ARTICLE |
THE INFLUENCE OF SOY
AND SODIUM ON URIC
ACID LEVELS IN
HUMANS

WINNING ARTICLE |
IDENTIFYING FACTORS
THAT INFLUENCE TREAT-
MENT ADHERENCE IN
TUBERCULOSIS PATIENTS
IN THE GREATER-ACCRA
REGION, GHANA

AMSj

Amsterdam
Medical
Student
journal

Index

Editorial

*The challenge is to stay positive
and keep the spirits high.
Sky high.*

*In times of need, in times of crisis,
but also in peaceful times
- with luxury and comfort –
to not lose the drive to thrive.*

Even though the appalling Corona crisis impacted many lives, both physically and emotionally, the commitment of the authors and the reviewers resulted again in an edition to be proud of. For this 19th edition of AMSj, several students made great efforts to submit their theses with challenging research subjects. The members of the editorial board have also done their utmost to write the content for this edition. This includes an interesting interview, Changing Perspectives, Radiology Image and several news items. Additionally, we are happy to reveal a new item in our journal, which is kicked off by Devica Umans with her own personal story. Can you guess the name of this new item?

I am happy to have experienced the exponential growth of AMSj, in both the editorial board as well as the general board. The collaboration with the educational institutions of the universities led to the organization of several thesis workshops with very positive feedback from the participants. The generosity of VGT Cursus contributed as well to the encouragement of research among students.

Furthermore, we are looking for several possibilities to improve the editions of AMSj and refine the way we provide scientific education. We really can't wait to reveal the results!

With the above mentioned, I am ready to hand over my function as Editor-in-Chief (location VUmc) to Elise Beijer. I am convinced that she and Devica Umans will empower AMSj with their great enthusiasm and motivation. I am extremely grateful to the general and editorial board for this great journey and definitely looking forward to future achievements of AMSj.

Take a moment and enjoy this 19th edition of AMSj!

Yours sincerely,

Zar Popal
**(Former)
Editor-in-Chief
Amsterdam UMC,
location VUmc**

NEWS NEWS NEWS

The association between COVID-19 and olfactory and gustatory dysfunction

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2. Department of Otolaryngology & Head and Neck Surgery, Amsterdam UMC, location VUmc

The global pandemic of COVID-19 now has more than one million confirmed cases. The most common clinical presentations at onset of illness are fever, fatigue, dry cough and breathing difficulties. However, multiple cases of olfactory dysfunction (OD) have been reported in pre-confirmed COVID-19 patients, resulting in missed diagnoses since these patients were not suspected for COVID-19. For this reason, Lechien *et al* analyzed the occurrence of OD and gustatory dysfunction (GD) in 417 confirmed COVID-19 patients in Europe.[1] In this study, 85.6% of the patients experienced OD and 88.8% experienced GD. OD was the first symptom of COVID-19 in 11.8%. Interestingly, 80% of the patients with OD had no other nasal symptoms such as rhinorrhea or nasal obstruction. Notably, females were significantly more likely to have OD and GD in comparison to their male counterparts. Most patients (73%) recovered from their OD within 8 days after resolution. These results suggest that OD and GD should be recognized as possible COVID-19 symptoms, especially in females. In addition, both olfactory and gustatory functions may be affected in COVID-19 patients without other nasal symptoms. However, exact pathophysiological mechanisms of OD and GD in COVID-19 infections remain unclear. Therefore, future research is needed to examine the pathophysiological background.

1.   Lechien JR, Chiesa-Estomba CM, De Siati DR et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol (2020).

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Reverse total shoulder arthroplasty for elderly with displaced proximal humerus fractures

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2. Department of Trauma Surgery, Amsterdam UMC, Location AMC

Proximal humerus fractures (PHF) are commonly encountered within the older population and until recently, it remained unclear what the best surgical technique or implant is to treat these fractures. The DELPHI study, a randomized controlled, multicenter, single blinded trial demonstrated that reverse total shoulder arthroplasty (TSA) is superior to open reduction and internal fixation (ORIF) with angular stable plates in older adults with a displaced PHF. Between 2013 and 2017, patients aged 65 to 85 with a displaced PHF were allocated to either reverse TSA or ORIF. The primary outcome measure was the Constant Murley Score (CMS), which is a score to evaluate shoulder function within a range from 0 to 100. A higher score represents a better shoulder function. After 2 years, the mean CMS in the reverse TSA group was 68.0 points and 54.6 in the ORIF group. This difference was statistically significant (p-value<0.001). Moreover, 7 complications occurred in the TSA group, whereas 12 complications occurred in the ORIF group. In conclusion, older adults with a displaced PHF have higher functional outcome scores after TSA compared to ORIF. It is therefore recommended that a reverse TSA should be the treatment of choice if a patient is treated surgically.[1]

1.   Fraser AN, Bjørdal J, Wagle TM, et al. 2020. Reverse Shoulder Arthroplasty Is Superior to Plate Fixation at 2 Years for Displaced Proximal Humeral Fractures in the Elderly: A Multicenter Randomized Controlled Trial. J Bone Joint Surg Am. 2020;102(6):477-485. doi:10.2106/JBJS.19.01071

◀

Cancer care during the coronavirus pandemic

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2. Department of Medical Oncology, Amsterdam UMC, location AMC

Cancer patients are highly vulnerable to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Therefore, the coronavirus pandemic poses a significant challenge for the provision of oncology services. Recently, several oncology societies have issued guidelines for the management of cancer patients. These have been summarized in The Lancet Oncology.[1] First, hospital visits for cancer patients should be reduced by offering telemedicine and telephone consultations. This is especially important for immunocompromised patients, such as patients with malignancies that inherently impair the immune system and patients with treatment-induced immunosuppression. Second, exposure to possible sources of infection should be reduced by offering home delivery of oral medication instead of intravenously administered drugs, whenever possible. Third, priority levels should be established for the provision of systemic treatments and radiotherapy: patients who are receiving treatment with curative intent and with high chances of success should be prioritized. Prolonging treatment intervals could also be an option if the patient's condition permits. On the other hand, patients awaiting noncurative therapy, with a low likelihood of clinically meaningful benefit, should be assigned to lower priority levels. In conclusion, these steps constitute several approaches for maintaining an optimal continuity of cancer care, while mitigating the risk of infection for cancer patients.

1.   Burki, T. K. (2020). Cancer guidelines during the COVID-19 pandemic. Lancet Oncol.

◀

Artificial intelligence on its way to revolutionizing our daily clinical care

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1. Department of Surgery, Amsterdam UMC, Location VUmc

Machine learning (ML) is the cornerstone of many big data services, including Google. It is the application of artificial intelligence (AI) in which machines analyze and learn from massive amounts of data by recognizing hidden patterns. It uses mathematical models to learn without human intervention to generate predictive models in a more effective and accurate way. As such, it is transforming our current approach towards diagnostics and patient-based therapeutics entirely. Liver diseases are complex diseases that develop under the susceptibility of - and the interaction between - many variables.[1] In contrast to conventional studies, ML transcends the assumption that such variables form a linear association with outcomes by unveiling the unseen patterns between variables. Using quantifiable color information and stiffness values from shear wave elastography images, ML was able to categorize patients with a sensitivity of 93.5% and specificity of 81.2%, compared to liver biopsy.[2] In the field of liver transplantation, algorithms that were generated using artificial neural networks on clinical databases predicted 3-month graft survival and loss with AUC values of 0.81 and 0.82, respectively.[3] Evidently, ML has remarkable potential. Be aware, however, that the algorithm learns from data and that its performance depends on the quality of the data provided.

1.   Spann A, Yasodhara A, Kang J, et al. 2020. Applying Machine Learning in Liver Disease and Transplantation: a Comprehensive Review. Hepatology. 2020;71(3):1093-1105.
2.   Gatos I, Tsantis S, Spiliopoulos S, et al. 2017. A machine-learning algorithm toward color analysis for chronic liver disease classification, employing ultrasound shear wave elastography. Ultrasound Med Biol. 2017;43:1297-1810.
3.   Lau L, Kankanige Y, Rubistein B, et al. 2017. Machine-learning algorithms predict graft failure after liver transplantation. Transplantation. 2017;101:125-132.

◀

The impact of underlying cardiovascular disease and myocardial injury on COVID-19

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1. Department of Cardiology, Amsterdam UMC, Location AMC
2. Department of Cardiology, Amsterdam UMC, Location VUmc

Since the rapid spread of the newly recognized virus SARS-CoV-2, causing COVID-19, the number of fatalities caused by this virus has increased. The condition of some COVID-19 patients can deteriorate at a fast pace. Considerable concern regarding cardiovascular manifestations has been raised by clinical data of respiratory failure caused by this virus. Guo and colleagues studied 187 confirmed COVID-19 patients in the period of January 23rd to February 23rd 2020, of which 35% had underlying cardiovascular disease.[1] 28% of all patients presented with increased Troponin-T levels, assumedly associated with myocardial injury. Elevated Troponin-T levels were more often seen in patients with underlying cardiovascular disease compared to patients without cardiovascular disease (55% vs. 13%). Individuals with increased Troponin-T levels developed organ failure more frequently. Additionally, an elevated Troponin-T was associated with a staggering 60% mortality rate, compared to 9% if Troponin-T was normal. Unfortunately, this study could not demonstrate whether myocardial injury as expressed by an elevated Troponin-T level had a causal relationship with mortality, or whether this was merely indicating clinical deterioration, for example related to COVID-19-induced myocarditis, septic shock or severe hypoxemic respiratory failure. In conclusion, this study demonstrated a significant association between fatal outcomes due to COVID-19 and elevated Troponin-T levels, while the prognosis of individuals with normal Troponin-T levels was more favorable.

1. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020 Mar 27. doi:10.1001/jamacardio.2020.1017

PUBLISH YOUR CASE REPORT

Educational case? Interesting patient? Publish it!
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An unorthodox alarming symptom

Devica S. Umans[1]
1. Faculty of Medicine, Amsterdam UMC, Location AMC, University of Amsterdam

A few years ago, I worked at the General Practice Emergency Center (GPEC), where I performed telephone triage. I decided with what urgency patients needed to be seen by a physician.

I enjoyed this challenging work. One of the challenges was to make a clinical assessment of a patient I could not physically examine. Therefore, I was drilled to think in the urgency with which full clinical assessment is necessary, rather than to think in diagnoses. In triage, assessing alarming symptoms is emphasized, such as shortness of breath or throat ache with inability to swallow.

A second challenge was the constant time pressure. Telephone calls with patients were to take no longer than 10 minutes. The reason for this stringent time limit were the ever-growing wait times – on my worst days more than 45 minutes.

The wait times are a shame, but as I learned during my years at the GPEC, they can be valuable too.

To explain this, I must take you back to a patient whose parents called on a Thursday night. He was a young and healthy man in his twenties. He had had a fever, cold chills and muscle pains for a few days, but no alarming symptoms were present: no shortness of breath, adequate consciousness, he had been drinking and urinating. There was nothing that could make me assume this was more than a normal flu, with no immediate examination necessary. Yet there was something I couldn't put my finger on. So, I manually increased the urgency in the computer system and had him examined at the GPEC. He was found to have severe tachycardia and hypotension and was admitted to the hospital.

I had to think for a long time about what it was that made me know that this man needed further examination. After a while it finally clicked for me: this man's parents, who had raised him and who had undoubtedly seen him be sick growing up, looked at him and decided it was worth it to wait 45 minutes to receive care. The alarming symptom was the hurdle to receive health care.

Since then, I have always factored in this hurdle in my patient assessment, whether it's telephone wait times, uninsured patients, or patients leaving work to seek care. And now, I share this teachable moment with you in the hopes it may improve your own clinical practice.

Prof. dr. Rob van Hulst, MD, PhD

Interviewed by Larissa Heideman[1]
1. Faculty of Medicine, Amsterdam UMC, location AMC, University of Amsterdam, Amsterdam

Function as specialist:
Military specialist in diving and hyperbaric medicine

Current position:
- Head of the hyperbaric department and senior researcher anesthesiology Amsterdam UMC, Location AMC
- Medical consultant of the Navy, diving medical consultant NFI, Nederlands Forensisch Instituut

Publications: 70 papers

What are your research interests?
Pulmonary oxygen toxicity in divers and clinical patients, hyperbaric oxygen in wound healing, and hyperbaric oxygen in Crohn's disease and cerebral air embolism.

How did you become involved in hyperbaric medicine and research?
During my medical studies I learned to scuba dive and became an instructor. Before my clinical training (1980), I worked as a diving instructor at the Costa Brava in Spain for six months. During that period I was confronted with some diving accidents and therefore I became interested in the physiology of diving. I did a residency in the Navy (1983) for three months and they offered me a contract for six years including a two-year specialism in diving and submarine medicine.

As a Navy physician I also worked at the Naval base as a general practitioner (1986), sailed on board of a Naval ship for a one-year period (1987) and was part of a UN mission in Cambodia (1993) for six months with the Marines. I was selected for the Naval staff school for the higher and managing positions (1992). Because diving medicine became

a part of the occupational service of the Navy, I had to obtain my degree in occupational medicine. From 1996 onwards I was the director of the Diving and Submarine Medical Center in Den Helder. Meanwhile I did my PhD part-time, during a period of four years (1999-2003) in Rotterdam at the department of Experimental Anesthesiology. From June 2005 I had a position in the AMC, dept. of Anesthesiology for one day for research and clinical hyperbaric oxygen therapy (HBO). After my retirement from the Navy I continued my work and extended this to three days per week.

What have you learned from your experience at the Navy?
There are several things I learned in the Navy: (1) regularly train different exercises in case of the worst scenarios (''train as you fight''); (2) you have to improvise under certain difficult circumstances; (3) the people who you work with are important, be honest and grateful.

In 2015 you became an endowed professor of Anesthesiology with a special interest in hyperbaric medicine. How did you achieve this?
The Navy would like to continue research in diving medicine and therefore they were willing to finance a professorship for five years, which has recently been extended for another five years. Meanwhile I have PhD students who are basically navy physicians, doing part time research on military medicine items which have operational relevance. The field of hyperbaric and diving medicine covers two different worlds: hyperbaric medicine, which is more clinically focused, and includes

Prof. dr. Rob van Hulst, MD, PhD

CURRICULUM VITAE	
1957	Birth
1984	Graduation Medicine, University of Groningen (Rijksuniversiteit Groningen, RUG)
1996	Occupational physician
1985-2013	Joined the Navy (as colonel physician)
2003	PhD, Cerebral air embolism in an animal model, Erasmus Rotterdam
2014-present	Staff member dept anesthesiology
2015	Fellow Hyperbaric and Undersea Medicine (FUHM), USA
2015-present	Professor

treatment of wound healing and late radiation tissue injuries, while diving medicine is on decompression illness and oxygen toxicity. Both fields are more extended but you have to focus on a few topics.

As a professor you've had multiple publications attached to your name. Is there one in particular which has a special interest to you?
There are two publications: the first is by Thijs Wingelaar, navy doctor, who recently defended his PhD. He wrote an exhaustive review on pulmonary oxygen toxicity in divers (Wingelaar TT, et al. 2018. Frontiers in Psychology). The second is a publication on a protocol for treating Crohn's disease with HBO. This is a new indication for HBO

and I'm convinced that it will be ground-breaking in due time (Lansdorp N, et al. 2019. Undersea Hyperbaric Medicine).

How do you envision the future of hyperbaric medicine?
Hyperbaric medicine was a niche subject in the field and was not taken very seriously by a lot of colleagues, both in the Netherlands as well as internationally. By doing serious research involving young doctors, hopefully this field will be more academically based within five to ten years.

You've achieved a lot of things over the course of your career. What further ambitions do you have?
Starting as a young doctor with scuba diving as a hobby and ending as a professor in this field is a nice career, I realize. The ambition I have left for the upcoming years is to motivate young physicians to do research in this field.

Looking back on your career, is there anything you'd advise students?
It is still a big cliché but: "Work hard and follow your heart!"
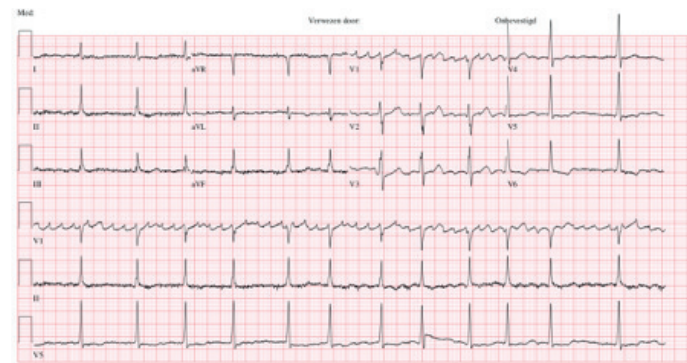
"Train as you fight"

VGT Practice Questions

QUESTION 1

What abnormality do you see on this ECG?
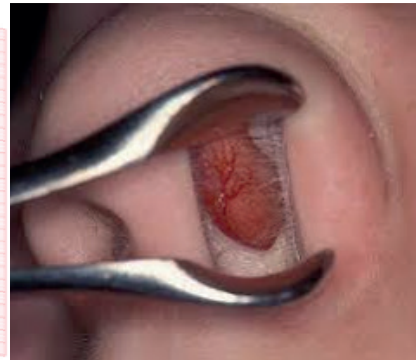
Tip: Try to always evaluate ECGs systematically

A.   Atrial fibrillation
B.   Atrial flutter
C.   Atrial tachycardia
D.   Sinus tachycardia

QUESTION 2

A 14-year-old boy visits the otorhinolaryngology (ENT) outpatient clinic due to recurrent epistaxis. Through inspection (rhinoscopia anterior) you find a certain structure to be the likely cause of the recurring nosebleeds. Which structure is in most cases the cause of nosebleeds in (young) children?

A.   Arteria ethmoidalis anterior
B.   Concha media
C.   Kiesselbach's plexus (locus Kiesselbachi)

EXPLANATION

Q1: Answer: A

What we see is a 12 lead ECG. Evaluating the ECG systematically:
- Frequency: approximately 70 bpm
- P wave: there are no clear P waves
- QRS complex: narrow QRS complexes (< 120 ms)
- Heart axis: normal (QRS is positive in I and aVF)
- R wave: normal R wave progression (R wave is larger than S wave in V3)
- ST segment: no ST elevations
- T wave: no T wave inversions

Conclusion: atrial fibrillation with a slow ventricular rate (70 bpm). Imperative for atrial fibrillation is the absence of P waves, indicated by minute oscillations, and a totally irregular ventricular rate. Usually the ventricular rate is abnormally high rather than low or normal.

EXPLANATION

Q2: Answer: C

The arteria ethmoidalis anterior and posterior anastomose with the septal branch of the arteria labia superior and the arteria sphenopalatina to form a plexus that is called 'locus Kiesselbachi'. In this region nosebleeds frequently occur, particularly in children. The cause is usually not one individual artery, but rather this plexus that is formed by multiple arteries.

The concha media is located on the lateral side of the nose, not on the septal side. Nosebleeds usually occur on the septal side. 90% of all nosebleeds occur in the locus Kiesselbachi. This is explained by external factors, mainly exposure to dry air through inhalation and mechanical trauma induced by fingernails through the habit of nose picking.

Changing perspectives in geriatric medicine - prescription habits

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2. DEPARTMENT OF NEUROLOGY, ALZHEIMER CENTER AMSTERDAM, AMSTERDAM UMC, LOCATION VUMC

As medical professionals want best for their patients, available medicines are prescribed generously when indicated, including preventive medicines. Guidelines describing treatment regimens are tenaciously followed, and this is where a problem arises when treating older patients. When following the guidelines, almost every older patient should receive large amounts of pills, resulting in polypharmacy and negative side effects.[1] Fortunately, the perspective on prescribing every indicated pill is changing.

One of the most striking examples of this changing perspective, is observed in the prescription of statins to reduce mortality and morbidity due to cardiovascular diseases. As these benefits do not hold true for every older patient, doctors now tend to be more cautious in prescribing statins.[2, 3]

In conclusion, there is a growing awareness of the fact that treatment effects are different in older patients due to the interplay of medical history, multimorbidity and polypharmacy. Prevention of mortality might not be the most important goal when life expectancy is short. To improve health of older patients, not every single guideline must be followed. Doctors should realize that sometimes it is better to stop medicine intake instead of prescribing it, thereby focusing on quality of life instead of lifespan.

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Identifying factors that influence treatment adherence in tuberculosis patients in the Greater-Accra Region, Ghana: A mixed method study

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BEST MANUSCRIPT OF EDITION 19!
We are proud to publish this exquisite manuscript by Jelle Nederstigt et al., which has been named the best article of edition 19! Therefore, Jelle is awarded a VGT Cursus FlexPack, which includes subscription to the course, a VGT Cursus Handbook and access to the E-learning with over 500 typical exam questions explained. Congratulations, Jelle!

ABSTRACT

INTRODUCTION There are theories attempting to understand the lack of adherence to treatment of tuberculosis (TB) in Ghana. None of these theories have proven useful and practically applicable, although shorter home-to-clinic distance has been associated with lower default rate. This research aims to identify and investigate factors contributing to treatment adherence of TB in the Greater-Accra Region, comparing urban and rural communities.
METHODS This was a cross-sectional mixed methods study used to identify factors contributing to treatment adherence in urban and rural communities. Participants included were patients with symptomatic pulmonary TB, confirmed by chest X-Ray or GeneXpert, between 18-70 years of age. The clinics were purposively selected and the default rate was determined by consulting the clinic's existing data. The data outcome was analyzed by a chi-squared test and a multinomial logistic regression. The interviews were recorded and analyzed for key themes.
RESULTS There was a non-significant result for default between communities. The qualitative analysis showed no difference between communities in correlation between default or death. Analysis of the quantitative design complemented by the in-depth qualitive analysis for both communities showed that a non-germ theory of disease, financial challenges, lack of support, co-morbidity and obstacles accessing health care in addition to an increase or decrease of symptoms can result in default of TB treatment.
CONCLUSION To increase treatment adherence the factors associated with default should be addressed irrespective of community.

INTRODUCTION

In Ghana, tuberculosis (TB) is still one of the biggest health challenges.[1, 2] With a current population of approximately 28 million people, an estimated 44,000 individuals are suffering from TB.[3] The National Tuberculosis Health Sector Strategic Plan for Ghana has the goal to reduce the 2012 TB mortality rate baseline of 4 deaths per 100,000 people by 35% by 2020 and of ending the TB epidemic in Ghana by 2035.[4] To realize these goals the default rate, defined as treatment interruption for at least two consecutive months, has to decrease. The de-fault rate of treatment in the Greater-Accra Region rose over the last three years from 1.6% in 2015 to 2.9% in 2017.[5] This is a substantial increase because the lack of treatment adherence causes an increase in drug resistant TB and higher mortality from TB.[6] According to previous research, the financial situation of the patient and cost of seeking and sustaining treatment is one of the factors influencing the default rate.[7, 8] Currently 64.1% of the TB patients in Ghana still face 'catastrophic financial costs'[9] and TB services are not covered by health insurance.[4] The relationship between public health insurance and treatment adherence in low-income countries is unclear.[10] Public health insurance is mandatory by design but there is no legal enforcement, thus deciding to obtain health insurance is still optional.[11]

There is little data available on factors influencing treatment adherence in Ghana.[7, 8, 12, 13] Additionally, there is no information about geographic influence on adherence, e.g. between urban and rural communities. This study aimed to answer two research questions: which factors influence treatment adherence in the Greater-Accra Region and what is the effect of residence in urban or rural communities in this area on TB treatment adherence? It was hypothesized that rural communities have a higher default rate due to a longer home-to-clinic distance[7] and that factors negatively influencing treatment adherence were: gender, increased costs, little knowledge of TB, non-germ theory of disease, experiencing obstacles accessing health care and addiction.[7, 8]

METHODS
Study setting
This study was conducted in the Greater-Accra Region of Ghana, the region with the third highest incidence rate in the country. Three hospitals and three clinics were selected through purposive sampling. These were preferred because these facilities had a high rate of TB patients attending, used the same patient registration system and were located in the same population cluster. A rural clinic was defined as a clinic in a distinct population cluster with less than 5,000 inhabitants.[14] The urban facilities were La General Hospital in the La Dade-Kotopon District and Lekma Hospital in the Lekma District. The rural clinics selected were Ga West Municipal Hospital, Pokuase Health Clinic, Amamorley Community Clinic and Oduman Polyclinic, all in the Ga West District.

Study design
This was a mixed methods study consisting of a quantitative retrospective cross-sectional study (phase 1) and a qualitative study with a partial concurrent-dependent design (phase 2&3).[15, 16] The quantitative study was used to identify a correlation between the factors emerging from the hypothesis including demographic questions and treatment adherence. The qualitative study was done to provide an in-depth understanding of how these factors influenced treatment adherence, using two semi-structured interviews, an entry-interview (phase 2) and an exit interview (phase 3).

Patient selection
Patients with symptomatic pulmonary TB, confirmed by chest X-Ray or GeneXpert, between 18-70 years of age, and who had signed informed consent for participation were included. Patients with a treatment duration longer than nine months were excluded. Patients attending the clinics were included in both study designs after diagnosis or collecting medication. Participants were not randomized. All participants were included during the intensive phase of treatment in which they attended the hospitals and clinics daily to pick up TB medication with exception of weekends. The intensive phase was the first two months for participants suffering from susceptible TB and four months for participants suffering from resistant TB. Participants attended facilities weekly to pick up TB-medication during the continuous phase of treatment, which were the remaining months of treatment.[17, 18] All participants were included during the first five weeks of this study. All patients in the Ga West District attended the Ga West Municipal hospital for diagnostic tests, but participants would pick up their medication in a hospital or clinic closest to their house. This facility determined in which community participants were included as participants attended the clinic with the shortest home-to-clinic distance.

Outcome Measures
The primary outcome measure of this study was patient default. Participants were considered defaulters if appointments to pick up their TB medication were missed for two consecutive months. Every appointment was documented by the facility, and this data was used to determine default. The secondary outcome measure was death.

Phase 1. Quantitative study
A questionnaire was developed for the quantitative part of this study to correlate the factors[7, 8, 19, 20] that were hypothesized to negatively influence treatment adherence with default. The main topics in the structured survey corresponded with the differ-

ent factors and were: demographic questions, socioeconomic status, mental and financial support, medical history, travel duration, socio-cultural beliefs and addiction.

Statistical analysis

A statistical analysis was performed for defaulters and non-defaulters in the whole population group and for each community to determine correlation with the different factors. This was done to correlate the different factors contributing to default for each community and to make a comparison between communities. Differences in factors were examined by using a chi-squared test and multinomial logistic regression with an alpha level of 0.05. The difference between the rural and urban communities in treatment adherence and the difference in factors contributing to default were examined using a chi-square test and logistic regression, respectively. A chi-square test was conducted for all categorical data. A multinomial logistic regression was conducted for all continuous data. To execute these tests the program Statistical Package for the Social Sciences (SPSS) (version 25) was used. The different topics of the survey were numbered and inserted in SPSS. This was done for the participants of the two areas separately and collectively. After data input, the program was run on the whole group to search for differences per factor.

Phase 2&3. Qualitative study

All interviews were conducted, recorded[21], transcribed and edited by the first author (JN). All non-English speaking participants were interviewed with the help of two translators who were trained TB health workers. Interviews were transcribed and checked with the interpreters for validation. All phase 1 participants were included in phase 2&3 if they had consented to the interview. The semi-structured interview in phase 2 was made with questions corresponding to survey topics. For example, when participants indicated on the survey that they believed that disease is caused by something else than germs, the researcher searched for an explanation for why the participant had this theory and why they had come to the clinic despite this belief. A deductive approach[22] was used to analyze the data in phase 2. A codebook was developed to analyze the data generated. The questions in the semi-structured interview in phase

3 were developed from the phase 2 code book and the preliminary statistical analysis. This interview corresponded to the phase 2 interview in codes and solely asked questions about factors assumed to be correlated with default. In both phases completers and defaulters were interviewed.

Sample size calculation

To calculate the sample size for this study, data of previous similar research was used.[23] A non-inferiority design[24], with the null hypothesis that there was no difference in default between area, was used. The response rate of a standard treatment group was 0.4. This meant that, to gain a power of 80% with a statistical significance of 95%, the study had to include 50 participants, 25 in each arm.

RESULTS
Phase 1. Quantitative study
Descriptive statistics of the study population
The mean age of the study population (n=50) was 40 years with 70% being male, which was consistent with TB patient demographics in Ghana (SUPPLEMENTARY TABLE 1).[25] There were no significant differences in demographic characteristics between communities. The majority of the participants defined themselves as lower class (58%). This corresponded with data showing that the majority of the TB patients is of lower class and higher-class patients are more likely to attend a private facility.[4] Over half of the population had health insurance (56%). Around two thirds of the population had challenges with money, such as difficulties buying food or paying for transport to work, in the recent year. A total of 88% reported a home-to-clinic distance of less than one hour. Only a smaller portion (18%) consulted a spiritualist, a shrine or other care providers such as the pharmacy before presentation at the hospital, although more than double of this percentage (39%) believed in another theory of disease than germ theory.

TB treatment adherence
Complete study population
In the total study group 4% of the participants defaulted and 6% died. There was no overall significant difference in default or death between the communities (p = 0.84). There was no significant difference in default or death between the commu-

nities according to gender (p = 0.64), having health insurance (p = 0.25), challenges with money over the last year(p = 0.46), support from relatives (p = 0.69), support from friends (p = 0.34), support from health care workers (p = 0.13), smoking behavior (p = 0.69), frequency of drinking alcohol (p = 0.92), amount of alcohol use (p = 0.53), hard drug use (p = 0.77) and travel time (p = 0.73). A non-significant effect was seen for the initial care provider (p = 0.058) while post-hoc testing showed a significant correlation between default and attending a faith healer prior to treatment (p = 0.00). Theory of disease (p = 0.10) did not reach significance although the group with supernatural beliefs was close to reaching significance for default (p = 0.0099), with a significance level of (p = 0.0056) due to correction for type 1 error. There was a significant effect of presence of comorbidity on death, with patients with another disease being more likely to die (p = 0.02). The regression showed a significant effect for taking drugs besides treatment and death (p = 0.03). SUPPLEMENTARY TABLE 2 shows a complete overview of the correlation between the questions of the questionnaire and treatment outcome.

Urban community
Within the urban community there was a non-significant effect of gender (p = 0.58), having health insurance (p = 0.24), challenges with money over the last year (p = 0.70), support from relatives (p = 0.72), support from friends (p = 0.36), support from health care workers (p = 0.93), other disease (p = 0.50), travel time (p = 0.84), initial care provider (p = 0.96), theory of disease (p = 0.29), smoking behavior (p = 0.86), frequency of drinking (p = 0.91), amount of alcohol use (p = 0.76), hard drug use (p = 0.79) and presence of comorbidity (p = 0.50) on default or death. The regression showed a significant effect for taking drugs besides TB medication treatment and death (p = 0.04).

Rural community
Within the rural community gender (p = 0.54), having health insurance (p = 0.31), challenges with money over the last year (p = 0.51), support from relatives (p = 0.91), support from friends (p = 0.36), travel time (p = 0.65), smoking behavior (p = 0.81), frequency of drinking (p = 0.92), amount of alcohol use (p = 0.49), hard drug use (p = 0.95)

and taking drugs besides TB medication (p = 0.23) all had a non-significant effect on default or death. There was a significant correlation between having witchcraft as a theory of disease (p = 0.00), attending a faith healer before clinical presentation (p = 0.02), and default. There was a significant correlation between feeling no support from health workers (p = 0.00), presence of comorbidity (p = 0.02), and death.

Phase 2&3. Qualitative study
The characteristics of the population in the qualitative study were roughly similar to the characteristics of that in the quantitative study. Twenty-four participants were recruited into two treatment groups. A total of 28 interviews were conducted with 5 participants in phase 2 (months 1-2 of treatment) and 10 in phase 3 (months 5-6 of treatment) (FIGURE 1). The issues that emanated from the interview with regard to the views of participants on TB treatment adherence were discussed per code. A total of seven main codes were developed with six of them being significantly correlated to the outcome measures. The code addiction was not correlated to either default or death in both phases. SUPPLEMENTARY TABLE 3 shows a complete overview of the codes and the correlation of subcodes to the outcome measures.

Costs
Phase 2: In the total population 70% indicated having financial problems adhering to treatment. In the urban community 100% of the participants indicated financial problems adhering to treatment with all of the participants having problems paying for transport to the clinic. These financial problems in the urban community were correlated with default and death.
Phase 3: TB symptoms made 18 out of 20 participants lose their income, which was correlated to default in the rural community. Despite having financial support from relatives this was nonetheless correlated with default in the rural community (80%). Prior to treatment, in the rural community, 30% incurred high cost at other health care providers and 50% at the pharmacy, which was both correlated to default. One defaulted participant explained:
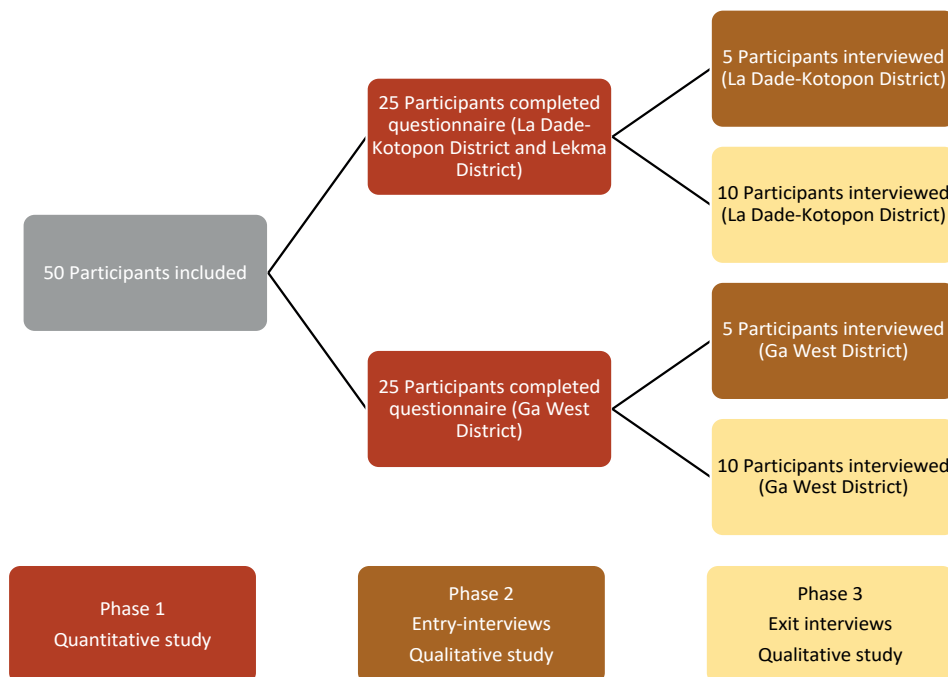
"I stopped treatment. As I stopped having symp-

FIGURE 1 Overview of selection procedure

toms, I started working full-time again. I had to make up for the debts made at the pharmacy and private hospital prior to treatment as I lost a part of my income due to TB. My mum was supporting me financially but she was not able to make up for all cost made. I am currently not able to pay for the rent of the house".

Knowledge
Phase 2: Non-germ theories of disease were correlated with death in the urban community (20%). In the rural community, 60% had a low awareness of TB symptoms which was correlated with default.
Phase 3: All participants had misconceptions about TB (100%). Over half (70%) were not aware they could possibly get sick and 40% had a non-germ theory of disease. All were associated with default. A belief in the curing ability of TB medication did not prevent participants in the urban community from defaulting (20%), as was explained:

"As I did not have any symptoms anymore, I believe that God has healed me. My belief in God was right and I am healed now but before God can heal you, you have to believe in him and have faith

in him and not everybody has such faith, so these people should continue treatment".

Obstacles
Phase 2: In the urban community, 40% of the respondents reported the hospital as being inaccessible as it was too far, which was correlated with death.
Phase 3: In both communities, 11 out of 20 (55%) participants described the hospital as being inaccessible. However, 9 out of these 11 (82%) stated that the chest unit was easily accessible. An inaccessible facility and chest clinic were both correlated with default. Two participants explained the chest unit was inaccessible due to inconvenient opening hours.

Postponing hospital visit
Phase 2: In the urban community, 60% treated themselves with non-TB treatment prior to clinical presentation. This was associated with death.
Phase 3: In both communities, 6 out of 20 participants treated themselves with non-TB treatment, which was correlated with default. Delaying initial clinical presentation due to financial reasons or self-treatment with over-the-counter drugs was not

associated with default or death.

Suffering of disease
Phase 2: In the rural community, a decrease of symptoms led to default for 20% of the participants. In the urban community, symptoms of a comorbid disease increased for 40% of the participants which was associated with death.
Phase 3: In both communities, an increase and a decrease of symptoms were correlated with default. In the urban community half of the participants experienced an increase in symptoms of comorbid disease which was associated with default. An increase of symptoms was explained as treatment failure.
A change in symptoms was always linked with one of the other codes explaining default in both phases (see quotes knowledge and costs).

Support
Phase 2: Support from friends, relatives and health workers was not correlated with the outcome measures.
Phase 3: All respondents that completed treatment (90%) felt supported by their health workers. Half of all the participants that defaulted from treatment did not feel supported by their health workers.

DISCUSSION
To increase TB treatment adherence, the significant factors contributing to default should be addressed. The factors negatively correlated with treatment adherence were: non-germ theory of disease, financial challenges, lack of support from health workers, comorbidity and obstacles accessing health care. This research did not find a difference in treatment adherence between urban and rural communities or different factors contributing to default in these communities in the Greater-Accra Region.

Quantitative findings did not show a significant difference in home-to-clinic distance or a difference in default rate between urban and rural communities. This was supported by qualitative findings as money paid for transport was a factor influencing treatment adherence whilst duration or distance was not. Transport cost was a significant cost, especially during the intensive phase where the clinic had to be visited daily to pick up med-

ication for treatment. This result showed that to increase treatment adherence the costs of transportation should be compensated for patients having difficulties affording transport to the clinic.

Quantitative findings did not show a correlation between challenges with money and treatment outcome. Qualitative findings, however, showed both communities were affected, in terms of treatment adherence and death, by the high financial burden caused by TB. This inconsistency in outcome could be explained as the survey was held at the beginning of treatment and the financial burden increases during treatment, as 90% of the participants lost their income. An increasing financial burden increased the likelihood of default as symptoms decrease. Health insurance could play a role in compensating TB patients. However, it solely covers drugs treating TB side-effects and not any of these additional costs. This could be an explanation for why having health insurance was not correlated to treatment adherence. Steps should be made to achieve universal health coverage in Ghana and reduce the financial risk for patients suffering from TB.[26]

A non-germ theory of disease led to default in both communities. The phase two and three analysis illustrated that participants with non-germ theories who completed treatment, did this due to either a change in their belief in a germ theory of disease or the belief that spiritual treatment alone was not sufficient. Participants were likely to change their opinion about theory of disease when there was no improvement in their symptoms. To address these issues health care providers should emphasize to patients that improvement of symptoms takes time and spiritual and medical healing are able to co-exist. In addition, low awareness of TB results in default and death, independent of community. Low awareness and misconceptions were independent of education level, indicating the need for an increase in knowledge of TB among all levels of Ghanaian society.

Feeling no support from health workers resulted in an increased likelihood of dying or defaulting in the rural community. The qualitative analysis showed that the influence of health workers on patients should not be underestimated. As there was

often only one TB health worker in the community clinic patients were attending, these health workers had a big impact on the participants. A good relationship between patients and health workers contributed to completing treatment; a bad relationship, however, created barriers and made TB patients more likely to default. With no participants in the urban community feeling a lack of support by their health worker a comparison could not be made. Health care workers should be aware that a good professional relationship with TB patients is essential for treatment adherence.

Qualitative analysis showed that the change in symptoms before and during treatment was a central factor in treatment adherence. A low burden of symptoms caused treatment delay whereas a high burden of symptoms resulted in clinical presentation. The decrease in symptoms could be misinterpreted as being cured or could mean patients prioritize other difficulties, such as having financial problems, over treatment. An increase in symptoms could be explained as treatment failure. We suggest a two-factorial model, with change in symptoms as one of the two factors, to predict the likelihood of default (FIGURE 2).

For the secondary outcome measures, a significant positive correlation was observed between having a comorbidity and death. In the urban community there was a significant difference between the mean amount of drugs taken, besides TB drugs, in the group that died and the group that completed treatment. The mean amount of drugs was significantly lower in the group that completed treatment. This can be expected since participants who were taking medication presumably suffered from another disease besides TB. The difference between urban and rural areas could be due to the fact that participants in the rural area suffered from more

or other comorbidities or participants in the urban area took more drugs for a comorbid disease. This study however did not research if mortality increases with the amount of comorbidities the patient is suffering from, and neither did it investigate which comorbidities are related to death. It could be suggested that the awareness of the association between comorbid diseases other than HIV and death is low. This may further explain why this study did not find a relationship between suffering from HIV, in addition to TB, and death, as this comorbidity is well known to health workers. Disease interactions, for example between Diabetes Mellitus and TB, have a high prevalence[27], but are not routinely checked for upon TB diagnosis, while HIV is. This relationship should be further examined in future studies.

Quantitative and qualitative analyses showed no correlation between addiction and treatment adherence or death.

Limitations and strengths

This study was limited to a maximum of 50 participants in two communities, which means the significance threshold might not have been met for every analysis. The study population does not represent the rural society of Ghana as the researched community is the densest community of Ghana and has a high TB burden. The clinics were picked through purposive sampling and not through randomization, which could have led to selection bias. The strengths of this study were the mixed method study design in which the quantitative and qualitative data were partly concurrently obtained and partly sequentially. Although this was a small study, extensive data was obtained through both quantitative and qualitative methods. This data gave a comprehensive view of TB treatment adherence in the Greater-Accra Region.
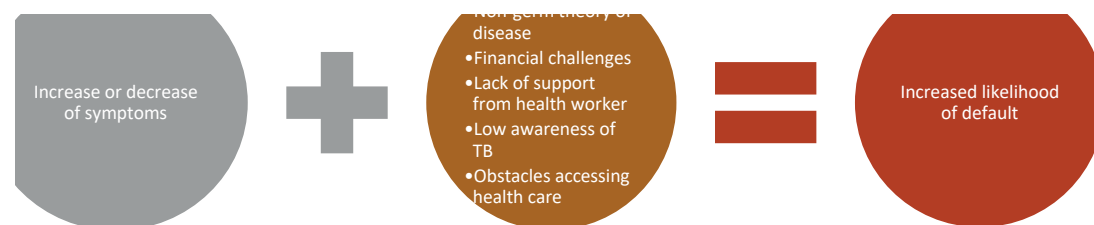

FIGURE 2 The two factorial model predicting TB treatment default

Increase or decrease of symptoms

+

Non germ theory of disease
•Financial challenges
•Lack of support from health worker
•Low awareness of TB
•Obstacles accessing health care

=

Increased likelihood of default

CONCLUSION

To increase treatment adherence and to end the TB epidemic by 2035[4], the catastrophic costs affecting TB patients, obstacles accessing health care and lack of support from health care workers should be addressed. Furthermore, knowledge about TB in patients and in society should be increased, especially towards the spread and treatment of germs causing TB. Further research should be conducted about the correlation between comorbidity and TB mortality.

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Shortness of breath in a 45 y/o female

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CASE
In March 2020, a 45-year-old female with no medical history presented at the ER complaining of shortness of breath and coughing. Symptoms had started a few days before and progressed over time. Upon physical examination a fever was found. A lung CT was performed.

QUESTION 1
What do you see? (multiple answers are correct)
A. Ground-glass opacity
B. Multifocal consolidations
C. Pleural effusion
D. Atelectasis
E. *Fleischner sign*
F. *Hampton hump*
G. *Enlarged lymph nodes*

Hint: What do you expect to see based on the symptoms?
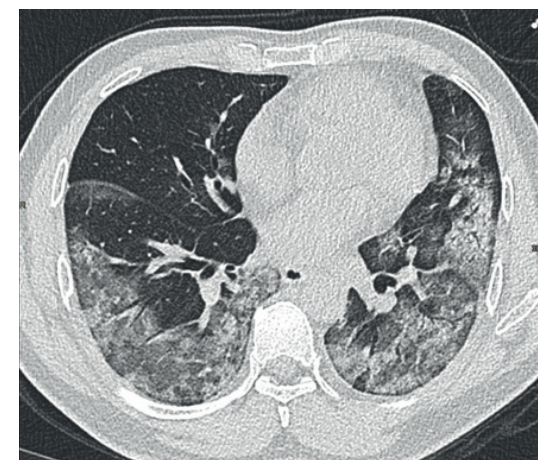
QUESTION 2
What is your diagnosis?
A. Pulmonary embolus
B. Lung carcinoma
C. Pneumothorax
D. Pneumonia

Hint: Which parts of the lungs are involved?

QUESTION 3
What would be most likely the cause?
A. Blunt trauma
B. Sharp trauma
C. Virus
D. Bacterium

E. Auto-immune
F. Lifestyle
G. Smoking behavior
H. Cholesterol
I. Immobiliza- tion

Hint: When did the patient present?

Letter to the editor

Respected Editors,

I have been studying the latest research on COVID-19 since its outbreak and have been a member of "Pakistan Corona Virus Research Outlook" (a team of medical professionals providing research information in simple language to the public via social media). At this point in the pandemic, various statistical graphs have been published. On observing graphs, such as FIGURE 1, I made a peculiar finding. The coronavirus deaths in developed countries are very high. How can this be possible? Despite being developed, why are these countries unable to control the virus?

Discussing this with my professor, Dr. Qudsia, we drew the following hypotheses:

- Vaccines: Because of hygiene in the developed countries, they are not given certain vaccines (e.g. BCG) that are still given in underdeveloped countries. This creates a better immunity in the underdeveloped countries.
- Age group: The population of the developed country has a higher proportion of individuals who are in old age due to better health facilities. As the elderly are more susceptible to disease, a relatively older population could also be the reason for a high death rate.

Finally, I want to propose a suggestion. The importance of quarantine and measures to be taken in quarantine must be a part of academic teaching. This might ensure a better way to combat such outbreaks in the future.

Sincerely,

Haleema Anwar
Dr. Qudsia Umeira Khan
CMH Lahore Medical and
Dental College, Pakistan

Coronavirus deaths as of 14 April 5 pm BST
Cumulative deaths, by number of days since 20th death

Note: Only selected countries are shown
Source: New Scientist analysis of Johns Hopkins University, CSSE; Worldometers

NewScientist
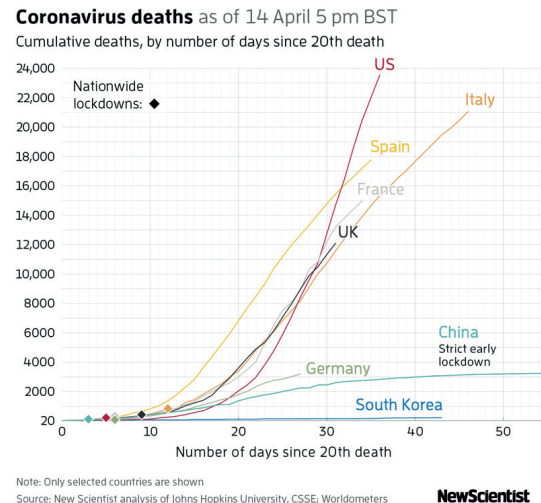
FIGURE 1 Coronavirus deaths

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Letter to the editor - Response

Dear Editors,

We have read the letter of Ms. Anwar, Dr Khan and the members of the Pakistan Corona Virus Research Outlook with great interest, and would like to clarify our theories about the question raised in this letter.

The following question was raised: How is it possible that the mortality numbers of COVID-19 in developed countries are higher compared to less developed countries? In other words: why are these countries unable to control the virus? Two hypotheses were stated: the lack of the Bacille Calmette-Guérin (BCG) vaccine administration in the developed countries, and the higher proportion of elderly in the developed countries. After research on this matter, we have come to a couple of conclusions.

The first hypothesis states a higher mortality number because of the lack of administered BCG vaccine. This is being researched in multiple clinical trials.[1-4] Results of both in vitro and in vivo studies suggest that the BCG vaccine has so called 'non-specific effects' on the immune system, which resulted in a decrease of respiratory tract infections and reduced viremia in experimental human models.[1] However, these effects have not been well characterized and their clinical relevance is unknown. The World Health Organization (WHO) will evaluate the evidence when it is available. In the absence of evidence, the WHO does not recommend BCG vaccination for the prevention of COVID-19.

The second hypothesis states that the high mortality number might be a result of the fact that the population of developed countries is older compared to the population of less developed countries.[5] With ageing, the immune system declines which results in a weakened response to the virus. Furthermore, elderly are more likely to suffer from underlying diseases that hinder the body to cope with and recover from other diseases.[6, 7] We agree that this might be one of the reasons why the mortality is relatively high in developed coun-

tries. However, this hypothesis has not undergone rigorous evaluation yet.

In addition to these two hypotheses there might be several other reasons why the mortality numbers in developed countries are higher. One theory is that because of better hygiene and better health care systems in developed countries, the immune system of people there is not as challenged as the immune system of people in less developed countries. This might result in a weaker immune response.

Finally, you proposed the importance of education on pandemics for health care workers. We could not agree more. Future health care workers should learn from this situation.

Respectfully,

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Amsterdam UMC, Location VUmc

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The influence of soy and sodium on uric acid levels in humans: A literature review

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2. Professor Nutrition and Health, Dept. Health Sciences, Amsterdam UMC, Location VUmc

ABSTRACT

INTRODUCTION Hyperuricemia has been established as a risk factor for multiple metabolic diseases, yet a direct link between food intake and serum uric acid remains unclear. Since the interest in plant-based products is widely increasing, a better understanding of how ingredients affect uric acid levels is needed in order to give people better advice about the food choices they make.
METHODS We retrieved 124 studies from databases PubMed and Embase, filtered for clinical trials within the last 10 years. Eight studies were selected for final assessment: four studies focused on soy intake and the other four on sodium intake, all in relation to effects on uric acid levels. Seven studies were RCTs, one was a prospective cohort study.
RESULTS A distinction between long-term and short-term effects of soy products on serum uric acid was established, both reporting subsequent reductions. Among the studies examining the influence of sodium one reported an overall increase, two reported a significant increase right after ingestion followed by a decrease at 2 and 3 hours post-ingestion, and one study reported that the increases in blood pressure were independently related to a change in uric acid levels and sodium intake.
CONCLUSION The consumption of meat substitutes might be linked to changes in serum uric acid levels in humans. However, a clear association between intake of these nutrients and uric acid levels tends to be more complex. To offer sensible dietary advice about a causal link between food intake and hyperuricemia, further clarified research is indicated.

INTRODUCTION

Uric acid is defined as the final product of purine catabolism in the liver.[1] When the metabolic pathway of uric acid production or its renal excretion is irregular, it can accumulate in the bloodstream. This abnormally high level of uric acid is termed hyperuricemia.[2]

Hyperuricemia can be a high-risk factor for cardiovascular diseases, gout and severe chronic kidney diseases.[3] Medication is often prescribed to reduce symptoms, yet prevention of hyperuricemia by dietary adjustments is a relatively neglected topic.[4] Some studies suggest that meat and fish consumption is possibly related to hyperuricemia.[5, 6, 7] A diet including plant-based substitutes would tend to be a healthier alternative, but such products often contain high amounts of soybeans and added sodium; 100g of soybeans contains 50-150 mg purine, whereas 100g of red meat contains 100-250 mg purine.[8, 9, 10, 11]

The risk of too much sodium is also linked to hypertension.[12] Studies also suggest that uric acid acts as a biomarker in endothelial dysfunction, a known risk factor for developing hypertension.[13] This review aimed to assess whether meat substitutes could be a suitable alternative to limit the development of hyperuricemia by evaluating randomized, controlled trial-based studies on the influence of both soy and sodium on uric acid levels in humans. It is hypothesized that the consumption of soy or sodium, which are moderately present in plant-based meat substitutes, does not affect uric acid levels in terms of hyperuricemia development.

METHODS

A systematic search was conducted using databases PubMed and Embase, including the search terms "hyperuricemia AND "Plant-based diet"" (SUPPLEMENTARY TABLE 1). Several inclusion criteria, such as "full text availability", "within 10 years" and "Randomized controlled trials or observational studies", were used to exclude records. In order to end up with eight eligible studies that only focused on soy or sodium in relation to uric acid, full-text articles were omitted using the exclusion criteria "studies not tested on humans", "medicated interventions" and "studies using nutrients other than sodium and soy" (SUPPLEMENTARY TABLE 2).

RESULTS

The search yielded 119 unique records (FIGURE 1). The use of several inclusion criteria resulted in a final number of eight eligible studies for the qualitative synthesis: four studies focused on the association between soy intake and uric acid, the other four on the potential association between sodium intake and uric acid. Seven studies were RCTs; one was a prospective cohort study (SUPPLEMENTARY TABLE 3).

Soy intake
Long-term effects
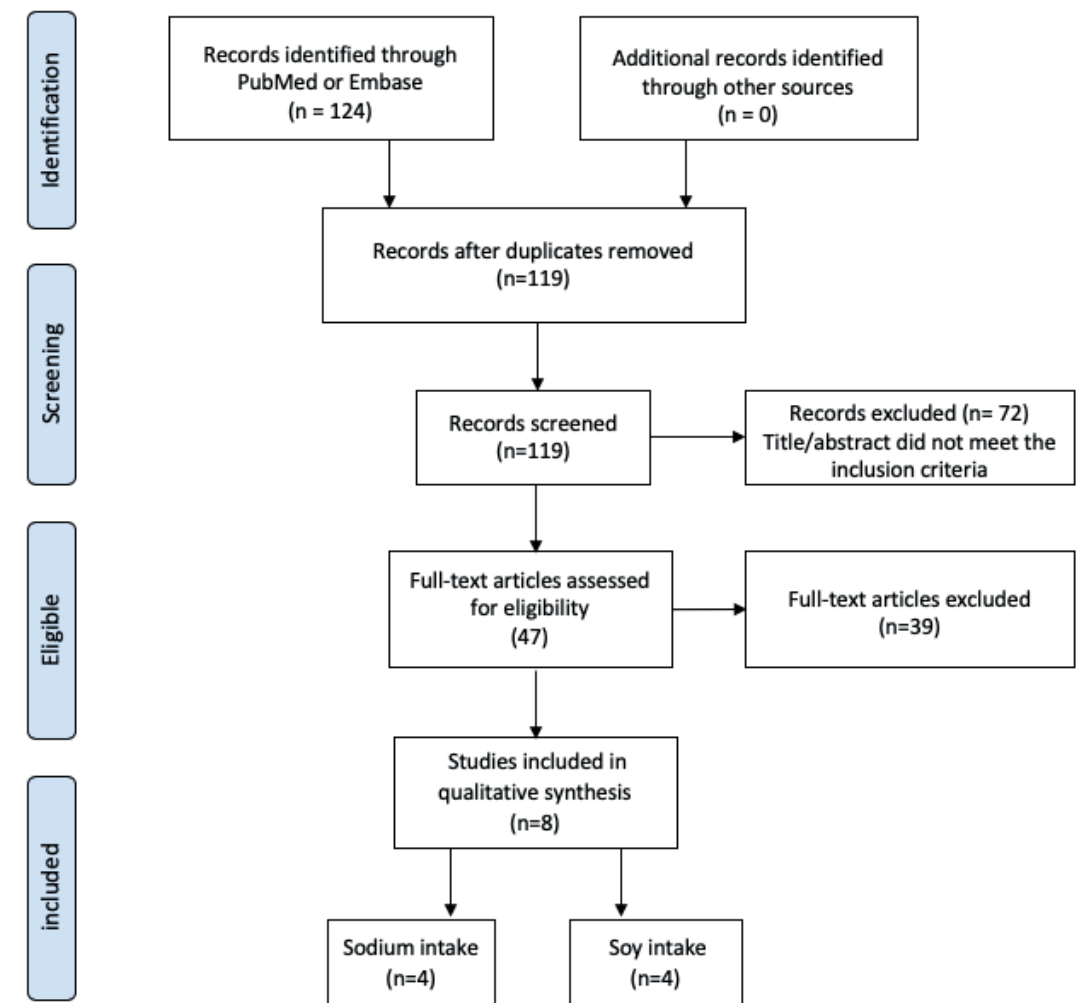The first study on soy intake was a six-month dou-

FIGURE 1 Flowchart

ble-blind, placebo-controlled RCT among 450 postmenopausal women.[14] After three months an increase of 1.22% serum uric acid was found in the soy protein trial, compared to a 4.28% and 4.82% decrease in the soy flour and placebo group. A pooled data analysis showed that the initial increase became non-significant when tested again six months later.

A second RCT compared two diets – a standard diet and another containing high amounts of fruit and soybeans – among 187 asymptomatic Chinese participants.[15] After a 3-month intervention results revealed no significant differences in uric acid between the two diet groups (p=0.732). Both groups individually showed reduction in uric acid levels at the end of the trial.

Short-term effects
A Canadian study investigated the direct effect (in hours) of three different purine-containing foods (haddock, liver, soybeans) on uric acid levels among 18 healthy males.[16] Results showed that the mean serum uric acid significantly increased in all groups (P<0.05) and the type of purines caused differentiation in serum elevation – and yet after three hours all values had returned back to their initial baselines.

The final study was an RCT in which participants were assigned to consume one of six products: water, soybeans, and four other different kinds of soy products.[17] Results showed a significant increase in uric acid levels after ingestion of all soy products, most notably after one hour, yet here too all values regularly decreased by two hours post-ingestion.

Sodium intake
The first study on sodium intake was a prospective cohort study among 4062 people from the general population of Groningen, the Netherlands, in which sodium intake was measured by analyzing urinary excretions.[18] This study suggests that an increase in sodium intake is independently associated with higher levels of uric acid, which is known to be a marker of endothelial dysfunction and vascular risks.[19]

The second study examines the influence of salt intake on uric acid and cardiovascular risks, report-ing for the first time that an increase in dietary sodium enhanced the correlations between uric acid and high blood pressures.[20] Hence lowering uric acid levels to prevent cardiovascular risks needs to be accompanied by a reduced dietary salt intake, particularly during treatment for hyperuricemia.

The third study investigated the association between dietary sodium and blood serum uric acid concentrations.[21] After the four-week trial, results revealed that participants' uric acid levels had been significantly modified by the sodium intake. Accordingly, uric acid concentrations dropped the most with the highest sodium intake, with an overall change of 14%. A reduction in dietary sodium intake to 60mmol/day or less (1 gr ≈ 43 mmol) might result in elevated uric acid levels in blood serum, entailing potential physiological risks later on.

The last study investigated uric acid levels as an independent factor for raising blood pressure, resulting from changes in sodium intake.[22] The used methods were similar to the third study. Results evidenced an increased sodium intake leading to a significant drop in serum uric acid, yet the overall blood pressure significantly increased in the intervention group. Changes in participants' blood pressure were independently related to changes in uric acid levels, therefore disclaiming the potential association between uric acid levels and high blood pressure related to sodium intake.

DISCUSSION
Consumption of meat substitutes containing moderate amounts of soy and sodium might be linked to changes in serum uric acid levels in humans. However, a clear association between the intake of these popular nutrients and uric acid levels tends to be more complex, due to involved metabolic factors and their limited documented evidence. In order to offer patients and healthcare professionals sensible dietary advice about the long-term effects of different nutrients on serum uric acid, a longitudinal crossover study is recommended. In this way, the potential independent associations between dietary adjustments and uric acid levels can be determined.

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Meet the reviewers - Dr. Niek H. Sperna Weiland MD, PhD

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It might be difficult to imagine during the current SARS-CoV-2 pandemic, but the public health effects associated with climate change pose the biggest threat to public health in the 21st century.[1] Extreme weather conditions, such as drought, are decreasing crop yield and causing people to (mass) migrate to more temperate environments. Rising sea levels lead to devastating floods and humanitarian disasters in densely populated coastal areas and increasing temperatures create suitable environments for insects such as the *Anopheles* mosquito, the vector for malaria.

> "We are the first generation to feel the impact of climate change, and the last generation that can do something about it"

As an industry, health care is responsible for 3-8% of global greenhouse gas emissions, tripling emissions caused by aviation.[2,3] The relative contribution of the Dutch health care sector currently outranks every other nation on the planet. This leads to a striking paradox; in our efforts to treat disease, we pollute the environment, potentially causing disease elsewhere. This is at odds with one of the main principles in our Hippocratic oath: *primum non nocere* (do no harm).

Dr. Niek H. Sperna Weiland

CURRICULUM VITAE

1988	Birth
2005-2012	Medical school, University of Amsterdam
2012-2018	Recidency in anesthesiology, Amsterdam UMC
2018-present	Staff Anesthesiologist Amsterdam UMC (Location AMC)
2019	PhD thesis 'Cerebral hemodynamics during anesthesia'

Inspired by this knowledge and fueled by my experiences working as an anesthesiologist in the operating room of the Amsterdam UMC, I decided to take action. Together with a group of enthusiastic co-workers from different backgrounds, we founded a *Green Team* and started to quantify the carbon footprint of the operating room in our own hospital.[4] This helped us to focus our energy on impactful matters.

After a year, I am very proud of the results that we are already able to report: the use of volatile anesthetics, highly potent greenhouse gases,[5] declined by 42% and energy consumption was reduced 460.000 kWh by optimizing ventilation and air conditioning on the operating room. Currently, we are working on reducing waste by eliminating disposables in favor of reusables.

Our efforts not only changed things in our own hospital, but we also aimed to inspire colleagues in other hospitals as well. We were able to generate some national media attention in the television program *Nieuwsuur*[6] and our project appeared on the front page of the newspaper *Het Parool*.[7] We set up a research line on sustainable surgery, collaborating with TU Delft and various pharmaceutical companies. In the coming year we hope to establish a center of excellence for sustainability in healthcare to bring these collaborations one step further.

All in all, working on sustainability within my own department and profession has taught me a lot about how things in our hospital are organized. It has been inspiring and fun to work with people from different backgrounds on his subject. We put a lot of effort and time into the project, but this investment repaid itself many times over. I would like to invite anyone with green intentions to get in touch and join in on the movement we are currently creating in Amsterdam UMC.

To quote Barack Obama, *'We are the first generation to feel the impact of climate change, and the last generation that can do something about it'*.

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Answers 'Shortness of breath in a 45 y/o female'

SANNE VAN BEEM AND MARIO MAAS

Correct answers: 1AB, 2D, 3C.

EXPLANATION
QUESTION 1

The chest CT shows bilateral multifocal consolidations and ground-glass opacity, which is, in combination with the symptoms, indicative for a viral pneumonia.

CT patterns of a viral pneumonia differ per virus, depending on how the virus spreads through the lungs and what tissues it invades. Respiratory syncytial virus (RSV) pneumonia for example usually presents with ground-glass opacity and multifocal consolidations as a result of activating the inflammatory response in lung tissue, whereas influenza pneumonia usually presents with consolidation as a result of necrotizing bronchitis and diffuse alveolar damage.[1] The distinction between a viral and bacterial pneumonia is often based on a chest x-ray or CT (viral pneumonia often shows a more diffuse image, with involvement of both lungs, where a bacterial pneumonia is often more lobular or limited to one lung), clinical signs and laboratory findings such as CRP.

Because the patient presented amidst the COVID-19 pandemic, she was highly suspected of a COVID-19 infection.

COVID-19 is caused by the SARS-CoV-19, a single stranded RNA virus that is mostly transmitted via droplets. The presentation of COVID-19 ranges from a common cold to acute respiratory distress syndrome (ARDS) in some patients. Most commonly reported symptoms include coughing, fever and dyspnea. Asymptomatic infections have been reported as well.[2]

A study in Wuhan, where the pandemic originated, concluded that most chest CT's of COVID-19 positive patients show multiple lesions, mostly located in the peripheral lung tissue, bilateral patchy ground-glass opacity and consolidations. They found that an imaging pattern of multifocal peripheral ground glass or mixed consolidation is highly suspicious of COVID-19 and that the image changes quickly over the course of days.[3]

Recently, a standardized reporting system for COVID-19 on a chest CT was established: the CO-RADS classification. This classification helps to determine the level of COVID-19 suspicion, ranging from 1 (very low suspicion) to 5 (very high) and also helps in determining the stage and severity of the disease. As our case shows multifocal ground-glass opacity and consolidation, it would most likely be classified as CO-RADS 5, although this is hard to determine based on one slice. At the time of writing, this classification system is still under development.[4]

The official diagnosis of COVID-19 is based on a PCR-based viral nucleic acid assay; however, this is a time-consuming test subjected to scarcity which is not suitable for a rapidly growing population of suspected patients. Furthermore, the test has shown false-negative results in patients with highly suspicious CT images. Thus, a chest CT is considered a more sensitive, indispensable tool in the screening and diagnosis of COVID-19.[5]

[separate side note]

Two of the answer options under question 1 are interesting radiology phenomena as well. The Fleischner sign is often seen when the central pulmonary artery is enlarged, something that commonly happens in pulmonary hypertension or a large pulmonary embolus. The Hampton hump is a pleural-based opacification shaped as a dome. It is seen in pulmonary embolisms and lung infarctions.[6, 7]

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Colophon