário em coleta de urina de 24 horas realizada concomitante ao terceiro dia de RA (17) e tem sido largamente utilizado em estudos transversais (22-25) e ensaios clínicos com manipulação de quantidade e tipo de proteínas da dieta (26-29).

Além da simples comparação entre as estimativas de ingestão obtidas pelos inquéritos dietéticos e biomarcador, em 1997 foi proposto o cálculo de correlação entre a ingestão estimada pelo instrumento de avaliação de consumo alimentar com a ingestão real (39). Este coeficiente de validade (ρ) é determinado a partir do método das tríades que considera os coeficientes de correlação entre as três variáveis (QFA, método de referência e biomarcador) e seus erros independentes de estimativa, pressupondo linearidade entre as três variáveis (40).

Além da validade da informação, a reprodutibilidade ou confiabilidade da informação obtida a partir da aplicação do QFA também precisa ser testada. Esta análise da reprodutibilidade consiste na coleta de informação dietética do mesmo indivíduo com a aplicação do QFA em momentos distintos (7). Neste sentido, sugere-se que estudos de reprodutibilidade em curto prazo sejam realizados com intervalo de tempo de 15 a 45 dias. Já no caso de estudos de reprodutibilidade de

longo prazo, o intervalo de tempo de 12 meses tem sido o mais adotado (35), principalmente em países de clima temperado.

QFAs validados na população brasileira

Até a presente data, 23 estudos de validação de QFA realizados para a população brasileira foram encontrados na literatura (31-33, 41-60), entretanto, nenhum desses QFAs foi elaborado para a população com diabetes - um grupo de indivíduos em que claramente preconizam-se modificações alimentares para o autocuidado desde o diagnóstico (3). Também, cabe ressaltar que esses questionários foram desenvolvidos em regiões distintas do país que possuem diferenças relevantes no padrão de despesa com grupos alimentares entre as famílias (61) e esta influência regional precisa ser considerada na lista de alimentos do QFA a ser utilizado (34).

Dentre os QFAs brasileiros, três deles foram realizados no Rio Grande do Sul (31, 32, 50) e estes foram adaptados a partir de um QFA construído com informações alimentares de recordatórios de 24 horas aplicados em uma população do Rio de Janeiro (41) para avaliar o consumo alimentar de gestantes (50), adultos (31, 32), adolescentes e idosos (32) da região metropolitana de Porto Alegre.

QFAs validados para pacientes com Diabetes no mundo

Foram encontrados quatro QFAs que foram validados em pacientes com diabetes em populações de etnias e culturas distintas (62-65). As características da população, do instrumento desenvolvido, do padrão de referência utilizado e os principais resultados obtidos e apresentados nos estudos de validação estão descritas na **Tabela 1**. Destaca-se que os padrões de referência utilizados foram RA com pesagem de alimentos (62) ou sem pesagem dos alimentos (63, 65) e recordatório alimentar de 48 horas (64). Nenhum desses QFAs avaliou o desempenho da estimativa de índice glicêmico e/ou a carga glicêmica da dieta dos participantes.

A validade da informação foi avaliada em todos os estudos através da comparação com padrões de referência relativa (62-65) e a reproduzibilidade de dois QFAs foi testada (62, 63). Os coeficientes de correlação obtidos para a ingestão de calorias e macronutrientes variaram de 0,16 (63) a 0,74 (65). É importante ressaltar que QFAs com boa validade são aqueles cuja estimativa do consumo alimentar é equiparável àquela obtida com o padrão de referência e esperam-se valores de coeficientes de correlação moderados - entre 0,40 e 0,70 (34).

Tabela 1. Questionários de Frequência Alimentar validados para pacientes com diabetes no mundo

Referência	População	QFA construído	Padrão de referência	Principais resultados apresentados ^a
Riley et al., 1995 (62)	n = 84 DM tipo 1 53,6% de homens 17-73 anos Origem: Austrália	Semiquantitativo, 153 itens Desenvolvido a partir de outro instrumento para população australiana (Baghurst et al., 1984)	RA de 2 dias com pesagem dos alimentos	Calorias: $r=0,46$ Proteínas: $r=0,38$ Lipídeos: $r=0,50$ Carboidratos: $r=0,45$ *Valores ajustados para calorias e correlações deatenuadas
Yamaoka et al., 2000 (63) <i>[abstract]</i>	n = 71 DM tipo 2 100% homens Idade: ND Origem: Japão	Semiquantitativo, 65 itens Auto-aplicado Lista de alimentos construída	RA de 7 dias	Calorias: $r=0,64$ Proteínas: $r=0,16$ Lipídeos: ND Carboidratos: ND *Valores ajustados para calorias
Coulibaly et al., 2007 (64)	n = 57 DM tipo 2 83,3 % homens 25-75 anos Origem: República de Mali	Quantitativo, 53 itens Lista de alimentos construída a partir de 7 diários alimentares para identificar fontes proteicas de origem animal e vegetal	Recordatório de 48h	Calorias: ND Proteínas: $r=0,63$ Lipídeos: ND Carboidratos: ND * Valores brutos
Hong et al., 2010 (65)	n = 85 DM tipo 2 55,3% homens 33-70 anos Origem: Coréia	Semiquantitativo, 85 itens Desenvolvido a partir de outro instrumento (Kim & Yang, 1998) considerando dados nacionais (NHANES, 2005)	RA de 3 dias (2 dias de semana e 1 dia de final de semana)	Calorias: $r=0,74$ Proteínas: $r=0,37$ Lipídeos: $r=0,44$ Carboidratos: $r=0,59$ * Valores brutos

DM = Diabetes Melito; RA = registros alimentar; ND = não descrito; ^aCoeficientes de correlação (r) encontrados entre QFA e padrão de referência (validação).

REFERÊNCIAS

1. International Diabetes Federation. The Global Burden. 2011. Disponível em: <http://www.idf.org/diabetesatlas/5e/the-global-burden>. Acessado em: Abril de 2012
2. Emerging Risk Factors Collaboration, Seshasai SR, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, Whincup PH, Mukamal KJ, Gillum RF, Holme I, Njølstad I, Fletcher A, Nilsson P, Lewington S, Collins R, Gudnason V, Thompson SG, Sattar N, Selvin E, Hu FB, Danesh J. Diabetes mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med.* 2011; 364(9):829-41.
3. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care.* 2012; 35 Suppl 1:S11-63.
4. Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, Lafont S, Bergeonneau C, Kassaï B, Erpeldinger S, Wright JM, Gueyffier F, Cornu C. Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials. *BMJ.* 2011; 343:d4169.
5. Gross JL, Kramer CK, Leitão CB, Hawkins N, Viana LV, Schaan BD, Pinto LC, Rodrigues TC, Azevedo MJ - Diabetes and Endocrinology Meta-analysis Group (DEMA). Effect of antihyperglycemic agents added to metformin and a sulfonylurea on glycemic control and weight gain in type 2 diabetes: a network meta-analysis. *Ann Intern Med.* 2011; 154:672-9.
6. Mendes ABV, Fittipaldi JAS, Neves RCS, Chacra AR, Moreira-Jr ED. Prevalence and correlates of inadequate glycemic control: results from nationwide survey in 6,671 adults with diabetes in Brazil. *Acta Diabetol.* 2010; 47: 137-45.
7. Kac G, Sichieri R, Gigante DP. Epidemiologia Nutricional. Rio de Janeiro: Fiocruz e Atheneu; 2007.
8. Fisberg RM, Marchiori DML, Colucci ACA. Assessment of food consumption and nutrient intake in clinical practice. *Arq Bras Endocrinol Metab.* 2009; 53:617-24.

9. Jonnalagadda SS, Mitchell DC, Smiciklas-Wright H, et al. Accuracy of energy intake data estimated by a multiple-pass, 24-hour dietary recall technique. *J Am Diet Assoc.* 2000; 100(3):303-8.
10. Conway JM, Ingwersen LA, Vinyard BT, et al. Effectiveness of the US Department of Agriculture 5-step multiple-pass method in assessing food intake in obese and nonobese women. *Am J Clin Nutr* 2003; 77:1171–8.
11. Fisberg RM, Slater B, Marchioni DML, Martini LA. Inquéritos Alimentares: métodos e bases científicos. São Paulo: Manole; 2005.
12. Zhu F, Mariappan A, Boushey CJ, Kerr D, Lutes KD, Ebert DS, Delp EJ. Technology-Assisted Dietary Assessment. *Proc SPIE.* 2008; 20:6811:14.
13. Shriver BJ, Roman-Shriver CR, Long JD. Technology-based methods of dietary assessment: recent developments and considerations for clinical practice. *Curr Opin Clin Nutr Metab Care.* 2010; 13(5):548-51.
14. Boushey CJ, Kerr DA, Wright J, et al. Use of technology in children's dietary assessment. *Eur J Clin Nutr.* 2009; 63(Suppl 1): S50–S57.
15. Basiotis PP, Welsh SO, Cronin FK, et al. Number of Days of Food Intake Records Required to Estimate Individual and Group Nutrient Intakes with Defined Confidence. *J Nutr.* 1987; 117:1638-41.
16. Goris AH, Westerterp-Plantenga MS, Westerterp KR. Underrating and under recording of habitual food intake in obese men: selective underreporting of fat intake. *Am J Clin Nutr.* 2000; 71 (1): 130-4.
17. Vaz JS, Bittencourt M, Almeida JC, Gross JL, Azevedo MJ, Zelmanovitz T. Protein Intake Estimated by Weighed Diet Records in Type 2 Diabetic Patients: Misreporting and Intra-Individual Variability Using 24-Hour Nitrogen Output as Criterion Standart. *J Am Diet Assoc.* 2008; 108(5): 867-72.

18. Johansson L, Solvoll K, Bjorneboe GE, Grevon CA. Under- and overreporting of energy intake related to weight status and lifestyle in a nationwide sample. *Am J Clin Nutr.* 1998; 68(2): 266-74.
19. Scagliusi FB, Ferriolli E, Pfrimer K, Laureano C, Cunha CS, Gualano B, et al. Underreporting of energy intake in Brazilian women varies according to dietary assessment: a cross-sectional study using doubly labeled water. *J Am Diet Assoc.* 2008; 108:2031-40.
20. Slater B, Philippi ST, Marchioni DML, Fisberg RM. Validação de Questionários de Freqüência Alimentar - QFA: considerações metodológicas. *Rev Bras Epidemiol.* 2003; 6(3):200-8.
21. Moulin CC, Tiskievicz F, Zelmanovitz T, de Oliveira J, Azevedo MJ, Gross JL. Use of weighed diet records in the evaluation of diets with different protein contents in patients with type 2 diabetes. *Am J Clin Nutr.* 1998; 67(5):853-7.
22. Almeida JC, Zelmanovitz T, Vaz JS, Steemburgo T, Perassolo MS, Gross JL, Azevedo MJ. Sources of protein and polyunsaturated fatty acids of the diet and microalbuminuria in type 2 diabetes mellitus. *J Am Coll Nutr.* 2008; 27(5):528-37.
23. Steemburgo T, Dall'Alba V, Almeida JC, Zelmanovitz T, Gross JL, de Azevedo MJ. Intake of soluble fibers has a protective role for the presence of metabolic syndrome in patients with type 2 diabetes. *Eur J Clin Nutr.* 2009; 63(1):127-33.
24. Silva FM, Steemburgo T, de Mello VD, Tonding SF, Gross JL, Azevedo MJ. High dietary glycemic index and low fiber content are associated with metabolic syndrome in patients with type 2 diabetes. *J Am Coll Nutr.* 2011; 30(2):141-8.
25. de Paula TP, Steemburgo T, de Almeida JC, Dall'alba V, Gross JL, de Azevedo MJ. The role of Dietary Approaches to Stop Hypertension (DASH) diet food groups in blood pressure in type 2 diabetes. *Br J Nutr.* 2011; 6:1-8.
26. Pecis M, de Azevedo MJ, Gross JL. Chicken and fish diet reduces glomerular hyperfiltration in IDDM patients. *Diabetes Care.* 1994; 17(7):665-72.

27. Gross JL, Zelmanovitz T, Moulin CC, De Mello V, Perassolo M, Leitão C, Hoefel A, Paggi A, Azevedo MJ. Effect of a chicken-based diet on renal function and lipid profile in patients with type 2 diabetes: a randomized crossover trial. *Diabetes Care*. 2002; 25(4):645-51.
28. de Mello VD, Zelmanovitz T, Azevedo MJ, de Paula TP, Gross JL. Long-term effect of a chicken-based diet versus enalapril on albuminuria in type 2 diabetic patients with microalbuminuria. *J Ren Nutr*. 2008; 18(5):440-7.
29. de Mello VD, Zelmanovitz T, Perassolo MS, Azevedo MJ, Gross JL. Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria. *Am J Clin Nutr*. 2006; 83(5):1032-8.
30. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilization of food-frequency questionnaires – a review. *Public Health Nutr*. 2002; 5(4):567-87.
31. Zanolla AF, Olinto MTA, Henn RL, Wahrlich V, Anjos LA. Avaliação de reprodutibilidade e validade de um questionário de freqüência alimentar em adultos residentes em Porto Alegre, Rio Grande do Sul, Brasil. *Cad Saúde Pública*. 2009; 25:840-8.
32. Henn RL, Fuchs SC, Moreira LB, Fuchs FD. Development and validation of a food frequency questionnaire (FFQ-Porto Alegre) for adolescent, adult and elderly populations from Southern Brazil. *Cad. Saúde Pública*. 2010; 26(11):2068-79.
33. Pereira GA, Genaro PS, Santos LC, Sarkis KS, Pinheiro MM, Szjenfeld VL, Schuch NJ, Martini LA. Validation of a food frequency questionnaire for women with osteoporosis. *J Nutr Health Aging*. 2009; 13(5):403-7.
34. Willett WC. *Nutritional epidemiology*. Oxford: Oxford University Press; 1998.
35. Burley V & Cade J. Consensus document on the development, validation, and utilization of food frequency questionnaires. In: The Fourth International Conference on Dietary Assessment Methods. 2000, p. 17-20.
36. Jenab M, Slimani N, Bictash M, Ferrari P, Bingham S. Biomarkers in nutritional epidemiology: applications, needs and new horizons. *Human Genet*. 2009; 125:507-25.

37. Potischman N. Biologic and methodologic issues for nutritional biomarkers. *J Nutr.* 2003; 133 Suppl 3:875S-80S.
38. Bingham SA. Urine nitrogen as a biomarker for the validation of dietary protein intake. *J Nutr.* 2003; 133 Suppl 3:921S-4S.
39. Kaaks RJ. Biochemical markers as additional measurements in studies of the accuracy of dietary questionnaire measurements: conceptual issues. *Am J Clin Nutr.* 1997; 65(4 Suppl):1232S-9S.
40. Yokota RTC, Miyazaki ES, Ito MK. Applying the triads method in the validation of dietary intake using biomarkers. *Cad. Saúde Pública.* 2010; 26(11):2027-37.
41. Sichieri R, Everhart JE. Validity of a Brazilian food frequency questionnaire against dietary recalls and estimated energy intake. *Nutr Res.* 1998; 18:1649-59.
42. Cardoso MA, Kida AA, Tomita LY, Stocco PR. Reproducibility and validity of a food frequency questionnaire among women of Japanese ancestry living in Brazil. *Nutrition Research.* 2001; 21:725-33.
43. Salvo VL, Gimeno SG. Reproducibility and validity of a food frequency questionnaire. *Rev Saúde Pública.* 2002; 36(4):505-12.
44. Fornés NS, Stringhini MLF, Elias BM. Reproducibility and validity of a food-frequency questionnaire among low-income Brazilian workers. *Public Health Nutr.* 2003; 6:821-7.
45. Slater B, Philippi ST, Fisberg RM, Latorre MRDO. Validation of a semi-quantitative adolescent food frequency questionnaire applied at a public school in São Paulo, Brazil. *Eur J Clin Nutr.* 2003; 57:629-35.
46. Ribeiro A, Sávio K, Rodrigues M, Costa T, Schivitz B. Validação de um questionário de freqüência de consumo alimentar para população adulta. *Rev Nutr.* 2006; 19:553-62.
47. Matarazzo HCZ, Marchioni DML, Figueiredo RAO, Slater B, Neto JE, Filho VW. Reprodutibilidade e validade do questionário de freqüência de consumo alimentar utilizado

- em estudo caso-controle de câncer oral. Revista Brasileira de Epidemiologia. 2006; 9(3):316-24.
48. Lima FEL, Slater B, Latorre MRDO, Fisberg RM. Validade de um questionário quantitativo de freqüência alimentar desenvolvido para população feminina no nordeste do Brasil. Revista Brasileira de Epidemiologia. 2007; 10(4):483-90.
49. Marchioni DML, Voci SM, Lima FEL, Fisberg RM, Slater B. Reproducibility of a food frequency questionnaire for adolescents. Cad Saúde Pública. 2007; 23(9):2187-96.
50. Teixeira MH, Veiga GV, Sichieri R. Avaliação de um questionário simplificado de freqüência de consumo alimentar como preditor de hipercolesterolemia em adolescentes. Arquivos Brasileiros de Cardiologia. 2007; 88:66-71.
51. Giacomello A, Schmidt MI, Nunes MAA, Duncan BB, Soares RM, Manzolli P, Camey S. Validação relativa de Questionário de Freqüência Alimentar em gestantes usuárias de serviços do Sistema Único de Saúde em dois municípios no Rio Grande do Sul, Brasil. Revista Brasileira de Saúde Materno Infantil. 2008; 8(4):445-54.
52. Voci SM, Enes CC, Slater B. Validação do Questionário de Freqüência Alimentar para Adolescentes (QFAA) por grupos de alimentos em uma população de escolares. Revista Brasileira Epidemiologia. 2008; 11(4):561-72.
53. Fumagalli F, Monteiro JP, Sartorelli DS, Vieira MNCM, Bianchi MLP. Validation of a food frequency questionnaire for assessing dietary nutrients in Brazilian children 5 to 10 years of age. Nutrition. 2008; 24(5):427-32.
54. Ishihara J, Iwasaki M, Kunieda CM, Hamada GS, Tsugane S. Food frequency questionnaire questionnaire is a valid tool in the nutritional assessment of Brazilian women of diverse ethnicity. Asia Pac J Clin Nutr. 2009; 18(1):76-80.
55. Crispim SP, Ribeiro RCL, Panato E, Silva MMS, Rosado LEFP, Rosado GP. Validação relativa de um questionário de freqüência alimentar para utilização em adultos. Revista de Nutrição. 2009; 22(1):81-95.

56. Ferreira-Sae MC, Gallani MC, Nadruz W, Rodrigues RC, Franchini KG, Cabral PC, Sales ML. Reliability and validity of a semi-quantitative FFQ for sodium intake in low-income and low-literacy Brazilian hypertensive subjects. *Public Health Nutrition*. 2009; 12(11):2168-73.
57. Cardoso MA, Tomita LY, Laguna EC. Assessing the validity of a food frequency questionnaire among low-income women in São Paulo, Southeastern Brazil. *Cad Saude Publica*. 2010; 26(11):2059-67.
58. Araujo MC, Yokoo EM, Pereira RA. Validation and calibration of a semiquantitative food frequency questionnaire designed for adolescents. *Journal American Diet Association*. 2010; 110(8):1170-77.
59. Slater B, Enes CC, López RVM, Damasceno NRT, Voci SM. Validation of a food frequency questionnaire to assess the consumption of carotenoids, fruits and vegetables among adolescents: the method of triads. *Cadernos Saúde Pública*. 2010; 26(11):2090-100.
60. Scagliusi FB, Garcia MT, Indiani AL, Cardoso MA. Relative validity of a food-frequency questionnaire developed to assess food intake of schoolchildren living in the Brazilian Western Amazon. *Cad Saude Publica*. 2011; 27(11):2197-206.
61. Brasil. Ministério do Planejamento, Orçamento e Gestão. Instituto Brasileiro de Geografia e Estatística – IBGE. Diretoria de Pesquisas. Coordenação de Trabalho e Rendimento. Pesquisa de Orçamentos Familiares 2008-2009. Rio de Janeiro, 2010.
62. Riley MD, Blizzard L. Comparative validity of a food frequency questionnaire for adults with IDDM. *Diabetes Care*. 1995; 18(9):1249-54.
63. Yamaoka K, Tango T, Watanabe M, Yokotsuka M. Validity and reproducibility of a semi-quantitative food frequency questionnaire for nutritional education of patients of diabetes mellitus (FFQW65). *Nihon Koshu Eisei Zasshi*. 2000; 47(3):230-44.

64. Coulibaly A, Turgeon O'Brien H, Galibois I. Validation of an FFQ to assess dietary protein intake in type 2 diabetic subjects attending primary health-care services in Mali. *Public Health Nutr.* 2008; 12(5):644-50.
65. Hong S et al. Development and validation of a semi-quantitative food frequency questionnaire to assess diets of Korean type 2 diabetic patients. *Korean Diabetes J.* 2010; 34(1):32-9.

Capítulo II

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**Development of a quantitative food frequency questionnaire for Brazilian patients with type 2
diabetes**

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ABSTRACT

Objective: To elaborate a quantitative food frequency questionnaire (FFQ) for patients with type 2 diabetes.

Design: Dietary data using 3-day weighed diet records (WDR) from 188 outpatients with type 2 diabetes were used to construct the list of usually consumed foods. Foods were initially clustered into eight groups: “cereals, tubers, roots, and derivatives”; “vegetables”; “fruits”; “beans”; “meat and eggs”; “milk and dairy products”; “oils and fats”, and “sugars and sweets”. The frequency of food intake and the relative contribution of each food item to the total energy and nutrient intakes were calculated. A food was included if it contributed at least 80% to total energy or nutrient content in its respective food group. Portion sizes were determined according to the 25th, 50th, 75th, and 95th percentiles of intake for each food item.

Setting: GNE - Group of Nutrition in Endocrinology - cohort - Southern Brazil.

Subjects: Outpatients with type 2 diabetes.

Results: A total of 62 food items were selected based on the 3-day WDR and another 27 foods or their preparation options and nine beverages were included after the expert examination, and accounted for 95% of total energy and nutrient intakes. Also, a portfolio with food photos of each included food item and its portion sizes was created to support the patients in identifying the consumed portion.

Conclusions: We developed a practical quantitative FFQ and portfolio with photos of 98 food items covering the past 12 months of the most commonly consumed food items. This dietary method will be valuable to assess the usual diet pattern of patients with type 2 diabetes in Southern Brazil.

Keywords: food frequency questionnaire; type 2 diabetes mellitus; food record; epidemiologic methods

INTRODUCTION

The field of nutritional epidemiology has been developed because of an interest in the concept that aspects of diet may influence the occurrence of human disease ⁽¹⁾. In the case of patients with diabetes, dietary advices and assessment of compliance with these recommendations are important for achieving metabolic goals, especially the glycemic control ⁽²⁾. However, the relationship between dietary components and micro- and macrovascular complications has not been completely elucidated.

There are several methods for the assessment of food and nutrient consumption as well as energy intake, including 24-hour recall, food records, food frequency questionnaire (FFQ), and biomarkers ⁽³⁾. To investigate the association between dietary components and development of chronic diabetic complications, the dietary evaluation should include a long period, months or years, as is the case of FFQ. To date, four FFQs involving patients with diabetes have been validated and published in specific populations: Australian ⁽⁴⁾, Japanese ⁽⁵⁾, Malian ⁽⁶⁾, and Korean ⁽⁷⁾; however, none was elaborated for the Brazilian population. In fact, the FFQ should represent the regional habits and the accuracy of such data needs to take this into account ⁽⁸⁾.

In elaborating FFQ, careful attention must be given to the choice of foods, the clearness of the questions, and the format of the frequency response section. In addition, the choice of foods, especially if FFQ is constructed to also include quantitative or semi-quantitative dietary evaluation, should be based in an accurate dietary tool ⁽⁹⁾. In this way, the present manuscript aims to create a FFQ and a portfolio with food photos to assess the usual intake pattern of Brazilian patients with diabetes to be used in future studies.

EXPERIMENTAL METHODS

Study population

Patients were identified from Group of Nutrition in Endocrinology (GNE) cohort of outpatients with type 2 diabetes in southern Brazil⁽¹⁰⁾. That study was planned to evaluate possible associations of dietary factors with diabetic chronic complications. From a previous constructed database of 225 patients with type 2 diabetes⁽¹¹⁾ data from consecutive registered patients who reported a plausible ratio of protein intake estimated from the 3-day weighed diet records (WDR) to protein intake from urinary nitrogen⁽¹²⁾ were selected. Also the same gender proportion (1:1 males and females) and equal seasonal distribution (1:1:1:1 spring, summer, autumn, and winter) were considered as inclusion criteria. Therefore, records from 188 patients with type 2 diabetes were analyzed.

The new instrument: food frequency questionnaire

The most frequently consumed foods and their respective portion sizes were extracted from 3-day WDR (two nonconsecutive weekdays and one day-off) to create the FFQ and the food portfolio photo. All registered foods were listed and clustered in eight groups as proposed by the Food Guide for the Brazilian Population⁽¹³⁾: “cereals, tubers, roots, and derivatives”; “vegetables”; “fruits”; “beans”; “meat and eggs”; “milk and dairy products”; “oils and fats” and “sugars and sweets”. The caloric and non caloric beverages were added into a new group, according to the WDR description (“beverages group”).

A food item was classified according to its relative contribution, at least 80%, for daily energy or intake of selected relevant nutrient (K nutrient) in its respective food group. The relative contribution was calculated by the equation proposed by Block et al.⁽¹⁴⁾ [$\% K \text{ nutrient contribution by food} = (\text{amount of the } K \text{ nutrient provided by food} \times 100) / \text{amount of the } K \text{ nutrient provided by all foods}$]. The most relevant nutrients in each food group were selected considering their influence on glucose metabolism⁽¹⁵⁻¹⁸⁾ and/or diabetic complications^(15,19-22) and are described in **Table 1**. Information about nutritional composition of each food and regional preparation ingredients was based on *NutriBase Clinical®* software⁽²³⁾.

The servings size of each food item was classified according to its respective weight distribution as registered in the WDR: small = 25th percentile, medium = 50th percentile, large = 75th percentile, and extra large = 95th percentile ⁽²⁴⁾. **Figure 1** shows a food example of portions as illustrated in the food portfolio photo. The amount in grams or milliliters of each portion was transformed into household measures using the *Table for Assessment of Food Intake in Household Measures* ⁽²⁵⁾. The FFQ also included open questions about the frequency of food consumption and an option to include new foods according to personal eating habits. The frequency was described as the number of times the food was consumed and also if the intake occurred daily, weekly, monthly, or yearly.

In order to obtain an expert examination, the constructed FFQ was submitted to health researchers used to dealing with diabetes care: endocrinologists, nutritionists, and researchers from GNE ⁽¹⁰⁾. After the experts' meeting, changes were made in the food list and definition of portion sizes. Also, regional dishes and seasonal foods were included according to suggestions.

Portfolio with food photos

The construction of the portfolio with food photos was based on the methodology suggested by Monteiro et al. ⁽²⁶⁾. Digital photographs were taken of each portion of food from the FFQ and organized in the same order of citation, considering the four portion sizes and food groups (**Figure 1**). Also, a numerical legend was created to explain details about the each portion (amount in grams or milliliters). The food portions were determined with an analytical scale (Marte ®, from 0.01 to 2000 g) and measuring cup (50-250 mL; Marinex, Brazil).

RESULTS

We evaluated the 3-day WDR of 188 outpatients with type 2 diabetes consecutively seen by nutrition researchers (GNE) in the Endocrinology Division of Hospital de Clínicas de Porto Alegre.

The WDR were performed during all seasons: 25% (n = 141) in winter, 25% (n = 141) in spring, 25% (n = 141) in summer, and 25% (n = 141) in autumn. The main features of patients were: 61.1 ± 10.1 years of age, males 50.0%, 12 years (6-18 years) of DM duration, BMI of $28.8 \pm 4.3 \text{ kg/m}^2$; HbA1c of $7.5 \pm 1.4\%$, 42.5% from lower middle class, and 84.4% self-identified as whites.

Initially, a list of 177 different food items was compiled based on data from the WDR and the number of food items in each food cluster were as follows: “cereals, tubers, roots, and derivatives” - 39 food items; “vegetables” - 34 food items; “fruits”- 22 food items; “beans” - 5 food items; “meat and eggs” - 27 food items; “milk and dairy products” - 14 food items; “oils and fats” - 7 food items; “sugars and sweets”- 16 food items; “beverages” - 13 food items. Subsequently, only 62 food types were included in the FFQ, considering the 80% cutoff contribution in its respective food group. The reported frequency of each included food item with respective relevant nutrient is shown in **Table 2**. The most frequently consumed foods by patients with diabetes included white rice (94.1 %), papaya (87.2 %), beans (78.2 %), French or Vienna bread (75.5 %), banana (71.8 %), and tomato (71.3 %). Furthermore, another four food items (lettuce, beef, chicken, and margarine) were reported by more than 50% of this patient sample. After the expert examination, 21 regional foods (fruits, vegetables, sweets, and fats), six different types of food preparations, and nine beverages were included in the food list. The final version of the FFQ consisted of 98 food items and beverages divided into nine groups: eight food groups and one of beverages. All included food items account for 95% of the total energy and nutrient intake as follows: total energy (94.2%), protein (96.8%), carbohydrate (92.8%), fat (94.6%), fiber (90.3%), iron (93.4%), calcium (95.3%), and potassium (92.2%). The portions of each food in grams or milliliters and its respective number of portions in household measures are shown in **Table 3**.

The FFQ also included open questions about frequency of food consumption and eight queries about food preferences and usual dietary practices: number of meals per day, type of sweetener added in beverages, type and amount of fat used in food preparation, if intake of visible

fat from meats, the habit of salt added in prepared foods and salads, and other foods not listed but consumed on a regular basis.

DISCUSSION

Patients with diabetes are encouraged to comply with specific dietary recommendations to achieve optimal glucose, lipid, and blood pressure control as well as a healthy body weight ⁽²⁾. These aspects can modify the food intake of patients with DM as compared to the general population. We constructed a quantitative FFQ and a portfolio with photos of 98 food items distributed into nine food groups and based on WDR. This is the first FFQ for Brazilian diabetes patients.

The development of a FFQ should consider some important aspects such as the elaboration of the food list, definition of portion intake ⁽⁸⁾, and how representative of the dietary habits of a population-based sample is the food list ⁽¹⁾. Our FFQ took into account the foods most commonly consumed by patients with type 2 diabetes and, as recommended, represents the regional dietary habits ⁽¹⁾ in Southern Brazil. In addition, the reliability of food items included in our FFQ was assured by using as reference the 3-day WDR, a dietary instrument previously standardized, validated ^(27,12), and largely used in diabetic patients by our research group ^(11,28-30). It is also important to keep in mind that these WDR were performed throughout the year because it is known that portion sizes and food types can vary according seasonality ⁽³¹⁾ and the gender distribution was equal, since gender also influences food intake ⁽³¹⁾.

The final food list was elaborated considering the contribution criteria of each relevant nutrient to minimize the omission of usually consumed food ⁽¹⁴⁾. It should be noted that nutrients known to influence glucose, lipid, or blood pressure control, or that have been associated with chronic diabetic complications were considered to choose the relevant nutrients for the food list. The number of food items in the final version of the FFQ is appropriate according to suggestions

found in the literature⁽³²⁾ and similar to other FFQs for diabetes around the world⁽⁵⁻⁷⁾. Small food lists (less than 50 items) may underestimate food intake, and very large lists (more than 100 items) may tire respondents and overestimate food intake⁽³²⁾.

The FFQ in the present study also includes a quantitative evaluation of food intake. The size of portions (quartiles of intake) was based on the weight of consumed foods assessed by 3-day WDR. These portions, specific for each food item, were shown as photos and as household measures in the food portfolio and can be easily used for respondents to select their own portion size⁽⁸⁾. Finally, the FFQ structure including open questions provides greater freedom to choose the actual frequency of food intake and reduces the error of consumption categories by the patients⁽³²⁾. This relatively long-term evaluation of food intake can be particularly relevant for prospective studies that evaluate associations of diet with chronic diabetic complications. However, this dietary instrument should be validated in other samples of patients.

In conclusion, we developed a practical quantitative FFQ and a portfolio with 98 food items covering the past 12 months and representing the usual food intake of patients with type 2 diabetes in Southern Brazil.

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contributed to the initial idea and study design. M.J.A. contributed the interpretation of results and final version of the manuscript. J.C.A. contributed to the study design and each step of the FFQ elaboration as well as proof-reading the manuscript. All authors contributed to revising the manuscript and approved the final version.

REFERENCES

1. Willett WC. Nutritional epidemiology. Oxford: Oxford University Press; 1998.
2. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2012; 35 Suppl 1:S11-63.
3. Pereira RA, Sichieri R. Métodos de avaliação do consumo alimentar. In: Kac G, Sichieri R, Gigante DP. Epidemiologia Nutricional. Rio de Janeiro: Fiocruz e Atheneu; 2007. p. 181-200.
4. Riley MD, Blizzard L. Comparative validity of a food frequency questionnaire for adults with IDDM. *Diabetes Care*. 1995; 18(9):1249-54.
5. Yamaoka K, Tango T, Watanabe M, Yokotsuka M. Validity and reproducibility of a semi-quantitative food frequency questionnaire for nutritional education of patients of diabetes mellitus (FFQW65). *Nihun Koshu Eisei Zasshi*. 2000; 47(3):230-44.
6. Coulibaly A, Turgeon O'Brien H, Galibois I. Validation of an FFQ to assess dietary protein intake in type 2 diabetic subjects attending primary health-care services in Mali. *Public Health Nutr*. 2008; 12(5):644-50.
7. Hong S et al. Development and validation of a semi-quantitative food frequency questionnaire to assess diets of Korean type 2 diabetic patients. *Korean Diabetes J*. 2010; 34(1):32-9.
8. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilization of food-frequency questionnaires – a review. *Public Health Nutr*. 2002; 5(4):567–87.
9. Lopes ACS, Caiaffa WT, Mingoti SA, Lima-Costa MFF. Ingestão Alimentar em Estudos Epidemiológicos. *Rev Bras Epidemiol*. 2003; 6(3): 209-19.
10. Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq. Diretório de Grupos de Pesquisa no Brasil. Grupo de Nutrição em Endocrinologia (GNE). Available in: <http://dgp.cnpq.br/buscaoperacional/detalhegrupo.jsp?grupo=01924053KT5EMV#identificacao> Accessed in: June 26, 2012.

11. de Paula TP, Steemburgo T, de Almeida JC, Dall'alba V, Gross JL, de Azevedo MJ. The role of Dietary Approaches to Stop Hypertension (DASH) diet food groups in blood pressure in type 2 diabetes. *Br J Nutr.* 2011; 6:1-8.
12. Vaz JS, Bittencourt M, Almeida JC, Gross JL, Azevedo MJ, Zelmanovitz T. Protein Intake Estimated by Weighed Diet Records in Type 2 Diabetic Patients: Misreporting and Intra-Individual Variability Using 24-Hour Nitrogen Output as Criterion Standart. *J Am Diet Assoc.* 2008; 108(5): 867-72.
13. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Coordenação Geral da Política de Alimentação e Nutrição. Guia Alimentar para a População Brasileira: promovendo a alimentação saudável. Brasília, 2006.
14. Block G, Dresser CM, Hartman AM, Carroll MD. Nutrient sources in the American diet: quantitative data from the NHANES II survey. *Am J Epidemiol.* 1985; 122:13-26.
15. Bantle JP, Wylie-Rosett J, Albright AL, Apovian CM, Clark NG, Franz MJ, Hoogwerf BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, Wheeler ML. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. *Diabetes Care.* 2008; 31 (Suppl. 1):S61–S78.
16. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The Role of Vitamin D and Calcium in Type 2 Diabetes. A Systematic Review and Meta-Analysis. *J Clin Endocrinol Metab.* 2007; 92:2017-29.
17. Zillich AJ, Garg J, Basu J, Barkis GL, Carter BL. Thiazide diuretics, potassium, and the development of diabetes: a quantitative review. *Hypertension.* 2006; 48:219–24.
18. Mello VD, Laaksonen DE. [Dietary fibers: current trends and health benefits in the metabolic syndrome and type 2 diabetes]. *Arq Bras Endocrinol Metabol.* 2009; 53(5):509-18.
19. Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. *Cochrane Database Syst Rev.* 2007; 17(4):CD002181.

20. de Mello VD, Zelmanovitz T, Perassolo MS, Azevedo MJ, Gross JL. Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria. *Am J Clin Nutr.* 2006; 83(5):1032-8.
21. de Mello VD, Zelmanovitz T, Azevedo MJ, de Paula TP, Gross JL. Long-term effect of a chicken-based diet versus enalapril on albuminuria in type 2 diabetic patients with microalbuminuria. *J Ren Nutr.* 2008; 18(5):440-7.
22. Liu Q, Sun L, Tan Y, Wang G, Lin X, Cai L. Role of Iron Deficiency and Overload in the Pathogenesis of Diabetes and Diabetic Complications. *Current Medicinal Chemistry.* 2009; 16:113-29.
23. USDA SR 17 Research Quality Nutrient Data. The Agricultural Research Service: Composition of Foods, Agricultural Handbook no 8 Washington, DC, US Department of Agriculture. 2006.
24. Cardoso MA, Stocco PR. Desenvolvimento de um questionário quantitativo de freqüência alimentar em imigrantes japoneses e seus descendentes residentes em São Paulo, Brasil. *Cad Saúde Pública.* 2000; 16(1):107-14.
25. Pinheiro ABV, Lacerda EMA, Benzecry EH, Gomes MCS, Costa VM. Tabela para avaliação de consumo alimentar em medidas caseiras. 3^a Ed. Rio de Janeiro: Editora Atheneu; 2004.
26. Monteiro JP. Nutrição e Metabolismo: Consumo Alimentar: Visualizando Porções. 1 ed. Rio de Janeiro: Guanabara Koogan; 2007.
27. Moulin CC, Tiskievicz F, Zelmanovitz T, de Oliveira J, Azevedo MJ, Gross JL. Use of weighed diet records in the evaluation of diets with different protein contents in patients with type 2 diabetes. *Am J Clin Nutr.* 1998; 67(5):853-7.
28. Almeida JC, Zelmanovitz T, Vaz JS, Steemburgo T, Perassolo MS, Gross JL, Azevedo MJ. Sources of protein and polyunsaturated fatty acids of the diet and microalbuminuria in type 2 diabetes mellitus. *J Am Coll Nutr.* 2008; 27(5):528-37.

29. Steemburgo T, Dall'Alba V, Almeida JC, Zelmanovitz T, Gross JL, de Azevedo MJ. Intake of soluble fibers has a protective role for the presence of metabolic syndrome in patients with type 2 diabetes. *Eur J Clin Nutr.* 2009; 63(1):127-33.
30. Silva FM, Steemburgo T, de Mello VD, Tonding SF, Gross JL, Azevedo MJ. High dietary glycemic index and low fiber content are associated with metabolic syndrome in patients with type 2 diabetes. *J Am Coll Nutr.* 2011; 30(2):141-8.
31. Slater B, Philippi ST, Marchioni DML, Fisberg RM. Validação de Questionários de Freqüência Alimentar - QFA: considerações metodológicas. *Rev Bras Epidemiol.* 2003; 6(3):200-8.
32. Fisberg RM, Slater B, Marchioni DML, Martini LA. Inquéritos Alimentares: métodos e bases científicos. São Paulo: Manole; 2005.

Table 1. Most relevant nutrients in each food group

Food group	Nutrients
Cereals, tubers, roots and derivatives	Carbohydrate
Vegetables	Fiber, iron, calcium, and potassium
Fruits	Carbohydrate, fiber, and potassium
Beans	Protein, fibers, and iron
Meat and eggs	Protein, lipids, and iron
Milk and dairy products	Protein, lipids, and calcium
Oils and fats	Lipids
Sugars and sweets	Carbohydrate

Table 2. Food list from Food Frequency Questionnaire for Diabetes: consumption frequency registered of 188 patients with type 2 diabetes and nutrients contribution

Foods	Nutrients Contribution*									
	n	%	Calories	Carbohydrate	Protein	Lipid	Fiber	Iron	Calcium	Potassium
Cereals, tubers, roots and derivatives										
White rice	177	94.1	yes	yes	yes	no	yes	yes	no	yes
French or Vienna bread	142	75.5	yes	yes	yes	yes	yes	yes	yes	yes
Spaghetti pasta	76	40.4	yes	yes	yes	no	yes	yes	no	yes
Wheat cracker	82	43.6	yes	yes	yes	yes	yes	yes	yes	yes
Whole bread	78	41.4	yes	yes	yes	yes	yes	yes	yes	yes
Cassava, boiled	41	21.8	yes	yes	no	no	yes	no	no	yes
Cake	35	18.6	yes	yes	no	yes	yes	yes	no	yes
<i>Polenta</i>	23	12.2	yes	yes	no	no	yes	yes	no	yes
Potato, boiled/baked	82	43.6	yes	yes	no	no	yes	no	no	yes
Homemade bread	24	12.7	yes	yes	no	no	no	yes	no	no
White bread	35	18.6	yes	yes	no	no	no	yes	yes	no
Milk cracker	27	14.3	yes	yes	no	yes	no	yes	yes	no
Vegetables										
Carrot	77	40.9	no	no	no	no	yes	no	yes	yes
Cabbage	56	29.7	no	no	no	no	yes	yes	yes	yes
Tomato	134	71.2	no	no	no	no	yes	no	no	yes
Chayote	34	18.0	no	no	no	no	yes	no	no	yes
Lettuce	112	59.5	no	no	no	no	no	yes	yes	yes
Kale	37	19.6	no	yes	no	no	no	yes	yes	yes
Broccoli	22	11.7	no	no	no	no	no	no	no	yes
Pumpkin	17	9.0	no	no	no	no	no	no	no	yes
Beet	20	10.6	no	no	no	no	no	no	no	yes
Fruits										
Banana	135	71.8	yes	no	no	no	yes	yes	no	yes
Apple	92	48.9	yes	yes	no	no	yes	no	no	yes
Orange	58	30.8	yes	yes	no	no	yes	no	yes	yes
Tangerine	51	27.1	yes	yes	no	no	yes	no	yes	yes
Papaya	164	87.2	yes	yes	no	no	yes	no	yes	yes
Mango	16	8.5	no	no	yes	no	no	no	no	no
Pear	19	10.1	no	no	no	no	yes	no	no	no
Beans										
Beans (all types)	147	78.1	yes	yes	yes	no	yes	yes	yes	yes
Lentil	16	8.5	yes	yes	no	no	yes	yes	no	yes

Meat and eggs										
Beef, boiled/baked	122	64.8	yes	no	yes	yes	no	yes	yes	yes
Chicken, boiled/baked	123	65.4	yes	no	yes	yes	no	yes	yes	yes
Ground beef	63	33.5	yes	no	yes	yes	no	yes	yes	yes
Beef steak	64	34.0	yes	no	yes	yes	no	yes	no	yes
Luncheon/bologna	43	22.8	yes	no	yes	yes	no	yes	no	yes
Fish, boiled/baked	21	11.1	yes	no	yes	yes	no	no	no	yes
Pork	28	14.8	yes	no	yes	yes	no	yes	no	yes
Fish, fried	9	4.7	yes	no	no	yes	no	no	no	yes
Chicken, fried	14	7.4	yes	no	yes	no	no	no	no	yes
Frankfurter wiener, hot dog	15	7.9	no	no	no	yes	no	no	no	no
Mortadella	35	18.6	no	no	no	yes	no	no	no	no
Salami	23	12.2	no	no	no	yes	no	no	no	no
Beef, fried	8	4.2	no	no	no	yes	no	no	no	no
Egg, boiled/fried	22	11.7	no	no	no	yes	no	no	no	no
Beef liver	6	3.1	no	no	no	no	no	yes	no	no
Ham	48	25.5	no	no	no	no	no	no	no	yes
Milk and dairy products										
Muenster cheese	76	40.4	yes	no	yes	yes	no	no	yes	no
Milk, fluid, 3.25% fat	73	38.8	yes	yes	yes	yes	no	no	yes	yes
Milk, fluid, nonfat	78	41.4	yes	yes	yes	no	no	no	yes	yes
Goat cheese, soft type	32	17.0	no	no	no	yes	no	no	yes	no
Muenster cheese	12	6.3	no	no	no	yes	no	no	yes	no
Milk, fluid, 2% fat	19	10.1	no	no	no	no	no	no	yes	yes
Yogurt, plain	10	5.3	no	no	no	no	no	no	yes	no
Milk type C	10	5.3	no	no	no	no	no	no	yes	no
Yogurt, plain, skim	8	4.2	no	no	no	no	no	no	yes	no
Milk, dry, whole	10	5.3	no	no	no	no	no	no	yes	no
Yogurt, fruit	6	3.1	no	no	no	no	no	no	yes	no
American cheese	11	5.8	no	no	no	no	no	no	yes	no
Oils and fats										
Margarine	101	53.7	yes	no	no	yes	no	no	no	no
Goose pate	23	12.3	no	no	no	yes	no	no	no	no
Mayonnaise	19	10.1	no	no	no	yes	no	no	no	no
Sugars and sweets										
Flan and/or pudding diet	8	4.2	no	no	no	no	no	no	yes	no

*Nutrient contribution defined as contribution of at least 80% of total energy or relevant nutrient intake in the respective food group.

Table 3. Final food list in the Food Frequency Questionnaire: portions in grams or milliliters and household measures

Food group	Small (25 th)	Medium (50 th)	Large (75 th)	Extra large (95 th)
Cereals, tubers, roots, and derivatives				
White rice	2 tablespoon full	50 g	4 tablespoon full	100 g
Spaghetti pasta	3 tablespoon full	75 g	4 tablespoon full	100 g
Cassava, boiled/fried	2 pieces	60 g	3 pieces	90 g
Potato, boiled/baked/fried	2 tablespoon full	60 g	3 tablespoon full	90 g
Polenta, boiled/fried	1 serving spoon	60 g	2 tablespoon full	90 g
French or Vienna bread	½ unit	25 g	1 unit	50 g
White bread	1 slice	25 g	2 slice	50 g
Whole bread	½ slice	15 g	1 slice	30 g
Homemade bread	2/3 slice	60 g	1 slice	68 g
Cake	1 small slice	50 g	1 medium slice	70 g
Wheat cracker	4 units	20 g	6 units	30 g
Milk cracker	5 units	25 g	8 units	40 g
Vegetables				
Carrot	2 tablespoon full	24 g	3 tablespoon full	36 g
Tomato	3 small slices	30 g	5 small slices	50 g
Chayote	1 tablespoon full	30 g	2 tablespoon full	60 g
Cabbage	4 tablespoon full	40 g	7 tablespoon full	70 g
Lettuce	1 tagger	20 g	2 taggers	30 g
Watercress	1 full dessert plate	20 g	2 taggers	30 g
Kale, spinach	2 tablespoon full	40 g	3 tablespoon full	60 g
Broccoli, cauliflower	1 small bunch	30 g	1 medium bunch	60 g
Snap bean	2 level tablespoon	30 g	2 tablespoon full	40 g
Pumpkin	1 medium piece	50 g	2 medium pieces	100 g
Beet	2 medium slices	30 g	5 medium slices	60 g
Fruits				
Banana	1 small unit	40 g	1 medium unit	70 g
Apple, pear	1 small unit	90 g	1 and ½ small unit	135 g
Orange, tangerine	1 small unit	90 g	1 and ½ small unit	135 g
Papaya	½ small slice	80 g	1 medium slice	100 g
Mango	1 small piece	60 g	2 small pieces	120 g
Grape	8 units	64 g	14 units	112 g
Persimmon	1 small unit	85 g	1 large unit	150 g
Casaba melon	½ small slice	78 g	1 small slice	125 g
Watermelon	1 small slice	143 g	1 medium slice	200 g
Beans				
Beans (all types)	1 small full scoop	65 g	1 level medium scoop	80 g
				2 small full scoop
				130 g
				2 level medium scoop
				160 g

Lentil	1 level medium scoop	100 g	1 medium full scoop	160 g	2 level medium scoop	200 g	2 medium full scoop	320 g
Meat and eggs								
Beef, boiled/baked/fried	1 small slice	70 g	4 small pieces	80 g	1 large slice	135 g	2 large slices	270 g
Ground beef	2 tablespoon full	50 g	3 tablespoon full	75 g	4 tablespoon full	100 g	8 tablespoon full	200 g
Beef steak	½ small unit	40 g	1 small unit	80 g	1 medium unit	100 g	2 medium units	200 g
Beef liver	½ large unit	75 g	1 small unit	80 g	1 medium unit	100 g	1 large unit	150 g
Chicken thigh, boiled/baked/fried	1 medium piece	60 g	1 large piece	95 g	2 medium pieces	110 g	3 medium pieces	180 g
Chicken breast, boiled/baked/fried	1 medium piece	60 g	1 large piece	95 g	2 medium pieces	110 g	3 medium pieces	180 g
Fish, boiled/baked/fried	½ small piece	60 g	1 small piece	100 g	1 large piece	155 g	2 large pieces	310 g
Pork, boiled/baked/fried	1 small slice	60 g	1 medium slice	90 g	1 large slice	120 g	2 medium slices	180 g
Luncheon/bologna	½ unit	30 g	1 unit	60 g	1 and ½ units	90 g	2 and ½ units	150 g
Frankfurter wiener, hot dog	1 unit	42 g	1 and ½ unit	63 g	2 units	84 g	3 and ½ units	147 g
Mortadella, ham, salami	1 medium slice	15 g	1 large slice	25 g	2 medium slices	30 g	2 large slices	50 g
Egg, boiled/fried	½ unit	25 g	1 unit	50 g	1 and ½ unit	75 g	3 units	150 g
Milk and dairy products								
Milk, fluid, 3.25% fat	½ cup	100 ml	¾ cup	150 ml	1 cup	200 ml	1 mug	300 ml
Milk, fluid, 2% fat	½ cup	100 ml	¾ cup	150 ml	1 cup	200 ml	1 mug	300 ml
Milk, fluid, nonfat	¾ cup	150 ml	1 cup	200 ml	1 glass	240 ml	1 and ½ cups	250 ml
Milk, dry	1 tablespoon full	16 g	2 full dessert spoon	18 g	2 tablespoon full	32 g	4 tablespoon full	36 g
Mozzarella/muenster cheese	1 slice	20 g	1 and ½ slice	30 g	2 slices	40 g	3 slices	60 g
Ricotta cheese	1 small slice	15 g	1 medium slice	35 g	1 large slice	45 g	2 large slices	90 g
Muenster cheese	1 small slice	25 g	1 medium slice	35 g	1 large slice	50 g	2 medium large slices	70 g
Sour cultured, Cream half-half	1 teaspoon	10 g	1 level tablespoon	15 g	1 tablespoon full	25 g	4 level tablespoon	60 g
American cheese	1 level dessert spoon	10 g	1 level tablespoon	15 g	1 tablespoon full	30 g	2 tablespoon full	60 g
Yogurt, plain	½ pot	100 g	1 pot	200 g	1 and ½ pots	300 g	2 pots	400 g
Yogurt, fruit	1 pot	100 g	1 and ½ pots	150 g	2 pots	200 g	3 pots	300 g
Oils and fats								
Margarine	1 level teaspoon	4 g	1 full teaspoon	8 g	1 level dessert spoon	13 g	1 full dessert spoon	23 g
Butter	1 level teaspoon	4 g	1 full teaspoon	8 g	1 level dessert spoon	13 g	1 full dessert spoon	23 g
Mayonnaise	1 full teaspoon	6 g	2 full teaspoon	12 g	1 full dessert spoon	17 g	2 full dessert spoon	34 g
Goose pate	1 full teaspoon	8 g	2 full teaspoon	16 g	1 full dessert spoon	21 g	3 full dessert spoon	63 g
Oil, add	1 teaspoon	2 ml	2 teaspoon	4 ml	1 dessert spoon	5 ml	1 tablespoon	8 ml
Sugars and sweets								
Sago	3 tablespoon full	90 g	4 tablespoon full	120 g	5 tablespoon full	150 g	6 tablespoon full	180 g
Chocolate	2 pieces	15 g	3 pieces	30 g	4 pieces	40 g	8 pieces	80 g
Flan, pudding	1 tablespoon full	50 g	2 tablespoon full	90 g	3 tablespoon full	130 g	5 tablespoon full	220 g
Ice cream	1 tablespoon full	55 g	1 bola	75 g	1 cup	100 g	2 bolas	150 g
Gelatin	2 tablespoon full	50 g	3 tablespoon full	75 g	5 tablespoon full	125 g	12 tablespoon full	300 g
Condensed milk	1 level teaspoon	10 g	1 level dessert spoon	15 g	1 tablespoon full	40 g	2 full dessert spoon	50 g
Jelly	1 full teaspoon	10 g	2 full teaspoon	20 g	1 tablespoon full	34 g	2 tablespoon full	68 g
Honey	1 dessert spoon	10 g	1 tablespoon	15 g	2 dessert spoon	20 g	2 tablespoon	30 g

Chocolate, dry	1 level dessert spoon	7 g	1 level tablespoon	11 g	1 tablespoon full	16 g	2 tablespoon full	32 g
Beverages								
Coffee, brewed	¼ cup	50 ml	½ cup	100 ml	¾ cup	150 ml	1 cup	200 ml
Coffee, instant	1 teaspoon	1.5 g	2 teaspoon	3 g	4 teaspoon	6 g	6 teaspoon	9 g
Tea	¾ cup	150 ml	1 cup	200 ml	1 and ¼ cups	250 ml	1 mug	300 ml
Refrigerant	1 cup	200 ml	1 full glass	250 ml	1 can	350 ml	2 full glass	500 ml
Fruit juice raw	¾ cup	150 ml	1 cup	200 ml	1 full glass	250 ml	2 cups	400 ml
Fruit juice artificial	¾ cup	150 ml	1 cup	200 ml	1 full glass	250 ml	2 full glass	500 ml
Soymilk	¾ cup	150 ml	½ glass	175 ml	1 cup	200 ml	1 full glass	250 ml
Beer	1 glass	300 ml	1 bottle	600 ml	1 and ½ bottles	900 ml	6 bottles	3600 ml
Wine	½ glass	75 ml	¾ glass	115 ml	1 glass	150 ml	2 glass	300 ml

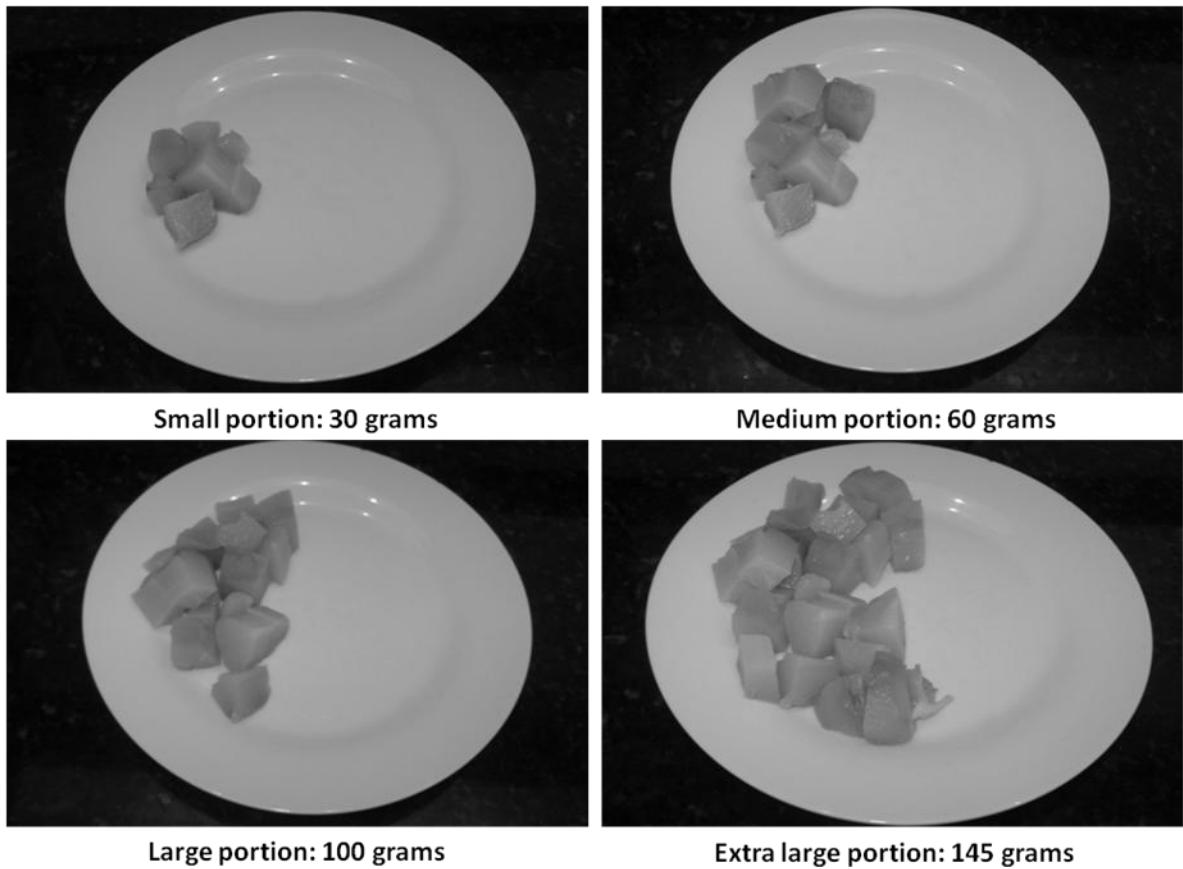


Figure 1. Illustration of four portions of the same food (chayote, cooked) photographed and included on the food portfolio

Capítulo III

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**Reproducibility and validity of a quantitative food frequency questionnaire designed for
patients with type 2 diabetes from Southern of Brazil**

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SUMMARY

Background: Food frequency questionnaires (FFQ), a dietary tool widely used to evaluate usual diet, should be directed at the specifically studied population. Moreover, after it is created, the FFQ must be validated in a different sample of subjects from the same population. The present study aims to evaluate the performance (validity and reproducibility) of a previously constructed FFQ to assess the usual diet of patients with type 2 diabetes mellitus (T2DM).

Methods: Consecutive T2DM patients, without previous dietary assessment, were selected to answer two quantitative FFQs (one-month interval) supported by a portfolio with food photos and, subsequently, to perform 3-day weighed diet records (WDR) and collect 24-h urine (urinary nitrogen output measurement). The dietary intake from FFQ was compared (t-test, correlation coefficients, and Bland-Altman agreement) with WDR and protein intake estimated from 24-hour urine, both used as reference criteria. The validity coefficient of protein intake from FFQ was calculated (method of triads) using values from FFQ, WDR, and 24-hour urinary nitrogen (protein intake biomarker). **Results:** From a total of 104 eligible T2DM outpatients, 88 patients were included in the evaluation of FFQ reproducibility (58% women; aged 63 ± 9 years; BMI 29.6 ± 3.9 kg/m²; HbA1c $8.9\pm2.0\%$) and 72 patients provided data for the validity study. The intake estimated from the 1st and 2nd FFQ did not differ ($P>0.05$). Correlation coefficients between the two FFQs were significant ($P<0.01$) for energy and nutrients ranging from 0.451 (soluble fiber) to 0.936 (polyunsaturated fatty acids). Regarding the validity evaluation, the consumption information from FFQ was higher than from WDR for total (28.3%), soluble (27.4%) and insoluble fibers (29.1%), saturated (13.5%), monounsaturated (11.1%), and total lipids (9.2%) ($P <0.05$ for all). There were significant correlation coefficients between FFQ and WDR for all nutrients, adjusted for energy intake and de-attenuated for intra- and inter-individual variances ($P<0.05$ for all). Also, the agreement plots between FFQ and WDR for energy and macronutrient intakes showed that these two methods are interchangeable. Considering the protein intake biomarker, the mean of difference

with FFQ was -3.8 g (-60.1, 52.4 g) and to WDR it was -1.0 g (-59.7, 57.7 g), without difference between them ($P=0.551$). The validity coefficient for the FFQ protein intake was 0.522 (95% CI 0.414-0.597). **Conclusions:** This quantitative FFQ performed an accurate assessment of the usual diet of patients with T2DM, according to its validity and reproducibility.

Keywords: type 2 diabetes mellitus; food frequency questionnaire; food records; nutritional epidemiology.

INTRODUCTION

The influence of diet in the development of human disease has been the central focus of nutritional epidemiology¹. There are several methods to evaluate food and nutrient consumption as well as the energy intake, including 24-hour recall, diet records, food frequency questionnaire (FFQ)², and biomarkers³. Dietary assessment is often carried out to develop and implement nutritional advice, promote health, prevent illness, and improve the nutritional status⁴.

The management of patients with diabetes included, besides pharmacological therapy, lifestyle changes^{5,6}. The intensive control of hyperglycemia and hypertension reduce or halt the development of diabetic chronic complications⁶. The best pharmacological strategy to lower glucose in patients with type 2 diabetes (T2DM) has been continuously evaluated⁷, but few patients reach the suggested targets. In fact, only 24% of the Brazilian diabetic patients had an HbA1c lower than the recommended target (HbA1c <7%)⁸. In this sense, lifestyle changes, especially dietary intervention, should be reinforced⁶. However, the relationship between diet and diabetes complications has not been completely elucidated.

To investigate the association between the components of diet and development of chronic diabetic complications, the dietary evaluation should cover a long period, months or years, as is the case of FFQ¹. The FFQ should be based in a specific population and its validity and reproducibility should always be tested¹. The validity is examined by comparing FFQ data with a reference method and/or biomarkers⁹. The weighed-diet record (WDR) has been considered the best dietary tool for the validation procedure¹⁰. Biomarkers evaluate specific nutrients, such as urinary urea estimating the protein intake¹¹. Finally, to evaluate the FFQ reproducibility, the dietary instrument should be tested at least on two separate occasions¹².

To date, only four FFQs were developed and validated for patients with diabetes in specific ethnic populations¹³⁻¹⁶. We recently constructed a Brazilian FFQ for diabetes¹⁷. Therefore, the present study aims to evaluate the performance (validity and reproducibility) of this FFQ in the

assessment of the usual diet of patients with T2DM comparing it with WDR and a protein intake biomarker.

METHODS

Patients

The present study was conducted in patients with T2DM, defined as subjects over 30 years of age at onset of diabetes, no previous episode of ketoacidosis or documented ketonuria and, if insulin users, the treatment with insulin began five years after diagnosis. The study recruited outpatients who consecutively attended the Endocrinology Division of the Hospital de Clínicas de Porto Alegre, Brazil, and who had not previously been submitted to any dietary assessment.

The inclusion criteria were: age <80 years, serum creatinine <2.0 mg/dL, and BMI <40 kg/m². Patients using corticosteroid drugs and with orthostatic hypotension or gastrointestinal symptoms suggestive of autonomic diabetic neuropathy were excluded. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients were approved by the Hospital Ethics Committee. Written informed consent was obtained from all patients.

Patients were submitted to clinical, lifestyle, and anthropometric evaluation. Information about clinical data (co-morbidities associated with diabetes and medication use) was collected from the patient's most recent medical records. Patients were classified as current smokers or not (former and nonsmokers) and were self-identified as white or non-white. Economic status was evaluated by a standardized Brazilian questionnaire¹⁸ and physical activity level was classified according to the short version of the International Physical Activity Questionnaire¹⁹ culturally adapted to the Brazilian population²⁰. Physical activity was graded in three levels: low, moderate, and high, according to activities during a typical week¹⁹. The body weight and height of patients (light clothing and without shoes) were obtained with measurements recorded to the nearest 100 g for

weight and to the nearest 0.1 cm for height. BMI (kg/m^2) was then calculated. Waist circumference was measured at the midpoint between the iliac crest and the last floating rib. Also, hip circumference was measured at the largest circumference of the buttocks. Flexible and non-stretch fiberglass tape was used for these measurements.

Dietary assessment

The usual patient's diet was assessed by FFQ (study factor), 3-day WDR (used as relative reference), and by a biomarker for protein intake (urinary nitrogen output) from February/2010 to May/2011. The FFQ was constructed with dietary data from a sample of T2DM patients as previously described¹⁷. Briefly, dietary data using 3-day WDR from 188 T2DM outpatients were used to construct a quantitative FFQ and a portfolio with photos of 98 food items covering the past 12 months of the most commonly consumed food items¹⁷. The FFQ was applied by a nutritionist (R.A.S.) twice with one-month interval. After this, the patients underwent a 3-day WDR (two non-consecutive weekdays and one day-off at an interval of three weeks) as previously standardized²¹. Compliance with the WDR technique was confirmed by comparison between protein intake estimate from WDR and 24-h urinary nitrogen output¹¹. To be included in the validity evaluation of the FFQ, misreporting should be excluded. Misreporting was defined when the ratio of protein intake from WDR to estimated protein intake by urinary nitrogen was < 0.79 or > 1.26 ²². The protein intake estimated from urinary nitrogen was also used as a biomarker to evaluate the agreement of protein intake from FFQ and WDR.

The food intake reported in dietary instruments (FFQ and WDR) was converted into daily intake and their nutritional composition was calculated by *Nutribase Clinical®* 2007 USDA SR²³. The amount of *trans*-unsaturated fatty acids was derived from “Tabela de Composição dos Alimentos - TACO”²⁴, U.S. Department of Agriculture²⁵, Slover et al.²⁶, and the TRANSFAIR Study²⁷. The total, soluble, and insoluble dietary fiber content were estimated from data available in the CRC Handbook of Dietary Fiber in Human Nutrition²⁸. The glycemic index (GI) and load (GL)

were obtained from the international table²⁹. When the GI of foods present in the instruments was not found, we used data from food with a similar composition.

Laboratory evaluation

Blood samples were obtained after a 12-h fast. Plasma glucose was determined by a glucose oxidase method, serum and urinary creatinine level by Jaffe's reaction, HbA1C test by HPLC (Tosoh 2.2 Plus HbA1c; Tosoh Corporation, Tokyo Japan; reference values 4.8 to 6%), total cholesterol and triglycerides were measured by enzymatic-colorimetric methods, and HDL-cholesterol by homogeneous direct method. LDL-cholesterol was calculated using the Friedewald's formula: LDL-cholesterol = total cholesterol - HDL-cholesterol - (triglyceride/5)³⁰ only for patients with triglycerides values <400 mg/dl. Urinary albumin excretion was measured by immunoturbidimetry [MicroAlb Sera-Pak® immuno microalbuminuria; Bayer, Tarrytown, NY on Cobas Mira Plus (Roche®)] and urinary urea was measured by an enzymatic ultraviolet method.

Statistical analysis

Results are expressed as mean \pm SD or median (interquartile range) and the Gaussian distribution was verified by the One-Sample Kolmogorov-Smirnov test. Data were log-transformed before analyses to normalize distribution. All data analyses were performed using the SPSS statistical software package version 18.0 (SPSS Inc., Chicago, IL, USA) and the type I error rate fixed at $P \leq 0.05$ (2-tailed).

To evaluate the FFQ reproducibility, data from 1st and 2nd FFQ were compared by Student's *t*-test or Wilcoxon *U*-test for paired-samples and Pearson correlation coefficients were calculated with crude and adjusted data for energy intake according to residual method¹.

In the validity study, data from 2nd FFQ, WDR (relative reference) and biomarker (only for protein intake) were evaluated comparing these dietary tools using Student's *t*-test or Wilcoxon *U*-test for paired-samples, Pearson correlations coefficients, and their agreement by Bland-Altman

plots³¹. Pearson correlation coefficients were calculated using crude data and data adjusted to energy intake¹. Correlation values were corrected by the ratio of the intra- and inter-individual variances, obtained by analysis of 3-day WDR, through the following equation: $[r_d = r_o (1 + \lambda/n)^{1/2}]$; where r_d is the de-attenuated correlation, r_o is the correlation observed between FFQ and WDR, λ is the intra- and inter-individual variance ratio in the WDR, and n is the number of replicates, which comprised three food records¹. Further, the correlation between the protein intake estimated from FFQ and true protein intake was performed according to the method of triads, considering protein intake estimate by 2nd FFQ, WDR, and measured using biomarker - urinary nitrogen output³².

In the sample size calculation a minimum correlation coefficient of 0.40¹ between the protein intake estimates by FFQ and by WDR, a type I error (two-tailed) of 5% and a type II error of 10% were taken into account. For the validity study, 62 patients were required; for the reproducibility evaluation, considering a 20% dropout, 75 patients needed to be studied.

RESULTS

Patients

Out of a total of 104 participants eligible for the study, three patients (2.9%) refused to participate and 13 patients (12.5%) agreed to participate but they did not return for another visit to answer the 2nd FFQ. Furthermore, 16 patients (15.4%) performed unsatisfactory WDR and they were not included in the validity evaluation. Therefore, 88 patients were included for the reproducibility evaluation and 72 patients provided complete data for the validity study. The demographic, clinical, anthropometric, and laboratory characteristics of patients included in each study were shown in **Table 1**. We did not observe differences between the patients included in the reproducibility evaluation as compared to patients included in the validity study.

Reproducibility evaluation

The daily intake data obtained from the 1st and 2nd FFQ were compared and are shown in **Table 2**. The reported intake of energy, macronutrients, fibers, GI and GL were not different between the two applications of FFQ. The correlation coefficients between the nutrients reported in the 1st FFQ and 2nd FFQ were calculated and are also shown in **Table 2**. All the correlation coefficients are significant before and after the energy adjustment ($P < 0.05$ for all analyses). The polyunsaturated fatty acid values showed a strong correlation ($r = 0.936$) and most nutrients showed moderate correlation values: the highest value was for total lipids ($r = 0.658$) and the lowest was for insoluble fiber ($r = 0.451$).

Validity study

The data of daily intake from 2nd FFQ were compared with the mean of 3-day WDR in the validity evaluation and are shown in **Table 3**. The mean values of nutrient intakes reported from FFQ for total (28.3%), soluble (27.4%) and insoluble fibers (29.1%), saturated fatty acids (13.5%), monounsaturated fatty acids (11.1%), and total lipids (9.2%) were higher as compared to values from WDR ($P < 0.05$ for all comparisons). Only the GI values reported in the FFQ were 2.6% lower than WDR ($P = 0.041$).

Regarding correlations, the de-attenuation improved the values for all dietary data and these results are also shown in **Table 3**. However, only soluble and insoluble fibers did not show significant correlations between FFQ and WDR values after energy adjustment. The total lipids ($r = 0.855$) and polyunsaturated fatty acids ($r = 0.912$) showed strong correlations, while most nutrients had moderate correlation coefficient values: the highest value was for monounsaturated fatty acids ($r = 0.762$) and the lowest value was for total fiber ($r = 0.400$).

Figure 1 shows the good agreement, according to Bland-Altman plots, between the intake of energy and macronutrients (energy-adjusted) from FFQ and WDR. The difference means (agreement range) observed between reported and registered data were: 152.2 kcal (-1152.8, 1457.2

kcal) for energy, -2.9 g (-45.8, 40.1 g) for proteins, 27.1 g (-62.6, 116.8 g) for carbohydrates and 7.5 g (-20.9, 35.9 g) for total lipids.

Considering urinary nitrogen output as a biomarker for protein intake, no differences were observed between data from FFQ (96.2 ± 39.2 g) and biomarker (100.1 ± 29.0 g; $P = 0.368$), as well as between data from WDR (99.1 ± 37.1 g) and biomarker ($P = 0.792$). **Figure 2** shows graphically (Bland-Altman plots) that FFQ and WDR are interchangeable: the mean difference (agreement range) obtained in protein intake by a biomarker with FFQ [-3.8 g (-60.1, 52.4 g)] and with WDR [-1.0 g (-59.7, 57.7 g)] were not different ($P = 0.551$). Regarding estimated protein intake, the correlation coefficient between the values obtained from FFQ and WDR was 0.597 ($P = 0.001$), between values reported from FFQ and estimated from a biomarker it was 0.414 ($P < 0.001$), and between values from WDR and estimated from a biomarker it was 0.907 ($P < 0.001$). Therefore, the correlation between the protein intake from FFQ and the true intake was 0.522 (95% CI 0.414-0.597), according to the formula proposed by the method of triads³².

DISCUSSION

The FFQ constructed to evaluate the usual diet of Brazilian TDM2 had adequate validity (moderate correlation values and appropriate agreement with the references standards) and reproducibility to assess the last month intake of energy, macronutrients, GI, and GL of patients with T2DM. This is the first FFQ elaborated based on the usual intake of patients with diabetes in Brazil.

In our study, some methodological cautions were taken into account: we tested the accuracy of FFQ in a different sample considering the sample where the FFQ was constructed¹⁷, but in the same population; we selected a sample of diabetic patients without previous experience in dietary records; we used reference standards, WDR and nitrogen output biomarker, previously standardized in patients with diabetes^{21,22} and largely used in diabetic patients by our research group³³⁻³⁶; finally, we included the influence of seasonality on validity evaluation of the FFQ¹⁰.

The correlation coefficients observed in the present study were within an acceptable range for calibration studies of diet, between 0.39 and 0.70¹, although the energy adjustment method has reduced the correlation values in reproducibility (see Table 2) and validity (see Table 3) studies. Possibly, this occurs when the variability of the nutrient is affected by systematic errors of under-recording or over-reporting of food consumption¹. Our results were similar to others studies to evaluate FFQ performance^{13,37,38}.

We observed differences higher than 10% between the intakes from FFQ and WDR for some nutrients that could be explained by under-recording the WDR^{39,40} or by overestimation by FFQ. In fact, previous studies demonstrated that the FFQ tended to overestimate energy and nutrient intake when compared to different dietary assessment methods⁴¹⁻⁴³. In this way, an additional assessment using a biochemical measure can be extremely valuable, considering that no dietary measure is without error¹. In this sense, the method of triads is a technique that has been used in studies to validate dietary nutrient intake⁴⁴⁻⁴⁶. This method adds a third variable – a biomarker – with an independent error from FFQ and the reference method (WDR) to assess the performance to estimate the true (but unknown) intake by calculating the validity coefficient (ρ)⁴⁷. In fact, the biomarkers should be used as additional measures because not all nutrients have biological markers and many are influenced by factors other than intake, such as bioavailability, metabolism, and genetic factors³. Our result from the correlation of the FFQ measurement with the true intake for protein ($\rho = 0.522$) was moderate and similar to that described by other authors^{48,49}.

Regarding the reproducibility of the FFQ, an important aspect that influences the results is the time elapsed between applications of FFQ. If the interval is too short, the reproducibility could be overestimated, since the participant remembers the answers of the first questionnaire. On the other hand, long intervals can reduce the correlations as a consequence of a real change in dietary patterns¹². In this sense, it is suggested that short-term reproducibility studies should be performed with a time interval of 15-45 days⁵⁰. In our study, the FFQ was validated for assessment of habitual diet of the previous month (short term).

When we analyzed the relative validity of the FFQ, significant correlations were observed for most analyzed nutrients and greater values were obtained after the de-attenuation procedure. These results are in accordance with the known influence of daily intra- and inter-individual variability of intake¹ with that observed by others^{37,51}.

Some limitations of the present study can be identified. We did not evaluate other biomarkers beyond protein intake. Though, we have used the estimation of protein intake from urinary urea as a marker of compliance with the WDR technique in many studies^{21,22,33-36} to confirm the adequacy of dietary records. However, future comparisons with other biomarkers, such as serum fatty acids and micronutrients or energy expenditure must be performed. Another possible limitation is that in the current study reproducibility data were derived from a relatively short-term period. Long-term reproducibility of the instrument (at least one year) should be also evaluated.

In conclusion, we demonstrated that the quantitative FFQ previously constructed was valid and precise to assess the usual diet of patients with T2DM. In addition, this easily applied FFQ can replace the WDR technique, a more laborious dietary tool.

REFERENCES

1. Willett WC. Nutritional epidemiology. Oxford: Oxford University Press; 1998.
2. Biró G, Hulshof KF, Ovesen L, Amorim Cruz JA; EFCOSUM Group. Selection of methodology to assess food intake. *Eur J Clin Nutr*. 2002; 56 Suppl 2:S25-32.
3. Jenab M, Slimani N, Bictash M, Ferrari P, Bingham S. Biomarkers in nutritional epidemiology: applications, needs and new horizons. *Human Genet*. 2009; 125:507-25.
4. Fisberg RM, Marchiori DML, Colucci ACA. Assessment of food consumption and nutrient intake in clinical practice. *Arq Bras Endocrinol Metab*. 2009; 53:617-624.
5. Bantle JP, Wylie-Rosett J, Albright AL, Apovian CM, Clark NG, Franz MJ, Hoogwerf BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, Wheeler ML. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. *Diabetes Care*. 2008; 31 (Suppl. 1):S61–S78.
6. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2012; 35 Suppl 1:S11-63.
7. Gross JL, Kramer CK, Leitão CB, Hawkins N, Viana LV, Schaan BD, Pinto LC, Rodrigues TC, Azevedo MJ - Diabetes and Endocrinology Meta-analysis Group (DEMA). Effect of antihyperglycemic agents added to metformin and a sulfonylurea on glycemic control and weight gain in type 2 diabetes: a network meta-analysis. *Ann Intern Med*. 2011; 154:672-679.
8. Mendes ABV, Fittipaldi JAS, Neves RCS, Chacra AR, Moreira-Jr ED. Prevalence and correlates of inadequate glycemic control: results from a nationwide survey in 6,671 adults with diabetes in Brazil. *Acta Diabetol*. 2010; 47:137-145.
9. Cardoso MA. Desenvolvimento, validação e aplicações de questionários de freqüência alimentar em estudos epidemiológicos. In: Gilberto Kac; Rosely Sichieri; Denise Gigante. Epidemiologia Nutricional. 1 ed. Rio de Janeiro: Fiocruz/Atheneu, 2007, p. 201-212.

10. Slater B, Philippi S, Marchioni D. Validação de Questionários de Freqüência Alimentar – QFA: considerações metodológicas. *Rev Bras Epidemiol* 2003; 6:200-8.
11. Maroni BJ, Steinman TL, Mitch WE. A method for estimating nitrogen intake of patients with chronic renal failure. *Kidney Int*. 1985; 2:58-65.
12. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilization of food-frequency questionnaires - a review. *Public Health Nutr*. 2002; 5:567-87.
13. Riley MD, Blizzard L. Comparative validity of a food frequency questionnaire for adults with IDDM. *Diabetes Care*. 1995; 18(9):1249-54.
14. Yamaoka K, Tango T, Watanabe M, Yokotsuka M. Validity and reproducibility of a semi-quantitative food frequency questionnaire for nutritional education of patients of diabetes mellitus (FFQW65). *Nihun Koshu Eisei Zasshi*. 2000; 47(3):230-44.
15. Coulibaly A, Turgeon O'Brien H, Galibois I. Validation of an FFQ to assess dietary protein intake in type 2 diabetic subjects attending primary health-care services in Mali. *Public Health Nutr*. 2008; 12(5):644-50.
16. Hong S et al. Development and validation of a semi-quantitative food frequency questionnaire to assess diets of Korean type 2 diabetic patients. *Korean Diabetes J*. 2010; 34(1):32-9.
17. Sarmento RA, Riboldi BP, Rodrigues TC, Azevedo MJ, Almeida JC. Development of a quantitative food frequency questionnaire for Brazilian patients with type 2 diabetes. 2012 [submitted].
18. ABEP – Associação Brasileira das Empresas de Pesquisa 2008. Available in: www.abep.org. Accessed in: March, 2009.
19. IPAQ – International Physical Activity Questionnaire. Available in: <http://www.ipaq.ki.se/ipaq.htm>. Accessed in: October, 2009.

20. Hallal PC, Matsudo SM, Matsudo VKR, Araújo TL, Andrade DR, Bertoldi AD. Physical activity in adults from two Brazilian areas: similarities and differences. *Cad Saúde Pública*. 2005; 21(2): 573-580.
21. Moulin CC, Tiskievicz F, Zelmanovitz T, Oliveira J, Azevedo MJ, Gross JL. Use of weighed diet records in the evalution of diets with different protein contents in patients with type 2 diabetes. *Am J Clin Nutrition*. 1998; 67: 853-857.
22. Vaz JS, Bittencourt M, Almeida JC, Gross JL, Azevedo MJ, Zelmanovitz T. Protein Intake Estimated by Weighed Diet Records in Type 2 Diabetic Patients: Misreporting and Individual Variability Using 24-Hour Nitrogen Output as Criterion Standart. *J Am Diet Assoc*. 2008; 108(5): 867-72.
23. USDA SR 17 Research Quality Nutrient Data. The Agricultural Research Service: Composition of Foods, Agricultural Handbook no 8 Washington, DC, US Department of Agriculture, 2006.
24. Lima DM. Tabela de Composição dos Alimentos - TACO. Versão II, 2a. Edição, Campinas, SP: NEPA - UNICAMP, 2006.
25. Exler J, Lemar L, and Smith J: USDA. Fat and Fatty Acid Content of Selected Foods Containing Trans-Fatty Acids. U.S. Department of Agriculture; Agricultural Research Service: samples collected between 1989–1993. Available in: http://www.nal.usda.gov/fnic/foodcomp/Data/Other/trans_fa.pdf. Accessed in: March. 2007.
26. Slover HT, Thompson JR, Davis CS and Merola GV. Lipids in Margarines and Margarine-like foods. *J AOAC Int*. 1985;62:775–786.
27. Van Poppel G, Van Erp-Baart M-A, Leth T, Gevers E, Van Amelsvoort J, Lanzmann-Petithory D, Kafatos A, Aroa A. Trans fatty acids in foods in Europe: the TRANSFAIR Study. *J Food Compos Anal*. 1998; 11:112–136.
28. Schakel S, Sievert YA, Buzzard IM. Dietary fiber values for common foods. In: CRC Handbook of Dietary Fiber in Human Nutrition. (ed). Spiller GA: 2001, pp 615-648.

29. Atkinson FS, Foster-Powell K, Brand-Miller JC. International Tables of Glycemic Index and Glycemic Load Values. *Diabetes Care*. 2008; 31(12):1-58.
30. Friedewald WT, Levy RI, Fredrickson DS (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972; 18:499-502.
31. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res*. 1999; 8(2):135-60.
32. Kaaks RJ. Biochemical markers as additional measurements in studies of the accuracy of dietary questionnaire measurements: conceptual issues. *Am J Clin Nutr*. 1997; 65(4 Suppl):1232S-9S.
33. Almeida JC, Zelmanovitz T, Vaz JS, Steemburgo T, Perassolo MS, Gross JL, Azevedo MJ. Sources of protein and polyunsaturated fatty acids of the diet and microalbuminuria in type 2 diabetes mellitus. *J Am Coll Nutr*. 2008; 27(5):528-37.
34. Steemburgo T, Dall'Alba V, Almeida JC, Zelmanovitz T, Gross JL, de Azevedo MJ. Intake of soluble fibers has a protective role for the presence of metabolic syndrome in patients with type 2 diabetes. *Eur J Clin Nutr*. 2009; 63(1):127-33.
35. Silva FM, Steemburgo T, de Mello VD, Tonding SF, Gross JL, Azevedo MJ. High dietary glycemic index and low fiber content are associated with metabolic syndrome in patients with type 2 diabetes. *J Am Coll Nutr*. 2011; 30(2):141-8.
36. de Paula TP, Steemburgo T, de Almeida JC, Dall'alba V, Gross JL, de Azevedo MJ. The role of Dietary Approaches to Stop Hypertension (DASH) diet food groups in blood pressure in type 2 diabetes. *Br J Nutr*. 2011;6:1-8.
37. Cardoso MA, Kida AA, Tomita LY, Stocco PR. Reproducibility and validity of a food frequency questionnaire among women of Japanese ancestry living in Brazil. *Nutrition Research*. 2001; 21:725-33.

38. Fornés NS, Stringhini MLF, Elias BM. Reproducibility and validity of a food-frequency questionnaire among low-income Brazilian workers. *Public Health Nutr.* 2003; 6:821-7.
39. Goris AH, Westerterp-Plantenga MS, Westerterp KR. Underrating and under recording of habitual food intake in obese men: selective underreporting of fat intake. *Am J Clin Nutr.* 2000; 71(1):130-4.
40. Scagliusi FB, Ferriolli E, Pfrimer K, Laureano C, Cunha CS, Gualano B, et al. Underreporting of energy intake in Brazilian women varies according to dietary assessment: a cross-sectional study using doubly labeled water. *J Am Diet Assoc.* 2008; 108:2031-40.
41. Pereira GA, Genaro PS, Santos LC, Sarkis KS, Pinheiro MM, Szjenfeld VL, Schuch NJ, Martini LA. Validation of a food frequency questionnaire for women with osteoporosis. *J Nutr Health Aging.* 2009; 13(5):403-7.
42. Zanolla AF, Olinto MTA, Henn RL, Wahrlich V, Anjos LA. Avaliação de reproduzibilidade e validade de um questionário de freqüência alimentar em adultos residentes em Porto Alegre, Rio Grande do Sul, Brasil. *Cad Saúde Pública.* 2009; 25:840-8.
43. Henn RL, Fuchs SC, Moreira LB, Fuchs FD. Development and validation of a food frequency questionnaire (FFQ-Porto Alegre) for adolescent, adult and elderly populations from Southern Brazil. *Cad. Saúde Pública.* 2010; 26(11):2068-79.
44. Pufulate M, Emery PW, Nelson M, Sanders AB. Validation of a short food frequency questionnaire to assess folate intake. *Br J Nutr.* 2002; 87:383-90.
45. Andersen LF, Veierod MB, Johansson L, Sakhi A, Solvoll K, Drevon CA. Evaluation of three dietary assessment methods and serum biomarkers as measures of fruit and vegetable intake, using the method of triads. *Br J Nutr.* 2005; 93:519-27.
46. McNaughton SA, Hughes MC, Marks GC. Validation of a FFQ to estimate the intake of PUFA using plasma phospholipid fatty acids and weighed food records. *Br J Nutr.* 2007; 97:561-8.

47. Yokota RTC, Miyazaki ES, Ito MK. Applying the triads method in the validation of dietary intake using biomarkers. *Cad. Saúde Pública*. 2010; 26(11):2027-2037.
48. Shai I, Rosner BA, Shahar DR, Vardi H, Azrad AB, Kanfi A, et al. Dietary evaluation and attenuation of relative risk: multiple comparisons between blood and urinary biomarkers, food frequency, and 24-hour recall questionnaires: the DEARR Study. *J Nutr*. 2005; 135:573-9.
49. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran Lipid and Glucose Study. *Public Health Nutr*. 2010; 13:654-62.
50. Burley V & Cade J. Consensus document on the development, validation, and utilization of food frequency questionnaires. In: The Fourth International Conference on Dietary Assessment Methods. 2000, p. 17-20.
51. Takachi R, Ishihara J, Iwasaki M, Hosoi S, Ishii Y, Sasazuki S, Sawada N, Yamaji T, Shimazu T, Inoue M, Tsugane S. Validity of a self-administered food frequency questionnaire for middle-aged urban cancer screenees: comparison with 4-day weighed dietary records. *J Epidemiol*. 2011; 21(6):447-58.

Table 1. Demographic, clinical, anthropometric, and laboratory characteristics of patients included in reproducibility and validity studies

Characteristics	Reproducibility study	Validity study	P value
n	88	72	-
Females	51 (58.0)	40 (55.6)	0.885 ^a
Age (years)	63.3 ± 8.5	61.9 ± 9.3	0.322 ^b
Diabetes duration (years)	10 (3-17)	10 (3-17)	1.000 ^c
Whites	63 (71.6)	53 (73.6)	0.917 ^a
Hypertension	79 (89.8)	63 (87.5)	0.836 ^a
Micro- or macroalbuminuria	28 (31.8)	24 (33.4)	0.963 ^a
Diabetes treatment			
Diet	2 (2.3)	2 (2.8)	
Oral hypoglycemic drugs	39 (44.3)	31 (43.1)	0.302 ^a
Insulin	7 (8.0)	7 (9.7)	
Insulin and oral hypoglycemic drugs	40 (40.5)	32 (44.4)	
Economic status			
Upper and upper-middle class	42 (47.7)	40 (55.6)	
Middle class	41 (46.6)	28 (38.9)	0.980 ^a
Lower-middle and lower class	5 (5.7)	4 (5.6)	
Current smoking	6 (6.8)	4 (5.6)	0.987 ^a
Physical activity: low level	50 (60.2)	38 (55.9)	0.698 ^a
Body mass index (kg/m ²)	29.6 ± 3.9	28.8 ± 4.3	0.219 ^b
Waist circumference (cm)			
Male	102.9 ± 10.7	102.3 ± 10.7	0.724 ^b
Female	100.1 ± 9.6	100.3 ± 10.0	0.897 ^b
Hip circumference (cm)			
Male	103.3 ± 7.1	103.3 ± 7.4	1.000 ^b
Female	106.7 ± 8.0	106.9 ± 8.1	0.875 ^b
Fasting plasma glucose (mg/dL)	163.1 ± 69.2	145.8 ± 59.3	0.095 ^b
Total cholesterol (mg/dL)	177.5 ± 36.9	183.1 ± 45.9	0.393 ^b
HDL-cholesterol (mg/dL)			
Male	42.3 ± 10.7	42.4 ± 11.3	0.954 ^b
Female	47.3 ± 12.5	46.6 ± 13.3	0.732 ^b
LDL-cholesterol (mg/dL)	103.7 ± 31.9	109.3 ± 36.3	0.300 ^b
Triglyceride (mg/dL)	131.0 (95.0-180.0)	119.0 (94.0-178.0)	0.874 ^c
HbA1c (%)	8.9 ± 2.0	8.5 ± 2.0	0.210 ^b
Serum creatinine (mg/dL)	0.9 ± 0.2	0.8 ± 0.2	0.753 ^b

Data are expressed as means ± standard deviation, median (interquartile range) or number of patients with analyzed characteristic (%).

^aChi-square test; ^bStudent's t-test; ^cMann-Whitney test.

Table 2. Energy intake, macronutrients, fiber, glycemic index and glycemic load estimated from the two food frequency questionnaires (FFQ) applied at an interval of one month in patients with type 2 diabetes (reproducibility study, $n = 88$)

Nutrients	1 st FFQ	2 nd FFQ	<i>P</i> value	Pearson correlations ^c	
				Crude data	Adjusted
Energy (kcal)	2205.0 ± 796.5	2137.9 ± 719.3	0.241 ^a	0.725	-
Protein (g)	90.9 (68.0 – 106.2)	86.6 (70.4 – 118.1)	0.396 ^b	0.693	0.602
Carbohydrate (g)	264.7 (212.6 – 308.3)	244.5 (198.6 – 295.2)	0.121 ^b	0.595	0.520
Total fiber (g)	26.4 ± 10.0	25.4 ± 9.5	0.256 ^a	0.563	0.505
Soluble fiber (g)	9.4 ± 3.5	8.9 ± 3.4	0.226 ^a	0.534	0.471
Insoluble fiber (g)	17.0 ± 6.8	16.2 ± 6.5	0.238 ^a	0.536	0.451
Total lipids (g)	81.5 ± 33.6	80.3 ± 25.6	0.582 ^a	0.783	0.658
Saturated fatty acids (g)	24.2 ± 13.4	24.0 ± 9.8	0.802 ^a	0.749	0.609
Monounsaturated fatty acids (g)	26.7 ± 11.6	26.6 ± 8.8	0.919 ^a	0.725	0.634
Polyunsaturated fatty acids (g)	21.4 ± 9.0	21.5 ± 8.2	0.680 ^a	0.925	0.936
<i>Trans</i> -unsaturated fatty acids	1.5 (0.9 – 2.2)	1.6 (1.1 – 2.4)	0.302 ^b	0.683	0.629
Glycemic index (%)	56.5 ± 5.5	55.9 ± 4.6	0.142 ^a	0.623	0.618
Glycemic load (g)	125.7 (96.7 – 167.5)	120.7 (93.5 – 142.2)	0.112 ^b	0.633	0.561

Data are expressed as means ± standard deviation or median (interquartile range).

^aStudent's *t*-test for paired samples; ^bWilcoxon *U*-test for paired samples.

^cThe energy and nutrient values were log-transformed to normalize the distribution and calculate the correlation coefficients. All Pearson correlations are $P < 0.001$

Table 3. Energy intake, macronutrients, fibers, glycemic index, and glycemic load estimated from the 2nd food frequency questionnaire (FFQ) *versus* 3-day mean of weighed dietary records (WDR) by patients with type 2 diabetes (validity study, n = 72)

Nutrients	FFQ	WDR	% of difference ^a	P value	Pearson correlations ^d		
					Crude data	Adjusted	De-attenuated
Energy (kcal)	2175.5 ± 765.3	2023.4 ± 612.9	6.9	0.052 ^b	0.474**	-	0.671
Protein (g)	96.2 ± 39.2	99.1 ± 37.1	-3.0	0.536 ^b	0.432**	0.383**	0.597
Carbohydrate (g)	246.1 (195.7 – 299.1)	235.5 (178.2 – 290.2)	4.3	0.060 ^c	0.398**	0.338*	0.543
Total fiber (g)	25.8 ± 10.1	18.5 ± 8.0	28.3	<0.001 ^b	0.215	0.271*	0.400
Soluble fiber (g)	9.1 ± 3.6	6.6 ± 2.6	27.4	<0.001 ^b	0.246*	0.185	0.302
Insoluble fiber (g)	16.5 ± 6.8	11.7 ± 6.1	29.1	<0.001 ^b	0.126	0.196	0.287
Total lipids (g)	81.2 ± 27.2	73.7 ± 27.1	9.2	0.010 ^b	0.534**	0.552**	0.855
Saturated fatty acids (g)	24.4 ± 10.3	21.1 ± 9.2	13.5	0.005 ^b	0.491**	0.434**	0.687
Monounsaturated fatty acids (g)	27.0 ± 9.1	24.0 ± 8.8	11.1	0.008 ^b	0.407**	0.457**	0.762
Polyunsaturated fatty acids (g)	21.3 ± 8.7	21.2 ± 9.1	0.4	0.854 ^b	0.696**	0.683**	0.912
Trans-unsaturated fatty acids	1.9 ± 0.9	2.0 ± 1.1	-5.2	0.630 ^b	0.329**	0.290*	0.549
Glycemic index (%)	55.8 ± 4.5	57.3 ± 5.0	-2.6	0.041 ^b	0.236*	0.251*	0.481
Glycemic load (g)	120.7 (93.5 – 142.1)	117.4 (92.5 – 159.9)	2.7	0.469 ^c	0.326**	0.308**	0.455

Data are expressed as means ± standard deviation or median (interquartile range).

^aDifference (expressed by %) = [(value from FFQ) – (value of mean from 3-day WDR)]/value from FFQ*100

^b Student's t-test for paired samples; ^cWilcoxon U-test for paired samples.

^dThe energy and nutrients values were log-transformed to normalize the distribution and calculate the correlation coefficients. *P < 0,05; **P < 0,01

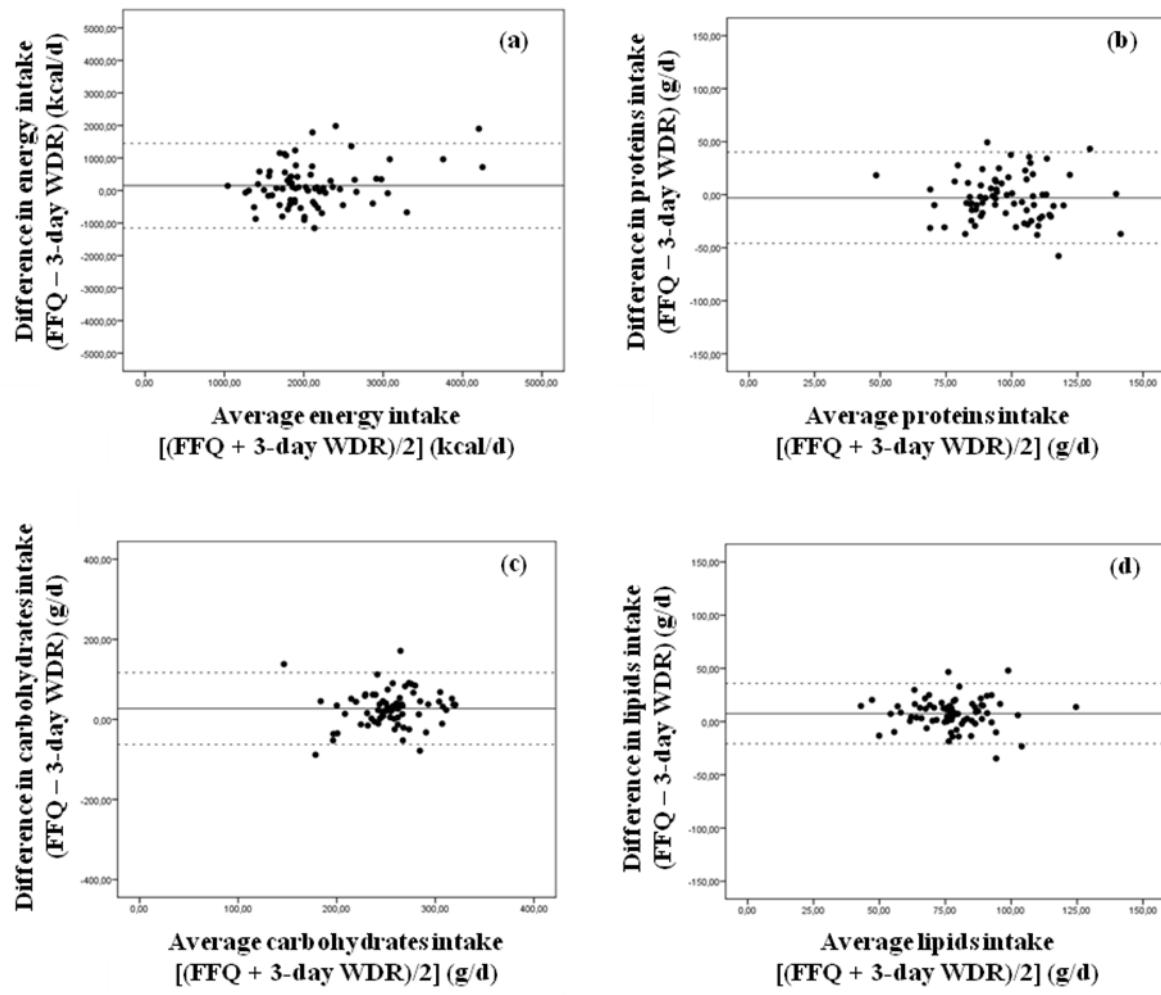


Figure 1. Bland–Altman plots to evaluate the agreement between the values of nutrient intake reported from 2nd food frequency questionnaire (FFQ) with values recorded from 3-day weighed diet record (WDR) in validity study; $n = 72$: (a) energy, (b) proteins, (c) carbohydrates, and (d) total lipids. The mean of the differences (continuous line) and their limits of agreement (dotted lines) are shown. The macronutrient values were energy-adjusted.

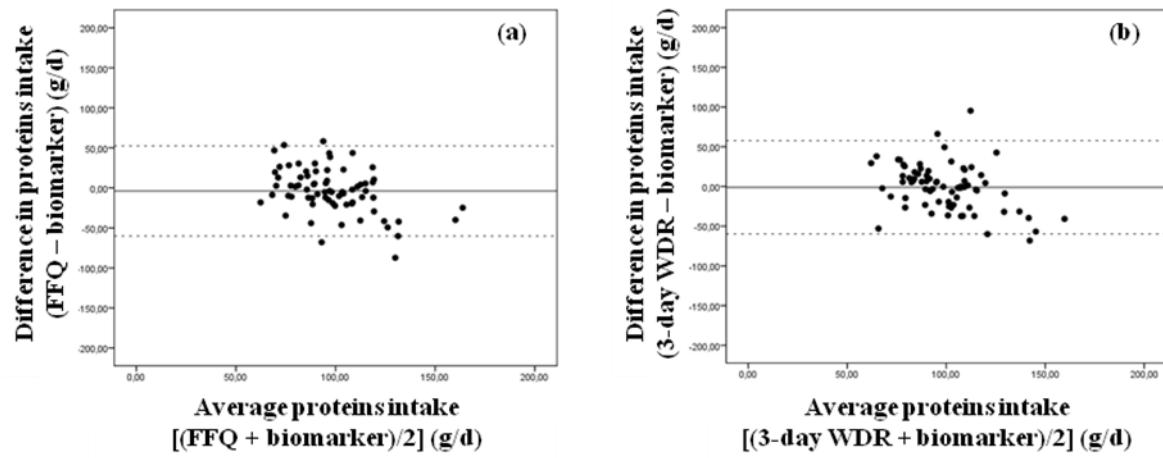


Figure 2. Bland-Altman plots to evaluate the agreement between the values of protein intake estimates from: (a) 2nd food frequency questionnaire (FFQ) with 24-h nitrogen output as biomarker; (b) mean of 3-day weighed diet record (WDR) with 24-h nitrogen output as biomarker (validity study; $n = 72$). The mean of the differences (continuous line) and their limits of agreement (dotted lines) are shown. The values of protein intake estimate from FFQ and WDR were energy-adjusted.