Diabetes prevention, screening and management

A handbook for pharmacists

2021

FIP Development Goals

Diabetes

FIP Practice Transformation Programme on NCDs

fip
International Pharmaceutical Federation

Colophon

International Pharmaceutical Federation (FIP)
Andries Bickerweg 5
2517 JP The Hague
The Netherlands
www.fip.org

Authors:
Lauren Blum, PharmD (University of North Carolina Eshelman School of Pharmacy, USA)
Aniekan Ekpenyong, FIP Practice Transformation Projects Coordinator

Editor:
Gonçalo Sousa Pinto, Lead for Practice Development and Transformation, FIP

Recommended citation
International Pharmaceutical Federation (FIP). Diabetes prevention, screening, and management: A handbook for pharmacists. The Hague: International Pharmaceutical Federation; 2021

Cover image:
© Proxima Studio | shutterstock.com

Contents

Executive summary

Diabetes is a significant public health issue that affects approximately one in 10 adults globally, with type 2 diabetes accounting for 90–95% of cases. This chronic condition causes considerable morbidity and mortality and is growing in impact, with cases projected to rise from 537 million in 2021 to 784 million by 2045.[1] As cases rise, it is imperative to ensure the healthcare workforce is prepared to care for affected individuals. However, there is a growing global shortage of healthcare workers, which was estimated, pre pandemic, to reach 15 million by 2030.[2] Therefore, all of the healthcare workforce will need to be utilised to their fullest potential in order to address the growing global burden of diabetes. Pharmacists will continue to be essential in this endeavour.

While pharmacists are primarily trained to address health concerns with appropriate, safe medicines, they also have the necessary skills and knowledge to provide prevention and screening services. Pharmacists are uniquely positioned to provide a wide array of services to prevent, identify and manage both type 1 and type 2 diabetes as well as support the care provided by other members of the healthcare team. They can also play an important role in referring patients to other healthcare providers for diagnosis of diabetes or specialist care. By leveraging their accessibility and trust, pharmacists can promote the importance of following a healthy lifestyle, including consuming a healthy diet and participating in regular physical activity, to prevent the development of type 2 diabetes, which is particularly important as most cases of type 2 diabetes could be prevented through these measures.

Pharmacists can also assess patients' risks for developing diabetes as well as signs and symptoms that may indicate they have the condition. From this, pharmacists can then offer screening and detection services that aim to identify those who may have diabetes but have not previously been diagnosed. This is especially important because, in 2019, more than one in two adults living with diabetes were not aware they had the condition, with most of these individuals found to have type 2 diabetes.[3] Once individuals with elevated blood glucose levels are identified, pharmacists can refer them to other members of the healthcare team to be formally diagnosed and initiated on appropriate treatment.

Beyond prevention and screening, pharmacists can utilise their medicines expertise to support primary care providers with the development of a diabetes care plan and evaluate the efficacy of the plan that was initiated. As part of this evaluation, pharmacists can ensure patients are remaining adherent to their prescribed medication, achieving their therapeutic goals, and not experiencing any adverse effects or symptoms that may be associated with diabetes complications. Pharmacists can also provide guidance to primary care providers regarding which medicines may be most appropriate to initiate in a particular patient to achieve desired results. Finally, pharmacists can recommend non-pharmacological measures that patients may pursue in conjunction with their prescribed medicines to improve their glycaemic control and health outcomes.

In all, pharmacists have the necessary knowledge and skills to address diabetes in their community by providing prevention, screening and treatment support services as well as working in collaboration with other members of the healthcare team to mitigate the impact of diabetes on individuals who have the condition. Through these efforts, pharmacists can have a significant impact on public health by contributing to the reduction of the global burden of diabetes.

Acknowledgements

FIP would like to thank the invaluable contributions and expertise of the following individuals and organisations, who served on the Expert Advisory Group for this programme and publication.

Prof. A. Patricia Acuña Johnson
Professor
School of Chemistry and Pharmacy, Faculty of Pharmacy
Universidad de Valparaiso
Chile

Ms Syireen Alwi
Pharmacy lecturer
Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy
Universiti Malaya
Malaysia

Mr Chima Meshach Amadi
FIP Worforce Development Hub lead for FIP DG13 (Policy development)
National Institute of Pharmaceutical Research and Development
Nigeria

Mrs Anna Busquets i Casso
Community pharmacist
Spokesperson of the Diabetes Group
Spanish Society of Clinical, Family and Community Pharmacy (SEFAC)
Spain

Dr Astrid Czock
FIP Workforce Development Hub lead for FIP DG8 (Working with others)
CEO, QualiCCare
Switzerland

Dr Mariet Eksteen
FIP Workforce Development Hub Lead for DG7 (Service provision), and workforce education and training
Pharmaceutical Society of South Africa
South Africa

Dr Zeyad Elgamal
Lead clinical staff pharmacist
Cleveland Clinic
Abu Dhabi
United Arab Emirates

Dr Julien Fonsart, PharmD, PhD
President
FIP Clinical Biology Section
France

Dr Manjiri Gharat
FIP vice president
Vice president and chair, Community Pharmacy Division, Indian Pharmaceutical Association
India

Dr Sanah Hasan
Assistant professor
Ajman University, College of Pharmacy and Health Sciences
United Arab Emirates

Dr Mohamed Hassan Elnaem
Lecturer
Department of Pharmacy Practice, Faculty of Pharmacy
International Islamic University
Malaysia

Ms Rute Horta
Executive director
Centre for Medicines Information and Health Interventions (CEDIME)
National Association of Pharmacies
Portugal

Mr Abdulhakeem A. Ikolaba
Consultant clinical pharmacist
Pillbox Pharmacy,
Lagos
Nigeria

FDI World Dental Federation
Switzerland

Dr Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDCES, FADCES, FCCP
Endocrine clinical pharmacy specialist, Continuous Glucose Monitoring and remote monitoring program coordinator
Cleveland Clinic Endocrinology & Metabolism Institute
United States

Prof. Tomohisa Ishikawa
Dean
Graduate Division of Pharmaceutical Sciences
Department of Pharmacology School of Pharmaceutical Sciences
University of Shizuoka
Japan

Ms Isabel Jacinto
Executive director
Graduate School of Health and Management
National Association of Pharmacies
Portugal

Dr Francisco Javier Jiménez, Pharm.D., BCPS, CDCES(CDE)
Professor
Department of Pharmacy Practice
University of Puerto Rico School of Pharmacy
Puerto Rico

Mr Peter Karegwa
Pharmacy technologist
Kenya

Ms Salliane Kavanagh
Diabetes Committee member
National Institute for Health and Care Excellence,
UK Senior lecturer in pharmacy practice and clinical pharmacy
University of Huddersfield
Former committee chair
United Kingdom Clinical Pharmacy Association
Diabetes and Endocrinology Group
United Kingdom

Dr. Navin Kumar Loganadan
Clinical pharmacist
Putrajaya Hospital,
Kuala Lumpur
Malaysia

Ms Minh-Hien Le, HonBSc, BScPhm, PharmD, RPh
Professional practice specialist
Canadian Society of Hospital Pharmacists
Adjunct lecturer
Leslie Dan Faculty of Pharmacy,
University of Toronto
Canada

Ms Antria Pavlidou, MSc
Clinical pharmacist
Pharmaceutical Services,
Ministry of Health
Cyprus

Ms Diane De Rivera-Gargya BPharm, GradCertDiabetesEd, MClinPharm
Pharmacy specialisation expert
Philippine Pharmacists Association
Philippines

Dr Pascale Salameh, PharmD, MPH, PhD, HDR
Professor of epidemiology
Lebanese University
Academic associate
University of Nicosia Medical School, Cyprus
Founder and director
Institut National de Santé Publique,
Epidémiologie Clinique et Toxicologie (INSPECT-LB)
Lebanon

Mr Paul Sinclair
Chair of the FIP Board of Pharmaceutical Practice
Australia

Dr Dallas Smith, PharmD
Clinical pharmacy and pharmacognosy lecturer,
Department of Pharmacy,
Kamuzu University of Health Sciences Blantyre
Malawi

Ms Jennifer Tan
Community pharmacist and digital pharmacy specialist
Malaysia

Dr Iryna Vlasenko, PhD
PhD in Pharmaceutical Technology and Organisation of Pharmaceutical Business
Associate professor, National Academy of Post-Graduate Education, Ukraine
Vice president
International Diabetes Federation
Belgium

Ms Margaret Wonah
Pharmacist
Diabetes Care Network
Nigeria

Foreword

By the president of the International Diabetes Federation

You need only spend a few minutes at your local pharmacy to appreciate the significant role the community pharmacist plays in supporting community health. You will observe that the role extends way beyond the filling of prescriptions and dispensing of pharmaceutical products. This is not to say that the work of the pharmacist to improve health outcomes by ensuring effective, safe, and cost-effective pharmacological therapy is not important — it clearly is. However, pharmacists do much more. They are active members of the healthcare team, providing trusted advice into a community to which, more often than not, they also belong.

From a diabetes care perspective, it is a key role. Diabetes is a serious life-long condition, with potentially life-threatening complications. People with diabetes have an increased risk of developing a number of serious health problems. Consistently high blood glucose levels can lead to serious diseases affecting the heart and blood vessels, eyes, kidneys, nerves and teeth. Diabetes is a leading cause of cardiovascular disease, blindness, kidney failure and lower-limb amputation.

Unfortunately, type 2 diabetes, which accounts for between 90% and 95% of the total diabetes burden, often goes undetected until it is too late, perhaps when complications are already present and, once detected, it is not always taken seriously, foolishly dismissed as something inevitable “for older people” or “just a touch of sugar”. The good news is that type 2 diabetes is largely preventable.

Pharmacists are ideally placed to raise awareness of diabetes as a serious threat to health, to support the detection and management of diabetes in their community, and to counsel community members on what action should be taken to either prevent type 2 diabetes or, if diabetes is present, to help the person prevent or at least delay the onset of complications. Advice, of course, should be based on the best available evidence. This publication from the International Pharmaceutical Federation provides pharmacists with everything they need to know to help guide community members to make healthy choices and adopt healthy habits.

Close to one in 10 adults worldwide (20–79 years of age) are currently living with diabetes. This adds up to around 537 million people and represents a 60% increase over the past 10 years. Fuelled by urbanisation, low levels of physical activity and increasing levels of overweight and obesity, it is forecast that an additional 115 million people will be living with diabetes by 2030 unless sufficient and effective action is taken.

In 2019, the total global cost of diabetes reached an estimated USD 760bn per year (USD 100 billion more than the annual revenues of Apple, Google, Facebook and Amazon combined). The cost is forecast to rise by 9% within the next 10 years to USD 825bn.

It is now well established that preventive action — including early diagnosis and screening of people at risk, as well as interventions that are adapted to the local context and designed to help reduce modifiable risk factors — is successful and cost-effective. Preventing type 2 diabetes and the complications associated with all types of diabetes requires a life-course approach. From early in life, when eating and physical activity habits are established, people need ongoing support to become aware of their potential risk of health issues and how to manage them should they arise. As the first point of contact for health information in many communities. pharmacists have a very important role to play in promoting awareness and facilitating healthy habits.

Tackling and reducing the impact of diabetes requires the involvement and commitment of all sectors of society. The International Diabetes Federation welcomes the development and implementation of this toolkit and looks forward to working together with the global pharmacist community to improve the lives of the millions affected by diabetes and the many more at risk.

Prof. Andrew Boulton, MD, DSc (Hon), FACP, FICP, FRCP

Foreword

By the president of the International Pharmaceutical Federation

According to the International Diabetes Federation (IDF), there are approximately 537 million adults (around one in 10), aged 20–79 years, living with diabetes globally and this number is expected to rise to 784 million by 2045. Over the past 20 years, the number of adults living with diabetes has more than tripled, making it one of the fastest growing global health challenges.[1, 3]

According to the World Health Organization (WHO), diabetes is one of the main non-communicable diseases (NCDs) in terms of global prevalence and mortality).[4] The WHO also states that Investing in better management of NCDs is critical and that high impact essential NCD interventions can be delivered through a primary health care approach to strengthen early detection and timely treatment.[4]

Prevention and control of NCDs require interventions that are therapeutically cost-effective, affordable and feasible for patients and health systems. Interventions need to be framed within national policies and in line with both NCD and risk-factor indicators, and they should contribute to improving equity in health care in targeted populations and individuals, and to improving health outcomes.

It is imperative for the efficiency and sustainability of health systems to leverage the accessibility and expertise of pharmacists to participate in primary health care strategies, including the prevention, screening and management of NCDs. This is the rationale behind FIP's commitment to the WHO Declaration of Astana on Primary Health Care.[5] In many parts of the world, pharmacists already play this important role in NCDs, in this instance the area of diabetes.[6]

To further expand and consolidate this role, FIP launched the FIP Practice Transformation Programme on NCDs, with the aim of providing tools and strategic support to FIP member organisations and individual pharmacists from around the world to develop and implement pharmacy services. These services can have a sustained positive impact in the prevention, screening, management and treatment optimisation of NCDs (in this case, diabetes), for improved patient outcomes and health systems efficiency and sustainability. While the project will have a particular focus on low- and middle-income countries, it will of course be applicable to and encourage implementation by countries of all income levels.

This project also aims to foster a collaborative interprofessional approach to the management of NCDs that is aligned with FIP Development Goal 15 (Patient-centred care). The interventions described in this handbook will be implemented through a structured approach that will not only include a strategy for building local capacity through workforce development, but also provide the tools to facilitate service delivery and the mechanisms for evaluating and long-term monitoring of the impact of this programme through data generation and analysis. The overall aim, as the programme name states, is not simply to deliver a set of valuable professional services, but to transform pharmacy practice in a sustainable manner.

Although this programme is primarily linked to FIP DG15, it is also linked to several other FIP development goals: DG7 (Advancing integrated services), DG18 (Access to medicines, devices and services), DG5 (Competency development), DG8 (Working with others), DG11 (Impact and outcomes) and DG12 (Pharmacy intelligence).

This handbook describes interventions by pharmacists in diabetes prevention, screening and management that are supported by robust evidence and can contribute not only to reducing the prevalence of diabetes, but also to improving the health and quality of life of people living with diabetes.

I take this opportunity to thank the authors and the large group of experts from around the world who have reviewed and contributed to this landmark publication.

I also thank the invaluable support and collaboration of the IDF, which not only contributed directly to this publication and kindly authorised FIP to include some of the tools it developed and validated, but also formally supported this programme by participating in our Expert Advisory Group. We truly value this important recognition of the role of pharmacists in diabetes.

I am confident that you will find this handbook to be a valuable resource to support pharmacy practice and better serve your community. I invite you to find and use this and other resources that you may find at FIP's new website dedicated to NCDs: https://ncd.fip.org.

Dominique Jordan

Diabetes

FIP Practice Transformation Programme on NCDs

1 Background

1.1 Diabetes prevalence and impact

Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin, or when the body cannot make good use of the insulin it produces. Insulin is a hormone that regulates blood glucose so when an individual is not able to produce insulin, or use it effectively, they experience raised glucose levels in the blood (hyperglycaemia). Over the long-term, high glucose levels can lead to damage to the body and failure of various organs and tissues. There are two main types of diabetes: type 1 and type 2.

Type 1 diabetes occurs as a result of the body's immune system destroying the beta cells in the pancreas. Beta cells are the cells responsible for producing insulin. When these are destroyed, the body is no longer able to produce insulin and regulate blood glucose, leading to hyperglycaemia. Because of this, individuals with type 1 diabetes are dependent on insulin and must administer it daily. Currently, there is no known cure for type 1 diabetes and the exact cause is unknown, but is speculated to be a result of genetic and environmental factors.[7, 8] Diagnosis of type 1 diabetes most commonly occurs in children and young adults, but can be diagnosed at any age.[9]

Type 2 diabetes occurs when the body is not able to effectively use or respond to insulin released by the body. Over time, individuals can develop insulin resistance, which is when the muscles, liver and fat cells do not use insulin well and require more insulin to help glucose enter cells. The pancreas will attempt to keep up with this increased demand, but the efficacy of beta cells to secrete sufficient amounts of insulin will wane over time.[8] Type 2 diabetes is the most common type of diabetes, representing about 90–95% of all diabetes cases and is most commonly found in older adults. However, it is also increasingly being seen in younger adults, children and adolescents as a result of rising levels of obesity, physical inactivity and poor diet worldwide.[10] In addition to these two main types of diabetes, there is a range of other types of diabetes, including gestational diabetes, which occurs during pregnancy in women who have not previously been diagnosed with diabetes.[11]

According to the International Diabetes Federation (IDF), there are approximately 537 million adults (around one in 10), aged 20–79 years, living with diabetes globally and this number is expected to rise to 784 million by 2045. Over the past 20 years, the number of adults living with diabetes has more than tripled, making it one of the fastest growing global health challenges. Of adults living with diabetes, over 81% live in low- and middle-income countries and one in five is above 65 years old. IDF further estimates that diabetes and its complications contributed to approximately 6.7 million deaths in 2021, or one every five seconds.[1, 3]

The growing number of diabetes cases and deaths due to poorly controlled diabetes and its complications is contributing to increased healthcare expenditures. In 2021, diabetes resulted in at least USD 966bn in healthcare expenditures, a 316% increase over the last 15 years.[1] Given that diabetes is a leading cause of death and a major cause of blindness, kidney failure, heart attack, stroke and lower limb amputation, it is imperative that actions are taken to reduce rates of diabetes globally.[7]

Of further concern, it is estimated that one in two people with diabetes are undiagnosed and more than 374 million people are at increased risk of developing type 2 diabetes. People with type 2 diabetes almost always have prediabetes first, but this typically does not cause symptoms. Consequently, millions of people over the age of 20 years old have prediabetes, but 90% are not aware of their condition. Prediabetes treatment can prevent more serious health problems, including type 2 diabetes and problems with the heart, blood vessels, eyes and kidneys.[3]

Therefore, pharmacists are ideally placed to:

- Promote healthy lifestyles among their patients with prediabetes and diabetes;
- Screen patients for prediabetes and diabetes and, if elevated blood glucose levels are detected, refer them to a primary care provider for proper diagnosis and treatment to prevent subsequent complications;
- Assist primary care providers in the management of individuals with diabetes; and

- Ensure their patients are achieving optimal health outcomes.

1.2 Importance of pharmacist integration in diabetes care

As cases of diabetes continue to increase globally, with a disproportionate impact on those in lower-income countries, there will be a corresponding need for qualified healthcare providers to care for this growing patient population. However, there is also a growing global shortage of healthcare workers that is estimated to reach 15 million by 2030.[2] Therefore, it is more important than ever that pharmacists are included as key members of the healthcare team and are able to support the efforts of other healthcare workers in order to ensure all patients are receiving high quality healthcare. This is especially important for individuals with diabetes as they are often taking several different classes of medicines and require close monitoring to ensure their medicines are well managed, their blood glucose is under control, and they do not develop any life-limiting complications, including coma, amputation, kidney failure, stroke or blindness.

As underlined in the 2006 FIP Statement of Policy on the role of pharmacists in the prevention and treatment of chronic disease, and more recently in the 2019 FIP Statement of Policy on the role of pharmacists in non-communicable diseases, pharmacists are in an ideal position to relieve the increasing burden of diabetes on health systems due to their accessibility, knowledge, education, ability to provide direct patient care and competency level.[12, 13] Pharmacists are an essential part of the healthcare team, and any health programme should recognise that "pharmacists are the most accessible health care professional in a community. As such, they are in a position to provide early detection of chronic diseases and to identify unhealthy lifestyles. They can help patients reduce risk factors by prevention counselling when appropriate, e.g., weight and diet management, exercise and smoking. Pharmacists are a community-based knowledge resource that can help people understand the dangers of chronic disease and the importance of prevention. Pharmacists work with other members of the healthcare team and can refer patients' chronic disease related issues to them." [12]

Pharmacist-led management of patients with diabetes in different settings requires high levels of collaboration and coordination. The need for interprofessional collaboration was stressed in the 2010 FIP Statement of Policy on collaborative pharmacy practice, which states: "Pharmacists have particular expertise in the use of medicines. . . . This expertise and skill set makes pharmacists' contribution to the healthcare team important to both optimise therapy and to prevent medicine-related problems. No other profession has the understanding and expertise across the full range of medicines available, including the various formulations and products, as the pharmacist." [14]

It is widely known that collaborative approaches to care lead to improved health outcomes. Pharmacists provide a unique perspective and skillset to the healthcare team that can contribute to optimising treatment regimens, preventing adverse events and drug interactions, and monitoring the efficacy of medicines. Studies have shown that pharmacist-led interventions can lead to improved clinical outcomes specifically for patients with diabetes, including reductions in haemoglobin A1c (HbA1c), blood pressure and low-density lipoprotein (LDL) cholesterol.[15, 16] One meta-analysis further showed that pharmacist-led interventions to support self-management of diabetes, including education on diabetes complications, medicines and lifestyle, resulted in reduced HbA1c levels, blood pressure, and LDL and total cholesterol, and resulted in increased self-management skill development and medicine adherence.[17] Another meta-analysis showed that pharmacist interventions significantly reduced adverse events compared with usual care and improved quality of life.[18] Studies also suggest that pharmacist-provided services are cost-effective and may result in healthcare cost savings.[19, 20] Therefore, by including pharmacists as members of the healthcare team, whether that is in a hospital, ambulatory or community setting, there are many benefits to be gained by patients with diabetes. This importance is further reinforced by a Primary Care Diabetes Society publication which discusses best practices in the delivery of diabetes care and highlights the importance of including both pharmacists and pharmacy technicians as part of a multidisciplinary team to address diabetes.[21]

In all, pharmacists are increasingly equipped with the necessary skills and knowledge to participate in diabetes care in several ways, ranging from diabetes prevention, screenings and referrals to disease state management, all of which are outlined throughout this handbook. It should be noted that regulations may prevent pharmacists in certain countries from performing some of the services outlined. Finally, when services can be provided, they should not be conducted in a silo. Collaborative care is necessary to ensure optimal

outcomes for individuals with diabetes and pharmacists should take steps to coordinate their efforts with those of other members of the healthcare team and refer patients for additional care as needed.

2 Prevention of type 2 diabetes

Given the significant burden that type 2 diabetes can have on both patients and health systems, it is crucial that steps are taken to prevent the disease from developing in the first place and, when presented, prevented from worsening. Health promotion interventions that encourage strategies to prevent the development of diabetes should be considered an essential component of pharmacist-provided care. These efforts are especially important given that a majority of cases of type 2 diabetes can be prevented through healthy diets and physical activity. Type 1 diabetes, on the other hand, cannot be prevented so this section will focus solely on type 2 diabetes, but the recommendations discussed throughout this section may be recommended to all in order to promote healthy lifestyles.

Pharmacists can play an important role in making patients aware of the potential of preventing type 2 diabetes from developing as well as the steps that can be taken to prevent its progression. Pharmacists can also play a role in providing motivational counselling for patients who wish to make and sustain healthy lifestyle changes. The level to which pharmacists are involved in prevention efforts for diabetes can range from developing educational materials, such as pamphlets or flyers, to providing general education regarding healthy lifestyles, to providing more comprehensive and long-term counselling on lifestyle changes. The level of involvement will depend on each pharmacist's comfort level with the topic and time available to engage with patients.

While pharmacists should leverage their position as one of the most accessible healthcare professionals in many countries to promote efforts to prevent diabetes, they should also be aware of any structured prevention programmes that exist in their area. These programmes can provide individuals with an opportunity to work with trained educators or coaches on developing healthy lifestyle habits to prevent the onset of type 2 diabetes, or other chronic conditions.[22] One example of these programmes is the National Diabetes Prevention Programme in the United States. Through this programme, individuals participate in a Centers for Disease Control and Prevention (CDC)-recognised lifestyle change programme that focuses on healthy eating and physical activity. Individuals who participated in this programme cut their risk of developing type 2 diabetes by 58%, with this reduction rising to 71% for individuals over the age of 60.[23] Therefore, structured prevention programmes can have a significant impact on preventing type 2 diabetes and should be promoted to patients as a unique opportunity to improve their health.

This section will focus broadly on recommendations to prevent patients from developing type 2 diabetes by promoting healthy lifestyles, including healthy diets, adequate physical activity and a healthy body weight. Pharmacists should consider how it would be best to incorporate these recommendations into their practice site and how they would like to communicate with their patients about these important topics.

In order to disseminate this important information to the public, several different approaches can be taken, including posters, lectures, social media campaigns and informal conversations during counselling sessions. Advice for creating a successful public health campaign can be found in the WHO's "Effective communications participant handbook".[24]

2.1 Promoting healthy lifestyles

2.1.1 Nutrition

The WHO and the Food and Agriculture Organization recommend the following nutritional approaches for the prevention of type 2 diabetes:[4]

1. Limit saturated fatty acid intake to less than 10% of total energy intake. For high-risk groups, limit to less than 7%.
2. Reduce the intake of free sugars to less than 10% of total energy intake. A further reduction to below 5% could have additional health benefits.[5]
3. Consume a minimum daily intake of 20g of dietary fibre through regular consumption of wholegrain cereals, legumes, fruits and vegetables.

The IDF recommends that a healthy diet include reducing the amount of calories consumed if overweight, replacing saturated fats (e.g., cream, cheese, butter) with unsaturated fats (e.g. avocado, nuts, olive and vegetable oils), eating dietary fibre (e.g., fruit, vegetables, whole grains), and avoiding tobacco use, excessive alcohol and added sugar. [10]

Specifically, the IDF provides the following recommendations for the general population to prevent type 2 diabetes:[6]

- Choosing water, coffee or tea instead of fruit juice, soda or other sugar-sweetened beverages;
- Eating at least three servings of vegetables every day, including green leafy vegetables;
- Eating up to three servings of fresh fruit every day;
- Choosing nuts, a piece of fresh fruit, or unsweetened yoghurt for a snack;
- Limiting alcohol intake to a maximum of two standard drinks per day;
- Choosing lean cuts of white meat, poultry or seafood instead of red or processed meat;
- Choosing peanut butter instead of chocolate spread or jam;
- Choosing whole-grain bread, rice, or pasta instead of white bread, rice or pasta; and
- Choosing unsaturated fats (olive oil, canola oil, corn oil or sunflower oil) instead of saturated fats (butter, ghee, animal fat, coconut oil or palm oil).

These recommendations should be tailored to an individual patient's needs and small changes that can be easily sustained should be encouraged.

One simple method that can be promoted to patients to encourage them to follow a healthy diet is the plate method. This method recommends the following:[25]

- Fill half of the plate with non-starchy vegetables, such as salad, green beans, broccoli, cauliflower or cabbage;
- Fill one quarter of the plate with a lean protein, such as chicken, turkey, beans, tofu or eggs;
- Fill one quarter of the plate with carbohydrate foods, such as grains, starchy vegetables like potatoes or peas, rice, pasta, beans, fruits and yoghurt (a cup of milk counts as a carbohydrate food); and
- Choose water or a low-calorie, unsweetened drink to accompany your meal.

If needed, or requested by the patient, pharmacists can refer patients to a nutritionist or dietician for more individualised dietary counselling and recommendations.

2.1.2 Physical activity

It is widely known that physical activity has significant benefits on an individual's health and wellbeing, both physically and mentally. Therefore, while it is recommended that all individuals partake in some type of physical activity, it is even more important for individuals who might be at risk of developing type 2 diabetes. Physical activity, coupled with a healthy diet, may prevent a patient from progressing to type 2 diabetes and prevent, or delay, them from requiring pharmacological therapy.

The WHO and the Food and Agriculture Organization recommend practising an endurance activity at moderate or greater level of intensity (e.g., brisk walking) for one hour or more per day on most days per week.[4] Similarly, the IDF recommends physical activity take place at least three to five days per week, for a minimum of 30–45 minutes.[26] People should also endeavour to reduce the amount of time they spend sedentary.[27]

It should be recommended that patients who are new to physical activity gradually increase the amount and intensity of activity they partake in. Pharmacists should recommend that patients begin by walking to achieve 150 minutes of total activity per week, or less if 150 minutes is not initially feasible. If walking is difficult for patients, other activities that could be recommended include swimming, cycling, etc. After becoming comfortable with their initial exercise regimen, patients can increase their activity and incorporate both aerobic and muscle-strengthening exercises. Ultimately, patients should be reminded that any physical activity is better than no physical activity.[28]

2.1.3 Maintaining a healthy weight

Being overweight or obese can increase the risk of developing type 2 diabetes, as well as the risk for heart disease, stroke, high blood pressure and high cholesterol.[29] While it can be difficult, losing weight by following a healthy diet and completing adequate physical activity is one of the most important steps that can be taken to prevent the development of diabetes.

Overweight and obesity are generally identified based on an individual's body mass index (BMI). BMI is calculated by dividing a person's weight in kilograms by the square of their height in metres (kg/m^2). A BMI greater than $30kg/m^2$ is considered obese and a BMI between $25kg/m^2$ and $29.9kg/m^2$ is considered overweight.[30] However, it is important to be aware that BMI is not an ideal measurement for health as it does not take individual patient factors into account, such as muscle mass, body composition, ethnicity or age. Therefore, BMI is not a perfect correlate for an individual's health. Despite this, BMI is still a commonly used measurement in most healthcare settings. Pharmacists should be aware of the limitations associated with BMI and, if needed, should explore alternative measurements to supplement BMI, such as waist circumference.[31]

To prevent type 2 diabetes, the WHO and the Food and Agriculture Organization recommend the following weight loss measures:[4]

- Maintenance of an optimum BMI at the lower end of the normal range (for the adult population, this means maintaining a mean BMI in the range $21–23kg/m^2$ and avoiding weight gain >5kg in adult life); and
- Voluntary weight reduction in overweight or obese individuals with impaired glucose tolerance (although screening for such individuals may not be cost-effective in many countries).

Similarly, the IDF recommends patients aim to achieve at least a 5–7% reduction in weight through a healthy diet and increased physical activity.[22]

2.1.4 Smoking cessation

Smoking cessation is an important step individuals can take to reduce their risk of developing diabetes, along with many other diseases. People who smoke are 30–40% more likely to develop type 2 diabetes than those who do not smoke, with the risk of developing diabetes increasing with the number of cigarettes smoked per day.[32] To assist patients with quitting, pharmacists can utilise the WHO's 5A model (Ask, Advise, Assess, Assist, Arrange) to help patients get ready to quit and the 5R model (Relevance, Risks, Rewards, Roadblocks, Repetition) to increase motivation to quit. Details on these strategies can be found in the WHO "Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care". [33]

3 Screening and referral

Pharmacists can not only leverage their accessibility and knowledge to prevent diabetes, but they can also play a role in identifying individuals who may have diabetes but have not been previously diagnosed and referring them for further evaluation and care. To participate in screening and referral services, pharmacists must be aware of who is at risk of potentially having diabetes, who should be screened, what to do if a test indicates a patient may have diabetes, and how to conduct point-of-care screenings.

For those with type 2 diabetes, screening is especially important as this condition develops slowly over time and individuals can be asymptomatic for several years and not be aware of their condition. For those with type 1 diabetes, the age of diagnosis is usually much younger than for those with type 2 diabetes so it is less likely they would be identified through a pharmacy-based screening. But this is not always the case. Even though diagnosis of type 1 diabetes often occurs in children and young adults, it can also occur in older adults, so it is important that pharmacists keep this in mind. Individuals with type 1 diabetes who have high blood glucose when screened can often be misdiagnosed with type 2 diabetes which further reinforces the importance of referring patients who have high blood glucose or HbA1c to a primary care provider for confirmatory testing.[9]

In 2019, more than one in two adults living with diabetes were not aware they had this condition, with most of these individuals having type 2 diabetes. Globally, rates of adults with undiagnosed diabetes were highest in Africa (60%), followed by South-East Asia (57%), Western Pacific (56%), Middle East and North Africa (45%), Europe (41%), and North America and the Caribbean (38%). As can be seen, undiagnosed diabetes is most common in low-income countries, where nearly 67% are estimated to be undiagnosed compared with approximately 38% in high-income countries and nearly 53% in middle-income countries.[34]

Undiagnosed diabetes is dangerous as it can lead to several microvascular and macrovascular complications that can be life-threatening and cause significant morbidity and mortality.[34] Therefore, it is essential that pharmacists utilise their role as a trusted, accessible healthcare professional to increase awareness of the prevalence of diabetes and work to ensure all individuals in their communities with diabetes are identified and receive the care they need in order to live a healthy life.

3.1 Assessing risk factors, signs and symptoms

When pharmacists are considering which patients to screen for diabetes, they should focus their efforts on those who are at highest risk of having the disease. This can be determined by assessing patients for certain risk factors that may put them at increased risk of developing diabetes and looking for signs and symptoms that may be indicative of diabetes.

3.1.1 Type 2 diabetes risk factors

3.1.1.1 Modifiable risk factors

Modifiable risk factors, or those that patients can influence by making lifestyle changes, are the largest contributor to growing rates of type 2 diabetes globally. These risk factors include:[10]

- **Being overweight or obese** Being overweight or obese is often, but not always, the result of unhealthy diets and physical inactivity, and is the strongest risk factor a patient can have for developing type 2 diabetes as it can cause or aggravate insulin resistance.

- **Unhealthy diets** There are several dietary risk factors that can increase an individual's risk of developing diabetes, including high intake of saturated fatty acids, high total fat intake, inadequate consumption of dietary fibre, and high carbohydrate and refined sugar intake.

- **Physical inactivity** Those who are not physically active have a greater risk of type 2 diabetes as regular physical activity can reduce blood glucose and often contributes to individuals achieving and maintaining a healthy weight.

- **Smoking** Smokers are at increased risk of developing type 2 diabetes, with the risk being greatest among heavy smokers and this risk can remain elevated for around 10 years after quitting smoking.[35]

- **History of cardiovascular disease, hypertension, or dyslipidaemia** Individuals with hypertension or high cholesterol can have an increased risk of developing type 2 diabetes as well as an increased risk of developing complications from the disease.

- **Medicines** There are some medicines that can increase an individual's risk of developing type 2 diabetes, including glucocorticoids, thiazide diuretics at higher doses, beta blockers, some fluroquinolones, some HIV medicines, statins and atypical antipsychotics.[36-38]

3.1.1.2 Non-modifiable risk factors

While patients can reduce their risk of developing type 2 diabetes by addressing the modifiable risk factors outlined above, there are certain risk factors that they are unable to control, including:[10]

1) **Family history of diabetes** Patients with a first degree relative who has diabetes, including parents or siblings, can have an increased risk of developing type 2 diabetes.

2) **Ethnicity** Certain ethnicities are at higher risk of developing type 2 diabetes, including South Asian, Afro-Caribbean and Hispanic.[39] Additionally, certain regions of the world, including Western Europe and island states in the Pacific show higher rates of type 2 diabetes.[40]

3) **Age** As individuals age, their risk of developing type 2 diabetes also increases. Typically, once an individual is aged 45 or older, they are considered to be at increased risk of type 2 diabetes, which is often reflected in screening guidelines.[41]

4) **History of gestational diabetes** Women who have a history of gestational diabetes are more likely to develop type 2 diabetes than those who do not have a history of this condition.[42] One study found that the risk of developing type 2 diabetes was eight times higher among women with gestational diabetes, and this risk was highest in non-white European women and those who were overweight.[43]

There are several online resources that can be used to assess a patient's risk of developing type 2 diabetes. One example is an online risk assessment tool developed by the IDF, based on the Finnish Diabetes Risk Score, which aims to predict an individual's risk of developing type 2 diabetes in the next 10 years. This test, which takes a few minutes to complete, can be found at https://www.idf.org/type-2-diabetes-risk-assessment.

3.1.2 Diabetes symptoms

Identifying potential signs and symptoms of diabetes is an important consideration for pharmacists undertaking diabetes screening. Even though many individuals with undiagnosed diabetes may have mild symptoms, or none, there are several signs and symptoms pharmacists should be aware of that could potentially indicate patients have diabetes or are at high risk. Those who have type 1 diabetes may have experienced a rapid onset of these symptoms, whereas those with type 2 diabetes will experience a slower onset of symptoms. It is important for pharmacists to note that many patients can still have diabetes even if they present with no signs and symptoms.

Symptoms of diabetes include:

- Excessive thirst and dry mouth (polydipsia);
- Frequent urination (polyuria);
- Excessive hunger (polyphagia);
- Unexplained weight loss;

- Lack of energy, tiredness, fatigue;
- Slow healing wounds;
- Recurrent infections in the skin;
- Blurred vision; and
- Tingling or numbness in hands and feet.[41, 44]

Signs of diabetes include:

- Acute metabolic deterioration and/or acute presentation of chronic complications;
- Severe dehydration;
- Kussmaul's respirations (a deep, laboured breathing pattern associated with severe metabolic acidosis);[45]
- Altered level of consciousness; and
- Diabetic complications, which usually occur after years of having the disease, including acute coronary disease, stroke, kidney disease, vision loss and diabetic foot.[44]

3.2 Diabetes screening

3.2.1 Background

Once a pharmacist assesses a patient's risk for diabetes and determines if any signs or symptoms are present, they can then determine if the individual should be tested for diabetes. This decision can be based on a pharmacist's clinical judgment, a patient's wishes or existing guidelines. Recommendations of who should be screened vary depending on which guideline is referenced. For example, the WHO recommends screening (i) adults of any age who are symptomatic and (ii) adults aged over 40 years and who are overweight (BMI >25) or obese (BMI >30).[44] Similarly, the US Preventive Services Task Force recommends screening all adults aged 35 to 70 years who are overweight or obese.[46]

When considering who should be screened for diabetes, pharmacists should first determine if there are national guidelines specific to their country that they should follow. If there are none, site protocols, WHO guidelines, clinical judgement or online risk assessment tools can be used. Once it is determined that a patient should be screened, pharmacists must then determine the type of point-of-care testing they would like, and are able, to conduct.

Performing point-of-care screenings is an important role for pharmacists to play in global efforts to reduce rates of diabetes. Given that pharmacists are one of the most accessible healthcare professionals, providing these screenings within communities where patients are living makes it more likely individuals with undiagnosed diabetes will be uncovered. If pharmacists provide these services in an easily accessible location, patients who may not have otherwise sought care or received testing have the benefit of receiving care at their local pharmacy.

Pharmacists generally provide two main types of point-of-care screenings: blood glucose and HbA1c, which are discussed in more depth below. Based on the results obtained from these screenings, pharmacists can determine if a patient could potentially have pre-diabetes or diabetes and require a referral to another member of the healthcare team for diagnosis and confirmatory testing.

Venous plasma glucose is typically the standard method by which blood glucose levels are measured and reported.[39] Therefore, the diagnostic criteria outlined below in Table 1 by the WHO include values for plasma glucose levels which are typically obtained in a healthcare facility or laboratory. However, the WHO states that if laboratory services are not available, point-of-care devices that analyse capillary blood, like those used in pharmacies, can be used in lieu of laboratory testing.[44]

Table 1 - WHO criteria for a diagnosis of diabetes[39, 44]

Test	mmol/l	mg/dl
Fasting plasma glucose	≥7.0	≥126
Random plasma blood glucose	≥11.1	≥200
Venous plasma glucose 2 hours after a 75g oral glucose load (oral glucose tolerance test)	≥11.1	≥200
Capillary plasma glucose 2 hours after a 75g oral glucose load (oral glucose tolerance test)	≥12.2	≥220
Test	**mmol/mol**	**%**
Glycated haemoglobin A1c (HbA1c)	≥48	≥6.5

If elevated levels of any of the blood glucose tests are detected in a patient without symptoms, it is recommended that the same test is repeated as soon as possible on a future day to confirm the elevated value. If elevated HbA1c is detected, patients should be immediately referred to a primary care provider. An HbA1C level of 6.5% or higher on two separate tests indicates that a patient has diabetes. An HbA1C between 5.7% and 6.4% indicates the patient has prediabetes and 5.7%, or below, is considered normal.[47] Pharmacists should refer all patients with elevated HbA1c or repeated elevated blood glucose levels to a primary care provider for confirmatory laboratory testing and diagnosis.[7]

3.2.2 Blood glucose

Blood glucose testing measures the level of glucose in a patient's blood at one particular moment in time and there are multiple options available for conducting blood glucose screenings. As stated above, venous plasma glucose is typically the standard method by which blood glucose levels are measured and reported; however, capillary samples obtained through point-of-care devices are also acceptable for use.[39] The reference values for venous and capillary samples of fasting blood glucose will be the same; however, for those who are not fasting and a random plasma glucose test is conducted, the capillary test may provide higher results than a venous sample.[48]

- **Fasting plasma glucose (FPG)** An FPG test measures a patient's blood glucose when they are fasting. Patients should be instructed to not eat or drink anything, except water, for 8–14 hours before the test; therefore, these tests are often performed in the morning, with patients fasting overnight.[49] This test is typically the most practical option in limited resource settings given its low cost. However, pharmacists should take steps to confirm a patient has been fasting for the required amount of time to ensure the results are interpreted correctly.[44]

- **Random plasma glucose (RPG)** An RPG test measures a patient's blood glucose at any time of the day and does not require the patient to be fasting. Despite the convenience of an RPG test, this is one of the least accurate tests that can be performed to diagnose diabetes. This test is best used in patients who are exhibiting symptom of diabetes. However, a test that does not exceed the thresholds listed in Table 1 does not mean a patient has definitively tested negative for diabetes.[44]

- **Plasma glucose 2 hours after a 75g oral glucose load (oral glucose tolerance test, OGTT)** An OGTT measures a patient's blood glucose two hours after consuming a drink containing 75g of glucose.[49] While this test can provide a helpful insight into how a patient processes glucose, it is less practical and more costly than the FPG test.

The accuracy of a blood glucose test depends on a variety of factors (Table 2), including the quality of the meter and test strips used for point-of-care testing, how accurately the point of care test is performed, the methodology used for clinical laboratory testing, as well as some additional factors.

Table 2 - Factors that influence accuracy of blood glucose tests [50]

Factors	Description
Patients' haematocrit levels	If a patient is severely dehydrated or anaemic, their results may be less accurate.
Interfering substances	Some substances, such as vitamin C, acetaminophen/paracetamol and uric acid, may interfere with glucose testing.
Altitude, temperature, humidity	High altitude, low and high temperatures, and humidity can cause unpredictable effects on glucose results.
Storage	Devices and test strips should be stored according to the manufacturer's instructions. Test strip vials should always be closed when being stored and used prior to the expiration date.

Pharmacists should always carefully read the manuals and instructions for the specific device and test strips being used to determine the level to which these factors may interfere with results as well as whether there may be other factors affecting the accuracy of the results. For example, patients on dialysis with icodextrin, a specific peritoneal dialysis solution, may show falsely elevated blood glucose levels when using certain meters.[51, 52] To assess the performance and accuracy of a glucometer, there are several strategies that can be pursued, depending on availability, as seen below in Table 3.

Table 3 - Assessing a blood glucose meter's performance[50]

Strategy	Description
Liquid control solution	Liquid control solutions are recommended to be used: (i) every time a new container of test strips is opened, (ii) occasionally as the container of test strips is used, (iii) whenever the meter is dropped or damaged, and (iv) whenever unusual results are obtained. To use the liquid control solution, a drop of the solution is treated just as a drop of blood would be treated. The result that is given by the device should then match with the value range written on the test strip vial label.
Electronic checks	Every time a meter is turned on, it does an electronic check. If a problem is detected, it will show an error code. This error code can then be found in the device's manual where it will explain what the error is and how to fix it.
Comparison to a laboratory test	If possible, compare the results obtained from the blood glucose meter to those obtained using a clinical laboratory method, because laboratory tests are more accurate and less likely to be influenced by other factors. This method will likely need to be done in a healthcare setting, such as a laboratory or primary care provider's office, as the laboratory test will require venous blood.

3.2.3 HbA1c

Another test that can be used to screen patients for diabetes is a glycated haemoglobin (HbA1c) test. Haemoglobin is a protein that exists within red blood cells and carries oxygen throughout the body. Haemoglobin becomes glycated when it attaches to glucose in the blood. This test is able to measure a patient's average blood glucose levels over the previous two to three months because the glucose stays attached to the haemoglobin for the life of the red blood cell, which is typically around two to three months.

This test can be performed at any time of day and does not require that a patient is fasting. This test also benefits from the fact that it analyses a patient's average blood glucose over a period of time and is not subject to the daily fluctuations and variability that exist when testing blood glucose.

Although HbA1c is the preferred method for the screening and diagnosis of diabetes, and the best method for monitoring the condition, there are some limitations that must be considered, as highlighted in Table 4. First, this test is much more costly than blood glucose tests and therefore, is not widely available in many limited resource settings. Further, the results of an HbA1c test may not always be accurate in patients with certain haemoglobinopathies, anaemias or conditions associated with accelerated red blood cell turnover, including malaria.[53]

Table 4 - Factors that influence HbA1c and its measurement (a WHO adaptation from Gallagher et al)[53, 54]

Factors*	Increased HbA1c	Decreased HbA1c
Erythropoiesis	Iron or vitamin B12 deficiency, decreased erythropoiesis	Administration of erythropoietin, iron, vitamin B12, reticulocytosis, chronic liver disease.
Altered haemoglobin	Genetic or chemical alterations in haemoglobin — haemoglobinopathies, fetal haemoglobin, methaemoglobin — can increase or decrease HbA1c	
Glycation	Alcoholism, chronic renal failure, decreased intraerythrocyte pH	Aspirin, large doses of vitamins C and E, certain haemoglobinopathies, increased intra-erythrocyte pH
Erythrocyte destruction	Increased erythrocyte life span: splenectomy	Decreased erythrocyte life span: haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone. Pregnancy[55]
Assays	Hyperbilirubinaemia, carbamylated haemoglobin, chronic alcoholism, large doses of aspirin, chronic opiate use	Hypertriglyceridaemia

**Not all of these factors will influence results on every available device or method used to test HbA1c.*

While there are many factors that may influence HbA1c results, it can be broadly stated that any condition that shortens the life of erythrocytes or causes increased red blood cell turnover can cause falsely decreased HbA1c results, and vice versa. One of the most common reported conditions that causes falsely increased HbA1c results is iron deficiency anaemia. For falsely decreased HbA1c, renal failure and pregnancy are most common.[55]

3.2.4 Implementation

Even though laboratory testing provides the most accurate blood glucose and HbA1c testing results, it is not feasible to provide this testing within a community pharmacy setting as most laboratory testing requires costly and complicated devices. Therefore, point-of-care devices offer a quick and simple method by which patients can be conveniently screened for diabetes, but they also involve a certain number of risks to be controlled. The steps and supplies needed to provide these point-of-care tests are presented below in Table 5 . A visual representation of the steps to take when performing a capillary blood test can be found in the WHO "Guidelines for drawing blood".[56]

Table 5 - General guidance for conducting diabetes point-of-care screenings[56]

Action steps*	Description
Educate patient on the test to be provided	Obtain the patient's consent for the test and provide education on either blood glucose or HbA1c testing.
Gather supplies and prepare screening area	Supplies needed will likely include the point-of-care device, lancets, test strips, alcohol swabs, sticking plasters cotton balls, gloves and a sharps container.
Prepare patient and point-of-care device for testing	Patient: Use an alcohol swab on the patient's finger or have them wash their hands with soap and water. Device: Follow the packaged instructions for the device to ensure it is prepared for use and then insert the test strip.
Conduct test	Use a disposable lancet to prick the patient's finger (either on the side of the finger or tip, not directly in the middle), gently rub or massage their finger until a sufficient size

Action steps*	Description
	drop of capillary blood forms, then place the test strip at the edge of the drop and a sticking plaster the patient's finger as needed. Sampled capillary blood should be tested immediately in order to prevent inaccurate results. Discard materials as appropriate (e.g., lancets in the sharps container).
Counsel patient on results and identify next steps, if needed	Educate the patient on their results. If the results are elevated and the patient is asymptomatic, they may return on a subsequent day to be tested again. Patients with elevated results, especially those with symptoms, should be referred to a primary care provider for laboratory testing to determine if they should be diagnosed.

**Each device used to evaluate blood glucose and HbA1c may have different specifications to ensure accurate test results are obtained. Pharmacists should always refer to the device manufacturer's recommendations.*

When performing these point-of-care tests, pharmacists must follow the instructions for the specific device they are using and ensure, among other things, that they are using test strips specific to that device that have not expired, that the device and test strips have been stored properly, and that the device is appropriately calibrated. Additionally, some devices may allow blood to be obtained from sites other than the fingertip, including the palm, upper arm, forearm, thigh or calf. However, these sites should not be used at times when blood glucose may be rapidly changing, such as when a patient has just eaten, exercised or taken insulin.[50] Pharmacists should again refer to the device's manual to determine if this is allowed.

The accessibility of pharmacists provides an ideal opportunity to screen many patients who may not have otherwise been tested or considered themselves at risk for diabetes. Pharmacists should always make certain they are prepared to refer patients to primary care providers for diagnosis and additional care if their results come back elevated, as point-of-care testing should generally not be used to diagnose diabetes.

4 Medicines management

Once a patient is formally diagnosed with diabetes (or pre-diabetes), they are then placed on a comprehensive treatment plan that will likely include a combination of lifestyle changes and medicines. Management of diabetes requires patients to be closely monitored to ensure they are taking their medicines as directed, staying adherent to lifestyle modifications, reaching their goals for glycaemic control, and not experiencing complications due to the disease or medicines. Though pharmacists are not going to diagnose patients, they can play an essential role in supporting the treatment plan outlined by the patient's primary care provider, identifying potential medicines-related issues and, when allowed by regulations, adjusting therapies when necessary or ordering laboratory tests.

4.1 Patient assessment

One role that pharmacists can play in supporting a patient's treatment plan is performing an assessment of the patient to identify, prevent and, when possible, address their concerns and needs. Comprehensively assessing patients is the foundation for ensuring proper management of their diabetes. A pharmacist's assessment should primarily focus on factors associated with the patient's current treatment regimen but can also include additional factors that, if pertinent, could be shared with the patient's primary care provider.

The method by which these assessments are done can range from formal comprehensive medication management sessions to informal questions asked during medication counselling encounters. Regardless, pharmacists should leverage their frequent touchpoints with patients to identify potential issues that could be interfering with their diabetes treatment. Pharmacists should also have a plan to share any important information obtained through these assessments with the patient's primary care provider and, if any urgent issue arise, pharmacists should know where the patient should go to receive emergency care. Potential factors that could be included in these assessments are:

- **Medication adherence** Pharmacists are in an optimal position to evaluate a patient's adherence to treatment through refill records, direct conversations with the patient or other appropriate methods. If reliable records are not available, given how frequently patients visit their pharmacy, pharmacists can attempt to obtain a patient's self-reported adherence and have them share any adherence barriers they might be facing to taking their medicines as directed. Pharmacists can then suggest strategies to help patients overcome these barriers.

- **Clinical response to treatment** Pharmacists can, where regulations permit, test a patient's blood glucose or HbA1c to identify how well managed their diabetes is. They can also assess additional clinical parameters, including blood pressure, cholesterol or weight.
    - If regulations allow, pharmacists can order laboratory tests to further investigate a patient's current health status and response to treatment.
    - Additionally, if patients are self-monitoring their blood glucose at home, pharmacists can work with the patient to assess their results and provide education on potential strategies to improve their blood glucose control.
    - Beyond clinical values, pharmacists may also assess if a patient is experiencing any concerning symptoms that would indicate their diabetes is not well-controlled or they are experiencing a potential complication of the disease. If identified, pharmacists can then encourage patients to make an appointment with their primary care provider as soon as possible or, if severe enough, seek emergency care.

- **Opportunities for treatment optimisation** Given pharmacists' medicines expertise, they can address a wide variety of factors surrounding a patient's medicines and make recommendations to optimise their treatment.
    - **Medicines storage** Ensuring medicines are stored properly, typically in a cool, dry place, away from children and pets, is important to ensure patients are receiving the optimal benefit from their medicines. Storage is particularly important for patients taking insulin and should be frequently reinforced by pharmacists when patients are collecting their refills.

- **Adverse effects** Pharmacists should assess each medicine a patient is taking and determine if they are experiencing any adverse effects that may be related to the medicine. Pharmacists should be aware of the most common side effects of all medicines being taken by the patient and work to identify strategies to overcome these. For example, they could recommend a timing, dosage or treatment change to the patient's primary care provider or recommend an appropriate over-the-counter medicine. Depending on regulations, pharmacists should also consider reporting adverse effects to their respective pharmacovigilance systems.

- **Medicines administration and dosing** Some patients may have difficulty swallowing certain medicines so pharmacists can work with the patient to identify strategies to overcome this barrier, such as identifying formulations that can be split in half or crushed. Pharmacists should also assess how patients administer their insulin, or other injectable diabetes medicines, as it can often be difficult for some to adapt to using injectable medicines and some may be injecting their medicines incorrectly. Another opportunity for pharmacists is to ensure patients are taking their medicines at appropriate times during the day to ensure they are receiving optimal benefits from their treatment. For patients who have trouble with complicated dosing schedules that require multiple doses throughout the day, pharmacists may be able to identify opportunities for them to switch to a different medicine or formulation of a current medicine (i.e., immediate release to extended release) that would allow them to take their medicines less frequently.

- **Drug interactions** Pharmacists should assess whether any of the patient's prescription medicines interact with each other or with any over-the-counter medicines, herbals, supplements, vitamins, topicals, etc., the patient may be taking. Some patients may not think to tell their primary care provider about over-the-counter medicines they are taking, so pharmacists can play a key role in identifying potentially dangerous interactions. For example, common cough and cold syrups and lozenges contain sugar, which can increase blood glucose, so sugar-free formulations should be recommended.[57] Pharmacists should also assess if there are any drug-food interactions present that could affect the efficacy of a patient's treatment or cause adverse effects. If these interactions are present, pharmacists can educate the patient on these interactions and advise them on strategies to overcome them, i.e., taking the medicine on an empty stomach.

4.2 Developing and implementing a care plan

While pharmacists are not typically the primary healthcare provider who develops an initial care plan for a patient, they can still play an extremely important role in supporting the development of care plans and providing guidance to the healthcare providers who are developing the care plan.

Pharmacists are the medicines experts of the healthcare team and due to their knowledge of pharmacology, drug interactions and evidence-based care, pharmacists can recommend appropriate therapies and establish therapeutic goals in conjunction with other primary care providers. They can consider individual patient factors and assess which medicine would be best suited for that individual patient to meet their therapeutic goals. Pharmacists can also make recommendations to primary care providers to initiate, modify or discontinue certain medicines as well as recommend dosing adjustments. They can also take steps to prevent adverse effects, drug interactions and medication non-adherence, among many other things.

For assistance in developing a care plan, pharmacists should first refer to national or regional guidelines specific to where they practise pharmacy. They can also refer to the WHO's type 2 diabetes management protocol found in the WHO "Package of essential noncommunicable disease interventions for primary health care.[43] Of note, the only medicines included in this protocol are on the WHO's Model List of Essential Medicines and, depending on where you are practising, there may be several other therapy options available to trial.[44] Examples of additional protocols that are more comprehensive and could be adapted for use include the American Diabetes Association (ADA) guidelines for utilising glucose-lowering medicines in those with type 2 diabetes and intensifying injectable therapies,[58] the Australian "Type 2 diabetes glycaemic management

algorithm",[59] and the Diabetes Canada "Clinical practice guidelines for glycaemic management for adults with type 1 diabetes".[60]

4.2.1 Sick day care plans

In addition to supporting the development of a care plan for individuals with diabetes, pharmacists can also play a role in ensuring they have a plan in place for when they are sick. When individuals with diabetes have an illness or infection, their blood glucose levels increase as a result of hormones released by the body to fight the illness. Thus, they may need to adjust their regular diabetes management regimen to account for this increased blood glucose. Ideally, patients will develop their sick day plan in collaboration with their primary care provider. However, if this is not the case and an individual comes to the pharmacy while sick, pharmacists can recommend the following general guidelines per the IDF[61]:

- Continue to take diabetes medicines as prescribed, including insulin;
- Test blood glucose frequently (e.g., every four hours) and keep track of results;
- Drink extra (calorie-free) fluids to prevent dehydration and try to eat normally;
- Monitor weight every day as weight loss while eating normally can be a sign of hyperglycaemia; and
- Check temperature every morning and evening to see if a fever is present.

Those with type 1 diabetes should also frequently (e.g., every four hours) check for the presence of ketones using either blood or urine ketone test strips while they are sick. If urine ketones are present or blood ketones are between 1.5mmol/l and 3.0mmol/l at any point, the patient is an increased risk of diabetic ketoacidosis and should follow their sick day plan, contact their healthcare team as soon as possible, or report to the hospital for care. If values above 3.0mmol/l are obtained, the patient should go to a hospital immediately.[61]

If patients are experiencing any of the following symptoms, pharmacists should recommend they seek care immediately: difficulty breathing, moderate to high urine ketone levels, inability to keep any liquids down for more than four hours, losing 2.3kg or more during the illness, blood glucose less than 60mg/dl, vomiting or having severe diarrhoea for more than six hours, feeling too sick to eat normally and inability to keep food down for more than 24 hours, having a temperature over 38°C (101°F) for 24 hours, having a reduced level of consciousness, or breathing rapidly with fruity-smelling breath.[61, 62]

When patients present at the pharmacy and request over-the-counter medicines to address symptoms associated with an acute illness, pharmacists should ensure they are recommending products that will not exacerbate their hyperglycaemia. For example, many cough and cold products, including syrups and lozenges, have high levels of sugar so pharmacists should recommend sugar-free formulations of these products and encourage patients to review the ingredients of products they may have at home that could have high levels of sugar. Additionally, other medicines, such as the decongestant pseudoephedrine, can also increase blood glucose.[57]

4.3 Monitoring and evaluating a care plan

Pharmacists can play an extremely important role in monitoring and evaluating a care plan for efficacy and ensuring the care plan is helping a patient reach their therapeutic goals. Pharmacists can assess the factors discussed in the patient assessment section of this chapter, conduct blood glucose and HbA1c tests to determine a patient's response to therapy, and promote rational medicines use and medication adherence.

4.3.1 Blood glucose/HbA1c monitoring

Treatment goals for patients will all be slightly different, but the IDF and WHO both recommend that individuals with diabetes aim for an HbA1c below 7%. This level is considered adequate glycaemic control and will minimise the risk of developing complications.[22, 44] However, a higher HbA1c target (e.g., 7–8%) may be needed for those who are prone to serious hypoglycaemia, have co-morbidities, or are older. Tighter glucose control may be recommended for those who are younger or newly diagnosed. If a pharmacist is conducting HbA1c testing, they should verify with the patient, or their primary care provider, what the goal HbA1c level is.[63] If HbA1c is not able to be assessed, the WHO recommends that FPG should be <126mg/dl (7mmol/l).[44] Similarly, the ADA recommends a fasting blood glucose between 80 and 130mg/dl.[64]

The IDF recommends that HbA1c be assessed every two to six months depending on the previous reading, stability of blood glucose control and changes in therapy. It also recommends that treatment be reviewed and modified if HbA1c is above the agreed goal on two consecutive occasions.[63]

4.3.1.1 Self-monitoring of blood glucose

Monitoring a care plan is not only a role for a patient's primary care provider and pharmacist; patients themselves should also play a role through self-monitoring of blood glucose (SMBG). The IDF recommends that SMBG only be undertaken by patients who have the knowledge, skills and willingness to use the information obtained through testing to actively adjust treatment and assess the effectiveness of their management plan on glycaemic control. The purpose of this testing should be predetermined by the patient and their primary care provider.[63]

SMBG is most important for patients taking insulin; however, patients taking oral glucose-lowering medicines may also consider utilising SMBG as an optional test to: (i) provide information on, and help avoid, hypoglycaemia; (ii) assess changes in blood glucose control due to medicines and lifestyle changes; (iii) monitor the effects of foods on postprandial glycaemia; and (iv) monitor changes in blood glucose levels during illness.[63] Pharmacists can support patients with SMBG by improving their health literacy and educating them on how to conduct testing, as discussed in section 3.2, and how to interpret their results.

4.3.1.2 Continuous glucose monitoring

While SBMG has historically only included traditional finger-prick testing, new technologies continue to emerge that make it even easier for patients with diabetes to monitor their blood glucose. Continuous glucose monitors (CGMs) utilise an external device attached to the patient's body to monitor their blood glucose.[65] CGMs fall into two broad categories: real-time and intermittently scanned. Both categories of devices are continuously measuring blood glucose, but the intermittently scanned CGMs will only show blood glucose values when the sensor is scanned by a reader or smartphone.[66] CGMs will often have the capability of sounding an alarm when blood glucose levels are too high or too low. And data can usually be downloaded to a computer or smart device in order to more clearly evaluate trends in blood glucose.[67] Depending on the model being used, CGMs may still require finger-prick tests to calibrate the device or make treatment decisions, such as addressing hypoglycaemia. This is especially important as CGMs measure interstitial glucose which can lag behind blood glucose if glucose levels are rising or falling quickly. [66]

One important measurement to assess diabetes control that can be assessed by CGMs is time in range. This measurement evaluates the time an individual's blood glucose is within the blood glucose range identified by their physician. Those with either type 1 or type 2 diabetes should aim to achieve a time in range of at least 70%, but this target can vary for each individual.[65]

CGMs have shown benefits in reducing HbA1c and hypoglycaemia in those who utilise either multiple daily injections of insulin or continuous subcutaneous insulin infusions. Therefore, these devices are becoming increasingly more popular among individuals with diabetes, especially those with type 1 diabetes, as it reduces the need for frequent finger-prick tests and increases their ability to monitor their blood glucose. Pharmacists should ensure their patients are educated on how to use these devices properly and safely. Most manufacturers will have existing trainings and tutorials that can be used to educate both pharmacists and patients on how to properly use the CGM.[66]

4.3.2 Rational use of medicines

Rational medicines use is defined by the WHO as "patients receiv[ing] medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".[68] This definition also includes criteria for ensuring rational use and prescribing of medicines that are listed in Table 6.

Table 6 - WHO criteria for rational use of medicines [68]

Rational use criterion	Description
Appropriate indication	The decision to prescribe drug(s) is entirely based on medical rationale and the drug therapy is an effective and safe treatment.
Appropriate drug	The selection of drugs is based on efficacy, safety, suitability and cost considerations.
Appropriate patient	No contraindications exist, the likelihood of adverse reactions is minimal and the drug is acceptable to the patient.
Appropriate patient information	Patients are provided with relevant, accurate, important and clear information regarding their conditions and the medicine(s) that are prescribed.
Appropriate evaluation	The anticipated and unexpected effects of medicines are appropriately monitored and interpreted.

Irrational use of medicines is a significant problem globally, with the WHO estimating that half of all medicines are prescribed, dispensed or sold inappropriately and half of all patients are not taking them correctly. Medicine errors, specifically, are estimated to cost USD42bn annually. Through the WHO "Global patient safety challenge: Medication without harm", the three key action areas identified to address medication errors and promote rational use of medicines, include (i) polypharmacy, (ii) high-risk situations, and (iii) transitions of care, all of which pharmacists have an opportunity to participate in.[69]

Because of the significant risk and cost associated with irrational use of medicines, and the potential to cause harm to patients, pharmacists should ensure they are addressing each of the criteria for rational use with their patients in order to prevent future harm and ensure optimal outcomes.

4.3.3 Medication adherence

Medication adherence is critical during treatment for diabetes to achieve good disease control, minimise disease progression and prevent the development of complications. Pharmacists should take steps to promote adherence during all interactions with patients. The WHO estimates that nearly half of all patients do not take their medicines correctly. Specific to long-term therapy for chronic disease, it is estimated that, in high-income countries, adherence to treatment averages at 50%, with rates likely being much lower in low- and middle-income countries. These low rates of adherence lead to poor health outcomes as well as increased costs to health systems. Because of the far-reaching effects of non-adherence, interventions that focus on improving adherence may have a greater impact on a population's health than any improvement in medical treatment. Therefore, pharmacists should consider medication adherence as a critical component of caring for patients with diabetes.[70]

To address medication adherence with patients, pharmacists must be aware of the many factors that influence adherence and ensure they are supporting patients to improve it. Further, pharmacists must recognise that adherence for patients with diabetes goes beyond medicines and includes adherence to blood glucose monitoring, dietary changes, physical activity, weight loss goals (if applicable), regular foot care, eye examinations, blood pressure screenings, etc. Adherence also, importantly, includes regular follow-up visits with their primary care provider to ensure their condition remains under control.

To support pharmacists in identifying the factors that are contributing to an individual patient's non-adherence, the WHO outlines five dimensions of adherence, presented in Table 7.

Table 7 - WHO five dimensions of adherence[70]

Dimension	Select considerations	
Social/economic factors	• Low socioeconomic status, high cost of medicines • Illiteracy or low levels of education • Unemployment • Lack of effective social support networks • Unstable living conditions	• High cost of transportation or long distance from treatment centres • Culture, beliefs about illness and treatment • Family dysfunction
Health system/ healthcare team factors	• Poor patient-provider relationship • Short consultations/appointments • Poor medicines distribution systems • Lack of knowledge and training for healthcare providers	• Overworked healthcare providers • Weak system capacity to educate patients and provide follow-up • Lack of knowledge on adherence and effective interventions to improve it
Condition-related factors	• Severity of symptoms • Severity of disease • Level of disability (physical, psychological, social and vocational) • Rate of disease progression	• Availability of effective treatments • Patient's perceived risk • Co-morbidities, including depression or alcohol abuse, may influence adherence
Therapy-related factors	• Complexity of medication regimens • Duration of treatment • Previous treatment failures • Frequent changes in treatment	• Immediacy of beneficial effects • Side effects • Availability of medical support to deal with side effects
Patient-related factors	• Resources, knowledge, attitudes, beliefs, perceptions and expectations of patients • Forgetfulness, hopelessness • Psychosocial stress, anxieties about possible adverse effects • Low motivation • Inadequate knowledge or skills in managing the disease and treatment • Lack of perceived need for treatment or perceived effect of treatment	• Misunderstanding or non-acceptance of the disease, disbelief about diagnosis • Lack of perception of the health risk related to the disease • Anxiety over complexity of drug regimen, misunderstanding treatment instructions • Feeling stigmatised by the disease

As pharmacists work with patients to identify the underlying causes of their non-adherence, they must remember that promoting adherence requires engaging with the patient and understanding their concerns, beliefs, expectations and motivations. Adherence differentiates itself from compliance in that the patient plays an active role in the decision-making process and agrees to the plan that is developed in collaboration with their healthcare provider.[70]

Once the underlying cause of adherence is identified, pharmacists can work with the patient to determine a suitable solution that will support them in improving their adherence. Simple, but effective, strategies that pharmacists can recommend include pillboxes, blister packs, or reminders using phones or printouts placed in a notable location for the patient. Additional strategies may include filling medicines with higher quantities (e.g., 90-day supply vs. 30-day supply) or synchronising their medicines so they can come to the pharmacy at one time to get all of their refills. If amenable to the idea, the patient could also request support from a friend or family member and have them remind them to their take their medicines. Finally, the reasons for non-adherence may stem from a lack of knowledge about the medicine and its effectiveness or concerns about side effects or administration, which are concerns that pharmacists are highly qualified to address.

One strategy that has been used to promote medicine adherence in community pharmacies is the Indian Health Service counselling technique, which includes interactive components of counselling as opposed to pharmacists simply sharing information with the patient. This strategy resulted in 50% more patients with diabetes, high cholesterol or hypertension achieving an adherence rate of at least 80%, which is a generally considered an acceptable level of adherence.[71] Further, while this type of counselling may take longer than

traditional counselling, it has demonstrated significant improvements in memory recall among patients.[72] The main questions that guide this counselling strategy are:[71]

1. What did your doctor tell you this medicine was for?
2. How did your doctor tell you to take this medicine?
3. What did your doctor tell you to expect from this medicine?

Pharmacists can use these questions to guide patients into discussions of topics that may fall under each question. For example, after asking question 3, pharmacists can discuss adverse effects, drug interactions and strategies to monitor treatment efficacy. Additional information on this strategy can be found in the study by Colvin *et al*.[71]

Another strategy that can be used to promote adherence among patients is motivational interviewing, which has been defined as "a collaborative conversation style for strengthening a person's own motivation and commitment to change".[72] Motivational counselling aims to help people overcome their ambivalence to change. Ultimately, this approach would require pharmacists to engage with patients and talk with them about why they want to make certain changes in their health behaviours. These conversations must encompass the four main principles of motivational interviewing (partnership, acceptance, compassion and evocation) and utilise the four main processes (engaging, focusing, evoking and planning). "Engaging" requires establishing a working relationship with the person you are speaking with. "Focusing" means the conversation must be concentrated on a certain direction or area. "Evoking" requires that a person has the opportunity to discover their own motivations for change. "Planning" involves developing clear next steps to help make this change. Finally, motivational interviewing requires the utilisation of five key communication skills: open-ended questions, affirmations, reflective listening, summarising, and providing information and advice with permission.[73]

Another option pharmacists can utilise to ensure patients are retaining the information they are taught is the teach-back method. This strategy involves having patients explain the information that has been shared with them in their own words in order to assess their understanding. The Agency for Healthcare Research and Quality shares the following recommendations for implementing this practice:[74]

- **Plan your approach** Think about how you will ask your patients to teach back the information.
- **"Chunk and check"** Assess understanding several times during counselling sessions if a lot of information is conveyed.
- **Clarify and check again** If there is a misunderstanding, explain information again in a different way. If patients are copying your words exactly, it is possible they may not have understood.
- **Use show-me methods** Ask patients to show you how will they will use a certain medicine or device. Users of blood glucose monitors and insulin may benefit from this strategy.
- **Use handouts along with teach-back** If possible, provide patients with handouts for key information to help them remember instructions at home.

5 Diabetes medicines

There are many medicines available to treat diabetes; however, their availability and affordability vary throughout the world. This chapter will provide an overview of the main medicines used to treat diabetes. An overview chart of the risks and benefits of common medicines for type 2 diabetes, excluding insulin, can be found in Appendix 1. IDF Risks and Benefits of Common Diabetes Medicines[22].

5.1 Metformin

Metformin is typically the first drug of choice for someone who has been diagnosed with type 2 diabetes. It is a biguanide that reduces hepatic glucose production, reduces the intestinal absorption of glucose and increases insulin sensitivity, which leads to reduced blood glucose levels. Metformin, unlike sulfonylureas, does not increase the secretion of insulin and hence, does not cause hypoglycaemia. However, in combination with sulfonylureas or insulin, it may potentiate hypoglycaemic effects.

Metformin can have a great impact on reducing a patient's HbA1c, often between a 1% and 2% decrease; therefore, it is an important medicine to consider for all patients newly diagnosed with type 2 diabetes. Primary side effects of this medicine are gastrointestinal and include diarrhoea or, less likely, constipation, bloating, flatulence and abdominal cramping. It may also cause a metallic taste. To avoid these side effects, pharmacists may recommend titrating the dose slowly and having patients take this medicine with food. They can also recommend the use of an extended-release formulation as opposed to an immediate-release formulation.

Metformin should not be used in patients with reduced renal function (creatinine clearance <30ml/min), acute/decompensated heart failure or severe liver disease, or for 48 hours after the use of iodinated contrast due to the risk of lactic acidosis, which is rare but may be fatal. It should also be avoided in individuals with acute or chronic metabolic acidosis (including diabetic ketoacidosis). Given the risk of continuing metformin in those with reduced renal function, patients should be encouraged to have their renal function tested regularly while taking this medicine, especially those who are older in age. Metformin is generally considered safe in pregnancy. [75, 76]

5.2 Sulfonylureas

Sulfonylureas, including glipizide, glyburide, glimepiride, gliclazide and glibenclamide, are insulin secretagogues that reduce blood glucose by stimulating the beta cells of the pancreas to release insulin. Sulfonylureas increase both basal insulin secretion and postprandial insulin release, and they also increase peripheral glucose utilisation, decrease hepatic gluconeogenesis, and may increase the number and sensitivity of insulin receptors. Given that they increase the release of insulin, sulfonylureas come with a risk of hypoglycaemia and should be used with caution in combination with other medicines that reduce blood glucose. Sulfonylureas are typically quite effective and can reduce HbA1c by 1–2%.

Side effects associated with sulfonylureas primarily include weight gain and nausea; however, weight gain is generally less than that associated with insulin use. Hypoglycaemia is a concern with all sulfonylureas; therefore, patients should be counselled on factors that may increase their risk of hypoglycaemia, signs and symptoms of hypoglycaemia, and how to manage it should it occur. The risk of hypoglycaemia may be most elevated when a patient is fasting, skipping meals, or exercising. Sulfonylureas should be taken with breakfast, or the first meal of the day, in order to reduce the risk of hypoglycaemia. Glipizide immediate release should be taken 30 minutes before a meal. Patients may need to omit a dose if they are not planning to eat.

Preferred sulfonylureas are typically glipizide, gliclazide, and glimepiride as they have a shorter duration of action and lower risk of hypoglycaemia compared with longer-acting sulfonylureas, including glyburide. In patients with chronic kidney disease, glyburide can increase the risk of hypoglycaemia as its metabolites are active and renally excreted. Therefore, short-acting sulfonylureas, including glipizide and glimepiride, are

preferred. These two sulfonylureas are also metabolised by the liver and excreted in the urine as inactive metabolites.[77, 78]

5.3 Meglitinides

Meglitinides, including repaglinide and nateglinide, are insulin secretagogues and have a similar mechanism of action to that of sulfonylureas; however, they have a more rapid onset and shorter duration of action. Therefore, they are most efficacious in reducing postprandial hyperglycaemia. The efficacy of meglitinides is similar to sulfonylureas, reducing HbA1c by around 1–2%, but they are generally more expensive, so they are used less often. These medicines may be used as initial monotherapy for those who are unable to take metformin or sulfonylureas.

Meglitinides should only be taken with meals and should be omitted if the patient is not eating. Similar to sulfonylureas, meglitinides can cause hypoglycaemia and weight gain. Patients may also experience upper respiratory tract infections. Further, those taking repaglinide may need to have their dose increased at one-week intervals based on their blood glucose levels. These patients may benefit from regular blood glucose monitoring in order to determine an optimal dose of the medicine. Finally, for those taking repaglinide, pharmacists should be aware that clopidogrel and gemfibrozil can reduce the clearance of repaglinide and cause hypoglycaemia. [79, 80]

5.4 Alpha-glucosidase inhibitors

Alpha-glucosidase inhibitors, including acarbose, voglibose and miglitol, exert their effects by inhibiting gastrointestinal enzymes, alpha-glucosidases, that covert complex carbohydrates into monosaccharides that can be absorbed. Therefore, these drugs slow the absorption of dietary carbohydrates, which, in turn, slows the rise of postprandial blood glucose concentrations. Compared with other therapeutic options, these medicines have a relatively low efficacy, lowering HbA1c by around 0.4–0.9%. However, they may play a beneficial role in those who consume high carbohydrates diets or have high postprandial glucose. [81]

Alpha-glucosidase inhibitors should be avoided in those with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or in patients predisposed to intestinal obstruction. They should also not be used in those who have a medical condition that could be worsened by increased gas formation in the intestine.[82]

The most common side effects associated with alpha-glucosidase inhibitors are gastrointestinal, including flatulence, diarrhoea and abdominal pain. Starting with a lower dose and increasing doses slowly may help to mitigate the severity of these side effects. These medicines are not known to cause hypoglycaemia; however, if hypoglycaemia occurs as a result of another medicine the patient is taking, they should ensure they use oral glucose (dextrose) instead of sucrose (cane sugar) to address the hypoglycaemia. Sucrose absorption will be slowed by the alpha-glucosidase inhibitor and so it will be unable to quickly correct hypoglycaemia. These medicines should be taken with the first bite of each meal of the day.[81, 83]

5.5 Thiazolidinediones

Thiazolidinediones (TZDs), including pioglitazone and rosiglitazone, are peroxisome proliferator-activated receptor gamma agonists that increase insulin sensitivity by increasing the uptake and utilisation of glucose by adipose tissue and muscle. They also play a small role in decreasing hepatic glucose production. As monotherapy, TZDs reduce HbA1c by 0.5–1.4%.

TZDs should not be used in those with heart failure, evidence of fluid overload or oedema, a history of fractures or high risk for fractures, liver disease, or active or prior history of bladder cancer. It should also not be used in those who are pregnant.[84] It should be noted that rosiglitazone is not often used given that there is evidence that it increases the risk of myocardial infarction.[85] Both TZDs increase the risk of heart failure.

Adverse effects associated with these medicines include weight gain, fluid retention, fractures and a potential increased risk of bladder cancer (pioglitazone). Macular oedema has also been reported in patients taking

TZDs. Given all of the contraindications and safety concerns associated with these medicines, TZDs are not common therapies for type 2 diabetes. In fact, the European Medicines Agency suspended the sale of rosiglitazone in 2010, followed by the French and German medicines agencies in 2011. However, both medicines are still available in the United States.[84]

5.6 Sodium-glucose co-transporter 2 inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors, including canagliflozin, dapagliflozin, empagliflozin and ertugliflozin, support the treatment of diabetes by promoting urinary glucose excretion. The SGLT2 protein is expressed in the proximal renal tubule and facilitates the reabsorption of the majority of filtered glucose. By inhibiting SGLT2, these medicines reduce the reabsorption of glucose, promote urinary glucose excretion and lower plasma blood glucose levels. Compared with first-line medicines, SGLT2 inhibitors have a modest effect on reducing HbA1c: between 0.4% and 1.1%. It is generally recommended that these medicines are taken in the morning and canagliflozin specifically should be taken before the first meal of the day.

These medicines, while not first-line agents, have some benefits for individuals with type 2 diabetes and cardiovascular disease. Empagliflozin and canagliflozin have evidence to support their efficacy in reducing the risk of atherosclerotic cardiovascular morbidity and mortality. However, empagliflozin is generally the preferred agent between these two because canagliflozin has been associated with an increased risk of lower limb amputations and fractures. SGLT2 inhibitors have also been shown to reduce weight, with one meta-analysis showing a significant reduction in weight, around 3kg, between SGLT2 inhibitors and placebo at two years.[86]

SGLT2 inhibitors should not be used in those with severe renal impairment (eGFR <30ml/min/1.73m^2). They should also be avoided, if possible, in those with frequent bacterial urinary tract infections or genitourinary yeast infections, low bone mineral density, high risk of fractures and falls, and foot ulcerations, and in those with factors that may make them more likely to have diabetic ketoacidosis. Adverse effects associated with these medicines include genital mycotic infections, urinary tract infections, hypotension, acute kidney injury, diabetic ketoacidosis and amputations (particularly with canagliflozin). Given the mechanism of action of these medicines, patients may also experience dehydration or thirst.[87]

5.7 Dipeptidyl peptidase 4 inhibitors

Dipeptidyl peptidase 4 (DPP4) inhibitors, including alogliptin, linagliptin, sitagliptin and saxagliptin, exert their effects through several mechanisms. DPP4 is an enzyme present on the surface of most cells that breaks down incretin hormones, including glucagon-like peptide 1 (GLP1) and gastric inhibitor peptide. These hormones play an important role in stimulating insulin release and reducing glucagon secretion after food is consumed. Therefore, by inhibiting the DPP4 enzyme, these hormones are not broken down and are able to exert their effect and reduce blood glucose. Through their effect on GLP1, these medicines may also help to slow gastric emptying. In general, DPP4 inhibitors modestly reduce HbA1c by around 0.5–0.8%.

DPP4 inhibitors are typically well-tolerated with limited side effects and no effects on body weight or hypoglycaemia if not being used with insulin or sulfonylureas. Potential side effects include headache, nasopharyngitis and upper respiratory tract infections. These medicines have been associated with acute pancreatitis, hepatic dysfunction (alogliptin), severe skin reactions, hypersensitivity reactions (anaphylaxis, angioedema, blistering skin conditions and Stevens-Johnson syndrome), severe joint paint, myalgias and muscle spasms/weakness. These medicines are also associated with an increased risk of hospitalisation for heart failure, especially saxagliptin and alogliptin. However, more research is needed to fully understand this risk. DPP4 inhibitors, except linagliptin, require dose adjustments in patients with chronic kidney disease.[88, 89]

5.8 Glucagon-like peptide 1 agonists

Glucagon-like peptide 1 (GLP1) agonists work on the same pathway as DPP4 inhibitors. GLP1, as stated above, is an incretin hormone that reduces blood glucose through several mechanisms, including by stimulating glucose-dependent insulin secretion, reducing postprandial glucagon secretion and slowing gastric emptying.

Medicines in this class include dulaglutide, exenatide, liraglutide, lixisenatide and semaglutide. These medicines are all given subcutaneously, except for the oral formulation of semaglutide. They are more effective than DPP4 inhibitors in reducing HbA1c, with reductions ranging from 0.8% to 1.6%.[90, 91]

GLP1 agonists broadly fall into two categories: short-acting and long-acting. Short-acting GLP1 agonists include exenatide twice daily and lixisenatide. These formulations tend to exert a greater impact on postprandial hyperglycaemia and gastric emptying as opposed to fasting glucose. Exenatide twice daily should be administered immediately before or within one hour before the patient's morning and evening meals. Lixisenatide is administered once daily within one hour before any meal and is not recommended for those with renal impairment.

Long-acting GLP1 agonists include exenatide once weekly, dulaglutide, liraglutide and semaglutide. These medicines have a greater effect on fasting glucose and a lesser effect on gastric emptying and postprandial glucose. These GLP1 agonist formulations are typically preferred for patients given the greater simplicity in dosing schedules compared with short-acting GLP1 agonists. Dulaglutide is administered once per week. Exenatide's long-acting formulation is administered once a week at any time without regard to meals. Of note, this medicine must be shaken immediately before being administered. Liraglutide is administered daily and requires a starting dose of 0.6mg once daily for one week to reduce the risk of gastrointestinal side effects. After this week, the dose can be increased to 1.2mg daily and further to 1.8mg daily if, after a week, blood glucose goals have not yet been met. Semaglutide has both a subcutaneous and oral formulation. The subcutaneous formulation is administered once weekly, and the oral formulation is taken daily. The oral formulation should be taken on an empty stomach with no more than 120ml of water at least 30 minutes before breakfast or taking any other oral medicines.

The most common side effects associated with these medicines include nausea, vomiting and diarrhoea. GLP1 agonists should not be used in those who have a history of pancreatitis or those with gastroparesis. Both formulations of exenatide should not be used in those with a creatinine clearance below 30ml/min. Liraglutide, dulaglutide, exenatide once weekly and semaglutide should be avoided in those who have a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2. Subcutaneous semaglutide should be used with caution in those with a history of diabetic retinopathy. Exenatide once weekly may be more likely than other GLP1 agonists to cause injection site reactions, including abscesses, cellulitis and necrosis, with or without subcutaneous nodules.[92-94]

Weight loss is common with these medicines and may be a result of its effects on slowing gastric emptying and increasing satiety. Weight loss can range from 1kg to 3kg. GLP1 agonists have also been shown to reduce systolic and diastolic blood pressure as well as lipid levels.[91] Liraglutide, semaglutide and dulaglutide have shown benefits for patients with atherosclerotic cardiovascular disease and may be a preferred choice for these patients.[92]

5.9 Insulin

Insulin is a hormone released by the beta cells of the pancreas that promotes glucose metabolism. In a healthy individual, the body releases a continuous supply of insulin throughout the day (basal) as well as higher amounts in response to food intake (bolus). In those with type 1 diabetes, the body's immune system destroys the beta cells and these individuals are not able to produce insulin and therefore require daily insulin administration. Individuals who have had type 2 diabetes for a long period may have reduced insulin sensitivity, which causes their blood glucose to remain high and reduces their body's ability to produce insulin naturally due to increased insulin demand and eventual beta cell exhaustion and destruction. In these individuals, insulin must be given as part of their treatment regimen.[8]

Insulin is available in two main forms: bolus (rapid or short acting) and basal (intermediate or long acting). These two types of insulins are used to mimic the body's natural release of insulin, with basal doses often given once or twice daily and bolus doses given around mealtimes. Table 8 describes the different types of insulin, their typical onset of action, peak time when the insulin is at its maximum strength, and the duration of how long the insulin works to lower blood glucose.

Table 8 - Types of insulin[95, 96]

Type of insulin	Onset	Peak	Duration	Examples
Rapid-acting	15 minutes	1–2 hours	2–4 hours	Aspart, glulisine, lispro
Regular or short-acting	30 minutes	2–3 hours	3–6 hours	Human regular
Intermediate acting	2–4 hours	4–12 hours	12–18 hours	NPH
Long acting	2 hours	Does not peak	Up to 24 hours	Degludec, detemir, glargine
Ultra-long acting	6 hours	Does not peak	36 hours or more	Glargine U-300

Insulin is a safe and effective medicine, but there are situations that can result in significant harm and, as such, insulin must be managed carefully. Doses that are too high can cause hypoglycaemia and doses that are too low can contribute to the patient experiencing hyperglycaemia. The dosing of insulin is specific to each person's individual needs. Therefore, patients who are on insulin will typically be instructed to monitor their blood glucose levels several times throughout the day, at a frequency determined by their primary care provider. Pharmacists can play a role in educating patients on how to properly perform these tests (as discussed in section 3.2) and on how to act based on the results of these tests.[97]

5.9.1 Insulin storage and administration

An important role that pharmacists can play is educating patients on how to safely store and administer their insulin. Patients should be reminded to store their insulin in a refrigerator if possible and to avoid placing it in areas where it will be exposed to extreme heat or extreme cold. This will help to ensure the efficacy and safety of the product. Insulin should also never be stored in a freezer or in direct sunlight.[98] When a vial of insulin is in use, it can be stored at room temperature; however, the amount of time a product is stable at room temperature is dependent on the product itself and should be verified with the manufacturer. Generally, insulin should be stored between 2° and 8°C (36° and 46°F). However, household refrigerators that are used to store insulin often have temperatures slightly below this range, 0° to 4°C (32° to 41°F) and can drop below freezing point. Compared with pharmaceutical refrigerators, household refrigerators are much more likely to have fluctuating temperatures.[99] Therefore, patients should be made aware of this potential and, according to IDF Europe, should take a few steps to help mitigate the risk of their insulin freezing and losing some of its potency, including:[99]

- Using an airtight container to store their insulin inside household refrigerators to reduce temperature fluctuations;
- Keeping a thermometer inside the refrigerator next to where the insulin is stored and measuring and logging the temperature frequently; and
- If using cool bags with ice or ice packs to transport insulin, making sure the vials or pens are not in direct contact with the ice packs.

When educating patients about how to properly administer insulin, pharmacists should first instruct them to inspect their insulin product (vial, cartridge or pen) for any potential changes, such as clumping, frosting, precipitation or changes in clarity or colour. If any of these changes is noticed, patients should be instructed to use a different vial, cartridge or pen of insulin. Patients should also be informed that rapid and short-acting insulin as well as long acting insulins like insulin glargine, detemir, and degludec, will appear clear in the vial, whereas some other types of insulin will be cloudy, like intermediate-acting insulin NPH.[100] They should also be sure to verify the expiration date of the product they will be using.

Insulin is most often administered subcutaneously using traditional insulin syringes or insulin pens; however, there are other options available, including jet injectors and insulin pumps. Because many patients will be using syringes to administer their insulin, pharmacists should ensure the patient knows how to correctly prepare and administer their prescribed dose (Table 9).[100] As part of this, pharmacists should ensure patients are using an appropriate needle length for a subcutaneous injection. Generally acceptable lengths include 4mm, 5mm, and 6mm. Longer needle lengths may be more painful for the patient and may increase the risk of inadvertent intramuscular injection and, subsequently, hypoglycaemia.[101]

The pharmacists can support those using insulin cartridges and pen devices by ensuring the device is working correctly and educating patients on how to prime the needle with insulin and how to check how much insulin is left in the device. Pharmacists can also support these individuals by providing education on how to appropriately store these devices.

Table 9 - Insulin injection technique (adapted from the American Diabetes Association) [100]

Action step	Description
Dose preparation	• Verify the label on the insulin to ensure the correct insulin product is being used and is the correct concentration. • Check the dose to be administered. • Visually inspect the product for any discoloration, clumping, frosting, etc. • If the insulin product being used is a suspension, gently roll the vial or pen in the palms of the hand to resuspend it. • Draw up air in the syringe equal to the dose of insulin. • Inject air into insulin vial and draw up the correct dose. • If air bubbles are present, gently flick the syringe to get rid of them (primarily to ensure the full dose of insulin is being received).

Injection site	• Insulin is injected into subcutaneous tissue, so injection sites can include the upper arms, the anterior and lateral aspects of the thigh, buttocks and abdomen (except for a 5 cm circle around the navel).
	  ○ The abdomen has the fastest absorption, followed by the arms, thighs and buttocks.
	• Injection sites should be rotated often to prevent lipohypertrophy or lipoatrophy.
	  ○ Dividing the abdomen into four quadrants and using a different quadrant each time.

Injection technique	• Clean hands and injection site.
	• Once the dose is ready and an injection site has been selected, most patients will be instructed to lightly pinch the skin where they are going to inject in order to prevent inadvertent intramuscular administration.
	• Patients should pinch the skin, push the needle into the skin, release the pinch, then inject the insulin at a 90-degree angle to the body.
	• The needle should stay in the skin for at least 5–10 seconds after the plunger is depressed.
	  ○ This is especially important for patients using insulin pens.
	  ○ Patients can be advised to count to 10 before pulling out the insulin syringe or pen at a 90-degree angle to avoid bleeding and leaking of insulin from the pen.

If an injection is painful or if bruising, soreness, welts, redness or pain occur at the injection site, one or more of the following, outlined by the ADA, may be tried:[100]

- Injecting insulin at room temperature;
- Ensuring there are no air bubbles in the syringe;
- Waiting until topical alcohol (if used) has completely evaporated;
- Keeping muscles in the injection area relaxed, not tense, when injecting;
- Penetrating the skin quickly;
- Avoiding changing direction of the needle during insertion or withdrawal; and
- Avoiding reusing needles.

Finally, patients should be instructed to dispose of their used needles and to not recap needles before disposing of them. Ideally, patients will dispose of their used needles after every injection and use a new needle for their next injection to ensure sterility and prevent potential infections from a contaminated needle. However, if this is not possible, the ADA has several recommendations to ensure needle reuse is done in a safe manner. First, patients should be reminded never to let the needle touch anything but the insulin vial and clean skin. The needle should also never be cleaned with alcohol as this can remove the coating that helps the needle slide into the skin. Needles should be recapped safely when not in use. Insulin syringes and needles should only be used by one person and never shared with others.[98]

Patients should dispose of syringes and needles in a sharps container, but if that is not available, they should use any thick plastic container as long needles are unable to break through it.[98] When this container is full, it should be sealed and disposed of according to local guidelines.[102]

5.9.2 Insulin pumps

Individuals who are taking insulin may also use insulin pumps to administer this medicine and pharmacists should be aware of these devices and how to educate patients on their use. Insulin pumps are devices that deliver continuous, subcutaneous basal and bolus insulin to patients throughout the day. Basal doses are provided in a steady manner throughout the day and bolus doses are provided around mealtimes and can be adjusted by the user. Through this system, the insulin pump is mirroring the body's natural release of insulin.[103] Insulin pumps generally utilise a rapid-acting or regular-acting insulin to provide both the basal and bolus doses. For bolus doses, patients calculate the amount of insulin needed based on their carbohydrate consumption and glucose levels. Some pumps will include a calculator that assists in calculating this dose.[104]

Using an insulin pump allows for increased precision and flexibility with insulin doses as well as fewer injections. Compared with multiple daily insulin injections, insulin pumps have been shown to improve glycaemic control and reduce hypoglycaemia in both children and adults.[104] Complications associated with the use of insulin pumps include dislodgement or occlusion of the device, which can put the patient at an increased risk of diabetic ketoacidosis, lipohypertrophy and less often, lipoatrophy, and pump site infections. However, with appropriate management and use of the device, these risks can be mitigated.[66]

These devices are most often used by those with type 1 diabetes but can be used by those with type 2 diabetes who are on multiple daily injections and are able to safely manage the device. [66] People who may benefit from the use of an insulin pump include active people who benefit from changes in basal rates or suspending the pump when exercising, people who have frequent hypoglycaemia, people with gastroparesis, and people planning to become pregnant.[103]

Some patients may couple their insulin pump with a CGM, otherwise known as a closed-loop system or artificial pancreas. These devices utilise an algorithm to calculate and adjust insulin delivery in real-time based on trends in blood glucose monitored by the CGM. Patients who use these devices benefit from insulin delivery being suspended when their blood glucose is low or increased when blood glucose is high. Similarly there are sensor-augmented pumps that suspend insulin when blood glucose levels are low or expected to be low within the next 30 minutes, which can be particularly helpful for patients who experience nocturnal hypoglycaemia.[66]

All these devices require extensive training and education to ensure their properly use and to achieve the maximum benefit for patients and prevent dangerous complications, including diabetic ketoacidosis. Pharmacists should refer patients to the educational resources developed by the manufacturer of a particular device and assist as needed. Additional resources can be found online, for example, the Association of Diabetes Care and Education Specialists has several insulin pump therapy resources.[105]

6 Prevention and management of diabetes complications

6.1 Hypoglycaemia

Hypoglycaemia, or abnormally low blood glucose, is a common complication of diabetes, particularly among patients who are taking sulfonylureas or insulin. It is a dangerous condition as it can cause loss of consciousness or coma and can be life-threatening if left untreated. Signs and symptoms of hypoglycaemia include:[39, 106]

- **Symptoms** Headache, hunger, irritability, anxiety, paraesthesia, palpitations, light-headedness or dizziness, nausea, fatigue
- **Signs** Sweating, chills, clamminess, trembling, difficulty speaking, confusion, ataxia, stupor, pallor, seizures, coma

These signs and symptoms may appear at different glucose levels for each individual, so all patients should be made aware of them so they can take action to correct the hypoglycaemia and prevent progression to a more severe episode. Hypoglycaemia is most commonly defined as a plasma glucose level of ≤70mg/dl (3.9mmol/l) and when patients are at this point, regardless of the presence of signs or symptoms, steps should be taken to raise blood glucose levels. [39]

Hypoglycaemia unawareness occurs when a person does not experience or perceive the symptoms of hypoglycaemia, even if their blood glucose levels are dangerously low. It is an especially dangerous condition that can occur in those with type 1 or type 2 diabetes, but is more common in those with type 1 diabetes. It is most common in those who have had diabetes for many years, have a history of frequent hypoglycaemia, are taking an intensive diabetes treatment regimen, or are older in age. As would be expected, these individuals are at a greater risk for severe hypoglycaemic complications, including seizures, coma and cardiac arrhythmias.[107]

The primary method by which hypoglycaemia is managed is through the consumption of simple carbohydrates. However, if a patient is severely hypoglycaemic and is not able to swallow, hypertonic glucose could be administered intravenously, or glucagon could be administered subcutaneously, intramuscularly or intranasally. Specifically, the WHO recommends the following strategy to manage hypoglycaemia:[39, 44]

- Patients who are experiencing hypoglycaemia and are able to ingest food or drink should ingest 15–20g of glucose. If glucose is not available, they should be given oral simple carbohydrates that contain 15–20g of rapidly absorbing forms of glucose, for example, three teaspoons of sugar, eight to 10 raisins, fruit juice, one tablespoon of honey, or glucose tablets equivalent to 15g of carbohydrates. After that, plasma glucose levels will generally rise by 50mg/dl (2.8mmol/l) within 15 minutes. The patient or their caregiver should then check the glucose level and, if it is still low, the process should be repeated. Once the initial low blood glucose is corrected, patients should consume a small meal with complex carbohydrates (e.g., bread, rice or potatoes) and protein to prevent further hypoglycaemia.

To remember this strategy, pharmacists can think of the “15-15 rule,” which states that patients should have 15g of carbohydrates to raise their blood glucose, which should be checked after 15 minutes. Patients should be encouraged to wait for these 15 minutes after they eat before checking their blood glucose in order to prevent their blood glucose rebounding and going too high.[106]

Another option that can be used to address severe hypoglycaemia is glucagon. Glucagon is a hormone produced in the pancreas that stimulates the liver to release stored glucose into the bloodstream, thereby increasing blood glucose levels. This medicine is available in several formulations and can be administered subcutaneously, intramuscularly or intranasally. Of note is that glucagon may cause patients to experience nausea, vomiting, headaches or upper respiratory system symptoms. If possible, patients should be recommended to have glucagon at home in case a severe hypoglycaemic episode occurs. Patients and their caregivers should be adequately trained to administer glucagon when needed.[106, 108] While not included in the

WHO's recommendations below, glucagon is an important and effective option to manage hypoglycaemia for patients who are unconscious or not able to consume food.

If a patient has severe hypoglycaemia (plasma glucose <50mg/dl or 2.8mmol/l), the WHO recommends pursuing the following:

- If the patient is conscious, give a sugar-sweetened drink.
- If the patient is unconscious, give 20–50ml of 50% of glucose (dextrose) IV over 1–3 minutes. If this concentration is not available, any hypertonic glucose solution may be used. Should this not be possible, the pharmacist should immediately call an ambulance.

6.2 Hyperglycaemia

Hyperglycaemia, or high blood glucose, is not only a concern prior to a patient's diagnosis with diabetes, it can also lead to a medical emergency after their diagnosis. Uncontrolled diabetes with chronic hyperglycaemia can lead to long-term complications involving vision, kidneys, nerves, blood vessels and heart. The absolute or relative insulin deficiency and the increase in counter-regulatory stress hormones during an infection can lead to potentially life-threatening hyperglycaemic emergencies called diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS).

DKA occurs when plasma glucose levels are ≥250mg/dl (13.9mmol/l), or occasionally lower, and urine/serum ketones are positive. DKA is much more common in individuals with type 1 diabetes but can also rarely occur in patients with type 2 diabetes.[39] The risk of DKA is also elevated for those taking SGLT2 inhibitors.[87]

- **Potential causes** Ketoacidosis is usually caused by the patient omitting insulin or having an acute illness or infection that causes an increase in counter-regulatory hormones such as cortisol, catecholamines, glucagon and growth hormone.[109]
- **Early signs/symptoms** Thirst, dry mouth, frequent urination, high blood glucose levels, high levels of ketones in the urine or blood.[39, 110]
- **Later signs/symptoms** Constantly feeling tired, dry or flushed skin, nausea, vomiting, abdominal pain, difficulty breathing, fruity odour on breath, difficulty concentrating, confusion.[39, 110]

HHS occurs when plasma glucose levels are ≥600mg/dl (33.3mmol/l) and urine/serum ketones are negative or weakly positive.[39] HHS is a complication most often seen in individuals with type 2 diabetes who do not have their blood glucose well controlled. Symptoms of HHS may develop slowly and worsen over days or weeks.

- **Potential causes** Infection (e.g., pneumonia or urinary tract infections), other illnesses (such as heart attacks or stroke), medicines that decrease the effect of insulin on the body, medicines or conditions that increase fluid loss, not taking prescribed diabetes medicines.[111]
- **Signs/symptoms** Increased thirst and urination (early symptom), feeling weak, nausea, weight loss, dry mouth/tongue, fever, seizures, confusion, altered consciousness (stupor or coma), loss of feeling or function of muscles, problems with movement, speech impairment.[111]

Both DKA and HHS can be fatal, so all patients with suspected hyperglycaemic emergencies should be immediately referred to a hospital so they can receive proper care. Once at the hospital, patients will typically have their dehydration and electrolyte imbalances corrected and receive insulin.[39]

6.3 Cardiovascular diseases

According to the IDF, people with diabetes have a significantly increased risk of cardiovascular diseases (CVD) compared with those without diabetes, two to three times the relative risk. Further, CVD events tend to happen at earlier ages in those with diabetes. CVD is a class of diseases that involve the heart or blood vessels with the three main types of CVD being cerebrovascular disease, coronary heart disease and peripheral arterial disease.[112]

- **Risk factors** Age, family history of CVD, being overweight or obese, chronic kidney disease, hypertension, dyslipidaemia, smoking, prior CVD event.

To combat these major causes of morbidity and mortality, patients should take steps to lower their blood pressure, control their cholesterol and, if recommended, pursue antiplatelet treatment.
Controlling blood pressure in patients with diabetes reduces the risk of future microvascular or macrovascular complications. While blood pressure control may be sustained through lifestyle changes alone, patients often need dual therapy, commonly with a thiazide diuretic and ACE inhibitor to keep their blood pressure at goal. Controlling a patient's cholesterol is best done through initiating a statin, which is typically recommended for all patients aged 40 years or older with diabetes. However, if this is not possible, those at highest risk should be the priority for initiating statins.[39, 44]

All patients with diabetes should have their blood pressure checked at every visit with their primary care provider as well as when they visit the pharmacy, if regulations allow pharmacists to perform such screenings.[44] Blood pressure is considered elevated when it is ≥140/90mmHg on two different days.[113, 114] Frequency of cholesterol screenings may vary based on the recommendations of a patient's primary care provider, but it is generally checked at least every year.[115, 116] To help patients lower their chances of a heart attack or stroke, pharmacists can remember the ABCs of diabetes management (Table 10).

Table 10 - National Institute of Diabetes and Digestive and Kidney Disease diabetes management recommendations [117]

ABCs of diabetes management	
A1c testing	Patients should get their HbA1c levels tested frequently, typically every 3–6 months, and work to meet the treatment goals set by their primary care provider.
Blood pressure	Through a combination of a healthy diet, physical activity and medicines, patients should work to keep their blood pressure at the goal level set by their primary care provider.
Cholesterol	All individuals over the age of 40 with diabetes should be started on a statin to control their cholesterol and protect their heart. Some individuals may need to start this medicine at an earlier age.
Stop smoking	Smoking can further exacerbate complications caused by diabetes and contribute not only to CVD complications, but also to kidney-, eye- and nerve-related complications.

6.4 Diabetic nephropathy

Diabetic nephropathy (or kidney disease) is a microvascular complication of diabetes where damage occurs to the small blood vessels in the kidneys and renders them less effective or causes them to fail. Individuals with diabetes are much more likely to have kidney disease than those without diabetes. It is estimated that up to 40% of people with diabetes will develop chronic kidney disease and the prevalence of end-stage renal disease (ESRD) is up to 10 times higher in people with diabetes.[118] Unfortunately, in ESRD, dialysis or kidney transplantation may be required to remove body toxins and waste products.

In the early stages of diabetic kidney disease, patients may experience increased blood pressure and moderately increased urine albumin excretion as well as nausea, itching and anorexia (symptoms of uraemia). At later stages, peripheral oedema will occur.[39] Additional symptoms may include loss of sleep, upset stomach, weakness and difficulty concentrating. However, it is possible that patients may be asymptomatic or may overlook these non-specific symptoms; therefore, regular screenings are necessary. Primary care providers can check a patient's blood pressure, their urine for the presence of protein, and their organs for other complications of diabetes. [119]

In order to prevent the development of diabetic kidney disease and to slow its progression, patients must be encouraged to have good glycaemic control, maintain blood pressure at levels <130/80mmHg, and manage other major CVD risk factors such as dyslipidaemia and smoking.[39] Maintaining recommended glycaemic control has been shown to reduce the risk of microalbuminuria by one-third and for those who already had microalbuminuria, the risk of progressing to macroalbuminuria was halved.[119] Another strategy to reduce the risk of diabetic kidney disease is through the initiation of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB). In those with type 2 diabetes, ACEs and ARBs can both reduce the risk of diabetic kidney disease and the occurrence of cardiovascular events. The renal protection properties of these medicines are independent of blood pressure reduction, and they exert their effects by reducing urinary albumin excretion and slowing the rate of progression to more advanced stages of diabetic kidney disease.[120]

The WHO recommends that patients with type 2 diabetes are tested for albuminuria annually and referred to a higher level of care if necessary.[44] Those with type 1 diabetes should be screened five years after being diagnosed and then annually.[121] Pharmacists can ensure their patients are aware of these screening recommendations and recommend they visit their primary care provider regularly in order to receive these tests.

6.5 Diabetic neuropathy and diabetic foot

6.5.1 Diabetic neuropathy

Diabetic neuropathy is nerve damage caused by diabetes and is found fairly frequently in those with diabetes, especially those who have had diabetes for a long period, have had poor glycaemic control, or are older. The most common types seen in patients are peripheral neuropathy and autonomic neuropathy.[122]

Peripheral neuropathy is the most commonly seen type of neuropathy in those with diabetes. It affects nerves in the hands, feet, legs and arms.[123] This type of neuropathy alters sensory function which causes abnormal feelings and progressive numbness, which can contribute to the development of ulcers and may progress to amputation.[124]

- **Signs/symptoms** Sensory loss, unsteadiness, pain, unpleasant sensation or burning, tingling or numbness.

Autonomic neuropathy affects the autonomic nervous system and affects the body's digestive system, urinary tract, heart and blood vessels, sweat glands, eyes, etc. The most common symptom of this type of neuropathy is increased bladder muscle tone, which causes urine to remain in the bladder for longer than is normal, leading to urinary tract infections.[125]

- **Signs/symptoms** Lack of awareness of hypoglycaemia, orthostatic hypotension and resting tachycardia, diarrhoea, constipation, faecal incontinence, erectile dysfunction, urinary incontinence, and bladder dysfunction [39]

Patients who are experiencing signs or symptoms of autonomic neuropathy should be referred to a primary care provider for specialised care. This is especially important for patients with hypoglycaemia unawareness who are unable to perceive any symptoms of hypoglycaemia that may be caused by autonomic nerve damage, thereby making them unable to address their hypoglycaemia before it progresses to dangerously low levels.[126]

6.5.2 Diabetic foot

Diabetic foot often manifests as ulcers or infections on the feet that have primarily resulted from peripheral neuropathy. Peripheral neuropathy can make patients unaware of injuries they may have on their feet due to an altered perception of feeling. Because of this, injuries on the feet can often progress unnoticed.[127] Further, neuropathy can also cause the foot to become deformed which results in patients walking in an abnormal way. This increased stress on certain areas of the foot can cause calluses, or thickened skin, which can then progress to ulcers. Ulcers can also be caused by minor traumas, such as ill-fitting shoes or acute injuries. A final potential cause of ulcers is peripheral arterial disease, which is typically a result of atherosclerosis. This condition, which can be seen in up to 50% of patients with a diabetic foot ulcer, can reduce the amount of blood flowing to the feet, which can make it even more difficult for injuries or infections to heal. Together, these factors can lead to patients developing ulcers or gangrene that do not improve with treatment, resulting in amputation.[127]

Amputations are estimated to be 10 to 20 times more common in people with diabetes than in those without the disease, and it is estimated that every 30 seconds a lower extremity amputation is taking place somewhere in the world as a result of diabetes.[124]

- **Risk factors for developing foot ulcers** Peripheral vascular disease, neuropathy, poor glycaemic control, cigarette smoking, diabetic nephropathy, previous foot ulceration/amputation.
- **Symptoms** Pain in the legs or cramping in the thighs or calves during physical activity, tingling, burning, or pain in the feet, loss of sense of touch or ability to feel heat or cold very well, a change in the shape of feet over time, dry cracked skin on the feet, a change in the colour and temperature of

the feet, thickened yellow toenails, fungal infections between the toes, blisters, sores, ulcers, infected corns, ingrown toenails.

Pharmacists should ensure they are educating all patients with diabetes on the importance of proper foot care. Table 11 provides diabetes foot care counselling tips pharmacists can use. If regulations allow, they can also provide foot screenings for their patients. For additional information on how to conduct these screenings, you can refer to the IDF's Clinical Practice Recommendations on the Diabetic Foot.[128]

Table 11 - WHO diabetes foot care tips[39]

Diabetes foot care counselling tips	
Inspect your feet daily. Check for cuts, blisters, redness, swelling or nail problems. Use a magnifying hand mirror to look at the bottom of your feet.	Shake out your shoes and feel the insides before wearing. Remember, your feet may not be able to feel a pebble or other foreign object, so always inspect your shoes before putting them on.
Bathe feet in lukewarm, never hot, water. Keep your feet clean by washing them daily. Use only lukewarm water — the temperature you would use on a new-born baby.	Wear socks and appropriate footwear. The inside length of the shoe should be 1–2cm longer than your foot and should be neither too tight nor too loose.
Be gentle when bathing your feet. Wash them using a soft washcloth or sponge. Dry by blotting or patting, and dry carefully between the toes.	Keep your feet warm and dry.
Moisturise your feet but not between your toes. Use a moisturiser daily to keep dry skin from itching or cracking. But don't moisturise between the toes — that could encourage a fungal infection.	Never walk barefoot, not even at home. Always wear shoes or slippers. You could step on something and get a scratch or cut.
Cut nails carefully. Cut them straight across and file the edges. Don't cut nails too short, as this could lead to ingrown toenails. If you have concerns about your nails, consult your doctor.	Take care of your diabetes. Keep your blood glucose levels under control.
Never treat corns or calluses yourself. No "bathroom surgery" or medicated pads. Visit your doctor for appropriate treatment.	Do not smoke. Smoking restricts blood flow in your feet.

Patients should be immediately referred to acute care if they have an infected ulcer, an infection that is spreading, critical limb ischaemia, gangrene, suspicion of acute Charcot arthropathy (changes in the shape of the feet), or an unexplained red swollen foot.[39] Patients should also be encouraged to contact their primary care provider if they have a cut, a blister or bruise on their foot that does not start to heal after a few days, or a callus containing dried blood. [127]

The WHO recommends that: (i) patients' feet be examined for ulcers at every visit and if ulcers are present, they should be referred to a higher level of care; and (ii) patients be assessed for their risk of lower limb amputation annually (foot pulses, sensory neuropathy by monofilament, presence of healed or open ulcers, calluses) and referred to a higher level of care if ulcers are present or pulse is absent.[44]

6.6 Diabetic retinopathy and eye complications

Diabetic retinopathy is a microvascular complication that encompasses all disorders of the retina caused by diabetes and is a leading cause of blindness globally. It is caused by high levels of blood glucose which, over time, can damage the retina.[129] The early stages of diabetic retinopathy are considered to be non-proliferative because microvascular complications are limited to the retina only. Proliferative diabetic retinopathy occurs when microvascular complications cause blood flow to the retina to be restricted and, as a result, the retina is deprived of oxygen. To combat this, new blood vessels are formed that start from the retina and go into the vitreous cavity. This can result in vision loss through vitreous haemorrhage, tractional retinal detachment and neovascular glaucoma.[130]

All individuals with diabetes are at risk of developing diabetic retinopathy and this risk increases the longer an individual has the disease. It is estimated that more than half of people with diabetes will develop diabetic retinopathy, but this risk can be reduced through good management of a patient's diabetes.[129]

- **Risk factors** Duration of diabetes, poor glycaemic control, hypertension, diabetic kidney disease, and dyslipidaemia.[39] Women with diabetes who become pregnant, or who develop gestational diabetes, are at an even greater risk for developing diabetic retinopathy later in the course of the disease. [129]

Patients with diabetic retinopathy often do not have symptoms in the early stages of the diseases, but some individuals may notice vision changes, such as trouble reading or difficulty seeing objects that are far away.[129] Other symptoms include blurred vision, dark spots or holes, flashes of light, seeing an increased amount of floaters or poor night vision.[131] However because diabetic retinopathy can often progress without symptoms, regular eye checks are imperative to prevent progression to blindness or permanent vision changes.

Diabetes can also lead to an increased risk of other vision-related conditions, including cataracts and glaucoma. High blood glucose levels can cause structural changes to the lens of the eye which can lead to cataracts developing quicker than normal. Symptoms of cataracts include cloudy or blurry vision, double vision in one eye, seeing halos around lights, extra sensitivity to light and glare, trouble seeing well at night, and bright colours seeming faded.[132] Glaucoma occurs when pressure builds up in the eye which can lead to gradual vision loss due to retina and optic nerve damage. Symptoms include blurry vision, halos around lights, blind spots in peripheral vision and sharp pain headaches.[133]

Given the serious effects diabetes can have on a patient's vision, they should be encouraged to receive regular eye examinations and, if any of the above symptoms are reported, pharmacists should refer patients to an optometrist or ophthalmologist as soon as possible.

The WHO recommends that patients with type 2 diabetes are referred for a dilated-pupil retinal examination upon diagnosis and every two years thereafter, or as per ophthalmologist recommendations.[44] For those with type 1 diabetes, the IDF recommends that an initial eye examination be completed within five years after being diagnosed, with regular examinations occurring every one to two years after the initial examination.[130]

6.7 Periodontal disease

Periodontal (gum) disease, including gingivitis and periodontitis, is a chronic inflammatory condition that affects the gums and bone that surround and support the teeth. Gingivitis is the early stage of this condition and is characterised by swollen and red gums that may bleed. Periodontitis is the more severe form of the condition and is characterised by the gums pulling away from the teeth, bone being lost, and teeth becoming loose or falling out. These conditions are caused by bacteria in the mouth that infect the tissues surrounding the teeth and consequently cause inflammation around the tooth that leads to periodontal disease.[134]

Diabetes is a key risk factor for developing periodontitis. In fact, it is suggested that those who have diabetes have two to three times the risk of developing periodontitis compared with those who do not have diabetes, with the risk being greatest if the individual with diabetes has poor glycaemic control. Diabetes also influences the number of teeth affected by periodontitis as well as the severity of the condition.[135] This may be due to the fact that glucose is present in saliva and when diabetes is not well controlled, high glucose levels in the saliva can lead to increased amounts of harmful bacteria in the mouth. When these bacteria combine with food, they form plaque, which can cause tooth decay, cavities and periodontal disease. When this plaque hardens and becomes tartar, it builds up above the gums and causes gingivitis, which can then progress to periodontitis. [136]

As periodontitis increases in severity, it also increases blood glucose levels and HbA1c in those with diabetes. This is thought to be due to bacteria from untreated periodontitis entering the circulation and causing inflammation that leads to impaired insulin signalling and increased insulin resistance[137]. This, in turn, can contribute to an increased likelihood of developing complications from diabetes, including periodontitis. Thus, there is a two-way relationship between periodontitis and diabetes, with each condition affecting the other. Treatment for periodontitis, on the other hand, can contribute to a reduction in HbA1c and improved glycaemic control, with several studies suggesting that this reduction is typically around 0.3–0.4% in the months following treatment.[137]

Pharmacists should ensure patients with diabetes are aware of their increased risk of periodontal disease and have an oral hygiene regimen that supports their oral health. Patients should be educated on the symptoms that may be associated with periodontal disease, including[136]:

- **Symptoms of gingivitis** Red, swollen and bleeding gums.
- **Symptoms of periodontitis** Red, swollen and bleeding gums; gums that have pulled away from the teeth, long-lasting infection between the teeth and gums, bad breath that will not go away, permanent teeth that are loose or moving away from one another, changes in the way the teeth fit together when biting, pus between the teeth and gums, changes in the fit of dentures.

Pharmacists can also educate patients on steps they can take to promote good oral health. These recommendations may include:[136, 138, 139]

- **Brushing teeth twice daily** Patients should brush their teeth twice daily, usually for around two minutes each time, with a manual or powered toothbrush to reduce plaque in the mouth. A fluoride toothpaste should be used to prevent tooth decay. Patients should use a toothbrush with soft bristles to prevent damage to the enamel on the teeth and should change their toothbrush every three months.
- **Flossing teeth or using interdental brushes once daily** Flossing or using interdental brushes will prevent the build-up of plaque and food between the teeth and along the gum line.
- **Visiting a dentist regularly** Ideally, patients should visit their dentist twice a year for a clean and check-up. Dentists can provide personalised recommendations to support a patient's oral health and can identify signs of periodontal disease, or other oral health conditions, that may need to be addressed.

7 Non-pharmacological management

Non-pharmacological management of diabetes typically involves patients making changes to improve their diet and increase the amount of physical activity they complete, often with the goal of losing weight. Making these lifestyle changes is an important component of diabetes care as it supports patients in achieving their therapeutic goals. Pharmacists can play an important role in promoting these health behaviour changes to their patients and educating them on the importance of supplementing their pharmacological treatment regimen with proper nutrition and exercise.

Similar to diabetes prevention efforts, the strategies by which pharmacists disseminate this information to patients can vary and may include developing educational materials, such as pamphlets or flyers, providing general education to patients regarding the importance of making these changes after being diagnosed with diabetes, or providing more comprehensive and long-term counselling on these lifestyle changes. The level of involvement will depend on each pharmacist's comfort level with the topic, patients' needs for information, and the time available to engage with patients. Advice for creating successful public health campaigns can be found in the WHO's "Effective communications participant handbook".[24]

Pharmacists also have a role to play in referring patients to other members of the healthcare team to receive additional guidance on how to make and sustain these lifestyle changes in a safe manner. Patients can be referred to dieticians, nutritionists, exercise physiologists, diabetes educators, or even structured group programmes to support individuals living with diabetes. Once these patients are referred, pharmacists can play an important role in following up with them frequently and providing encouragement and support in order to sustain any lifestyle changes they may have made.

7.1 Nutrition

Throughout this section, various dietary considerations will be presented. However, these considerations can have different interpretations and may need to be adapted for different population groups, including religious groups, or those with certain dietary restrictions, such as those with food intolerances or those who are vegetarian or vegan. It is not within the scope of this handbook to provide specific guidance for all of these groups, but general guidance will be presented that can be adapted to various situations as needed.

While primarily trained to address diabetes from a pharmacological perspective, pharmacists can also play a role in promoting healthy dietary approaches to their patients. Several studies have shown that patients with diabetes require reinforcement of diabetes education, including dietary management, from a variety of healthcare providers in order to facilitate their understanding of the disease and to improve outcomes. Therefore, pharmacists have an opportunity to reinforce the recommendations made by a patient's other healthcare providers to appropriately manage their diabetes.[140] Although no specific dietary approaches will work for all patients with diabetes, this section will explore some of the most common ones.

The IDF broadly recommends that all people with diabetes follow a healthy diet that includes reducing the intake of calories if the patient is overweight or obese, replacing saturated fats (e.g., cream, cheese, butter) with unsaturated fats (e.g., avocado, nuts, and olive and vegetable oils), eating dietary fibre (e.g., fruit, vegetables, whole grains), and avoiding tobacco use, excessive alcohol and added sugar.[10]

The American Diabetes Association and the European Association for the Study of Diabetes also note in a consensus statement on the management of hyperglycaemia that there is no single ratio of carbohydrates, proteins and fats that is optimal for every person with diabetes. Instead, they recommend individualised dietary approaches that "emphasise foods of demonstrated health benefit, that minimise foods of demonstrated harm, and that accommodate patient preference and metabolic needs, with the goal of identifying healthy dietary habits that are feasible and sustainable".[141]

In this section, several dietary approaches with evidence to support their impact on blood glucose, HbA1c and other clinical parameters will be discussed. Most of the research conducted on the impact of these dietary approaches is for individuals with type 2 diabetes, but they may still be recommended for those with type 1

diabetes to improve overall health. Currently, there is limited evidence to support recommending one dietary approach over another for those with type 1 diabetes.[142]

7.1.1 Calorie reduction

Dietary guidelines from the IDF recommend a low-calorie diet for patients with type 2 diabetes, with the goal of losing weight or reaching a healthy body weight. Overweight or obese patients with type 2 diabetes should generally reduce their daily caloric intake by about 500–600 calories; however, this will be dependent on current dietary intake and should also take into account the quality and type of food being consumed. People with diabetes should limit sugar, sweets, sweetened beverages and snacks. They may also wish to limit eating out at restaurants, cafes, etc. where the size and content of meals cannot be controlled. Overall, patients should select foods that are high in fibre and have a low glycaemic index, with a general goal of three to five daily portions of fruit and vegetables, and fish, grains and monosaturated fats.[10]

One simple strategy to help patients visualise their dietary intake and control portion sizes is the plate method discussed in section 2.1.1 [25]

7.1.2 Glycaemic index

Glycaemic index (GI) is used to measure how carbohydrates affect blood glucose levels. All carbohydrates are digested and absorbed at different rates and the GI is a way to represent how quicky a carbohydrate-based food or drink will raise blood glucose levels after it is ingested. The GI runs from 0 to 100 and typically uses pure glucose, with a GI of around 100, as a reference. Carbohydrates that are slowly absorbed have a low GI of 55 or below.[143] High GI carbohydrates cause blood glucose levels to spike and crash, whereas low GI carbohydrates cause blood glucose to be slowly released into the bloodstream. GI values are determined through scientific methods and cannot be estimated based on the composition of the food or nutrition information on food packaging.[144] A low-GI diet has been shown to be beneficial for people with diabetes, especially type 2 diabetes, but focusing only on the GI of foods can lead to an unbalanced diet that is high in fat and calories. This is due to the fact that fat lowers the GI of foods; for example, chocolate has a low GI. Protein also lowers the GI of foods, with milk and other dairy products having low GI due to their high protein and fat content.[143] Here are some examples of foods and their GIs:[145]

- High glycaemic index (>70) — white rice, white bread, potatoes, rice cakes.
- Moderate glycaemic index — brown rice, brown bread, sweet potatoes, bananas.
- Low glycaemic index (<55) — mushrooms, milk, apples, peanuts.

Research supports the effectiveness of a low-GI diet for individuals with diabetes. A systematic review and meta-analysis of 54 studies showed that low-GI diets effectively reduced HbA1c, fasting glucose, BMI, total cholesterol and LDL cholesterol in patients with prediabetes or diabetes, especially type 2 diabetes.[146] Another meta-analysis of 18 trials that compared low- and high-GI diets found that low-GI diets result in improved glycaemic control for patients with diabetes.[147]

Further, a high-GI diet has been shown to increase the risk of developing type 2 diabetes. One study showed that those who consumed the highest-GI diets had a 33% greater risk of developing type 2 diabetes than those who consumed the lowest-GI diets.[148] This is further supported by a meta-analysis of prospective cohort studies which states that food and nutrition advice that favours low-GI diets has the potential to produce cost savings for healthcare systems.[149, 150]

To support patients who wish to integrate more low-GI foods into their diet, there are many online tools and lists that include the GI of foods. Examples include the Glycaemic Index Search Tool developed by the University of Sydney,[151] and the Glycaemic Index Food Guide developed by Diabetes Canada.[152]

7.1.3 Mediterranean diet

The Mediterranean diet is a well-researched dietary approach that can be promoted to patients to improve their health and wellbeing. The Mediterranean diet originated in the olive-growing areas of the Mediterranean region and still has a strong cultural association with these areas. While definitions vary, the Mediterranean diet is generally characterised by a “high intake of plant-based foods (fruit, vegetables, nuts and cereals) and olive oil; a moderate intake of fish and poultry; a low intake of dairy products (principally yoghurt and cheese),

red meat, processed meats and sweets (for which fresh fruit is often substituted); and a moderate wine intake, normally consumed with meals".[153]

The Mediterranean diet has been shown to benefit patients with type 2 diabetes and has been associated with improvements in glycaemic control, cardiovascular risk factors and body weight in multiple meta-analyses.[154, 155] Another network meta-analysis compared nine dietary approaches and found that the Mediterranean diet was the most effective in improving glycaemic control in patients with type 2 diabetes.[156]

There are also social and cultural factors associated with the Mediterranean diet, including longer mealtimes, post-meal siestas, regular physical activity and shared eating practices.[157] The Mediterranean Diet Foundation has developed 10 recommendations to support individuals who wish to adopt the Mediterranean diet, that are listed in Table 12.

Table 12 - Mediterranean Diet Foundation's 10 basic recommendations[158]

Recommendation	Justification
Use olive oil as your main source of added fat	This is the most widely used oil in Mediterranean cuisine. It is rich in vitamin E, beta-carotenes and a type of vegetal fat (monounsaturated) that helps prevent cardiovascular diseases. It represents a treasure in the Mediterranean diet and has remained through centuries among regional gastronomical traditions, conferring on dishes unique tastes and aromas.
Eat plenty of fruits, vegetables, legumes and nuts	Fruits and vegetables are a main source of vitamins, minerals and fibre in our diets and they also provide us with a large amount of water. It is very important to consume five servings of fruits and vegetables daily. Thanks to their elevated content of antioxidants and fibre, they can contribute to prevent various cardiovascular diseases and certain cancers, among other conditions.
Bread and other grain products (pasta, rice, and whole grains) should be a part of your everyday diet	Daily consumption of pasta, rice and grain products in general is essential due to their high content in carbohydrates. They provide us with an important amount of energy needed for our daily activities. Keep in mind that whole grain products provide more fibre, vitamins and minerals.
Foods that have undergone minimal processing, that are fresh and locally produced are best	It is important to take advantage of in-season products since they are at their best in terms of nutrients, aroma and flavour.
Consume dairy products daily, mainly yoghurt and cheese	Dairy products are excellent sources of proteins, minerals (calcium, phosphorus, etc.) and vitamins. Fermented dairy products (yoghurt, bio, etc.) are associated with health benefits since they contain live microorganisms capable of improving the balance of our intestinal microflora.
Red meat should be consumed in moderation and, if possible, as part of stews and other recipes*	Processed meat should be consumed in small amounts and as a part of sandwiches or other dishes. Meat contains proteins, iron and animal fat in variable quantities. An excessive intake of animal fat is not healthy. Therefore, small amounts of meat are recommended, lean meat whenever possible and as a part of a dish with a cereal and vegetable base.
Consume fish abundantly and eggs in moderation	It is recommended to consume fatty (dark meat) fish at least once or twice a week since its fat — even though of animal origin — has properties quite similar to those of vegetable origin which are known to protect against heart disease. Eggs are rich in high quality proteins, fat and many vitamins and minerals that make them a very complete food item. Eating eggs three or four times a week is a good alternative to fish and meat.
Fresh fruit should be your everyday dessert, and sweets, cakes and dairy desserts should be consumed only on occasion	Fresh fruit should be our usual dessert, before sweets and pastries. Fruits are highly nutritious and bring colour and flavour to our diet as well as being a healthy snack alternative.

Recommendation	Justification
Water is the beverage par excellence in the Mediterranean diet	Water is fundamental to our diet. Wine should be taken in moderation and with meals. Wine is a traditional part of the Mediterranean diet that can provide health benefits, but it must be taken as a part of a balanced diet.
Be physically active every day, since it is just as important as eating well	Keeping physically fit and doing physical activity adapted to our needs every day is key to keeping healthy.

**The International Agency for Research on Cancer classifies processed meats as Group 1, carcinogenic to humans, and red meat as Group 2A, probably carcinogenic to humans. Therefore, it is recommended that individuals limit their consumption of these meats to small amounts.*[159]

7.1.4 Low-carbohydrate diets

A ketogenic diet is one that encourages a very low intake of carbohydrates. It is different from a typical low-carbohydrate diet as it encourages individuals to focus on eating fats and proteins while significantly reducing carbohydrates. The high intake of fat coupled with restrictions in carbohydrates puts the body in a metabolic state of ketosis, which is when the body burns fat for fuel instead of carbohydrates. This is hypothesised to benefit patients with type 2 diabetes because they will not be subject to the spikes and crashes of blood glucose levels associated with the breakdown of carbohydrates. Research on the effectiveness, safety and sustainability of the ketogenic diet has shown mixed results; therefore, this is a riskier option to recommend to patients compared with other dietary approaches, such as the Mediterranean diet.[160]

Further, the ketogenic diet requires individuals to limit eating high fibre, unrefined carbohydrates, such as whole grains, fruits, legumes, etc., which are some of the most health-promoting foods, especially for individuals with type 2 diabetes.[160] For example, a review of 45 prospective studies found that whole grains intake is associated with a dose-dependent reduction in the risk of coronary heart disease, cardiovascular disease, total cancer and all-cause mortality.[161] Specific to type 2 diabetes, prospective cohort studies have found that higher consumption of total whole grains and several whole grain foods, such as whole grain breakfast cereal, oatmeal, dark bread, brown rice, added bran, and wheat germ, is significantly associated with a lower risk of type 2 diabetes.[162] Finally, it has been seen that adherence to ketogenic diets appears to be poor and individuals will often revert to higher carbohydrate intake.[163] Therefore, if patients are interested in the ketogenic diet, it is best to refer them to their primary care provider, dietician or nutritionist.

While a ketogenic, or very low-carb diet can be a risky option for patients with type 2 diabetes, there is evidence to support a diet that is lower in carbohydrates. However, there are no clear, international guidelines that differentiate between a high-carb and low-carb diet or between low-carb and ketogenic diets. Thus, it can be difficult to accurately evaluate the literature surrounding this topic or make recommendations to patients. One study defined low-carbohydrate diets as those that include 50–150g of carbohydrates per day and ketogenic diets as those than include only 20–50g of carbohydrates per day.[163] Another definition of the ketogenic diet includes 55–60% fat, 30–35% protein and 5–10% carbohydrates. For example, in a 2,000 calorie per day diet, carbohydrates would amount to 20–50g.[164] However, again, definitions will vary, and these numbers should serve only as general guidance.

Studies have shown that low-carbohydrate diets can positively impact HbA1c, triglycerides and HDL cholesterol, but these diets do not have significant effects on long-term weight loss.[165] A recent systematic review has also shown that a low-carbohydrate diet (<40% from carbohydrates) might be slightly more effective than a low-fat diet (<30% from fat).[166] Patients should be encouraged to evaluate both the quantity and quality (high-GI vs low-GI) of the foods and carbohydrates they consume and work with their healthcare team to develop a healthy diet plan they will be able to adhere to for years to come.

7.1.5 Plant-based diets

Plant-based diets, such as vegetarian or vegan diets, are those that primarily include whole foods, such as legumes, whole grains, fruits, vegetables and nuts, and have limited or no intake of animal products. It has

been shown that plant-based diets are beneficial for both preventing and treating type 2 diabetes, while also providing other health benefits such as improvements in cardiovascular disease and cancer prevention.[167]

If a plant-based diet is recommended to patients, they should ensure they are including primarily healthy plant foods in their diet. Some individuals who follow vegetarian plant-based diets include less healthy plant foods, such as sweetened food and beverages, which can be harmful to health and defeat the health benefits of the diet. Data from three prospective cohort studies have shown that a diet that emphasises plant foods and is low in animal foods is associated with a 20% reduction of risk for developing diabetes. Specifically, those that followed a plant-based diet that emphasised healthy plant foods experienced a greater risk reduction, 34%, and those who followed a plant-based diet high in less healthy plant foods actually experienced a 16% increased risk of developing type 2 diabetes. Therefore, patients should aim to include primarily healthy plant-based foods in their diet. Broadly, this study considered healthy plant foods to include whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea and coffee. Less healthy plant foods include fruit juices, sugar-sweetened beverages, refined grains, potatoes and sweets or desserts.[168]

Plant-based diets, in conjunction with educational interventions, are associated with significant improvements in psychological health, quality of life, HbA1c, and weight for patients with type 2 diabetes. Plant-based diets could also potentially improve diabetic neuropathic pain and total cholesterol, LDL cholesterol and triglycerides.[169] Vegetarian diets specifically have shown similar results, with the diet causing significant reductions in HbA1c and improvements in overall glycaemic control, LDL cholesterol, non-HDL cholesterol and body weight/adiposity in individuals with diabetes.[170, 171] Finally, for people with diabetes who have chronic kidney disease, a plant-based diet can have positive effects on their health by delaying progression of the disease. It can also help to manage and prevent some symptoms and metabolic complications of chronic kidney disease.[167, 172]

7.2 Physical activity

Regular physical activity is very important for individuals with diabetes as it can lower blood glucose and blood pressure, improve tissue perfusion, burn calories to support weight loss, improve mood, decrease risk of falls, improve memory in older adults and support better sleep.[173]

The IDF recommends that individuals with diabetes do physical activity on three to five days a week, for a minimum of 30–45 minutes, as regular physical activity is essential to help keep blood glucose levels under control.[174] Physical activity is most effective when it includes a combination of both aerobic exercise (e.g., jogging, swimming, cycling) and resistance training (e.g., free weights, resistance bands, body weight exercise), as well as reduced amounts of time spent being inactive. If there are no contraindications, resistance training should take place two to three times per week on non-consecutive days. All individuals with diabetes should make efforts to reduce the amount of time spent being sedentary each day. For example, if sitting for long periods, efforts should be made to stand or walk around every 30 minutes. [36]

To ensure physical activity is sustained long-term, it is recommended that physical activity is introduced gradually, based on the patient's willingness and ability, with individualised and specific goals being set for a certain period. One way this can be implemented is recommending patients walk for at least 150 minutes per week, e.g., 20 minutes daily or 30 minutes five days of the week), or less if the patient feels this goal may not be achievable at first, and then increasing either the intensity or frequency of activity once a patient is confident they can maintain this level of activity. Patients should also be recommended to pursue physical activities that they enjoy and can see themselves sustaining for years to come. To support patients in making these changes, pharmacists can reference resources developed by Diabetes Canada, which include a sample walking plan that encourages patients to slowly increase their duration and intensity of exercise over time[175] as well as a brochure that explains how to safely begin resistance training and how to complete certain resistance exercises.[176] When participating in physical activity, patients should take care to wear footwear that fits properly as well as moisture wicking socks in order to prevent diabetic foot complications, including ulcers.[177]

Patients should also be educated on how to adjust their medicines, especially insulin, for physical activity and how adding timely carbohydrate intake may help them avoid hypoglycaemia.[22, 63] Physical activity lowers blood glucose, and a patient's blood glucose may become dangerously low if they are not prepared. Therefore,

patients may need to increase their frequency of blood glucose testing before and after physical activity. Hypoglycaemia can occur during or up to 24 hours after physical activity.[173]

7.3 Tobacco cessation

Smoking is not only a risk factor for developing type 2 diabetes, but it can also contribute to the progression of the disease as well as an increased risk of complications for those with type 1 or type 2 diabetes. All individuals with diabetes should be advised to not use cigarettes, tobacco products or e-cigarettes. Being exposed to high levels of nicotine causes the body to require larger doses of insulin to control blood glucose levels as insulin is less effective in the presence of nicotine. Further, those who smoke and have diabetes are more likely to experience complications of the disease, including heart and kidney complications, diabetic foot infections or ulcers, potential amputation of the toes or feet, retinopathy and peripheral neuropathies.[32] They may also have a greater risk of premature death.[36] To assist patients with quitting, pharmacists can utilise the WHO's 5A model (Ask, Advise, Assess, Assist, Arrange) to help patients get ready to quit and the 5R model (Relevance, Risks, Rewards, Roadblocks, Repetition) to increase motivation to quit. Details on these strategies can be found in the WHO "Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care".[33]

8 Barriers to delivering pharmacist-provided diabetes services

There are various factors that enable or hinder the delivery of pharmacist-provided diabetes services in the community. To ensure that the role of pharmacists in providing care for patients with diabetes is optimised, there is a need to outline the various barriers influencing pharmacists' ability to establish and provide diabetes management services in the community. Pharmacists should evaluate whether these factors may be present where they would be providing diabetes services and identify strategies to overcome these barriers in order to facilitate the delivery of diabetes services in their community. These factors include, but are not limited to, the following:

Lack of a convenient space for private consultation and counselling The lack of a consulting space in the pharmacy where pharmacists can engage, interact with and counsel patients has been identified as an impediment to providing diabetes services.[178] This is because patients are more likely to share details regarding their health status and medicines in a safe and convenient environment, where privacy is guaranteed.[179] Hence, pharmacy premises lacking a counselling space might impede the type of services provided by the pharmacist, especially those requiring ample engagement time. In situations where there are no private spaces on the pharmacy floor, pharmacists will have to be innovative in providing alternative solutions that still allow for some privacy.[179] Some examples include the use of temporary structures to differentiate between the pharmacy floor and areas for consultation, and the deployment of telephone appointments for consultation.

Insufficient time and heavy workload Due to the busy nature of most pharmacies, pharmacists might not have the ability to commit sufficient time to engaging with patients during counselling sessions.[178] These time constraints may result in an inability to provide specific diabetes services such as counselling or medicine assessments.[180] Community pharmacists are busy professionals, addressing a myriad of health concerns presented by their patients, while also providing leadership and managing the day-to-day activities in the pharmacy. Therefore, running a separate or additional service to manage a specific disease condition might be challenging and, hence, serve as a demotivating factor. This challenge is exacerbated in the absence of pharmacy support staff, leaving the pharmacist to grapple with both patient care and administrative functions. While this is a difficult challenge to address, pharmacists can take steps to introduce initiatives that require limited time. For example, they can work with their national pharmacy association to see if there are existing diabetes educational materials that could be shared with their patient population. If pharmacists do this, their patients still benefit from learning more about diabetes and pharmacists are not adding significant amounts of work to their existing heavy workload.

Remuneration Pharmacists are already poorly remunerated for providing additional services in the pharmacy, with product-based remuneration remaining the most common remuneration model globally.[181] This serves as a huge barrier in the delivery of diabetes services, which in most cases present in the form of an extra service provided by pharmacists. Several studies carried out to understand the barriers preventing the delivery of diabetes services have indicated poor remuneration as an important barrier to pharmacists committing their time and resources to addressing diabetes in their community.[180, 182] In situations where a remuneration model for such services exists, the benefits usually go to pharmacy owners and not the pharmacists themselves.[183] As a result of this, pharmacists may not feel motivated to provide services to improve diabetes in the community, alongside the myriad of other services they are already providing, given that they have no financial incentive to do so.

However, pharmacists have been shown to provide an increased number of diabetes services when they are properly remunerated, according to a study carried out in Canada.[182] Remunerated services typically included the development of an annual care plan and prescription renewal assessment. These services were likely to be provided by certified pharmacists (see below), thereby elevating a need for the institution of a reimbursement plan that is consistent with the level of services provided.[182] Pharmacists should endeavour to work with various pharmacy and healthcare stakeholders to advocate increased remuneration for pharmacist-provided services so they have a greater ability to provide services, such as diabetes screenings, to improve health in their community.

Accreditation and training Evidence demonstrates that pharmacists who are accredited with a specialised certification are more likely to deliver an increased number of diabetes management services in the community, compared with pharmacists who are unaccredited.[184] A study conducted in Alberta, Canada demonstrated that pharmacists who were certified diabetes educators, now called "certified diabetes care and educator specialists", or had additional prescribing authority, initiated significantly more diabetes management services than other pharmacists. Pharmacists surveyed in Kuwait in 2017 identified the need for advanced specialist skills in diabetes patient education as an enabler for offering diabetes management services within the community.[185] This extra level of accreditation provides pharmacists with the knowledge, credibility and motivation to provide these services. Evidence consistently demonstrates a greater likelihood of pharmacists with specialised knowledge providing specialised services in disease-specific areas compared with pharmacists without expert knowledge, which emphasises the need for additional training and certification to assure pharmacists' adequate knowledge, skill and confidence.[186-188]

Enrolling in training activities, such as seminars, conferences, symposia and continuing professional development initiatives, prepares and equips pharmacists to provide diabetes-related roles. When pharmacists are trained, they become confident and willing to lead on the provision of diabetes management services. Therefore, sustaining a culture of continuous learning among pharmacists can benefit pharmacists and patients in preventing and managing diabetes and its complications.

Patients' perception of pharmacists' role The way pharmacists are perceived regarding their role in patient care can serve as an impediment or facilitator to providing diabetes services. Where pharmacists are regarded as dispensers of medicines, rather than providers of pharmaceutical care, it might impact the interaction and engagement level of patients with pharmacists.[185] Studies conducted in Kuwait cited patients' perception of pharmacists as dispensers as a barrier to the provision of diabetes services.[185, 189] An implication of this is the lack of trust in the ability of pharmacists to provide patient care for diabetic patients. Addressing this challenge will require pharmacists to educate their patients about their role in the provision of pharmaceutical care and gain their trust as medicines experts. However, in most communities, patients have come to understand and appreciate the role of pharmacists in providing diabetes management services and have indicated acceptance of services, serving as an enabler for renewed interest by pharmacists to offer their time and expertise.[190-192]

9 Conclusion

With growing rates of diabetes globally, it is imperative that pharmacists leverage their accessibility and expertise to address this pressing global health issue in their communities. Pharmacists are ideally positioned and qualified to provide diabetes services, ranging from preventive services to screenings and referrals for pharmacological and non-pharmacological treatments.

Pharmacists also have an opportunity to collaborate with other healthcare professionals to provide comprehensive, holistic care for those with diabetes. While there are barriers to widespread adoption of pharmacist-provided diabetes services, there is an enormous beneficial public health potential to be had if these services are integrated into pharmacy practice globally.

Pharmacists should begin to consider how they might incorporate the services discussed throughout this handbook into their approach to care and how these services might benefit their patients. Ultimately, pharmacists have an immense opportunity to further their role as public health professionals and healthcare providers by taking steps to prevent, identify and treat diabetes in their community.

10 References

1. International Diabetes Federation. IDF Diabetes Atlas - 10th Edition: 2021. updated [accessed: 3 November 2021]. Available at: https://diabetesatlas.org/.
2. Liu JX, Goryakin Y, Maeda A et al. Global Health Workforce Labor Market Projections for 2030. Human Resources for Health. 2017;15(1):11. [Cited: 19 March 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/28159017/.
3. International Diabetes Federation. IDF Diabetes Atlas - Ninth Edition. 2019. [Cited: 21 July 2021]. Available at: https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf.
4. Organization WH. Noncommunicable Diseases Geneva: WHO; 2021. updated [accessed: 26 Oct]. Available at: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases.
5. Organization WH. Declaration of Astana - Global Conference on Primary Health Care. [Internet]. 2018. [Cited: Available at: https://www.who.int/docs/default-source/primary-health/declaration/gcphc-declaration.pdf.
6. Federation IP. Beating non-communicable diseases in the community — The contribution of pharmacists. [Internet]. 2019. [Cited: Available at: https://www.fip.org/file/4694.
7. World Health Organization. Diabetes Geneva: World Health Organization; 2021. updated 2021/04/13/. [accessed: 19 March 2021]. Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes.
8. National Institute of Diabetes and Digestive and Kidney Diseases. Symptoms and Causes of Diabetes: 2016. updated [accessed: 24 October 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/symptoms-causes.
9. National Institute of Diabetes and Digestive and Kidney Diseases. Type 1 Diabetes: 2017. updated [accessed: 24 October 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/type-1-diabetes.
10. International Diabetes Federation. Type 2 diabetes: 2020. updated 2020/10/16/. [accessed: 19 March 2021]. Available at: https://www.idf.org/aboutdiabetes/type-2-diabetes.html.
11. Centers for Disease Control and Prevention. Gestational Diabetes: 2019. updated 2019/05/30/. [accessed: 13 July 2021]. Available at: https://www.cdc.gov/diabetes/basics/gestational.html.
12. International Pharmaceutical Federation. FIP Statement of Policy - The role of pharmacists in non-communicable diseases. 2019. [Cited: 20 July 2021]. Available at: https://www.fip.org/file/4338.
13. International Pharmaceutical Federation. FIP Statement of Policy – The role of the pharmacist in the prevention and treatment of chronic disease: 2006. updated [accessed: 20 July 2021]. Available at: https://www.fip.org/file/1468.
14. International Pharmaceutical Federation. FIP Statement of Policy - Collaborative Pharmacy Practice. [Internet]. 2010. [Cited: 20 July 2021]. Available at: https://www.fip.org/file/1492.
15. Fazel MT, Bagalagel A, Lee JK et al. Impact of Diabetes Care by Pharmacists as Part of Health Care Team in Ambulatory Settings: A Systematic Review and Meta-analysis. Ann Pharmacother. 2017;51(10):890-907. [Cited: Available at: https://pubmed.ncbi.nlm.nih.gov/28573873/.
16. Chisholm-Burns MA, Kim Lee J, Spivey CA et al. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. Med Care. 2010;48(10):923-33. [Cited: Available at: https://pubmed.ncbi.nlm.nih.gov/20720510/.
17. van Eikenhorst L, Taxis K, van Dijk L et al. Pharmacist-Led Self-management Interventions to Improve Diabetes Outcomes. A Systematic Literature Review and Meta-Analysis. Front Pharmacol. 2017;8:891. [Cited: 21 August 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/29311916.
18. Desse TA, Vakil K, Mc Namara K et al. Impact of clinical pharmacy interventions on health and economic outcomes in type 2 diabetes: A systematic review and meta-analysis. Diabet Med. 2021;38(6):e14526. [Cited: 21 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/33470480/.

19. Wang Y, Yeo QQ, Ko Y. Economic evaluations of pharmacist-managed services in people with diabetes mellitus: a systematic review. Diabet Med. 2016;33(4):421-7. [Cited: 20 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/26433008/.
20. Abdulrhim S, Sankaralingam S, Ibrahim MIM et al. The impact of pharmacist care on diabetes outcomes in primary care settings: An umbrella review of published systematic reviews. Prim Care Diabetes. 2020;14(5):393-400. [Cited: 20 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/31926868/.
21. Primary Care Diabetes Society. Best Practice in the Delivery of Diabetes Care in the Primary Care Network. [Internet]. 2021. [Cited: 24 October 2021]. Available at: https://www.pcdsociety.org/resources/details/glance-guide-best-practice-delivery-diabetes-care-primary-care-network.
22. International Diabetes Federation. IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. [Internet]. 2017. [Cited: 19 March 2021]. Available at: http://www.idf.org/managing-type2-diabetes.
23. Centers for Disease Control and Prevention. National Diabetes Prevention Program - Diabetes DDT: 2019. updated 2019/08/02/T06:30:40Z. [accessed: 22 August 2021]. Available at: https://www.cdc.gov/diabetes/prevention/about.htm.
24. World Health Organization. WHO Effective Communications Participant Handbook. Geneva: Organization WH [Internet]. 2015. [Cited: 20 March 2021]. Available at: https://www.who.int/communicating-for-health/resources/participant-handbook-english.pdf?ua=1.
25. Centers for Disease Control and Prevention. Diabetes Meal Planning: 2021. updated 2021/03/11/. [accessed: 27 April 2021]. Available at: https://www.cdc.gov/diabetes/managing/eat-well/meal-plan-method.html.
26. International Diabetes Federation. Type 2 Diabetes Prevention: 2020. updated [accessed: 21 August 2021]. Available at: https://idf.org/our-activities/care-prevention/prevention.html.
27. American Diabetes Association. 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021;44(Supplement 1):S34-S9. [Cited: 23 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/44/Supplement_1/S34.full.pdf.
28. Bull FC, Al-Ansari SS, Biddle S et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020;54(24):1451-62. [Cited: 23 August 2021]. Available at: https://bjsm.bmj.com/content/bjsports/54/24/1451.full.pdf.
29. American Diabetes Association. Extra Weight, Extra Risk: updated [accessed: 23 August 2021]. Available at: https://www.diabetes.org/diabetes-risk/prevention/overweight.
30. World Health Organization. Body mass index - BMI [Internet]. Copenhagen: World Health Organization; updated [accessed: 25 April 2021]. Available at: https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi.
31. World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation. Geneva: Organization WH [Internet]. 2011. [Cited: 13 April 2021]. Available at: https://www.who.int/publications/i/item/9789241501491.
32. Centers for Disease Control and Prevention. Smoking and Diabetes: 2014. updated [accessed: 23 August 2021]. Available at: https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/pdfs/fs_smoking_diabetes_508.pdf.
33. World Health Organization. Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care. 2014. [Cited: 22 August 2021]. Available at: https://apps.who.int/iris/bitstream/handle/10665/112835/9789241506953_eng.pdf?sequence=1.
34. International Diabetes Federation. IDF Diabetes Atlas, 9th edn: 2019. updated 2019. [accessed: 26 April 2021]. Available at: https://www.diabetesatlas.org.
35. World Health Organization. Global report on diabetes. Geneva: Organization WH [Internet]. 2016. [Cited: 19 March 2021]. Available at: https://www.who.int/publications-detail-redirect/9789241565257.

36. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes. Diabetes Care. 2021;44(Supplement 1):S15-S33. [Cited: 21 July 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/33298413.
37. Rehman A, Setter SM, Vue MH. Drug-Induced Glucose Alterations Part 2: Drug-Induced Hyperglycemia. Diabetes Spectrum. 2011;24(4):234-8. [Cited: 21 October 2021]. Available at: https://spectrum.diabetesjournals.org/content/diaspect/24/4/234.full.pdf.
38. U.S. Food and Drug Administration. FDA Drug Safety Communication: Important safety label changes to cholesterol-lowering statin drugs: 2016. updated [accessed: 23 October 2021]. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-important-safety-label-changes-cholesterol-lowering-statin-drugs.
39. World Health Organization. HEARTS D: Diagnosis and management of type 2 diabetes. 2020. [Cited: 21 July 2021]. Available at: https://www.who.int/publications-detail-redirect/who-ucn-ncd-20.1.
40. Khan MAB, Hashim MJ, King JK et al. Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020;10(1):107-11. [Cited: 22 August 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7310804/.
41. National Institute of Diabetes and Digestive and Kidney Diseases. Type 2 Diabetes: 2017. updated [accessed: 22 August 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/type-2-diabetes.
42. Noctor E, Dunne FP. Type 2 diabetes after gestational diabetes: The influence of changing diagnostic criteria. World J Diabetes. 2015;6(2):234-44. [Cited: 22 August 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4360417/.
43. Dennison RA, Chen ES, Green ME et al. The absolute and relative risk of type 2 diabetes after gestational diabetes: A systematic review and meta-analysis of 129 studies. Diabetes Research and Clinical Practice. 2021;171. [Cited: 22 August 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/33333204.
44. World Health Organization. WHO Package of Essential Noncommunicable (PEN) Disease Interventions For Primary Health Care. 2020. [Cited: 20 July 2021]. Available at: https://apps.who.int/iris/bitstream/handle/10665/334186/9789240009226.eng.pdf?sequence=1&isAllowed=y.
45. Centers for Disease Control and Prevention. Respiratory Rate: updated [accessed: 22 July 2021]. Available at: https://www.cdc.gov/dengue/training/cme/ccm/page57286.html.
46. United States Preventive Services Taskforce. Draft Recommendation: Screening for Prediabetes and Type 2 Diabetes Mellitus 2021. updated [accessed: 27 July 2021]. Available at: https://uspreventiveservicestaskforce.org/uspstf/draft-update-summary/prediabetes-and-type-2-diabetes-screening.
47. Centers for Disease Control and Prevention. Diabetes - All About Your A1c: 2021. updated [accessed: 23 October 2021]. Available at: https://www.cdc.gov/diabetes/managing/managing-blood-sugar/a1c.html.
48. World Health Organization and International Diabetes Federation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia : report of a WHO/IDF consultation. Geneva: [Internet]. 2006. [Cited: 18 October 2021]. Available at: https://apps.who.int/iris/handle/10665/43588.
49. American Diabetes Association. Diagnosis: updated [accessed: 17 October 2021]. Available at: https://www.diabetes.org/a1c/diagnosis.
50. U.S. Food and Drug Administration. Blood Glucose Monitoring Devices: 2019. updated 2019/05/03/Fri, -10:30. [accessed: 22 August 2021]. Available at: https://www.fda.gov/medical-devices/in-vitro-diagnostics/blood-glucose-monitoring-devices.
51. Dogan K, Kayalp D, Ceylan G et al. Falsely Elevated Glucose Concentrations in Peritoneal Dialysis Patients Using Icodextrin. J Clin Lab Anal. 2016;30(5):506-9. [Cited: 18 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/26511081/.
52. Perera NJ, Stewart PM, Williams PF et al. The danger of using inappropriate point-of-care glucose meters in patients on icodextrin dialysis. Diabet Med. 2011;28(10):1272-6. [Cited: 17 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/21679233/.

53. World Health Organization and International Diabetes Federation. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. Diabetes Research and Clinical Practice. 2011;93(3):299-309. [Cited: 16 August 2021]. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0168822711001318.

54. Gallagher EJ, Le Roith D, Bloomgarden Z. Review of hemoglobin A(1c) in the management of diabetes. J Diabetes. 2009;1(1):9-17. [Cited: 27 August 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20923515.

55. Radin MS. Pitfalls in Hemoglobin A1c Measurement: When Results may be Misleading. J Gen Intern Med. 2014;29(2):388-94. [Cited: 22 August 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912281/.

56. World Health Organization. WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy. Chapter 7 - Capillary Sampling. 2010. [Cited: 23 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK138654/.

57. Terrie Y. Cough and Cold Products for Patients with Diabetes: 2008. updated [accessed: 23 October 2021]. Available at: https://www.pharmacytimes.com/view/2008-10-8700.

58. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes 2021. Diabetes Care. 2021;44(Supplement 1):S111-S24. [Cited: 17 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/44/Supplement_1/S111.full.pdf.

59. Australian Diabetes Society and Diabetes Australia. Australian Type 2 Diabetes Glycaemic Management Algorithm: 2021. updated [accessed: 18 October 2021]. Available at: https://diabetessociety.com.au/downloads/20211014%20T2D%20Management%20Algorithm.pdf.

60. McGibbon A AL, Ingersoll K, Kader T, Tugwell B, . Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Glycemic Management in Adults With Type 1 Diabetes: 2018. updated [accessed: 24 October 2021]. Available at: https://guidelines.diabetes.ca/cpg/chapter12.

61. International Diabetes Federation Europe. How to manage diabetes during an illness? : updated [accessed: 23 October 2021]. Available at: https://www.idf.org/component/attachments/?task=download&id=2155:IDFE-Sick-day-management.

62. Centers for Disease Control and Prevention. Managing Sick Days: 2020. updated [accessed: 23 October 2021]. Available at: https://www.cdc.gov/diabetes/managing/flu-sick-days.html.

63. International Diabetes Federation. Global guideline for type 2 diabetes. 2017. [Cited: 23 August 2021]. Available at: https://www.idf.org/e-library/guidelines/79-global-guideline-for-type-2-diabetes.

64. American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021;44(Supplement 1):S73-S84. [Cited: 23 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/44/Supplement_1/S73.full.pdf.

65. American Diabetes Association. CGM & Time in Range: updated [accessed: 24 October 2021]. Available at: https://www.diabetes.org/healthy-living/devices-technology/cgm-time-in-range.

66. Association AD. 7. Diabetes Technology: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021;44(Supplement 1):S85-S99. [Cited: 24 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/44/Supplement_1/S85.full.pdf.

67. National Institute of Diabetes and Digestive and Kidney Diseases. Continuous Glucose Monitoring: 2017. updated [accessed: 24 October 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/managing-diabetes/continuous-glucose-monitoring.

68. World Health Organization. Problems of Irrational Drug Use - Session Guide. 2010. [Cited: 23 August 2021]. Available at: https://www.paho.org/hq/dmdocuments/2010/3_IrrationalSG.pdf.

69. World Health Organization. Medication Without Harm: 2017. updated [accessed: 23 August 2021]. Available at: https://www.who.int/initiatives/medication-without-harm.

70. World Health Organization. Adherence to Long-Term Therapies - Evidence for Action. 2003. [Cited: 23 August 2021]. Available at: https://www.who.int/chp/knowledge/publications/adherence_full_report.pdf.

71. Colvin NN, Mospan CM, Buxton JA et al. Using Indian Health Service (IHS) counseling techniques in an independent community pharmacy to improve adherence rates among patients with diabetes, hypertension, or hyperlipidemia. Journal of the American Pharmacists Association. 2018;58(4):S59-S63.e2. [Cited: 23 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/29895481/.
72. Lam N, Muravez SN, Boyce RW. A comparison of the Indian Health Service counseling technique with traditional, lecture-style counseling. J Am Pharm Assoc (2003). 2015;55(5):503-10. [Cited: 24 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/26359960/.
73. Miller WR RS. Motivational Interviewing: Helping People Change. [Internet]. 2012. [Cited: 18 October 2021]. Available at: https://books.google.com/books/about/Motivational_Interviewing.html?id=01-ZpM7QqVQC.
74. Agency for Healthcare Research and Quality. Use the Teach-Back Method: 2020. updated [accessed: 23 August 2021]. Available at: https://www.ahrq.gov/health-literacy/improve/precautions/tool5.html.
75. DrugBank. Metformin: 2021. updated [accessed: 29 August 2021]. Available at: https://go.drugbank.com/drugs/DB00331.
76. MedlinePlus. Metformin: 2020. updated [accessed: 29 August 2021]. Available at: https://medlineplus.gov/druginfo/meds/a696005.html.
77. Costello RA, Nicolas S, Shivkumar A. Sulfonylureas: StatPearls. 2021. [Cited: 29 August 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK513225/.
78. DrugBank. Gliclazide: 2021. updated [accessed: 29 August 2021]. Available at: https://go.drugbank.com/drugs/DB01120.
79. Wexler DJ. Sulfonylureas and meglitinides in the treatment of type 2 diabetes mellitus: UpToDate; 2021. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/sulfonylureas-and-meglitinides-in-the-treatment-of-type-2-diabetes-mellitus.
80. Milner Z AH. Repaglinide. StatPearls. 2021. [Cited: 17 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK559305/.
81. Lipska KJ. Alpha-glucosidase inhibitors for treatment of diabetes mellitus: UpToDate; 2021. updated [accessed: 19 October 2021]. Available at: https://www.uptodate.com/contents/alpha-glucosidase-inhibitors-for-treatment-of-diabetes-mellitus.
82. Pharmaceuticals BH. Precose (acarbose tablets): 2011. updated [accessed: 19 October 2021]. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020482s024lbl.pdf.
83. Akmal M WR. Alpha Glucosidase Inhibitors. StatPearls. 2021. [Cited: 19 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK557848/.
84. Inzucchi SE LB. Thiazolidinediones in the treatment of type 2 diabetes mellitus: UpToDate; 2020. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/thiazolidinediones-in-the-treatment-of-type-2-diabetes-mellitus.
85. Wallach JD, Wang K, Zhang AD et al. Updating insights into rosiglitazone and cardiovascular risk through shared data: individual patient and summary level meta-analyses. BMJ. 2020;368:l7078. [Cited: 20 October 2021]. Available at: https://www.bmj.com/content/bmj/368/bmj.l7078.full.pdf.
86. Liu XY, Zhang N, Chen R et al. Efficacy and safety of sodium-glucose cotransporter 2 inhibitors in type 2 diabetes: a meta-analysis of randomized controlled trials for 1 to 2years. J Diabetes Complications. 2015;29(8):1295-303. [Cited: 21 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/26365905/.
87. DeSantis A. Sodium-glucose co-transporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus: UpToDate; 2020. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/sodium-glucose-co-transporter-2-inhibitors-for-the-treatment-of-hyperglycemia-in-type-2-diabetes-mellitus.
88. Dungan K DA. Dipeptidyl peptidase 4 (DPP-4) inhibitors for the treatment of type 2 diabetes mellitus: UpToDate; 2021. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/dipeptidyl-peptidase-4-dpp-4-inhibitors-for-the-treatment-of-type-2-diabetes-mellitus.

89. Kasina SVSK BK. Dipeptidyl Peptidase IV (DPP IV) Inhibitors. StatPearls. 2021. [Cited: 17 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK542331/.

90. Tran S, Retnakaran R, Zinman B et al. Efficacy of glucagon-like peptide-1 receptor agonists compared to dipeptidyl peptidase-4 inhibitors for the management of type 2 diabetes: A meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2018;20 Suppl 1:68-76. [Cited: 23 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/29364587/.

91. Hinnen D. Glucagon-Like Peptide 1 Receptor Agonists for Type 2 Diabetes. Diabetes Spectrum. 2017;30(3):202-10. [Cited: 23 October 2021]. Available at: https://spectrum.diabetesjournals.org/content/diaspect/30/3/202.full.pdf.

92. Dungan K DA. Glucagon-like peptide 1 receptor agonists for the treatment of type 2 diabetes mellitus: UpToDate; 2021. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/glucagon-like-peptide-1-receptor-agonists-for-the-treatment-of-type-2-diabetes-mellitus.

93. Latif W LK, Rodriguez R,. Compare And Contrast the Glucagon-like Peptide-1 Receptor Agonists (GLP1RAs). StatPearls. 2021. [Cited: 17 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK572151/.

94. Collins L CR. Glucagon-like Peptide-1 Receptor Agonists. StatPearls. 2021. [Cited: 17 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK551568/.

95. American Diabetes Association. Insulin Basics: updated [accessed: 20 October 2021]. Available at: https://www.diabetes.org/healthy-living/medication-treatments/insulin-other-injectables/insulin-basics.

96. Centers for Disease Control and Prevention. Types of Insulin: 2021. updated [accessed: 20 October 2021]. Available at: https://www.cdc.gov/diabetes/basics/type-1-types-of-insulin.html.

97. DrugBank. Insulin: 2021. updated [accessed: 29 August 2021]. Available at: https://go.drugbank.com/drugs/DB00030.

98. American Diabetes Association. Insulin Storage and Syringe Safety: updated [accessed: 21 October 2021]. Available at: https://www.diabetes.org/healthy-living/medication-treatments/insulin-other-injectables/insulin-storage-and-syringe-safety.

99. Krämer L VI, Zayani A,. Storage of Insulin: IDF Europe Awareness Paper [Internet]. 2019. [Cited: 21 October 2021]. Available at: https://idf.org/images/IDF_Europe/Storage_of_Insulin_-_IDF_Europe_Awareness_Paper_-_FINAL.pdf.

100. American Diabetes Association. Insulin Administration. Diabetes Care. 2003;26(suppl 1):s121-s4. [Cited: 31 August 2021]. Available at: https://care.diabetesjournals.org/content/diacare/26/suppl_1/s121.full.pdf.

101. Frid AH, Kreugel G, Grassi G et al. New Insulin Delivery Recommendations. Mayo Clin Proc. 2016;91(9):1231-55. [Cited: 21 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/27594187/.

102. Association of Diabetes Care & Education Specialists. Insulin Injection Know-How: 2020. updated [accessed: 31 August 2021]. Available at: https://www.diabeteseducator.org/docs/default-source/living-with-diabetes/tip-sheets/insulin-injections/insulin_injection_how_to_aade.pdf?sfvrsn=8.

103. American Diabetes Association. Insulin Pumps: Relief and Choice: updated [accessed: 24 October 2021]. Available at: https://www.diabetes.org/healthy-living/medication-treatments/insulin-other-injectables/insulin-pumps-relief-and-choice.

104. Berget C, Messer LH, Forlenza GP. A Clinical Overview of Insulin Pump Therapy for the Management of Diabetes: Past, Present, and Future of Intensive Therapy. Diabetes Spectrum. 2019;32(3):194-204. [Cited: 24 October 2021]. Available at: https://spectrum.diabetesjournals.org/content/diaspect/32/3/194.full.pdf.

105. Association of Diabetes Care and Education Specialists. Insulin Delivery: updated [accessed: 24 October 2021]. Available at: https://www.diabeteseducator.org/practice/practice-tools/diabetes-management-tools/ipt-resources.

106. American Diabetes Association. Hypoglycemia (Low Blood Glucose): updated [accessed: 22 August 2021]. Available at: https://www.diabetes.org/healthy-living/medication-treatments/blood-glucose-testing-and-control/hypoglycemia.

107. Martín-Timón I, Del Cañizo-Gómez FJ. Mechanisms of hypoglycemia unawareness and implications in diabetic patients. World J Diabetes. 2015;6(7):912-26. [Cited: 17 October 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/26185599/.

108. LexiComp. Glucagon: Drug Information UpToDate: 2021. updated [accessed: 17 October 2021]. Available at: https://www.uptodate.com/contents/glucagon-drug-information.

109. Gosmanov AR KA. Diabetic Ketoacidosis. 2018. [Cited: 23 October 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK279146/.

110. American Diabetes Association. DKA (Ketoacidosis) & Ketones: updated [accessed: 22 August 2021]. Available at: https://www.diabetes.org/diabetes/complications/dka-ketoacidosis-ketones.

111. U.S. National Library of Medicine. Diabetic hyperglycemic hyperosmolar syndrome: MedlinePlus Medical Encyclopedia: 2020. updated [accessed: 22 August 2021]. Available at: https://medlineplus.gov/ency/article/000304.htm.

112. International Diabetes Federation. Diabetes and Cardiovascular Disease Report. 2016. [Cited: 23 August 2021]. Available at: https://idf.org/our-activities/care-prevention/cardiovascular-disease/cvd-report.html#sub-content-tab-nav.

113. de Boer IH, Bangalore S, Benetos A et al. Diabetes and Hypertension: A Position Statement by the American Diabetes Association. Diabetes Care. 2017;40(9):1273-84. [Cited: 24 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/40/9/1273.full.pdf.

114. World Health Organization. Hypertension: updated [accessed: 24 October 2021]. Available at: https://www.who.int/health-topics/hypertension#tab=tab_1.

115. American Diabetes Association. Dyslipidemia Management in Adults With Diabetes. Diabetes Care. 2004;27(suppl 1):s68-s71. [Cited: 24 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/27/suppl_1/s68.full.pdf.

116. Diabetes UK. Screening for Cholesterol: 2019. updated [accessed: 24 October 2021]. Available at: https://www.diabetes.co.uk/diabetes-complications/cholesterol-screening.html#:~:text=As%20someone%20with%20diabetes%2C%20your,test%20for%20your%20HbA1c%20level.

117. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes, Heart Disease, & Stroke: 2021. updated [accessed: 23 August 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/heart-disease-stroke.

118. International Diabetes Federation. Diabetes and the Kidneys: 2021. updated [accessed: 23 August 2021]. Available at: https://idf.org/our-activities/care-prevention/diabetes-and-the-kidney.html.

119. American Diabetes Association. Kidney Disease (Nephropathy): updated [accessed: 21 August 2021]. Available at: https://www.diabetes.org/diabetes/complications/kidney-disease-nephropathy.

120. Gross JL, de Azevedo MJ, Silveiro SP et al. Diabetic Nephropathy: Diagnosis, Prevention, and Treatment. Diabetes Care. 2005;28(1):164-76. [Cited: 17 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/28/1/164.full.pdf.

121. Kramer H, Molitch ME. Screening for Kidney Disease in Adults With Diabetes. Diabetes Care. 2005;28(7):1813-6. [Cited: 24 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/28/7/1813.full.pdf.

122. American Diabetes Association. Neuropathy: updated [accessed: 22 August 2021]. Available at: https://www.diabetes.org/diabetes/complications/neuropathy.

123. American Diabetes Association. Peripheral Neuropathy: updated [accessed: 21 August 2021]. Available at: https://www.diabetes.org/diabetes/complications/neuropathy/peripheral-neuropathy.

124. International Diabetes Federation. Diabetic Foot: 2020. updated [accessed: 22 August 2021]. Available at: https://idf.org/our-activities/care-prevention/diabetic-foot.html.

125. American Diabetes Association. Autonomic Neuropathy: updated [accessed: 22 August 2021]. Available at: https://www.diabetes.org/diabetes/complications/neuropathy/autonomic-neuropathy.

126. National Institute of Diabetes and Digestive and Kidney Diseases. Autonomic Neuropathy: 2018. updated [accessed: 22 August 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/nerve-damage-diabetic-neuropathies/autonomic-neuropathy.

127. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes and Foot Problems: 2017. updated [accessed: 23 August 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/foot-problems.

128. International Diabetes Federation. IDF Clinical Practice Recommendations on the Diabetic Foot 2017. 2017. [Cited: 23 August 2021]. Available at: https://www.idf.org/e-library/guidelines/119-idf-clinical-practice-recommendations-on-diabetic-foot-2017.html.

129. National Eye Institute. Diabetic Retinopathy: 2021. updated [accessed: 23 August 2021]. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy.

130. International Diabetes Federation and The Fred Hollows Foundation. Diabetes eye health: A guide for health care professionals. [Internet]. 2015. [Cited: 17 October 2021]. Available at: https://idf.org/our-activities/care-prevention/eye-health/eye-health-guide.html.

131. American Diabetes Association. Eye Health: updated [accessed: 23 August 2021]. Available at: https://diabetes.org/diabetes/eye-health.

132. American Diabetes Association. Curious about Cataracts? : updated [accessed: 22 August 2021]. Available at: https://diabetes.org/diabetes/eye-health/understand-eye-conditions/curious-about-cataracts.

133. American Diabetes Association. What is Glaucoma? : updated [accessed: 22 August 2021]. Available at: https://diabetes.org/diabetes/eye-health/understand-eye-conditions/what-is-glaucoma.

134. Centers for Disease Control and Prevention. Periodontal Disease: 2013. updated [accessed: 22 October 2021]. Available at: https://www.cdc.gov/oralhealth/conditions/periodontal-disease.html.

135. Casanova L, Hughes FJ, Preshaw PM. Diabetes and periodontal disease: a two-way relationship. British Dental Journal. 2014;217(8):433-7. [Cited: 23 October 2021]. Available at: https://doi.org/10.1038/sj.bdj.2014.907.

136. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes, Gum Disease, & Other Dental Problems: 2014. updated [accessed: 23 October 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/gum-disease-dental-problems.

137. Preshaw PM, Bissett SM. Periodontitis and diabetes. British Dental Journal. 2019;227(7):577-84. [Cited: 23 October 2021]. Available at: https://doi.org/10.1038/s41415-019-0794-5.

138. Herrera D MJ, Renvert S, Jin L,. White Paper on Prevention and Management of Periodontal Diseases for Oral Health and General Health. [Internet]. 2020. [Cited: 23 October 2021]. Available at: https://www.fdiworlddental.org/sites/default/files/2020-11/gphp-2018-white_paper-en.pdf.

139. American Diabetes Association. Diabetes and Oral Health: updated [accessed: 23 October 2021]. Available at: https://www.diabetes.org/diabetes/complications/keeping-your-mouth-healthy#:~:text=If%20you%20have%20diabetes%2C%20you,made%20up%20mostly%20of%20bacteria.

140. Sami W, Ansari T, Butt NS et al. Effect of diet on type 2 diabetes mellitus: A review. Int J Health Sci (Qassim). 2017;11(2):65-71. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5426415/.

141. Davies MJ, D'Alessio DA, Fradkin J et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018;41(12):2669-701. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/30291106.

142. Association AD. 5. Lifestyle Management: Standards of Medical Care in Diabetes—2019. Diabetes Care. 2019;42(Supplement 1):S46-S60. [Cited: 24 October 2021]. Available at: https://care.diabetesjournals.org/content/diacare/42/Supplement_1/S46.full.pdf.

143. Diabetes UK. Glycaemic index and diabetes [Internet]. updated [accessed: 27 April 2021]. Available at: https://www.diabetes.org.uk/guide-to-diabetes/enjoy-food/carbohydrates-and-diabetes/glycaemic-index-and-diabetes.

144. Glycaemic Index Foundation. Low Gi Explained: updated [accessed: 27 April 2021]. Available at: https://www.gisymbol.com/low-gi-explained/.

145. World Health Organization Regional Office for the Western Pacific. Healthy Eating Habits for Patients with Diabetes [Internet]. Manila: World Health Organization; 2017. updated 2017. [accessed: 27 April 2021]. Available at: https://iris.wpro.who.int/bitstream/handle/10665.1/13561/9789290618072-diab-mod4-eng.pdf.

146. Zafar MI, Mills KE, Zheng J et al. Low-glycemic index diets as an intervention for diabetes: a systematic review and meta-analysis. The American Journal of Clinical Nutrition. 2019;110(4):891-902. [Cited: 27 April 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/31374573/.

147. Wang Q, Xia W, Zhao Z et al. Effects comparison between low glycemic index diets and high glycemic index diets on HbA1c and fructosamine for patients with diabetes: A systematic review and meta-analysis. Primary Care Diabetes. 2015;9(5):362-9. [Cited: 26 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25524422.

148. Bhupathiraju SN, Tobias DK, Malik VS et al. Glycemic index, glycemic load, and risk of type 2 diabetes: results from 3 large US cohorts and an updated meta-analysis123. The American Journal of Clinical Nutrition. 2014;100(1):218-32. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4144100/.

149. Livesey G, Taylor R, Livesey HF et al. Dietary Glycemic Index and Load and the Risk of Type 2 Diabetes: Assessment of Causal Relations. Nutrients. 2019;11(6). [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6628270/.

150. Livesey G, Taylor R, Livesey HF et al. Dietary Glycemic Index and Load and the Risk of Type 2 Diabetes: A Systematic Review and Updated Meta-Analyses of Prospective Cohort Studies. Nutrients. 2019;11(6). [Cited: 26 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/31195724.

151. The University of Sydney. GI Database Search [Internet]. updated [accessed: 27 April 2021]. Available at: https://www.glycemicindex.com/foodSearch.php.

152. Diabetes Canada. Glycemic Index Food Guide [Internet]. updated [accessed: 27 April 2021]. Available at: https://guidelines.diabetes.ca/docs/patient-resources/glycemic-index-food-guide.pdf.

153. Renzella J, Townsend N, Jewell J et al. What national and subnational interventions and policies based on Mediterranean and Nordic diets are recommended or implemented in the WHO European Region, and is there evidence of effectiveness in reducing noncommunicable diseases? Health Evidence Network Synthesis Report 58. 2018. [Cited: 19 March 2021]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK519076/.

154. Esposito K, Maiorino MI, Bellastella G et al. A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. BMJ Open. 2015;5(8):e008222. [Cited: 19 March 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26260349.

155. Huo R, Du T, Xu Y et al. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. Eur J Clin Nutr. 2015;69(11):1200-8. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25369829.

156. Schwingshackl L, Chaimani A, Hoffmann G et al. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. Eur J Epidemiol. 2018;33(2):157-70. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5871653/.

157. Fundación Dieta Mediterránea. Mediterranean Diet Pyramid: A Lifestyle for Today: 2010. updated 2010. [accessed: 19 March 2021]. Available at: https://dietamediterranea.com/piramidedm/piramide_INGLES.pdf.

158. Fundación Dieta Mediterránea. What's The Mediterranean Diet? 10 Basics: updated [accessed: 19 March 2021]. Available at: https://dietamediterranea.com/en/nutrition/.

159. World Health Organization. Cancer: Carcinogenicity of the consumption of red meat and processed meat [Internet]. Geneva: World Health Organization; 2015. updated 2015/10//. [accessed: 12 April 2021]. Available at: https://www.who.int/news-room/q-a-detail/cancer-carcinogenicity-of-the-consumption-of-red-meat-and-processed-meat.

160. Joshi S, Ostfeld RJ, McMacken M. The Ketogenic Diet for Obesity and Diabetes-Enthusiasm Outpaces Evidence. JAMA Intern Med. 2019. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/31305866.

161. Aune D, Keum N, Giovannucci E et al. Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies. BMJ (Clinical research ed). 2016;353:i2716. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27301975.

162. Hu Y, Ding M, Sampson L et al. Intake of whole grain foods and risk of type 2 diabetes: results from three prospective cohort studies. BMJ (Clinical research ed). 2020;370:m2206. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/32641435.

163. Brouns F. Overweight and diabetes prevention: is a low-carbohydrate–high-fat diet recommendable? Eur J Nutr. 2018;57(4):1301-12. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5959976/.

164. Masood W, Annamaraju P, Uppaluri KR. Ketogenic Diet. StatPearls. 2021. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK499830/.

165. Meng Y, Bai H, Wang S et al. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes Research and Clinical Practice. 2017;131:124-31. [Cited: 19 March 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/28750216.

166. van Zuuren EJ, Fedorowicz Z, Kuijpers T et al. Effects of low-carbohydrate- compared with low-fat-diet interventions on metabolic control in people with type 2 diabetes: a systematic review including GRADE assessments. The American Journal of Clinical Nutrition. 2018;108(2):300-31. [Cited: 19 March 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/30007275.

167. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. J Geriatr Cardiol. 2017;14(5):342-54. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5466941/.

168. Satija A, Bhupathiraju SN, Rimm EB et al. Plant-Based Dietary Patterns and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies. PLOS Medicine. 2016;13(6):e1002039. [Cited: 27 April 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/27299701/.

169. Toumpanakis A, Turnbull T, Alba-Barba I. Effectiveness of plant-based diets in promoting well-being in the management of type 2 diabetes: a systematic review. BMJ Open Diabetes Research and Care. 2018;6(1):e000534. [Cited: 27 April 2021]. Available at: https://drc.bmj.com/content/6/1/e000534.

170. Yokoyama Y, Barnard ND, Levin SM et al. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. Cardiovasc Diagn Ther. 2014;4(5):373-82. [Cited: 27 April 2021]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4221319/.

171. Viguiliouk E, Kendall CW, Kahleová H et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. Clin Nutr. 2019;38(3):1133-45. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/29960809.

172. Carrero JJ, González-Ortiz A, Avesani CM et al. Plant-based diets to manage the risks and complications of chronic kidney disease. Nat Rev Nephrol. 2020;16(9):525-42. [Cited: 27 April 2021]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/32528189.

173. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes Diet, Eating, & Physical Activity: 2016. updated [accessed: 23 August 2021]. Available at: https://www.niddk.nih.gov/health-information/diabetes/overview/diet-eating-physical-activity.

174. International Diabetes Federation. Diabetes Prevention [Internet]. Brussels: International Diabetes Federation; 2019. updated 2019/07//. [accessed: 12 April 2021]. Available at: https://www.idf.org/aboutdiabetes/prevention.html.

175. Diabetes Canada. Planning for Regular Physical Activity: updated [accessed: 17 October 2021]. Available at: https://www.diabetes.ca/diabetescanadawebsite/media/managing-my-diabetes/tools%20and%20resources/planning-for-physical-activity.pdf?ext=.pdf.

176. Diabetes Canada. Introductory Resistance Program: updated [accessed: 17 October 2021]. Available at: https://www.diabetes.ca/diabetescanadawebsite/media/managing-my-diabetes/tools%20and%20resources/introductory-resistance-program.pdf?ext=.pdf.

177. American Diabetes Association. Foot Complications: updated [accessed: 23 October 2021]. Available at: https://www.diabetes.org/diabetes/complications/foot-complications.

178. Dhippayom T, Krass I. Supporting self management of type 2 diabetes: is there a role for the community pharmacist? Patient Prefer Adherence. 2015:1085. [Cited: 20 August 2021]. Available at: https://dx.doi.org/10.2147/ppa.s88071.

179. Hattingh HL, Emmerton L, Ng Cheong Tin P et al. Utilization of community pharmacy space to enhance privacy: a qualitative study. Health Expectations. 2016;19(5):1098-110. [Cited: 20 August 2021]. Available at: https://dx.doi.org/10.1111/hex.12401.

180. Plake KS, Chesnut RJ, Odorzynski M. Barriers to Community Pharmacists' Provision of Diabetes Care Services in Iowa. Journal of Pharmacy Technology. 2007;23(6):327-38. [Cited: 20 August 2021]. Available at: https://journals.sagepub.com/doi/abs/10.1177/875512250702300602.

181. International Pharmaceutical Federation. Community pharmacy at a glance 2021 - Regulation, scope of practice, remuneration and distribution of medicines through community pharmacies and other outlers: 2021. updated [accessed: 31 August 2021]. Available at: https://www.fip.org/file/5015.

182. Bharadia R, Lorenz K, Cor K et al. Financial remuneration is positively correlated with the number of clinical activities: an example from diabetes management in Alberta community pharmacies. International Journal of Pharmacy Practice. 2018;26(1):77-80. [Cited: 20 August 2021]. Available at: https://dx.doi.org/10.1111/ijpp.12331.

183. MacCallum L, Mathers A, Kellar J et al. Pharmacists report lack of reinforcement and the work environment as the biggest barriers to routine monitoring and follow-up for people with diabetes: A survey of community pharmacists. Research in Social and Administrative Pharmacy. 2021;17(2):332-43. [Cited: 3 August 2021]. Available at: https://www.sciencedirect.com/science/article/pii/S1551741119311143.

184. Lo A, Lorenz K, Cor K et al. Factors Affecting Number of Diabetes Management Activities Provided by Pharmacists. Can J Diabetes. 2016;40(6):535-42. [Cited: 20 August 2021]. Available at: https://pubmed.ncbi.nlm.nih.gov/27373434/.

185. Al Haqan AA, Al-Taweel DM, Awad A et al. Pharmacists' Attitudes and Role in Diabetes Management in Kuwait. Medical Principles and Practice. 2017;26(3):273-9. [Cited: 20 August 2021]. Available at: https://dx.doi.org/10.1159/000456088.

186. Jacobi J. CLINICAL PHARMACISTS: PRACTITIONERS WHO ARE ESSENTIAL MEMBERS OF YOUR CLINICAL CARE TEAM. Revista Médica Clínica Las Condes. 2016;27(5):571-7. [Cited: 20 August 2021]. Available at: https://www.sciencedirect.com/science/article/pii/S0716864016300827.

187. Gilchrist M, Wade P, Ashiru-Oredope D et al. Antimicrobial Stewardship from Policy to Practice: Experiences from UK Antimicrobial Pharmacists. Infectious Diseases and Therapy. 2015;4(1):51-64. [Cited: 19 August 2021]. Available at: https://doi.org/10.1007/s40121-015-0080-z.

188. Emmerton LM, Smith L, LeMay KS et al. Experiences of community pharmacists involved in the delivery of a specialist asthma service in Australia. BMC Health Services Research. 2012;12(1):164. [Cited: 20 August 2021]. Available at: https://doi.org/10.1186/1472-6963-12-164.

189. Alsairafi Z, Waheedi M, Alsaleh F. The perspectives of patients and physicians on the role of pharmacists in improving medication adherence in type 2 diabetes: a qualitative study . Patient Prefer Adherence. 2019;Volume 13:1527-43. [Cited: 20 August 2021]. Available at: https://dx.doi.org/10.2147/ppa.s218068.

190. Mehralian G, Sheikhi S, Peiravian F. Diabetic Patients' Views on Services Provided by Community Pharmacies. Journal of Pharmaceutical Health Services Research. 2018;9(4):335-40. [Cited: 3 August 2021]. Available at: https://doi.org/10.1111/jphs.12229.

191. Siaw MYL, Toh JH, Lee JY-C. Patients' perceptions of pharmacist-managed diabetes services in the ambulatory care and community settings within Singapore. Int J Clin Pharm. 2018;40(2):403-11. [Cited: 20 August 2021]. Available at: https://doi.org/10.1007/s11096-018-0591-2.

192. Twigg MJ, Poland F, Bhattacharya D et al. The current and future roles of community pharmacists: Views and experiences of patients with type 2 diabetes. Research in Social and Administrative Pharmacy. 2013;9(6):777-89. [Cited: 20 August 2021]. Available at: https://www.sciencedirect.com/science/article/pii/S155174111200321X.

11 Appendix 1. IDF Risks and Benefits of Common Diabetes Medicines[22]

Developed by the International Diabetes Federation (IDF) and reproduced with their permission, this table describes the main risks and benefits associated with common glucose lowering medicines pharmacists may encounter in their practice.

	Metformin	Sulfonylureas	Meglitinides	Pioglitazone	Alpha-glucosidase inhibitors	DPP4 inhibitors	GLP1 receptor agonists	SGLT2 inhibitors
Hypoglycaemia	Neutral	Moderate/ severe	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral
Weight	Slight loss	Gain	Gain	Gain	Neutral	Neutral	Loss	Loss
Chronic kidney disease stages 3A, 3B	Reduce dose in 3A Contraindicated in 3B	Caution, higher risk of hypoglycaemia	Caution, higher risk of hypoglycaemia	Neutral	Neutral	Neutral, but must reduce dose except linagliptin	Caution with exenatide ER	Contraindicated in 3B
Chronic kidney disease stages 4,5	Contraindicated	Contraindicated except glipizide and gliclazide	Contraindicated	Neutral	Contraindicated	Neutral, but must reduce dose except linagliptin	Contraindicated	Contraindicated
Gastro-intestinal side effects	Moderate	Neutral	Neutral	Neutral	Moderate	Neutral	Moderate	Neutral
Other side effects				Edema and bone fracture		Pancreatitis Heart failure (not a class effect)		Mycotic genital infections, fractures, amputations Bone Fractures and Amputations (may not be a class effect)
Major cardiovascular events	Benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Benefit (2 RCT*)	Benefit (2 randomised controlled trials*)
Chronic heart failure	Neutral	Neutral	Neutral	Increased risk	Neutral	Neutral	Neutral	Benefit (2 randomised controlled trials†)

*Reduced risk in RCTs designed for non-inferiority with liraglutide, semaglutide, empagliflozin and canagliflozin

†Reduced risk in RCT designed for non-inferiority with empagliflozin and canagliflozin

International
Pharmaceutical
Federation

Fédération
Internationale
Pharmaceutique

Andries Bickerweg 5
2517 JP The Hague
The Netherlands
-
T +31 (0)70 302 19 70
F +31 (0)70 302 19 99
fip@fip.org
-
www.fip.org