Chapter 31

DIABETIC CARE

Technology Will Improve Diabetics' Quality of Life

Golo von Basum[1], Rufus Driessen[1], Francisco Morales[1], Begonya Otal[2] and Kristiane Schmidt[1]

[1]Philips Research, Eindhoven, The Netherlands; [2]Philips Research, Aachen, Germany

Abstract: According to the WHO, diabetes is one of the most growing diseases today population-wise[1]. Looking at estimations there will be more than 333 million diabetics by 2025. This justifies efforts to develop new technologies in helping diabetics in their daily life. We briefly describe the background of diabetes, show a potential segmentation of the diabetic population and illustrate their primary needs. Amongst them, we identify the three most important unmet needs, i.e. painless glucose monitoring, decision support, and lifestyle support. We believe that new technological solutions have the potential to fulfill these unmet needs. This will make meaningful contributions by reducing the daily burdens of diabetes management, reducing long-term complications and generally improving the quality of life for diabetics.

Keywords: Diabetes, lifestyle, decision support, non-invasive, diabetes management

1. BACKGROUND ON DIABETES

Diabetes is a metabolic disorder in which the human body either fails to produce or to properly use insulin; a hormone that regulates uptake and transport of glucose. Currently, diabetes affects more than 194 million people worldwide[2]. The number of people suffering from diabetes is rapidly increasing, and is estimated to exceed 333 million by 2025[2]. At least 50% of all people with diabetes are unaware of their condition.

In the long term, diabetes can cause a variety of severe complications, such as blindness, cardiovascular diseases, kidney failure, and lower limb amputations. In most developed countries, diabetes and its complications are already the fourth main cause of death[3].

G. Spekowius and T. Wendler (Eds.), Advances in Healthcare Technology, 517-532.

Apart from the enormous physical and emotional burden of the disease and its complications for the individual, diabetes also has a major impact on Healthcare infrastructure and Healthcare expenditures. The American Diabetes Association estimated that in 2002 diabetes cost the US Healthcare System and economy approximately $132 billion[4].

1.1 Types of diabetes

About 5-15% of diabetics are afflicted by what is known as type 1 diabetes[2]. Type 1 diabetes is an autoimmune disease, in which the body's immune system destroys the insulin producing β cells of the pancreas. This results in an inability to produce insulin. Type 1 diabetes tends to occur in people of less than 20 years of age.

The majority of diabetics however suffer from type 2 diabetes, which is usually associated with insulin resistance. In this condition the pancreas cells are able to produce insulin, but the insulin cannot stimulate the uptake of glucose into muscle and adipose cells[5]. Type 2 diabetes is often, but not always, associated with obesity, which in itself can cause insulin resistance. Usually, the condition is diagnosed after the age of 40, and its prevalence increases with age. However, the number of young people and even children with type 2 diabetes is increasing, most likely due to obesity and physical inactivity.

Type 2 diabetes is often preceded by pre-diabetes, an asymptotic condition where blood glucose levels are elevated. Individuals with pre-diabetes are at high risk of progressing to type 2 diabetes, although such progression is not inevitable. Probably over 30% of these individuals will return to normal glucose tolerance over a period of several years[6]. In 2003, worldwide about 314 million people had impaired glucose tolerance (IGT)[2]. Several clinical studies have shown that type 2 diabetes can be prevented or at least delayed by lifestyle changes[7].

Gestational diabetes is defined as IGT that is first detected during pregnancy. About 7% of all pregnancies are affected by gestational diabetes, which is strongly associated with both maternal and fetal complications[8].

1.2 Pathophysiology and complications of diabetes

Without treatment, diabetes results in hyperglycemia, which is a very high level of glucose in the blood (above 10 mmol/l; 180 mg/dl). Even slight hyperglycemia is strongly associated with long-term complications of diabetes[9]. Diabetic people often also suffer from hypoglycemia, which is too low blood glucose levels (below 3 mmol/l; 54 mg/dl). Hypoglycemia is mainly caused by too much insulin and/or too little food intake and can easily be treated by carbohydrate intake. However, if a diabetic person is not able to feel hypoglycemia or if hypoglycemic episodes occur during the night, a life threatening condition could occur.

Insulin stimulates the uptake of glucose into muscle and adipose tissue. In addition, insulin suppresses the release of glucose from the liver and of fatty acids from adipose tissue[10]. The latter explains why most diabetic people also have elevated lipid levels, i.e. cholesterol and triglycerides. Insulin also stimulates nitric oxide (NO) synthase in the vascular endothelium and thus may increase tissue perfusion[11].

Table 31-1 summarizes the long-term complications of diabetes. Microvascular complications are caused by dysfunction of the capillaries and small blood vessels. The main cause for these complications is hyperglycemia. Macrovascular complications are due to alterations in the large blood vessels, for instance arteriosclerosis. Besides hyperglycemia, dyslipidemia (abnormal lipid levels) and hypertension (high blood pressure) are involved in macrovascular complications [5].

Table 31-1. Long-term complications of diabetes.

	Complication	Description
Microvascular	Retinopathy	Damage of eye capillaries, leading cause of blindness.
	Neuropathy	Impairment of nerves, especially in the lower extremities. Loss of sensation, pain (tingling), numbness. Foot ulcers, leading cause for lower limb amputation.
	Nephropathy	Impairment of kidney function. Most common single cause for end-stage renal disease. May require dialysis or kidney transplantation.
Macrovascular	Coronary heart disease	Heart attack, myocardial infarction. Major complication in type 2 diabetes.
	Peripheral arterial disease	Decreased perfusion of lower extremities. Foot ulcers, leading cause for lower limb amputation.
	Cerebrovascular disease	Blockage of blood vessels in the brain. Transient ischemic attacks, stroke.

1.3 Treatment

Until now, there is no cure for diabetes, but optimized treatment can greatly reduce long-term complications. The main target for the treatment of all types of diabetes is glycaemic control, which means bringing the blood glucose levels as close as possible to normal. All type 1 diabetics need to be treated with multiple daily injections of exogenous insulin. The exact amount of insulin that is needed depends on the actual blood glucose level as well as the anticipated intake of carbohydrates (diet) and glucose consumption by the body (muscle activity). The diabetic person must also monitor her blood glucose levels at least three times per day by SMBG (self-monitoring of blood glucose).

For type 2 diabetics, the treatment depends on the severity of β cell failure. A minor fraction of type 2 diabetics requires insulin therapy as described above for type 1. The majority of people with type 2 diabetes use oral agents to lower their glucose levels. Again, the diabetic person has to control the effectiveness of the treatment by performing SMBG. Besides medication, the glucose levels can also be lowered by dietary changes (lowering the carbohydrate intake), weight loss and, most importantly, by physical exercise. During exercise, the uptake and metabolism of glucose is stimulated independently of insulin. In addition, exercise also has been reported to increase insulin sensitivity[5]. For the treatment of pre-diabetes, lifestyle modifications have been shown to be even more effective than treatment with oral agents[7]. For more detailed and in-depth information related to diabetes treatment, refer to the diabetes compendium by Berger[12].

2. NEEDS OF DIABETICS

2.1 Segmentation of diabetic population

The large population of diabetics consists of many different groups, each with different lifestyles and each dealing with diabetes their own way. We will show seven criteria for a possible segmentation (see Table 31-2) and give examples for specific *needs* and *technologies* in the different groups.

Table 31-2. Segmentation is based on 7 sets of classification criteria.

	Criteria	Range
1	Type of diabetes	Type 1 – type 2 – gestational – pre-diabetes
2	Insulin	Insulin-dependent versus non-insulin-dependent
3	Compliance level	Highly compliant … non-compliant
4	Type of glycaemic management	Self-management … assisted-management
5	Age	Children – adolescents – adults – elderly
6	Diagnosis	Diagnosed versus non-diagnosed
7	Type of chronic complications	Neuropathy, nephropathy, retinopathy, macrovascular

Type of diabetes. The most obvious and commonly used breakdown of the diabetic population is based on the type of the diabetes: type 1, type 2, gestational and pre-diabetes. The segmentation could be extended to those people who are at risk for developing diabetes. A first example for technology related to this criterion is *tight glycaemic control*, which plays an important role in the segments of type 1 diabetes and gestational diabetes. A second example is technology that *supports awareness* of the disease. This is of interest for newly diagnosed diabetics, but is also valid for pre-diabetes and part of the type 2 diabetics. An extension of this technology could be a solution to *support lifestyle*: this can play a role in the total diabetic population.

Insulin. The diabetic population can be divided into insulin-dependent and non-insulin-dependent. All of type 1 diabetics are insulin-dependent, as well as a part of type 2 diabetics. They require insulin therapy to control their blood glucose levels. Technologies for insulin-dependent diabetics could include *decision support* in dosing the right amount of insulin at the right time. Furthermore, a technology is required for *delivering insulin* and other medications into the body. A last example is a *non-invasive* and *quasi-continuous* glucose monitoring technology that would help realizing well-controlled insulin dosing.

Compliance level. The level of compliance in monitoring blood glucose values is a third consideration. While the recommended testing frequency may vary from eight times per day to once a week or even less, in general the actual finger-stick test frequency falls short. The compliance of a diabetic depends mostly on her disease awareness or denial. Also, personal motivation is important when discussing compliance. Although technology may help diabetics to be more motivated, technology by itself is not sufficient. Key technology drivers that will support compliance are *painless and bloodless monitoring*. For non-compliant diabetics, ignorance or denial shows up. Here technology may play a role in *personalizing education* and in *providing meaningful data* that matches the diabetics' compliance level.

Type of glycaemic management. Another way to look at diabetes is to define who is actually performing the day-to-day managing of blood glucose levels. This can either be the diabetic herself (self-management) or somebody else helping the diabetic (assisted-management). In the case of self-management, the user is the diabetic, who needs to integrate monitoring of glucose and administering of medication in daily life. Therefore, *portability* and other *ease-of-use* aspects are important. In the case of assisted glucose management, the user is not the diabetic, but somebody assisting her.

Age. Yet another way to divide the diabetic population is by age: children, adolescents, adults and elderly. Each age-group may require specific technology solutions. An example is that elderly people may require a user interface with *larger displays* and *buttons*.

Diagnosis. Another split of the population is the diagnosed versus the undiagnosed. The undiagnosed is suffering from the same disease as the diabetic but is not aware of it: her blood glucose level will make excursions outside of the normal range. A large part of the type 2 diabetics are undiagnosed. Technology to *screen* and to *identify people* with type 2 diabetes or pre-diabetes will help in reducing its impact.

Type of chronic complications. Finally, chronic complications related to diabetes is another set of classification criteria. A simplified classification is based on macrovascular diseases and microvascular complications. Each of these areas requires specific technologies to avoid, to reduce or to treat the complication. A specific example is technology for *early detection and treatment of foot ulcers*.

This possible segmentation of the diabetic population will help to address the diverse groups of diabetics with individualized technological solutions. Thus, it makes it easier to identify characteristic needs for the separate groups of diabetics.

2.2 Analysis of the diabetics' needs

For undiagnosed people, sometimes a complication of diabetes may give a clue to the presence of the disease. However, these complications are not unavoidable consequences. A healthy, active lifestyle is a lifetime plan. According to that, every diabetic person runs generally through the same basic needs in which lifestyle modifications are essential.

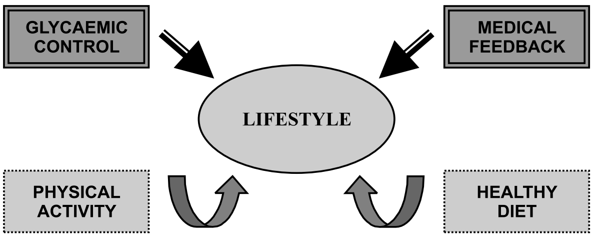

Figure 31-1. Basic diabetic needs, which every diabetic is confronted with.

Figure 31-1 shows the basic needs grouped in four main categories. These four needs, which every diabetic is daily confronted with, are generally described as follows:

Glycaemic control. Tight glycaemic control slows down the onset and progression of diabetes complications. Thus, good diabetes care always begins at home using SMBG. Glycaemic control is the cornerstone for preventing unwanted complications.

Medical feedback. The primary care team plays an important role in diabetes management. Ideally they should be offering step-by-step diabetes self-management education on the one hand, and personalized feedback on the other hand. First of all, they have to pay attention to behavioural changes of all diabetics, such as smoking cessation, adequate nutrition, enough exercise and, above all, right glycaemic control. Moreover, early diagnosis of diabetes is also essential in order to delay or even avoid long-term complications. Last but not least, diabetic people must be reminded of yearly and monthly visits when the time approaches, as a way to increase motivation and compliance.

Physical activity. Physical activity can lower blood glucose, blood pressure, and cholesterol. In addition, regular activity helps insulin to work better and improves blood circulation. Most doctors recommend diabetics to participate in regular aerobic exercise. There is a vital need in increasing motivation for committing to regular exercise and physical activity.

Healthy diet. Food and blood glucose levels are closely correlated. Knowing the food composition – the calories, carbohydrates, protein, and fat – will help in controlling blood glucose levels. Most diabetics will need to make some changes to their eating habits. However, this does not mean that they have to follow a special diet – the diet recommended for people with diabetes is a general healthy diet.

2.3 Key unmet needs

In the following, we will identify those main needs of a diabetic person that will enable her to improve quality of life accordingly to her type of diabetes and personal condition. Within the afore described four groups, the following three key unmet needs are identified:

Painless, blood-free glucose monitoring. Nowadays, diabetics use finger stick meters, which require a fingertip puncture to withdraw a drop of blood. This procedure causes pain and carries risk of infection. It also exposes a diabetic's surroundings to blood and creates an uncomfortable social situation that diabetics strongly avoid. The pain perception during a finger stick test is the major hurdle for frequent testing. Therefore, a painless and if possible non-invasive meter to determine blood glucose values is the most desired tool. Apart from this main feature, accuracy and portability are of fundamental interest. People want reliable blood glucose values, and to measure blood glucose everywhere and whenever it is required. This need is most present in the segments of type 1 and type 2 diabetics, as well as in the gestational diabetics. It also relates to the segment of compliance.

Decision support. Tight glycaemic control increases the risk of hypoglycaemic events[13]. Diabetics are therefore confronted with the difficulty of keeping their blood glucose values in a very defined regime. Food intake will influence their glucose values, as well as physical activity and of course insulin dosing. Bearing this in mind, every diabetic will find it beneficial not only to measure her current blood glucose level, but also to be able to anticipate its value one or two hours in advance. Easy, comfortable and nontime consuming prediction of blood glucose values is therefore another key unmet need.

Lifestyle support. The basis of managing diabetes nowadays is a change of the lifestyle of the diabetic to prevent long-term complications. These complications are to blame for a reduction in quality of life and in lifetime expectancy. A lifestyle support concept is also a key unmet need and probably the most ambitious to work on, because motivation and educational aspects play the essential role here. Every diabetic requires personalized and continuous coaching in order to manage her disease. Thus, there is on the one hand a need for facilitating relations among diabetics and medical care providers, and on the other hand a need for personal encouragement and responsibility for the own disease.

As portrayed in Figure 31-2, the lifestyle support concept will benefit from the previously identified needs. Generally depicted, the lifestyle support solution will help diabetics to delay or prevent serious complications associated with their disease by providing answers and explanations, as though one had a virtual nurse as a companion.

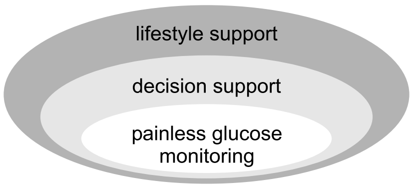

Figure 31-2. The key unmet needs from a diabetic perspective.

The three here presented key unmet needs are a step further in the direction of diabetes management, which will assist every diabetic to keep up with the suggested medical guidelines. These diabetic needs turned into technological solutions will help not only the person in her new way of living, but also the physician to manage the disease.

3. TECHNOLOGIES AND APPLICATIONS

In this section we describe potential solutions for the afore-mentioned most important unmet needs. These include technologies and applications to address:

- Painless, blood-free monitoring.
- Decision support.
- Lifestyle support.

3.1 Non-invasive glucose monitor

Diabetics from all types need to measure their blood glucose values frequently to ensure tight glycaemic control. From the analysis of the key unmet needs we derived the following three main issues related to glucose monitoring: painless, easy-to-use and sufficiently accurate technology. Such a technology will lead to a much higher acceptance and compliance by the diabetics compared to existing technologies, like finger stick devices. This will help encourage more frequent testing and thus a better control of the diabetes.

Figure 31-3 gives an example how inadequate testing could lead to problems in tracking the correct glucose values. The continuous trace shows the glucose values of a non-diabetic person recorded with a sample interval of five minutes (continuous). This data is taken from literature[14]. We additionally marked points at intervals of two hours. It is obvious that due to this undersampling nearly every excursion of the glucose value is missed. Gough et al. found, that the optimal sampling frequency is in the order of 10 minutes[15].

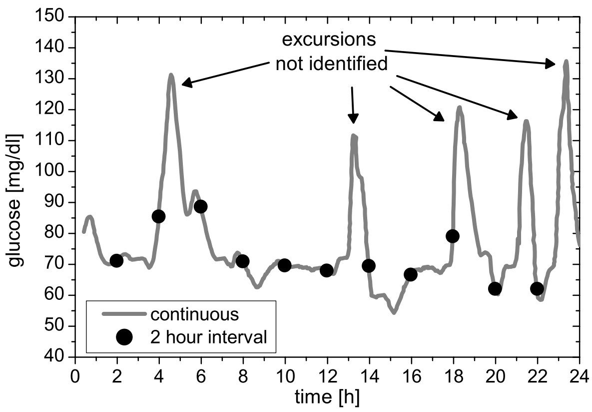

Figure 31-3. Example of undersampling[14].

In the analysis of potential solutions, we will focus on truly non-invasive technologies to ensure the aspect of painless monitoring and avoiding the risk of infection or contamination. This means that these technologies should not require any analyte extracted from the body (e.g. blood or interstitial fluid). Such techniques have been investigated extensively for many years. Khalil[16] has given an excellent overview of the recent developments in the area of non-invasive glucose measurement techniques. The most extensive investigated approaches are optical techniques, which make use of the specific absorption spectrum of glucose. The wavelength regions vary from near infrared (NIR, 800 – 2000 nm) up to the mid infrared (MIR, 2000 – 10000 nm). The optical techniques include diffuse back-reflectance spectroscopy, Raman spectroscopy, attenuated total reflectance (ATR) spectroscopy, optical coherence tomography (OCT), and photoacoustic spectroscopy. All of them assume to be able to measure directly the effect of glucose on the spectrum. Besides these, non-optical methods also have been reported, like *in vivo* electrical impedance measurements.

A common challenge for many non-invasive techniques relates to the measurement volume, where glucose is mainly present in interstitial fluid and capillary blood. When comparing these glucose values with values obtained directly from venous blood, they often show a lag time due to metabolism, vasoconstriction and perfusion. But recent research shows promising results to address this lag time issue[17]. Another difficulty arises from substances present in human skin, which may hamper a correct glucose determination. These factors add up to the challenge of sufficient accuracy and specificity.

Although none of the current non-invasive technologies, which are reported in literature, is able to solve all of these problems, major steps towards sufficient accuracy and specificity have been made[16]. Moreover, we believe that in near future, the problems related to truly non-invasive glucose measurements will be overcome.

3.2 Decision support technology

The second identified unmet need mainly addresses the issue of appropriate glycaemic control. This includes prediction of future glucose values, giving advice for food intake, alerting in case of hypoglycaemia, and advising insulin dosing. Decision support technology should give advice or recommendation to help regulate the blood glucose values on a short-term time scale (e.g. hours).

For any technology addressing this need, it is crucial to develop suitable algorithms helping to predict future glucose values. As for the painless, non-invasive glucose meter, work has been done in this area by different academic groups[15,18,19,20]. The basic scheme for a decision-supporting algorithm is shown in Figure 31-4.

The most important input parameter for a model to predict future glucose values is the history of measured glucose values. It is obvious that the shorter the measuring interval is, the better the prediction algorithms will perform. Thus, the most suited measuring method to enable a decision tool should be a quasi-continuous technology. Apart from pure measurements of glucose values, a good and simple logging of these values is needed. This will give the diabetic a better insight into her disease, and it will also help the care provider to evaluate and to set up the therapeutic treatment.

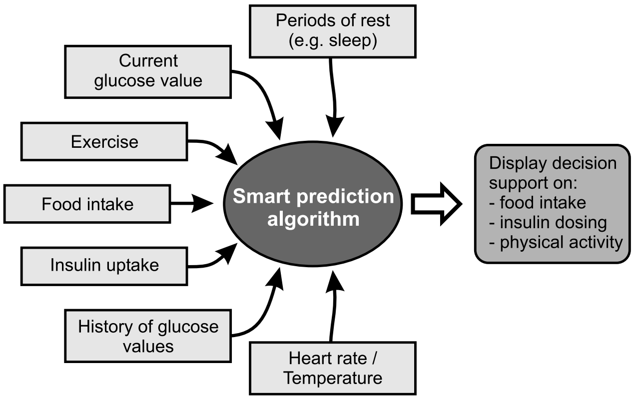

Figure 31-4. Overview of a decision support algorithm.

We mentioned already, that the development of diabetes is strongly affected by the physical condition of the diabetic person, the food intake, and the overall lifestyle situation. All this, of course, has consequences on the short-term change of the blood glucose values. Thus, additional input parameters will improve the prediction model significantly. A tool for decision support should include input for food intake, times and level of exercising, or periods of rest or sleep. Furthermore, other vital body signals like heart rate or temperature will improve the quality of prediction. A major challenge to gather this information is the development of unobtrusive sensors.

A very important point to keep in mind when investigating decision support algorithms, is the unique personal situation of every single diabetic. This requires highly personalized and adaptive tools, which for example take care of the individual metabolism, clinical history, lifestyle situation, or even changes of the diabetes in time. For good predictions, not only past or current actions should be transferred to the algorithm, but also actions planned in the near future. This information could then be considered when calculating glucose and insulin metabolism.

A further feature of decision support should be the advice when to use insulin. Zisser et al.[21] showed that run-to-run control of glucose levels as direct reaction of insulin intake could be used to calculate the personalized best insulin dosing prior to a meal based on the recorded history of the diabetic. The optimal solution would be an intelligent self-learning algorithm, which adapts to the personal situation of the individual diabetic. Apart from concrete actions to change glucose levels, the tool might also give advice on the most suitable measurement intervals, or give an alarm when the next measurement should be taken.

The goal of any new technology enabling decision support should be an easy-to-use and simple application from the diabetics' perspective, relieving them from risks and from the burden of worries. It needs to provide meaningful directives to the diabetic, which are actionable. This will also help to increase the quality of life by enhancing the confidence of a diabetic in taking action related to her condition. Currently there is no good and simple-to-use tool for decision support available on the market, but we believe that algorithms can be developed and implemented in devices for home use.

3.3 Lifestyle support

The life of a person dramatically changes from the moment she is diagnosed with diabetes. This is a very crucial moment in her life because she will be confronted with two major problems:

- You have a chronic, incurable disease that will accompany you for the rest of your life: If you do not change your lifestyle, it will not get better, but it may get worse.
- You have to change your lifestyle in order to keep on living and to avoid potential complications.

This section concentrates on technical options that can improve a diabetic's health during gradual changes in the lifestyle that will match her self-discipline and will empower her, taking away the burden of worries.

Besides the stigma of a chronic disease, the diabetic person has little support dealing with the disease, because almost everything is based on self-treatment. She defines whether to measures glucose levels and when. The calculation of calorie intake is based on her heuristic best guess. The amount of medication is self-dosed, hopefully according to the guidelines given by the general practitioner. She also has to estimate the amount of energy spent during more extenuating physical activity, thus lowering the need of additional amounts of medication. In summary, the disease is always very present in a diabetic's daily life due to the burden of responsibility.

Technology and education of diabetics will enable a change in today's diabetes management. Technology will additionally enable diabetics to start living a more normal life with fewer worries reducing the pressure of responsibility, while maintaining a healthy consciousness of the disease. The former will give people a self-assuring feeling, while the latter is important because diabetics learn to accept the disease rather than denying it. Depending on the level of disease awareness and education, specialized programs can coach diabetics while keeping them motivated to start new phases of treatment and to keep on learning about their disease, and thus inducing more positive changes in the diabetic's lifestyle.

We assume that solutions for lifestyle support must have an integral approach empowering diabetics with autonomy and independence, while keeping them mobile and assuring the right treatment at the right time. We can look at it from two different perspectives: from the diabetic's point of view and from the technological point of view. Furthermore, every perspective can be split in subcategories where the solutions will play a role. We foresee the subcategories as shown in Table 31-3.

Table 31-3. Technology perspectives and subcategories.

Perspective	Subcategory	Definition
Diabetics perspective	Advanced support and coaching	Set of solutions that will support diabetics in their lifestyle changes.
	Healthcare system	General Practitioner, specialists, nurses, hospitals, analysis laboratories.
Technology perspective	Diabetes companion	Portable device that diabetics carry around for lifestyle support.
	Home Health Center	Stationary set of infrastructure based at the diabetic's home that enables data transmission and further diagnostic at home.
	Telemedicine	Support infrastructure that assures that diabetics' data are saved and that proper reporting to the healthcare system occurs at the right time. This might include a two-way communication channel with a Healthcare center, but also a TV set.

Table 31-4 shows the two perspectives with the subcategories, and in addition, some examples of solutions by the technology offerings. These technological solutions will positively influence diabetics' lifestyle and hence their quality of life. We believe that technology and technology trends will make these solutions possible in a foreseeable time horizon. Key technologies that will definitively play an important role are:

- Optical techniques for diagnosis and measurement, but also for treatment
- Self-learning user interfaces that will adapt to diabetics' needs and awareness level
- Miniaturization of electronics for wearable devices and energy management

- Unobtrusive sensors to measure body signals
- Cost-effective biosensors for home use
- Integration of complex systems in meaningful architectures to bring components to an integral system.

Table 31-4. Technological solutions.

		Diabetics' perspective	
Technology perspective		*Advanced Support and Coaching*	*Healthcare system*
	Diabetes companion	• Measures glucose non-invasively • Provides decision support • Reminds that measurement has to be taken • Reminds to take medication • Coaches during exercise • Counts calorie intake • Counts calories consumption	• Downloads data to physician • Keeps track of diabetics' clinical history • Provides ubiquitous information access
	Home Health Center	• Provides decision support • Gives foot care (perfusion, pressure, etc.) • Detects extremity ulcers and decubitus • Measures additional blood analytes to secure compliance • Measures other body quantities	• Informs to contact healthcare provider in case some indicator surpasses a boundary • Broadcasts information to the healthcare provider
	Tele-medicine	• Provides education targeted to a specific diabetic person • Helps to configure • Coaches diabetics to set goals • Helps diabetics to keep motivated	• Physician can change medication / treatment • Education on early screening

Finally, these technological solutions will have to be integrated in the total Healthcare environment to create a diabetic-centered disease management.

4. CONCLUSIONS

Diabetes is one of the most growing diseases today population-wise. Looking at estimations there will be more than 333 million diabetics by 2025. This justifies efforts to develop new technologies helping people to improve their quality of life. We described a segmentation of the diabetic population, which allows for addressing the diverse groups of diabetics with individualized solutions. For this segmentations seven separate criteria are selected. From the numerous general needs of diabetics, we identified the three most important needs, which could be fulfilled by breakthrough inventions. These technologies include truly non-invasive blood glucose monitors, decision support tools and lifestyle support. All mentioned technologies are currently not available on the market, but we believe that it is possible to overcome most of the current restrictions. This will help the majority of diabetics reduce the burden of their disease, improve their daily living and significantly reduce long-term complications associated with elevated blood glucose values.

ACKNOWLEDGEMENTS

We would like to thank Gerald Lucassen, Rachel Thilwind, Markus Laubscher, Sieglinde Neerken and Dan Barton for their useful comments on the manuscript.

REFERENCES

1. World Health Organization (September 16, 2005); http ://www. who. int/ dietphysicalactivity/publications/ facts/diabetes.
2. International Diabetes Federation, *Diabetes Atlas, Second Edition* (International Diabetes Federation, Brussels, 2003).
3. International Diabetes Federation, *Diabetes and Cardiovascular Disease: Time to Act* (International Diabetes Federation, Brussels, 2001).
4. P. Hogan, T. Dall, P. Nikolov, Economic costs of diabetes in the US in 2002, *Diabetes Care* **26**(3), 917-932 (2003).
5. S.A. Ross, E.A. Gulve, M. Wang, Chemistry and biochemistry of type 2 diabetes, *Chem Rev* **104**(3), 1255-1282 (2004).
6. K.G. Alberti, The clinical implications of impaired glucose tolerance, *Diabet Med* **13**(11), 927-937 (1996).
7. M. Laakso, Prevention of type 2 diabetes, *Curr Mol Med* **5**(3), 365-374 (2005).
8. T.L. Setji, A.J. Brown, M.N. Feinglos, Gestational Diabetes Mellitus, *Clin Diabetes* **23**(1), 17-24 (2005).
9. I.M. Stratton, A.I. Adler, H.A. Neil, D.R. Matthews, S.E. Manley, C.A. Cull, D. Hadden, R.C. Turner, R.R. Holman, Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study, *B M J* **321**(7258), 405-412 (2000).
10. M. Stumvoll, B.J. Goldstein, T.W. van Haeften, Type 2 diabetes: principles of pathogenesis and therapy, *Lancet* **365**(9467), 1333-1346 (2005).
11. K. Shinozaki, K. Ayajiki, A. Kashiwagi, M. Masada, and T. Okamura, Malfunction of vascular control in lifestyle-related diseases: mechanisms underlying endothelial dysfunction in the insulin-resistant state, *J Pharmacol Sci* **96**(4), 401-405 (2004).

12. M. Berger, *Diabetes mellitus* (Urban & Fischer, München, 2000).
13. American Diabetes Association, Implications of the Diabetes Control and Complications Trial, *Diabetes Care* **25**(Supplement 1), 25-27 (2002).
14. Project for Glucose Monitoring and Control (September 16, 2005); http://www.glucosecontrol. ucsd.edu/data.html.
15. D.A. Gough, K. Kreutz-Delgado, T.M. Bremer, Frequency characterization of blood glucose dynamics, *Ann Biomed Eng* **31**(1), 91-97 (2003).
16. O.S. Khalil, Non-invasive glucose measurement technologies: an update from 1999 to the dawn of the new millennium, *Diabetes Technol Ther* **6**(5), 660-697 (2004).
17. P.J. Stout, J.R. Racchini, M.E. Hilgers, A novel approach to mitigating the physiological lag between blood and interstitial fluid glucose measurements, *Diabetes Technol Ther* **6**(5), 635-644 (2004).
18. C.C. Palerm, J.P. Willis, J. Desemone, B.W. Bequette, Hypoglycemia prediction and detection using optimal estimation, *Diabetes Technol Ther* **7**(1), 3-14 (2005).
19. E.J. Knobbe and B. Buckingham, The extended Kalman filter for continuous glucose monitoring, *Diabetes Technol Ther* **7**(1), 15-27 (2005).
20. C. Cobelli, D.M. Bier, and E. Ferrannini, Modeling glucose metabolism in man: theory and practice, *Horm Metab Res Suppl* **24**, 1-10 (1990).
21. H. Zisser, L. Jovanovic, F. Doyle, III, P. Ospina, C. Owens, Run-to-run control of meal-related insulin dosing, *Diabetes Technol Ther* **7**(1), 48-57 (2005).