The DHP assesses the impact of diabetes on everyday social and emotional functioning. Well suited to measure the impact of diabetes in a variety of settings from clinical practice to clinical trials, the DHP is simple to complete and score.

With proven psychometric and operational performance the DHP has a number of distinct advantages over other diabetes-specific measures of the psychological and behavioural impact of living with diabetes which include:

- A clearly defined conceptual framework of the measurement model which conforms to the FDA Final guidance for Industry
- The measurement of dysfunctional eating behaviour – which despite its importance in the management of diabetes is absent in other scales
- Content reported by patients as highly relevant to living with diabetes
- The exclusion of skip and hypothetical questions
- The use of straight forward language and simple phrasing
- Simple scoring algorithm
- Norm referenced database

diabetesprofile
Patient research

User Guide

The Diabetes Health Profile (DHP-1 and DHP-18)

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1

Background and development of the Diabetes Health Profile

Chapter 1

Background

Diabetes mellitus is a chronic disorder of the endocrine system in the regulation of blood glucose. The two main types of diabetes are Type 1 and Type 2. With Type 1 diabetes, the beta cells of the pancreas no longer make insulin because the body's immune system has attacked and destroyed them. Treatment for Type 1 diabetes is by regular insulin injections combined with food choices and regular exercise. Type 2 diabetes usually begins with insulin resistance, a condition in which fat, muscle, and liver cells do not use insulin effectively. This results in the pancreas to lose the ability to secrete enough insulin in response to meals. Treatment of Type 2 diabetes includes insulin injections, oral medication and diet.

Associated with long-term complications including blindness, heart and blood vessel disease, stroke, kidney failure, amputations, and nerve damage, diabetes is widely recognized as one of the leading causes of death and disability and in 2006 was the seventh leading cause of death in the USA.

Since 1996 the number of people diagnosed with diabetes in the UK has increased from **1.4 million to 2.6 million**. By 2025 it is estimated that over four million people will have diabetes of which the majority will be Type 2 diabetes, because of the ageing population and rapidly rising numbers of overweight and obese people. Worldwide, diabetes is expected to affect **438 million people by 2030**.

In addition to the physical limitations and complications, diabetes can have a significant impact on the psychological and behavioural functioning including emotional wellbeing, family and social functioning and psychological distress.

Because the management of diabetes requires the active participation of the patient, the importance of evaluating the impact of the disease on the psychological and behavioural functioning of the patient is increasingly being appreciated. This has resulted in the necessity to design instruments that can quantify the patient's psychological and behavioural functioning based on patient self-report, which as part of a larger group of measures, are referred to as patient reported outcomes (PROs).

As with any measure used to make clinical or research decisions, PRO instruments must be shown to be valid and reliable as well as satisfy the increased need for documentation from regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMEA).

The Diabetes Health Profile is one such instrument developed to evaluate the impact of living with diabetes on the psychological and behavioural functioning of living with diabetes.

In 2011, one in every 400 to 600 children were diagnosed with diabetes...

The Conceptual Model

Because of the difficulties and complexities of defining and measuring the patient's quality of life, the focus of the Diabetes Health Profile was the psychological and behavioural dysfunctioning of the person as a consequence of the impact of living daily with diabetes. Therefore, it was considered important that the measure contained content that reflected the outcome from the everyday dynamic interchange between the person with diabetes and the environment and as a result dysfunctional outcomes could be addressed or alleviated through appropriate educational or therapeutic intervention.

Therefore, the theoretical model chosen to under pin the development of the DHP is the "Transactional Theory of Stress and Coping" (Lazarus & Launier., 1978; Lazarus & Folkman., 1984) which views the person and the environment in a dynamic, mutually reciprocal, bidirectional relationship and where the person and environment and the person's relationship with it is constantly changing. The model involves attending to what is actually happening in a specific context and not what is happening in general.

Because many of the traditional approaches to coping have focused on either stable dispositions and or the unidirectional environmental influences, the transactional model in contrast not only affords equal importance to person-environmental factors in coping and adaptation, but also their relationship is seen as reciprocal and dynamic in determining outcome. Figure 1 shows the conceptual model underpinning the development of the DHP.

The rationale for the development of the DHP-18 was the same as the DHP-1 with the difference to develop an instrument using questions from the DHP-1 question set that would be suitable for use across both Type and Type 2 diabetes including insulin, oral and diet.

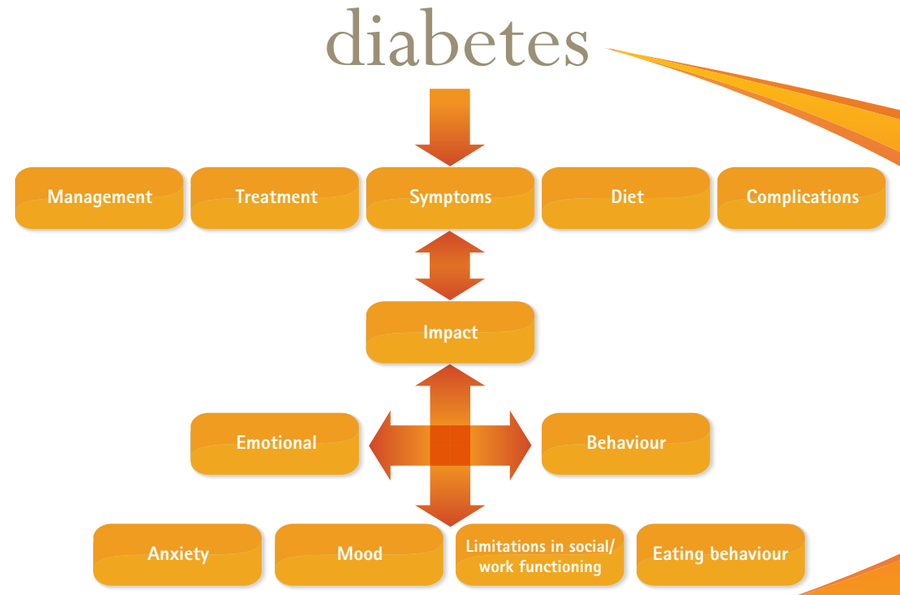


Figure 1.
Diabetes Health Profile
Conceptual Model

Test construction Standards

When the DHP-1 was initially developed the then current psychometric standards found in a number of texts including (Anastasi, 1961; Campbell & Fiske, 1959; Cattell, 1978; Cronbach, 1951; Cronbach & Meehl, 1955; Guildford, 1954) were used as a guide to scale construction. These standards include the elements of validity (content, criterion, discriminant and construct validity) and reliability (internal consistency and test-retest).

These standards are very similar to those proposed by the FDA's Guidance for Industry, Patient-reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims (FDA 2009). We continued this approach for the development of the DHP-18.

The FDA's final guidance also highlighted the importance of patient input in the development and selection of questions and post-construction cognitive debriefing of patients to determine how relevant and understandable the questions are to them. While cognitive debriefing was not part of the initial development of the DHP-1, seven patients were recruited to review questions and indicate those which were difficult to understand or answer. Only one question was identified as problematic. This review was carried out in parallel with a review of question ambiguity by a Diabetologist, Diabetes Nurse Specialist and Dietician. Subsequent research by Knowles & Brazier (2010) and cognitive debriefing as part of the translation of the DHP into other languages has allowed us to confirm both the relevance and understanding of the questions.

Recall Period

The optimal selection of the recall period to provide an accurate picture of the patient's psychological and behavioural functioning can be challenging as the appropriate recall period must take account of the patient burden and ability of the patient to easily and accurately recall the required information. Also within the same disease area, appropriate recall may vary depending on the measured concept or phenomenon of interest e.g. variability, frequency and intensity.

Based upon the above factors all the DHP questions were phrased in the present e.g. "Do you cry or feel like crying" enabling the respondent to provide their own frame of reference using the range of the available response options.

Response Options

The scoring method, which is applied to the Diabetes Health Profile (DHP), is based upon the widely used Likert method of summated scales in which each question is scored using a graded scale and summated to provide a total score for the specific domain (Likert, 1932).

Application of the Likert type scaling approach is based on a number of assumptions. The most important of these being (a) the question is graded on a linear or equal interval scale i.e. that the distance between each grade is the same (e.g. Never, Sometimes, Fairly often, Very often); (b) that it is appropriate to provide equal weights to each question. Both of these assumptions are questionable; nevertheless, it has been shown that simple linear scoring systems are sufficiently robust and suitable for many purposes (Dawes 1979).

For both the DHP-1 and DHP-18 a number of different "forced choice" adjective scales are used to measure either frequency or intensity which depend on the nature of the question asked. These are:

- Always, Usually, Sometimes, Never
- Very often, Often, Sometimes, Never
- Very much, A lot, a little, Not at all
- Never, Sometimes, Fairly often, Very often

Each question is scored 0–3 to provide scale scores of (0) No dysfunction – (100) Maximum dysfunction. Response options are reversed where appropriate.

For both the DHP-1 and DHP-18 the "forced choice" method - where there is no neutral option -was selected. The question whether to include or exclude a "don't know" or neutral option response to survey questions is one that has been considerably debated and has been the subject of both support and criticism. For example it can be seen either as an easy option to take when a respondent is unsure, or whether it can be considered as a true neutral option is questionable. However, it has been shown that when comparing between a 4-point and a 5-point Likert scale, where the former has the neutral option unavailable, the overall difference in the response is negligible. (Armstrong, 1987).

2

Administrating the Diabetes Health Profile

Chapter 2

Modes of Administration

Both the DHP-1 and DHP-18 can be administered in a number of formats, including traditional "paper-and-pencil" (either self-administration or research/clinical staff) and electronic formats (ePRO) such as telephone-based interactive voice response (IVR) systems, hand held devices, PC tablets, and Web-based applications.

Pencil-and-Paper forms

The traditional form of administration of the DHP is for the patient –or where necessary research/clinical staff – to fill in the paper form. The 0-3 scale is presented as tick boxes which are ticked by the patient or research/clinical staff. Research/clinical staff completing the form on the patient's behalf, whether in person or over the phone, are not permitted to direct the patient's responses in any way or to add to or attempt to explain the meaning of the questions.

ePRO

Despite evidence of patient acceptability, high question completion rates and the overall integrity of data collected using the paper version of the DHP, there is both a strong scientific and business case for the creation of a validated electronic version of the measure, which is underpinned by the use of electronic patient reported outcomes as increasingly being seen as essential by clinical trial sponsors for ensuring data integrity and regulatory support.

Benefits of an eDHP

Although paper based PROs are an established and accepted medium which are easy to reproduce and distribute, ePROs offer a number of distinct advantages over paper. Apart from enabling administration of the eDHP in a consistent, standardised and objective manner, a key advantage is the ability to date and time stamp PRO data to avoid the recognised limitation of paper-based PROs 'parking lot effect' where study participants retrospectively and prospectively enter data. As a result sponsors are assured that data are collected at the point of experience and as a result reduces variance in the data which can enhance the study's ability to show efficacy. An eDHP also offers less administrative and participant burden minimises missing data and reduces data entry errors.

Further and significant benefits of the DHP for electronic data capture include the ability to:

- Integrate eDHP data with other electronic data capture, for instance primary clinical endpoints such as patients HbA1c levels and
- Extend to web-browser data collection.

Migrating from paper to electronic data collection is a significant movement in the field of PRO measurement. To retain the integrity of the different administration modalities of the DHP, it can be administered for example using the PHT LogPad which is a hand held device for self-administration, the PHT SitePad which can be used for collecting data from respondents on one mobile device and PHT NetPRO for collecting data over the Internet. However, there is the requirement that sponsors provide evidence to support the comparability or measurement equivalence of the eDHP-18 to the paper-based version from which it has been adapted. It should however, be pointed out that the eDHP has not yet been fully validated.

Validating the eDHP

The level of evidence to support the comparability or measurement equivalence of the ePRO to the paper-based PRO from which it has been adapted will vary in accordance with the magnitude of the modification and its effect on the content, format and interpretation of the PRO questions and scales.

There is evidence however to suggest that the psychometric properties of the original measure will still hold for the ePRO version if only minor modifications have been carried out and that cognitive debriefing and usability testing will likely suffice as the level of evaluation. In cases where substantial modifications have been made, establishing the measurement equivalence of the ePRO is likely to include full psychometric evaluation (Food & Drugs Administration, 2009)

Instructions for Administration the Diabetes Health Profile by Research/ Clinical Staff

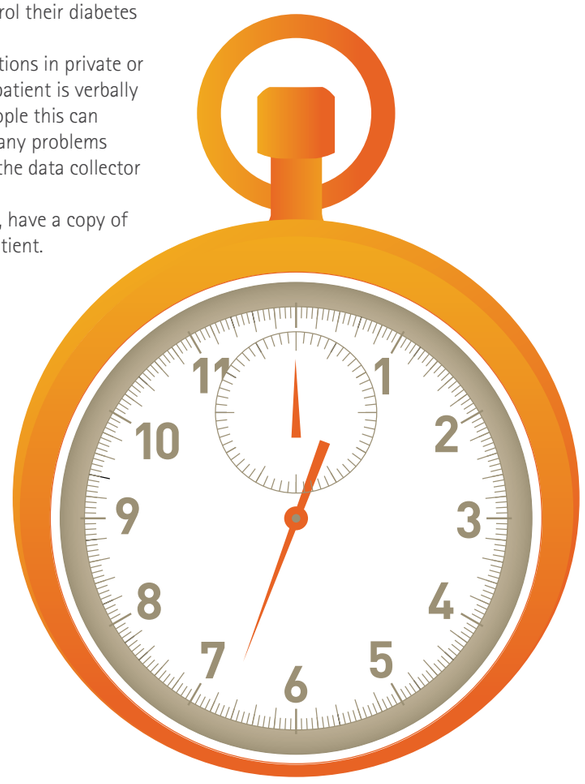
When administering the DHP by research/clinical staff it is essential that data is collected in a standardised way so that the respondent's responses to the questions are not influenced by the behaviour or words of the person collecting the data. It is therefore, important that the data collector remains as neutral as possible. Adherence to the following rubrics should help the data collector remain as neutral as possible.

- Do not respond to what the patient says with statements of concern or sympathy or other signs or indications of how severe you think their condition is as this can influence the patient's responses.
- Do not give specific answers to questions patients ask while answering the questionnaire, and do not offer additional information or clarification about the questions as this may cause them to respond to the questions differently than patients who do not have that information. Instead, simply ask the patient to answer the questions to the best of their ability.
- Do not offer advice on how to prevent, treat, or control their diabetes or other diabetes-related aspects.
- If at all possible, arrange for patients to answer questions in private or away from earshot of other people because when a patient is verbally answering the questions in the presence of other people this can influence the patient's answers and may report that any problems are less severe than they would report if no one but the data collector could hear the answers.
- If the questionnaire is to be completed on the phone, have a copy of the questionnaire available to read along with the patient.

Using a script to administer a questionnaire can help to ensure that patient interactions with a data collector are as uniform as possible. Examples of instructions and scripts for administration are included in Appendix C.

Assessment of Respondent Burden

Completion of the DHP-1 in pencil-and-paper format takes approximately 10-12 minutes and the DHP-18 approximately 6-7 minutes.



Dealing with missing data

Missing data can result because of either the whole questionnaires missing or when respondents fail to complete all the questions in the questionnaire. Missing data may or may not be related to the respondent's quality of life or health status however, when whole questionnaires are missing it is difficult to establish whether complete forms are missing accidentally, have not been received by respondents due to inaccurate sampling frames, respondents are too ill to complete the questionnaire or see little point in responding.

Missing data is of particular concern when carrying out longitudinal or repeated analysis as this can result in loss of power to detect change over time but most significantly where there is a lot of missing data is the extent to which the data received from respondents is representative of the total sample recruited to the study.

Patients who are experiencing a negative impact on their lives resulting from the disease or therapy are less likely to complete the questionnaire. However, missing data has not shown to be a significant problem with the DHP.

Missing questionnaires

When whole questionnaires are missing, there are no easy solutions to addressing the potential bias. As a result, it is essential that procedures are in place to ensure maximum compliance with completing the assessment. There is a considerable literature on improving response rates in questionnaire surveys addressing issues such as: ensuring appropriate administrative and management processes are in place, current name and address registers are used, effective recording of returned questionnaires is carried out, follow up reminders are sent out to non-responders, respondents are provided with clear instructions and guidance as to the purpose of the survey and how to complete the questionnaire.

It is also important to report the extent and reasons for missing data where possible to help identify factors, which contribute to non-response such as the time, questionnaires were sent out e.g. prior to religious holidays and the socio-demographics of non-responders, so that possible biases can be identified and addressed as well as being circumnavigated in future studies. Response rates to postal surveys of the DHP-1 has ranged from 79%-86% while for the DHP-18 which has included multiple questionnaire community surveys has averaged 67% (range 45%-82%) response rates.

Missing questionnaire questions

Respondents will when completing the DHP fail to answer a few questions. This can be due to the respondent simply missing the question or deliberatively omitting to answer the question for a particular reason.

In the initial validation study of the 43-question DHP-1 Meadows et al., (1996) reported that 9% of the sample omitted one-question and 6% two or more. With respect to the DHP-18 Hippisley-Cox et al., (2006) reported that every question in a domain was answered by at least 89% whilst in the UK and Danish samples (Meadows et al., 2000) <6% and 9% of patients respectively failed to answer one question.

Although it is important to distinguish whether questions are missed at random or are not answered for a particular reason, in practice it is difficult to determine the specific reason for missing values. However, generally, missing values can be assumed random, although before such an assumption is made, the nature of missing questions needs to be considered to determine whether a pattern is apparent that would indicate that omission is non-random. Where missing questions are considered to be occurring at random the investigator can calculate scores based on those questions that have been completed by imputing or estimating the missing values.

Various statistical methods can be applied for imputing missing values, but the different strategies can have implications for analysis of data when assessing outcome of interventions or psychometric properties of a questionnaire. With the former we require an unbiased outcome value, where as with latter our concerns are more to do with inter-correlations of the scale.

When undertaking psychometric analyses this will often involve correlational analysis and techniques such as regression may over-estimate the correlations involving missing questions, although this will be less of a problem if the number of missing values for an question is low.

> *Although it is important to distinguish whether questions are missed at random or are not answered for a particular reason, in practice it is difficult to determine the specific reason for missing values.*

There are a number of options for dealing with missing values. These include imputing the mean of the question responses from other respondents, regressing the missing question on remaining scale questions, treating the scores for that question as missing. For the former the limitations are that the imputed values will differ from study to study where as with the later, this could result in 20% or more of respondents scale scores missing with a questionnaire comprising 20 questions.

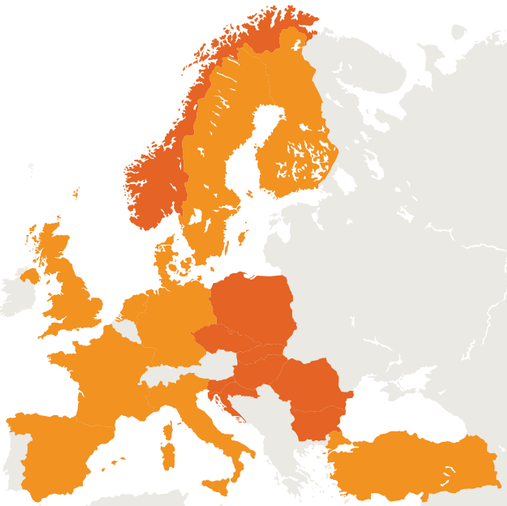
A commonly used strategy in dealing with missing values when not undertaking psychometric analysis is to substitute the missing value with the mean of the respondent's answered questions for the specific domain as long as half or more of the questions have been answered. This is also known as the 'half rule' where more than half the questions have missing values the score for the domain should be set to 'missing'. However, use of the 'half rule' should be used with caution when questions have been ordered hierarchically such as the ability to walk given distances or other levels of disability or dysfunctioning. The DHP does not have a hierarchical structure to the ordering of its questions and therefore, using the 'half rule' is the specified method for substituting missing values for all versions of the DHP.

Foreign Language Versions of the DHP

All language versions of the Diabetes Health Profile have undergone extensive linguistic validation in accordance with currently accepted methodology accepted by the MOT and other international groups, ISPOR guidelines and the standards accepted by regulatory agencies such as the FDA. All new translations must undergo the appropriate procedures in accordance with currently accepted methodology and guideline which will include forward and backward translations by native speakers, pilot testing with cognitive debriefing and international harmonization to ensure conceptual equivalence and proof reading by native translators.

Table 13. Current translations

DHP-1	DHP-18
-	Bulgarian
-	Croation
-	Czech
Danish	Danish
Dutch	Dutch
Dutch (Belgium)	Dutch (Belgium)
English (Canada)	English (Canada)
English (USA)	English (USA)
Finnish	Finnish
French	French
French (Belgium)	French (Belgium)
French (Canada)	French (Canada)
-	French (Swiss)
German	German
-	German (Austria)
-	German (Swiss)
-	Hungarian
Italian	Italian
-	Italian (Swiss)
-	Manderin
-	Norwegian
-	Polish
-	Romanian
Turkish (German)	Turkish (German)
-	Slovak
-	Slovenian
Spanish	Spanish
Spanish (USA)	Spanish (USA)
Swedish	Swedish



6

Foreign Language Versions of the DHP

Chapter 6