What contributes to lack of hypertension awareness in an urban population?

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UNIVERSITY OF ZAGREB

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What Contributes To Lack Of Hypertension Awareness In An Urban Population?

Graduate thesis



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Abbreviation

CVD	Cardiovascular disease
NCD	Non-communicable diseases
BP	Blood pressure
РН	Public health
НРТ	Hypertension
DALY	Disability adjusted life years
РНС	Public health care
НС	Health care
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
GFR	Glomerular filtration rate
CBC	Complete blood count
NHANES	National Health and Nutrition Examination Survey
CDC	Center for disease control
WHO	World health organization
НСР	Health care provider
GP	General practitioner

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Abstract

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Cardiovascular diseases (CVD) are responsible for the largest proportion of noncommunicable disease (NCD) related deaths below the age of 70 years. This primarily includes conditions caused by high blood pressure (BP), which is a major health implication within our ageing society.

Nations have implemented cost-efficient and applicable interventions, with success rates in improving public health (PH) and reducing BP, with implemented goals and action plan-programs; including comprehensive primary prevention for management over the last few decades; both pharmacologically and lifestyle changes.

There is an increase in awareness from the early 2000s till today. Improvements regarding awareness have occurred in urban population, as a result of programs implemented for primary prevention. But the numbers are far from optimal as high rates of morbidity and mortality of the diseases caused by hypertension (HPT) still contributes to the leading cause of CVD's. Prevalence of HPT is still high as population is growing, aging, and urbanization and globalization of unhealthy lifestyles increasing.

Increased prevalence of HPT and the fact that the 'rule of halves' still is valid in many urban populations, with still high numbers of unawareness, shows we still have not yet reached our goal of increasing awareness and decreasing uncontrolled HPT.

Amassed public knowledge and education by primary prevention intervention policies. Therefore, we still need improvements in screening criteria's and diagnostic protocols, education, and finally, adequate treatment.

Key words: Hypertension, Awareness, Primary prevention.

Sažetak

Naslov: Uzroci Neznanja o Postojanju Viskog Krvnog Tlak u Urban Populaciji

Autor: Tara Mhedin

Kardiovaskularne bolesti kao nezarazne bolesti glavni su uzrok smrtnosti osoba mlađih od 70 godina. Primarno uključuju stanja i bolesti uzrokovane visokim krvnim tlakom, što je važna zdravstvena implikacija u našem društvu koje stari. Mnoge nacije su implementirale novčano isplative i primjenjive intervencije koje su pokazale uspjeh u smanjenju krvnog tlaka i u poboljšanju javnog zdravstva. Tijekom posljednjih nekoliko desetljeća provedeni su programi i ciljevi akcijskog plana uključujući sveobuhvatnu primarnu prevenciju, farmakološki pristup i promjenu načina života.

Od ranih 2000-ih do danas cjelokupna populacija svjesnija je problema. Najveći pomak se odvio u urbanoj populaciji kao rezultat implementiranog programa za primarnu prevenciju. No, brojke su daleko od optimalnih, jer visoke stope morbiditeta i mortaliteta uzrokovane hipertenzijom i dalje pridonose vodećom uzroku kardiovaskularnih bolesti. Kako populacija brojčano raste, stari, a urbanizacija i globalizacija su kao nezdravi načini života u porastu, tako raste i rasprostranjenost visokog krvnog tlaka.

Povećana rasprostranjenost visokog krvnog tlaka i činjenica da je "pravilo polovica" i dalje važeće u urbanim sredinama, s još uvijek visokim brojem neinformiranih ljudi pokazuje nam da još uvijek nismo dostigli cilj o povećanju svjesnosti i smanjenju nekontrolirane hipertenzije.

Prikupljeno javno znanje i edukacija kroz primarnu preventivnu intervencijsku politiku pokazalo se uspješnim, ali su nam još uvijek potrebna dodatna poboljšanja kriterija za trijažu, te poboljšanja dijagnostičkih protokola, edukacije i odgovarajućeg liječenja.

Ključne riječi: Hipertenzija, svjesnost, primarna prevencija.

1.0 Introduction

NCD's today have become today's world leading cause of morbidity and mortality due to numerous factors, such as: growing urbanization, an aging population, increased income and globalization of increasing sedentary lifestyles and smoking and unhealthy diet [1,2]. HPT and its burden (effect mostly populations in low- and middle-income countries, where health systems and education systems are weaker) is perhaps the most significant risk factor for CVD's, (which is the number one cause of death) accounting for 45% of all heart disease-related deaths and 51% of deaths due to stroke [1,2,3].

HPT is however becoming a worldwide epidemic, even in high-income countries, as one of the leading behavioral risk factors to which 13% of the global deaths are attributed [1,2,3]. HPT, the primary cause of almost half of all ischemic heart diseases and strokes, also contributes to the development of hemorrhagic stroke, kidney failure, premature death and disability and metabolic syndrome [3,4]. HPT causes about 7.5-9.5 million deaths every year and accounts for 57 million disability adjusted life years (DALY) [5]. The 'rule of halves' although decreasing, is still valid in some urban populations [6], although the Asian-Indian paradox referring to high prevalence of heart diseases despite lower presence of the traditional risk factors also contributes to the high prevalence in those areas [7]. Primary health care (PHC) level is one affordable way to tackle today's urban HPT unawareness [8,9,10]. Collaboration between PHC and PH is seen as one strategy to address the principles of equity and access in health care (HC) and to meet the goals of "health for all" [11] as outlined in the Alma Ata Declaration.

1.1 Definition

Normal adult BP is defined as a systolic blood pressure (SBP) of 120 mm Hg and a diastolic blood pressure (DBP) of 80 mm Hg [12]. HPT is defined as a SBP of 140 mm Hg or more, or a DBP of 90 mm Hg or more, or taking antihypertensive medication [12].

HPT may be primary or secondary [13]. Depending on the cause, primary or essential HPT, which accounts for 90-95% of adult cases, develop as a result of environmental or genetic causes [13]. Secondary HPT has multiple etiologies, including renal, vascular, and endocrine causes [13].

1.2 Pathophysiology

In the majority of cases, there is no known cause for primary HPT [14]. In general terms, the harder the heart has to work in order to pump blood when the pressure in the blood vessels is higher [14]. Uncontrolled, HPT can lead to a heart attack, an enlargement of the heart and eventually heart failure [15]. The high BP in the blood vessels may lead to aneurysms causing them to clog, burst and cause blood to leak out into the brain causing a stroke [14]. HPT can also lead to kidney failure, blindness, rupture of blood vessels and cognitive impairment [14] and contributes to metabolic syndrome [4].

According to the WHO; the main Factors that contribute to the development of high blood pressure and its complications are [2]; *Social determinants and drivers* (globalization, urbanization, aging, education, income, housing) determining *behavioral risk factors* (unhealthy diet, tobacco use, physical inactivity and harmful use of drugs) that can increase the *metabolic risk factors* (High BP, obesity, diabetes, increased blood lipids) leading to *CVD*'s.

1.3 Risk Factors

CVD's are caused by many risk factors. Some are non-modifiable while some can be modified, treated and controlled.

The non-modifiable risk factors for HPT according to the World Heart Federation [15]:

Age

The probability of CVD's increases with advancing age. Physiological changes of the heart, comes with increasing age, even in the absence of disease. Stiffening of cardiac muscle causes a less efficient pumping of blood from the heart to the rest of the circulation.

Gender

The male sex is at greater risk of CVD's than a pre-menopausal woman. Post-menopausal women have lost the protective effects of estrogen and have the same risks as a man.

Family history

A positive history of first-degree blood relative before the age of 55 years (for a male relative) or 65 years (for a female relative) increases the risk of CVD development.

Modifiable risk factors for HPT according to the World Heart Federation [15]:

HPT, smoking, hyperglycemia, physical inactivity, unhealthy diet, high cholesterol and lipids, overweight and obesity; increases the chances of HPT and CVD's [15,16]. Changing or reducing risk factors for high BP can reduce the chances of CVD's. Patients should be encouraged to reduce factors contributing to CVD's.

According to the WHO global health observatory data, the risk factors for CVD's, doubles for each increased increment of 20/10 mmHg of BP starting as low as 115/75 mm Hg [16], with more than a twofold difference increased risk in CVD's with BP 130-139/85-89 when compared with BP 120/80 [17]. According to Framingham study population research, it is also important to distinguish between usual or average BP from normal or acceptable, which is the optimal one for avoiding the HPT related CVD's [18].

1.4 Symptoms of hypertension

This "invincible" disease rarely causes symptoms in early stages [2,5,14]. Once symptoms develop, it usually is a sign of organ damage and urgent treatment is needed. Symptoms when present can be headache, shortness of breath, dizziness, chest pain, palpitations of the heart and nose bleeds [2,5,12,14].

1.5 How to properly diagnose hypertension

Many tests are available in the evaluation of HPT. Critical approaches to laboratory and radiologic evaluation can avoid unnecessary expenses [19]. A proper evaluation involves performing a focused medical history and physical examination, accurate BP measuring, and results of routine laboratory studies including a 12-lead electrocardiogram [19].

Needed material for measurements:

There are electronic, mercury and aneroid devices that are used to measure BP. It is recommended to use electronic devices, given that mercury is toxic [18].

Hypertension workup primarily involves accurate BP measurement, a focused medical history, physical examination and a routine laboratory workup [20].

Accurately measuring the patient's BP [18,19,20].

- 1. Sitting quietly for 3-5 min
- 2. Inflate cuff 20-30 mmHg above loss of radial pulse
- 3. Deflate at 2 mmHg/second
- 4. 1st sound heard is SBP
- 5. Disappearance 2nd sound/ Korotkoff sound (phase5) is DBP

To confirm HPT, workup procedure should to be repeated about 2 months later for stage 1 and shorter if it is a new onset HPT or for higher stages. Further studies may be obtained if needed on basis of clinical findings and/or suspected secondary hypertension with evidence of end-organ damage [13]. Patients presenting with HPT should have a cardiovascular risk assessment, including tests for diabetes mellitus and other risk factors such using the risk prediction chart [21].

2.0 Epidemiological data on hypertension

2.1 Epidemiological data of hypertension prevalence

It is estimated that HPT causes about 7.5 million deaths every year and accounts for approximately 57 million DALYs [16]. National Health and Nutrition Examination Survey (NHANES) data through 1991, suggested that HPT prevalence was declining [22], while other reports indicate that people diagnosed with HPT has been increasing from 600 million in 1980 to 972 million people in 2000 [16,23]. This was more than 25% of the whole worlds population at that time. The prevalence of raised BP in adults aged 25 and over was around 40% in 2008 [16], and predicted to increase to 1.56 billion people by 2025, with the majority being in developing continents such as Africa and Asia [23,24]. This situation is starting to resemble the one observed in industrialized countries 20 years ago.

High prevalence and low control of HPT is attributed to factors [2,5,14] such as:

- population growth,
- ageing
- behavioral risk factors, such as increased average salary, unhealthy diet, harmful use of alcohol, lack of physical activity, excess weight and exposure to persistent stress (contributing to the negative effects of rapid urbanization)

2.2 Epidemiological data of uncontrolled hypertension

According to the center for disease control (CDC), more people with high BP (especially those 60 years or older) are aware of their condition today and receiving treatment for it [25].

Unfortunately, uncontrolled HPT is still high. Only about half of people with high BP have their condition controlled as data indicated that more then half of the patients

referred for a cardiac stress test had inadequate control and nearly one quarter had a BP above 160/100 mm Hg [26].

The aim of a study in England from May 2010 to July 2012 was to identify the characteristics of individuals who where missed by the general health check-ups with HPT without a previous history of CVD's in the general population. Out of 8933 hypertensive participants in the study, 408 where under no treatment [27]. Due to the fact that HPT is a 'hidden' disease, it was more likely to be diagnosed with more frequent consultations. The same study also concluded an association between patients with untreated HPT and living alone [27].

There seems to have been a slight decrease of uncontrolled HPT between the years of 1980 and 2008. However, due to growth and aging of the population, there is still a high prevalence of uncontrolled HPT [2,5].

As the cornerstones of primary prevention programs for CVD's has been populationbased approaches and intensive targeted strategies in PH by policies and guidelines [28], However reports show that even once diagnosed with HPT, many do not receive adequate BP lowering treatment for it to reach optimal levels [29].

2.3 Epidemiological data and contributions to unawareness

Population-based cross-sectional studies in low and middle income countries in Africa, Asia and south America showed that HPT awareness and treatment among those who were aware, widely varied between communities, and there is a clear need to focus on primary preventions [30]. Awareness levels differed from 33.5% in India to 69% in Peru [30]. HPT is one major modifiable risk factor for CVD's and provides a powerful basis for preventing CVD complications [30]. Yet not handled very efficiently.

Primary prevention of HPT; promotes, interrupts and prevents the continuous costly cycle of its management [30]. Applying complementary strategies targeting a population- level, an individual-level and high-risk groups for HPT, has been a very successful way to decrease the absolute risk for HPT (even small decrement in SBP result in considerable reduction of BP-related diseases) [30]. These strategies applied early in life provides the greatest long term potential for avoiding the HPT precursors [30].

However even with efficient interventions in improving PH and despite precise guidelines for the detection and prevention of HPT, recent studies have shown that awareness is far from optimal as the "rule of haves" still apply in some urban areas [6].

The "rule of halves" was first published in a classic paper by Wilber et al. [31]; observing:

- 1. only one half of the patients with high BP have been diagnosed,
- 2. only half of those detected have been treated,
- 3. only half of those treated are on adequate treatment to reach a normal BP

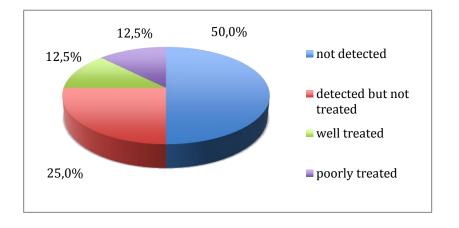


Chart 2: Rule of halves by Wilber and Barrow [31]:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3660552/

A study in Japan on HPT awareness from the national health survey in 1990s showed that more than 50% of men with HPT were unaware that they had high BP and less than 5% were under treatment [31]. The employed Canadian guidelines and criteria's of hypertension in Japan in 1990 was: A BP of 160/95 mmHg or being on medical treatment for hypertension, while the US had a stricter HPT criteria. Differences in guidelines may be attributed to the low awareness. The prevalence of SBP in Japan has decreased in all groups of men and women, but still high in people above 50 years of age [32].

Low rates of HPT treatment and control were the main causes of the high first-ever stroke incidence in China [33]. Women, a positive family history of HPT, obesity, diabetics and patients that suffered from a previous heart disease or stroke were less likely to be unaware of their hypertensive condition. During 2001-2010, the awareness of HPT in China increased from 69.8% to 74.5% in an urban elderly population [34]. A higher awareness of HPT was noted in higher educational levels, a higher BMI and positive family history of HPT.

In an urban population of Kerala (South India) in 2009, 33% of the hypertensive individuals were unaware of their condition [35]. Here the awareness was higher among the older population and low among the young. This could be explained by the popular belief that HPT only occurs in the elderly, with associated diabetes and the complete unawareness in the pre-hypertensive group about the needed and/or beneficial modifiable risk factors.

The general HPT awareness in Greece is very low compared the other western countries which strongly was associated with inadequate aspects of the HC systems today [36], again highlighting the importance of good prevention programs.

A cross sectional study conducted in a central city in Iran between 2005 and 2006 showing an increase in awareness, although still less then half of the hypertensive people being aware of their condition [37].

3.0 Discussion

NCD's is a global PH epidemic in the 21 century, with CVD's accounting for the majority of them and HPT being the leading risk factor for CVD's, causing 57 million DALYs [1,2,3,5].

The number of people diagnosed with HPT rose from being less then a million in 1980 to more than a billion in 2008 with a predicted increase to almost 1.6 billion by 2025 [16,23], with 75% being in low and middle income countries like the Asian African continents [24].

There is a rapid urbanization in China and India since 2014, with an expected additional increase of 292 million and 404 million people respectively by 2050 [38]. With the negative effects of rapid urbanization (which correlates with globalization of increasing sedentary lifestyles and smoking and the aging of population [1,2,5]), HPT and the treatment and control should urgently be recognized as a top priority in prevention and HC.

Governments today are overwhelmed and not able to keep up with the accelerating burden of NCD's [2]. It is clear that the financial burden will reach levels beyond the capacity of even wealthy countries to manage regarding this invincible killer. So the problem does not only lie in low- and middle-income countries.

HPT rarely causes symptoms in its early stages and is a "hidden" disease [2]. Misconceptions could be due to the terms "benign" or "essential" HPT (almost indicating that HPT is normal or even necessary with old age) or in criteria's with higher levels of BP to be considered as HPT. Therefore criteria's applied should be universally equal and maybe even stricter definitions and guidelines is required. Misbelieves about the condition of HPT only existing in elderly, the absolute involvement of other diseases (like diabetes) and that HPT always presents with symptoms [35], seems to be common. And therefore many people may go undiagnosed for a long time, allowing the worsening of the condition and following organ damage. The rule of halves, are decreasing but proven to still exist and therefore still be valid in some urban population [6]. Despite global efforts to tackle the challenge of NCD's the evolution of HPT rates are increasing [16,23,24].

Among untreated hypertensive subjects (which partially was due to unawareness) there was a significant association with; the male sex, age (<45 but below 60), less frequent visits to a health care provider (HCP) and general practitioner (GP) [39], dissatisfaction with recent medical care, high total cholesterol and lower body weights also lead to unawareness.

It is very understandable that people having dissatisfaction with medical care are less likely to back to for other medical advice, care or treatment. This emphasizes the importance of having ethical values when working in medicine and doctor-patient communication [40].

Has information not been adequate or the delivery of it from physicians? Is the information too expensive or has the disease been underestimated?

Despite abundant evidence demonstrating that CVD's and HPT can be prevented (by changing lifestyle behaviors and decreasing metabolic and physiological risk factors) many policy-makers still fail to consider NCD's as a global or national health priority [24]. Effective interventions such as tobacco control measures and salt reduction are available and abundant in many countries, but lacking adequate commitment [24].

The situation in developing countries is starting to resemble the one observed in industrialized countries 20 years ago and should alert serious concerns, considerations and commitments on all levels to preventing this growing epidemic.

4.0 Conclusion

HPT, the most significant risk factor for CVD's has been on a rise since the 1980s. This "Invincible killer" is predicted to increase to around 1.6 billion by 2025, increasing the burden even in high-income countries.

We have found that high prevalence is attributed to: rapid urbanization and globalization of behavioral and metabolic risk factors such as unhealthy lifestyles, smoking, aging of population, increased average income, higher exposure to stress and lower rates of physical activity.

Many people once finally diagnosed with HPT, is not always controlled to optimal levels and far too many people still today are unaware of their condition, even with access to cost-effective treatments and effective intervention programs available in urban communities due to the fact that they lack vital and adequate information about our times most common cause of morbidity and mortality.

To be the most successful, the general rule is to have the best information. Physicians and HC practitioners worldwide must understand the importance of conveying accurate and adequate information to the public about not only pharmacological treatments to HPT but also about the non-pharmacological ones, such as lifestyle modifications. The most superior proven intervention recommendations for prevention of HPT since 1993 has been; weight loss, reduction of dietary sodium intake, moderation in alcohol consumption and increased physical activity.

Doctor-patient communication is very important in conveying this type of information, how simple life style changes these individuals can make, have great impact on improving their BP and compliance.

There have been improvements in the prevalence, awareness, treatment and control over the past decades through primary intervention programs and better management plans. However the 'rule of halves' are still valid in many urban populations today and optimal levels of BP is far from satisfactory, even in countries where neither medical help and/or treatment costs is not an issue. HPT is not just an increase in BP, but it contributes to cardiovascular system and metabolic syndrome, thus much attention should be given to the high rates of prevalence and low rates of control, which are far from acceptable needing further research and improvements in HPT unawareness and control.

We have during this review acknowledged some contributions to the high level of prevalence and low levels of awareness that can help beat back the global threat of HPT and its burden.

By strengthened national surveillance programs and policies, with reliable information in monitoring and controlling the PH with HPT and increase the study of evidence based medicine in this area for better primary prevention.

• Decentralization of health care

Regulating the HC responsibilities from a central body to county level can off load the central and gives local governments more freedom in this area. It is important that every country and community understands their own local needs and find suitable solutions.

• Lack of commitment in government

WHO has acknowledged that many governments are overwhelmed by the speed of growth and rapidly growing urban cities and unable to keep pace with the expanding needs for newer policies, legislations, services and infrastructure that could help in overcoming CVD's. But governments must understand that there is significant financial and health gains associated with early detection, adequate treatment and good control of compared to secondary complication preventions which would include high budget surgical procedures. Programs to battle the problems of urbanization and globalization of unhealthy lifestyles early during the development of urban areas. People in developing countries are increasingly eating more and more unhealthy foods with higher levels of

total energy as well as being targeted by tobacco, alcohol and fast food marketing while availability of these products increases.

• Community wide changes in unhealthy behavior and risk factors

The National High Blood Pressure Program reports challenges in the prevention of HPT. These are factors at different levels of the HC system but also include people with different cultural norms, inadequate care, attention or understanding of the importance of health education, lack of reimbursement for HPT prevention services by the government.

HC professionals and policy developers must collaborate with the food industry to increase availability to products, which is healthier and contains less sodium.

Higher commitment is needed to prioritize effective and wide population intervention approaches to reduce high BP, similar to the ones addressing other major NCD's (since HPT is the leading cause of CVD's) such as salt reduction and physical activity.

• Improvements in resources and Primary prevention in PHC

According to National High Blood Pressure Program, PHC level (with increased collaboration between primary care and PH) is one affordable strategy to tackle still today's urban HPT unawareness and inadequate control. This way a large population can be reached. Unfortunately this seems to be the weakest level of the health system in many countries. By implementing integrated programs, systems and services in place to promote universal health and lead a multidisciplinary approach to support healthy lifestyles and to provide the population with access to adequate, good quality and cost effective HC and medications for management just as written in Alma Ata declaration.

Best buys- cost-effective strategy plans and policies should be implemented especially where availability of healthy food is restricted, for example in poor urban areas.

• Better management

Management is relatively good among industrialized countries, but lacking in many countries and cities with the rapid urbanization. The complexity of hospitals and HC systems should be studies as early as possible during the evolution of urbanization.

Medical practitioners still needs to improve in their doctor-patient communication (as less than half some treated hypertensive patients are on adequate control of their BP in some areas) and educate them that dissatisfaction with medical care should not ever be an issue for a patient, making them less likely to address their health issues after a previous dissatisfaction with HC or GP.

• Workplace health program's to reduce risk factor related behavior

No tolerance for tobacco smoking, support for physical activity and opportunities for healthy food areas. Workplace health programs have shown great success and therefore more focus should be given here.

• Focusing on all groups and not only the traditional high-risk ones

Among hypertensive subjects, unawareness was significantly associated with; the male sex (females can get detected more often due to extra checkups during pregnancy which can be a reason the prevalence is higher in men and the awareness lower), age (the common misconception that HPT only occurs in old age), less frequent visits to a HCP and GP (due to cultural differences or dissatisfaction with recent medical care), a high total cholesterol and low body weight (thinking they are healthy without knowing that the dangerous fat being the visceral one), no previous family history of HPT (thus not as enlightened in the matter of HPT) and smoking (which is a major risk factor) and last but not least, a lower level of education.

• Earlier detection

Earlier screening methods, rigorous strategies should begin in childhood and adolescence since it provides the greatest long term potential for lowering the overall burden of hypertensive related complications.

Focusing on younger men to raise the awareness of their higher prevalence and uncontrolled HPT.

• Misconceptions and misunderstood criteria's

Many people go undiagnosed because it rarely causes symptoms in the early stages. Increasing the public awareness about the silent nature of this disease that is occurring without symptoms. People seem to believe the disease is only of old age and always with accompanied symptoms and/ or diabetes mellitus. This could be a cause why awareness is lower in younger age. There could be a need for re-defining criteria's and standardization of BP measurements, informing about the Pathophysiology and mechanism increases the understanding of this disease that leads to HPT.

We all have a huge role to play in the prevention, awareness and control of HPT. This requires will and engagement not only on the part of governments and policy- makers, but also in HC workers whom are the physical forms and voices of health, the academic research community and families and individuals.

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To the apples of my eyes, Milo Mian and Matteo Mian. For my greatest wish, is the happiness of the two of you. Always dream big and aim for the stars and you will see new universes everyday.

In loving memory of Nahida Mhedin

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7.0 Curriculum Vitae

Tara Mhedin was born on January1982 to parents with Kurdish descent and lives in Stockholm, Sweden.

After graduating high school in Stockholm where she studied business and administration, she spent years living abroad to experience and learn about new cultures and languages. She spent some years in New York City, US and Malaga, Spain where she studied and worked. She started studying at the University of Stockholm, Stockholm Sweden during the years 2006-2008 where she took courses in Nature science as this branch of passion increased.

Tara started her medical studies in 2010 in Zagreb, Croatia at the University of Zagreb, School of medicine, English program. She studied physiology in Karolinska Institute as an exchange student in 2010 and 2011.