MEDICAL DEVICES FOR PHARMACY AND OTHER HEALTHCARE PROFESSIONS

Edited by

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To the late Professor Mohamed Azmi Ahmed Hassali (1974–2021) for his contribution in Pharmacy Practice and Social Pharmacy disciplines, and Dr. Yasser A. Ibrahim (1961–2021), one of the contributors of this book who passed away before completing his chapter.

Ahmed Ibrahim Fathelrahman

To my beloved father, Mohamed Ibrahim (1941–2018)
Forever missed
Thanks for everything

Mohamed Izham Mohamed Ibrahim

This book is dedicated to my wife Joaquima Serradell who has attended alone far too many concerts, plays, and other events, while I spent time on this endeavor. Thank you Joaquima.

Albert I. Wertheimer

Contents

Foreword

Not every pharmacist encounters medical devices as part of their daily practice—but with rapidly advancing technology and a growing number of products entering the market, many more soon will. That's why all pharmacists would be wise to keep a copy of *Medical Devices for Pharmacy and Other Healthcare Professions* on their bookshelves to be ready to serve the patients who depend on these devices.

This resource is just right for both experienced practitioners and beginners. My colleagues, Drs. Ahmed Ibrahim Fathelrahman, Mohamed Izham Mohamed Ibrahim, and Albert I. Wertheimer, have created a robust, handy guide for everything that's most important to know about medical devices. It also takes a deeper dive into medical devices' context within disparate health landscapes.

Medical devices—from the ubiquitous to the groundbreaking—pose untold opportunities for our changing profession and new methods to provide life-changing patient care. Pharmacists' skills in the evaluation of medications' efficacy, safety, affordability, and associated outcomes are a natural fit with optimizing the use of medical devices. Just as important is our experience counseling patients, responding to their concerns, and answering their questions in settings that are most compatible with daily life.

This is especially important given the evolution in healthcare delivery and the ways patients consume care. They're taking more control over their health, and healthcare technology is key to that. Our patients may use medical devices for the diagnosis, treatment, monitoring, and prevention of disease states, but realizing their full potential requires proficient operation and a deep understanding of their purposes and capabilities.

Just like they do with medications, patients need access to a health professional who can communicate complex information, use data to personalize care, and demonstrate proper usage of equipment. Booking an appointment with a primary care physician or specialist to get those services is impractical and can lead to suboptimal use and noncompliance. It's a no-brainer that patients should get them from the provider they see most, know best, and can reach most easily, especially those in rural and underserved areas.

With resources like *Medical Devices for Pharmacy and Other Healthcare Professions* at hand, pharmacists will be prepared to meet their needs, whether that means educating ourselves or ensuring our counseling is thorough, successful, and digestible. We are already armed with the framework to get the maximum value out of these devices. This book can help fill in the blanks.

I'm grateful that Drs. Ahmed Ibrahim Fathelrahman, Mohamed Izham Mohamed Ibrahim, and Albert I. Wertheimer are working to help us answer every question our patients and our fellow providers ask us. I'm excited to see the technological marvels to come and how they will affect pharmacy practice. Above all, I'm motivated to learn everything I can. Thankfully, I can grab this book and immediately benefit from its authors' knowledge and expertise—and so can you.

Scott Knoer, MS, PharmD, FASHP,
Executive Vice President and CEO of the
American Pharmacists Association

Preface

A profession can only survive for as long as the public feels that it adds value and utility. When it fails to deliver valued services, it declines or dies. For example, the blacksmith who attaches iron shoes to the bottom of horses' feet is nearly nonexistent, since there is a very limited need for these services today. This is the similar fate of the cooper, a person who makes wooden barrels. Today, large volumes of liquids are usually housed in glass or plastic containers and the only major use of wooden barrels is found in wine-making. The practicing pharmacist does not often become concerned or involved in many contemporary medical devices, but that is no reason why they should be ignorant about the topic.

Today, more than ever, the pharmacist is a full member of the health team and many of the pharmacist's patients are using cardiac pacemakers, TENS pain reduction devices, insulin pumps, and a host of other devices used in nearly all specialty areas of medicine and surgery. We cannot afford to be left behind and must stay current in the medical device area, even if devices come into play on intermittent, infrequent occasions. A physician may ask the pharmacist which medical device or technology would be most effective to improve medication adherence; or a pharmacist may be asked by a patient if he can clean his insulin pump, how he can keep it safe in hot weather, and which insulin smart pump would be more suitable for traveling. We must be prepared to answer questions such as these. It is acceptable to ask the patient to wait a few minutes while we check a reference source, since no one expects a pharmacist to be able to precisely answer every single question instantaneously.

This book is the answer to how the pharmacist and other healthcare providers can be familiar with the most common medical devices in current use. It is not enjoyable reading and was not intended to be read in one sitting. In actuality, it is better used as a nearby reference source that can be called upon when a device-related question arises. The editors hope that it will make the pharmacist reader as well as other healthcare providers as knowledgeable as possible about this important, evolving area of technology.

Moreover, this book can be used as a reference book for clinical training offered to pharmacy and medical students as a part of clinical skill lab settings. The images and illustrations provided in the book will be useful for students in becoming familiar with the features and designs of various devices and understanding how to operate them and interpret their readings and measures appropriately.

Ahmed Ibrahim Fathelrahman, Izham Ibrahim, and Albert I. Wertheimer

Editors

Ahmed Ibrahim Fathelrahman is currently an associate professor at the Department of Clinical Pharmacy, College of Pharmacy, Taif University, Saudi Arabia. Prior to that from September 2017 to August 2021, he was an assistant professor at the same department. From September 2011 to August 2017, he was an assistant professor and head of department of Pharmacy Practice, Qassim University, Saudi Arabia. Before joining Qassim University in 2011, he worked with the Ministry of Health, Sudan for 13 years in different units and departments such as the Central Medical Supplies Public Corporation (CMS) Sudan (1997–2000); the Revolving Drug Fund, Khartoum State (2000–2005); the General Directorate of Pharmacy and the Khartoum State Drug Information Centre, the Ministry of Health, Khartoum State (2005–2010), and the General Directorate of Planning and Development of the Khartoum State Ministry of Health (2010–2011). Ahmed Ibrahim Fathelrahman is the main author or co-author of more than 50 articles and titles that represent publications in international peer-reviewed journals, books, book chapters, or conference presentations besides other works published in some local journals. Ahmed Ibrahim Fathelrahman is a reviewer for a variety of international peer-reviewed journals from the fields of pharmacy, public health, tobacco control, and toxicology, and he acted as a member of review committees of various international scientific meetings regularly organized by international societies such as the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) and the Society for Research on Nicotine and Tobacco (SRNT). Ahmed Ibrahim Fathelrahman was also an editorial board member of Heliyon, an open-access multidisciplinary journal published by Elsevier. In April 2016, he produced together with Professor Mohamed Izham Mohamed Ibrahim from Qatar University and Professor Albert I. Wertheimer from College of Pharmacy, Nova Southeastern University, USA, an edited book published by Elsevier Science entitled *Pharmacy Practice in Developing Countries: Achievements and Challenges*. In 2018, they produced another edited book published by Elsevier Science entitled *Pharmacy Education in the Twenty First Century and Beyond: Global Achievements and Challenges*. Ahmed Ibrahim Fathelrahman was a winner of the Young Investigator Scholarship of the APACT 8th Asia Pacific Conference on Tobacco or Health, Taipei, Taiwan (17–20 October 2007); Universiti Sains Malaysia (USM) Research Fellowship (September 2007–December 2009), and the Sanggar Sanjung Award for Best Publication, Universiti Sains Malaysia, 2010. Ahmed Ibrahim Fathelrahman worked as a member of research ethics committees of each of the following: the Ministry of Health Khartoum State, the Community Medicine Council of Sudan Medical Specializations Board, the College of Pharmacy at Qassim University, and Al-Qassim Region, Saudi Arabia. Ahmed Ibrahim Fathelrahman supervised the research of more than 30 medical or pharmacy students in Sudan and Saudi Arabia at levels of Bachelor, Doctor of Pharmacy, Master of Science, Medical Doctor, and Fellowship.

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1 Introduction
Medical Devices History, Current Perspectives, and Shortages

Ahmed Ibrahim Fathelrahman and Mohamed Izham Mohamed Ibrahim

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BACKGROUND

The Global Harmonization Task Force (GHTF) is an expert group set up in 1992 jointly by regulatory authorities and the medical device industry.[1] In 2005, GHTF approved a definition of medical devices that received wide acceptance among stakeholders. The definition reveals the variety of forms and application of medical devices. According to GHTF, "A medical device is any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material, or another similar or related article that does not achieve its primary intended action in or on the human body solely by pharmacological, immunological, or metabolic means and that is intended for human beings for:

- The diagnosis, prevention, monitoring, treatment, or alleviation of disease.
- The diagnosis, monitoring, treatment, alleviation of, or compensation for an injury.
- The investigation, replacement, modification, or support of the anatomy or a physiological process.
- Supporting or sustaining life.
- Controlling conception.
- Disinfecting medical devices.
- Providing information for medical or diagnostic purposes using in vitro examination of specimens derived from the human body."

To understand what medical devices are, we need to distinguish between them and medications and pharmaceutical products from one hand, and distinguish between them and other consumers' products from another hand. According to Monsein, consumers' products are not medical devices if used for general purposes but are neither dedicated to nor intended or promoted for medical applications.[2] For example, a screw is considered a medical device when it is promoted for holding bones together rather than holding pieces of wood together.[2] On the other hand, medical devices are different from drugs in that they do not achieve their principal action through chemical action or metabolization in or on the body. For example, plaster cast used for bone healing is considered a device, while a topical ointment used to promote bone healing is considered a drug.[2] However, the differentiation between medical devices and drugs is not always easy, mainly because of the widespread use of several products straddling the borderline between a device and a drug, such as insulin pens and implantable drug delivery devices.[1]

HISTORICAL OVERVIEW ON THE USE OF MEDICAL DEVICES IN MANAGEMENT, CONTROL, PREVENTION, AND MONITORING OF DISEASES

There are several milestones in a long journey that witnessed the evolution and the revolution in the medical devices industry. Although some historians have backdated their appearance in the world to as far as 7000 BCE by the ancient Egyptians and Etruscans, the official appearance of medical

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TABLE 1.1
Important Milestones in Modern Medical Devices History According to the WHO[1]

No.	Important event	Years
1	First modern stethoscopes	1800–1850
2	X-rays discovery	1895
3	First cardiograph	1903
4	First modern respirator	1927
5	First cardiac catheterization	1928
6	First metallic hip replacement surgery	1940
7	First kidney dialysis machine	1945
8	First artificial hip replacement	1950
9	First commercially available artificial heart valve	1951
10	First successful external cardiac pacemaker	1952
11	First totally internal pacemaker	1960
12	First computerized axial tomography scanner	1970
13	First laparoscopic procedure	1972
14	First pulse oximeter	1972
15	First regulatory system for medical devices in the US	1976
16	First magnetic resonance imaging device for full body scan	1977
17	First multichannel cochlear implant	1978
18	First permanent artificial heart	1982
19	First implantable cardioverter defibrillator	1985
20	First robot-assisted surgical procedure	1985
21	First European Union regulatory system	1993

devices in modern history was in the 1700s.[3] According to the World Health Organization (WHO), the important milestones in medical device development started with the development of first modern stethoscopes (1800–1850), followed by X-rays discovery (1895).[1] Table 1.1 shows 21 important milestones in modern medical devices history.

THE TREMENDOUS DEVELOPMENT IN MEDICAL DEVICES TECHNOLOGY DURING THE LAST DECADES

Over the last five to six decades, the pharmaceutical and healthcare market witnessed a vast and fast development in medical devices. This was driven by certain factors, including a) the tremendous advancements in science and technology, b) changes in some health philosophies and the widespread existence of newer concepts such as teamwork and collaboration among healthcare providers, health promotion, and the self-care concept, and c) the globalization that produced populations with comparable cultures, health needs, challenges, and awareness about health and diseases. This last factor in producing one large global market with similar demand encouraged manufacturers to be involved in the large-scale production of products with variable user-specific characteristics to satisfy customers everywhere. The advancement in technology resulted in the production of sophisticated devices with a variety of capabilities. The information technology and informatics brought the healthcare team together and facilitated their collaboration to take care of patients and communities. The manufacturers used the new environment that encourages more patient involvement in caring for their health and produced devices for self-monitoring of various diseases and health conditions.

It has been estimated that the number of medical devices with different types, purposes, and versions reached about 1.5 million, divided into about 10,000 various categories.[1] Due to the rising concerns about self-care, the number of medical devices introduced to the community pharmacy to be operated there or sold to patients for home use increases quickly every year. This has put a particular concern about the pharmacists' essential role in managing and controlling the sale and use of such devices. Previously, medical devices were likely to be seen inside hospitals and other facilities providing monitoring, diagnosis, and treatment to the patients. Nowadays, medical devices are commonly seen in community pharmacies and as household products.

REGULATION OF MEDICAL DEVICES

Both drugs and medical devices are regulated in the United States by the US Food and Drug Administration (FDA). Although the regulation of drugs began in 1906, medical device regulations were not in place until 1938, when the Federal Food, Drug, and Cosmetic Act was approved.[4] However, such regulations were limited and intended only for controlling adulteration and misbranding in medical devices. An important amendment made in 1976 to fulfill some quality control standards in response to an increase in reports of injuries related to some medical devices.[4] At present, medical devices (like drugs) are required to comply with regulations regarding labeling, advertising, production, and post-marketing surveillance. However, if compared with regulations applied on drugs, medical device regulations are still limited.[4] For example, the demonstration of safety and efficacy in humans is required only with Class III medical devices (i.e., medical devices are classified into Class I, Class II, and Class III). In addition, no inspection is performed in the medical device industry.

THE GAPS IN KNOWLEDGE AND EXPERIENCE ABOUT MEDICAL DEVICE USE AMONG PATIENTS AND HEALTHCARE PROFESSIONALS

An overview of the literature reveals a significant gap in knowledge and associated skills required for efficient medical device technique use among patients. Inadequate experience with device technique was also evident among healthcare professionals. Many studies on patients' awareness and appropriate operation of medical devices focused on the devices commonly used by patients, such as asthma inhalers and the simple devices like those used to measure liquid medications at home. The following are examples of such literature.

An experimental study by Van Der Palen et al from the UK revealed high but variable rates of errors among participants concerning various inhaler device techniques. Ellipta showed lower errors among patients than Diskus (Accuhaler), metered-dose inhaler (MDI), and Turbuhaler.[5] This is likely due to variation in the easiness of handling the devices. Such variation was replicated again in a study by von Schantz et al. from Finland.[6] The researchers compared only dry-powder inhalers Diskus, Easyhaler, Ellipta, and Turbuhaler. The percentages of participants showing correct device techniques were as follows: Diskus 48%, Easyhaler 19%, Ellipta 55% and Turbuhaler 16%. Patients' preferences of the devices seem to be related to the easiness of use and ability to use the device correctly.

Bryant et al. from New Zealand assessed the inhaler technique among patients presented to community pharmacies.[7] They found high rates of inappropriate performance with marked variation in the proportions of patients showing good techniques regarding turbuhaler and MDI with or without a spacer. Most participants received initial instructions from their doctors, but a lower proportion of them recalled having their inhaler technique rechecked.

Plaza et al. conducted a systematic review of the literature assessing errors in inhalers techniques among healthcare professionals.[8] Using the data from 55 studies involving more than 6,000 healthcare professionals, they estimated that the inhaler technique was considered correct in only 15.5% of cases (95% confidence interval; 12–19.3). The authors concluded that inhaler technique skills among professionals have worsened in recent years despite extensive training efforts. The authors raised the attention to the urgent need for efficient strategies to improve healthcare professionals' training in the appropriate use of inhalers.

Almazrou and associates conducted a study to assess Saudi mothers' experiences with measuring cups, syringes, and droppers for oral liquid medications.[9] One of the study objectives was to compare the accuracy of dosing across these devices. The researchers found low rates of accurate measurements among participants, with only 58%, 50%, and 51% of participants measuring an accurate dose of paracetamol using oral dosing syringe, dropper, and dosing cup, respectively. Participants measured more than the anticipated dose with the dosing cup and less than the anticipated dose with the dropper. Dosing correctness for each type of devices was significantly affected by the participants' education status. Most of them had not had previous counseling on the use of liquid medication measuring devices.

ACCESS TO RELIABLE INFORMATION ABOUT MEDICAL DEVICES

Having reliable information is very important in all aspects of patient management. Credible information and communication are critical points in evidence-based medicine and practice. Medical devices or equipment (e.g., wheelchair, blood glucose meter, X-ray machine, pacemaker, surgical gloves) and pharmaceuticals are important approaches used to manage patients in either in-patient, out-patient, or home care. Patients and healthcare providers use medical devices for medical purposes. There is a rapid increase in the array, variety, and complexity of medical devices. These devices are used for diagnosing, preventing, monitoring, or treatment of disease. There are also devices used as an aid, such as equipment for people with a disability (e.g., crutches, three-wheel walker). Generally, they have a mechanical or physical effect on the body of the users. Therefore, it is important to ensure that these medical devices are of quality, safe, and effective.

Accordingly, FDA classifies medical devices into three classes: Class I, II, and III.[10] These categories are based on the risk aspects, safety, and effectiveness; Class I has the lowest risk, while Class III has the highest risk. International and national regulatory agencies should manage safety issues using a medical device vigilance system. Information regarding malfunction or deterioration or inconsistency in labeling or instructions needs to be recorded in the system, which later will be helpful for users.

Other important information for users is the list of manufacturers, wholesalers, retailers of medical devices, and registered medical devices in the country. A website would be a good source of information for the community. It should contain information related to the regulations, clinical studies, quality auditing and surveillance, designated and authorized agency, advice and support for patients, healthcare professionals and industry, and educational materials for the public.

Table 1.2 lists a few sites that provide valuable and reliable information on medical devices.

TABLE 1.2
Source of Information Related to Medical Devices

Organization	Link
Government of the United Kingdom	www.gov.uk/guidance/medical-devices-information-for-users-and-patients#:~:text=A%20medical%20device%20is%20a,physical%20impairments%20become%20more%20independent
United States Food and Drug Administration (USFDA)	www.fda.gov/medical-devices
Australian Therapeutic Goods Administration (TGA)	www.tga.gov.au/medical-devices
European Commission	https://ec.europa.eu/health/md_sector/overview_en
European Medicines Agency	www.ema.europa.eu/en/human-regulatory/overview/medical-devices
National Medical Products Administration of China	http://english.nmpa.gov.cn/medicaldevices.html
Pharmaceuticals and Medical Devices Agency of Japan	www.pmda.go.jp/english/
Medtech Regulatory Special Interest Group (SIG)	www.med-technews.com/topics/medtech-regulatory-special-interest-group-sig/

MEDICAL DEVICES IN HEALTH PROFESSION STUDENTS' CURRICULA

Should we teach health profession students topics on medical devices and technologies? Should the aspects of medical devices and technologies be part of the curriculum? If yes, then what topics, and how should they be taught to students?

The latest medical technologies applied in the healthcare system include virtual reality, precision medicines, artificial organs, sensors, smart inhalers, health wearables, and many more. These technologies, which involve a fusion of biomedical and material sciences, will continue to be the key method used in patient management and the primary market in the future.

There are academic institutions that offer degrees at the undergraduate and graduate levels in health/medical technologies. These programs should be taught (e.g., skills and concepts) in multidisciplinary approaches involving experts in medicine, engineering, life sciences, physical sciences, and business.

There are a few methods of teaching that can be utilized in teaching medical device technologies to students. These include a combination of lecture materials, observational learning, problem-solving, hands-on training, experiential learning, medical simulations, industry guest expertise, texts and readings, and internet-based searches to develop their understanding of the problem and design their solutions. Such approaches are expected to successfully provide a significantly increased knowledge base and competence of medical device design.[11–13] According to May-Newman and Cornwall, teaching courses related to medical device design are very challenging and using traditional educational approaches might not be effective.[12] Some colleges provide training in the research, development, and manufacturing of medical devices. These programs and courses are open for healthcare professionals, engineers involved in biomedical product design and development, regulatory officers, manufacturing professionals, etc.

Individuals interested in the field can use their knowledge and skills to invent and design medical devices (e.g., producing prototypes). Others can also proceed to manufacture, test, and commercialize the product.

Colleges offering courses related to medical technologies include topics such as the following in their curricula:

- Fundamental knowledge of engineering, biomedicine, and biotechnology
- Regulatory aspects
- Principles of product design and development
- Microelectromechanical system fabrication techniques
- Manufacturing
- Technology innovation management
- Technology macroenvironment
- Quality aspects
- Safety aspects
- Entrepreneurship

Here are examples of colleges or institutes which offer programs in medical device technologies:

www.mtu.edu/engineering/graduate/certificates/medical-devices/
https://cse.umn.edu/tli/medical-device-innovation-curriculum
www.birmingham.ac.uk/postgraduate/courses/taught/chemical-engineering/healthcare-technology.aspx
www.auckland.ac.nz/en/study/study-options/find-a-study-option/medical-devices-technologies.html
www.strath.ac.uk/engineering/biomedicalengineering/strathclydeinstituteofmedicaldevices/
www.ncad.ie/postgraduate/school-of-design/msc-medical-device-design/
www.uclaextension.edu/engineering/bioengineering/certificate/medical-device-engineering
www.seas.harvard.edu/news/2014/05/medical-mechanics
https://extension.ucsd.edu/courses-and-programs/regulatory-affairs-for-medical-devices
www.tp.edu.sg/schools-and-courses/adult-learners/all-courses/skillsfuture-series/medical-device-school.html

ABOUT THE BOOK IN YOUR HAND

1. The primary readers are pharmacists and pharmacy personnel practicing in various settings, and pharmacy students worldwide. This book is intended to provide information, knowledge, and guidance on the safest and best way to use medical devices for the diagnosis, prevention, monitoring, and treatment of common diseases and conditions.
2. It is intended to be a comprehensive review of medical devices that pharmacists and pharmacy personnel may deal with in various working settings to provide pharmaceutical care, including hospitals, community pharmacies, and other settings and at points of care testing.
3. Devices under pharmaceutical care represent the core part of the book. They are presented according to a clinical specialty such as endocrinology, cardiology, orthopedics, and nephrology; and within each therapeutic area, devices are presented according to common conditions and diseases (e.g., diabetes devices and those for growth disorder under endocrinology), by purposes (e.g., blood pressure monitoring and pulse oximetry under cardiology), or according to body organs like the chapter on gastroenterology and hepatology devices.
4. This book contains a section on medical devices for specialized services and purposes that links devices used collectively while providing services such as smoking cessation and anticoagulation clinics, and those used for particular purposes such as those improving adherence.

5. This book is intended to provide descriptions of different devices, including but not limited to the important features, purposes of use, how to use or operate properly, maintenance, interpretation of their readings, and more.
6. This book is intended to be a practical and concise guide for pharmacists and users to simplify information about devices and provide the information needed for proper use.
7. This book is intended to act as an atlas that illustrates information textually and graphically using photographic pictures, diagrams, and drawings.
8. This book provides the available evidence on the effectiveness and cost-effectiveness and the latest information in medical devices.
9. Besides the medical devices that pharmacists come in direct contact with, each chapter on the particular therapeutic area includes some medical devices that are not related directly to pharmacy, but which pharmacists should know (devices that pharmacists might not come in direct contact with, but should know about if their patients have or use them so they can understand what they are experiencing such as pacemakers, defibrillators, left ventricle assist devices, deep brain stimulation devices for seizure disorders, bone density testing devices for osteoporosis, pulse oxygenation measurement, blood pressure and temperature devices, vascular filters, artificial heart valves, etc.
10. For devices that are usually used by patients or which patients need to know about (such as insulin syringes, insulin pens, and glucose monitoring devices) there is a special part in every chapter ready to be conveyed by pharmacists who want to educate and counsel patients entitled "Special tips for patient counseling."

WHO SHOULD READ THIS BOOK?

1. Pharmacists practicing in different settings as well as other interested practicing medical professionals
2. Pharmacy and medical students (e.g., can be used as a teaching source in pharmacy practice and clinical courses such as patient assessment, hospital pharmacy, community pharmacy, responding to symptoms, over-the-counter medications and devices, clinical skills lab, industrial pharmacy, etc.)
3. Pharmacy and medical educators
4. Administrative authorities in academic institutions and the inventory control departments in such institutions (medical and pharmacy colleges) as a primary list of instruments/devices and technologies needed for training in students' practical laboratories and clinical skills labs.
5. Nursing and nurse practitioner programs may be interested in a product such as this. Perhaps medical technology programs as well.

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Section I

Medical Devices for Specialized Services and Purposes

2 Medical Devices for Pharmacy-Based Anticoagulant Services

Hazem Fathy Elewa

CONTENTS

BACKGROUND

Oral anticoagulation therapy is used to prevent thromboembolism in patients with variety of disorders, including atrial fibrillation, prosthetic heart valves, coronary artery disease, and venous thromboembolism.[1,2] Warfarin is the mainstay oral anticoagulant medication and one of the most widely prescribed medications all over the world.[3] Because of the narrow therapeutic index of warfarin and large interpatient variability, close and consistent monitoring of anticoagulation is mandated to ensure optimal outcomes and minimize the risks associated with inappropriate management. International normalized ratio (INR) is a reliable surrogate marker that has been used for decades as an indicator for warfarin's therapeutic effect to ensure optimal outcomes for anticoagulated patients.[2] Guidelines recommend that healthcare providers involved in the management of oral anticoagulation therapy should do so in a systematic and coordinated fashion, incorporating patient education, systematic INR testing, tracking, follow-up, and good patient communication of results and dosing decisions.[4] The challenging management of oral anticoagulation therapy has led to the development of a variety of models including patient self-management, specialized anticoagulation clinics, and pharmacist-managed anticoagulation clinics.[5] Many studies have indicated that specialized anticoagulation clinics can reduce complications associated with inappropriate warfarin use and improve its efficacy.[6] Pharmacist-managed anticoagulation clinic represents a model that provides patients with more consistent management, closer monitoring, more education, and awareness especially in regards to interacting drugs and food that can alter warfarin efficacy and safety.[5,7–9] Overall flow in specialized anticoagulation clinics starts with patient check-in, measurement of INR, patient interview and data gathering, assessment of warfarin therapy, making a therapeutic plan, and scheduling a follow-up appointment for the patient.[10] INR can be measured through venipuncture at the laboratory or through finger stick point-of-care (POC) testing. POC testing is considered to be a faster, more patient-friendly and reliable alternative to the venipuncture measurement of the INR.[11] Since the 1990s, POC devices started to be introduced as self-testing devices as well which allowed patients to measure their INR at home. In the practice of self-monitoring, a patient tests the INR at home then contacts the clinic to report it and gets instruction on appropriate dose adjustment, and in self-managing, a patient tests the INR at home then makes adjustment to the dose based on a predetermined instruction scheme.[12,13] Both INR venipuncture and POC instruments work essentially through the same mechanism by measuring primarily the prothrombin time (PT). The PT measures the recalcification and clotting time of a patient's plasma in the presence of thromboplastin (a potent tissue procoagulant extract).[14] Due to lack of standardization of commercial thromboplastin used by the different laboratories, PT results differ significantly from one facility to another. Based on international collaborative study, the use of INR was proposed and adopted by the World Health Organization (WHO) in the early 1980s.[15] INR system is defined as the ratio of the PT to the geometric

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FIGURE 2.1 CoaguCheck System™ including testing, lancing device, and test strips.

Source: www.shutterstock.com/image-photo/khonkaen-thailand-january-27-2018-drop-1010736280

FIGURE 2.2 CoaguCheck System™ with a strip inserted into the device and the testing in progress.

Source: www.shutterstock.com/image-photo/heiligenhaus-nrw-germany-november-30-2018-1288429105

mean of prothrombin time of at least 20 adult normal subjects calculated in terms of the appropriate International Sensitivity Index (ISI). It can be calculated using the following formula, INR = (patient's PT/mean PT)^{ISI}. The ISI is a numerical value that calibrates the responsiveness of any given commercial thromboplastin system relative to the international standard. It takes into account the variability in results obtained using different commercial systems in calculating the results. With the INR system, results from different laboratories and countries can be compared with very minimal variabilities.

DEVICE DESCRIPTION

A typical portable POC INR test device is a battery-operated meter that has an electrical charging dock. It has a screen that displays the results and an opening for the testing strips. Meters are typically supplies with a lancing device, test strips, and standards for calibration. A test strip is inserted into the meter, then the lancing device is used to obtain a capillary blood droplet which is applied directly to the test strip. The meter reads the test strip and measures the time it takes the blood to form a clot then presents the results on the screen as INR (and PT in some meters). Among the most common POC INR test devices are CoaguChek System™ by Roche Diagnostics, Hemochron™ by International Technidyne Corporation (ITC), and Alere™ by Abott.

HOW TO USE/OPERATIONAL REQUIREMENTS

The following steps will explain how to use the POC INR meter.

1. Turn on the device using the on/off switch. Alternatively, insert a test strip and the device will automatically turn –on.
2. Wash hands using warm water and soap. Dry hands thoroughly.
3. Apply alcohol swab to the finger that will be pricked by the lancing device.
4. Remove the test strip from the container and insert it into the designated opening in the meter.
5. Confirm that the code chip number displayed on the device screen matches the batch number on the test strip container.
6. Prick the tip of the finger with the lancing device and discard the lancet in a sharps or plastic container.
7. Wait until the device gives the signal that it is ready (For example: showing a figure of a blood drop on the screen, or beeping. The signal may differ from one device to another).
8. Apply the blood sample to the target area of the test strip within 15 seconds of pricking the fingertip.
9. Keep applying the blood to the strip until the device beeps signaling that the sample is being processed.
10. Wait until the INR results appear on the screen which may take 30–60 seconds, and record the result.
11. Remove the test strip and dispose of it appropriately.

INTERPRETATION OF READINGS

As previously explained, POC INR testing devices measure the PT/INR with some newer models equipped to measure the partial thromboplastin time (PTT) and activated partial thromboplastin time (aPTT). PT/INR measures the time it takes the blood to clot. Since INR is a ratio taking into account the PT of healthy individuals, a normal INR of a healthy subject is (or very close to) 1.[14]

INR is used in clinical settings to measure the anticoagulation effect of vitamin K antagonists such as warfarin. INR targets of 2.5 (2–3) or 3 (2.5–3.5) are the most common therapeutic targets used in the different thromboembolic conditions requiring warfarin therapy.[16] INR below therapeutic target indicates reduced anticoagulation effect of warfarin which may be associated with increased risk of thrombosis (especially with INR below 1.5). On the other hand, INR above therapeutic target indicates augmented anticoagulation effect of warfarin which may be associated with increased risk of bleeding (especially with INR above 4.5).[17]

IMPORTANT SAFETY ISSUES

Here are some important safety tips that should be followed to achieve adequate operation of the POC INR device.

1. The meter should be operated at room temperature.
2. The meter should be kept horizontal when testing is in process.
3. The meter should not be used near a strong magnetic field.
4. Avoid using a code chip from a box of test strips other the one that is actually used.
5. Avoid touching the test strip with wet hands.
6. Avoid removing the test strip while measurement is in process.
7. Do not delay the application of the blood onto the test strip by more than 15 seconds.
8. Blood sample application should be done all at once.
9. Avoid addition of more blood sample once the measurement is in process.
10. Avoid touching buttons on the meter while the device is testing.

STORAGE CONDITIONS AND MAINTENANCE

Meters should be stored at room temperature. Avoid storing the meter in damp or humid conditions (more than 85% humidity). Meters should be kept in a clean, dust-free area. Meters should be regularly cleaned especially if it is dirty or has any remaining blood spots. Use a swab or damp cloth for cleaning and avoid using sprays of any kind. The appropriate cleansing agents include 70% isopropyl alcohol and 10% hypochlorite solution (1 part bleach to 9 parts distilled water). Wipe the device from the outside after being turned off and avoid the accumulation of liquids near any openings. Dry the exterior with a lint-free cloth and wipe away any residual liquid or moisture. INR meters require routine performance of quality control (QC); however, devices differ in how often QC is required and how it is performed. Some devices have internal electronic QC run with every PT/INR check while others may require daily and/or weekly manual QC. QC is performed through the addition of one or more standard solutions that should yield certain readings in order to pass the QC. Refer to the individual meter manual for more detailed instructions.

Important Features and Special Advantages

Here are some of the most important features and advantages of POC INR devices.

1. Most meters automatically store the results (up to 100 readings or more).
2. Most meters have the ability to scan the medical record number to store the results to the corresponding patient.
3. Most meters have the ability to interface with the electronic medical record system used at the healthcare facility and migrate the results to the corresponding patient medical record.
4. Compared to the conventional venipuncture INR performed in the laboratory, POC INR meters require much less blood volume (around 10 mcl), require less processing time and labor, and are more convenient for the patient.
5. POC INR meters can function with a capillary blood sample (retrieved through finger prick) which is less painful and more convenient for the patients than the venipuncture INR performed at the laboratory.
6. Many POC INR meters have also the ability to measure PTT and aPTT.

SPECIAL TIPS FOR PATIENT COUNSELING

Here are some important tips that should be considered by the practitioner performing the INR POC testing or communicated to the patient/family if performing self-testing.[18]

1. Make sure that the fingers are not too cold by massaging the hands, holding hands under the arm, or washing hands with warm water.
2. Avoid squeezing or "milking" the fingers to get sufficient amount of blood.
3. Avoid switching to another spot on the same finger or to a different finger if unable to get a sufficient amount of blood from the initial spot.
4. POC INR meter readings may be affected by some factors/medical conditions such as hematocrit, anemia, antiphospholipid antibody syndrome, malignancy, infection, and inflammatory conditions.
5. Laboratory INR may need to be performed occasionally to confirm INR readings in the conditions stated previously.
6. Laboratory INR is also recommended for confirmation of POC INR readings above 5 since INR readings may be less accurate above this value in most POC meters.
7. Encourage patients using self-testing meters to get their INR compared occasionally to laboratory INR values to confirm accuracy of their meters.

AVAILABLE EVIDENCE ON THE EFFECTIVENESS AND SAFETY

Warfarin is the cornerstone prevention and treatment of a wide variety of thromboembolic disease such as deep venous thrombosis, pulmonary embolism, and stroke. Because of the narrow therapeutic index of warfarin and large interpatient variability, close and consistent monitoring of anticoagulation through the INR is mandated to ensure optimal efficacy and safety.[19,20] Thus, it is very important to use INR testing devices with high accuracy and precision to ensure results' validity when making clinical recommendations for warfarin patients.[21] POC INR testing devices were introduced to the market in the 1990s to meet the increased demand for oral anticoagulant (warfarin) use. Due to the ease of their use by healthcare providers, convenience for the patient (requires only a finger prick) and short time from test to result, a majority of clinics managing warfarin patients rely heavily on POC INR testing devices. And while the precision and accuracy of the POC INR testing devices are slightly lower than that achieved with the automated INR laboratory instruments,[11,21] their clinical advantages have helped many patients to be more consistent with and adherent to their INR follow-up measurements. This in turn translates into better effectiveness and safety outcomes. It is worth mentioning, however, that it is very important to calibrate POC INR testing devices as instructed by the manufacturer and to routinely compare the POC INR testing device results with a laboratory test to eliminate potential imprecision errors.

ECONOMIC EVALUATION

As explained in the introduction of this chapter, there are various types of INR testing strategies: laboratory INR testing; POC clinic-based INR testing; POC self-monitoring home INR testing; and POC self-managing home INR testing. Although the same POC device may be used in the last 3 strategies, the strategy itself may yield different clinical and economical outcomes. In a cost utility analysis that was conducted comparing these 4 strategies by the Canadian ministry of health, it was found that the laboratory INR testing had the least cost ($7,033 per patient). On the other hand, self-managing POC INR testing strategy had the greatest number of quality-adjusted life-years (QALYs) (4.2136) but was only marginally higher than the laboratory INR testing (4.1957) with an additional cost of $233. This led to an incremental cost-effectiveness ratio (ICER) of $13,028 per QALY gained for the self-managing strategy. The POC clinic-based INR testing and the POC self-monitoring home INR testing were dominated by the self-managing strategy with total incremental cost of $575 and $968 more per patient and fewer QALY gains.[22]

As in any economic model, these results cannot be considered generalizable since they may differ based on the healthcare setting, country, payer perspective, frequency of INR checks, and time in therapeutic range.

CHALLENGES TO THE PHARMACISTS AND USERS

POC INR testing meters are not without challenges to the pharmacists and the users. Among the most common challenges are the following:

1. Capillary blood sample should be accessed within 15 seconds which may not be sufficient period of time especially for untrained users. In this case, another finger should be pricked and the initial test strip may need to be discarded if it came into contact with the initial blood sample.
2. Laboratory INR is also recommended for confirmation of POC INR readings above 5 since INR readings may be less accurate above this value in most POC meters.
3. POC INR meters reading may be affected by some factors/medical conditions such as hematocrit, anemia, antiphospholipid antibody syndrome, malignancy, infection, and inflammatory conditions.
4. Laboratory INR may need to be performed occasionally to confirm INR readings in the conditions stated here.

Recommendations: The Way Forward

While warfarin is still used for patients requiring treatment with oral anticoagulants, direct oral anticoagulants are now becoming more frequently used and there may be future POC testing devices to measure the effect of these drugs.

CONCLUSION

The aims of POC testing are convenience for the patient, faster test results to the healthcare provider, and potentially more timely clinical decision-making, all of which improve clinical outcomes and reduce healthcare resource use. The site of POC is not restricted to the bedside, but can occur in a variety of locations, as long as the technology is in close proximity to the patient: in a hospital, a doctor's office, a pharmacy, the patient's home, a community clinic, or an anticoagulation clinic.

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3 Self-Testing Medical Devices for the Detection, Diagnosis or Management of Health Conditions

A Public Health Perspective

Silvia E. Rabionet

CONTENTS

INTRODUCTION

Self-tests, also known as home tests, are typically sold over the counter (OTC) in pharmacies and allow users to test self-collected specimens and interpret the results in the comfort of their homes without the need of a trained or licensed health professional. These tests differ from home collection tests, which require mailing or taking the sample to a laboratory or clinic for processing analysis and interpretation.[1]

In this chapter I will present medical devices in the form of self-tests approved by the FDA for diagnosis and monitoring of illnesses that constitute public health threats and that have a global impact. Specifically, I will be presenting the evolution and current use of self-tests in monitoring diabetes and in identifying new cases of HIV and COVID-19. These testing technologies involve self-collection of a biological samples such as blood, oral fluid, or urine; self-testing of the sample; and interpretation of the results by the individual tested. The products include inserts of self-explanatory instructions provided by the manufacturer. I will also be discussing the impact that these devices can play in curtailing current epidemics and review some challenges associated with their widespread use. The discussion will consider their significance in creating the capacity for self-care. These discussions will be contextualized by describing the public health burden of the selected illnesses. Self-testing technologies have proven their diagnostic capabilities, but also are a powerful tool for clinical prevention, avoiding complications of diseases like diabetes, and preventing spread of infectious diseases like HIV and COVID-19.

DIABETES AND SELF-TESTING AND MONITORING

Diabetes is a chronic disease that leads to uncontrolled blood glucose. It occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. It is estimated that 422 million people worldwide are suffering from diabetes. Diabetes has been associated with damage to the heart, blood vessels, eyes, kidneys, and nerves. According to the World Health Organization,[2] people with diabetes have a two- to three-fold increased risk of heart attacks and strokes. Poor blood flow and neuropathy in the feet increases the chance of foot ulcers and infections, eventually leading to amputations. It is the cause of 2.6% of global blindness due to diabetic retinopathy that results in accumulated damage to the retina. Diabetes is also among the leading causes of kidney illnesses and failure.[3,4]

Currently, more than 34 million Americans have diabetes, representing 10.5% of the United States population. This percentage increases with age, reaching 28.8% among people 65 and over. Approximately 90–95% of them have type 2 diabetes. People over age 45 are at a greater risk of developing diabetes, but increasingly more children and younger adults are also developing it. It is estimated that 7.3 million adults are not aware that they have diabetes.[5]

Diabetes management requires glucose level monitoring and adequate insulin dosing. For people who already have a diagnosis of diabetes, a home blood glucose test enables them to monitor their blood sugar levels. Self-monitoring blood glucose (SMBG) devices play an important role in the management of diabetes and in the reduction of risk of

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serious secondary clinical complications.[6] This can not only benefit individual patients but can result in reduced expenditures at the primary care level and in hospitalizations. Meter and reagent strip systems to monitor blood glucose were developed in the late 1960s, making it a viable first step for diabetes self-monitoring with instant clinical information. This technology has experienced significant development in design and dissemination over the past 60 years. The first portable glucose meter was the Ames Reflectance Meter and became widely available in 1970. They are regulated by the US Food and Drug Administration (FDA). The FDA issues warnings and educational material to encourage adequate use.[7,8] Figure 3.1 illustrates a SGBM meter.

SMBG is the most widely used method for monitoring how effectively the body is processing glucose in the comfort of the home. SMBG meters are portable devices that measure blood glucose concentration in a drop of blood using finger-stick blood samples and test strips. Over the past six decades, enormous progress has been made in glucose meters' technology. The size of SBGM meters have been reduced, and its accuracy has significantly improved. Many meters are now affordable and have integrated advanced data-handling capabilities and features to record daily doses of insulin, intake of carbohydrates, and workout history. Most meters allow for recording results on cellular smartphones, using apps. There is evidence of the impact of lower cost on increased use, enabling patients to monitor their blood glucose levels. Despite their benefits Clarke et al. argue that

> a number of barriers to optimal adherence to SMBG have been identified and include demographic factors, notably in ethnic minority groups, and significantly psychosocial elements such as anxiety, self-perception of diabetes and vulnerability to complications, and the quality of support available by the healthcare provider and family. Patients may be stressed by the responsibility of self-care and the demands of regular and possibly repeated painful finger-prick, or lack the motivation and discipline required.[9]

FIGURE 3.1 Glucose monitoring meter and strips.

Source: www.fda.gov/consumers/consumer-updates/how-safely-use-glucose-meters-and-test-strips-diabetes

The advent of real-time continuous glucose monitoring (CGM) systems that measure glucose levels continuously constitute an important breakthrough and revolutionary development in diabetes self-home-care technology. They are especially beneficial for people with type 1 diabetes. However, the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), and American College of Endocrinology (ACE) have reported its benefit for people on intensive insulin treatment. CGM comprises a glucose-sensing device inserted in the abdomen or on the arm, electrochemically measuring glucose levels in subcutaneous tissues; it eliminates the need for continuous finger-sticks. The Guardian Real-Time System (Medtronic MiniMed) got FDA approval in 1999 as the first CGM device.[10] Since then, the accuracy of CGM technologies has remarkably improved, reaching the performance of SMBG devices. CGM devices currently in the market provide alerts to the patients helping them detect hypo- and hyperglycemic events. Some of the most commonly used systems with integrated alerts are the Dexcom G5 Mobile and G6, the Medtronic Enlite and Guardian, FreeStyle Libre 2, and the Senseonics Eversense (refer to Figure 3.2). Cappon et al. Claim, "CGM devices have been proved to improve safety and effectiveness of diabetes therapy, reduce hypoglycemia incidence and duration, and decrease glycemic variability. Furthermore, the real-time availability of blood glucose values has been stimulating the realization of new tools to provide patients with decision support to improve insulin dosage tuning and infusion."[11,12]

Research and development continue to provide innovative ways to advance autonomous devices. The healthcare systems need to promote their use and find alternatives for dissemination, reduce costs, and guarantee widespread availability of the newer technologies as they emerge. The data collected by these devices provide options for patient-provider communication and allow for the potential of improving the health and quality of life of the patient with diabetes. In addition, I claim that the collected data could be useful in making epidemiological decision at the micro and macro levels.

FIGURE 3.2 Example of a continuous glucose monitoring system.

HIV AND DIAGNOSTIC SELF-TESTING

The human immunodeficiency virus (HIV) attacks the body's immune system. HIV is found in blood, semen, preseminal fluid, vaginal fluid, rectal fluid, and breast milk. It is transmitted person to person, underscoring the importance of screening and awareness of having the disease. If HIV is not treated, it can lead to AIDS (acquired immunodeficiency syndrome). There is currently no effective cure for HIV. HIV disease continues to be a serious health issue for parts of the world. However, with proper medical care and adherence to antiretroviral therapy, HIV can be controlled.

Worldwide, there are about 1.7 million new reported cases each year. About 37.9 million people were living with HIV around the world, and 24.5 million are receiving antiretroviral therapy (ART). An estimated 770,000 people have died from AIDS-related illnesses since the start of the epidemic. In the United States it is estimated that 1.2 million live with HIV; of those about 14% (1 in 7) were unaware that they had HIV.[13]

Screening and early diagnosis is key for controlling the progression of the illness in individuals and for curtailing the epidemic at the population level. The gap in screening has been explained by lack of access to care, poor knowledge about risks, and the stigma associated with having HIV. Self-testing for HIV can be a powerful tool for closing the gap on early screening. Although the US Food and Drug Administration (FDA)-approved HIV home-collection tests have been on the market since 1996, various concerns have prevented the approval of a home test until recently, including that people that tested positive might delay contacting the healthcare provider. Since July 2012, the FDA approved the OraQuick® In-Home HIV Test for rapid home-testing, manufactured by OraSure Technologies, Inc. It remains the only approved test in the United States. There is authorization to sell in stores and online to people over 17 years or age. The FDA describes the OraQuick® In-Home HIV Test as "an in-vitro diagnostic home-use test for HIV (HIV-1 and HIV-2) in oral fluid. This test works by looking for your body's response (antibodies) to fighting the HIV virus. A positive result is preliminary and follow-up confirmatory testing is needed."[14] The FDA reported specificity of the test to be 99.8% (indicating one in 5,000 results may be a false positive. The FDA conducted a Monte Carlo mathematical simulation model of self-test use that demonstrated that 4,000 infections might be prevented in the first year of its use.[15]

After self-testing, linkage to healthcare clinical service should follow, independently of the results. Confirmatory tests are needed if positive, and if the confirmatory test is positive treatment should be offered. In the case of a negative test, the option to receive FDA-approved PrEP (or pre-exposure prophylaxis) drugs should be offered and evaluated.

The CDC recommends "that everyone between the ages of 13 and 64 years old be screened for HIV at least once as part of their routine health care." Home self-testing should facilitate and promote population level compliance of this recommendation. More frequent testing is recommended for people who have a higher risk of infection because of behaviors such as having sex without condoms, having sex with multiple partners, or using injectable drugs with shared needles.[16] For this test, the person must swab his or her gums to collect an oral fluid sample and use the materials in the kit (stick and tube with testing solution) to test the oral fluid sample and the results will be available in 20 to 40 minutes. The test is not reliable at detecting HIV infections within 3 months of onset of exposure. Refer to Figures 3.3 and 3.4.

Issues of global adoption, dissemination, implementation, and benefits of home self-testing have been widely

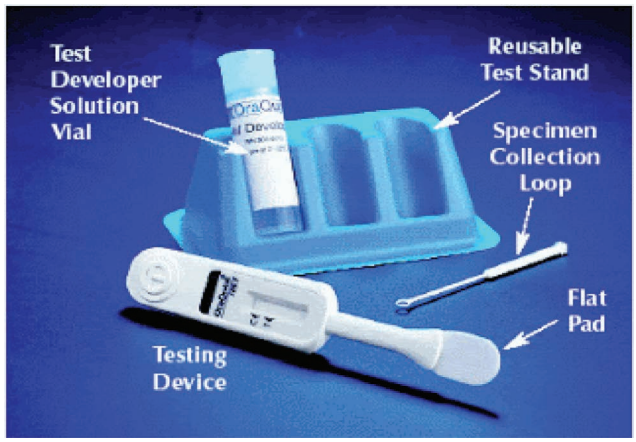

FIGURE 3.3 The contents of the The OraQuick® In-Home HIV Test.

Source: OraQuick Home HIV Test Kit (drugabusecontrol.com)

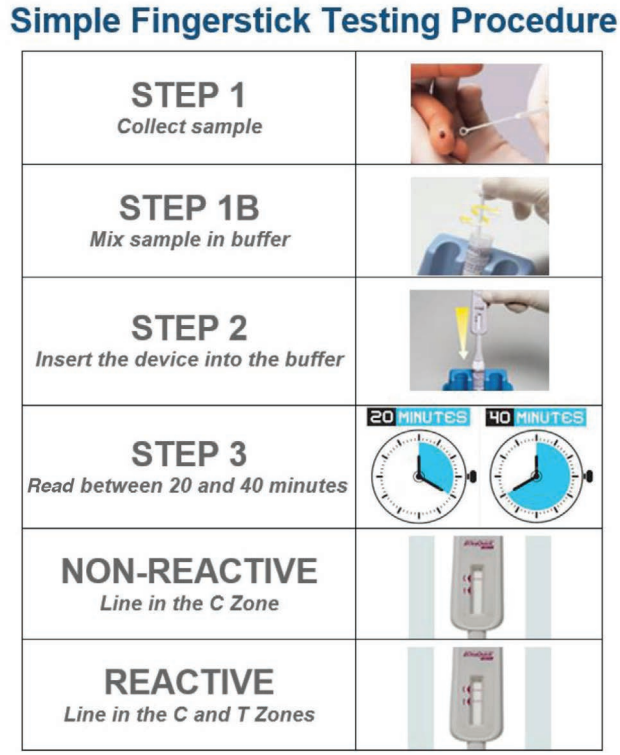

FIGURE 3.4 Educational step-by-step testing procedure.

Source: simple-finger-stick.png (633×805) (knscanada.com)

discussed in the scientific and lay literature.[17] Salient issues are the appropriate and coordinated linkage to culturally sensitive care, the generalized stigma associated with HIV, and the lack of mental health support. These issues are barriers that are shared by other interventions and innovations to address the HIV epidemic.[18] These issues underscore the need to continue workforce development, targeted health education, scaling of resources, and revised data-driven policies. The home self-testing technology is a promising tool for a coordinated response to HIV. In the United States, the product is sold in pharmacies, increasing the possibility of pharmacists' involvement while significantly contributing to screening as prevention from a population perspective. Pharmacists, with the right level of awareness and health education skills, can contribute to the dissemination, adopting, and appropriate use of home self-testing.

SELF-TESTING FOR COVID-19

Since 2019, the whole world has been addressing the COVID-19 epidemic, a dangerous disease caused by SARS-CoV-2 virus discovered in Wuhan, China. It is very contagious and has quickly spread around to all continents.[19] Since its onset there has been an untiring and constant race to address the health consequences and the social disruptions caused by the virus responsible for COVID-19.

In September 2021, the United States reported nearly 40.8 million accumulated diagnosed cases, and 656,318 deaths. Worldwide 173.4 million people have reported having COVID-19 and the deaths are quickly approaching 3.8 million. COVID-19 most often causes respiratory symptoms that can feel much like a cold, the flu, or pneumonia, but COVID-19 can also harm other parts of the body. Older adults and some specific groups, like minorities and people living in underdeveloped countries, have suffered a disproportionate burden of the disease.[20] The massive response has included preventive measures like mandated mask-wearing, social distancing, school and business closings, and travel bans, among others. Rapid and unprecedented resources have been devoted to biomedical research and the development of vaccines. The US FDA have provided emergency-use authorization to three different vaccines. Vaccination plans have been rolled out around the world, with different levels of success. Treatment protocols to address the multiple symptoms are constantly under revision, and some have avoided hospitalizations and deaths.

Within this context, we cannot minimize the role of testing and screening for COVID-19 as a diagnostic measure and as one of the pillars for reducing the spread of the virus. The FDA is actively authorizing COVID-19 tests understanding the importance of it as a public health measure, jointly with other prevention strategies. This includes emergency-use authorizations for COVID-19 tests in which some or all testing processes can be performed at home. A negative result means the test did not detect the SARS-CoV-2 virus, and a positive result means the test did detect the SARS-CoV-2 virus. The FDA

02/11/2021	Ellume Limited	Ellume COVID-19 Home Test 12/15/2020	Lateral Flow, Fluorescence, Instrument Read, Over the Counter (OTC) Home Testing, Screening	Home, H, M, W
04/12/2021	Abbott Diagnostics Scarborough, Inc.	BinaxNOW COVID-19 Ag Card Home Test 12/16/2020	Lateral Flow, Visual Read, Prescription Home Testing	Home, H, M, W
03/01/2021	Quidel Corporation	QuickVue At-Home COVID-19 Test 03/01/2021	Lateral Flow, Visual Read, Prescription Home Testing	Home, H, M, W
03/31/2021	Quidel Corporation	QuickVue At-Home OTC COVID-19 Test 03/31/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening	Home, H, M, W
04/01/2021	Abbott Diagnostics Scarborough, Inc.	BinaxNOW COVID-19 Antigen Self Test 03/31/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening	Home, H, M, W
03/31/2021	Abbott Diagnostics Scarborough, Inc.	BinaxNOW COVID-19 Ag Card 2 Home Test 03/31/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Telehealth Proctor Supervised, Serial Screening	Home, H, M, W
06/04/2021	OraSure Technologies, Inc.	InteliSwab COVID-19 Rapid Test Rx 06/04/2021	Lateral Flow, Visual Read, Prescription Home Testing	Home, H, M, W
06/04/2021	OraSure Technologies, Inc.	InteliSwab COVID-19 Rapid Test 06/04/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening	Home, H, M, W

FIGURE 3.5 Individual EUAs for antigen diagnostic tests for SARS-CoV-2 authorized for home testing as of June 4, 2021.

Source: www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2

"cautions patients against using the results from any serology test as an indication that they can stop taking steps to protect themselves and others, such as stopping social distancing or discontinuing wearing masks."[21] Refer to Figure 3.5 for a list of current home tests approved by the FDA. It should be highlighted that this list is rapidly changing and expanding.

Currently, most of the OTC testing options are not covered by health insurances in the United States. Some COVID-19 collection kits are available for a $0 upfront charge if prescribed or if the person to be tested meets symptoms-related screening criteria for COVID-19 testing. They have not been designed to test the efficacy of the COVID-19 vaccination, a common misconception among the population. The role of the chain and independent pharmacies has been recognized during this pandemic and has been instrumental in the testing and screening. With the addition of OTC testing options that can be conducted from the comfort of home the pharmacies remain a critical component of the pandemic response nationally and internationally.

The applicability and accuracy of a self-testing strategy for SARS-CoV-2 from a population perspective merits further study, due to the newness of the technology and the changing patterns of the epidemic.[22] It has been argued by some that the expansion and investment in SARS-CoV-2 testing programs with more frequent and rapid tests across diverse communities, in conjunction with the self-isolation of individuals with confirmed infection. are essential for alleviating the COVID-19 pandemic.[23,24]

CONCLUSION

Self-testing for monitoring and diagnosis of diseases cannot be ignored as a prevention tool. As primary healthcare services patient-centered care and shared clinical decision making are accepted as best practices, the ability to empower patients with point of care tests becomes an indispensable tool. In the case of monitoring diabetes, patients have embraced the technology and its evolution in such a way that self-monitoring has become the norm. This is not necessarily the case when it comes to infectious diseases like HIV and COVID-19. Barriers associated with financing and linkage to care remain the greatest concerns.

Tests by themselves are not a solution to improve health. They have to be embedded in coordinated public health strategies that consider the social determinants of health. In order for the benefits of self-testing for chronic and infectious diseases to be maximized, there is a need to empower patients to understand and manage their self-diagnosis with appropriate resources. Patients need to trust the system, set clear health objectives, be transparent, share the results, and be skillful in communicating with health professionals. Furthermore, psychological support must be readily available to ensure that patients are prepared to receive their results and engage in appropriate management. Concurrently to the dissemination of the technology, there is a need to educate patients to use, understand, and manage the diagnostic results. To fully benefit from self-testing technology, there is a need for systemic approaches to improving health outcomes.

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4 Medical Devices for Management of Tobacco Use Disorder

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CONTENTS

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GENERAL BACKGROUND

Smoking is a leading cause of preventable mortality and morbidity, mainly from various vascular and respiratory diseases and cancer. Despite available scientific evidence on the health hazards of cigarette smoking, its prevalence is still high in many parts of the world, especially in low- to middle-income countries.

Nicotine addiction involves being dependent on nicotine, a naturally found psychoactive substance in tobacco. Nicotine stimulates the central nervous system at the commonly delivered doses by tobacco products to exert pleasure; improve mood, memory, and concentration; reduce anxiety and appetite; and induce other short-lived feelings of well-being. The addictive nature of nicotine includes drug-reinforced behavior, obsessive use and reoccurring use after abstaining from it, withdrawal symptoms, physical dependence, and tolerance.[1]

Based on the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), tobacco use disorder is diagnosed when an individual uses tobacco for more than a year, and a minimum of two (2) of the eleven (11) following sub-features appear:

1. More amounts of tobacco over a longer timeframe than planned
2. Inability to quit or lessen the amount of tobacco use despite efforts to do so
3. An excessive amount of time spent on attaining or using tobacco
4. Craving or a strong desire or urge to use tobacco
5. Relinquishing responsibilities because of tobacco use
6. Persistent use of tobacco despite its negative impacts both socially and in relationships
7. Abandoning career, social, and other activities to use tobacco
8. Use of tobacco in harmful situations/settings
9. Persistent use of tobacco even in the face of physical or emotional difficulties related to tobacco use
10. Tolerance, as defined by either the need for markedly increased amounts of tobacco to achieve the desired effect or a markedly diminished effect with continued use of the same amount of tobacco
11. Withdrawal, as manifested by either the characteristic withdrawal syndrome or the use of tobacco to relieve or avoid withdrawal symptoms

Tobacco withdrawal occurs when an individual experiences the following symptoms upon cessation, including craving, problems concentrating/focusing, anxiousness, headaches, weight gain (mainly due to increased appetite), reduced heart rate, difficulties sleeping (e.g., insomnia), agitation or mood disturbance, and depression. The symptoms spike in the first several days and gradually fade around 4 to 8 weeks of continued smoking abstinence.

According to the American Psychiatric Association, tobacco use disorder is separated into three categories: mild, moderate, and severe. If two or three symptoms from the criteria exist, the tobacco use disorder is considered mild. The disorder is classified as moderate when four to five of the symptoms from the criteria are met. With six or more of the criteria, the diagnosis of severe tobacco use disorder is made.[1]

Clinical intervention that can be offered to the smokers by the healthcare professionals can be divided into three levels depending on the intensity and service provided: very brief, brief, and intensive clinical intervention.[2] Brief clinical intervention by the healthcare professionals including pharmacists increases quit rates effectively.[3] Pharmacists must act to identify those who use tobacco and offer treatment to them.

One of the strategies is based on the 5A's approach (ask, advise, assess, assist, and arrange follow-up) intended to be brief and taking minimum time from healthcare providers (Table 4.1). Upon identifying a smoker, pharmacists can provide opportunistic advice for quitting, offer assistance, make a referral (e.g., to a quit-smoking clinic), recommend pharmacotherapy, and arrange a follow-up. This opportunistic advice focuses on increasing smokers' motivation to stop smoking to improve their quitting success rate.[4] Evidence shown that such brief intervention increases overall tobacco abstinence rates.[5] There is high-quality evidence that individually delivered smoking cessation counseling can assist smokers to quit. There is moderate-quality evidence of a smaller relative benefit when counseling is used in addition to pharmacotherapy and of more intensive counseling (longer and multiple sessions) compared to a brief counseling intervention.[6]

STEP 1: ASK ABOUT TOBACCO SMOKING

Pharmacists and other healthcare providers should ask all their patients about smoking status, and they should document such information as much as possible. This should be provided as convenient during customers' routine visits regardless of their intentions to quit and whether they ask for assistance or not. Changes in smoking status should be reported continuously at each visit as smokers progress from no intention through interest in quitting, to quit attempts, to quitting, to preventing relapse. All healthcare settings should adopt good systems for documentation to ensure that smoking status is perfectly recorded at every visit.[7,8]

STEP 2: ADVICE TO QUIT

The healthcare providers should offer all patients found to be smoking clear advice about quitting. Evidence shown that advice by healthcare providers including pharmacist improves quit rates. The length of person-to-person contact sessions has been found to be associated with successful treatment outcomes and such association has been

described to represent a strong dose-response relationship.[8] Collaboration between healthcare providers in providing advice has a further-strengthening effect on such rates. Healthcare providers are encouraged to provide at least a brief intervention constituting concise cessation advice to all tobacco users. However, maximum effectiveness is achieved when intensive interventions are offered whenever possible because smokers' thoughts, perceptions, and emotions towards smoking and quitting are always inconsistent (Table 4.2).[9] Face-to-face treatment sessions repeated at least four times appears to be more effective in increasing cessation. Thus, when feasible, smoking cessation service providers should make efforts in arranging for at least four sessions with patients stopping tobacco.[10]

Pharmacists should be trained to deliver brief advice effectively in order to assist smokers. This training should provide them with knowledge and skills on various types of smoking cessation advice to trigger a quit attempt.[11]

STEP 3: ASSESS WILLINGNESS TO MAKE A QUIT ATTEMPT

Various models have been proposed regarding the motivation of smokers and their willingness to quit. The Transtheoretical Model of Change or "Stage of Change" model has been used to determine smokers' willingness to quit. This model suggests that the smoker goes through a series of phases during his/her smoking cessation process: pre-contemplative (the smoker does not contemplate quitting smoking), contemplative (the smoker begins thinking about quitting smoking within the next six months), preparative (the smoker is prepared to quit smoking), smoking cessation, and the eventual relapses that restart the cycle.[12] Those in the pre-contemplation and contemplation stages are considered to have a lower willingness to quit than those in the preparation stage. However, there is no sufficient evidence that motivating smokers based on stage of change model has successful outcomes, indicating that readiness or motivation to stop smoking may not be integral for quitting.[13]

Interestingly, motivational interviewing (MI) has been used as a counseling style that helps smokers explore and resolve their uncertainties about quitting. MI may modestly increase the likelihood of long-term smoking cessation when used with other smoking cessation intervention components or when compared with non-MI smoking cessation interventions.[14] However, there is also the possibility that MI may reduce quit rates relative to other smoking cessation interventions. Further evidence is likely to strengthen or weaken this idea.

Trained pharmacists involved with tobacco use disorder treatment should assist smokers regardless of the smoker's motivation at any given time. In addition to assessment of motivation level to quit smoking, pharmacists should also assess the level of nicotine dependence. The Fagerström Test for Nicotine Dependence (FTND) is still widely used to assess the level of nicotine dependence among cigarette smokers despite having some issues concerning its validity and reliability.[15] The FTND incorporates two crucial questions, i.e., the Heaviness of Smoking Index (HSI), to assess the number of cigarettes smoked per day and the time to first cigarette (TTFC).[16]

A useful tool in assessment of smoking is the carbon monoxide (CO) analyzer. It is a simple, noninvasive, and relatively inexpensive method to assess recent tobacco smoking and also to validate smoking cessation.[17,18] Carbon monoxide is produced by incomplete combustion of organic materials, including tobacco leaves. The CO level detected in exhaled air by CO-oximetry can be used to evaluate the heaviness or intensity of smoking. In general, there is a direct relationship between the levels of CO and the number of cigarettes smoked.[17] It has been observed that the measurement of CO in exhaled air in smokers could be an indicative test of immediate and future harm to their health as a consequence of smoking[19] and this could increase their motivation to stop smoking, which could lead to smoking cessation in these patients.

However, available studies have provided mixed results regarding the effect of biomedical risk assessment as an aid for smoking cessation. A recent Cochrane systematic review concluded that moderate-certainty evidence limited by risk of bias did not detect an effect of feedback on smoking exposure by CO monitoring.[20] Nonetheless, it is still considered an important part of smoking cessation service given its practicality and affordability.

> The measurement of CO levels in exhaled air by CO-oximetry is an inexpensive, noninvasive, and rapid technique that requires little technical training, making it a technique for risk assessment in smokers that can be easily applied in primary care and could serve as a reinforcement aid in smoking cessation intervention activities.

STEP 4: ASSIST IN QUIT ATTEMPT

First step in assisting smokers to quit is setting a quit date. The quit date is preferred to be set within two weeks from being interested in quitting.[21] Smokers' counseling is a core part in smoking cessation interventions. It can be offered individually, in a group, or via telephone. Using multiple approaches in delivering smoking cessation interventions increases abstinence rates; thus, it should be encouraged. However, evidence indicates that individual counseling results in better quitting outcomes than group or phone counseling and self-help.[10,22]

Telephone counseling can take on one of two approaches: either "proactive counseling" or "reactive counseling." Smokers receive regular calls from smoking cessation service providers on a scheduled basis when a proactive approach is followed. When a "reactive counseling" approach is desired, smokers seek help or advice via initiating calls to a helpline. Proactive services have been

evaluated widely compared to reactive services because they can be controlled easier. According to an available evidence, behavioral counseling formats should include proactive telephone counseling elements.[23]

STEP 5: ARRANGE FOLLOW UP

Lapsing and/or relapsing are common occurrences among smokers attempting to quit. Lapsing refers to returning to the smoking habits temporarily before being able to quit again whereas relapsing refers to a permanent or long-term return to smoking. Continuous abstinence is accomplished when a patient stops smoking for at least six months. Within the first few weeks of quitting smokers are at higher risk of relapse. Thus, they should be offered a support from families, friends, and healthcare providers in the first week of quitting. Research indicated that abstinence for as long as twelve months is a strong predictor of long-term abstinence.[24]

Research suggest that the smoking abstinence rate and its effectiveness can be enhanced by using multiple treatment sessions. More than eight sessions within six months (intensive interventions) may result in a greater quitting rate. Nevertheless, fewer smokers might benefit from such interventions (i.e., having limited reach) and may not be viable in some primary care settings.[7] National Centre for Smoking Cessation and Training (NCSCT) of the UK recommends evidence-based behavior change techniques delivered via at least six (6) sessions while dealing with smokers looking for assistance with quitting as described here:[25]

First session:	1 or 2 weeks before Quit Date (Pre-Quit Assessment)
Second session:	Quit Date
Third session:	1 week after Quit Date
Fourth session:	2 weeks after Quit Date
Fifth session:	3 weeks after Quit Date
Sixth session:	4 weeks after Quit Date

Activities at each session differ accordingly, e.g., the earlier session is to get the smoker to commit to abrupt cessation (or gradual reduction with pharmacotherapy) while later on is about the "not a puff" rule to prevent lapse and relapse. As mentioned earlier, the CO breath analyzer can be used at each session to assess any recent smoking activity.[26] CO tests at every visit are helpful to show the patient objective proof of improved health after they have stopped smoking completely and to check whether they have stopped smoking.[26]

At the end of the 6-month follow-up post quit date, final verification of abstinence can be done using the CO breath analyzer and/or the cotinine level in body fluids. Cotinine is the primary metabolite of nicotine. When cigarette smoke is inhaled, nicotine is absorbed through the lungs and undergoes extensive metabolism in the liver. Typically, 70–80% of nicotine is metabolized into cotinine.[27] Cotinine detection is generally preferred over nicotine due to its longer average half-life, which is estimated to be 15–40 hours.[27,28]

In comparison, the average half-life for nicotine is only 2 hours.[27] Although samples for cotinine detection can be obtained from the blood, urine, or saliva, salivary cotinine test is preferred in the clinical setting since it is the most noninvasive and easiest to perform in the community pharmacy setting. Evidence shows that cotinine is the preferred method for determining smoking status over CO monitoring.[28,29]

Research suggests that intensive tobacco dependence treatment has more impact than brief treatment. Such intensiveness can be fulfilled via increasing the length of individual treatment sessions, increasing number of sessions, and incorporating specialized behavioral therapies. Intensive clinical interventions could be offered by any adequately trained healthcare provider who has the facilities available to offer intensive interventions suitable for any tobacco user ready to participate in them.[7]

TABLE 4.1
The "5A's" for Brief Intervention

1. Ask about tobacco use.
   - Identify and document tobacco use status for every patient at every visit, including the adolescents.
   - Where appropriate, ask the patient's caretaker about tobacco use or exposure to tobacco smoke in living and/or working environment.
2. Advise to quit.

In a clear, strong, and personalized manner urge every tobacco user to quit.

Advice should be:

- Clear—for example: "I believe it is crucial for you to quit smoking immediately, and my staff and I can assist you," or perhaps, "Reducing the number of cigarettes while you are unwell or sick is not enough."
- Strong—for example: "As your pharmacist, I know that quitting smoking is the most important action you can take to improve your condition/ health now as well as in the future. We are here to help you quit successfully."
- Personalized—Linking tobacco usage with existing health problems/illness, social norms, social rejection, and/or other social and economic consequences, motivation level/ readiness to quit, and/or the effect of tobacco use on kids and family members.

3. Assess willingness to make a quit attempt.

Is the patient willing to make a quit attempt currently?

- Provide support if the patient is willing to make a quit attempt.
- Offer intensive treatment or refer to intensive intervention.
- Apply motivational interviewing using the "5 R's" (relevance, risks, rewards, roadblocks, and repetition) if the patient is unwilling to make a quit attempt yet.

4. Assist in quit attempt.
   - Offer counseling with pharmacotherapy (unless medication is contraindicated) for the smoker willing to make a quit attempt.

Preparations for quitting: STAR (Set, Tell, Anticipate, Remove)

- **Set** a quit date. A quit date must be set as soon as possible or within two (2) weeks of the first session. Smokers may choose between abrupt quitting (cold turkey) or gradual reduction, i.e., cutting down the number of cigarettes gradually until the set date. Preferably, get the smoker to quit abruptly.
- **Tell** family members, acquaintances, and coworkers about quitting to obtain understanding and support. In addition, assist smokers in getting extratreatment social support from self-help groups, if available. If there are other smokers (e.g., in the household), encourage them to quit together and request others not to smoke in his/her presence to reduce the risk of therapeutic failure and exposure to secondhand smoke.
- **Anticipate** challenges to a proposed quit attempt, especially during the critical first few weeks. Challenges include nicotine withdrawal symptoms. Talk with the smoker about challenges/causes and how he or she will effectively conquer them. Offer exercises on problem-solving/skills.
- **Remove** tobacco products from his or her environment. Preceding quitting, avoid smoking in sites where much of the patient's time is spent such as at work, in the house, or in the car.
- Provide a supportive healthcare environment while reassuring the patient in his or her quit attempt.
- Total abstinence is very important. Explain the "not a single puff" rule after the quit date to prevent lapse and relapse.
- Discuss previous experiences with quitting. Identify what assisted and what prohibited quitting in the former attempts.
- Discuss alcohol. The smoker should consider decreasing or abstaining from drinking alcohol during the quit attempt because it may cause lapse and relapse.
- Advise the use of authorized smoking cessation medications, when indicated. Describe how such pharmacotherapies reduce craving and withdrawal symptoms, increasing smoking cessation success.
- Provide supplementary materials and information, if available.

5. Arrange follow-up.
   - Timing is important. Follow-up appointments should be scheduled weekly until the quit date, if possible, and within the first week after the quit date.
   - Subsequent appointments are recommended every week within the first month, and then every 2 weeks for the second and third month, and every month after that up to 6 months.
   - Appointments should be in person whenever possible, or via telephone, etc.
   - Actions during follow-up:
   - Congratulate success.
   - If tobacco use has occurred, review circumstances and provoke a commitment for complete quitting.
   - Inform the smoker that any lapse that occurred can be viewed as a learning experience.
   - Identify obstacles already faced and foresee obstacles in the near future.
   - Assess medication use and any associated difficulties, including side effects.
   - Think of incorporating more intensive treatment; in the event of failure, a referral is recommended.

Source: Adapted from Fiore et al.[7] and NCSCT.[25]

TABLE 4.2
Elements of an Intensive Tobacco Dependence Intervention

Assessment	• The willingness of tobacco users to make a quit attempt using an intensive treatment strategy should be assessed. • Other assessments can deliver useful information in counseling (e.g., anxiety, addiction).
Program clinicians	• The involvement of various kinds of clinicians should be efficient. • Having a healthcare provider present to convey a solid message about quitting, information about health risks of smoking and benefits of quitting, and recommending and prescribing medications is a possible counseling strategy that should be endorsed. • Additional counseling interventions can be delivered by nonmedical personnel.
Program intensity	There is evidence of a strong dose-response relationship; thus, when possible, the program intensity should be as follows: • In terms of length, sessions should be extended to more than 10 minutes. • In terms of number, sessions should be at least 4.
Program format	• Group or individual counseling can be offered. • Counseling via telephone calls is effective and is complementary to the treatments provided in the clinical setting. • The provision of self-help materials and the use of cessation web sites are possible additional options. • Follow-up interventions should be scheduled.
Type of counseling and behavioral therapy	Counseling should include practical counseling (problem solving/skills training) integrated with social support during treatment.
Medication	• Every smoker should be offered cessation pharmacotherapy, when indicated. There is insufficient evidence of effectiveness among some groups like pregnant women, smokeless tobacco users, mild smokers, and adolescents. • The pharmacist should describe how medications assist in reducing withdrawal symptoms and craving, and as so improving quitting success. • Combining counseling and medication increases abstinence rates, as well as certain combinations of cessation medications when indicated.
Population	Intensive intervention programs can be offered to any tobacco user wanting to make such an effort.

Source: Adapted from Fiore et al.[7]