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Editorial: Family Medicine in the Middle East—From Fragmented Systems to a Unified Vision for Primary Care and Healthy Aging

Family medicine in the Middle East and Eastern Mediterranean Region (EMR) is undergoing a profound transformation. The collection of papers in this issue offers an impressive, multi-layered narrative that spans diverse national contexts—from Oman's internationally recognized primary health-care achievements to Egypt's ambitious system-wide reforms, Kuwait's structured and expanding residency programs, Jordan's evolving training pathways, Iraq's post-conflict rebuilding efforts, and the broader region's response to demographic transition and dementia. Together, these contributions form a compelling statement: **the future of sustainable health-care in the Middle East rests on the strength of family medicine and its integration into national primary care systems.**

The collective insights across the papers reveal not only the historical roots and evolving competencies of family medicine but also the challenges that continue to impede full realization of its potential. Importantly, they present a shared roadmap for progress—one grounded in evidence, regional collaboration, and the emerging needs of aging populations. This editorial synthesizes the key themes emerging from all contributions and situates them within a broader vision for the future of family medicine in the region.

A Region Rich in Progress Yet Marked by Uneven Trajectories

The central review, *Advancing Family Medicine in the Middle East*, provides the foundation for understanding the regional mosaic.

From Lebanon and Bahrain's early adoption of family medicine in the 1980s to Oman's establishment of one of the earliest academic departments in 1987, the region has achieved milestones that position it well for future integration of primary care as the first point of contact. Yet, as the review highlights, this progress is uneven—shaped by political instability, economic constraints, and differing levels of policy commitment.

The country-specific papers deepen this picture:

Egypt

Egypt's model illustrates the complexities of scaling family medicine in a large, heterogeneous nation. Since the 1970s, reform efforts—including expansion of training programs, the Egyptian Fellowship, University-based departments, and the Universal Health Insurance Law—have strengthened primary care capacity. Yet challenges persist: limited faculty numbers, inadequate undergraduate exposure, and fragmented public perception of family medicine's role.

Kuwait

Kuwait's experience showcases a robust and structured postgraduate training ecosystem. Its Family Medicine Residency Program, developed with the Royal College of General Practitioners (MRCGP INT) and expanded to 60 specialized training centers with over 420 enrolled residents, stands as one of the region's most comprehensive. Innovative projects—such as the Ideal Family Medicine Clinic model—demonstrate how operational redesign can reduce waiting times, enhance continuity, and improve patient satisfaction. Yet systemic gaps remain in academic leadership, digital integration, and continuity of care.

Oman

Oman provides a narrative of pioneering success. With widespread PHC coverage, early academic leadership at Sultan Qaboos University, and WHO recognition for health system performance, the country exemplifies what long-term investment in PHC can achieve. However, Oman too faces

growing pressures related to chronic disease burdens, geographic disparities, and the need for digital transformation in primary care.

Jordan

Jordan's well-structured, four-year FM residency programs accredited by the Jordan Medical Council form the backbone of the country's PHC workforce. Yet training capacity remains insufficient for its rapidly expanding population and refugee-resettlement pressures. Public awareness and academic visibility continue to lag behind the demonstrated effectiveness of family medicine in delivering comprehensive, preventive care.

Iraq

Iraq's family medicine system is shaped by years of conflict, political transitions, and economic constraints. Despite this, the country maintains thousands of PHC centers, established family medicine boards, and growing WHO-supported diploma pathways. The resilience of Iraqi family physicians—delivering care through home visits, telemedicine, and community outreach during crises—highlights the specialty's adaptability and essential role in health system recovery.

Together, these papers remind us that family medicine in the Middle East is not a static specialty but a dynamic, context-responsive discipline shaped by economic cycles, conflict, migration, and demographic transitions.

Shared Challenges: Workforce, Structure, and Systemic Barriers

Despite meaningful progress, the concurrent challenges identified across submissions are strikingly consistent:

1. Workforce Shortages and Training Gaps

Every country reports an insufficient number of trained family physicians relative to population needs. This shortage is exacerbated by:

- limited training positions
- shortages of qualified trainers
- inadequate academic departments
- emigration of specialists
- limited incentives for graduates to choose family medicine

Egypt, Jordan, and Iraq highlight stark demand–capacity gaps, while Kuwait and Oman acknowledge the need for expanded postgraduate pathways and academic autonomy.

2. Limited Public Awareness and Misconceptions

Across the region, patients frequently bypass family physicians to directly access specialists—a reflection of healthcare culture and structural issues. Jordan and Lebanon, for example, report persistent misconceptions about the scope and qualifications of family physicians.

3. Fragmented Systems and Weak Gatekeeping

Most EMR countries lack a true gatekeeping system, leading to:

- duplication of services
- unnecessary specialist referrals
- higher costs
- compromised continuity of care

Kuwait and Egypt note that despite structured programs, large segments of care remain hospital-centric.

4. Insufficient Use of Digital Health and Data Systems

Although Kuwait, Oman, and some Gulf states have made progress, the region generally lacks integrated electronic health records and data systems essential for chronic disease management and coordination.

International Partnerships: A Cornerstone of Regional Success

One of the strongest and most hopeful themes running across all papers is the transformative role of global and regional partnerships.

The Arab Board of Health Specializations, RCGP collaborations, WHO-supported training, and international academic exchanges have strengthened curricula, standardized competencies, and facilitated cross-border knowledge sharing. Lebanon, Oman, Bahrain, and Kuwait have benefited immensely from these long-standing collaborations.

Jordan, Syria, and Iraq emphasize how partnerships are particularly vital in crisis settings—providing training opportunities, access to updated curricula, and reinforcement of PHC service delivery. These partnerships are not simply educational—they form the backbone of capacity-building, system strengthening, and professional identity.

The continuing integration of WONCA, international research networks, and cross-country residency pathways reflects a region increasingly committed

to global alignment and harmonization of competencies.

Family Medicine and the Challenge of Dementia: A New Frontier

The paper, Genetics and Risk Factors of Dementia, situates family medicine within one of the 21st century's greatest health challenges: the rising burden of dementia.

The paper emphasizes a crucial paradigm shift—dementia is not purely a result of aging but a multifactorial condition shaped by:

- genetic predispositions
- modifiable vascular and metabolic risks
- lifestyle factors
- psychosocial and environmental determinants

With dementia cases in MENA expected to rise by 125% by 2050, family physicians will be at the forefront of screening, prevention, early diagnosis, and longitudinal management.

The review highlights the importance of:

- APOE genotyping and risk counseling
- the life-course model of brain health
- management of modifiable risk factors such as hypertension, obesity, hearing loss, diabetes, smoking, and social isolation

The integration of dementia knowledge into family medicine curricula, screening programs, and public health strategies is urgently needed. This aligns naturally with the broader regional vision of strengthening PHC for chronic disease and aging.

A Unified Vision for the Future

Drawing on the evidence across all contributions, a shared roadmap for strengthening family medicine in the Middle East becomes clear:

1. Establish family medicine as the foundation of PHC

- Mandate family physicians as the first point of contact
- Expand gatekeeping systems
- Integrate PHC networks with hospital services

2. Strengthen academic infrastructure

- Establish independent family medicine departments in all medical schools
- Expand training capacity
- Integrate FM into undergraduate curricula

3. Scale up workforce development

- Incentivize FM residency enrollment
- Offer fellowships, research pathways, and academic career tracks
- Enhance trainer qualifications

4. Leverage digital transformation

- Implement integrated national electronic health records
- Use digital platforms for chronic disease management
- Expand telemedicine and home-based care

5. Advance healthy aging and dementia prevention

- Train FM physicians in risk assessment, screening, and counseling
- Incorporate the MIND diet, physical activity, and social engagement into PHC counseling
- Develop memory clinics and community-based geriatrics programs

6. Deepen international and regional partnerships

- Expand joint training initiatives
- Strengthen collaborations with RCGP, WHO, WONCA
- Support cross-border faculty development

Conclusion: A Region Poised for Transformation

The papers in this issue collectively affirm that **family medicine is not merely a specialty—it is the backbone of a resilient, equitable**, and cost-effective healthcare system. Across the Middle East, the momentum is unmistakable. Despite structural barriers, financial challenges, and geopolitical instability, countries are investing in PHC, expanding training, and embracing international collaboration.

At the intersection of rising chronic disease burdens, demographic aging, and the need for accessible community-based care, family medicine emerges as a transformative force. The integration of dementia prevention and brain-health frameworks further positions the specialty at the forefront of tomorrow's public health agenda.

This issue, through the contributions of leading educators, clinicians, and policymakers across the region, provides not only an academic analysis but a blueprint for action—one that moves the Middle East closer to the vision of resilient, people-centered, and future-ready healthcare systems.

Advancing Family Medicine in the Middle East: A Comprehensive Analysis of Development, Challenges, and International Partnerships

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Abstract

Family medicine has become essential to the health-care systems across the Middle East, providing comprehensive, continuous care and addressing a broad range of health issues. This paper explores the historical evolution, challenges, advocacy efforts, and impact of family medicine in several Middle Eastern countries, namely Lebanon, Bahrain, Egypt, Oman, Jordan, Syria, Kuwait, and Iraq. By examining these diverse national experiences, we assess how family medicine has influenced population health, navigated barriers, and fostered international collaborations. By analyzing the experiences of these countries, we identify successful efforts, ongoing challenges, and international collaborations that can strengthen the field of family medicine across the region.

Keywords: Family medicine, healthcare systems, comprehensive analysis, development, challenges, international partnerships, Middle East

Introduction

Family medicine is a vital healthcare specialty focused on delivering continuous and comprehensive care to individuals and families. It covers a broad spectrum of health concerns across all ages, organ systems, and diseases, with a strong focus on preventive care. This paper explores the historical evolution, educational advancements, public health impact, encountered challenges, and creative solutions achieved through international collaborations. It provides an analysis of the progress, barriers, and innovative practices in family medicine across eight Middle Eastern countries (1). Family medicine is a vital healthcare specialty focused on delivering continuous and comprehensive care to individuals and families. It covers a broad spectrum of health concerns across all ages, organ systems, and diseases, with a strong focus on preventive care. This paper explores the historical evolution, educational advancements, public health impact, encountered challenges, and creative solutions achieved through international collaborations. It provides an analysis of the progress, barriers, and innovative practices in family medicine across eight Middle Eastern countries (1).

Historical Background and Challenges Faced

In 1978, the Alma Ata Conference in Kazakhstan highlighted the critical role of Primary Health Care (PHC) in addressing the root causes of poor health. At this conference, 134 countries adopted a resolution for “health for all by the year 2000,” prioritizing efforts to address social, economic, and political determinants of health (2).

The first family medicine academic program was established in Canada in 1967, followed by the United States in 1969. When the model reached the Middle East, Lebanon and Bahrain were early adopters in the 1980s. In the region FM has faced several challenges, including economic instability, fragmented healthcare systems, resistance from established healthcare sectors, and a shortage of trained family physicians. Each country has encountered distinct obstacles, shaping the development of family medicine practice within unique contexts (1,3).

Successful efforts

Countries such as Lebanon, Bahrain, and Oman have developed comprehensive family medicine (FM) training programs, with notable contributions from universities and international partners.

The “Arab Board of Health Specialisations (ABHS)” was established in 1978 by the Council of Arab Health Ministers to enhance medical standards across the Arab world. In 1985, the Family Medicine Council within ABHS was created to aid Arab countries in developing FM services, accrediting programs, and producing competent FM specialists through standardized exams.

Country by Country analysis

Lebanon:

Family medicine was introduced in 1979 and key universities, have lead FM training. Established in 1991, the Lebanese Society of Family Medicine advocates for FM as a primary care foundation, collaborating with the Ministry of Public Health. As of 2021, Lebanon had five FM training programs and approximately 96 FM physicians actively practicing. However, challenges persist, including economic instability, physician emigration, and a culture where patients often bypass family doctors to consult specialists directly (1,4).

Bahrain:

Primary healthcare (PHC) services have been available in Bahrain for over 40 years, with family medicine formally introduced in 1981 through the Family Practice Residency Program (FPRP). Bahrain's FM program at Arabian Gulf University integrates problem-based learning and community-focused care. Bahrain played a leading role in establishing the Arab Board of Health Specializations, which has helped extend FM training across the region. The program's emphasis on research-oriented training and academic rigor has become a model for other countries (5). Bahrain still faces a shortage of family physicians, limited funding, and lack of public awareness of family physicians' role (5,6).

Egypt:

Egypt's focus on FM started in the 1990s when the Supreme Council of Universities recommended that each medical school establish a training program for general practice. By 2004, Egypt's FM initiative had expanded, with medical faculties urged to establish dedicated FM departments and curricula (13,14). Currently challenges include fragmented healthcare structures, a shortage of trained professionals, and low public awareness of family medicine's role in primary care (7).

Oman:

Oman's FM training, started in 1987 at Sultan Qaboos University. The first locally trained family physicians graduated in 1998. The program received RACP recognition in 2001, making it the first regional provider of the MRCGP (INT) exam (17). By 2016, Oman had increased its PHC centers to 206 and improved its general practitioner ratio significantly. Oman still faces resource shortages and a rising burden of non-communicable diseases, with ongoing efforts focusing on technology integration and disease management (8).

Jordan:

Family medicine residency programs started in Jordan in the early 1980s, and the specialty has since become central to primary healthcare. Currently, four residency programs exist at Jordan University. The Jordan Medical Council accredits structured FM residency programs, which include both hospital and primary care settings. Jordan's FM residency curriculum spans four years, with

residents completing three years in hospitals and one year in primary healthcare settings. The residency culminates in board exams, with initial assessment at the end of the second year and a final evaluation after the fourth year. To bridge the gap of 1 FM doctor per 12,138 patients, the WHO and Jordan's Ministry of Health offer a two-year Professional Diploma in Family Medicine. However, limited training resources, financial constraints, and a preference for higher-paying specialties among graduates present ongoing challenges.

Syria:

With support from the Ministry of Health and WHO, Syria's family medicine program began in 1992. Family physicians undergo four years of training in Ministry hospitals and PHC centers. By 2008, the program produced 400 family physicians. Despite ongoing conflict, Syria has maintained a family medicine residency program with support from the Syrian Association of Family Medicine, which promotes training and development in the field. The University of Damascus introduced a Masters degree in FM in 1998, later expanded to a four-year program. In 2004, the Scientific Council of Family Medicine began conferring Masters and Doctoral degrees, with a PhD program added in 2017.

Kuwait:

The Kuwait Board of Family Medicine was founded in 1983, and achieved MRCGP (INT) accreditation in 2005. Kuwait has made significant advances in FM by establishing specialized training centers and expanding residency programs, with support from international bodies. Kuwait has 60 specialized FM training centers, 85 trainers, and 19 assistant trainers (P. Trainers) enhancing mentorship and instructional quality. Since the programs began, approximately 665 graduates have joined the FM workforce. The Kuwait Association of Family Medicine has been instrumental in advocating for FM's integration into medical education and the development of residency programs (1,18). Currently there are 420 residents. The program duration is 5 years. Barriers remain, including insufficient training facilities, a shortage of family doctors, low financial incentives, and challenges of integration (1,4,10).

Iraq:

Introduced in 1995, family medicine gained the Arab Board Specialization in 2008. However, the specialty faces obstacles, including limited resources, political instability, and a system that still favours specialized care. Efforts are underway to integrate family medicine across all healthcare levels, but structural challenges remain heightened by economic instability (11). Despite these challenges, Iraq has seen a growing interest in FM, supported by the Arab Board of Health Specializations and the Iraqi Family Medicine Society (Table 1).

Table 1: Historical Development of Family Medicine in the Middle East

Country	Year Family Medicine Introduced	Key Milestones	Challenges
Lebanon	1979	Structured program with support from the American University of Beirut.	Economic instability, physician emigration, patients bypassing family doctors.
Bahrain	1981	Family Practice Residency Program (FPRP) established.	Shortage of family physicians, limited funding, low public awareness.
Egypt	1980s	Programs at Suez Canal University expanded to other institutions.	Fragmented healthcare, shortage of trained professionals, low public awareness.
Oman	1980s	PHC network strengthened, 206 PHC centres by 2016.	Resource shortages, rising burden of non-communicable diseases.
Jordan	Early 1980s	Residency programs established. WHO support for training.	Limited training resources, financial constraints, preference for higher-paying specialties.
Syria	1992	Ministry of Health and WHO support, 400 family physicians by 2008.	Political instability, resource shortages.
Kuwait	1983	Kuwait Board of Family Medicine founded MRCGP accreditation in 2005.	Insufficient training facilities, shortage of family doctors, low financial incentives.
Iraq	1995	Arab Board Specialization in 2008.	Limited resources, political instability, preference for specialized care.

Comparative Analysis and recommendations

- Challenges: Funding, public perception, and professional.
- Strategies: Effective international partnerships, policy support, and educational reforms.
- Recommendations: Enhance collaborations, increase public awareness, and strengthen government support (Table 2).

Table 2: Family Medicine Training Programs in the Middle East

Country	Key Institutions	Training Duration	Accreditation	Graduates (Approx.)
Lebanon	American University of Beirut, Saint Joseph University	3-4 years	Lebanese Society of Family Medicine	96
Bahrain	Arabian Gulf University	3-4 years	Arab Board of Health Specializations	N/A
Egypt	Suez Canal University, Menoufia University	3-4 years	Egyptian Fellowship Board	N/A
Oman	Sultan Qaboos University	4 years	Royal College of General Practitioners (MRCGP)	300+
Jordan	Jordan University, Royal Medical Services	4 years	Jordan Medical Council	N/A
Syria	University of Damascus	4 years	Scientific Council of Family Medicine	100+
Kuwait	Kuwait Institute for Medical Specialisations	5 years	Royal College of General Practitioners	655
Iraq	University of Baghdad	4 years	Arab Board of Health Specializations	200+

Impact Assessment of Family Medicine on Populations

The introduction of Family Medicine has led to significant health improvements across the Arab region, particularly in managing chronic diseases and enhancing preventive care. FM's emphasis on continuous, community-based care has proven especially valuable in rural areas previously lacking healthcare access (Table 3).

Table 3: Impact of Family Medicine on Population Health

Country	Key Health Improvements	Challenges
Lebanon	- Improved chronic disease management. - Enhanced preventive healthcare.	Accessibility gaps in rural areas.
Bahrain	- High-quality PHC services. - Improved population health standards.	Limited public awareness of family medicine.
Egypt	- Increased healthcare access in underserved areas. - Reduced healthcare costs.	Fragmented healthcare system.
Oman	- Lower mortality rates. - Improved disease management in rural areas.	High burden of non-communicable diseases.
Jordan	- Improved access to primary care. - Reduced disparities in underserved regions.	Strain from refugee influx, economic hardships.
Syria	- Maintained primary care services despite conflict. - Mobile clinics reaching conflict zones.	Devastated healthcare infrastructure, brain drain.
Kuwait	- Enhanced continuity of care. - High patient satisfaction in chronic disease management.	Overreliance on expatriate workforce, integration issues.
Iraq	- Strengthened primary healthcare. - Critical support during COVID-19.	Political instability, resource shortages.

Lebanon & Bahrain:

FM has improved health outcomes in Lebanon and Bahrain, focusing on managing chronic conditions and promoting preventive healthcare. In Bahrain PHC services supervised by qualified FPs have continuously been able to offer a variety of high-quality easily accessible healthcare services. FPs across the country have started gaining a good reputation for providing efficient and high-quality health services that have helped in promoting the standard of health of the population. However, accessibility gaps remain in rural areas (1,5).

Egypt:

FM has increased healthcare access in Egypt, especially in underserved areas by providing comprehensive, continuous, and community-centered care, thereby addressing both immediate and long-term health needs. Emphasizing preventive care and early intervention, FM has reduced healthcare costs and improved public health outcomes. The Healthcare Authority reported that over 35.5 million family medicine services were delivered through healthcare units and centers in governorates implementing the Universal Health Insurance System (21).

Oman:

FM has significantly boosted Oman's healthcare, lowering mortality rates and improving disease management. Community-oriented care has shown marked benefits in rural areas. Oman's healthcare system was ranked seventh globally by the WHO in its 2000 report, recognizing its achievements (22). The integration of noncommunicable diseases (NCDs) into primary care in Oman has proven to be a valuable approach for data collection and surveillance of selected NCDs.

Jordan, Syria & Iraq:

Although FM is still developing in Jordan, Syria, and Iraq, it has improved access to primary care and reduced disparities in underserved regions. During COVID-19, FM practitioners in Iraq provided critical support through home visits and telemedicine (20,24).

Kuwait:

FM in Kuwait has enhanced continuity of care and patient satisfaction, particularly in specialized clinics managing chronic conditions. As per a 2018 World Health Organization Review in the Eastern Mediterranean, 90 percent of PHC centres in Kuwait provided dental and diabetes care, with 38 percent providing gynaecological and obstetric care (24,25). PHC centres use an electronic health file which can be accessed across all centres and is planned to be linked to hospitals. A majority (90 percent) of PHC centres are open until midnight, with all centres offering walk-in services (26).

Barriers to Family Medicine Training and Implementation

Despite advancements in Family Medicine, several barriers persist, including limited resources, policy issues, financial disincentives, and lack of public awareness. Solutions include infrastructure investment, policy reforms to prioritize family physicians as first contacts, and public campaigns to raise FM's profile.

Primary challenges affecting FM across the region:

- **Limited Resources:** A lack of infrastructure, training facilities, and technological tools like telemedicine hinders FM development. Increased investment is essential.
- **Shortage of Trainers:** Many countries, including Egypt, face a shortage of trained FM educators and adequate training programs due to underrepresentation in medical education (13).
- **Limited Undergraduate Exposure:** Students receive minimal exposure in medical schools, often limited to brief rotations, impacting its visibility as a career path.
- **Healthcare System Modernization:** A centralized FM system could better serve as the first point of patient contact.
- **Insufficient Specialists:** Expanding postgraduate FM programs and offering incentives can help increase the number of family medicine specialists.
- **Independent Departments:** In several countries, FM departments are not autonomous within universities, limiting their influence.
- **Policy Challenges:** In Lebanon, Egypt, and Syria, policies do not mandate FM as the initial patient contact, reducing FM's role.
- **Financial Disincentives:** Low salaries and limited career growth discourage physicians from FM.
- **Economic Crises:** Financial strain in countries like Lebanon, Syria, and Egypt has impacted healthcare, raising costs and limiting access to FM services.
- **Physician Emigration:** Economic and political instability in Lebanon, Syria, and Egypt has led many doctors to emigrate.
- **General Practitioner vs. Family Medicine:** In the region, general practitioners (GPs) often lack the advanced training of FM physicians, leading to a role distinction that can affect public understanding.
- **Public Perception:** Low awareness among policymakers and the public limits FM's perceived value. Public health campaigns could improve understanding of FM's role.

Creative Partnership Approaches and International Collaborations

International partnerships have played a vital role in advancing family medicine (FM) education and raising practice standards in the Middle East. Collaborations with established institutions like the Royal College of General Practitioners (RCGP) have enabled knowledge sharing, curriculum development, and international exposure, aligning training with global standards (Table 4).

Table 4: International Collaborations and Partnerships

Country	Key Collaborations	Impact	Challenges
Lebanon	WHO, Médecins Sans Frontières (MSF).	Strengthened PHC system, mental health, and chronic disease management.	Economic instability, refugee crisis.
Bahrain	Gulf Health Council, WHO.	98% immunization coverage, 90% PHC access within 5 km.	Limited funding, low public awareness.
Oman	Royal College of General Practitioners, University of Sydney.	Over 300 family physicians trained reduced infant mortality.	Geographic challenges, retaining physicians in rural areas.
Kuwait	Royal College of General Practitioners, University of London.	95% immunization coverage, 85% PHC access.	Overreliance on expatriate workforce, patient preference for specialists.
Jordan	WHO, UNHCR, MSF.	Enhanced PHC in refugee-hosting areas.	Strain from refugee influx, economic hardships.
Syria	WHO, MSF, UNICEF.	Over 500,000 patients served annually, mobile clinics in conflict zones.	Devastated infrastructure, economic sanctions.
Egypt	WHO, international universities.	Improved training quality, resource sharing.	Fragmented healthcare system, low public awareness.
Iraq	WHO, Arab Board, MSF.	Over 1,200 PHC centres established, 200+ family physicians trained.	Political instability, resource shortages.

Lebanon, Bahrain, Oman, and Kuwait have benefited from partnerships with organizations such as RCGP and WONCA. These collaborations have enabled standardized curricula, knowledge exchange, and best practices sharing, enhancing FM training quality and providing physicians with international exposure.

In Lebanon, partnerships and collaborations, particularly with the WHO, have been crucial in strengthening its primary healthcare system amid challenges like the Syrian refugee crisis and the aftermath of the Beirut explosion in 2020. NGOs like Médecins Sans Frontières and International Medical Corps also play a significant role, with MSF operating 12 centres serving 200,000 patients each year (28).

Bahrain collaborates with Gulf Cooperation Council (GCC) countries through the Gulf Health Council to share best practices in family medicine, achieving a notable 98% immunization coverage. The World Bank and WHO have supported the strengthening of primary healthcare infrastructure, ensuring over 90% of Bahrain's population has primary healthcare access within 5 km (29).

Oman has significantly advanced its primary healthcare system with WHO support, reducing infant mortality from 118 per 1,000 live births in 1970 to 9.7 in 2020. The Oman Medical Specialty Board collaborates with the RCGP, training over 300 family physicians. Sultan Qaboos University's collaboration with the University of Sydney has produced over 50 primary care research papers. Despite these advances, Oman struggles with geographic challenges in remote areas, a high chronic disease burden, and retaining trained family physicians in rural settings (30,31).

In Kuwait, the collaboration with GCC countries through the Gulf Health Council has led to a 95% immunization coverage rate. WHO support has helped strengthen its primary healthcare system, with over 85% of the population having access to primary care. Kuwait University's partnership with the University of London has developed a robust family medicine program, graduating approximately 50 physicians annually with a current yearly intake of around 100 new residents. The current expected increase in the coming years is 70–80 graduates per year.

The Family Medicine Residency Program in Kuwait is administered by the Kuwait Institute for Medical Specializations (KIMS) in collaboration with the Royal College of General Practitioners (RCGP – International Accreditation). Kuwait faces challenges such as an overreliance on an expatriate healthcare workforce, patients preferring specialist care, and the integration of healthcare services (32).

Lebanon, Bahrain, Oman, and Kuwait have made significant progress in family medicine through **creative partnerships and international collaborations**. These efforts have improved access to care, chronic disease management, and health outcomes. However, challenges such as workforce shortages, chronic disease burdens, and integration issues persist.

Regional Collaboration

In the Gulf, countries like Kuwait, Oman, Saudi Arabia, and Qatar have fostered partnerships to share resources, training methods, and expertise, strengthening FM education regionally. Bahrain and Lebanon maintain a long-term collaboration, reinforcing their FM programs.

Jordan and Syria:

Exchange programs allow FM residents in Jordan and Syria to gain experience in countries with established FM systems. The Royal Medical Services in Jordan has previously sent family physicians abroad for advanced training in specialties like geriatrics, facilitated by WONCA conferences and other international forums.

Jordan has become a regional leader in healthcare due to its response to the Syrian refugee crisis, with family medicine at the forefront of its strategy. WHO, NGOs like Médecins Sans Frontières, and international organizations such as the UNHCR have been pivotal, enhancing primary healthcare, especially in refugee-hosting areas. However, the influx of refugees strains the healthcare system, compounded by economic hardships and a shortage of trained family physicians in rural and refugee-hosting areas (33, 34).

Despite ongoing conflict, Syria continues to maintain primary care services through international aid and collaborations. WHO and NGOs like Médecins Sans Frontières and UNICEF have been instrumental, with MSF operating eight primary healthcare centers serving over 500,000 patients yearly. Academic partnerships, continue to produce healthcare professionals, with over 100 family physicians graduating in the past decade. Mobile clinics and outreach programs have reached over a million people in conflict zones. Yet, the war has devastated healthcare infrastructure, economic sanctions restrict medical supplies, and a significant brain drain due to unsafe conditions and poor work environments persists (35-37).

Egypt:

Egypt's FM training has benefited from partnerships with institutions abroad, providing exposure to advanced educational practices. Joint research initiatives and conferences help foster an international dialogue on best practices in FM education, improving training quality and resource sharing (38). The WHO has collaborated with Egypt to bolster public health and family medicine services, to provide equitable access to quality healthcare for all Egyptians (39).

Iraq:

With support from the Arab Board and WHO, Iraq has developed its FM training program, though additional international partnerships are needed to address the country's healthcare professional shortages. Iraq has made significant progress in strengthening family

medicine and primary healthcare despite enduring decades of conflict, economic instability, and infrastructure damage. Key partnerships with the WHO have led to the establishment of over 1,200 primary healthcare centers, significantly impacting millions annually. NGOs like Médecins Sans Frontières and International Medical Corps, alongside academic institutions like the University of Baghdad, have crucially supported family medicine services and training, with over 200 family physicians graduating from Baghdad in the last decade. Collaborations with regional bodies and global entities like the World Bank have further supported these initiatives (40-42).

Despite significant progress through international collaborations and improvements in access to care and chronic disease management, challenges like workforce shortages, chronic disease burdens, and integration issues remain.

Limitations

While the paper provides valuable insights, we confronted several limitations, including unreliable data, especially from conflict-affected areas like Syria, Iraq, and Lebanon. This region's diversity in healthcare systems and economic conditions also challenges the generalizability of findings. There is lack of longitudinal data, and insufficient consideration of cultural factors and patient perspectives.

Finally, ethical concerns in conflict zones and the challenge of implementing policy recommendations due to resource constraints are significant hurdles. Addressing these limitations would necessitate a comprehensive, nuanced approach involving mixed methods and local stakeholder engagement.

Conclusions

Family Medicine (FM) in the EMRO region has demonstrated remarkable resilience and growth despite significant challenges. This progress is largely due to the commitment of policymakers who prioritize health accessibility for all. Many countries within the EMRO region have integrated family practice as a foundational element of their primary healthcare delivery systems. In conflict zones, family physicians often expand their roles to adapt their services to the specific health needs created by war-related injuries, underscoring their versatility and critical importance.

Overcoming these barriers will require detailed and strategic efforts across several fronts:

1. Policy Support: Specific actions such as the implementation of favorable regulatory frameworks can empower family physicians. Additionally, policies that recognize and financially support the broad scope of services provided by family physicians will ensure their roles are both sustainable and impactful.

2. Strategic Resource Allocation: Effective resource allocation is crucial for the enhancement of Family Medicine. This might include investing in medical infrastructure that supports telemedicine technologies, which are particularly beneficial in remote or conflict-impacted regions. Allocating funds for research into local health challenges and the efficacy of family medicine practices in these contexts can also provide data to further optimize healthcare delivery.

3. Education and Training: Investing in education involves both the initial training of family physicians and their ongoing education. Enhancements in training programs to include specialized modules on managing chronic diseases, mental health, and trauma related to conflicts can prepare physicians for the wide range of challenges they face in the region. Further, creating partnerships with international medical schools and institutions can enrich local training programs with global best practices and innovations in family medicine.

Addressing these areas through comprehensive policy support, strategic resource allocation, and targeted educational investments will sustain and significantly enhance the effectiveness of Family Medicine. Such efforts are crucial for improving the overall health of populations across the region and ensuring the long-term viability and influence of Family Medicine.

References

1. Abyad, A., Al-Baho, A.K., Unluoglu, I., Tarawneh, M., and Al Hilfy, T.K.Y. 2007. "Development of Family Medicine in the Middle East." *Family Medicine* 39 (10): 736–41.
2. 1-Rifkin SB. Alma Ata after 40 years: Primary Health Care and Health for All-from Consensus to Complexity. *BMJ Glob Health*. 2018 Dec 20;3(Suppl 3):e001188. <https://pubmed.ncbi.nlm.nih.gov/30622747/>
3. Arya N, Gibson C, Ponka D, Haq C, Hansel S, Dahlman B, et al. Family medicine around the world: Overview by region: The Besrou papers: A series on the state of family medicine in the world. *Can Fam Physician* 2017;63:436 41.
4. Abyad A. Family medicine in the Middle East: Reflections on the experiences of several countries. *J Am Board Fam Pract* 1996;9:289 97.
5. Alnasir F. Family Medicine in the Arab World, Is it a Luxury? *Journal of the Bahrain Medical Society*.2009;21(1); 191-2
6. Hunt V. Bahraini's Family Medicine Residency Program. *Bahrain Medical Bulletin* 1981; 3(2):60-8.
7. Farahat TM. The history of family medicine in Egypt. *Egyptian Family Medicine Journal*. 2017;1(2). doi:10.21608/efmj.2017.120050.
8. Al-Shafae M. Family Medicine Practice in Oman: Present and future. *Sultan Qaboos Univ Med J*. 2009 Aug;9(2):116-8. Epub 2009 Jun 30. PMID: 21509286; PMCID: PMC3074766.
9. Obeidat, N A, M A Habashneh, R A Shihab, and F I Hawari. n.d. "Are Jordanian Primary Healthcare Practitioners Fulfilling Their Potential in Cancer Prevention

and Community Health? Findings from a Cross-Sectional Survey." *BMJ Open Access*. Accessed December 2, 2018. <https://doi.org/10.1136/bmjopen-2016-015269>

10. "Family Medicine Residency Program Trainers' & Residents' Guide to the Curriculum." Accessed October 9, 2018. <http://kims.org.kw/pge/uploads/pdf/pdf-117699728.pdf>.

11. World Health Organization. WHO strengthens the capacity of family physicians in Iraq as an approach towards achieving universal health coverage. Accessed March 30, 2018. <https://reliefweb.int/report/iraq/who-strengthens-capacity-family-physicians-iraq-approach-towards-achieving-universal>

12. Helou, Mariana, and Grace Abi Rizk. 2016. "State of Family Medicine Practice in Lebanon." *Journal of Family Medicine and Primary Care* 5 (1): 51–55. <https://doi.org/10.4103/2249-4863.184623>.

13. Farahat TM. The history of family medicine in Egypt. *Egyptian Family Medicine Journal*. 2017;1(2). doi:10.21608/efmj.2017.120050.

14. Elkhawaga G, Bernard B, El-Gilany AH. House officers' attitude towards family medicine and its choice as a career in Egypt. *Family Practice*. 2015;32(2):198-204. doi:10.1093/fampra/cmv007.

15. Soliman SSA, Hopayian K. Egypt: on the brink of universal family medicine. *Br J Gen Pract*. 2019;69(679):82. doi:10.3399/bjgp19X701069.

16. Khalifa AY, Jabbour JY, Mataria A, Bakr M, Farid M, Mathauer I. Purchasing health services under Egypt's new Universal Health Insurance law: implications for universal health coverage. *Int J Health Plann Manage*. 2022 Mar;37(2):619-31. doi:10.1002/hpm.3287.

17. Al-Shafae M. Family Medicine Practice in Oman: Present and future. *Sultan Qaboos Univ Med J*. 2009 Aug;9(2):116-8. Epub 2009 Jun 30. PMID: 21509286; PMCID: PMC3074766.

18. "Family Medicine Residency Program Trainers' & Residents' Guide to the Curriculum." Accessed October 9, 2018. <http://kims.org.kw/pge/uploads/pdf/pdf-117699728.pdf>.

19. "KuwaitAssociationOfFamilyandGeneralPractitioners." Kuwait Medical Association. Accessed October 9, 2018. <http://kma.org.kw/en-US/AssociationsDetails.aspx?id=12>.

20. Osman, Hibah & Romani, Maya & Hlais, Sani. (2011). Family Medicine in Arab Countries. *Family medicine*. 43. 37-42.

21. Egyptian Health Authority. (n.d). 35.5M family services. Retrieved from https://eha.gov.eg/en/news/35-5m-family-services/?utm_source=chatgpt.com

22. Al-Shafae M. Family Medicine Practice in Oman: Present and future. *Sultan Qaboos Univ Med J*. 2009 Aug;9(2):116-8. Epub 2009 Jun 30. PMID: 21509286; PMCID: PMC3074766.

23. World Health Organization Eastern Mediterranean Regional Office. (n.d.). NCD surveillance at primary care level in Oman: Strengthening healthcare. Retrieved from <https://www.emro.who.int/fr/noncommunicable-diseases/highlights/ncd-surveillance-at-primary-care-level-in-oman-strengthening-healthcare.html>

24. Barghouti FF, Almasri NA, Takruri DH. Exploring agendas of patients attending family medicine clinics in Jordan. A qualitative content analysis study. *Saudi Med J*. 2019Aug;40(8):844-848. doi: 10.15537/smj.2019.8.24328. PMID: 31423524; PMCID: PMC6718862.

25. World Health Organization. (2019). Report on primary healthcare in the Eastern Mediterranean Region: review of progress over the last decade (2008-2018).

26. Salah, K. & Kidd, M. (2019). Family Practice in the Eastern Mediterranean Region: Universal health coverage and quality primary care. Taylor & Francis Group, Florida, USA.

27. World Health Organization. (n.d.). WHO Lebanon Country Cooperation Strategy. Retrieved from <https://www.who.int/countries/lbn/>

28. Médecins Sans Frontières. (n.d.). MSF Lebanon Reports. Retrieved from <https://www.msf.org/lebanon>

29. Ministry of Health, Bahrain. (n.d.). Annual Reports. Retrieved <https://www.moh.gov.bh/home>

30. World Health Organization. (n.d.). WHO Oman Country Cooperation Strategy. Retrieved from <https://www.who.int/countries/omn/>

31. World Health Organization. (n.d.). Oman Ministry of Health Reports. Retrieved <https://moh.gov.om/en/statistics/annual-health-reports/>

32. Ministry of Health, Kuwait. (n.d.). Kuwait Ministry of Health Reports. Retrieved from <https://www.moh.gov.kw/en/Pages/default.aspx>

33. World Health Organization. (n.d.). WHO Jordan Country Cooperation Strategy. Retrieved from <https://www.who.int/countries/jor/>

34. Médecins Sans Frontières. (n.d.). MSF Jordan Reports. Retrieved from <https://www.msf.org/jordan>

35. World Health Organization. (n.d.). WHO Syria Country Cooperation Strategy: WHO Syria. Retrieved from <https://www.who.int/publications/i/item/9789292742003>

36. Médecins Sans Frontières. (n.d.). MSF Syria Reports: MSF Syria. Retrieved from <https://www.msf.org/syria>

37. United Nations Children's Fund. (n.d.). UNICEF Syria Reports. Retrieved from [https://www.google.com/search?client=safari&rls=en&q=37.+United+Nations+Children+%27s+Fund.+\(n.d.\).+UNICEF+Syria+Reports&ie=UTF-8&oe=UTF-8](https://www.google.com/search?client=safari&rls=en&q=37.+United+Nations+Children+%27s+Fund.+(n.d.).+UNICEF+Syria+Reports&ie=UTF-8&oe=UTF-8)

38. Lie DA, Boker JR, Lenahan PM, Dow E, Scherger JE. An international physician education program to support the recent introduction of family medicine in Egypt. *Fam Med*. 2004 Nov-Dec;36(10):739-46. PMID:15531990.

39. World Health Organization. (n.d.). Statement by Egypt at the WHO Executive Board Session. Retrieved from https://apps.who.int/gb/statements/EB156/PDF/Egypt-6.pdf?utm_source=chatgpt.com

40. World Health Organization. (n.d.). WHO Iraq Country Cooperation Strategy. Retrieved from <https://www.emro.who.int/annual-report/2014/index.html>

41. Médecins Sans Frontières. (n.d.). MSF Iraq Reports. Retrieved from <https://www.msf.org/iraq>

42. United Nations Children's Fund. (n.d.). UNICEF Iraq Reports. Retrieved from <https://www.unicef.org/iraq/research-and-reports>

Family Medicine in Bahrain

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Healthy living is defined as a life free from illness characterized by good social, mental, and physical well-being for everyone in every community. To achieve such a goal, health authorities must develop a comprehensive health service that provides sickness prevention, treatment, rehabilitation, and palliative care using a holistic approach. These elements form the main principles of Primary Health Care services (PHC). PHC is a healthcare service that focuses on maintaining and restoring people's general well-being via early identification of health problems and providing treatment at the earliest stages of illness development. Moreover, it emphasizes ongoing medical care that is person-centered and personalized, but within the family context. It is a cost-effective way of providing healthcare services while maintaining intersectoral cooperation, population equity, and community engagement that responds to community-based health needs initiatives.

With the worldwide attention on the importance of PHC especially after the 1978 Alma Ata Conference on PHC in Kazakhstan, 134 nations unanimously agreed on a resolution declaring the need for coordinated efforts to address the social, economic, and political causes of ill health. The concept of "health for all by the year 2000" was eventually agreed upon as the primary principle aiming to develop a healthy society in member countries [1].

PHC services have been available in the Kingdom of Bahrain for over 40 years in many health centers that were distributed across the island [2]. However, such services were provided by doctors who were non-specialized general practitioners. In 1979, the Ministry of Health decided to begin a structured training program for general practitioners and newly graduated doctors called the Family Practice Residency Program (FPRP). The

program aimed at graduating qualified family physicians (FPs) responsible for providing quality PHC services to the population [3]. Bahrain was one of the first countries in the Arab world to start a structured training in Family Medicine

for healthcare professionals, especially physicians to equip them with the necessary skills enabling them to provide efficient primary healthcare services. Bahrain and the Republic of Lebanon launched the first FPRP in 1980. It was a three-year training program which was increased to four years after some time. Subsequently, many more Arab nations took that initiative.

The FPRP program became more academized after the foundation of the first medical school in the Kingdom in 1983, the College of Medicine and Medical Sciences (CMMS) of the Arabian Gulf University. Principles of problem-based learning and community orientation were emphasized in the program. The CMMS also played a major role in promoting a research-oriented training program within the FPRP [4-6].

Bahrain also had a major role in the foundation of the "Arab Board of Health Specializations (ABHS)" in 1978, which was started by a decree from the Council of the Arab Health Ministers of the Arab League. The main goal of ABHS was to work on raising the level of medical science and practice in the Arab world to upgrade the health services provided to the population. In addition, to assist and encourage the Arab nations in creating and establishing FM services and initiating FPRP programs, the Family Medicine Council within the Arab Board was founded in 1985. It assumed responsibility for helping Arab nations establish FM discipline, initiating and accrediting FPRP programs, and was accountable for graduating competent FP specialists by offering end-of-program standardized examinations [7,8].

PHC services supervised by qualified FPs have continuously proved to be able to offer a variety of high-quality, easily accessible healthcare services. Over the years FPs across the country have started gaining a good reputation for providing efficient and high-quality health services that have helped in promoting the standard of health of the population. However, many challenges are still hindering the fully-fledged implementation of PHC and

Family Medicine services. The most important remains the shortage in the number of FPs, and the lack of funding and supplies [9]. The inadequate understanding of the role of family medicine was also the reason why many policymakers remain unconvinced about PHC [7,10]. Moreover, the roles and responsibilities of the FP are still ambiguous, while the identity of the discipline is still unclear. For example, a major part of FPRP training occurs in hospitals (the secondary or tertiary care units) apart from PHC centers [7,11] because it is challenging for the training program to teach and train physicians in a range of subjects and on a variety of clinical cases while maintaining their level of proficiency when it takes place only in the primary healthcare facility [12].

Nevertheless, it is encouraging to know that most of the aforementioned problems started gradually and progressively being resolved because of a greater awareness of PHC's benefits.

In the long term, should the Family Medicine discipline be strengthened it is crucial to understand that each of the stated difficulties must be resolved to overcome the many health problems that the country is suffering from, such as hereditary blood diseases, non-communicable diseases and obesity.

References

- 1- Rifkin SB. Alma Ata after 40 years: Primary Health Care and Health for All-from Consensus to Complexity. *BMJ Glob Health*. 2018 Dec 20;3(Suppl 3):e001188. <https://pubmed.ncbi.nlm.nih.gov/30622747/>
- 2- Alnasir F. Family Medicine in the Arab World, Is it a Luxury? *Journal of the Bahrain Medical Society*. 2009;21(1); 191-2
- 3- Hunt V. Bahraini's Family Medicine Residency Program. *Bahrain Medical Bulletin* 1981; 3(2):60-8
- 4- Alnasir F. The Watched Structured Clinical Examination (WASCE) as a tool of assessment. *Saudi Medical Journal* 2004;25(1):71-4
- 5- Alnasir FA., Robertson AS. Can selection assessments predict students' achievements in the premedical year? A study at the Arabian Gulf University. *Education for Health* 2001;14(2):277-86
- 6- Alnasir F, Jaradat A. Prediction of medical students' performances in the medical school. *Family Medicine & Medical Sciences Research* 2013;2:113
- 7- Cecilia Gutierrez & Peter Scheid. The History of Family Medicine and Its Impact in US Health Care Delivery. <https://www.aafpfoundation.org/content/dam/foundation/documents/who-we-are/cfhm/FMImpactGutierrezScheid.pdf>
- 8- Family Medicine Scientific Council. <https://www.arab-board.org/Specialties/Family-Medicine>
- 9- Qidwai W, Khoja Tawfik A M, Rawaf Salman, Alnaser Faisal A, et al. Primary Health Care in Pandemics: Barriers, Challenges, and Opportunities. *World Family Medicine*. 2021; 19(8): 6-11
- 10- Arya N, Gibson C, Ponka D, Haq C, Hansel S, Dahlman B, Rouleau K. Family medicine around the world: overview by region: The Besroul Papers: a series on the state of family medicine in the world. *Can Fam Physician*. 2017 Jun;63(6):436-441. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5471080/>
- 11- Mohammadibakhsh R, Aryankhesal A, Sohrabi R, Alihosseini S, Behzadifar M. Implementation Challenges of Family Physician Program: A Systematic Review on Global Evidence. *Med J Islam Repub Iran*. 2023 Mar 13; 37:21. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10167646/>
- 12- Stevens RA. (2001). The Americanization of Family Medicine: Contradictions, Challenges, and Change, 1969- 2000. *Family medicine*. 33. 232-43.

Family Medicine in Egypt: A Comprehensive Overview

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Historical background and Challenges Faced

Since the mid-1970s, Family Medicine in Egypt has seen significant development, driven by the recognized need for comprehensive primary healthcare. The 1978 Declaration of Alma-Ata highlighted the importance of primary care, shaping Egyptian health policy and leading to the introduction of the first family medicine curriculum at Suez Canal University in 1979, followed by similar programs at Menoufia and Cairo universities, and subsequently at other institutions. The evolution of family medicine in Egypt began in the 1990s, with a recommendation from the Supreme Council of Universities for each medical school to establish a training program for general practice. By 2004, this initiative had expanded, urging medical faculties to develop family medicine departments and curricula [1].

However, early efforts faced several challenges. A major obstacle was the lack of awareness and understanding of the role of family physicians. The prevailing healthcare system was fragmented, with specialists managing specific health issues, leading to inefficiencies and gaps in patient care. Additionally, there was a shortage of trained family trainers and insufficient training programs, as family medicine was under-represented in medical education [1,2]. The healthcare system's structure, which prioritized specialized and hospital-based care, further complicated the implementation of a primary care model. Limited resources, including trained personnel, facilities, and funding, also constrained the development of family medicine [1-3].

Successful Efforts to Advocate for Family Medicine Education and Training

Despite challenges, substantial progress has been made in advancing family medicine education and training in Egypt. The Egyptian government has been instrumental in establishing family medicine departments in medical schools, notably at institutions like Suez Canal University, Menoufia University, and Cairo University. The creation of residency and master's programs in family medicine represents a key achievement, providing structured education and training for future family physicians [1-3]. Additionally, the Egyptian Ministry of Health and Population established the Egyptian Fellowship Board in 1998 and has been involved in developing national guidelines for primary care [4].

There is also Professional Organizations in the form of The Egyptian Family Medicine Association (EFMA), established in 2006, which has been vital in promoting and advocating for family medicine [5]. Also, the enactment of the Universal Health Insurance Law, which aims to provide comprehensive health coverage, has further increased the demand for family medicine specialists. This legislative shift has sparked heightened interest among medical students and young physicians, leading to a growing number of graduates pursuing careers in family medicine [6].

Impact Assessment of Family Medicine on Populations Served

Family medicine has significantly increased access to primary care services, particularly in rural and underserved areas. This has led to better management of chronic diseases, preventive care, and overall health outcomes. The Egyptian Health Sector Reform program and the initiative "Healthy Egyptian 2010" aim to assure universal access to primary and family health care, providing a basic package of services based on needs. Over 90% of Egypt's population has access to Ministry of Health primary health care units, which are crucial for improving healthcare access in rural areas [7]. Family medicine emphasizes preventive care and early intervention, contributing to cost savings in the healthcare system. This approach reduces the burden on specialized and hospital-based services. The establishment of family medicine units under the new Universal Health Insurance Law aims to provide comprehensive care, which is expected to lead to significant cost reductions by decreasing reliance on secondary care [6].

Barriers to Family Medicine Training and Evidence-Based Solutions

Despite the progress made, several barriers to family medicine training in Egypt persist. These include a lack of awareness about the role of family medicine among medical students, insufficient faculty training, and limited resources for practical training [1]. The establishment of family medicine as a specialty in Egypt has been met with challenges, including the need for increased awareness and training among medical students and faculty [8-9]. Addressing these challenges requires increased investment in family medicine education from both the government and private sector. Policy changes and advocacy efforts to elevate the status of family physicians can attract more medical graduates to the specialty. Moreover, forming partnerships with international institutions can provide access to additional resources, expertise, and training opportunities [6].

Creative Partnership Approaches to Strengthen Training Across Borders

International collaboration has emerged as a vital strategy for strengthening family medicine training in Egypt. Partnerships with institutions in countries with established family medicine programs can facilitate knowledge exchange and resource sharing. For instance, training programs that involve exchanges between Egyptian medical schools and abroad institutions provide Egyptian students and faculty with exposure to advanced practices and educational methodologies [10].

Furthermore, joint research initiatives and conferences can foster a global dialogue on best practices in family medicine education. These partnerships not only enhance the quality of training but also contribute to the development of a robust family medicine network that can address common challenges faced by healthcare systems worldwide [11,12].

References

1. Farahat TM. The history of family medicine in Egypt. *Egyptian Family Medicine Journal*. 2017;1(2). doi:10.21608/efmj.2017.120050.
2. Ahmed M, Mostafa M, El-Sayed S, Mohamed R. House officers' choice of family medicine specialty amid the implementation of the new Universal Health Insurance Law. *J Prim Care Community Health*. 2021;12:21501327211018940. doi:10.1177/21501327211018940.
3. Elkhawaga G, Bernard B, El-Gilany AH. House officers' attitude towards family medicine and its choice as a career in Egypt. *Family Practice*. 2015;32(2):198-204. doi:10.1093/fampra/cmv007.
4. Soliman SSA, Hopayian K. Egypt: on the brink of universal family medicine. *Br J Gen Pract*. 2019;69(679):82. doi:10.3399/bjgp19X701069.
5. WONCA East Mediterranean Region. Available from: <https://www.globalfamilydoctor.com/AboutWonca/Regions/EastMediterranean2.aspx>. Accessed August 20, 2024.
6. Khalifa AY, Jabbour JY, Mataria A, Bakr M, Farid M, Mathauer I. Purchasing health services under Egypt's new Universal Health Insurance law: implications for universal health coverage. *Int J Health Plann Manage*. 2022 Mar;37(2):619-31. doi:10.1002/hpm.3287.
7. Galal SB, Al-Gamal N. Health problems and health care provider choices: a comparative study of urban and rural households in Egypt. *J Epidemiol Glob Health*. 2014;4(2):141-9. doi:10.1016/j.jegh.2013.12.002.
8. Hegazy N, Elden N, Mowafy M. Family medicine postgraduate clinical training in two universities in Egypt: physicians' perspectives. *Egyptian J Hosp Med*. 2022;86(1):147-55. doi:10.21608/ejhm.2022.210791.
9. Alkot MM, Gouda MA, KhalafAllah MT, Zahran MS, Kallaf MM, Zayed AM. Family medicine in Egypt from medical students' perspective: a nationwide survey. *Teach Learn Med*. 2015;27(3):264-73. doi:10.1080/10401334.2015.1044654.
10. Lie DA, Boker JR, Lenahan PM, Dow E, Scherger JE. An international physician education program to support the recent introduction of family medicine in Egypt. *Fam Med*. 2004 Nov-Dec;36(10):739-46. PMID:15531990.
11. van Weel C, Alnasir F, Farahat T, Usta J, Osman M, Abdulmalik M, Kassai R. Primary healthcare policy implementation in the Eastern Mediterranean region: experiences of six countries. *Eur J Gen Pract*. 2017;24(1):39-44. doi:10.1080/13814788.2017.1397624.
12. Nashat N, Hadjij R, Al Dabbagh AM, Tarawneh MR, Alduwaisan H, Zohra F, Rawaf S. Primary care healthcare policy implementation in the Eastern Mediterranean region: experiences of six countries: Part II. *Eur J Gen Pract*. 2019;26(1):1-6. doi:10.1080/13814788.2019.1640210.

Advancing Family Medicine in Kuwait: A Comprehensive Review

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Historical Background and Challenges

Family medicine in Kuwait has evolved over recent decades from a predominantly hospital-centered system to one increasingly recognizing the importance of primary care. Historically, the Kuwaiti healthcare system was heavily focused on specialized care in hospitals, with limited emphasis on preventive and continuous care provided by primary care centers. The shift towards valuing primary care has been driven by the need for more accessible and preventative health services as the population grows and healthcare demands increase. Challenges faced by primary care centers in Kuwait include a shortage of trained family medicine professionals, lack of unified digital system, and a healthcare infrastructure that was traditionally oriented towards specialized care rather than comprehensive primary care. The system has struggled with integrating family medicine into its core offerings due to these entrenched practices.

Kuwait's Vision 2035 "New Kuwait", launched in 2017, outlines a comprehensive national development plan that prioritizes enhancing the quality, efficiency, and accessibility of healthcare services, expanding national capacity, and addressing the growing burden of non-communicable diseases in a cost-effective manner (Alnashmi et al., 2022). Over recent decades, family medicine in Kuwait has evolved from a predominantly hospital-centered system to one that increasingly recognizes the importance of primary care as a cornerstone of sustainable health development. Historically, the healthcare system was largely focused on specialized hospital-based services, with limited attention given to preventive and continuous care delivered through primary care centers. This gradual shift toward valuing primary care has been driven by the need for more accessible, preventive, and community-based health services amid a growing population and rising healthcare demands. However, challenges persist, including a shortage of trained family medicine professionals, the absence of a unified digital health system, and a legacy infrastructure oriented toward specialized rather than comprehensive primary care. In my view, achieving the ambitions of Vision 2035 will only be possible through

strengthening the primary healthcare system, ensuring it becomes the foundation for accessible, high-quality, and cost-effective healthcare delivery across Kuwait.

Successful Efforts in Family Medicine Education and Training

The Family Medicine Residency Program (FMRP) in Kuwait was established nearly four decades ago by the Kuwait Institute for Medical Specialization (KIMS) in collaboration with the Royal College of General Practitioners (RCGP). Initially designed as a three-year residency program, it was later extended to four years in 2001 to meet evolving educational and clinical training standards. In 2010, the program underwent further development, extending its duration to five years to align with international benchmarks in postgraduate medical education. Notably, the program achieved MRCGP [International] accreditation in 2005, marking a significant milestone in recognizing the program's adherence to global standards of excellence in family medicine training. (Kuwait Family Medicine Residency Program – Since 1983, n.d.)

In recent years, Kuwait has made substantial progress in advancing family medicine education and training, reflecting a strong national commitment to strengthening primary healthcare through the preparation of competent and well-trained physicians. A total of 60 specialized family medicine training centers have been established, providing comprehensive environments for clinical education, mentorship, and professional development. The number of trainers has increased to 85, along with 19 program trainers (P. Trainers), which has contributed to improving the overall quality of supervision and training. Currently, there are 420 residents enrolled in accredited family medicine programs, while the total number of graduates has reached 655, signifying the program's success in expanding Kuwait's family medicine workforce. (Kuwait Family Medicine Residency Program – Since 1983, n.d.)

In alignment with national health priorities, the Ministry of Health (MOH) has issued specific directives to increase the number of trainees in all residency programs, with particular emphasis on family medicine, aiming to enroll

approximately 70 to 100 new physicians each year. The Kuwait Association of Family Medicine continues to play a vital role in promoting the integration of family medicine into medical education, strengthening residency programs, and fostering research and continuous professional development. These efforts collectively demonstrate Kuwait's strategic vision to enhance the quality, sustainability, and accessibility of primary healthcare services.

Impact Assessment of Family Medicine

The integration of family medicine has had a noticeable impact on the Kuwaiti population. The Ideal Family Medicine Clinic (IFMC) project was implemented between 2016 and 2018 at Al-Yarmouk Health Center as part of my Master's degree in Leadership from the Institute of Leadership at the Royal College of Surgeons. The initiative aimed to transform the conventional walk-in primary care system into an appointment-based model, enhancing efficiency and quality of care. The project achieved remarkable outcomes, including a reduction in average waiting time from 19.03 to 9.8 minutes, an increase in consultation time from 3.35 to 14.27 minutes, and an improvement in electronic medical record completion rates from 9.6% to 76.7%. These operational improvements resulted in high satisfaction levels among both patients (95%) and healthcare staff (95.24%), confirming that sustainable quality improvement in primary care requires effective leadership, structured processes, and active team engagement.

Following the successful implementation at Al-Yarmouk Health Center, the IFMC model has continued to operate under the same system and has been replicated in several other primary healthcare centers across Kuwait. However, the initiative has not yet been fully scaled to all centers nationwide. The project's findings and outcomes were presented to the Ministers of Health and senior primary healthcare leaders for further evaluation and consideration as a potential framework for national primary care reform. The sustained success of the IFMC underscores its potential as a scalable, evidence-based model for improving patient-centered care and operational efficiency in Kuwait's healthcare system.

Barriers to Family Medicine Training and Evidence-Based Solutions

Despite the significant progress achieved in recent years, several barriers continue to impede the growth and advancement of family medicine training in Kuwait. One of the major challenges is the absence of fellowship programs in the country and the limited culture of encouragement for pursuing fellowships abroad, coupled with the lack of linkage between career promotion and the attainment of advanced qualifications. Moreover, there is a limited emphasis on scientific research, which is neither integrated into the promotion system nor established as a mandatory requirement for board certification. Additionally, graduates of the parallel diploma program, who represent the majority of primary healthcare providers in Kuwait, do not receive

recognition or incentives comparable to other medical professionals, which may affect motivation and career satisfaction. Compounding these challenges, continuity of care remains weak, as patients rarely maintain long-term relationships with a single family physician, reflecting a public perception that primary care providers have limited expertise—particularly in managing chronic conditions such as diabetes and cardiovascular diseases (Mossialos et al., 2018).

Another significant challenge facing the advancement of family medicine education in Kuwait is the absence of a dedicated Department of Primary Care or Family Medicine at Kuwait University. Currently, primary care training and teaching fall under the umbrella of another academic department, which limits the visibility, autonomy, and strategic development of the discipline within the undergraduate medical curriculum. This structural gap has been recognized as a major obstacle to strengthening academic leadership, research capacity, and curriculum integration in primary care. Efforts are currently underway in collaboration with key stakeholders and academic leaders to establish an independent department for primary healthcare and family medicine, which would serve as a foundational step toward aligning medical education with the evolving needs of Kuwait's healthcare system.

Another critical barrier lies in the financial disparities between family physicians and hospital-based specialists. The lower salary structure and limited allowances for family doctors may discourage new graduates from entering family medicine residency programs. Furthermore, there is a lack of technology integration in training and education, particularly in the use of digital platforms for remote learning, virtual clinical supervision, and e-training modules. Addressing these challenges requires policy reform, structured incentives, and the adoption of innovative educational technologies to enhance accessibility, motivation, and professional development in family medicine. Implementing these evidence-based strategies would not only strengthen training capacity but also promote the long-term sustainability and appeal of family medicine as a vital discipline within Kuwait's healthcare system.

Creative Partnership approaches

Strengthening family medicine training in Kuwait can be significantly enhanced through innovative and collaborative international partnerships. Establishing formal cooperation with family medicine board and fellowship programs in other Gulf Cooperation Council (GCC) countries or other Arab countries, as well as exploring partnerships with recognized international institutions such as the American, Canadian, and Australian family medicine boards, would provide valuable opportunities for knowledge exchange, curriculum development, and faculty capacity building. Such collaborations could also facilitate joint training initiatives, shared accreditation standards, and exposure to global best practices in primary healthcare delivery and education.

In addition to international partnerships, engaging with non-governmental and non profit organizations—including the Kuwait Medical Association, the Kuwait Association of Family Medicine, the Gulf association of Family Medicine, and the World Organization of Family Doctors (WONCA)—can further strengthen national training frameworks. The experience of the Gulf association of Family Medicine serves as an exemplary model, demonstrating how regional collaboration through knowledge exchange, scientific conferences, research support, and policy harmonization can drive meaningful progress. Moreover, integrating representatives from those non profit associations into scientific councils and board committees could enhance stakeholder engagement, ensure alignment with community needs, and foster a more holistic and sustainable approach to developing family medicine training programs in Kuwait.

References

- Alnashmi, M., Salman, A., Alhumaidi, H., Yunis, M., & Al-Enezi, N. (2022). Exploring the Health Information Management System of Kuwait: Lessons and Opportunities. *Applied System Innovation* 2022, Vol. 5, Page 25, 5(1), 25. <https://doi.org/10.3390/ASI5010025>
- Kuwait Family Medicine Residency Program – Since 1983. (n.d.). Retrieved November 13, 2025, from <https://kfmrp.com/>
- Mossialos, E., Cheatley, J., Reka, H., Alsabab, A., & Patel, N. (2018). Kuwait: health system review.

Family Medicine in Oman

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Family Medicine in Oman

The effectiveness of any healthcare system is deeply rooted in the strength of its primary health care (PHC) system. PHC serves as the first point of contact for patients, offering a comprehensive range of services that include preventive care, treatment for common conditions, and coordination with specialized services when needed. The core attributes of PHC -community proximity, accessibility, comprehensiveness, and continuity of care (1) are crucial for efficiently meeting diverse healthcare needs.

Family Medicine has emerged as a cornerstone of PHC, with family physicians playing a pivotal role in delivering these essential services. Numerous studies have demonstrated the advantages of a robust PHC system; countries with strong PHC infrastructures typically enjoy healthier populations, lower mortality rates, and reduced healthcare costs (2-6). For instance, an increase in the number of primary care physicians has been linked to lower overall mortality and fewer deaths from major diseases such as heart disease and cancer (2-6).

In Oman, a comprehensive network of PHC centers has been established nationwide, initially focusing on urgent health concerns like infectious diseases, childhood immunization, and maternal care. While most centers were designed as outpatient facilities, some in remote areas were equipped to function as small hospitals, with a few beds and facilities for labour and delivery. By 2016, the total number of PHC centers had grown to 206, and the number of general practitioners per 10,000 population had surged from 0.2 in 1970 to 10.8 in 2016 (7).

To underscore Oman's commitment to PHC, the Department of Family Medicine and Community Health (later renamed Family Medicine and Public Health) was established in 1987 as one of the first five clinical departments at Sultan Qaboos University's College of Medicine and Health Sciences (8). This department has played a significant role in the education and training of

medical students and laid the foundation for the Family Medicine residency program. The first cohort of locally trained family physicians graduated in 1998, and by 2001, the program had earned recognition from the Royal College of General Practitioners (UK), making Oman the first country to offer the MRCGP (INT) Examination (8).

Oman gained international recognition for its exceptional achievements in healthcare. In the World Health Report titled "Health Systems: Improving Performance," released in 2000, the World Health Organization (WHO) ranked Oman's healthcare system eighth out of 191 member countries (9). This ranking was based on various criteria, including overall health system performance, responsiveness, and the equitable distribution of health across the population. Additionally, UNICEF commended Oman for its outstanding success in childhood immunization, particularly noting the high coverage rates and the effectiveness of its national immunization program (10).

Despite these successes, challenges remain, such as the need for increased resources, clearer definitions of catchment areas for PHC centers, and better integration of technology to enhance care coordination and patient management. To further strengthen PHC in Oman, it is essential to increase the number of qualified family physicians, broaden the scope of services offered, and incorporate advanced digital tools. Additionally, addressing the rising prevalence of non-communicable diseases (NCDs) through effective screening and prevention programs is crucial. Promoting a team-based approach and improving the training and retention of family physicians will also lead to better patient outcomes.

In summary, PHC is the cornerstone of Oman's healthcare system. By addressing the current challenges and reinforcing its foundations, Oman can ensure improved care quality and better health outcomes for its population.

References

1. Jimenez G, Matchar D, Koh GCH, et al. Revisiting the four core functions (4Cs) of primary care: operational definitions and complexities. *Prim Health Care Res Dev*. 2021;22:e68. doi:10.1017/S1463423621000669.
2. Starfield B, Shi L, Macinko J. Contribution of primary care to health systems and health. *Milbank Q*. 2005;83(3):457-502. doi:10.1111/j.1468-0009.2005.00409.x.
3. Franks P, Fiscella K. Primary care physicians and specialists as personal physicians. Health care expenditures and mortality experience. *J Fam Pract*. 1998;47(2):105-109.
4. Shi L, Macinko J, Starfield B, Wulu J, Regan J, Politzer R. The relationship between primary care, income inequality, and mortality in US States, 1980-1995. *J Am Board Fam Pract*. 2003;16(5):412-422. doi:10.3122/jabfm.16.5.412.
5. Gulliford MC. Availability of primary care doctors and population health in England: is there an association?. *J Public Health Med*. 2002;24(4):252-254. doi:10.1093/pubmed/24.4.252.
6. Ferrante JM, Gonzalez EC, Pal N, Roetzheim RG. Effects of physician supply on early detection of breast cancer. *J Am Board Fam Pract*. 2000;13(6):408-414. doi:10.3122/15572625-13-6-408.
7. Al-Mahrezi, A., & Al-Kiyumi, M. (2019). Primary Health Care in Oman: Shaping the Future. *Oman medical journal*, 34(6), 479–481. <https://doi.org/10.5001/omj.2019.89>.
8. Al-Shafae M. (2009). Family Medicine Practice in Oman: Present and future. *Sultan Qaboos University medical journal*, 9(2), 116–118.
9. The World Health Report 2000: Health Systems – Improving Performance. World Health Organization (2000). Geneva: WHO.
10. United Nations Children's Fund (UNICEF). Situational analysis of children and women in the Sultanate of Oman. Muscat: UNICEF Oman Country Office; 2017. <https://www.unicef.org/oman/media/296/file/Situational%20Analysis%20of%20Children%20and%20Women%20in%20the%20Sultanate%20of%20Oman%202017.pdf>. Accessed November 11, 2025.

Family Medicine in Syria: Entry Points and Priorities for Support and Way Forward

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In Syria, the Family Medicine program started in 1992. The specialty of family medicine was established in the mid-1990s in partnership with the Ministry of Health and the World Health Organization (WHO). Residents receive integrated training in six medical areas: pediatrics, obstetrics and gynecology, internal medicine, psychiatry and neurology, surgery, and community medicine. The FM doctor trained for three years, spending 29 months in hospitals and 7 months in Primary Health Care Centers. Starting in 1996, FM doctors must complete a four-year training in Ministry of Health hospitals and centers to obtain a specialization certificate in Family Medicine. The program admitted 40-50 doctors annually and produced 400 family doctors by 2008, with 60% practicing abroad. The Master's Degree in Family Medicine was added to the University of Damascus in 1998, offering a 3-year training program in educational university hospitals. In 2001, the Higher Education Council mandated that master's programs at Syrian universities last 4 years. However, since the opening of the Master's Degree in Family Medicine until 2023, there have been only around 50 graduates. The Scientific Council of Family Medicine was formed in 2004, and both certificates are now awarded by the Syrian Board. A four-year Ph.D. The Family Medicine program opened in 2017 with only two Ph.D. students(1). Family medicine clinics have been established in medical centers across the country. This project has been successfully implemented in areas such as Damascus, Hama, Latakia, Daraa and As-Suwayda. The Family Medicine program at Damascus University consists of nine accredited health training centers. These centers train students and residents in specialized Family Medicine. A committee is responsible for overseeing curriculum standardization, training, and center equipment. Two family medicine training centers were accredited in Aleppo in 2007 for Family Physicians at the eastern and northern regions. These centers offer comprehensive care, diagnose and manage around 80% of common diseases, and provide individual and family-centered healthcare as the first point of contact with the family doctor. Families are registered in the file system and individuals have medical

records. Referrals for specialists are made by the family doctor and recorded. Most graduates worked in less than 5% of primary care centers, but the number of residents decreased in the eastern governorates. In 2007, there were 178 residents. By 2009, this number decreased to 99 residents. Due to the crisis in Syria and limited access to certain areas, the family medicine project has been negatively affected. Graduates are currently working in medical centers or have traveled to Gulf countries(1).

The Syrian Association of Family Medicine, established in 2007, is connected to the Syrian Medical Syndicate and operates throughout all Syrian governorates, with its headquarters in Damascus. The association collaborates with the Ministry of Health's Department of Rehabilitation and Training, as well as the Syrian Medical Specialties Commission, to ensure that doctors earn educational points for participating in scientific events and receive certification(1).

The number of family doctors currently affiliated with the Association is about 160 doctors from different governorates: 60 doctors in the southern region; 33 doctors in the central region (Homs - Hama); 70 doctors in the coast (Latakia and Tartous); 25 doctors in Aleppo. It was assessed that Syria needs 7,000 family doctors, with one family doctor for every 1,500 - 2,500 members to activate the program(1).

Analysis of the current situation of family medicine in Syria (2)

The structure of the health system in Syria is not consistent with the requirements of family practice. There is a lack of Technical Skills to apply family practices, and ignorance of the benefits of family medicine for doctors, citizens and those who will benefit from this specialty; also there is the weak financial income of family medicine compared to some other specialties.

Main Challenges and Gaps in Family Medicine Practice in Syria (2)

There is a **lack of a supportive political decision**, as the specialty of family medicine was adopted as a new specialty, but the interest and desire of decision-makers clearly diminished, as well as instability imposed new priorities on the ground; also the **economic negligence** of family doctors by the **Ministry of Health** and the failure to make a decision found them not working with a full quorum. **Misunderstanding** with the failure to define the importance of specialization. There were problems with how to deal with family medicine residents, such as a **lack of a clear reference or curriculum** for study. Failure to adopt the **subspecialty of family medicine** (geriatrics, nutrition, sports medicine). **Lack of sufficient motivation** for experienced skilled family doctors and the need to work in private clinics and health care centers. **Lack of public or private initiatives** to encourage family doctors and empower family medicine, and to prioritize recruitment of family doctors in health insurance companies.

Therefore, family doctors prefer to work abroad to achieve satisfaction at all levels, and the conditions of war led to the emigration of many doctors, including family doctors.

There are few studies on the specialty of family medicine in Syria due to the limited adoption of the family medicine program by decision makers; **some studies have been conducted by the Center for Strategic Health Studies** in Damascus, such as the *survey of beneficiaries' satisfaction with the centers that provide family medicine services*. There was higher satisfaction in those centers compared to lower satisfaction in centers that do not provide family medicine program services.

Also, there is a **cross-sectional study** conducted in the **Department of Family and Community Medicine at the Faculty of Medicine at Damascus University** on a selective sample of 102 patients visiting family medicine clinics in 2009 covering aspects of accessibility and nursing care, communication with the doctor, empathy, respect for patient privacy, doctor's technical skills, information provision, family inclusion and overall satisfaction. **A Survey was carried out by the Aga Khan Foundation in cooperation with the Syrian Medical Syndicate and Syrian Family Medicine Association in July 2022⁽⁹⁾**. Out of 160 registered doctors in SAFM, 131 family doctors participated in the study. Most were female (77%) and aged 46-60 years old, from Damascus and Latakia. The majority received training in Damascus and specialized in the Ministry of Health for 4 years. Doctors considered the curriculum as a significant strength for specialization, while learning methods and teaching staff were identified as the weakest areas. Most participants chose to study this discipline because of its comprehensiveness(3).

Regarding the adequacy and quality of the training modules for the family medicine curriculum, 75% of participants found it acceptable to good in women's health and sexual health

promotion. 65% found common internal diseases, mental health, ophthalmic and neurological diseases, emergency care, geriatric care, and surgical care acceptable to good. 50% found training in palliative care, nutrition, risk management, critical care, adolescent health, men's health, and health systems management acceptable to poor. Over 70% lacked training in sonography, laboratory, sports medicine, disaster medicine, and physician welfare. 80% enjoyed practicing the specialty and most agreed on the absence of supportive health policies or family medicine protocols(3).

The capacities of family medicine(2)

There is a lack of scientific research methods and research capabilities among doctors, as a result of not receiving adequate training in this field during the residency period. Family medicine is sometimes considered a less favored and respected medicine by the other medical community. Doctors in this specialty may face challenges in building their professional identity and dealing with professional challenges. Family medicine faces tension and conflict with other specialties, as some think that family medicine will take their place. Physicians in this specialty need to make additional efforts to advocate and promote their role and importance in the healthcare system. Economic and physical conditions can be challenging for physicians in family medicine in Syria. They may have difficulty providing resources for professional development and continuing training. Some family medicine doctors suffer from fear of participating in scientific seminars as lecturers, due to the feeling of lack of necessary knowledge and skills. They may have to work on developing their scientific and professional confidence to participate confidently in these events. Some doctors in family medicine may lack adequate training in the field of scientific research during the period of specialized training. They may need to support and enhance their skills in conducting research and publishing scientific findings. Some family medicine physicians may have poor English language skills and their ability to access scholarly resources and updated information. It may require them to enhance their capabilities in this regard. In addition, they face financial constraints in subscribing to paid sites that provide reliable medical information.

References

1. Presentation by Dr. Samar Al Moazen, Chairperson of Syrian Family Medicine Association SFMA during AKHS meeting in Beirut, July 2023.)
2. Results of KILs with Family Medicine Syrian Scientific Board member and postgraduate studies' teaching supervisor, conducted by AKHS TA'MIN project research team, July 2023).
3. Aboumayaleh, M, AlMoazen,S ,AGA KHAN HEALTH SERVICES- Syria, Samar, Syrian Association of Family Medicine SAFM, Damascus, Syria, Need Assessment for Family Physicians in Syria, 2022.

Family medicine and primary health care in Iraq

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Primary Health Care (PHC) in Iraq is based on the principle of "Health for All," which emphasizes equitable access to essential health services at a cost people can afford. Iraq formally adopted PHC as a national strategy following the Alma-Ata Declaration in 1978, after which a wide network of health institutions was established to meet population needs (1).

In earlier decades, PHC services were mainly delivered by general practitioners with basic medical qualifications (1). PHC centers provide maternal and child health care, school health services, adult health care, immunization, infectious disease control, management of common health problems, public health education, screening for specific diseases, and selected clinical interventions (1,2).

Family medicine, as a medical specialty, delivers continuous, comprehensive health care to all individuals regardless of age or sex, with particular emphasis on the family unit. In Iraq, family medicine operates as a core component of primary care (3). The specialty was officially introduced in Iraq in 1995 through the Iraqi Board of Medical Specializations, followed by the establishment of the Arab Board specialization in 2008 (3).

Most postgraduate family physicians now serve in Primary Health Care Centers (PHCCs), while others contribute to administrative and academic sectors. With the introduction of family medicine practice in many PHCCs, improvements such as computerized medical records and referral systems were implemented, although full system requirements for efficient family medicine practice have not yet been achieved (4).

The Aged-Friendly PHC Project was introduced to improve services for older adults. Health workers in these centers receive training to conduct home visits for elderly care and follow-up (5). During the COVID-19 pandemic, several areas in Baghdad adopted home-based follow-up and telemedicine delivered by family physicians, which significantly increased public awareness of the importance of family medicine and its role in supporting individuals and families throughout diverse health challenges (6).

Family medicine also exists academically within undergraduate curricula, typically integrated into community and family medicine departments, though independent family medicine departments have not yet been established (7). Subspecialty components—including mental health, geriatrics, cancer screening, nutrition and aviation medicine—are validated training areas for family doctors. After completing two years of structured training, graduates serve in hospitals or family medicine centers (3).

The Iraqi Family Physicians Society, founded in 2012, collaborates with other medical organizations nationally and internationally through conferences, workshops, and scientific meetings (8). In 2018, Iraq hosted the WONCA East Mediterranean Regional Conference in Baghdad, with participation from Iraqi and international family physicians (8).

In 2024, the Professional Diploma of Family Medicine was launched by the Arab Board of Health Specializations in collaboration with WHO and WONCA EMR to enhance the clinical skills and competencies of practicing physicians (9). The Society of Iraqi Family Physicians currently has 2,300 registered members, including consultants, specialists, and general practitioners. According to the World Health Organization, Iraq requires 10,000 family physicians in the next ten years to meet public health and health insurance demands (9).

Nationally, Iraq has approximately 3,600 PHC centers, corresponding to 0.7 centers per 10,000 population, which remains below the international standard of 2–3 centers per 10,000 population (1). Although family medicine practice does not yet fully cover all aspects of primary care—such as continuity, comprehensiveness, person-centeredness, high quality, and cost-effectiveness—it is still considered essential to any modernization of the Iraqi health system (10).

A major challenge for the Ministry of Health is the full integration of family medicine into all PHC centers, supported by a structured referral system linking primary, secondary, and tertiary care levels and reinforcing the role of the family physician as a gatekeeper (4,10). Additional challenges include increasing the number of family medicine specialists by expanding postgraduate training

capacity and offering incentives to encourage physicians to enter the field (9). Establishing independent family medicine departments in medical colleges and updating curricula are essential steps toward producing graduates with a strong orientation toward family medicine practice (7).

Public education about family medicine and the role of family physicians is also recommended through mass media campaigns and PHC-based health promotion activities (10).

References

1. University of Anbar. Primary Health Care in Iraq. Available at: <https://www.uoanbar.edu.iq>1.
2. World Health Organization. Basic Health Services Package for Iraq.
3. Iraqi Board for Medical Specializations. History of Family Medicine Training in Iraq.
4. BMC International Health & Human Rights. Primary care policy implementation challenges in Iraq.
5. Ministry of Health Iraq. Age-Friendly Primary Health Care Initiative.
6. COVID-19 Field Reports, Baghdad PHC Directorate, 2020–2021.
7. Medical Colleges of Iraq. Undergraduate Curriculum for Community and Family Medicine.
8. Iraqi Family Physicians Society. Annual Reports 2012–2024.
9. Arab Board of Health Specializations. Professional Diploma of Family Medicine Program 2024.
10. WHO & Iraqi Ministry of Health. Health System Modernization and Family Medicine Strategy Reports.

Family Medicine in Jordan

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Background

Jordan is an upper-middle-income country located in the Middle East with an estimated population of 11.4 million in 2023, which is projected to increase to about 12.9 million by mid-2030. Jordan's healthcare system is made up of a combination of the public, private, international, and charity sectors, as well as councils and institutions. The Jordan Ministry of Health (MoH) provides health services to 60% of Jordanians. Primary healthcare (PHC) is provided through a network of facilities managed by the MoH, including comprehensive health centers providing the broadest range of services and primary health centers and village health centers providing limited services.

Jordan Medical Council (JMC), which is the umbrella that covers all medical specialties, created the postgraduate curriculum for family medicine residency program in the early 1980s. In the year 1994 the family medicine program was established as one of the activities of the department of community medicine at Jordan university. Currently, four family medicine residency programs exist. Family physicians are trained to provide continuous, comprehensive care for individuals and families.

Family doctors often work in polyclinics alongside nurses, midwives, and general practitioners. Ultimately, their role is much like that of a general practitioner. They manage patients' care, promote healthy living and perform routine assessments to ensure early detection and management of diseases. They provide continuous, comprehensive care for individuals and families; patients benefit from consistent and coordinated care, ensuring that their healthcare needs are addressed comprehensively over time. Prevention is a cornerstone of family medicine, and they are dedicated to promoting health and wellness through preventive screenings, vaccinations, and lifestyle counseling.

The factors advocating for family medicine education and training in Jordan:

In Jordan the family medicine residents are well trained through structured curricula; the JMC approved the training programs in different entities such as MOH, RMS and universities. The residents spend 4 years in this program, three years in hospitals and one year in a Primary Health Care setting. They should pass 2 part board exams, the first one at the end of year 2 and the second part at the end of fourth year of residency program. MOH policy to accommodate more family medicine residents in its program is good approach, however there are still many challenges such as insufficient number of training centers and insufficient number of trainers. The graduates from all programs are not sufficient to cover the needs. The Family doctor to patient's ratio is 1 physician:12,138 patients. To address the gap the WHO in close collaboration with the MOH are giving practicing general physicians a convenient route to become family practitioners through providing Professional Diploma in Family Medicine. Diploma takes two years (24 months). It is divided into eight terms with two six-week blocks per term. It is designed to give participants the knowledge, skills and attitudes they need to provide comprehensive, continuous and appropriate health care to individuals and families. The content has been developed by family physicians affiliated with renowned academic institutions in the Region, and the curriculum is based on the competencies of Family Medicine/General Practitioner doctor as defined by the World Organization of Family Doctors (WONCA), the Accreditation Council for Graduate Medical Education (ACGME) and the College of Family Physicians of Canada for the specialty of Family Medicine.

Although the number of family medicine training programs is increasing, the number of graduates remains inadequate to meet population needs.

Impact assessment of family medicine on populations served

Overall satisfaction at MOH comprehensive health centers that have been conducted through accreditation process, who depend on the family physicians to provide essential services is very good, however in Jordan there are no accurate statistics to measure the impact of family medicine on the population served. The primary health care services are provided mainly by MOH and the private sector. The catchment areas for PHC centers are not well defined.

Barriers to family medicine training and evidence-based solutions to navigating those barriers

Barriers to FM training; short period of FM training in the undergraduate firstly, most postgraduates prefer other specialties with medical procedures because of their better income as follows:

- ♦ Lack of exposure of the specialty in the undergraduate curriculum for medical students; some medical schools have 2 weeks period of training others have 4 weeks,
- ♦ Universities do not have Departments of Family Medicine; the exception is Jordan University and JUST
- ♦ Insufficient awareness of public on family medicine roles.
- ♦ Insufficient knowledge among decision makers of the importance and cost effectiveness of FM.
- ♦ Insufficient amount of allocated budget for PHC overall, and family medicine training.

In the last few years, successful efforts have been taken to update the FM training curricula to fit the progress of the specialty in the country, as well health decision makers configure the impact of family physicians as an important health provider and a unique gate keeper into the health system through PHC, where the health authority planned to augment the candidate numbers in the FMRP to fulfill the quota of 3 family doctors to 10,000 population. In the MOH the integration of Non-Communicable Diseases, psychiatry and maternity as examples showed the urgent need for family doctor services to tackle most of the above-mentioned diseases.

Creative partnership approaches to strengthen training between education programs located across international borders

Exchange training with other intra or international partnership helps to update and to strengthen family medicine knowledge such as scholarships to western countries. As an example the Royal Medical Services used to send 2-3 family doctors to receive further education either in Europe or USA and Australia, so other medical schools in JU and JUST send abroad family doctors to receive more knowledge and education for more specific branches such as geriatrics, family planning, etc. The World Organization of family doctors (WONCA) is providing opportunities to accredit training programs and exchange experiences through regional and international conferences too.

Genetics and Risk Factors of Dementia

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Abstract

Dementia is one of the most significant public health challenges of the 21st century, affecting older adults disproportionately and imposing profound consequences on individuals, families, healthcare systems, and society. Although increasing age is the strongest risk factor, advancing scientific knowledge has revealed dementia to be a disorder driven by multifactorial and modifiable determinants rather than a simple consequence of aging. A better understanding of these risk pathways enables clinicians to implement prevention-focused, person-centered care and population-level strategies, especially in regions undergoing rapid demographic transition such as the Middle East and North Africa (MENA).

Dementia is not a single disease but a clinical syndrome characterized by progressive decline in cognition, function, and behaviour. Alzheimer's disease (AD) remains the most common etiology, followed by vascular dementia, dementia with Lewy bodies, and frontotemporal dementia. Modern geriatric medicine conceptualizes dementia as a bio-psychosocial condition, integrating molecular pathology, vascular burden, metabolic dysfunction, psychosocial stressors, and environmental influences across the lifespan.

Keywords: dementia, risk factors, genetics

Introduction: The Interplay of Genes and Lifestyle

Dementia, a syndrome characterized by a decline in cognitive function severe enough to interfere with daily life, is not an inevitable consequence of aging. Rather, it is the result of a complex and dynamic interplay between our genetic blueprint and the lives we lead (Livingston et al., 2020). For decades, the quest to understand dementia has traversed two parallel paths: one exploring the intricate code of our DNA, and the other investigating the environmental and lifestyle factors we encounter from birth to old age. Today, these paths have converged, revealing that our risk for developing dementia is not written solely in our genes but is profoundly shaped by a lifetime of choices, experiences, and exposures.

This chapter delves into the multifaceted landscape of genetic and risk factors for dementia. We begin by exploring the fundamental genetic architecture, distinguishing between rare genes that virtually guarantee disease and common gene variants that merely increase susceptibility. We will then clarify the often-misunderstood concepts of familial and sporadic dementia. The chapter's core will focus on the empowering science of modifiable risk factors - the aspects of our physical and mental health that we can influence to build resilience against cognitive decline (Livingston et al., 2020). Finally, we will examine broader environmental and lifestyle influences, synthesizing this knowledge into the unifying concept of cognitive reserve (Stern, 2012). By the end of this chapter, the reader will appreciate that while we cannot change our genes, we have significant agency in modulating our risk for dementia through informed, proactive lifestyle decisions.

This reviews:

- Genetic architecture and heritable risk factors
- Distinction between familial and sporadic dementia
- Vascular, metabolic, and lifestyle-based risk factors
- Environmental and psychosocial determinants
- Biomarkers and the evolving role of precision medicine
- Regional risks and public health implications in the MENA region
- Clinical screening pathways in primary and geriatric care

The objective is to provide geriatric clinicians with a comprehensive and pragmatic framework for identifying risk, counseling patients, and implementing early-intervention and prevention-focused strategies.

Epidemiological Perspective

Worldwide dementia prevalence is rising due to global population aging and increased survival rates into advanced age. According to the WHO, over 55 million people currently live with dementia, with 10 million new cases annually. Prevalence doubles approximately every five years after age 65, with nearly one-third of adults over 85 affected.

Changing Understanding of Dementia Risk

Historically regarded as inevitable with aging, dementia is now recognized as partially preventable. Landmark longitudinal studies and meta-analyses estimate that up to 40% of dementia cases may be delayed or prevented by addressing modifiable risk factors.

Key concepts shaping modern epidemiology include:

- Life-course model of brain health — cognitive reserve shaped early in life
- Vascular-metabolic hypothesis — brain aging mirrors cardiovascular health
- Neuro-inflammation and oxidative stress — amplified by chronic disease
- Social determinants of health — education, occupation, social engagement

With elderly populations expanding rapidly in the Gulf region, Levant, and North Africa, MENA nations face a projected 125% increase in dementia cases by 2050, making early-risk identification and prevention a regional healthcare priority.

The Genetic Blueprint: Predispositions and Deterministic Genes

Genetics provides the foundational code for all biological processes, including those that maintain brain health. In the context of dementia, genetic influences can be broadly categorized into two groups: risk genes and deterministic genes (National Institute on Aging, 2023). Understanding this distinction is crucial for accurate risk assessment, counseling, and research (Table 1).

1. Risk Genes (Genetic Predispositions): These are gene variants that increase an individual's likelihood of developing a disease but do not guarantee it. They are common in the general population. Having one or even two copies of a risk gene elevates risk, but other factors—such as other genes, lifestyle, and environment—play a decisive role in whether the disease manifests. The most prominent example in Alzheimer's disease is the APOE gene.

2. Deterministic Genes (Autosomal Dominant Mutations): These are much rarer, inherited mutations in specific genes that directly cause a disease. If a parent carries a deterministic gene, each child has a 50% chance of inheriting it. Virtually everyone who inherits such a mutation will develop the disease, often at a younger age (early-onset, before 65). These are primarily linked to familial forms of Alzheimer's disease and some forms of Frontotemporal dementia (Bateman et al., 2011).

Table 1. Genetic Classification of Dementia

Category	Description	Examples	Clinical Implication
Risk Genes (Predispositional)	Increase the likelihood of disease but are not causative.	APOE-e4, TREM2, ABCA7	Guide lifestyle interventions and risk counseling.
Deterministic Genes (Causative)	Directly cause disease with autosomal dominant inheritance.	APP, PSEN1, PSEN2, MAPT, GRN, C9orf72	Indicate early-onset familial dementia; require genetic counseling.

The following sections will explore these genetic factors in detail, beginning with the most significant genetic risk factor for late-onset Alzheimer's disease.

3.1 Deep Dive: The APOE-e4 Allele and Alzheimer’s Disease

The **Apolipoprotein E (APOE) gene**, located on chromosome 19, is instrumental in lipid metabolism and neuronal repair (Liu, Kanekiyo, Xu, & Bu, 2013). It comes in three common forms, or alleles: **e2, e3, and e4** (Table 2).

- **APOE-e3:** This is the most common allele and is considered neutral in terms of Alzheimer’s risk.
- **APOE-e2:** This relatively rare allele appears to have a protective effect, reducing the risk of developing Alzheimer’s.
- **APOE-e4:** This allele is the strongest known genetic risk factor for late-onset sporadic Alzheimer’s disease.

How APOE-e4 Influences Risk:

- **Dose-Dependent Effect:** Risk increases with the number of e4 alleles (Liu et al., 2013).
 - **One copy of e4 (approximately 25% of the population):** Risk is increased 2- to 3-fold.
 - **Two copies of e4 (approximately 2-3% of the population):** Risk is increased 8- to 12-fold, and the age of onset is typically younger.

Table 2. APOE Genotype and Relative Alzheimer’s Risk

Genotype	Population Frequency	Relative Risk	Clinical Notes
ε2/ε3	~10%	Protective	May reduce amyloid accumulation.
ε3/ε3	~60%	Baseline	Most common, neutral effect.
ε3/ε4	~25%	2–3× increased risk	Earlier onset possible.
ε4/ε4	~2–3%	8–12× increased risk	Strongest known genetic risk factor.

- **Biological Mechanisms:** The e4 allele is believed to contribute to Alzheimer’s pathology through several mechanisms (Liu et al., 2013):
 - 1. Amyloid-Beta Plaque Accumulation:** APOE protein is involved in clearing amyloid-beta peptides from the brain. The APOE-e4 isoform is less efficient at this clearance, leading to increased plaque deposition.
 - 2. Tau Tangles:** It may also promote the hyperphosphorylation of tau protein, leading to the formation of neurofibrillary tangles.
 - 3. Neuronal Inflammation and Dysfunction:** APOE-e4 is associated with increased neuroinflammation and impaired synaptic repair and lipid transport.

It is critical to emphasize that APOE-e4 is a risk gene, not a deterministic one. Many people with one or even two e4 alleles never develop Alzheimer’s, while many people with the disease have no e4 alleles. This highlights the essential role of non-genetic factors.

3.2 Early-Onset Familial Alzheimer's Disease

A minority of dementia cases follow autosomal dominant inheritance with mutations in:

Table 3. Autosomal dominant inheritance

Gene	Function
APP	Amyloid precursor protein cleavage
PSEN1	γ -secretase component
PSEN2	γ -secretase component

These mutations cause overproduction of amyloid- β 42, resulting in early onset (30–60 years) and rapid progression.

Red flags for genetic forms:

- Onset <65 years
- ≥ 2 affected first-degree relatives
- Rapid decline or atypical features

3.3 Other Neurodegenerative Gene Associations

Table 4. Other gene association

Disorder	Genes	Key Pathology
Frontotemporal dementia	MAPT, GRN, C9orf72	Tau or TDP-43 pathology
Lewy body dementia	GBA, SNCA	α-synuclein deposition
Vascular dementia (CADASIL)	NOTCH3	Small-vessel arteriopathy

Genetic testing is considered in geriatric practice when clinical features strongly suggest hereditary disease. Routine testing of older adults without red-flag features is **not recommended**.

3.4 Beyond APOE: Other Genetic Risk Factors

While APOE-e4 is the most significant player, genome-wide association studies (GWAS) have identified dozens of other genetic loci that contribute to the risk of Alzheimer's disease and other dementias (Kunkle et al., 2019). These genes often have small individual effects but can act in concert to significantly influence overall risk and are involved in various biological pathways.

Key Pathways and Example Genes:

- **Immune Response and Inflammation:** The brain's immune cells, microglia, play a key role in Alzheimer's pathology. Genes like TREM2 (Triggering Receptor Expressed on Myeloid cells 2) are critical for microglial function. Certain variants of TREM2 significantly increase risk, potentially by impairing the brain's ability to clear amyloid plaques and manage inflammation (Ulland & Colonna, 2018).
- **Lipid Metabolism and Endocytosis:** Genes involved in processing fats and cellular membrane trafficking are also implicated. Examples include ABCA7 (which helps transport cholesterol) and PICALM (involved in synaptic vesicle formation and amyloid precursor protein processing). Dysfunction in these processes can disrupt neuronal communication and plaque clearance (Kunkle et al., 2019).
- **Tau Pathology:** While most strong genetic links are with amyloid, some genes are more directly associated with tau pathology, a hallmark of several dementias. The MAPT gene, which codes for the tau protein itself, is a key locus for Frontotemporal dementia (Strang et al., 2019).
- **Vascular Dementia Genetics:** Risk for vascular dementia is heavily influenced by genes that affect cardiovascular health, such as those involved in hypertension (e.g., ACE), cholesterol metabolism, and diabetes. The interplay between these and Alzheimer's genes is a critical area of research (Raz et al., 2016). The identification of these multiple risk genes underscores that Alzheimer's and other dementias are polygenic disorders, resulting from the combined effect of many genetic variants.

3.5 Familial vs. Sporadic Dementia

Dementia can broadly be classified into familial (inherited) and sporadic forms. Understanding this distinction is critical for geriatric clinicians who frequently field questions regarding heritability and screening among older adults.

Sporadic Dementia

Sporadic dementia comprises 90–95% of cases. While genetic predisposition plays a role (e.g., APOE-ε4), sporadic dementia arises from interacting biological and lifestyle factors across the lifespan.

- **Definition:** This is the most common form of dementia, accounting for over 90% of all cases, particularly Late-Onset Alzheimer's Disease (LOAD). "Sporadic" means the disease occurs without a clear, inherited pattern in the family.
- **Genetic Role:** Sporadic dementia is not "non-genetic." It involves a complex combination of genetic risk factors (like APOE-e4 and others) and non-genetic factors (lifestyle, environment, age). An individual may have a higher genetic risk load but still require environmental triggers for the disease to develop.
- **Age of Onset:** Typically later in life (after 65).

Familial Dementia (Familial Aggregation)

Definition: This term refers to dementia that clusters in families. It includes two sub-categories:

1. **Familial with a Strong Genetic Component:** This includes both the rare autosomal dominant forms caused by deterministic genes and families where there is a high load of common risk genes (e.g., multiple members with APOE-e4).
2. **Familial due to Shared Environment/Lifestyle:** Families may share risk not through genes, but through common habits (e.g., diet, smoking), exposures (e.g., to toxins), or socioeconomic factors (e.g., access to education and healthcare) (Livingston et al., 2020).

Familial dementia accounts for 5–10% of all cases and typically involves autosomal dominant inheritance patterns.

These cases often display:

- Earlier onset (usually before age 65)
- Faster progression
- Multiple affected first-degree relatives
- Genetic mutations involving APP, PSEN1, PSEN2, MAPT, GRN, or C9 or f72

Key Takeaway: Having a family history of dementia increases one's risk, but it does not mean the disease is inevitable. Conversely, having no family history does not confer immunity, as sporadic cases are very common.

3.6 Rare Deterministic Genes in Early-Onset Familial Alzheimer's Disease

In less than 1% of all Alzheimer's cases, the disease is caused by a single, inherited mutation in one of three genes (Bateman et al., 2011). These are autosomal dominant mutations, meaning only one copy of the mutated gene, inherited from either parent, is sufficient to cause the disease. This form is known as Autosomal Dominant Alzheimer's Disease (ADAD) or Familial Alzheimer's Disease (FAD).

The Three Primary Genes:

1. Amyloid Precursor Protein (APP) on chromosome 21: The APP protein is cleaved to produce amyloid-beta peptides. Mutations in APP lead to overproduction or altered cleavage of amyloid-beta, directly driving plaque formation. The fact that individuals with Down syndrome (trisomy 21) have an extra copy of the APP gene and universally develop Alzheimer's pathology by middle age strongly supports the central role of APP and amyloid.

2. Presenilin 1 (PSEN1) on chromosome 14: This is the most common cause of ADAD. The PSEN1 protein is a component of the gamma-secretase complex, which is one of the enzymes that cleaves APP. Mutations in PSEN1 alter the gamma-secretase activity, leading to the production of longer, more sticky forms of amyloid-beta that aggregate easily.

3. Presenilin 2 (PSEN2) on chromosome 1: Similar to PSEN1, PSEN2 is part of the gamma-secretase complex. Mutations here are rarer and can sometimes result in a more variable age of onset.

Implications:

- **Age of Onset:** ADAD typically results in early-onset disease, often between a person's 30s and 50s (Bateman et al., 2011).
- **Genetic Testing and Counseling:** Because these are deterministic genes, genetic testing is available. However, it involves profound ethical, psychological, and social considerations and is always preceded and followed by extensive genetic counseling.
- **Research:** The study of these families has been invaluable, leading to the "amyloid cascade hypothesis" and providing cohorts for preventative clinical trials.

4. The Power of Modifiability: Introduction to Risk Factors

While our genetic makeup is fixed at conception, the story of our brain health is far from predetermined. A paradigm shift in dementia research has been the growing evidence that a substantial proportion of cases could be prevented or delayed by addressing modifiable risk factors. The landmark 2020 report from The Lancet Commission identified 12 key modifiable risk factors that, if addressed, could prevent or delay up to 40% of dementia cases worldwide (Livingston et al., 2020) (Table 5).

Table 5. Key Modifiable Risk Factors for Dementia (Lancet Commission, 2020)

Life Stage	Modifiable Risk Factor	Mechanism	Preventive Strategy
Early Life (0–20 yrs)	Low education	Reduced cognitive reserve	Promote access to quality education.
Midlife (40–65 yrs)	Hypertension, obesity, hearing loss, TBI, alcohol misuse, smoking, depression	Vascular and metabolic damage; neuroinflammation	Manage blood pressure, maintain healthy weight, use hearing aids, avoid smoking/alcohol excess, address depression.
Later Life (65+ yrs)	Social isolation, inactivity, diabetes, smoking, air pollution	Reduced cognitive stimulation; vascular damage	Maintain social engagement, physical activity, and manage diabetes.

These factors act across the entire lifespan, from childhood to late life, highlighting that it is never too early or too late to take action.

A Lifespan Approach to Risk:

- **Early Life (Childhood and Adolescence):** Factors like education level set the stage for cognitive reserve.
- **Midlife (Ages 45-65):** This is a critical window for addressing cardiovascular and metabolic health.
- **Later Life (Ages 65+):** Continuing healthy habits and managing sensory and social health becomes paramount.

The following sections will explore the most significant modifiable risk factors, beginning with the cornerstone of physical health: cardiovascular function.

4.1 Modifiable Risk Factor 1: Cardiovascular Health

The link between a healthy heart and a healthy brain is unequivocal (Gorelick et al., 2017). The brain is one of the most metabolically active organs, consuming 20% of the body's oxygen and nutrients supplied by blood. Conditions that damage the heart and blood vessels invariably impair this critical supply chain (Table 6).

Key Cardiovascular Risk Factors:

- **Hypertension (High Blood Pressure):** Chronic high pressure damages the delicate small blood vessels in the brain, leading to tiny strokes (microinfarcts), white matter lesions, and blood-brain barrier disruption. Midlife hypertension is one of the strongest risk factors for both vascular dementia and Alzheimer's disease (Livingston et al., 2020).
- **Hypercholesterolemia (High Cholesterol):** High levels of LDL ("bad") cholesterol can contribute to atherosclerosis (hardening of the arteries) in both heart and brain vessels, increasing the risk of stroke. Cholesterol also interacts with the APOE protein and is involved in amyloid pathology.
- **Diabetes and Insulin Resistance:** Type 2 diabetes doubles the risk of dementia (Chatterjee et al., 2016). High blood sugar causes inflammation and oxidative stress, damages blood vessels, and may lead to "Type 3 Diabetes," a proposed term for insulin resistance in the brain that impairs neuronal function and promotes amyloid accumulation.
- **Atrial Fibrillation and Heart Disease:** Irregular heart rhythms and other cardiac conditions can lead to the formation of blood clots that can cause strokes, directly causing vascular cognitive impairment.

Mechanisms: The pathways linking cardiovascular risk to dementia include (Gorelick et al., 2017):

1. **Reduced Cerebral Blood Flow:** Limiting delivery of oxygen and glucose.
2. **Cerebrovascular Disease:** Strokes and micro-injuries.
3. **Neuroinflammation:** Systemic inflammation from vascular disease affects the brain.
4. **Amyloid Dysregulation:** Vascular dysfunction impairs the clearance of amyloid-beta.

Managing these conditions through medication, diet, and exercise is one of the most effective strategies for preserving cognitive health.

Table 6. Cardiovascular Risk Factors and Mechanisms

Condition	Mechanism of Brain Injury	Dementia Type Associated	Key Management Approach
Hypertension	Microvascular damage, white matter lesions	Vascular & Alzheimer's	Blood pressure control (ACE inhibitors, ARBs).
Hyperlipidemia	Atherosclerosis, impaired amyloid clearance	Vascular	Statin therapy, dietary control.
Diabetes Mellitus	Insulin resistance, oxidative stress	Alzheimer's & mixed	Glycemic control, weight management.
Atrial Fibrillation	Embolic stroke, hypoperfusion	Vascular	Anticoagulation, rhythm management.

4.2 Modifiable Risk Factor 2: Physical Activity and Exercise

Regular physical activity is a powerful, evidence-based pillar of dementia prevention (Erickson et al., 2019). Its benefits are mediated through multiple direct and indirect pathways in the brain (Table 7).

Direct Neurobiological Benefits:

- **Increased Cerebral Blood Flow:** Exercise boosts blood flow to the brain, delivering oxygen and nutrients while removing metabolic waste.
- **Neurogenesis and Brain-Derived Neurotrophic Factor (BDNF):** Aerobic exercise, in particular, stimulates the production of BDNF, a protein that supports the survival of existing neurons and encourages the growth and differentiation of new neurons and synapses, primarily in the hippocampus—a key memory center (Erickson et al., 2019).
- **Reduction of Pathologies:** In animal models, exercise has been shown to reduce both amyloid-beta and tau pathology.
- **Reduced Inflammation:** Exercise has a systemic anti-inflammatory effect.

Indirect Benefits:

- **Improved Cardiovascular Health:** It helps control weight, blood pressure, and cholesterol.
- **Improved Sleep:** Regular activity promotes healthier sleep patterns, which are critical for amyloid clearance.
- **Reduced Stress and Depression:** Exercise is a potent modulator of stress hormones and mood.

Exercise Recommendations (World Health Organization, 2020):

- **Aerobic Exercise:** At least 150 minutes of moderate-intensity (e.g., brisk walking, cycling) or 75 minutes of vigorous-intensity exercise per week.
- **Strength Training:** Muscle-strengthening activities at least two days per week.
- **Balance and Coordination:** Activities like tai chi are also beneficial, especially for fall prevention in older adults.

The key message is that any movement is better than none, and benefits are seen at all ages.

Table 7. Physical Activity Recommendations (WHO, 2020)

Type	Frequency	Examples	Cognitive Benefit
Aerobic	≥150 min/week (moderate) or 75 min (vigorous)	Walking, cycling, swimming	Improves blood flow, promotes neurogenesis.
Strength Training	≥2 days/week	Resistance bands, light weights	Improves muscle tone and metabolism.
Balance/Coordination	Regularly	Tai chi, yoga	Reduces fall risk, improves motor planning.

4.3 Modifiable Risk Factor 3: Diet and Nutrition

“What is good for the heart is good for the brain” is a guiding principle for nutritional strategies to reduce dementia risk. The brain is susceptible to oxidative stress and inflammation, both of which can be modulated by diet.

The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diet:

This hybrid of the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets is specifically designed for brain health (Morris et al., 2015) (Table 8). It emphasizes:

- **Foods to Encourage:**
 - o Green Leafy Vegetables (e.g., spinach, kale): ≥6 servings/week.
 - o Other Vegetables: ≥1 serving/day.
 - o Berries (especially blueberries and strawberries): ≥2 servings/week; high in flavonoids.
 - o Nuts: ≥5 servings/week; source of healthy fats and vitamin E.
 - o Olive Oil as primary cooking oil.
 - o Whole Grains: ≥3 servings/day.
 - o Fish: ≥1 serving/week; source of omega-3 fatty acids (DHA).
 - o Beans: ≥4 servings/week.
 - o Poultry: ≥2 servings/week.
- **Foods to Limit:**
 - o Red meat and processed meats.
 - o Butter and margarine.
 - o Cheese.
 - o Pastries and sweets.
 - o Fried or fast food.

Table 8. MIND Diet Components

Food Group	Recommended Intake	Cognitive Benefit
Green leafy vegetables	≥6 servings/week	Antioxidant and anti-inflammatory.
Berries	≥2 servings/week	Rich in flavonoids; reduces oxidative stress
Nuts	≥5 servings/week	Vitamin E and healthy fats.
Fish	≥1 serving/week	Omega-3s improve synaptic function.
Olive oil	Primary oil	Reduces vascular inflammation.
Red meat, butter, sweets	Limit	Reduce vascular burden.

Proposed Mechanisms (Morris et al., 2015):

- **Antioxidant Effects:** Berries and leafy greens combat oxidative stress.
- **Anti-Inflammatory Effects:** Omega-3s from fish and monounsaturated fats from olive oil reduce neuroinflammation.
- **Vascular Health:** The diet supports healthy blood pressure and cholesterol.
- **Amyloid Reduction:** Some studies suggest the MIND diet is associated with lower levels of amyloid plaques.

4.4 Modifiable Risk Factor 4: Cognitive and Social Engagement

A mentally and socially active life builds a “cognitive reserve” that helps the brain become more resilient to pathology (Stern, 2012). The principle of “use it or lose it” appears to hold true for neural circuits (Table 9).

Cognitive Engagement:

- **Concept:** Challenging the brain with novel and complex activities strengthens synaptic connections and promotes neuroplasticity.
- **Activities:** Formal education, lifelong learning, reading, playing musical instruments, learning a new language, doing puzzles, and engaging in strategic games (e.g., chess).
- **Evidence:** Higher levels of education and engagement in cognitively stimulating activities are consistently linked to a lower risk of dementia (Livingston et al., 2020). It is believed that a more robust neural network can better compensate for the damage caused by disease, delaying the onset of symptoms.

Social Engagement:

- **Concept:** Maintaining strong social networks and frequent social interaction is protective against cognitive decline.
- **Activities:** Having a strong social support system, participating in group activities, volunteering, maintaining friendships, and engaging in community life.
- **Mechanisms (Frattiglioni, Paillard-Borg, & Winblad, 2004):**
 1. **Cognitive Stimulation:** Social interaction is itself a complex cognitive task requiring attention, memory, and emotional regulation.
 2. **Stress Buffering:** Social support can mitigate the harmful effects of chronic stress.
 3. **Behavioural Reinforcement:** Social networks often encourage healthy behaviours (e.g., friends to exercise with) and discourage unhealthy ones.

Loneliness and social isolation, conversely, are significant risk factors for depression, cognitive decline, and earlier mortality.

Table 9. Cognitive and Social Engagement Factors

Domain	Examples	Mechanism	Impact
Cognitive	Reading, learning, puzzles	Strengthens synaptic connections	Builds cognitive reserve.
Social	Group activities, volunteering	Reduces stress and isolation	Enhances resilience and mood.

5. Other Critical Modifiable Factors: Smoking, Alcohol, and Sleep

Smoking:

Tobacco smoking is a major risk factor for dementia (Livingston et al., 2020). The harmful effects are multifold:

- **Vascular Damage:** It accelerates atherosclerosis and increases the risk of stroke.
 - **Oxidative Stress and Inflammation:** Tobacco smoke contains numerous neurotoxins and pro-inflammatory compounds.
 - **Direct Toxicity:** Some compounds in smoke may have a direct toxic effect on neurons.
- The good news is that quitting smoking, even later in life, can significantly reduce the elevated risk.

Alcohol Consumption:

The relationship between alcohol and dementia is J-shaped. Heavy drinking (>21 units per week for men, >14 for women) is detrimental, increasing the risk through neurotoxicity, vitamin B1 (thiamine) deficiency, and increased risk of stroke and liver disease (Livingston et al., 2020). However, light to moderate consumption (particularly red wine, with its polyphenols like resveratrol) has been associated in some studies with a reduced risk, likely due to beneficial cardiovascular effects. Given the risks of alcohol, it is not recommended to start drinking for health benefits, and for those who do drink, moderation is key.

Sleep:

Quality sleep is essential for brain maintenance. During deep sleep, the brain's glymphatic system—a waste-clearance system—becomes highly active, flushing out metabolic byproducts, including amyloid-beta (Xie et al., 2013) (Table 10).

- **Sleep Disorders:** Chronic insomnia and sleep-disordered breathing (e.g., sleep apnea) are linked to an increased risk of cognitive decline. Sleep apnea causes repeated drops in oxygen levels, damaging the hippocampus.
- **Recommendation:** 7-9 hours of quality sleep per night is considered a cornerstone of brain health.

Table 10. Sleep and Mental Health Factors

Factor	Mechanism	Dementia Risk Link	Intervention
Poor sleep	Impaired glymphatic clearance of amyloid	↑ Alzheimer's risk	Sleep hygiene, treat apnea.
Depression	Hippocampal atrophy, inflammation	Independent risk factor	Therapy, antidepressants.
Chronic stress	Cortisol-mediated neuronal damage	Cognitive decline	Stress management, mindfulness.

6. Environmental Influences: Air Pollution and Heavy Metals

Beyond personal lifestyle choices, the broader environment we live in can influence dementia risk. The evidence for many environmental toxins is still evolving, but several strong candidates have emerged.

Air Pollution:

Fine particulate matter (PM_{2.5}) and other pollutants from vehicle exhaust, industrial emissions, and wildfires can enter the bloodstream and, via the nose, directly access the brain (Underwood, 2017).

• Proposed Mechanisms:

1. **Systemic Inflammation:** Pollutants trigger a body-wide inflammatory response that affects the brain.
2. **Oxidative Stress:** Particles generate reactive oxygen species that damage neurons.
3. **Direct Entry to Brain:** Ultrafine particles can travel up the olfactory nerve directly into the brain, potentially carrying toxic metals.
4. **Amyloid Pathology:** Animal studies show exposure to air pollution can increase amyloid plaque formation.

Heavy Metals:

- **Lead:** Childhood exposure to lead (in paint, water, or soil) has been linked to lower cognitive performance and increased risk of neurodegeneration later in life. Lead is a potent neurotoxin.
- **Other Metals:** The evidence for other metals like mercury and aluminum is more controversial. While high-level exposure is neurotoxic, a definitive causal link to common forms of dementia like Alzheimer's at typical environmental levels remains unproven. Aluminum, in particular, has been the subject of much speculation but little conclusive human evidence.

Mitigating these risks involves policy-level changes (e.g., cleaner air regulations) and individual actions (e.g., using air purifiers, being aware of lead in older homes).

6. The Role of Traumatic Brain Injury (TBI)

Traumatic Brain Injury, particularly moderate to severe or repeated mild TBI (such as in contact sports), is a well-established environmental risk factor for dementia (Livingston et al., 2020).

The Link to Neurodegeneration:

- **Acute Effects:** TBI causes immediate damage through shearing and tearing of neuronal axons, contusions, and bleeding.

- **Chronic Effects:** *It triggers a cascade of pathological events that can persist for years, including (Smith, Johnson, & Stewart, 2013):*

- o **Amyloid Pathology:** The brain may rapidly produce amyloid-beta plaques in response to injury.

- o **Tau Pathology:** TBI is a strong driver of tau tangles. A condition known as Chronic Traumatic Encephalopathy (CTE), found in athletes and military veterans with repeated head trauma, is characterized by extensive tau pathology.

- o **Neuroinflammation:** A persistent inflammatory state can be activated after TBI.

- o **Vascular Damage:** Injuries can damage the brain's blood vessels.

Risk and Severity:

A single, severe TBI increases the risk of developing dementia later in life. The risk is substantially higher with repeated injuries. This has major implications for sports safety, military veterans, and fall prevention in the elderly. The use of helmets and other protective gear is a critical modifiable behaviour to mitigate this risk.

7. The Impact of Mental Health: Depression and Chronic Stress

Psychological well-being is inextricably linked to cognitive health. Chronic negative mental states can exert a tangible, damaging effect on the brain.

Depression:

Late-life depression is both a potential early symptom of dementia and an independent risk factor for its development (Livingston et al., 2020).

• Mechanisms:

- o **Hippocampal Atrophy:** Depression is associated with elevated cortisol levels (a stress hormone), which can be toxic to hippocampal cells, leading to volume loss in this critical memory region.
- o **Inflammation:** Major depression is linked to a chronic, low-grade inflammatory state.
- o **Vascular Factors:** Depression is associated with worse cardiovascular health.
- o **Social Withdrawal:** It can lead to reduced cognitive and social engagement.

Chronic Stress:

The body's stress response system, the hypothalamic-pituitary-adrenal (HPA) axis, is designed for short-term threats. Chronic activation leads to dysregulation.

• **Cortisol:** Persistently high cortisol levels impair memory, reduce hippocampal volume, and increase blood pressure.

• **Lifestyle Mediators:** Chronic stress often leads to poor sleep, unhealthy eating, and physical inactivity, creating a cascade of risk.

Effectively managing mental health through therapy, medication, mindfulness, and social support is therefore a vital component of dementia risk reduction.

8. Sensory Health: Hearing and Vision Loss

Emerging evidence strongly suggests that addressing sensory impairments is a critical, and often overlooked, strategy for preserving cognitive function (Livingston et al., 2020).

Hearing Loss:

Age-related hearing loss is one of the top modifiable risk factors for dementia.

• Proposed Causal Pathways (Livingston et al., 2020):

1. **Cognitive Load:** The brain must expend more resources to decode sounds, diverting cognitive resources away from memory and thinking processes.
2. **Brain Atrophy:** Lack of auditory input may lead to accelerated atrophy in auditory regions of the brain, which can spread to other areas.
3. **Social Isolation:** Hearing loss makes communication difficult, leading to social withdrawal and reduced cognitive stimulation.

Studies show that the use of hearing aids is associated with a reduced risk of cognitive decline, likely by counteracting these pathways.

Vision Loss:

Similar to hearing loss, impaired vision can contribute to risk through:

- **Reduced Cognitive Stimulation:** It limits activities like reading, puzzles, and driving.
- **Social Isolation:** Difficulty recognizing faces and navigating social situations can lead to withdrawal.
- **Shared Neurodegeneration:** The same vascular or neurodegenerative processes affecting the brain may also affect the eyes (e.g., retinopathy).

Regular screening for hearing and vision and the consistent use of corrective devices (hearing aids, glasses) are simple yet powerful interventions.

9. Synthesizing the Evidence: The Concept of Cognitive Reserve

How can one person have significant Alzheimer's pathology at autopsy yet show few cognitive symptoms in life, while another with minimal pathology had severe dementia? The answer lies in the concept of Cognitive Reserve (Stern, 2012).

Definition: Cognitive reserve is the brain's ability to improvise and find alternative ways of getting a job done. It is the mental resilience that allows some individuals to withstand more age-related brain changes or disease pathology before showing clinical symptoms of decline.

What Builds Cognitive Reserve?

The modifiable factors discussed throughout this chapter are the primary builders of reserve:

- **High Educational and Occupational Attainment**
- **Lifelong Engagement in Cognitively Stimulating Hobbies**
- **Rich Social Networks**
- **Physical Activity**

Mechanisms: Reserve is not a physical entity but a functional characteristic, believed to be underpinned by (Stern, 2012):

1. **Neural Reserve:** More efficient or robust brain networks in healthy individuals.
2. **Neural Compensation:** The ability to recruit alternative brain networks or use different cognitive strategies to compensate for damage.

This concept powerfully reframes the goal of risk reduction: it is not necessarily to prevent all pathology, but to build a brain that is resilient enough to cope with it, thereby delaying or preventing the onset of disabling symptoms.

10. A Lifespan Model of Risk and Resilience

Dementia risk is not static; it accumulates and can be modified across the entire human lifespan. The following model illustrates how risk factors (in red) and protective/resilience factors (in green) interact from childhood to old age, as conceptualized by the Lancet Commission (Livingston et al., 2020).

- **Early Life (0-20 years):**
 - o **Risk:** Low childhood education, childhood lead exposure.
 - o **Resilience:** High-quality education, cognitive stimulation, good nutrition.
 - o *This period builds the foundational brain structure and initial cognitive reserve.*
- **Midlife (40-65 years):**
 - o **Risk:** Hypertension, obesity, hearing loss, TBI, alcohol misuse, smoking, depression.
 - o **Resilience:** Managing cardiovascular health, staying physically and cognitively active, healthy diet, strong social ties.
 - o *This is a critical period for intervention, as addressing these risks can have a massive impact on late-life outcomes.*
- **Later Life (65+ years):**
 - o **Risk:** Social isolation, physical inactivity, diabetes, depression, smoking, air pollution.
 - o **Resilience:** Continued cognitive engagement, managing sensory loss, treating depression, maintaining social connections.
 - o *It is never too late; lifestyle changes in later life still confer significant benefit.*

This model underscores that prevention is a lifelong endeavour.

11. Clinical Implications and Public Health Perspective

The knowledge of genetic and modifiable risk factors has profound implications for clinical practice and public health policy.

Clinical Implications:

- **Genetic Counseling:** For individuals with a strong family history of early-onset dementia, genetic counseling is essential to discuss the pros and cons of testing for deterministic genes. For APOE, routine testing is not recommended for risk assessment in asymptomatic individuals due to its limited predictive value and potential for psychological harm (Goldman et al., 2011).
- **Risk Assessment and Patient Counseling:** Clinicians should move beyond family history and actively assess modifiable risk factors (e.g., blood pressure, hearing, physical activity levels, diet, social engagement) during patient visits.
- **Personalized Prevention Plans:** Healthcare providers can work with patients to create tailored plans focusing on their most impactful modifiable risks (e.g., “Let’s focus on getting your blood pressure under control and increasing your weekly walks”).

Public Health Perspective:

Addressing dementia risk requires a population-level approach (Livingston et al., 2020).

- **Policy Initiatives:** Governments can promote brain health through policies that improve air quality, fund public education campaigns, ensure access to early childhood education, and create age-friendly communities that promote social and physical activity.
- **Economic Impact:** A small reduction in the overall rate of dementia through preventative strategies would have an enormous positive economic impact by reducing the future burden of care.
- **Health Equity:** Many risk factors disproportionately affect socioeconomically disadvantaged populations. Public health efforts must focus on reducing these disparities to ensure equitable brain health for all.

12. Conclusion and Key Takeaways

This chapter has explored the complex tapestry of factors that influence an individual's risk of developing dementia. The key takeaways are:

1. **Genetics Sets the Stage, But Doesn't Write the Script:** While deterministic genes cause a small percentage of dementia cases (Bateman et al., 2011), for the vast majority, genetic risk (e.g., APOE-e4) represents a predisposition that interacts with lifestyle and environment.
2. **Familial vs. Sporadic is a Spectrum:** Family history increases risk, but most dementia is sporadic, arising from a combination of common genetic variants and modifiable factors.
3. **Modifiable Risk Factors are Paramount:** Up to 40% of dementia cases could be prevented by addressing 12 key modifiable factors across the lifespan (Livingston et al., 2020). The most significant include:
 - o Less education in early life.
 - o Midlife hypertension, obesity, hearing loss, and excessive alcohol use.
 - o Later life smoking, depression, physical inactivity, social isolation, diabetes, and air pollution.
4. **The Brain-Body Connection is Inseparable:** Cardiovascular health is brain health (Gorelick et al., 2017). Physical activity (Erickson et al., 2019), a heart-healthy diet (like the MIND diet) (Morris et al., 2015), and good sleep are foundational.
5. **"Use It or Lose It" is Scientifically Valid:** A mentally, socially, and cognitively engaged life builds cognitive reserve (Stern, 2012), making the brain more resilient to pathology.
6. **Prevention is a Lifelong Journey:** Interventions at any stage of life can be beneficial, but midlife represents a particularly critical window of opportunity.

In conclusion, the fear of dementia, often fueled by a sense of genetic determinism, can be replaced with a sense of empowerment. By understanding and actively managing our modifiable risk factors, we can all take meaningful steps toward preserving our cognitive health for years to come.

References

- Bateman, R. J., Aisen, P. S., De Strooper, B., Fox, N. C., Lemere, C. A., Ringman, J. M., ... & Xiong, C. (2011). Autosomal-dominant Alzheimer's disease: a review and proposal for the prevention of Alzheimer's disease. *Alzheimer's Research & Therapy*, 3(1), 1.
- Chatterjee, S., Peters, S. A., Woodward, M., Mejia Arango, S., Batty, G. D., Beckett, N., ... & Huxley, R. R. (2016). Type 2 diabetes as a risk factor for dementia in women compared with men: a pooled analysis of 2.3 million people comprising more than 100,000 cases of dementia. *Diabetes Care*, 39(2), 300-307.
- Erickson, K. I., Hillman, C., Stillman, C. M., Ballard, R. M., Bloodgood, B., Conroy, D. E., ... & Physical Activity Guidelines Advisory Committee. (2019). Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Medicine and Science in Sports and Exercise*, 51(6), 1242.
- Frattiglioni, L., Paillard-Borg, S., & Winblad, B. (2004). An active and socially integrated lifestyle in late life might protect against dementia. *The Lancet Neurology*, 3(6), 343-353.
- Goldman, J. S., Hahn, S. E., Catania, J. W., LaRusse-Eckert, S., Butson, M. B., Rumbaugh, M., ... & Bird, T. (2011). Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genetics in Medicine*, 13(6), 597-605.
- Gorelick, P. B., Furie, K. L., Iadecola, C., Smith, E. E., Waddy, S. P., Lloyd-Jones, D. M., ... & American Heart Association/American Stroke Association. (2017). Defining optimal brain health in adults: a presidential advisory from the American Heart Association/American Stroke Association. *Stroke*, 48(10), e284-e303.
- Kunkle, B. W., Grenier-Boley, B., Sims, R., Bis, J. C., Damotte, V., Naj, A. C., ... & Genetic and Environmental Risk in AD/Defining Genetic, Polygenic and Environmental Risk for Alzheimer's Disease Consortium (GERAD/PERADES). (2019). Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates A β , tau, immunity and lipid processing. *Nature Genetics*, 51(3), 414-430.
- Liu, C. C., Kanekiyo, T., Xu, H., & Bu, G. (2013). Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. *Nature Reviews Neurology*, 9(2), 106-118.
- Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., ... & Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, 396(10248), 413-446.
- Morris, M. C., Tangney, C. C., Wang, Y., Sacks, F. M., Barnes, L. L., Bennett, D. A., & Aggarwal, N. T. (2015). MIND diet slows cognitive decline with aging. *Alzheimer's & Dementia*, 11(9), 1015-1022.
- National Institute on Aging. (2023). Alzheimer's Disease Genetics Fact Sheet. U.S. Department of Health and Human Services. Retrieved from <https://www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet>
- Raz, L., Knoefel, J., & Bhaskar, K. (2016). The neuropathology and cerebrovascular mechanisms of dementia. *Journal of Cerebral Blood Flow & Metabolism*, 36(1), 172-186.
- Smith, D. H., Johnson, V. E., & Stewart, W. (2013). Chronic neuropathologies of single and repetitive TBI: substrates of dementia?. *Nature Reviews Neurology*, 9(4), 211-221.
- Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *The Lancet Neurology*, 11(11), 1006-1012.
- Strang, K. H., Golde, T. E., & Giasson, B. I. (2019). MAPT mutations, tauopathy, and mechanisms of neurodegeneration. *Laboratory Investigation*, 99(7), 912-928.
- Ulland, T. K., & Colonna, M. (2018). TREM2 — a key player in microglial biology and Alzheimer disease. *Nature Reviews Neurology*, 14(11), 667-675.
- Underwood, E. (2017). The polluted brain. *Science*, 355(6323), 342-345.
- World Health Organization. (2020). Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization.
- Xie, L., Kang, H., Xu, Q., Chen, M. J., Liao, Y., Thiyagarajan, M., ... & Nedergaard, M. (2013). Sleep drives metabolite clearance from the adult brain. *Science*, 342(6156), 373-377.

Early phase of diabetes mellitus may just be a reversible insufficiency of pancreas against excess fat tissue

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Abstract

Background: Excess fat tissue may be a reversible etiology of early diabetes mellitus (DM).

Methods: Sick cell diseases (SCD) patients were studied.

Results: We studied 222 males and 212 females (30.8 vs 30.3 years of age, $p>0.05$, respectively). Smoking (23.8% vs 6.1%, $p<0.001$), alcohol (4.9% vs 0.4%, $p<0.001$), transfused red blood cells (RBC) in their lives (48.1 vs 28.5 units, $p=0.000$), disseminated teeth losses (5.4% vs 1.4%, $p<0.001$), ileus (7.2% vs 1.4%, $p<0.001$), stroke (12.1% vs 7.5%, $p<0.05$), chronic renal disease (CRD) (9.9% vs 6.1%, $p<0.05$), cirrhosis (8.1% vs 1.8%, $p<0.001$), chronic obstructive pulmonary disease (25.2% vs 7.0%, $p<0.001$), coronary heart disease (18.0% vs 13.2%, $p<0.05$), leg ulcers (19.8% vs 7.0%, $p<0.001$), and clubbing (14.8% vs 6.6%, $p<0.001$) were all higher in males.

Conclusion: As a prototype of accelerated atherosclerosis, hardened RBC-induced capillary endothelial cell damage terminates with end-organ deficiencies in early decades in SCD. Although atherosclerotic endpoints are so common, we detected no case of DM probably due to lower excess fat. As the most common cause of CRD, DM may be a reversible insufficiency of pancreas against excess fat tissue in early phases. Increased blood and insulin needs of excess fat in contrast to decreased blood supply of excess tissue and pancreas both due to excess pressure on vasculature, externally and atherosclerosis, internally may be important in DM. Acarbose and metformin are safe, cheap, oral, long-term used, and effective drugs for excess fat which may be curative in early phases of DM before development of other atherosclerotic endpoints.

Key words: Sick cell diseases, early diabetes mellitus, excess fat tissue, acarbose, metformin, capillary endothelial cell inflammation, atherosclerotic endpoints

Introduction

Chronic endothelial damage starting at birth may be the most common cause of early aging and shortened survival by means of the atherosclerotic endpoints in the body (1). Much higher blood pressures (BP) of the arterial system may be the strongest accelerating factor via the repeated injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the catastrophic process. Thus venosclerosis is not a significant health problem in medicine. Due to the chronic endothelial damage, inflammation, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures, which terminally reduce blood supply to the end-organs, and increase systolic and decrease diastolic BP further. Some of the well-known accelerating factors of the inflammatory process are physical inactivity, emotional stress, animal-rich diet, smoking, alcohol, excess fat tissue, chronic inflammation, prolonged infection, and cancers for the development of atherosclerotic endpoints including obesity, hypertension (HT), diabetes mellitus (DM), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, chronic obstructive pulmonary disease (COPD), peripheral artery disease (PAD), stroke, abdominal angina, osteoporosis, dementia, early aging, and shortened survival (2, 3). Although early withdrawal of the accelerating factors can delay the atherosclerotic endpoints, the endothelial changes can not be reversed, completely due to fibrotic natures. The accelerating factor and atherosclerotic endpoints have been researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature, extensively (4-6). Similarly, sickle cell diseases (SCD) are highly catastrophic process on vascular endothelial cells initiating at birth and terminating with an accelerated atherosclerosis-induced end-organ deficiencies even at childhood (7, 8). Hemoglobin S causes loss of elastic and biconcave disc shaped structures of red blood cells (RBC). Loss of elasticity instead of shape may be the major problem since the sickling is rare in peripheral blood samples of patients with associated thalassemia minors (TM), and survival is not affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present during whole lifespan, but exaggerated with inflammation, infection, cancer, surgery, and emotional stress. The hardened RBC-induced chronic endothelial damage, inflammation, and fibrosis terminate with tissue hypoxia all over the body (9). As a difference from other causes of chronic endothelial damage, SCD keep vascular endothelium particularly at the capillary level since the capillary system is the main distributor of the hardened RBC into the body (10, 11). The hardened RBC-induced chronic endothelial damage builds up an accelerated atherosclerosis in much earlier decades. Vascular narrowing and obstructions-induced tissue ischemia and end-organ insufficiencies are the terminal consequences, so the mean life expectancy is decreased 30 years or more in the SCD because we have patients with the age of 96 years without the SCD but just with the age of 59 years with the SCD (8).

Material and Methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and June 2016. All patients with the SCD were included. SCD are diagnosed with the hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC). Smoking, alcohol, acute painful crises per year, transfused units of RBC in their lifespans, leg ulcers, stroke, surgeries, deep venous thrombosis (DVT), epilepsy, and priapism were searched in all cases. Cases with a history of one pack-year and one drink-year were accepted as smoker and drinkers, respectively. A physical examination was performed by the Same Internist, and patients with disseminated teeth losses (<20 teeth present) were detected. Patients with acute painful crisis or any other inflammatory or infectious process were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. Check up procedures including serum iron, iron binding capacity, ferritin, creatinine, liver function tests, markers of hepatitis viruses A, B, and C, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure systolic BP of pulmonary artery, an abdominal ultrasonography, a venous Doppler ultrasonography of the lower limbs, a computed tomography (CT) of brain, and magnetic resonance imagings (MRI) of brain and hips were performed. Other bones for avascular necrosis were scanned according to the patients' complaints. Avascular necrosis of bones is diagnosed via MRI (12). Associated TM were detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed via HPLC since SCD with associated TM come with milder clinics than the sickle cell anemia (SCA) (Hb SS) alone (13). Systolic BP of the pulmonary artery of 40 mmHg or greater are accepted as pulmonary hypertension (14). Cirrhosis is diagnosed with full physical examination, laboratory parameters, and ultrasonographic evaluation of the liver. The criterion for diagnosis of COPD is a post-bronchodilator forced expiratory volume in one second/forced vital capacity of lower than 70% (15). Acute chest syndrome (ACS) is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum, dyspnea, and hypoxia (16). An x-ray film of abdomen in upright position was taken just in patients with abdominal distention or discomfort, vomiting, obstipation, or lack of bowel movement, and ileus is diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity. CRD is diagnosed with a permanently elevated serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter of higher than 1.0, and with the presence of Schamroth's sign (17, 18). An exercise electrocardiogram is taken in case of an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is performed in case of a positive exercise electrocardiogram. As a result, CHD was diagnosed either angiographically or with the Doppler

echocardiographic findings as movement disorders in the heart walls. Rheumatic heart disease is diagnosed with the echocardiographic findings, too. Stroke is diagnosed by the CT and/or MRI of the brain. Sick cell retinopathy is diagnosed with ophthalmologic examination in case of visual complaints. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

We included 222 males and 212 females with similar mean ages (30.8 vs 30.3 years, $p>0.05$, respectively) into the study, and there was no patient above the age of 59 years. Associated TM were detected with similar prevalences in both genders (72.5% vs 67.9%, $p>0.05$, respectively). Smoking (23.8% vs 6.1%) and alcohol (4.9% vs 0.4%) were both higher in males ($p<0.001$ for both) (Table 1). Transfused units of RBC in their lives (48.1 vs 28.5, $p=0.000$), disseminated teeth losses (5.4% vs 1.4%, $p<0.001$), ileus (7.2% vs 1.4%, $p<0.001$), CRD (9.9% vs 6.1%, $p<0.05$), cirrhosis (8.1% vs 1.8%, $p<0.001$), COPD (25.2% vs 7.0%, $p<0.001$), CHD (18.0% vs 13.2%, $p<0.05$), leg ulcers (19.8% vs 7.0%, $p<0.001$), digital clubbing (14.8% vs 6.6%, $p<0.001$), and stroke (12.1% vs 7.5%, $p<0.05$) were all higher in males, significantly. Although the mean age of mortality (30.2 vs 33.3 years) was lower in males, the difference was nonsignificant, probably due to the small sample sizes (Table 2). On the other hand, the mean ages of the atherosclerotic endpoints were shown in Table 3.

Table 1: Characteristic features of the study patients

Variables	Males with the SCD*	p-value	Females with the SCD
Prevalence	51.1% (222)	Ns†	48.8% (212)
Mean age (year)	30.8 ± 10.0 (5-58)	Ns	30.3 ± 9.9 (8-59)
Associated TM‡	72.5% (161)	Ns	67.9% (144)
<u>Smoking</u>	<u>23.8% (53)</u>	<u><0.001</u>	<u>6.1% (13)</u>
<u>Alcoholism</u>	<u>4.9% (11)</u>	<u><0.001</u>	<u>0.4% (1)</u>

*Sickle cell diseases †Nonsignificant ($p>0.05$) ‡Thalassemia minors

Table 2: Associated pathologies of the study patients

Variables	Males with the SCD*	p-value	Females with the SCD
Painful crises per year	5.0 ± 7.1 (0-36)	Ns†	4.9 ± 8.6 (0-52)
<u>Transfused units of RBC‡</u>	<u>48.1 ± 61.8 (0-434)</u>	<u>0.000</u>	<u>28.5 ± 35.8 (0-206)</u>
<u>Disseminated teeth losses (<20 teeth present)</u>	<u>5.4% (12)</u>	<u><0.001</u>	<u>1.4% (3)</u>
<u>CHD§</u>	<u>18.0% (40)</u>	<u><0.05</u>	<u>13.2% (28)</u>
<u>Cirrhosis</u>	<u>8.1% (18)</u>	<u><0.001</u>	<u>1.8% (4)</u>
<u>COPD¶</u>	<u>25.2% (56)</u>	<u><0.001</u>	<u>7.0% (15)</u>
<u>Ileus</u>	<u>7.2% (16)</u>	<u><0.001</u>	<u>1.4% (3)</u>
<u>Leg ulcers</u>	<u>19.8% (44)</u>	<u><0.001</u>	<u>7.0% (15)</u>
<u>Digital clubbing</u>	<u>14.8% (33)</u>	<u><0.001</u>	<u>6.6% (14)</u>
<u>CRD**</u>	<u>9.9% (22)</u>	<u><0.05</u>	<u>6.1% (13)</u>
<u>Stroke</u>	<u>12.1% (27)</u>	<u><0.05</u>	<u>7.5% (16)</u>
PHT***	12.6% (28)	Ns	11.7% (25)
Autosplenectomy	50.4% (112)	Ns	53.3% (113)
DVT**** and/or varices and/or telangiectasias	9.0% (20)	Ns	6.6% (14)
Rheumatic heart disease	6.7% (15)	Ns	5.6% (12)
Avascular necrosis of bones	24.3% (54)	Ns	25.4% (54)
Sickle cell retinopathy	0.9% (2)	Ns	0.9% (2)
Epilepsy	2.7% (6)	Ns	2.3% (5)
ACS*****	2.7% (6)	Ns	3.7% (8)
Mortality	7.6% (17)	Ns	6.6% (14)
Mean age of mortality (year)	30.2 ± 8.4 (19-50)	Ns	33.3 ± 9.2 (19-47)

*Sickle cell diseases †Nonsignificant (p>0.05) ‡Red blood cells §Coronary heart disease ¶Chronic obstructive pulmonary disease **Chronic renal disease ***Pulmonary hypertension ****Deep venous thrombosis *****Acute chest syndrome

Table 3: Mean ages of endpoints of the sickle cell diseases

Variables	Mean age (year)
Ileus	29.8 ± 9.8 (18-53)
Hepatomegaly	30.2 ± 9.5 (5-59)
ACS*	30.3 ± 10.0 (5-59)
Sickle cell retinopathy	31.5 ± 10.8 (21-46)
Rheumatic heart disease	31.9 ± 8.4 (20-49)
Autosplenectomy	32.5 ± 9.5 (15-59)
Disseminated teeth losses (<20 teeth present)	32.6 ± 12.7 (11-58)
Avascular necrosis of bones	32.8 ± 9.8 (13-58)
Epilepsy	33.2 ± 11.6 (18-54)
Priapism	33.4 ± 7.9 (18-51)
Left lobe hypertrophy of the liver	33.4 ± 10.7 (19-56)
Stroke	33.5 ± 11.9 (9-58)
COPD†	33.6 ± 9.2 (13-58)
PHT‡	34.0 ± 10.0 (18-56)
Leg ulcers	35.3 ± 8.8 (17-58)
Digital clubbing	35.4 ± 10.7 (18-56)
CHD§	35.7 ± 10.8 (17-59)
DVT¶ and/or varices and/or telangiectasias	37.0 ± 8.4 (17-50)
Cirrhosis	37.0 ± 11.5 (19-56)
CRD**	39.4 ± 9.7 (19-59)

*Acute chest syndrome †Chronic obstructive pulmonary disease ‡Pulmonary hypertension
 §Coronary heart disease ¶Deep venous thrombosis **Chronic renal disease

Discussion

Excess fat tissue may be the most common cause of vasculitis, aging, and death. It causes both excess pressure on the vasculature, externally and an exaggerated atherosclerosis, internally in addition to the increased blood and insulin requirements of the excess tissue. DM may just be an atherosclerotic endpoint of excess fat tissue in whole body rather than the pancreas alone. Although all kinds of the atherosclerotic endpoints are common with the SCD, we have detected no case of DM, probably due to the lower body mass indexes (BMI) (10). The BMI were 20.7 vs 24.9 kg/m² in the SCD and control groups, respectively with the mean age of 28.6 years ($p=0.000$ for both) (10). The heights were similar in both groups (166.1 vs 168.5 cm, respectively, $p>0.05$) which may powerfully indicate that the body height is determined, genetically (10). Similarly, just 20% of elderly have DM, but 55% of patients with DM are obese. So excess fat tissue may be more harmful than smoking, alcohol, or chronic inflammatory or infectious processes for atherosclerosis. Excess fat tissue leads to a chronic and low-grade inflammation on vascular endothelium, and risk of death from all causes increases parallel to its severity (19). The low-grade chronic inflammation may also cause genetic changes on the endothelial cells, and the systemic atherosclerotic process may even decrease clearance of malignant cells by the natural killers (20). The chronic inflammatory process is characterized by lipid-induced injury, invasion of macrophages, proliferation of smooth muscle cells, endothelial dysfunction, and increased atherogenicity (21, 22). Excess fat tissue is considered as a strong factor for controlling of C-reactive protein (CRP) since the excess tissue produces biologically active leptin, tumor necrosis factor- α , plasminogen activator inhibitor-1, and adiponectin-like cytokines (23, 24). On the other hand, excess fat tissue will also aggravate myocardial hypertrophy and decrease cardiac compliance further. Fasting plasma glucose (FPG) and serum cholesterol increased and high density lipoproteins (HDL) decreased parallel to the severity of BMI (25). Similarly, CHD and stroke increased parallel to the severity of BMI (26). Eventually, the risk of death from all causes increased parallel to the severity of excess fat tissue in all age groups, and people with underweight may even have lower biological ages and longer overall survival (27). Similarly, calorie restriction prolongs survival and retards age-related chronic sicknesses (28). So the term of excess weight should be replaced with the excess fat tissue because there are nearly 19 kg of excess fat even between lower and upper borders of normal weight in adults.

Smoking may be the second most common cause of vasculitis all over the world. It causes a systemic inflammation on vascular endothelium terminating with atherosclerotic endpoints in early decades (29). Its atherosclerotic effect is the most obvious in the Buerger's disease and COPD (30). Buerger's disease is

an obliterative vasculitis in the small and medium-sized arteries and veins, and it has never been reported in the absence of smoking. Its characteristic features are chemical toxicity, inflammation, fibrosis, and narrowing and occlusions of arteries and veins. Claudication is the most significant symptom with a severe pain in feet and hands caused by insufficient blood supply, particularly by walking in the feet. It may also radiate to central areas in advanced cases. Numbness or tingling of the limbs is also common. Skin ulcerations and gangrene of fingers or toes are the terminal endpoints. Similar to the venous ulcers, diabetic ulcers, leg ulcers of the SCD, digital clubbing, onychomycosis, and delayed wound and fracture healings of the lower extremities, pooling of blood due to the gravity may be the main cause of Buerger's disease, particularly in the lower extremities. Several narrowing and occlusions of the arm and legs are diagnostic in the angiogram. Skin biopsies may be risky, because a poorly perfused area will not heal, completely. Although most patients are heavy smokers, the limited smoking history of some patients may support the hypothesis that Buerger's disease may be an autoimmune reaction triggered by some constituent of tobacco. Although the only treatment way is complete cessation of smoking, the already developed narrowing and occlusions are irreversible. Due to the well-known role of inflammation, anti-inflammatory dose of aspirin in addition to the low-dose warfarin may even be life threatening by preventing microvascular infarctions. On the other hand, FPG and HDL may be negative whereas triglycerides, low density lipoproteins (LDL), erythrocyte sedimentation rate, and CRP positive acute phase reactants (APR) in smokers (31). Similarly, smoking was associated with the lower BMI due to the systemic inflammatory effects (32, 33). An increased heart rate was detected just after smoking even at rest (34). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (35). Nicotine may lengthen intermeal time, and decrease amount of meal eaten (36). Smoking may be associated with a postcessation weight gain, but the risk is the highest during the first year, and decreases with the following years (37). Although the CHD was detected with similar prevalences in both genders, prevalences of smoking and COPD were higher in males against the higher white coat hypertension, BMI, LDL, triglycerides, HT, and DM in females (38). The risk of myocardial infarction is increased three-fold in men and six-fold in women with smoking probably due to the higher BMI in women (39). Chemical toxicity of smoking can affect all organ systems. For example, it is usually associated with depression, irritable bowel syndrome (IBS), chronic gastritis, hemorrhoids, and urolithiasis with several possible mechanisms (40). First of all, smoking may also have some anxiolytic properties. Secondly, smoking-induced vascular inflammation may disturb epithelial absorption and excretion in the gastrointestinal (GI) and genitourinary (GU) tracts (41). Thirdly, diarrheal losses-induced urinary changes may cause urolithiasis (42). Fourthly, smoking-induced sympathetic nervous system activation may cause motility problems in the GI

GI and GU tracts terminating with IBS and urolithiasis. Finally, immunosuppression secondary to smoking may terminate with the GI and GU tract infections and urolithiasis since some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits. Actually, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced by the urease producing bacteria. As a result, urolithiasis was higher in the IBS patients (17.9% vs 11.6%, $p < 0.01$) (40).

CHD is the other major cause of death in the human being together with the stroke. The most common triggering cause is the disruption of an atherosclerotic plaque in an epicardial coronary artery, which leads to a clotting cascade. The plaques are the gradual and unstable collection of lipids, fibrous tissue, and white blood cells (WBC), particularly the macrophages in arterial walls in decades of life. Stretching and relaxation of arteries with each heart beat increases mechanical shear stress on atheromas to rupture. After the myocardial infarction, a collagen scar tissue takes its place which may also cause life threatening arrhythmias because the scar tissue conducts electrical impulses more slowly. The difference in conduction velocity between the injured and uninjured tissues can trigger re-entry or a feedback loop that is believed to be the cause of lethal arrhythmias. Ventricular fibrillation is the most serious arrhythmia that is the leading cause of sudden cardiac death. It is an extremely fast and chaotic heart rhythm. Ventricular tachycardia may also cause sudden cardiac death that usually results in rapid heart rates preventing effective cardiac pumping. Cardiac output and BP may fall to dangerous levels which can lead to further coronary ischemia and extension of the infarct. This scar tissue may even cause ventricular aneurysm and rupture. Aging, physical inactivity, animal-rich diet, excess fat tissue, smoking, alcohol, emotional stress, prolonged infection, chronic inflammation, and cancers are important in atherosclerotic plaque formation. Moderate physical exercise is associated with a 50% reduced incidence of CHD (43). Probably, excess fat tissue may be the most important cause of CHD because there are nearly 19 kg of excess fat between the lower and upper borders of normal weight, nearly 33 kg between the lower borders of normal weight and obesity, nearly 66 kg between the lower borders of normal weight and morbid obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$), and nearly 81 kg between the lower borders of normal weight and super obesity ($\text{BMI} \geq 45 \text{ kg/m}^2$) in adults. In other definition, there is a huge percentage of adults with heavier fat than their lean body masses that brings a heavy stress on the heart, liver, kidneys, lungs, brain, and pancreas.

DM is the most common cause of blindness, non-traumatic amputation, and renal dialysis in adults. As the most common cause of CRD, DM may just be an atherosclerotic endpoint affecting the pancreas, too. Increased blood and insulin requirements of the excess fat tissue in contrast to the decreased blood supply of the excess tissue and pancreas due to excess pressure on the vasculature, externally and atherosclerosis, internally may be the underlying mechanisms in the development of DM. For

example, excess fat tissue in the liver and pancreas are called as non-alcoholic fatty liver disease (NAFLD) and non-alcoholic fatty pancreas disease (NAFPD). They are usually accepted as components of the metabolic syndrome. NAFLD progresses to steatohepatitis, cirrhosis, and hepatocellular carcinoma. Blocking triglycerides secretion, subcellular lipid sequestration, lipolysis deficiency, enhanced lipogenesis, gluconeogenesis defects, or inhibition of fatty acid oxidation may be some of the development mechanisms (44). NAFLD may just be an atherosclerotic process, and strongly associated with an accelerated atherosclerotic process not only in the liver instead all over the body. For example, NAFLD is seen in one-third of cases with hepatitis B virus-related chronic liver disease (45). Similarly, higher fatty liver ratios were observed in children with non-Hodgkin lymphomas (46). The liver density on contrast abdominopelvic CT of colorectal cancer patients was low that is consistent with the NAFLD (47). As one of the APR, serum thrombopoietin levels increased in the NAFLD (48). Although serum levels of oxidizing agents including nitrate and advanced oxidation protein products increased, serum nitrite did not adequately increase as an antioxidant agent in the NAFLD (49). As a result, NAFLD is associated with an impaired carotid intima-media thickness (IMT) and flow-mediated dilation which are considered as early markers of systemic atherosclerosis (50). Carotid IMT was correlated with the BMI ($p < 0.001$), age ($p = 0.001$), and grade 2-3 NAFLD ($p < 0.001$) (51). Patients with the NAFLD have more complex CHD, and carotid IMT and grade 2-3 NAFLD were associated with the severity of CHD ($p < 0.001$ for both) (51-53). Similarly, there were reductions in hepatic artery flow volume, portal vein flow volume, and total flow volume in contrast to the increased NAFLD (54). As the most common pathology of pancreas in adults, there may be reductions in flow volume of pancreatic arteries in the NAFPD, too (55). NAFPD is usually associated with the aging, increased BMI, and insulin resistance (56). Replacement of more than 25% of pancreas by fat tissue is associated with systemic atherosclerosis and risk of DM (57). Insulin is stored in vacuoles in beta cells of islets of Langerhans in whole pancreas and released via exocytosis. Pancreatic fat infiltration may lead to a reduced insulin secretion (58). NAFPD may lead to exocrine pancreatic insufficiency by fat droplet accumulation in pancreatic acinar cells and consequent lipotoxicity, destruction of acinar cells by both inflammation and fatty replacement, and by negative paracrine effect of adipocytes (59). It is unsurprising that the NAFPD may even cause pancreatic fibrosis and cancers. NAFPD causes a higher risk of DM (57), and newly diagnosed patients with DM have higher pancreatic fat (60). At least early phases of DM may actually be a relative insufficiency of the pancreas against the excess fat tissue in whole body. Age-related impairment of beta cells may actually be an atherosclerotic endpoint since 20% of elderly have DM, and just 55% of patients with DM are obese. Glucose tolerance progressively decreases by aging. It may be due to the progressively decreased physical and mental activity-induced excess fat tissue secreting adipokines. There is no term of malnutrition-related DM. DM can be cured by gastric bypass surgery

in 90% of morbid obese cases (61). The effect is not due to the weight loss instead decreased insulin requirement since it usually occurs just after days of the surgery. This surgery reduced death rate from all causes by 40% (61). NAFLD is an independent risk factor for CHD, too (62). Similarly, NAFLD is associated with increased aortic IMT and epicardial fat tissue (63). As a result, NAFLD, cirrhosis, NAFLD, and DM may be atherosclerotic endpoints in human body (64).

Acute painful crises are nearly pathognomonic for the SCD. Although some authors reported that pain itself may not be life threatening directly, infections, medical or surgical emergencies, or emotional stresses are the most common precipitating factors of the crises (65). The increased basal metabolic rate during such stresses aggravates the sickling and capillary endothelial cell damage, inflammation, and edema terminating with tissue hypoxia and end-organ deficiencies. So the risk of mortality is much higher during the crises. Actually, each crisis may complicate with the following crises by leaving significant sequelae on the capillary endothelial system in whole body. After a period of time, the sequelae may terminate with end-organ failures and sudden death with an acute painful crisis that may even be silent, clinically. Similarly, after a 20-year experience on such patients, the deaths seem sudden and unexpected events in the SCD. Unfortunately, most of the deaths develop just after the hospital admission, and majority of them are patients without hydroxyurea therapy (66, 67). Rapid RBC supports are usually life-saving for such patients, although preparation of RBC units for transfusion usually takes time. Beside that RBC supports in emergencies become much more difficult in terminal cases due to the repeated transfusions-induced blood group mismatch. Actually, transfusion of each unit of RBC complicates the following transfusions by means of the blood subgroup mismatch. Due to the significant efficacy of hydroxyurea therapy, RBC transfusions should be preserved just for acute stresses and emergencies (66-68). According to our experiences, simple and repeated transfusions are superior to RBC exchange (69, 70). First of all, preparation of one or two units of RBC suspensions in each time rather than preparation of six units or higher provides time to clinicians by preventing sudden death of such high-risk patients. Secondly, transfusions of one or two units of RBC suspensions in each time decrease the severity of pain, and relax the patients and their relatives since RBC transfusions probably have the strongest analgesic effects during such crises (71). Actually, the decreased severity of pain by transfusions also indicates the decreased severity of inflammation in whole body. Thirdly, transfusions of lesser units of RBC suspensions by means of the simple transfusions will decrease transfusion-related complications including infections, iron overload, and blood group mismatch. Fourthly, transfusions of RBC suspensions in the secondary health centers prevent deaths developed during the transport to the tertiary centers for the exchange. Terminally, cost of the simple transfusions on insurance system is much lower than the exchange which needs trained staff and

additional devices. On the other hand, pain is the result of complex and poorly understood interactions between RBC, WBC, platelets (PLT), and endothelial cells, yet. Probably, leukocytosis contributes to the pathogenesis by releasing cytotoxic enzymes. The adverse effects of WBC on vascular endothelium are of particular interest for atherosclerotic endpoints. For example, leukocytosis even in the absence of any infection was an independent predictor of the severity of the SCD (72), and it was associated with the risk of stroke (73). Disseminated tissue hypoxia, releasing of inflammatory mediators, bone infarctions, and activation of afferent nerves may take role in the pathophysiology of the intolerable pain. Due to the severity of pain, narcotic analgesics are usually required (74), but simple RBC transfusions are effective both to relieve pain and to prevent sudden deaths which may develop due to the end-organ failures on atherosclerotic background of the SCD.

Hydroxyurea is the life-saving drug for the SCD. It interferes with the cell division by blocking the formation of deoxyribonucleotides by means of inhibition of ribonucleotide reductase. The deoxyribonucleotides are the building blocks of DNA. Hydroxyurea mainly affects hyperproliferating cells. Although the action way of hydroxyurea is thought to be the increase in gamma-globin synthesis for fetal hemoglobin (Hb F), its main action may be the suppression of leukocytosis and thrombocytosis by blocking the DNA synthesis (75, 76). Due to the same action way, hydroxyurea is also used in moderate and severe psoriasis to suppress hyperproliferating skin cells. As in the viral hepatitis cases, although presence of a continuous damage of sickle cells on the capillary endothelium, the severity of catastrophic process is probably exaggerated by the patients' own WBC and PLT. So suppression of proliferation of them can limit the endothelial cells damage-induced edema, ischemia, and infarctions (77). Similarly, Hb F levels in hydroxyurea users did not differ from their pretreatment levels (78). The Multicenter Study of Hydroxyurea (MSH) studied 299 severely affected adults with the SCA, and compared the results of patients treated with hydroxyurea or placebo (79). The study particularly researched effects of hydroxyurea on painful crises, ACS, and requirement of blood transfusion. The outcomes were so overwhelming in the favour of hydroxyurea group that the study was terminated after 22 months, and hydroxyurea was initiated for all patients. The MSH also demonstrated that patients treated with hydroxyurea had a 44% decrease in hospitalizations (79). In multivariable analyses, there was a strong and independent association of lower neutrophil counts with the lower crisis rates (79). But this study was performed just in severe SCA cases alone, and the rate of painful crises was decreased from 4.5 to 2.5, annually (79). Whereas we used all subtypes of the SCD with all clinical severity, and the rate of painful crises was decreased from 10.3 to 1.7, annually ($p<0.000$) with an additional decreased severity of them (7.8/10 vs 2.2/10, $p<0.000$) (66). Similarly, adults using hydroxyurea for frequent painful crises appear to have reduced mortality rate after a 9-year follow-up period (80). Although the

genetic severity remains as the main factor to determine prognosis, hydroxyurea may decrease severity of disease and prolong survival (80). The complications start to be seen even after birth. For example, infants with lower hemoglobin levels were more likely to have higher incidences of ACS, painful crises, and lower neuropsychological scores, and hydroxyurea reduced the incidences of all (81). If started early, hydroxyurea may protect splenic function, improve growth, and delay atherosclerotic endpoints. But due to the risks of infections, iron overload, and development of allo-antibodies causing subsequent transfusions difficult, RBC transfusions should be preserved for acute stress and emergencies as the most effective weapon in our hands.

Aspirin is a member of nonsteroidal anti-inflammatory drugs (NSAID). Although aspirin has similar anti-inflammatory effects with the other NSAID, it also suppresses the normal functions of PLT, irreversibly. Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the cyclooxygenase (COX) enzyme. Aspirin inactivates the COX enzyme, irreversibly, which is required for the synthesis of prostaglandins (PG) and thromboxanes (TX). PG are the locally produced hormones with some diverse effects, including the transmission of pain into the brain and modulation of the hypothalamic thermostat and inflammation. TX are responsible for the aggregation of PLT to form blood clots. Low-dose aspirin irreversibly blocks the formation of TXA₂ in the PLT, producing an inhibitory effect on the PLT aggregation during whole lifespan of the affected PLT (8-9 days). Since PLT do not have nucleus and DNA, they are unable to synthesize new COX enzyme anymore. But aspirin has no effect on the blood viscosity. The antithrombotic property is useful to reduce the risks of myocardial infarction, transient ischemic attack, and stroke (82). Low-dose of aspirin is effective to prevent the second myocardial infarction, too (83). Aspirin may also be effective in prevention of colorectal cancers (84). On the other hand, aspirin has some side effects including gastric ulcers, gastric bleeding, worsening of asthma, and Reye syndrome in childhood and adolescence. Due to the risk of Reye syndrome, the US Food and Drug Administration recommends that aspirin should not be prescribed for febrile patients under the age of 12 years (85), and it was only recommended for Kawasaki disease (86). Reye syndrome is a rapidly worsening brain disease (86). The first detailed description of Reye syndrome was in 1963 by an Australian pathologist, Douglas Reye (87). The syndrome mostly affects children, but it can only affect fewer than one in a million children, annually (87). Symptoms of Reye syndrome may include personality changes, confusion, seizures, and loss of consciousness (86). Although the liver toxicity and enlargement typically occurs in most cases, jaundice is usually not seen (86). Although the death occurs in 20-40% of affected cases, about one third of survivors get a significant degree of brain damage (86). It usually starts just after recovery from a viral infection, such as influenza or chicken pox. About 90% of children are associated with an aspirin use (87, 88). Inborn errors of metabolism are also the other risk factors, and the genetic testing for inborn errors of

metabolism became available in developed countries in the 1980s (86). When aspirin use was withdrawn for children in the US and UK in the 1980s, a decrease of more than 90% in rates of Reye syndrome was seen (87). Due to the low risk of Reye syndrome but higher risk of death, aspirin should be added into the acute and chronic treatments of the SCD with an anti-inflammatory dose even in children (89).

Warfarin is an anticoagulant, and it has no effect on blood viscosity, too. It is the best suited for anticoagulation in areas of slowly flowing blood such as veins and the pooled blood behind artificial and natural valves and dysfunctional cardiac atria. It is commonly used to prevent DVT and pulmonary embolism, and against stroke in atrial fibrillation (AF), valvular heart disease, and artificial heart valves. It is additionally used following ST-segment elevation myocardial infarction and orthopedic surgeries. Initiation regimens are simple, safe, and suitable to be used in the ambulatory settings (90). It should be initiated with a 5 mg dose, or 2 to 4 mg in the elderly. In the protocol of low-dose warfarin, the target international normalized ratio (INR) is between 2.0 and 2.5, whereas in the protocol of standard-dose warfarin, the target INR is between 2.5 and 3.5 (91). Simple discontinuation of the drug for five days is enough to reverse the effect, and causes INR to drop below 1.5 (92). Its effects can be reversed with phytonadione (vitamin K₁), fresh frozen plasma, or prothrombin complex concentrate, rapidly. Warfarin decreases blood clotting by blocking vitamin K epoxide reductase, an enzyme that reactivates vitamin K₁. Without sufficient active vitamin K₁, abilities of clotting factors II, VII, IX, and X are decreased. The abilities of anticlotting protein C and S are also inhibited, but to a lesser degree. A few days are required for full effect which is lasting up to five days. The consensus agrees that current self-testing and management devices are effective providing outcomes possibly better than achieved, clinically. The risk of severe bleeding is just 1-3%, annually, and the severest ones are those involving the central nervous system (92, 93). The risk is particularly increased once the INR exceeds 4.5 (93). The risk of bleeding is increased further when warfarin is combined with antiplatelet drugs such as clopidogrel or aspirin (94). Thirteen publications from 11 cohorts including more than 48,500 patients with more than 11,600 warfarin users were included in the meta-analysis in which warfarin resulted with a lower risk of ischemic stroke ($p=0.004$) and mortality ($p<0.00001$), but had no effect on major bleeding ($p>0.05$) in patients with AF and non-end-stage CRD (95). Warfarin is associated with significant reductions in ischemic stroke even in patients with warfarin-associated intracranial hemorrhage (ICH), and recurrent ICH occurred in 6.7% of warfarin users and 7.7% of the others ($p>0.05$) (96). On the other hand, patients with cerebral venous thrombosis (CVT) anticoagulated either with warfarin or dabigatran had lower risk of recurrent venous thrombotic events (VTE), and the risks of bleeding were similar in both regimens (97). Additionally, an INR value of 1.5 achieved with an average daily dose of 4.6 mg warfarin, has resulted with no increase in the number of men ever reporting minor

bleeding episodes (98). Non-rheumatic AF increases the risk of stroke, presumably from atrial thromboemboli, and long-term use of low-dose warfarin is highly effective and safe with a reduction of 86% in the risk of stroke ($p=0.0022$) (99). The mortality rate was markedly lower in the warfarin group, too ($p=0.005$) (99). The frequencies of bleedings that required hospitalization or transfusions were similar in both groups ($p>0.05$) (99). Additionally, very-low-dose warfarin was safe and effective for prevention of thromboembolism in metastatic breast cancer in which the average daily dose was 2.6 mg, and the mean INR value was 1.5 (100). On the other hand, new oral anticoagulants had a favourable risk-benefit profile with significant reductions in stroke, ICH, and mortality, and with similar major bleedings as for warfarin, but increased GI bleeding (101). Interestingly, rivaroxaban and low-dose apixaban were associated with increased risks of all cause mortality compared with warfarin (102). The mortality rates were 4.1%, 3.7%, and 3.6% per year in the warfarin, 110 mg of dabigatran, and 150 mg of dabigatran groups, respectively ($p>0.05$ for both) with AF (103). Eventually, infection, inflammation, medical or surgical emergency, and emotional stress-induced increased basal metabolic rate accelerates sickling, and an exaggerated capillary endothelial edema-induced myocardial infarction or stroke may cause sudden deaths (104). So anti-inflammatory dose of aspirin plus low-dose warfarin may be the other life-saving regimen to prevent atherosclerotic endpoints even at childhood in SCD (105).

COPD is the third leading cause of death in human being (106). Aging, smoking, alcohol, male gender, excess fat tissue, chronic inflammation, prolonged infection, and cancers may be the main causes. Atherosclerotic effects of smoking may be the most obvious in the COPD and Buerger's disease, probably due to the higher concentrations of toxic substances in the lungs and pooling of blood in the extremities. After smoking, excess fat tissue may be the second common cause of COPD due to the excess fat tissue-induced atherosclerotic endpoints all over the body. Since an estimated 25-45% of patients with the COPD have never smoked (107). Regular alcohol consumption may be the third leading cause of the systemic accelerated atherosclerotic process and COPD, since COPD was one of the most common diagnoses in alcohol dependence (108). Furthermore, 30-day readmission rates were higher in the COPD patients with alcoholism (109). Probably an accelerated atherosclerotic process is the main structural background of functional changes that are characteristics of the COPD. The inflammatory process of vascular endothelial cells is exaggerated by release of various chemicals by inflammatory cells, and it terminates with an advanced fibrosis, atherosclerosis, and pulmonary losses. COPD may actually be the pulmonary endpoint of the systemic atherosclerotic process. Beside the accelerated atherosclerotic process of the pulmonary vasculature, there are several reports about coexistence of associated endothelial inflammation all over the body in COPD (110). For instance, there may be close relationships between COPD, CHD, PAD, and stroke (111). Furthermore, two-third of mortality cases were caused by cardiovascular

diseases and lung cancers in the COPD, and the CHD was the most common cause in a multicenter study of 5.887 smokers (112). When hospitalizations were researched, the most common causes were the cardiovascular diseases, again (112). In another study, 27% of mortality cases were due to the cardiovascular diseases in the moderate and severe COPD (113). Finally, COPD may also be an atherosclerotic endpoint of SCD (106).

Leg ulcers are seen in 10% to 20% of the SCD, and its prevalence increases with aging, male gender, and SCA (114, 115). The leg ulcers have an intractable nature, and around 97% of them relapse in a period of one year (114). Similar to Buerger's disease, the leg ulcers occur in the distal segments of the body with a lesser collateral blood flow (114). The hardened RBC-induced chronic endothelial damage, inflammation, edema, and fibrosis at the capillaries may be the chief causes (115). Prolonged exposure to the hardened bodies due to the pooling of blood in the lower extremities may also explain the leg but not arm ulcers in the SCD. The hardened RBC-induced venous insufficiencies may also accelerate the process by pooling of causative bodies in the legs, and vice versa. Pooling of blood may also be important for the development of venous ulcers, diabetic ulcers, Buerger's disease, digital clubbing, and onychomycosis in the lower extremities. Furthermore, pooling of blood may be the cause of delayed wound and fracture healings in the lower extremities. Smoking and alcohol probably have some additional atherosclerotic effects on the leg ulcers in males. Hydroxyurea is the first drug that was approved by Food and Drug Administration in the SCD (116). It is an oral, cheap, safe, and effective drug that blocks cell division by suppressing formation of deoxyribonucleotides which are the building blocks of DNA (11). Its main action may be the suppression of hyperproliferative WBC and PLT in the SCD (117). Although presence of a continuous damage of hardened RBC on vascular endothelial cells, severity of the destructive process is probably exaggerated by the immune system. Similarly, lower WBC counts were associated with lower crisis rates, and if a tissue infarct occurs, lower WBC counts may decrease severity of tissue damage and pain (78). Prolonged resolution of leg ulcers with hydroxyurea may also suggest that the ulcers may be secondary to increased WBC and PLT counts-induced exaggerated capillary endothelial cell edema.

Clubbing is characterized by the increased normal angle of 165° between nailbed and fold, increased convexity of the nail fold, and thickening of the whole distal finger (118). Although the exact cause and significance is unknown, the chronic tissue hypoxia is highly suspected (119). In the previous study, only 40% of clubbing cases turned out to have significant underlying diseases while 60% remained well over the subsequent years (18). But according to our experiences, clubbing is frequently associated with the pulmonary, cardiac, renal and hepatic diseases, and smoking those are characterized with chronic tissue hypoxia (5). As an explanation for that hypothesis, lungs, heart, kidneys, and liver are closely related organs which affect their functions in a short period of time.

On the other hand, clubbing is also common in the SCD with a prevalence of 10.8% in the present study, too. It probably shows chronic tissue hypoxia caused by disseminated endothelial damage, edema, and fibrosis, particularly at the capillary level in the SCD. Beside the effects of SCD, smoking, alcohol, cirrhosis, CRD, CHD, and COPD, the higher digital clubbing in males (14.8% vs 6.6%, $p < 0.001$) may also indicate some additional role of male gender for the atherosclerotic endpoints.

CRD is increasing which can be explained by prolonged survival and increased prevalence of excess fat in human being, too (120). Aging, animal-rich diet, excess fat tissue, smoking, alcohol, chronic inflammatory or infectious process, and cancers may be the major causes of the renal endothelial inflammation, too. The inflammatory process is enhanced by release of various chemicals by lymphocytes to repair the damaged endothelial cells of the renal arteriols. Due to the continuous irritation of the vascular endothelial cells, prominent changes develop in the architecture of the renal tissues with advanced atherosclerosis, tissue hypoxia, and infarcts (121). Excess fat tissue-induced hyperglycemia, dyslipidemia, elevated BP, and insulin resistance can cause tissue inflammation and immune cell activation (122). Age ($p = 0.04$), high-sensitivity CRP ($p = 0.01$), mean arterial BP ($p = 0.003$), and DM ($p = 0.02$) had significant correlations with the CIMT (120). Increased renal tubular sodium reabsorption, impaired pressure natriuresis, volume expansion due to the activations of sympathetic nervous system and renin-angiotensin system, and physical compression of kidneys by visceral fat tissue may be some mechanisms of the increased BP with excess fat tissue (123). Excess fat tissue also causes renal vasodilation and glomerular hyperfiltration which initially serve as compensatory mechanisms to maintain sodium balance due to the increased tubular reabsorption (123). However, along with the increased BP, these changes cause a hemodynamic burden on the kidneys in long term that causes chronic endothelial damage (124). With prolonged excess fat tissue, there are increased urinary protein excretion, loss of nephron function, and exacerbated HT. With the development of dyslipidemia and DM, CRD progresses more easily (123). The systemic inflammatory effects of smoking on endothelial cells is also important in the CRD (125). Although the presence of some opposite reports (125), alcohol can give harm to the renal vascular endothelium, too. Chronic inflammatory or infectious processes may also terminate with atherosclerotic endpoints in kidneys (124). There are close relationships between CRD and other atherosclerotic endpoints (126, 127). The most common causes of death were CHD and stroke in CRD, again (128). The hardened RBC-induced capillary endothelial damage may be the major cause of CRD in SCD, again (129).

Stroke is the other terminal cause of death, together with the CHD, and it develops as an acute thromboembolic event on the chronic atherosclerotic background. Aging, male gender, smoking, alcohol, excess fat tissue, chronic inflammatory or infectious process, cancer, and emotional stress may be the major causes. Stroke is also a common

atherosclerotic endpoint of the SCD (130). Similar to the leg ulcers, stroke is particularly higher in cases with the SCA and higher WBC counts (131). Sickling-induced capillary endothelial damage, activations of WBC, PLT, and coagulation system, and hemolysis may terminate with chronic capillary endothelial damage, edema, and fibrosis (132). Stroke may not have a macrovascular origin, and an acute onset diffuse capillary endothelial edema may be more important in the SCD. Thus permanent neurological deficits are rare with stroke in the SCD. Infection, inflammation, medical or surgical emergency, and emotional stress may cause by increasing basal metabolic rate and sickling. Low risk of stroke with hydroxyurea can also suggest that a significant proportion is developed due to the increased WBC and PLT counts-induced an acute capillary endothelial edema (133).

Acarbose is a pseudotetrasaccharide produced as a natural microbial product of *Actinoplanes* strain SE 50. It binds to oligosaccharide binding site of alpha-glucosidase enzymes in the brush border of the small intestinal mucosa with a dose-dependent manner, reversibly and competitively. It inhibits glycoamylase, sucrase, maltase, dextranase, and pancreatic alpha-amylase. It has little affinity for isomaltase but does not have any effect on beta-glucosidases such as lactase. By this way, it delays the intestinal hydrolysis of oligo- and disaccharides mainly in the upper half of the small intestine. As a result, the absorption of monosaccharides is delayed, and transport into the circulation is interrupted. Its effects may prolong up to 5 hours. The suppression of alpha-glucosidases is persistent with long-term use. Its usage results with carbohydrates appearing in the colon where bacterial fermentation occurs, and causes flatulence, loose stool, and abdominal discomfort (134). If started with a lower dosage and titrated slowly, side effects are tolerable (135). Long-term use increases colonic bacterial mass that of lactobacteria in particular. The finally impaired carbohydrate absorption, increased bacterial carbohydrate fermentation, and fecal acidification mimic effects of lactulose in portosystemic encephalopathy. So acarbose has a favourable therapeutic profile for the long-term use even in cirrhosis. Similarly, observed changes in bacterial flora and decreased stool pH and beta-hydroxybutyrate may be associated with anti-proliferative effects on the epithelial cells of colon that may potentially decrease carcinogenesis. After oral administration, less than 2% of the unchanged drug enters into the circulation. Therefore there is no need for dosage adjustment in mild renal insufficiency. After a high carbohydrate meal, acarbose lowers the postprandial rise in blood glucose by 20% and secondarily FPG by 15% (136). The initial improvement in blood glucose tends to be modest, but efficacy steadily improves with the long-term use. Its beneficial effects on serum lipids were also seen with a dose-dependent manner (136), because dietary carbohydrates are key precursors of lipogenesis, and insulin plays a central role for postprandial lipid metabolism. Carbohydrate-induced postprandial triglycerides synthesis is reduced for several hours, so acarbose lowers plasma triglycerides levels (136). The same beneficial effect is also seen in

non-diabetic patients with hypertriglyceridemia, and acarbose reduced LDL significantly, and HDL remained as unchanged in hyperinsulinemic and overweight patients with impaired glucose tolerance (IGT) (137). Significantly elevated ursocholic acids in the stool appear to be the additive endpoint of a decreased rate of absorption and increased intestinal motility due to the changes of intestinal flora. Acarbose may lower LDL via increased fecal bifido bacteria and biliary acids. Acarbose together with insulin was identified to be associated with a greater improvement in the oxidative stress and inflammation in DM (138). Probably, acarbose improves release of glucagon-like peptide-1, inhibits PLT activation, increases epithelial nitrous oxide synthase activity and nitrous oxide concentrations, promotes weight loss, decreases BP, and eventually prevents endothelial dysfunction (136). So it prevents atherosclerotic endpoints of excess fat tissue even in the absence of IGT or DM (139, 140). Although some authors reported as opposite (141), it should be used as the first-line antidiabetic agent. Based on more than 40 years of use, numerous studies did not show any significant side effect or toxicity (142). Although 25.9% of patients stopped metformin due to excessive anorexia (143), only 10.6% stopped acarbose due to an excessive flatulence or loose stool (144).

Metformin is a biguanide, and it is not metabolized, and 90% of absorbed drug is eliminated as unchanged in the urine. Plasma protein binding is negligible, so the drug is dialyzable. According to literature, antihyperglycemic effect of metformin is largely caused by inhibition of hepatic gluconeogenesis, increased insulin-mediated glucose disposal, inhibition of fatty acid oxidation, and reduction of intestinal glucose absorption (145, 146). Precise mechanism of intracellular action of metformin remains as unknown. Interestingly, 25.9% of patients stopped metformin due to the excessively lost appetite (143). Additionally, 14.1% of patients with overweight or obesity in the metformin group rose either to normal weight or overweight group by weight loss without a diet regimen (143). According to our opinion, the major effect of metformin is an inhibition of appetite. Similar results indicating the beneficial effects on the BMI, BP, FPG, and lipids were also reported (147, 148). Probably the major component of the metabolic syndrome may be the excess fat tissue. So treatment of excess fat tissue with acarbose plus metformin will probably prevent not only IGT or DM but also the other atherosclerotic endpoints.

As a conclusion, hardened RBC-induced capillary endothelial cell damage terminates with end-organ deficiencies in early decades in the SCD. Although atherosclerotic endpoints are so common, we detected no case of DM probably due to lower excess fat tissue. As the most common cause of CRD, DM may be a reversible insufficiency of pancreas against excess fat tissue in early phases. Increased blood and insulin needs of excess fat tissue in contrast to decreased blood supply of excess tissue and pancreas both due to excess pressure on vasculature, externally and atherosclerosis, internally may be important in the development of DM. Acarbose

and metformin are safe, cheap, oral, long-term used, and effective drugs for loss of excess fat tissue which may even be curative in early phases of DM before development of other atherosclerotic endpoints.

References

1. Widlansky ME, Gokce N, Keaney JF Jr, Vita JA. The clinical implications of endothelial dysfunction. *J Am Coll Cardiol* 2003; 42(7): 1149-60.
2. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005; 365(9468): 1415-28.
3. Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. *J Hypertens* 2006; 24(10): 2009-16.
4. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; 106(25): 3143-421.
5. Helvacı MR, Aydın LY, Aydın Y. Digital clubbing may be an indicator of systemic atherosclerosis even at microvascular level. *HealthMED* 2012; 6(12): 3977-81.
6. Anderson RN, Smith BL. Deaths: leading causes for 2001. *Natl Vital Stat Rep* 2003; 52(9): 1-85.
7. Helvacı MR, Gokce C, Davran R, Akkucuk S, Ugur M, Oruc C. Mortal quintet of sickle cell diseases. *Int J Clin Exp Med* 2015; 8(7): 11442-8.
8. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. *N Engl J Med* 1994; 330(23): 1639-44.
9. Helvacı MR, Yaprak M, Abyad A, Pocock L. Atherosclerotic background of hepatosteatosis in sickle cell diseases. *World Family Med* 2018; 16(3): 12-8.
10. Helvacı MR, Kaya H. Effect of sickle cell diseases on height and weight. *Pak J Med Sci* 2011; 27(2): 361-4.
11. Helvacı MR, Aydın Y, Ayyıldız O. Hydroxyurea may prolong survival of sickle cell patients by decreasing frequency of painful crises. *HealthMED* 2013; 7(8): 2327-32.
12. Mankad VN, Williams JP, Harpen MD, Mancini E, Longenecker G, Moore RB, et al. Magnetic resonance imaging of bone marrow in sickle cell disease: clinical, hematologic, and pathologic correlations. *Blood* 1990; 75(1): 274-83.
13. Helvacı MR, Aydın Y, Ayyıldız O. Clinical severity of sickle cell anemia alone and sickle cell diseases with thalassemias. *HealthMED* 2013; 7(7): 2028-33.
14. Fisher MR, Forfia PR, Chamera E, Houston-Harris T, Champion HC, Girgis RE, et al. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. *Am J Respir Crit Care Med* 2009; 179(7): 615-21.
15. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013; 187(4): 347-65.
16. Davies SC, Luce PJ, Win AA, Riordan JF, Brozovic M. Acute chest syndrome in sickle-cell disease. *Lancet* 1984; 1(8367): 36-8.

17. Vandemergel X, Renneboog B. Prevalence, aetiologies and significance of clubbing in a department of general internal medicine. *Eur J Intern Med* 2008; 19(5): 325-9.
18. Schamroth L. Personal experience. *S Afr Med J* 1976; 50(9): 297-300.
19. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999; 341(15): 1097-105.
20. Helvacı MR, Aydın Y, Gundogdu M. Smoking induced atherosclerosis in cancers. *HealthMED* 2012; 6(11): 3744-9.
21. Ross R. Atherosclerosis--an inflammatory disease. *N Engl J Med* 1999; 340(2): 115-26.
22. Ridker PM. High-sensitivity C-reactive protein: Potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. *Circulation* 2001; 103(13): 1813-8.
23. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. *JAMA* 1998; 279(18): 1477-82.
24. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *JAMA* 1999; 282(22): 2131-5.
25. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. *Obes Rev* 2002; 3(3): 147-56.
26. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. *Biomed Environ Sci* 2002; 15(3): 245-52.
27. Helvacı MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. *Int Heart J* 2007; 48(5): 605-13.
28. Heilbronn LK, Ravussin E. Calorie restriction and aging: review of the literature and implications for studies in humans. *Am J Clin Nutr* 2003; 78(3): 361-9.
29. Fodor JG, Tzerovska R, Dorner T, Rieder A. Do we diagnose and treat coronary heart disease differently in men and women? *Wien Med Wochenschr* 2004; 154(17-18): 423-5.
30. Helvacı MR, Aydın LY, Aydın Y. Chronic obstructive pulmonary disease may be one of the terminal end points of metabolic syndrome. *Pak J Med Sci* 2012; 28(3): 376-9.
31. Helvacı MR, Kayabasi Y, Celik O, Sencan H, Abyad A, Pocock L. Smoking causes a moderate or severe inflammatory process in human body. *Am J Biomed Sci & Res* 2023; 7(6): 694-702.
32. Grunberg NE, Greenwood MR, Collins F, Epstein LH, Hatsukami D, Niaura R, et al. National working conference on smoking and body weight. Task Force 1: Mechanisms relevant to the relations between cigarette smoking and body weight. *Health Psychol* 1992; 11: 4-9.
33. Helvacı MR, Camci C, Nisa EK, Ersahin T, Atabay A, Alrawii I, Ture Y, Abyad A, Pocock L. Severity of sickle cell diseases restricts smoking. *Ann Med Medical Res* 2024; 7: 1074.
34. Walker JF, Collins LC, Rowell PP, Goldsmith LJ, Moffatt RJ, Stamford BA. The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity. *Nicotine Tob Res* 1999; 1(4): 365-70.
35. Hughes JR, Hatsukami DK. Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight. *J Subst Abuse* 1997; 9: 151-9.
36. Miyata G, Meguid MM, Varma M, Fetissov SO, Kim HJ. Nicotine alters the usual reciprocity between meal size and meal number in female rat. *Physiol Behav* 2001; 74(1-2): 169-76.
37. Froom P, Melamed S, Benbassat J. Smoking cessation and weight gain. *J Fam Pract* 1998; 46(6): 460-4.
38. Helvacı MR, Kaya H, Gundogdu M. Gender differences in coronary heart disease in Turkey. *Pak J Med Sci* 2012; 28(1): 40-4.
39. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. *BMJ* 1998; 316(7137): 1043-7.
40. Helvacı MR, Kabay S, Gulcan E. A physiologic events' cascade, irritable bowel syndrome, may even terminate with urolithiasis. *J Health Sci* 2006; 52(4): 478-81.
41. Helvacı MR, Dede G, Yildirim Y, Salaz S, Abyad A, Pocock L. Smoking may even cause irritable bowel syndrome. *World Family Med* 2019; 17(3): 28-33.
42. Helvacı MR, Algin MC, Kaya H. Irritable bowel syndrome and chronic gastritis, hemorrhoid, urolithiasis. *Eurasian J Med* 2009; 41(3): 158-61.
43. Kamimura D, Loprinzi PD, Wang W, Suzuki T, Butler KR, Mosley TH, et al. Physical activity is associated with reduced left ventricular mass in obese and hypertensive African Americans. *Am J Hypertens* 2017; 30(6): 617-23.
44. Sun Z, Lazar MA. Dissociating fatty liver and diabetes. *Trends Endocrinol Metab* 2013; 24(1): 4-12.
45. Rastogi A, Sakhuja P, Kumar A, Hissar S, Jain A, Gondal R, et al. Steatosis in chronic hepatitis B: prevalence and correlation with biochemical, histologic, viral, and metabolic parameters. *Indian J Pathol Microbiol* 2011; 54(3): 454-9.
46. Köse D, Erol C, Kaya F, Koplay M, Köksal Y. Development of fatty liver in children with non-Hodgkin lymphoma. *Turk J Pediatr* 2014; 56(4): 399-403.
47. Aktas E, Uzman M, Yildirim O, Sahin B, Buyukcam F, Aktas B, et al. Assessment of hepatic steatosis on contrast enhanced computed tomography in patients with colorectal cancer. *Int J Clin Exp Med* 2014; 7(11): 4342-6.
48. Balcik OS, Akdeniz D, Cipil H, Ikizek M, Uysal S, Kosar A, et al. Serum thrombopoietin levels in patients with non-alcoholic fatty liver disease. *Saudi Med J* 2012; 33(1): 30-3.
49. Çiftci A, Yılmaz B, Köklü S, Yüksel O, Özsoy M, Erden G, et al. Serum levels of nitrate, nitrite and advanced oxidation protein products (AOPP) in patients with nonalcoholic fatty liver disease. *Acta Gastroenterol Belg* 2015; 78(2): 201-5.
50. Kucukazman M, Ata N, Yavuz B, Dal K, Sen O, Deveci OS, et al. Evaluation of early atherosclerosis markers in patients with nonalcoholic fatty liver disease. *Eur J Gastroenterol Hepatol* 2013; 25(2): 147-51.

51. Ağaç MT, Korkmaz L, Cavusoglu G, Karadeniz AG, Ağaç S, Bektas H, et al. Association between nonalcoholic fatty liver disease and coronary artery disease complexity in patients with acute coronary syndrome: a pilot study. *Angiology* 2013; 64(8): 604-8.
52. Inci MF, Özkan F, Ark B, Vurdem ÜE, Ege MR, Sincer I, et al. Sonographic evaluation for predicting the presence and severity of coronary artery disease. *Ultrasound Q* 2013; 29(2): 125-30.
53. Öztürk H, Gümrükçüoğlu HA, Yaman M, Akyol A, Öztürk Ş, Akdağ S, et al. Hepatosteatos and carotid intima-media thickness in patients with myocardial infarction. *J Med Ultrason* (2001) 2016; 43(1): 77-82.
54. Karasin M, Tokgoz O, Serifoglu I, Oz I, Erdem O. The Doppler ultrasonographic evaluation of hemodynamic changes in hepatic vascular structures in patients with hepatosteatos. *Pol J Radiol* 2014; 79: 299-304.
55. Ozbulbul NI, Yurdakul M, Tola M. Does the visceral fat tissue show better correlation with the fatty replacement of the pancreas than with BMI? *Eurasian J Med* 2010; 42(1): 24-7.
56. Van Geenen EJ, Smits MM, Schreuder TC, van der Peet DL, Bloemena E, Mulder CJ. Nonalcoholic fatty liver disease is related to nonalcoholic fatty pancreas disease. *Pancreas* 2010; 39(8): 1185-90.
57. Stamm BH. Incidence and diagnostic significance of minor pathologic changes in the adult pancreas at autopsy: a systematic study of 112 autopsies in patients without known pancreatic disease. *Hum Pathol* 1984; 15(7): 677-83.
58. Lameloise N, Muzzin P, Prentki M, Assimacopoulos-Jeannet F. Uncoupling protein 2: a possible link between fatty acid excess and impaired glucose-induced insulin secretion? *Diabetes* 2001; 50(4): 803-9.
59. Aubert A, Garnet JM, Hammel P, Levy P, O'Toole D, Ruzsniowski P, et al. Diffuse primary fat replacement of the pancreas: an unusual cause of steatorrhea. *Gastroenterol Clin Biol* 2007; 31(3): 303-6.
60. Chai J, Liu P, Jin E, Su T, Zhang J, Shi K, et al. MRI chemical shift imaging of the fat content of the pancreas and liver of patients with type 2 diabetes mellitus. *Exp Ther Med* 2016; 11(2): 476-80.
61. Quintero JHR, Grosser R, Velez GR, Ramos-Santillan VO, Pereira X, Flores FM, et al. Safety and efficacy of roux-en-y gastric bypass in older aged patients. *Rev Col Bras Cir* 2022; 49: e20223332.
62. Kim MK, Chun HJ, Park JH, Yea DM, Baek KH, Song KH, et al. The association between ectopic fat in the pancreas and subclinical atherosclerosis in type 2 diabetes. *Diabetes Res Clin Pract* 2014; 106(3): 590-6.
63. Selim Kul, Aysegül Karadeniz, İhsan Dursun, Sinan Şahin, Ömer Faruk Çirakoğlu, Muhammet Raşit Sayın, et al. Non-Alcoholic Fatty Pancreas Disease is associated with Increased Epicardial Adipose Tissue and Aortic Intima-Media Thickness. *Acta Cardiol Sin* 2019; 35(2): 118-25.
64. Pezzilli R, Calculli L. Pancreatic steatosis: Is it related to either obesity or diabetes mellitus? *World J Diabetes* 2014; 5(4): 415-9.
65. Parfrey NA, Moore W, Hutchins GM. Is pain crisis a cause of death in sickle cell disease? *Am J Clin Pathol* 1985; 84(2): 209-12.
66. Helvacı MR, Ayyıldız O, Gundogdu M. Hydroxyurea therapy and parameters of health in sickle cell patients. *HealthMED* 2014; 8(4): 451-6.
67. Helvacı MR, Tonyali O, Yaprak M, Abyad A, Pocock L. Increased sexual performance of sickle cell patients with hydroxyurea. *World Family Med* 2019; 17(4): 28-33.
68. Helvacı MR, Aydın Y, Aydın LY, Sevinc A, Camci C, Abyad A, Pocock L. Red blood cell transfusions should be preserved just for emergencies in sickle cell diseases. *World Family Med* 2025; 23(4): 40-53.
69. Helvacı MR, Atci N, Ayyıldız O, Muftuoglu OE, Pocock L. Red blood cell supports in severe clinical conditions in sickle cell diseases. *World Family Med* 2016; 14(5): 11-8.
70. Helvacı MR, Ayyıldız O, Gundogdu M. Red blood cell transfusions and survival of sickle cell patients. *HealthMED* 2013; 7(11): 2907-12.
71. Helvacı MR, Cayir S, Halici H, Sevinc A, Camci C, Abyad A, Pocock L. Red blood cell transfusions may have the strongest analgesic effect during acute painful crises in sickle cell diseases. *Ann Clin Med Case Rep* 2024; V13(12): 1-12.
72. Miller ST, Sleeper LA, Pegelow CH, Enos LE, Wang WC, Weiner SJ, et al. Prediction of adverse outcomes in children with sickle cell disease. *N Engl J Med* 2000; 342(2): 83-9.
73. Balkaran B, Char G, Morris JS, Thomas PW, Serjeant BE, Serjeant GR. Stroke in a cohort of patients with homozygous sickle cell disease. *J Pediatr* 1992; 120(3): 360-6.
74. Cole TB, Sprinkle RH, Smith SJ, Buchanan GR. Intravenous narcotic therapy for children with severe sickle cell pain crisis. *Am J Dis Child* 1986; 140(12): 1255-9.
75. Miller BA, Platt O, Hope S, Dover G, Nathan DG. Influence of hydroxyurea on fetal hemoglobin production in vitro. *Blood* 1987; 70(6): 1824-9.
76. Platt OS. Is there treatment for sickle cell anemia? *N Engl J Med* 1988; 319(22): 1479-80.
77. Helvacı MR, Aydoğan F, Sevinc A, Camci C, Dilek I. Platelet and white blood cell counts in severity of sickle cell diseases. *Pren Med Argent* 2014; 100(1): 49-56.
78. Charache S. Mechanism of action of hydroxyurea in the management of sickle cell anemia in adults. *Semin Hematol* 1997; 34(3): 15-21.
79. Charache S, Barton FB, Moore RD, Terrin ML, Steinberg MH, Dover GJ, et al. Hydroxyurea and sickle cell anemia. Clinical utility of a myelosuppressive "switching" agent. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia. *Medicine (Baltimore)* 1996; 75(6): 300-26.
80. Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. *JAMA* 2003; 289(13): 1645-51.
81. Lebensburger JD, Miller ST, Howard TH, Casella JF, Brown RC, Lu M, et al; BABY HUG Investigators. Influence of severity of anemia on clinical findings in infants with sickle cell anemia: analyses from the BABY HUG study. *Pediatr Blood Cancer* 2012; 59(4): 675-8.

82. Toghi H, Konno S, Tamura K, Kimura B, Kawano K. Effects of low-to-high doses of aspirin on platelet aggregability and metabolites of thromboxane A2 and prostacyclin. *Stroke* 1992; 23(10): 1400-3.
83. Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009; 373(9678): 1849-60.
84. Algra AM, Rothwell PM. Effects of regular aspirin on long-term cancer incidence and metastasis: a systematic comparison of evidence from observational studies versus randomised trials. *Lancet Oncol* 2012; 13(5): 518-27.
85. Macdonald S. Aspirin use to be banned in under 16 year olds. *BMJ* 2002; 325(7371): 988.
86. Schrör K. Aspirin and Reye syndrome: a review of the evidence. *Paediatr Drugs* 2007; 9(3): 195-204.
87. Pugliese A, Beltramo T, Torre D. Reye's and Reye's-like syndromes. *Cell Biochem Funct* 2008; 26(7): 741-6.
88. Hurwitz ES. Reye's syndrome. *Epidemiol Rev* 1989; 11: 249-53.
89. Meremikwu MM, Okomo U. Sick cell disease. *BMJ Clin Evid* 2011; 2011: 2402.
90. Mohamed S, Fong CM, Ming YJ, Kori AN, Wahab SA, Ali ZM. Evaluation of an initiation regimen of warfarin for international normalized ratio target 2.0 to 3.0. *J Pharm Technol* 2021; 37(6): 286-92.
91. Chu MWA, Ruel M, Graeve A, Gerdisch MW, Ralph J, Damiano Jr RJ, Smith RL. Low-dose vs standard warfarin after mechanical mitral valve replacement: A randomized trial. *Ann Thorac Surg* 2023; 115(4): 929-38.
92. Crowther MA, Douketis JD, Schnurr T, Steidl L, Mera V, Ullrich C, et al. Oral vitamin K lowers the international normalized ratio more rapidly than subcutaneously vitamin K in the treatment of warfarin-associated coagulopathy. A randomized, controlled trial. *Ann Intern Med* 2002; 137(4): 251-4.
93. Brown DG, Wilkerson EC, Love WE. A review of traditional and novel oral anticoagulant and antiplatelet therapy for dermatologists and dermatologic surgeons. *J Am Acad Dermatol* 2015; 72(3): 524-34.
94. Delaney JA, Opatrný L, Brophy JM, Suissa S. Drug drug interactions between antithrombotic medications and the risk of gastrointestinal bleeding. *CMAJ* 2007; 177(4): 347-51.
95. Dahal K, Kunwar S, Rijal J, Schulman P, Lee J. Stroke, major bleeding, and mortality outcomes in warfarin users with atrial fibrillation and chronic kidney disease: a meta-analysis of observational studies. *Chest* 2016; 149(4): 951-9.
96. Chai-Adisaksopha C, Lorio A, Hillis C, Siegal D, Witt DM, Schulman S, et al. Warfarin resumption following anticoagulant-associated intracranial hemorrhage: A systematic review and meta-analysis. *Thromb Res* 2017; 160: 97-104.
97. Ferro JM, Coutinho JM, Dentali F, Kobayashi A, Alasheev A, Canhao P, et al. Safety and efficacy of dabigatran etexilate vs dose-adjusted warfarin in patients with cerebral venous thrombosis: A randomized clinical trial. *JAMA Neurol* 2019; 76(12): 1457-65.
98. Meade TW. Low-dose warfarin and low-dose aspirin in the primary prevention of ischemic heart disease. *Am J Cardiol* 1990; 65(6): 7C-11C.
99. Singer DE, Hughes RA, Gress DR, Sheehan MA, Oertel LB, Maraventano SW, et al. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1990; 323(22): 1505-11.
100. Levine M, Hirsh J, Gent M, Arnold A, Warr D, Falanya A, et al. Double-blind randomised trial of a very-low-dose warfarin for prevention of thromboembolism in stage IV breast cancer. *Lancet* 1994; 343(8902): 886-9.
101. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014; 383(9921): 955-62.
102. Vinogradova Y, Coupland C, Hill T, Hippisley-Cox J. Risks and benefits of direct oral anticoagulants versus warfarin in a real world setting: cohort study in primary care. *BMJ* 2018; 362: k2505.
103. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009; 361(12): 1139-51.
104. Helvacı MR, Cayir S, Halıcı H, Sevinc A, Camcı C, Abyad A, Pocock L. Terminal endpoints of systemic atherosclerotic processes in sickle cell diseases. *World Family Med* 2024; 22(5): 13-23.
105. Helvacı MR, Daglioglu MC, Halıcı H, Sevinc A, Camcı C, Abyad A, Pocock L. Low-dose aspirin plus low-dose warfarin may be the standard treatment regimen in Buerger's disease. *World Family Med* 2024; 22(6): 22-35.
106. Helvacı MR, Erden ES, Aydin LY. Atherosclerotic background of chronic obstructive pulmonary disease in sickle cell patients. *HealthMED* 2013; 7(2): 484-8.
107. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; 374(9691): 733-43.
108. Schoepf D, Heun R. Alcohol dependence and physical comorbidity: Increased prevalence but reduced relevance of individual comorbidities for hospital-based mortality during a 12.5-year observation period in general hospital admissions in urban North-West England. *Eur Psychiatry* 2015; 30(4): 459-68.
109. Singh G, Zhang W, Kuo YF, Sharma G. Association of Psychological Disorders With 30-Day Readmission Rates in Patients With COPD. *Chest* 2016; 149(4): 905-15.
110. Mannino DM, Watt G, Hole D, Gillis C, Hart C, McConnachie A, et al. The natural history of chronic obstructive pulmonary disease. *Eur Respir J* 2006; 27(3): 627-43.
111. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease. A case-control study in a health maintenance organization. *Arch Intern Med* 2000; 160(17): 2653-58.
112. Anthonisen NR, Connett JE, Enright PL, Manfreda J; Lung Health Study Research Group. Hospitalizations and mortality in the Lung Health Study. *Am J Respir Crit Care Med* 2002; 166(3): 333-9.

113. McGarvey LP, John M, Anderson JA, Zvarich M, Wise RA; TORCH Clinical Endpoint Committee. Ascertainment of cause-specific mortality in COPD: operations of the TORCH Clinical Endpoint Committee. *Thorax* 2007; 62(5): 411-5.
114. Trent JT, Kirsner RS. Leg ulcers in sickle cell disease. *Adv Skin Wound Care* 2004; 17(8): 410-6.
115. Minniti CP, Eckman J, Sebastiani P, Steinberg MH, Ballas SK. Leg ulcers in sickle cell disease. *Am J Hematol* 2010; 85(10): 831-3.
116. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA* 2014; 312(10): 1033-48.
117. Helvaci MR, Aydogan F, Sevinc A, Camci C, Dilek I. Platelet and white blood cell counts in severity of sickle cell diseases. *HealthMED* 2014; 8(4): 477-82.
118. Myers KA, Farquhar DR. The rational clinical examination. Does this patient have clubbing? *JAMA* 2001; 286(3): 341-7.
119. Toovey OT, Eisenhauer HJ. A new hypothesis on the mechanism of digital clubbing secondary to pulmonary pathologies. *Med Hypotheses* 2010; 75(6): 511-3.
120. Nassiri AA, Hakemi MS, Asadzadeh R, Faizei AM, Alatab S, Miri R, et al. Differences in cardiovascular disease risk factors associated with maximum and mean carotid intima-media thickness among hemodialysis patients. *Iran J Kidney Dis* 2012; 6(3): 203-8.
121. Helvaci MR, Gokce C, Sahan M, Hakimoglu S, Coskun M, Gozukara KH. Venous involvement in sickle cell diseases. *Int J Clin Exp Med* 2016; 9(6): 11950-7.
122. Xia M, Guerra N, Sukhova GK, Yang K, Miller CK, Shi GP, et al. Immune activation resulting from NKG2D/ligand interaction promotes atherosclerosis. *Circulation* 2011; 124(25): 2933-43.
123. Hall JE, Henegar JR, Dwyer TM, Liu J, da Silva AA, Kuo JJ, et al. Is obesity a major cause of chronic kidney disease? *Adv Ren Replace Ther* 2004; 11(1): 41-54.
124. Nerpin E, Ingelsson E, Risérus U, Helmersson-Karlqvist J, Sundström J, Jobs E, et al. Association between glomerular filtration rate and endothelial function in an elderly community cohort. *Atherosclerosis* 2012; 224(1): 242-6.
125. Stengel B, Tarver-Carr ME, Powe NR, Eberhardt MS, Brancati FL. Lifestyle factors, obesity and the risk of chronic kidney disease. *Epidemiology* 2003; 14(4): 479-87.
126. Bonora E, Targher G. Increased risk of cardiovascular disease and chronic kidney disease in NAFLD. *Nat Rev Gastroenterol Hepatol* 2012; 9(7): 372-81.
127. Helvaci MR, Cayir S, Halici H, Sevinc A, Camci C, Sencan H, Davran R, Abyad A, Pocock L. Acute chest syndrome and coronavirus disease may actually be genetically determined exaggerated immune response syndromes particularly in pulmonary capillaries. *World Family Med* 2024; 22(3): 6-16.
128. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, et al. Chronic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol* 2006; 17(7): 2034-47.
129. Helvaci MR, Aydin Y, Aydin LY. Atherosclerotic background of chronic kidney disease in sickle cell patients. *HealthMED* 2013; 7(9): 2532-7.
130. DeBaun MR, Gordon M, McKinstry RC, Noetzel MJ, White DA, Sarnaik SA, et al. Controlled trial of transfusions for silent cerebral infarcts in sickle cell anemia. *N Engl J Med* 2014; 371(8): 699-710.
131. Majumdar S, Miller M, Khan M, Gordon C, Forsythe A, Smith MG, et al. Outcome of overt stroke in sickle cell anaemia, a single institution's experience. *Br J Haematol* 2014; 165(5): 707-13.
132. Kossorotoff M, Grevent D, de Montalembert M. Cerebral vasculopathy in pediatric sickle-cell anemia. *Arch Pediatr* 2014; 21(4): 404-14.
133. Charache S, Terrin ML, Moore RD, Dover GJ, Barton FB, Eckert SV, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. *N Engl J Med* 1995; 332(20): 1317-22.
134. Rosak C, Mertes G. Critical evaluation of the role of acarbose in the treatment of diabetes: patient considerations. *Diabetes Metab Syndr Obes* 2012; 5: 357-67.
135. Salvatore T, Giugliano D. Pharmacokinetic-pharmacodynamic relationships of acarbose. *Clin Pharmacokinet* 1996; 30(2): 94-106.
136. DiNicolantonio JJ, Bhutani J, O'Keefe JH. Acarbose: safe and effective for lowering postprandial hyperglycaemia and improving cardiovascular outcomes. *Open Heart* 2015; 2(1): e000327.
137. Leonhardt W, Hanefeld M, Fischer S, Schulze J. Efficacy of alpha-glucosidase inhibitors on lipids in NIDDM subjects with moderate hyperlipidaemia. *Eur J Clin Invest* 1994; 24(3): 45-9.
138. Li FF, Fu LY, Xu XH, Su XF, Wu JD, Ye L, et al. Analysis of the add-on effect of alpha-glucosidase inhibitor, acarbose in insulin therapy: A pilot study. *Biomed Rep* 2016; 5(4): 461-6.
139. Standl E, Schnell O, Ceriello A. Postprandial hyperglycemia and glycemic variability: should we care? *Diabetes Care* 2011; 34(2): 120-7.
140. Helvaci MR, Halici H, Erdogan K, Sevinc A, Camci C, Abyad A, Pocock L. Acarbose in the treatment of chronic obstructive pulmonary disease. *World Family Med* 2025; 23(2): 37-52.
141. Wettergreen SA, Sheth S, Malveaux J. Effects of the addition of acarbose to insulin and non-insulin regimens in veterans with type 2 diabetes mellitus. *Pharm Pract (Granada)* 2016; 14(4): 832.
142. Van De Laar FA, Lucassen PL, Akkermans RP, Van de Lisdonk EH, Rutten GE, Van Weel C. Alpha-glucosidase inhibitors for patients with type 2 diabetes: results from a Cochrane systematic review and meta-analysis. *Diabetes Care* 2005; 28(1): 154-63.
143. Helvaci MR, Kaya H, Borazan A, Ozer C, Seyhanli M, Yalcin A. Metformin and parameters of physical health. *Intern Med* 2008; 47(8): 697-703.

144. Helvaci MR, Aydin Y, Varan G, Abyad A, Pocock L. Acarbose versus metformin in the treatment of metabolic syndrome. *World Family Med* 2018; 16(5): 10-15.
145. Stumvoll M, Nurjhan N, Perriello G, Dailey G, Gerich JE. Metabolic effects of metformin in non-insulin-dependent diabetes mellitus. *N Engl J Med* 1995; 333(9): 550-554.
146. Jackson RA, Hawa MI, Jaspan JB, Sim BM, Disilvio L, Featherbe D, et al. Mechanism of metformin action in non-insulin-dependent diabetes. *Diabetes* 1987; 36(5): 632-640.
147. Campbell IW, Howlett HC. Worldwide experience of metformin as an effective glucose-lowering agent: a meta-analysis. *Diabetes Metab Rev* 1995; 11(1): 57-62.
148. Helvaci MR, Kurt GD, Halici H, Sevinc A, Camci C, Abyad A, Pocock L. Metformin in the treatment of chronic renal disease. *World Family Med* 2025; 23(1): 12-27.

Rising Healthcare Costs: Need to Strengthen Health System More Today Than Ever Before

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We are passing through a challenging time with rising population, and limited resource expansion which is unable to meet growing needs of the world population, and quadruples disease burden, and climate change consequences among others(1). Healthcare needs of growing populations around the world are increasing and available resources are falling short to meet them. Governments are increasingly passing on healthcare burden to the private sector, with communities increasingly faced with out of pocket expenses to meet unmet healthcare needs.

Technological advancement is offering expensive diagnostic and treatment options (2). This is increasing healthcare costs, since lack of focus on health maintenance and disease prevention is causing need to diagnose and treat advanced disease at enormous costs, and disease outcomes are also far from satisfactory..

We are faced with quadruple disease burden having communicable diseases, non-communicable diseases, injuries and spiritual aspects needing to be addressed by healthcare professionals. This requires a comprehensive, holistic and multifaceted approach while dealing with healthcare issues at individual as well as a community level. It requires an approach that focuses on delivery of high quality, and cost effective and safe healthcare. Approaches should provide ongoing preventive, curative and rehabilitative healthcare. Such a scientific approach ensures not only efficient use of limited resources, it also positively impacts health related outcomes (3,4).

An effective population focused approach that effectively addresses and controls rising world population is long term solution to reduce burden on limited available resources (5). Population control can only be achieved with the active involvement of all stakeholders including governments, non-government organizations, private sector and academic institutions in particular. A human

development approach that focuses on education, health, social development and employment opportunities will be required to address increasing healthcare related challenges currently faced by our communities. An educated family that is gainfully employed and has access to resources, can efficiently manage healthcare needs. Women's education(6) is particularly important in development of communities and society.

Climate change(7) is again a growing challenge today. With rising global temperature, extreme weather conditions including droughts and floods cause food shortages and famines. Unless climate change is addressed on an urgent basis, healthcare provision and healthcare of individuals and communities will be compromised. Climate change consequences can be efficiently addressed with the active involvement of all stakeholders including governments, non-government organizations, private sector and academic institutions in particular. Carbon emissions and damage to ozone layer need to be addressed, with more focus on use of clean renewable energy resources.

Advent of Artificial Intelligence(8) is an opportunity to address growing healthcare needs of communities. It offers opportunity but at the same time there are challenges to ensure humane elements of healthcare are not compromised.

At healthcare delivery level, health system development is needed more today than ever before. It can help address enormous challenges we face today, to address growing healthcare needs on one hand and limited resources at the other.

Overall health system strengthening is required. It needs to be made operational and effective, so that it can positively impact health related outcomes.

Overall health systems need strengthening from primary health care, secondary, tertiary and Quaternary healthcare. Strengthening at various levels should be in proportion to requirement of health care needs. A primary health care focus should be on provision of cost effective, high quality and safe healthcare with positive impact on health related outcomes. Its focus on health maintenance and disease prevention reduces burden on other higher levels of healthcare that come with rising costs. Its strong focus on community based first contact care with individuals within community results in better healthcare related outcomes. Having a focus on strong communication skills and health education, healthcare interventions are better understood and followed by patients. A strong focus on person centered care(9) that not only addresses healthcare needs at individual level, ensures focus on health maintenance and disease prevention.

Secondary, tertiary and Quaternary healthcare levels are also very important for an effective health system. These higher levels of care require higher level of resources and come at higher costs. Therefore it becomes important to have an effective primary healthcare system, to effectively manage the majority of health care needs of the community, and at much lower costs and with positive health related outcomes. This will ensure that limited healthcare related disease burden is passed on to higher levels of health system, to ensure the efficient use of limited resources.

It is important to have an operational health system. The majority of healthcare needs of communities should be addressed at primary health care level and only those patients with need for higher levels of healthcare should be referred to higher levels of the health system. There should be provision for return to lower levels of health system once higher levels of health care are addressed. There should be provision for shared care that benefits patients.

A very strong focus is required on research(10) that addresses healthcare challenges and needs. Best practices based on latest evidence need to be implemented. Healthcare professional training programs are required to ensure presence of an effective healthcare delivery workforce. It is important to develop strong leadership skills among healthcare professionals to help bring positive health related change in society.

Today we stand at cross roads. Efforts we put in place today will determine how we effectively tackle rising healthcare related costs in a resource constrained world. We need to act now, to ensure health of future generations.

References

1. Sox HC. Understanding rising health care costs: introducing a series of articles. *Ann Intern Med.* 2005 May 17;142(10):865.
2. Pavel M, Jimison HB, Wactlar HD, Hayes TL, Barkis W, Skapik J, Kaye J. The role of technology and engineering models in transforming healthcare. *IEEE Rev Biomed Eng.* 2013;6:156-77.
3. Qidwai W. Delivering Healthcare Services in Resource Constraint Countries Like Pakistan: Sustainable Options. *J Coll Physicians Surg Pak.* 2015 Jun;25(6):393-4.
4. Qidwai W. Healthcare delivery system improvements: a way forward to improve health in developing countries and Pakistan. *J Coll Physicians Surg Pak.* 2013 May;23(5):313-4.
5. De Silva T, Tenreyro S. Population Control Policies and Fertility Convergence. *J Econ Perspect.* 2017;31(4):205-28.
6. Mayuzumi K. Rethinking literacy and women's health: a Bangladesh case study. *Health Care Women Int.* 2004 Jun-Jul;25(6):504-26.
7. Campbell-Lendrum D, Neville T, Schweizer C, Neira M. Climate change and health: three grand challenges. *Nat Med.* 2023 Jul;29(7):1631-1638.
8. Liu PR, Lu L, Zhang JY, Huo TT, Liu SX, Ye ZW. Application of Artificial Intelligence in Medicine: An Overview. *Curr Med Sci.* 2021 Dec;41(6):1105-1115. doi: 10.1007/s11596-021-2474-3. Epub 2021 Dec 6.
9. Qidwai, W., Kazmi, Z., Nanji, K. (2015). Patients' attitudes and perceptions regarding person centered care: results of a survey from an urban city of Pakistan. *European Journal for Person Centered Healthcare*, 3(1).
10. Kidd M, Manning G, Howe A, Qidwai W, Beasley JW, van Weel