AMSj

Amsterdam Medical Student journal

SOLVING STATISTICS |
ALL YOU HAVE TO KNOW ABOUT CONFOUNDERS, MODERATORS, AND MEDIATORS IN MEDICAL RESEARCH

CHANGING PERSPECTIVES |
3D PRINTED BREAST IMPLANTS: FICTION OR REALITY?

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The Amsterdam Medical Student journal (AMSj) is a scientific journal created and published by Amsterdam UMC staff members and students to promote research and to encourage other medical students to publish their clinical observations, research articles and case reports. Go to www.amsj.nl for publication options and to find out how you can contribute to AMSj as reviewer or member of the editorial board.

Editorial

Dear readership,

On behalf of the entire editorial board, I have the pleasure of welcoming you to the 31st edition of the Amsterdam Medical Student Journal! I want to thank all the reviewers and editorial members for the effort that they have put into this edition, and congratulate them on the result!

In this edition, we bring multiple interviews, Subject 101 items, and radiology quizzes! Firstly, Joost Piët, PhD candidate in pharmacotherapy, tells about his view on planetary health and sustainable healthcare and his efforts towards sustainable prescription writing and planetary health.

Furthermore, in a bony affair, we present interviews with both Prof. Dr. van den Bekerom, an orthopedic surgeon, and Prof. Dr. Bloemers, a trauma surgeon. Although they have different professions, they both hold a position in trauma surgery. Prof. van den Bekerom shares his area of expertise, views on current research, and advice for medical students on page 21. Prof. Bloemers looks back at his student time, the highlights of his career, and the research that he is most proud of. Read it on page 27!

In this edition's clinical image, you can acquaint yourself with orthopantomograms through an interesting orthomaxillofacial surgery case. Also, in this edition's radiology image, a case of abnormalities on the MRI of a young patient is presented. Find them on pages 15 and 9!
On page 11 prof. dr. Twisk of Epidemiology and Biostatistics writes about everything you need to know about confounding, moderation, and mediation. In just two pages, he has provided a comprehensible explanation of these mystic terms from the world of biostatistics.

At AMSj, we encourage students to start their own scientific journey, whether it is through research or education. We cordially invite you to submit your own original article to our journal and experience what goes into publishing scientific research. AMSj is also often looking for new colleagues, so are you interested in working as an editor or reviewer? Keep an eye on our social media channels for frequent vacancies. General questions about AMSj? Please, do not hesitate to contact the Editors-in-Chief through chief-editor@amsj.nl, we are very happy to help.

Lastly, the 31st edition of AMSj will sadly be the last edition for which I had the honor of serving as editor-in-chief VUmc. Due to my recent graduation and the beginning of my career as a professional physician, I will hand over my tasks to the next editor-in-chief. I am happy to share that from edition 32 and onward Tina Vekua will have the pleasure of fulfilling this position! I wish her all the best and hope to see AMSj flourish in the future. For now, enjoy the 31st edition of the Amsterdam Medical Student Journal

Yours Sincerely,

Mees Hesmerg, MD
Editor-in-Chief
Amsterdam UMC,
location VUmc

NEWSNEWSNEWS

The search for a vaccine against respiratory syncytial virus is almost over

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Respiratory syncytial virus (RSV) is the most common cause of infant respiratory hospitalization and continues to pester humans throughout life. RSV usually presents as the common cold in healthy adults, but in the elderly and immunocompromised it can lead to serious conditions like pneumonia. Currently, there is no approved vaccine.

An RSV prefusion F protein-based (RSVpreF) vaccine has previously shown high efficacy against symptomatic RSV infection in healthy adults aged 18-50, but elderly populations remained unstudied. Walsh et al.[1] conducted a phase 3 trial, in which the RSVpreF vaccine is being tested on adults aged >60. This trial has two primary endpoints: vaccine efficacy against RSV respiratory illness with ≥2 symptoms - and with ≥3 symptoms. The trial has shown a vaccine efficacy of 67% (96.7% CI, 28.8 to 85.8) and 86% (96.7% CI, 32.0 to 98.7), respectively. The vaccine is also successful in preventing acute RSV respiratory illness with a vaccine efficacy of 62% (95% CI, 37.1 to 77.9). With regard to safety and tolerability, there was an increase in short-term local reactions (12% versus 7% of participants). Otherwise, the rate of adverse events is similar in both groups.

Given the occurrence of RSV respiratory disease in the elderly, an approved vaccine could have a widespread effect on the quality of life, hospitalization costs, and mortality reduction.

1. Walsh EE, Marc GP, Zareba AM, et al., 2023. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. The New England Journal of Medicine, 388(16), 1465–1477.

Empagliflozin in acute myocardial infarction treatment

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1-3% of the adult population is diagnosed with heart failure, with myocardial infarction (MI) being one of the leading causes.[1] Guidelines recommend the use of sodium-glucose co-transport 2 inhibitors (SGLT2i) in heart failure patients with reduced, mildly reduced, and preserved ejection fractions. The EMMY trial investigated whether the use of empagliflozin as an addition to standard post-MI-treatment could improve N-terminal pro-hormone of brain natriuretic peptide (NT-proBNP) and echocardiographic parameters in patients with acute MI.

The trial randomized patients to either empagliflozin or a placebo on top of standard post-MI-treatment. Empagliflozin treatment led to a greater reduction of NT-proBNP as compared to placebo (15%, 95% CI -4.4 to -23.6; p= 0.026). Furthermore, a greater improvement in left-ventricular ejection fraction (Δ 1.5%, 95% CI 0.2-2.9%; p= 0.029) and left-ventricular diastolic function (6.8%, 95% CI 1.3-11.3%; p= 0.015) was observed in the empagliflozin group. Lastly, empagliflozin treatment led to a greater reduction of left-ventricular end-systolic volume (-7,5 mL, 95% CI -11.5 to -3.4 mL; p= 0.0003) and left-ventricular end-diastolic volume (-9.7 mL, 95% CI -15.7 to -3.7 mL; p= 0.0015).[2]

These results demonstrate that early SGLT2i treatment in patients with acute MI improves NT-proBNP and echocardiographic parameters as compared to placebo. Although this trial provides evidence that suggests the beneficial effects of empagliflozin in acute MI patients, future studies are warranted.

1. Eidizadeh A, Schnelle M, Leha A, et al. Biomarker profiles in heart failure with preserved vs. reduced ejection fraction: results from the DIAST-CHF study. ESC Heart Fail. 2023 Feb;10(1):200-210.
2. von Lewinski D, Kolesnik E, Tripolt NJ, et al. Empagliflozin in acute myocardial infarction: the EMMY trial. Eur Heart J. 2022 Nov 1;43(41):4421-4432. v

Can The Gut Microbiome Affect Your Mental Health?

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2. Department of Psychiatry, Amsterdam UMC, location AMC

Depression is a complex mental disorder and one of the leading causes of mental health issues, affecting approximately 280 million people worldwide. Recent studies have explored the connection between the gut microbiome and depression, with new evidence suggesting that gut microbe imbalances can contribute to mood disorders by producing metabolites that affect brain function and behavior. However, previous research focused on ethnically homogenous European populations, while demographic factors likely account for significant individual variation in the gut microbiome.

Therefore, researchers examined the link between gut microbiota diversity and depressive symptoms across different ethnicities by analyzing the fecal composition from six different ethnic groups in Amsterdam (N = 3211).[1] The findings revealed that lower gut microbiome variety within individuals (α-diversity) was significantly associated with depressive symptoms measured by the Patient Health Questionnaire-9 ($p < 0.001$). Additionally, the study found that differences in microbiota composition between individuals (β-diversity) were also associated with depressive symptoms, explaining 29%-18% of ethnic differences in symptom scores after adjusting for age and sex ($p < 0.001$). These findings suggest that variations in the microbiome may partly contribute to the disparities in depressive symptoms observed across ethnic groups. Specifically, certain bacterial genera, such as Christensenellaceae and Ruminococcacea, were positively correlated to depressive scores, whereas Coprococcus, containing anti-inflammatory butyrate-producing species, was inversely correlated with these scores.

In conclusion, this research highlights the association between the variety of gut microbiome composition and depressive symptoms among ethnicities, and understanding this relationship may lead to new targets for psychobiotic interventions to effectively treat depression.

1. Bosch JA, Nieuwdorp M, Zwinderman AH, et al. The gut microbiota and depressive symptoms across ethnic groups. Nat Commun. 2022;13:7129.

Finger-stick dried blood spots (DBS) as an alternative to venipuncture for the determination of CRP-levels

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C-reactive protein (CRP) is a biomarker used to monitor, diagnose and predict infections and cardiovascular diseases (CVD). In practice, CRP is measured from blood collected through venipuncture. Research has shown, however, that CRP can also be measured from capillary finger-stick DBS, which may enable effective patient follow-up in a minimally invasive way. In addition, this would potentially enable early detection through efficient screening programs.

In order to determine if finger-stick DBS CRP measurements can be used in everyday practice, Schakelaar et al.1 conducted a study in which CRP levels from DBS were compared to CRP levels from venous heparin plasma. For this comparison, blood was collected from 53 patients visiting the outpatient clinic of the University Medical Center Utrecht, and CRP was measured using both methods.

Using finger-stick DBS, at a cut-off of > 3mg/L the researchers found a sensitivity (95%CI) of 1.00 (1.00-1.00) and a specificity (95%CI) of 0.96 (0.89-1.03) for the prediction of high risk for CVD. In addition, at a cut-off of 10 mg/L a sensitivity (95%CI) of 0.92 (0.77-1.07) and a specificity (95%CI) of 1.00 (1.00-1.00) was found for the prediction of possible infections. Results were validated by, among others, evaluating the precision of measurement. The researchers concluded that CRP from DBS can be used as an alternative to venipuncture in everyday practice. This method enforces further patient participation, which is increasingly warranted nowadays. Besides better patient follow-up, DBS CRP may render effective and successful screening programs.

1. Schakelaar, Michael Y et al. "Analysis of C-reactive protein from finger stick dried blood spot to predict high risk of cardiovascular disease." Scientific Reports 13(1), 2515, 2023

The influence of a pathologist's personality on the interobserver variability of PD-L1 scoring in NSCLC

Ezgi Ulas[1] and Julia Driessen[2]
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2. Department of Hematology, Amsterdam UMC, location AMC

Immune checkpoint-based immunotherapy has changed the treatment landscape for non-small cell lung cancer (NSCLC). One of the ligands targeted by immunotherapy is the programmed death-ligand (PD-L1) on the surface of tumor cells, which binds to PD-1 on T-cells, inhibiting T-cell activation. PD-L1 expression by immunohistochemistry staining in a tumor biopsy can be used to predict response to immunotherapy and has become an important tool to make treatment decisions.

Although widely implemented, the use of PD-L1 expression as a biomarker to determine the possible treatment response is disputed. PD-L1 staining has shown high inter-assay and inter-laboratory variations in terms of scoring by pathologists. Different interpretations of the PD-L1 expression could have detrimental effects on the treatment decisions that are based on this.

A recent study investigated the impact of a pathologist's personality on interobserver variability and diagnostic accuracy of PD-L1 immunoscoring in NSCLC.[1] Seventeen pathologists performed PD-L1 scoring on 50 resected NSCLC tumors in three categories (PD-L1 expression in <1%, 1-49%, and ≥50% of tumor cells) and performed a personality test. Results show higher kappa values (i.e. higher interobserver agreement) among pathologists with high scores for conscientiousness, (p=0.009), and they scored fewer tumors as PD-L1 positive (p=0.03). Pathologists with a neuroticism personality scored a higher percentage of PD-L1 positive tumors (p=0.017) and had higher interobserver variability (p=0.2). These results indicate that a pathologist's personality influences PD-L1 scoring, which questions the validity of this specific biomarker.

1. Butter R, Hondelink, L.M., … Radonic, T (2022). The impact of a pathologist's personality on the interobserver variability and diagnostic accuracy of predictive PD-L1 immunohistochemistry in lung cancer. Lung Cancer, 166, 143–149.

New possibilities for cardiovascular risk reduction in statin-intolerant patients with bempedoic acid

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1. Faculty of Medicine, Amsterdam UMC, Amsterdam Medical Centre, The Netherlands
2. Department of Internal Medicine, Amsterdam UMC, Amsterdam, The Netherlands

Cardiovascular events, like myocardial infarction and stroke, are part of the most important non-communicable diseases among populations all over the world. Primary and secondary prevention strategies are widely used. One of these strategies is lowering blood cholesterol levels by using statins. However, many patients are unwilling to take statins due to myalgia. A recent study evaluated whether bempedoic acid, a prodrug of statin, could also be used to lower cholesterol levels and had fewer side effects.

The CLEAR Outcomes trial by Nissen et al. is a multinational double-blind, randomized, placebo-controlled trial involving statin-intolerant patients who had a high risk of cardiovascular disease.[1] A total of 13970 patients, of which 6992 received bempedoic acid and 6978 received placebo, were followed for a mean duration of 40.6 months. The reduction in LDL was 21% lower in the bempedoic acid group compared to the placebo group. In addition, this resulted in a lower incidence of primary end-point events (a four-component composite of major adverse events, i.e. cardiovascular cause, nonfatal myocardial infarction, nonfatal stroke, and coronary revascularization (11.7% vs. 13.3%; p=0.004). These findings suggest that bempedoic acid may be considered as an alternative for patients with statin intolerance. However, several aspects of the study should be considered For example, the intervention group showed more side effects, bempedoic acid had no significant effect on separate end-point events, and this study did not compare bempedoic acid to statins, ezetimibe, or PCSK9 inhibitors.

1. Nissen et al. (2023). Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. The New England Journal of Medicine.

Integrating Planetary Health and sustainability within Pharmacotherapy education

Joost D. Piët[1]
1. PhD Candidate and Teacher Pharmacotherapy at Amsterdam UMC, location VUmc

As a PhD candidate and teacher in Pharmacotherapy at the Amsterdam UMC, I teach medical students of the VUmc how to safely and effectively prescribe medication. Also I do research on how we can improve prescribing education in Europe. Before I started working here in March 2023, I chose to do the last elective internship of my medicine study on sustainability in healthcare, in which I attempted to provide suggestions on how to reduce medication waste on the intensive care unit. During this internship, I became aware of the major impact of our healthcare sector on the environment and this increased my interest in making planetary health a part of my future work in the healthcare sector.

Without any doubt, the climate crisis is the greatest challenge that we as humanity will face in the upcoming decades. In order to prevent ourselves from the potential disastrous consequences of this crisis, we have to take actions in each sector that has an impact on the environment. The healthcare sector in the Netherlands is responsible for 7% of the total greenhouse gas emissions of our country and medication has a large contribution to this percentage.1 Furthermore, many medicines have direct harmful effects when they end up in the environment. Therefore, reducing the environmental impact of medication will provide a significant benefit for planetary health.

Many initiatives are already initiated in order to reduce medication waste. However, no initiative yet exists on integrating planetary health in prescribing behavior and individual treatment choices. Therefore, at the Pharmacotherapy unit of the Amsterdam UMC (part of the Internal Medicine department), we started a new project with the aim of integrating planetary health and sustainability in pharmacotherapy education for (future) prescribers. Within this project, our intention is to provide concrete educational contributions towards reducing the environmental impact of medicines.

In order to enable the integration of planetary health in prescribing education, we want to reach widely supported international consensus on all criteria that are essential to compare different medicines with each other when taking planetary health into consideration. Afterwards, we will create and test a universal planetary health education format for prescribing and we will develop international teaching materials and programs about sustainable prescribing. Furthermore, we hope to launch the idea that medical students and teachers can be change agents in the process of taking planetary health into account during the prescribing of medication.

Together with 8 other European Universities and the Dutch National Institute for Public Health and the Environment, we submitted a proposal for this project, called PlanEd Prescribing (Planetary Health Education in Prescribing), in the hope to receive the financial aid that enables us to execute this project. The result of this application is expected to be announced at the end of July 2023. When we receive a positive result, we will be able to start the project in October 2023. Otherwise, the intention to implement these planetary health objectives in our work will remain and will be carried out through other projects.

REFERENCES

1. Rijksinstituut voor Volksgezondheid en Milieu RIVM. Het effect van de Nederlandse zorg op het milieu (The impact of Dutch healthcare on the environment), 2022

MEET OUR TEAM

Stella Jacobs,
Public Relations & Secretary of AMSj

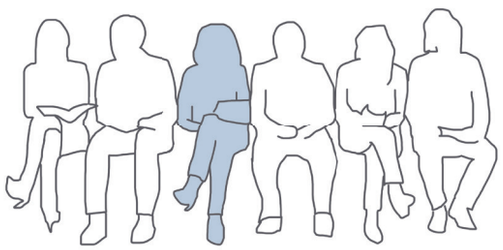
Dear readers,

It is with great pleasure that I introduce myself as part of the team of AMSj. My name is Stella, and I am a 25-year-old student studying interdisciplinary social sciences, and currently serving as the Secretary and PR of AMSj's general board. My passion lies in (clinical) neuropsychology. I am enthusiastic about learning more about the medical field from medical students and incorporating my social and psychological backgrounds in discussions on how to improve healthcare.

I was introduced to AMSj by my friend Dasha in October 2022 and was immediately excited to apply. As Secretary and PR, I am responsible for keeping records of meetings, updating the website and social media channels, and managing the info@amsj.nl email.

What I enjoy most about working at AMSj is the opportunity to collaborate with people from a different academic background. I would also like to emphasize that I find the publication process very interesting. It is a unique process where a team of students works towards a common goal.

I am grateful for the opportunity to be part of the AMSj team and hope you enjoy reading this edition. I believe that AMSj offers students excellent opportunities, including learning about the reviewing process of scientific articles, working towards a common goal in a team, and publishing their manuscripts in an accessible way. In the future, I hope to see AMSj grow as a platform for student manuscripts and achieve a level of notoriety without losing its acceptability.



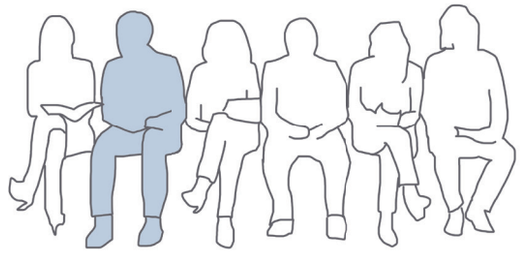
MEET OUR TEAM

Tycho ter Beek,
Treasurer of AMSj

It is with great pleasure that I can introduce myself to you here. My name is Tycho ter Beek, and I am honoured to fulfil the position as board member and treasurer of AMSj since January this year. Currently, I am a third-year medical student at the VU. Throughout my study, I have always been intrigued by the intersection of medicine and research. While actively looking for opportunities to engage in the world of research, I first came across AMSj through their website and journal. This captured my attention and prompted me to look at any vacancies. After meeting the team and seeing the dedication and professionalism of all members involved, I am glad to have applied for this position.

As treasurer, my job is to oversee all aspects of financial management of AMSj. This entails financial planning and reporting, accounting, and managing sponsors. In the future, I would like to see AMSj continue to grow and thrive, by expanding its reach and impact. My goal as treasurer is to implement strategies to enable AMSj to reach this goal and to ensure long-term sustainability. For example, I aim to streamline the budgeting process and to implement cost-cutting measures, while securing new sources of funding to support more initiatives and projects.

AMSj contributes to medical students not only by providing a platform to publish their research, but also by fostering a community of enthusiastic students. This helps students to hone their research and organizational skills, and also provides exposure to the peer-review and publication process. I hope that as a reader you find AMSj to be a valuable resource and platform for your own research endeavours.



Neurological abnormalities in a young patient

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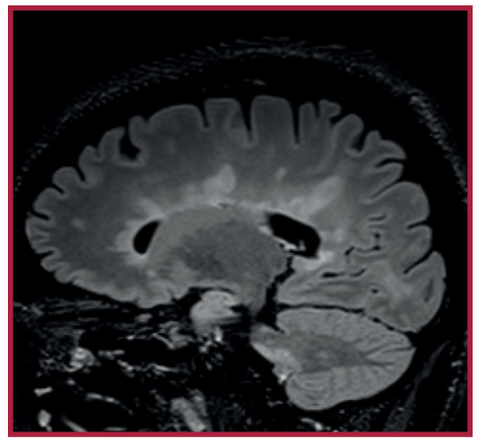
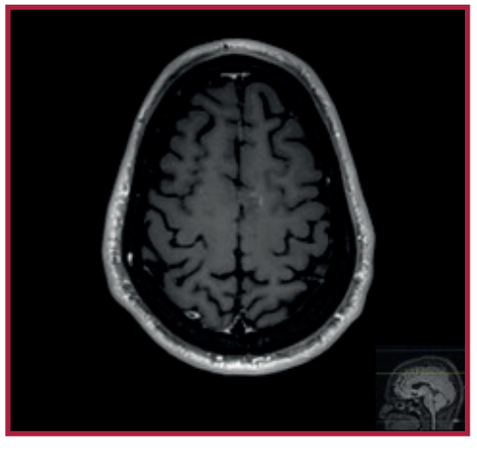
1. Faculty of Medicine, Amsterdam UMC, location AMC
2. Department of Radiology and Nuclear Medicine, Amsterdam UMC, location AMC

CASE

A 25-year-old female who has been experiencing fatigue for the past eight months, along with an unsteady gait and facial numbness, has presented for evaluation.

An MRI was performed, showing the following images...





QUESTION 1

Which of the following terms describes the white matter lesions observed in the sagittal FLAIR MRI image?

A. Plaques
B. Ischemia
C. Dawson's fingers
D. Granulomas

QUESTION 2

Look at the second MRI image; do you see any abnormalities and if so, how would you describe them?

A. No abnormalities
B. This is an axial post-contrast T1 image showing a lesion with open ring enhancement in the left frontal lobe
C. This is an axial FLAIR image showing T2-hyperintense juxtacortical lesions
D. This is an axial FLAIR image showing T2-hyperintense lesions in the periventricular white matter.

QUESTION 3

Review the imaging to identify the most likely diagnosis and determine whether the radiologic criteria for this disease are met.

Answer on page 32

Expecting the unexpected

Miyaada Abdi[1] and Marc Sirks[2]
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2. Department of Ophthalmology, Amsterdam UMC, location AMC

As medical students, we get clinical lectures from doctors every week who bring in patients to tell their stories. One week, I encountered a special patient. A 17-year-old patient - who was not much younger than me at the time - was presented with a genetic disease and a shortened life expectancy of about 40 to 50 years. He told his journey of being in and out of hospitals while juggling his relatively normal teenage life. Despite knowing he had a shortened life expectancy compared to his peers, he still seemed very optimistic. This positive mindset of the patient and the doctor moved me but also made me question: how do you tell a (pediatric) patient that he is not going to live very long? Then again, life and its duration are never guaranteed. This stuck with me and made me more intrigued by pediatrics.

A few months later, we were told this patient had suddenly died in an accident unrelated to his condition. I was taken aback by this news of how a patient who was most likely to die from his disease, died in the most unexpected way. I became aware of the fragility of life. Even the very experienced doctor who shared the news was visibly moved by it due to the long-term doctor-patient relationship they shared.

> "I was taken aback by this news of how a patient who was most likely to die from his disease, died in the most unexpected way"

This made me wonder whether I would be able to deal with the passing of patients, especially when it is outside of my control. At that moment, I learned the difference between having responsibility and having control over life's circumstances. Sometimes, the only thing medical professionals can provide is comfort to patients and their families. Perhaps these moments can't be fully taught but can only be experienced by yourself.

> "At that moment, I learned the difference between having responsibility and having control over life's circumstances"

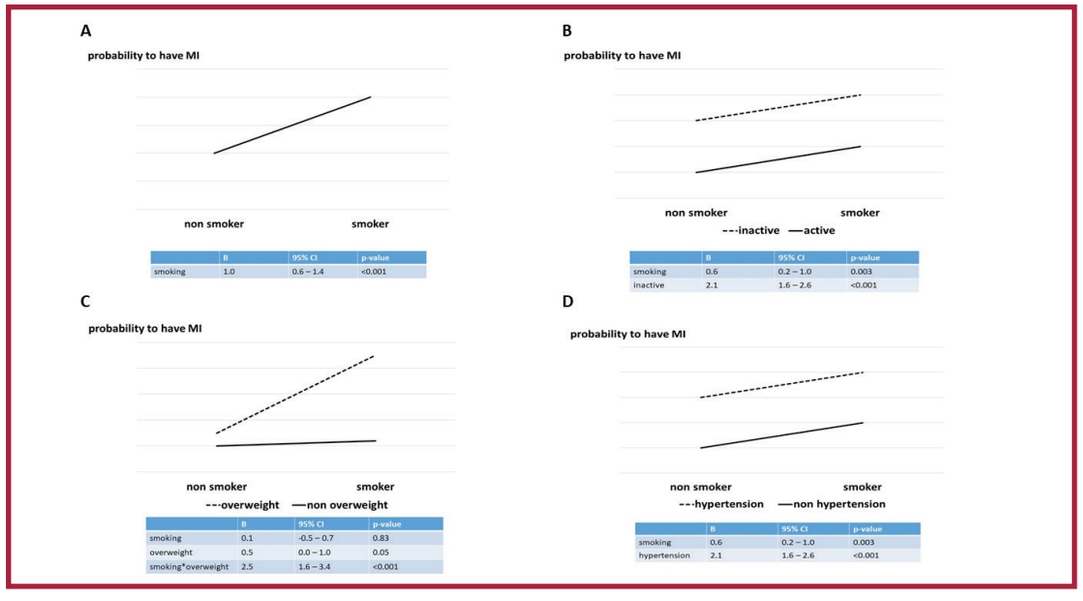
Fortunately, my university teaches and prepares students in delivering bad news to patients and dealing with death. Overall, dealing with the death of patients requires compassion, support, and care. Care for your patients, and their families, but also for yourself as a healthcare provider. Although coping with death might not become any easier throughout the years, it does become easier to appreciate that most patients will survive.

All you have to know about confounders, moderators, and mediators in medical research

Jos Twisk[1]
1. Department of Epidemiology and Data Science, Amsterdam UMC

Confounding, moderation, and mediation all influence the results of medical research in slightly different ways. The problem is that many medical researchers are a bit confused by the terminology. Therefore, the purpose of this column is to shed some light into the dark.

First of all, there is confounding. Suppose we perform a study to evaluate the relationship between smoking (which is the exposure) and the occurrence of myocardial infarction (which is the outcome). We probably will find a positive relationship between these two variables. Suppose now that smoking is part of what we call an unhealthy lifestyle cluster and it seems that in the study, smokers are more inactive than non-smokers. In that case, part of the effect observed for smoking can be due to inactivity. In this study, inactivity is a confounder in the relationship between smoking and the occurrence of myocardial infarction. Part of the effect of smoking is caused by something else, the confounder (in this case inactivity). So, the actual effect of smoking is less than observed in the first analysis. The 'real' effect of smoking can be obtained from an analysis including smoking and inactivity.



	B	95% CI	p-value
smoking	1.0	0.6 – 1.4	<0.001

	B	95% CI	p-value
smoking	0.6	0.2 – 1.0	0.003
inactive	2.1	1.6 – 2.6	<0.001

	B	95% CI	p-value
smoking	0.1	-0.5 – 0.7	0.83
overweight	0.5	0.0 – 1.0	0.05
smoking*overweight	2.5	1.6 – 3.4	<0.001

	B	95% CI	p-value
smoking	0.6	0.2 – 1.0	0.003
hypertension	2.1	1.6 – 2.6	<0.001

FIGURE 1 A: crude effect; B: confounding; C: moderation; D: mediation
MI = myocardial infarction

Confounding is often confused with mediation. The reason is that mediation and confounding can be investigated in exactly the same way. The difference between the two is based on a different definition. A mediator is in the causal path of the exposure and the outcome, while a confounder is not in the causal path. Let us look, for instance, at hypertension in the same example as mentioned before. Smokers have a higher probability to have hypertension compared to non-smokers. Basically the same as has been mentioned for inactivity. However, because hypertension is in the causal pathway of exposure (smoking) and outcome (myocardial infarction), hypertension is seen as a mediator in the relationship between smoking and myocardial infarction, i.e. part of the effect of smoking on myocardial infarction goes through hypertension. Basically the same idea, but a totally different interpretation.

> "A mediator is in the causal path of the exposure and the outcome, while a confounder is not in the causal path"

Confounding and mediation can be analyzed in the same way; the only difference is the interpretation. Moderation, on the other hand, is a totally different concept. Moderation is also known as effect modification and when a particular variable is a moderator it means that the effect of interest is different for other groups of the particular moderator. For instance, the relationship between smoking and myocardial infarction can be moderated by overweight. This means that the relationship between smoking and myocardial infarction is different for people with overweight and people without overweight.

It is important to realize that a particular variable can be a confounder and a moderator in a particular relationship. In many textbooks, it is more or less suggested that a variable is either a confounder or a moderator. That suggestion is not correct.

> "...when a particular variable is a moderator it means that the effect of interest is different for other groups of the particular moderator"

FIGURE 1 illustrates the principles of confounding, mediation, and moderation. FIGURE 1A shows the relationship between smoking and the probability of having a myocardial infarction (MI); this effect (i.e. a regression coefficient of 1.0) is known as the crude effect. FIGURE 1B shows the confounding effect of inactivity on the relationship between smoking and MI. It can be seen that the effect of smoking is attenuated by inactivity, i.e. the effect of smoking on MI is less strong (0.6 instead of 1.0) when an adjustment is made for inactivity. It can also be seen that the effect of smoking is equal for active and non-active subjects. So, inactivity is not a moderator in this relationship. This is different in FIGURE 1C, in which the relationship between smoking and MI is different for subjects that are overweight and subjects that are not overweight. Therefore, FIGURE 1C illustrates moderation, which is analyzed by adding an interaction term to the regression model. Based on the significance of the interaction term ($p<0.001$), there is significant moderation. FIGURE 1D is basically the same as FIGURE 1B; in both situations, the relationship between smoking and MI is attenuated by either inactivity or hypertension. The only difference is the interpretation of the influence of the third variable. Because hypertension is assumed to be in the causal pathway between smoking and MI, hypertension is interpreted as a mediator in this relationship. Inactivity, on the other hand, is assumed not to be in the causal pathway, so inactivity is interpreted as a confounder.

In the Erasmus Medical Centre, I ran into... Amir-Hossein Sadeghi, cardiothoracic surgery resident

Interviewed by Rahul A. Bhoera[1] and Wouter Bakhuis[2]
1. Faculty of Medicine, Amsterdam UMC, location VUmc, Vrije Universiteit Amsterdam
2. Department of Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam

As a final-year cardiothoracic surgery resident at the Erasmus Medical Center, Amir-Hossein Sadeghi will be able to call himself a cardiothoracic surgeon in less than a year. Apart from seeing patients and doing surgery, he is also active in the field of research and innovation within cardiothoracic surgery. He is the co-inventor of CardioVR and PulmoVR, a virtual reality and artificial intelligence-based tool that provides surgeons with 3D views of the anatomy of patients, based on CT scans, to improve surgical planning.

Could you talk about the journey that brought you where you are now in your career?

In 2010, I started studying Pharmacy at Utrecht University. During my Bachelor thesis internship, I got inspired by a physician who was also engaged in conducting biomedical research. That was the moment I decided to become a doctor and pursue a job where I would treat patients and maintain engagement in clinical research. After obtaining my Bachelor's degree, I got enrolled in SUMMA, a dual-degree Master's program at Utrecht University. In this way, I could reach my goal of becoming a physician and a clinical researcher. During this trajectory, my interest in cardiothoracic surgery found its origin when I attended coronary bypass surgery for the first time. After becoming a doctor I started working at the Erasmus MC as a junior physician (ANIOS).

Amir-Hossein Sadeghi, cardiothoracic surgery resident

In 2018 I got accepted to become a resident in training (AIOS). As I commenced my training, I experienced difficulties in using CT scans while preparing for complex lung surgery. Out of curiosity, I started investigating how I could improve this. After a while I came across the term 'virtual reality' and I thought maybe this could be the solution I was looking for. With Medical VR and cardiothoracic surgeons, I developed PulmoVR. Shortly after commencing my training, I started my PhD in immersive virtual reality in cardiothoracic surgery, which I successfully finished in 2021.

What has been the biggest struggle in your career?

The biggest struggle would be the insecurity during early residency as a resident not in training (ANIOS) Cardiothoracic surgery is very competitive when it comes to becoming a resident in training (AIOS). I wanted to fulfill my big dream of becoming a cardiothoracic surgeon. There was constant pressure, because as a candidate you have to constantly prove yourself and leave no space for errors. When I received the news that I got accepted to become a resident in training, it felt as if a huge burden fell off my shoulders. I was really relieved and grateful.

What do you consider to be the most beautiful aspect of cardiothoracic surgery?

As a cardiothoracic surgeon, it is a privilege and a great honor to literally take a patient's heart or lungs in your hands and fix it in order to save or improve someone's life. The best feeling in the world for me is to be able to see that after an operation, the patient is feeling better or sometimes 'relieved'. This, together with the gratitude of the patients, is an indescribable feeling that I find the most beautiful aspect of this humane specialty.

What is the most valuable lesson you learned during your career?

It is always important to work hard if you want to achieve a goal. Be eager to learn, stay humble, and remember that everything within cardiothoracic surgery is done with teamwork. That is why it is important to have a good understanding with your colleagues. These lessons all correlate with each other in order to function well in a team to provide optimal care for patients.

Do you have any advice for students with an interest in cardiothoracic surgery?

Start well in advance to explore how you want to profile yourself within the field. Doing research is not a must! You can also profile yourself by showing your interest and passion in other ways such as education, innovation, management, or anything else. Starting well in advance is key. Make sure you are well prepared when you are at the department and make sure that you are in the picture with the surgeons and residents. Go to the library, grab a book, and study. Really old school, but this will help you increase your knowledge of this specialism.

Pain: From toothache to suicide?

Mert Uluç[1]
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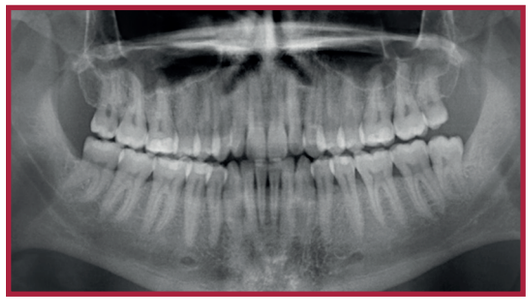
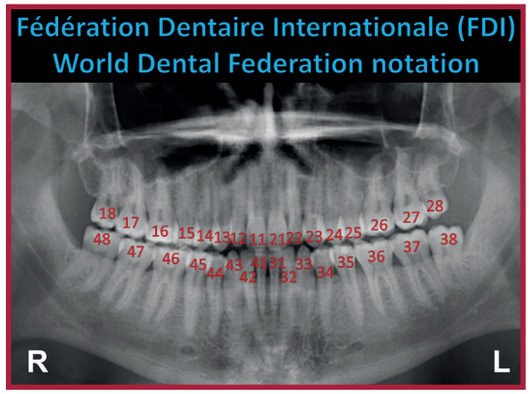
Case courtesy of Francis Deng, Radiopaedia.org, rID: 70397

CASE

Mr. A., 26 years old, seeks consultation regarding right mandibular pain, presumably due to the 48 (wisdom tooth).
You see the following orthopantomogram (OPT/OPG)





QUESTION 1

The OPT reveals:

A. Caries: Cavity in the 48, probably reaching the nerve.
B. Periodontitis: A radiolucency around the crown (pericoronal) of the 48 indicates vertical bone loss.
C. Temporomandibular Joint (TMJ) disorder: The TMJ has a sharp angle, indicating overuse of the lower jaw.
D. No notable findings.

No signs of local inflammation were observed (redness, swelling, pain, heat, and/or loss of function).
The pain is described as spontaneous intense bursts, lasting for less than a minute, with subsequent periods of significantly lower levels of pain.

Paracetamol, ibuprofen, and tramadol were completely ineffective. A slight touch, e.g. whilst brushing the teeth or shaving, can trigger the pain. The pain is so intense that he wants to repeatedly bonk his head to the wall. Suicidal thoughts, although briefly present, were also mentioned.

QUESTION 2

Knowing you were a very eager medical student, you quickly remember which diagnosis is most befitting and also its potential cause(s):

A. Overuse of the jaws
B. A blood vessel
C. A lack of sleep
D. Multiple sclerosis
E. Tumor
F. Idiopathic

QUESTION 3

A Jannetta procedure will take place soon. Which pharmaceutical option is indicated for suppressing the pain associated with the condition in the meantime?

A. Carbamazepine (anti-epileptic)
B. Sumatriptan (selective 5HT1-agonist)
C. Verapamil (calciumantagonist)
D. Morphine (opioid)

Answer on page 31

A joyful view of life – different patient perspectives

Soumaya Laabar[1] and Sanne Graaf[2]
1. Faculty of Medicine, Amsterdam University Medical Centers, location Academic Medical Center,Amsterdam, The Netherlands
2. Department of Pediatrics, Medical Center Leeuwarden, The Netherlands

> ‘‘Working as a medical professional allows us to experience a variety of memorable cases’’

> ‘‘The human perspective on disease is an exciting part of your work as a medical professional’’

Working as a medical professional allows us to experience a variety of memorable cases. For this section, I will describe a patient case Drs.. S. Graaf encountered working in the pediatric field.

‘’A 5-year-old girl was presented at the emergency department with dyspnea. She looked unwell and anxious. Her face was pale and she was not able to speak. There was marked chest recession, a respiratory rate of over 40 breaths per minute, and a low oxygen saturation of 88%. During the psychical examination, decreased breathing sounds were heard over de lungs. Oxygen support and salbutamol nebulization were started. Shortly after, she was admitted to the pediatric ward with bronchial hyperreactivity due to a viral respiratory infection. Over the night she needed higher oxygen support levels and the salbutamol nebulization frequency was increased. Luckily she was stable in the morning. We refrained from a transfer to the pediatric intensive care unit. During bed rounds, we came to her room. She looked out of the window, the sun was shining on her face. Because of the nasal oxygen cannula, she was not able to move freely. Nonetheless, she told us very happily ‘’I feel better already, I can go home now!’.

The human perspective on disease is an exciting part of your work as a medical professional. There is a wide variety due to demographic and cultural differences. This patient's case describes the resilience of the child. Even though physically she was not able to leave the hospital yet, she already felt better. I recommend everyone to work with children for an extended period of time. The beauty of this resilience is something we can learn from as adults.’’

Tetralogy of Fallot

Sally H. Khalaf, BSc[1] and Petra E. Habets, MD PhD[2]
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2. Department of Medical Biology, Clinical Anatomy and Embryology Section, Amsterdam UMC, Location AMC

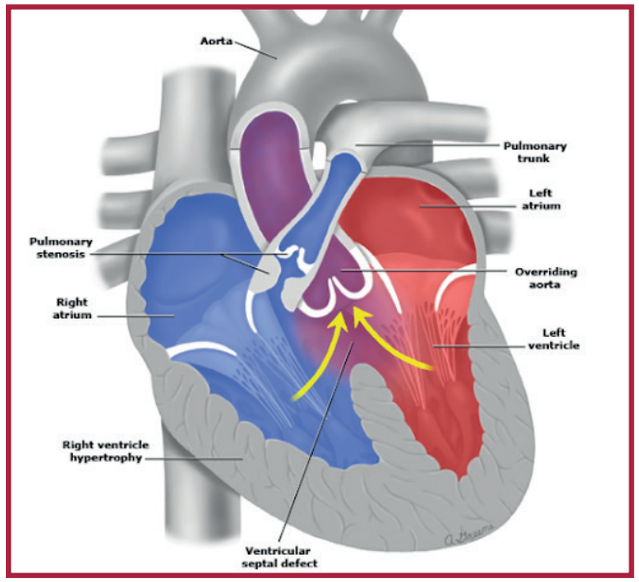

FIGURE 1 Anatomy of tetralogy of Fallot (UpToDate: Pathophysiology, clinical features, and diagnosis of tetralogy of Fallot).

DEFINITION

Tetralogy of Fallot is a cyanotic congenital heart defect characterized by the simultaneous occurrence of four anatomical construction defects. These defects include a right ventricular outflow tract obstruction, right ventricular hypertrophy, ventricular septal defect, and an overriding aorta.

EPIDEMIOLOGY

About 60 children are born with a tetralogy of Fallot in the Netherlands every year. With a prevalence rate ranging from 50 to 70%, this is the most frequently occurring cyanotic congenital heart defect worldwide. Roughly 7 to 10 percent of cases of all congenital heart diseases can be attributed to this defect.[1]

ANATOMY

The exact cause and embryology of these defects are unknown, but it is believed that during development, a deviation of the infundibular septum can lead to improper development of the septum, resulting in a “hole” in the septum or ventricular septal defect (VSD). Additionally, the aorta is displaced over the ventricular septal defect causing an overriding aorta, which can lead to right ventricular outflow tract (RVOT) obstruction. These defects put significant pressure on the right ventricle forcing it to work harder, eventually leading to hypertrophy or enlargement of the right ventricle.[2] For illustration see (FIGURE 1).

ETIOLOGY

Although the tetralogy of Fallot often occurs sporadically[3], it can also occur as part of a syndromic condition, often genetically determined such as Down syndrome and DiGeorge syndrome. Certain maternal risk factors are also associated with this condition, such as maternal alcohol consumption during pregnancy and phenylketonuria.[4]

> “Although the tetralogy of Fallot often occurs sporadically, it can also occur as part of a syndromic condition”

CLINICAL FINDINGS

Most patients with tetralogy of Fallot are diagnosed prenatally. Patients with a mild form may be initially asymptomatic. The severity of the symptoms depends on the degree of obstruction of the right ventricular outflow tract. In mild obstruction, left-right shunting of blood occurs through the VSD. Therefore, the patient might not show severe symptoms of cyanosis. In this case, the cyanosis may be seen mainly in the child's extremities. However, in severe obstruction, right-left shunting takes place making the cyanosis more pronounced. In addition, children may have attacks called "Tet spells", usually after a period of exercise where the right ventricle constricts, exacerbating the constriction already in place, and allowing more deoxygenated blood to enter the systemic circulation. This results in a child who is restless looks extra cyanotic, and has stuttering breathing. These attacks vary in duration and can sometimes be fatal.[5] Typically, the child then attempts to squat, a mechanism that increases peripheral vascular resistance and can lead to temporary reversed shunting and recovery.

TREATMENT AND PROGNOSIS

Fortunately, the severe attacks mentioned above are less common because children with tetralogy of Fallot usually undergo surgery during their first year of life to correct the ventricular septal defect and alleviate the pulmonary constriction. Without surgery, it is estimated that 50% of patients do not reach their third year of life. With the corrective operation, more than 90% of the patients reach the age of 25 years.[6,7]

> “With the corrective operation, more than 90% of the patients reach the age of 25 years.”

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The Expert's View – Marcel Levi[1]

1. President Dutch Research Council (NWO) and Professor of Medicine, University of Amsterdam and University College London

Uninformed consent

Randomized controlled clinical trials are often regarded as the most straightforward way to gather information on the efficacy or safety of medical treatment. Usually, before the trial starts a lot of care is given to the establishment of the most relevant outcome measures, choice of the right intervention and control groups, and adequate identification of eligible study subjects. After the initiation of the trial much effort is devoted to finding the right patients to participate, following all study procedures according to the protocol, and – after completion – analyzing the results as precisely as possible and publishing the results.

Nevertheless, not every clinical trial is a success. One of the biggest hurdles is often collecting the required number of trial participants. More than 85% of clinical studies that are included in clinical trial registers do not successfully include the number of patients within the pre-specified timeframe. Insufficient inclusion is the reason for the stopping and failure of about one-fifth of all clinical studies. The most frequent reason for insufficient inclusion is a too-optimistic estimate of eligible patients at the start of the trial. While almost every protocol starts by advertising that the disease of interest "… is one of the most frequently occurring problems in medicine …", patients seem to vanish like thin air as soon as a trial starts. The problem is further aggravated by too complex in- and exclusion criteria.

Failure of a clinical trial is not only a waste of time and energy of the investigators and a dissipation of scarce research money by funding agencies but also quite unfair towards the patients that did participate. In fact, they had agreed to be exposed to a new intervention (or placebo) and have often undergone additional trial procedures or hospital visits. They had done so because they were prepared to contribute to medical research, sometimes mostly in the interest of other, future, patients. But if their sacrifice did not at all contribute to an increase in medical knowledge because the trial failed, their effort was useless and their good faith is being compromised.

Another form of a failed trial is a trial that has been completed and analyzed but is eventually not published. Withholding publication of trial results may be at the request of a sponsoring company that wants to protect intellectual property. However, the current scientific code dictates that such interests can only justify a minor delay (a few months) in publication and that all results should be ultimately published. Nevertheless, a recent survey of 500 of the largest studies in the most important trial register (ClinicalTrials.gov) demonstrated that the results of 70 trials with a total number of approximately 90.000 participants were not yet published ten years after the completion of the study.

I am not sure whether participating patients are at all informed that they had participated in a failed study (including a study that was completed but not published). And it is even less certain that we warn patients of possible failure when we ask them to participate in a trial or that we promise them that trial results will always be published. I think it would be appropriate if ethical review boards would pay attention to adequately informing potentially participating patients that a trial is not always successfully completed and would ask for guarantees that all trial results would be published within a reasonable time frame. If not, patients are likely to provide uninformed consent when asked to participate in clinical research.

Updated recommendations for hiccups in a palliative setting

Sanne Roos[1] and Remco J. Molenaar[2]
1. Faculty of Medicine, Amsterdam UMC, Location VUmc, Amsterdam
2. Department of Oncology, Amsterdam UMC, Location AMC, Amsterdam

Hiccups are a common symptom among palliative oncology patients negatively impacting the quality of life. Prevalence ranges from 1 to 9%[1,2]. Recently, the guidelines for this symptom have been updated. When the underlying cause of hiccups cannot be addressed, non-drug measures such as vagal nerve stimulation (Valsalva maneuver), uvula stimulation (by tickling the pharynx with a cotton swab), or diaphragm inhibition (by swallowing crushed ice) are advised as first steps.[3] Several studies have explored the effectiveness of acupuncture as well.[3] However, there is insufficient evidence to recommend this, due to low-quality studies that only compare acupuncture to methylphenidate or anisodamine, which are not proven effective.[3]

> "Hiccups are a common symptom among palliative oncology patients negatively impacting the quality of life"

For pharmacological treatment, baclofen, gabapentin, and metoclopramide are the three options that are best supported by scientific evidence.[3] It is not clear whether one of these is superior to the other.[3] The choice should therefore be based on individual patient preferences and the pharmacological properties that best fit their characteristics.[3] Other drugs have been less extensively studied or exhibit a less favorable side-effect profile.[3] Chlorpromazine is the only registered drug for this indication, but it is less readily available in the Netherlands.[3] It may be considered if the above-mentioned drugs have not been effective, in which case, consultation with a pharmacist is recommended.[3] If pharmacological treatment options fail, unilateral blockade or electrical stimulation of the phrenic nerve should be considered even though anesthesiologists have limited experience with this intervention.[3] This recommendation is based on a study that demonstrated promising results.[4] This retrospective study showed that one session of 48-hour epidural blockade of C3-C5 resulted in the resolution of symptoms in 61% of cases, and for two sessions this result improved to 93%.[4] There was no control group, therefore no p-values were reported.[4]

In conclusion, the revision of the guideline resulted in the recommendation of three equally effective pharmacological options, and of phrenic nerve blockade as a potential next step. This revision makes the treatment of hiccups more evidence-based and therefore may improve the care for patients with this debilitating symptom.

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Prof. Dr. Michel van den Bekerom

Interviewd by Stijn R.J. Mennes[1,2] and Reinier W.A. Spek[1]
1. Department of Orthopedic Surgery, OLVG Amsterdam, The Netherlands
2. Department of Human Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Prof. Dr. Michel van den Bekerom, Orthopedic surgeon at OLVG hospital and Jan van Goyen clinics

Could you introduce yourself to our readers?
My name is Michel van den Bekerom. I have been an orthopedic surgeon for twelve years now. I work in the elbow and shoulder unit at OLVG Hospital and Jan van Goyen Clinics. I also enjoy doing and supervising scientific research. In my spare time, I spend time with my family, drink wine and make tours on my race bike.

What is your area of expertise?
During my fellowships, I have specialized in the operative treatment of both shoulder and elbow conditions. As a professor in sports traumatology, my main focus is on sports-related injuries. We treat a broad spectrum of diseases in patients both young and old, and also in amateur and professional athletes. These pathologies consist of fractures, ligament injuries, joint instability, and also related arthrosis. Sometimes a patient needs an operation and in other moments it may be better to not operate. As a surgeon, operating is one of the best parts of the job but a good surgeon also knows when not to operate.

> "As a surgeon, operating is one of the best parts of the job but a good surgeon also knows when not to operate."

Why is being an orthopedic surgeon so much fun?
For me, it is the variation within my workweek. One day, I work with my team in the operating room, while the next day, I see patients in the outpatient clinic or conduct research. The variety of conditions, ranging from relatively simple to complex ones, we treat at OLVG makes it a vigorous work environment. Additionally, in a teaching hospital, I have the opportunity to work with and educate young doctors and students, which is something that I enjoy tremendously. Another fun part of being an orthopedic surgeon is working in a team. Orthopedic patients often need a multidisciplinary team, which can consist of sports medicine physicians, radiologists, physiotherapists, anaesthesiologists, operating assistants, and so forth. You will get to work with many different colleagues!

> "Another fun part of being an orthopedic surgeon is working in a team"

Can you tell us something about your research focus?
The focus of our research is on shoulder- and elbow conditions. We try to understand the relationship between structural, functional, and mental problems. For instance, when we treat shoulder instability, we may surgically address the structural issue by fixing the labrum, and work with the patient's physiotherapist to address functional problems by training the rotator cuff and scapula muscles. However, a significant number of our patients may not fully recover and return to their normal activities due to the fear of re-dislocation, which can be considered a mental problem. We believe that the mental aspect of our patients' conditions is just as crucial as the structural and functional ones, and that's where our research is focused. We seek to understand which patients experience the fear of relapsing and how we can help them regain the confidence to return to their sport or work.

> "We believe that the mental aspect of our patients' conditions is just as crucial as the structural and functional ones"

Many of our readers are students, what would you advise them?
My advice is to keep an open mind during your internships and find a specialty that excites and suits you. Some specialties may look heroic or interesting during your internship but they have their downsides as well. Take your time and figure out what you find important in life.

CURRICULUM VITAE

1978	Birth
2004	Graduation medicine, KU Leuven, Belgium
2004	Residency (not in training) in orthopedic surgery, Gelre hospitals
2005	Residency in orthopedic surgery, AMC
2011	Registered orthopedic surgeon, fellowship shoulder and elbow surgery, Amphia hospital
2013	Staff member orthopedic surgery, shoulder and elbow unit, OLVG hospital
2019	PhD, University of Amsterdam
2021	Professor in sports traumatology of the upper extremity, VU Amsterdam

CURRENT POSITIONS: Orthopedic surgeon at OLVG hospital and Jan van Goyen clinics. Professor in sports traumatology of the upper extremity at VU Amsterdam.

E-MAIL ADDRESS: M.P.J.vandenBekerom@olvg.nl

Finally, can you mention something in your life you are particularly proud of?
While I work hard and certainly enjoy my job, I have learned to switch off the "doctor button" when I need to do something else. This has enabled me to be fully present with my family at home or my friends on vacation without having to think about work. As a result, I find that my work remains enjoyable, and I can get more satisfaction from my spare time. Achieving this balance between work and personal life is something that I am proud of, and I believe it has made me a better doctor and a happier person. ◀

3D Printed Breast Implants: Fiction or Reality?

Felicio Wildeboer[1] and Debby Bom[2]
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2. van Weel-Bethesda Hospital Department of Emergency Medicine Stationsweg 22, Dirksland

A great number of breast cancer patients prefer breast-conserving surgery. However, breast-conserving surgery is occasionally accompanied by post-operative problems such as infections, deformities, asymmetry, and pain. 3D printing (3DP) can mitigate these adverse effects by precision 3D scaffold printing where scaffolds can be altered according to the patient's wishes. Moreover, depending on the used print material these scaffolds are able to incorporate medication, such as antibiotics to mitigate the risk of infection, or chemotherapy, allowing shrinkage of the tumor. Furthermore, some used biopolymers can be incorporated with stem cells, allowing for the growth of breast-tissue-forming cells over time to enhance cosmesis. In recent studies, biodegradable scaffolds are used which are absorbed by the body over time, therefore reducing post-operative complications and the number of needed revisionary surgeries.

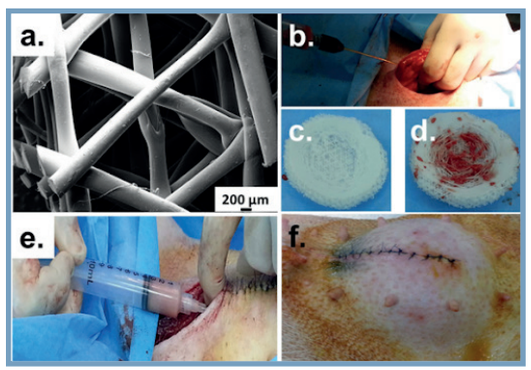

FIGURE 1 a) schematic overview of the pores of the scaffold; b) Liposuction procedure near the abdominal midline incision; c) empty scaffold; d) completely filled scaffold; e) fat injection in the prevascularizated + lipoaspirate scaffolds; f) the final form of scaffold adapting a natural breast shape.

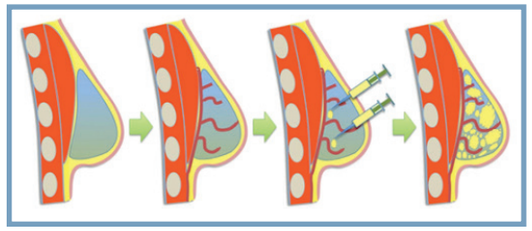

FIGURE 2 **Schematic overview of prevascularisation and delayed-fat injection step.** Firstly, the empty scaffold is implanted. Secondly, over the following 2-3 weeks connective tissue formation and neovascularization occurs within the pores of the scaffold. Then fat is injected into the pores. Pre-formed vascularization allows stabilization of the formed adipose tissue.

One of those studies was conducted by Chhaya et al. (2016) in which Bellaseno's medical-grade 75 cm3 polycaprolactone-based biodegradable implants (Senella) were implanted in six surgically created subglandular pockets on female swine (n = 4).[1] The four female pigs were evaluated with a follow-up of 24 weeks. Their results showed that all subjects tolerated the implantation and surgery with no clinical signs of infection. One swine developed seroma accumulation in one subglandular pocket (n = 1; 4.2%) 12 weeks post-surgery. Furthermore, prevascularisation and delayed fat-injection techniques with lipoaspirate were used and yielded promising adipose tissue regeneration on the scaffolds (FIGURE 1 AND 2). In 2022 Manufacturer Bellaseno announced that their 3DP Senella breast implants entered phase I human trials.[2] As shown in the study of Chhaya et al. the implants are biodegradable and therefore slowly absorbed by the body within three years while leaving behind the patient's own tissues by autologous fat injections. Last year these implants passed its first human trial, confirming the implant's efficacy and safety in human applications. Furthermore, these properties eliminate the risk of rupture and encapsulation, while weighing more than 90% less than silicone-based implants.

> "these properties eliminate the risk of rupture and encapsulation, while weighing more than 90% less than silicone-based implants"

These results are promising and show that we are one step closer to eradicating traditional materials and manufacturing methods used for implants in the field of plastic surgery. Consequently, reducing post-operative complications while possibly increasing cosmesis and patient satisfaction rate. Furthermore, the personalization of scaffold properties will further enhance treatment options in breast cancer patients. Nevertheless, more research is needed to further enhance the field of 3DP in order to completely replace traditional manufacturing methods.

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A helpful tool to assess pigmented skin lesions in primary care

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2. Department of general practice, section student education Vumc

"timely diagnosis and treatment are essential for improved patient outcomes"

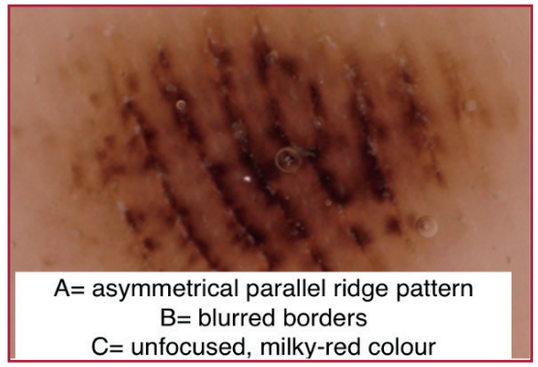
One of the most prevalent types of cancer worldwide is skin cancer, which encompasses melanoma, basal cell carcinoma, and cutaneous squamous cell carcinoma. According to the World Health Organization (WHO), there were an estimated 324,000 new cases of melanoma worldwide in 2020. Melanoma comprises just 1% of skin cancers but is responsible for the majority of skin cancer deaths.[1] In the Netherlands alone, 800 patients per year die due to melanomas.[2] As a result, timely diagnosis and treatment are essential for improved patient outcomes, especially for melanoma.

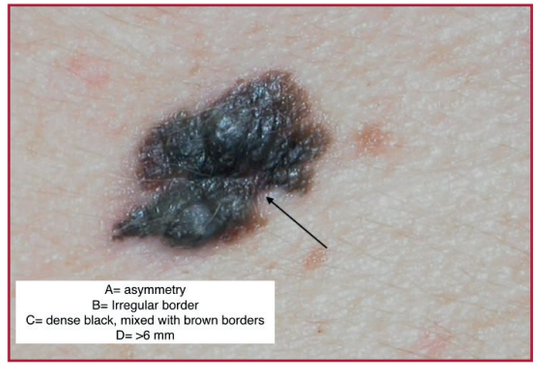
There are four types of melanomas to be identified: superficial spreading melanoma (SSM), nodular melanomas, lentigo melanomas, and acral lentiginous melanoma.[3,4] SMM is the most common type of invasive melanoma and often occurs at the trunk or legs. Nodular melanomas often present as a raised, firm, dark-colored bump that can rapidly increase in size and often occur on the head and neck of older patients. Lentigo maligna, on the other hand, progresses rapidly and is poorly

"There are four types of melanomas to be identified: superficial spreading melanoma (SSM), nodular melanomas, lentigo melanomas, and acral lentiginous melanoma"

defined and variably pigmented, often appearing after a slow-growing precursor-pigmented macule, also known as Hutchinson's freckle. It is more common in individuals aged 60 and over. Acral lentiginous melanomas, which are more common in the Asian population, are large pigmented macules that occur exclusively on the palms and soles and under nails and can mimic warts with a verrucous, non-pigmented appearance.[3,5]

In the general practice setting, the physical examination is the cornerstone of the evaluation of pigmented skin lesions and is systematized with the ABCDE rule.[3,4] The ABCDE rule stands for asymmetry, border irregularity, color variation (potentially cancerous mole or lesion may have varying shades of color, or may have black, blue, or white areas), diameter larger than 6mm, and





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evolving size, shape, or color. Lesions that exhibit any of these characteristics should be further evaluated, as they may indicate the presence of melanoma.

In conclusion, melanoma is a serious skin cancer that demands early detection and treatment for optimal outcomes. In general practice, a physical examination is crucial to spot suspicious lesions and check lymph nodes. Healthcare providers must know the features of melanoma and apply the ABCDE rule to detect potentially malignant lesions. Dermoscopy can also be valuable in diagnosis and management. With a thorough physical examination and diagnostic tools, healthcare providers play a vital role in the early detection and management of melanoma.[3]

"In general practice, a physical examination is crucial to spot suspicious lesions and check lymph nodes"

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Prof. dr. Frank W. Bloemers

INTERVIEWD BY ELISE BEIJER[1] AND FAY R.K. SANDERS[2]
1. FACULTY OF MEDICINE, VRIJE UNIVERSITEIT, AMSTERDAM
2. DEPARTMENT OF SURGERY, RADBOUD UMC, NIJMEGEN

CURRICULUM VITAE

1969	Year of birth, Amsterdam
1996	MD, University of Amsterdam
2004	PhD "Resorbable bone substitutes in trauma surgery", Free University Amsterdam
2005	Medical doctor Heli-MMT Lifeliner 1
2007	Senior staff member Trauma surgery, VUmc Amsterdam
2008	Consultant surgeon AFC AJAX
2011	MSc clinical epidemiology, Free University of Amsterdam
2012	Head Department of Trauma surgery, VUmc Amsterdam
2018	Chairman ROAZ region Northern and Western Netherlands
2019	Professor of Trauma surgery, Amsterdam UMC
2020	Head Department of Trauma surgery, Amsterdam UMC

CURRENT POSITIONS: professor in Trauma surgery, consultant surgeon AFC AJAX and head department of Trauma surgery Amsterdam UMC

AREA OF EXPERTISE: Trauma surgery, polytrauma patients, complex and spinal fractures, sports traumatology, education, research

Prof. dr. Frank W. Bloemers

Could you please introduce yourself?
My name is Frank Bloemers and I am a trauma surgeon, born and raised in Amsterdam.

Why is trauma surgery THE specialty for you?
What I particularly like about trauma surgery is that this specialty is the most comprehensive and exciting occupation. And, challenging and different every single day!

What kind of medical student were you during your studies?
I was the kind of medical student that enjoyed life; I was rowing at Nereus and living in a house together with my friends. But nevertheless, eager to learn every day!

Could you name the highlights of your career?
Besides the marks on my CV such as my time as a medical doctor at the Heli-MMT Lifeliner 1 and being the consultant surgeon of AFC AJAX, the real highlights in my career are the patients I treated. It brings me so much energy and positivity when I helped a patient successfully. This applies not only in cases of patients with life-threatening injuries but also to patients with relatively minor injuries.

What are you most proud of?
Recently, we succeeded in merging the trauma surgery departments of two enormous hospitals in Amsterdam: the VUmc and the AMC. We (from VUmc) did this together with the orthopaedic and the trauma surgeons in the AMC. This is a huge accomplishment; I am very proud of all the nurses, specialists, and other staff and people involved in making this the big success it is. We now are one of the largest trauma centers in Europe and treat patients with the highest possible quality of care.

> "We now are one of the largest trauma centers in Europe"

After all you have accomplished so far, what are your future ambitions?
My future ambitions include working hard on the optimization of many processes in the trauma surgery department of Amsterdam UMC. I strive to realize the best trauma center in Europe here in Amsterdam. Traumasurgeons will super specialize in specific topics, for example upper- or lower extremities. Or pelvic and children trauma surgery.

What was a big challenge in your career?
It is always challenging: every step you take in your career takes full devotion.

Is there something you would like to see changed in trauma surgery and/or your profession?
I think that our specialism needs a more scientific "body". It is important to keep improving our knowledge of e.g. treatment strategies in trauma surgery so that we ensure the best care for our patients. I would not be surprised if we will super specialize as trauma surgeons in, for instance, lower extremity injuries or pelvic fractures as mentioned before.

What are your main research interests?
My main research interests include spine and fracture healing, but also the influence of trauma on cellular processes and how we can target this and try to develop novel therapies to target these processes. Basic science is becoming more and more important, as well as translational studies providing new knowledge.

Any advice for medical students interested in research and/or trauma surgery?
Enjoy life and meanwhile develop yourself as a complete person. Do not rush, keep going steadily and keep curious about your environment!

In the outpatient clinic of the VUMC I ran into Ewa Platek, Rheumatology research nurse

Interviewed by Wouter van Binsbergen[1] and Özlem Bilir[2]
1. Department of Rheumatology and Clinical Immunology, Amsterdam UMC location VUMC.
2. Medical student, Amsterdam UMC location VUMC, Vrije Universiteit

In the outpatient clinic, I ran into Ewa Platek[1], a research nurse from the Dept. of Rheumatology and Clinical Immunology, and asked about his normal workday and participation in clinical research.

What does a research nurse do?

A research nurse assists their department in the creation and execution of clinical studies. They are involved in both the creation and execution of studies. They can create study documentation and submit it to the competent authority such as the Medical Ethics Board (METc). In addition, they administer study visits including physical exams, questionnaires, and general examination of study participants. Finally, they fill in, organize and archive study materials and documentation. In this fashion, they support PIs, post-docs, and PhD-students in research efforts.

What is involved in the creation of a study?

Well, the creation of a study requires a lot of different documentation, which was recently expanded with the ECTR (European Clinical Trial Regulation) for research involving medications. The documentation needs to be precise according to the regulations and then contained in the local study binder. Once all the appropriate documents have been created, signed, and dated, they must be submitted to the ethical committee. If you're lucky, it will be approved in the first round, if not, there will be further rounds of questions and re-submissions.

> "If you're lucky, it will be approved in the first round, if not, there will be further rounds of questions and re-submissions"

Once a study is approved, what are your responsibilities then?

Once a study has been approved, the real work begins. I contact patients and explain the study to them, following the complete informed consent procedure. Once a patient agrees, I plan study visits and compile both study documentation and the materials required for blood draws or sample collection. Especially when the clinical lab is not specifically involved in the study, precision and preparation of this part is vital. If I don't get all the proper information or samples, the study hypothesis can't be tested. Once all questions have been asked, all papers filled out and all samples taken to the lab, the data is then put into the appropriate database. Once all data for a study has been completed and analyses have been conducted, I am also responsible for the archiving of all related materials. In addition, for all study visits, there is not just the study admin to take care of, there is also the patient's medical file to update, for which we are responsible as well.

Ewa Platek, rheumatology research nurse

Does your work overlap with clinical care?

As just mentioned, I manage patient participation in studies. That does sometimes overlap with clinical care, especially considering that any action that is taken in the study, must be documented in the patient's file so that the treating physician can account for all potential information and changes. In addition, I am a research coordinator in EPIC, allowing me to oversee studies in the patient files, ensuring that the study is properly linked to the patient, and to all actions taken for the study. There is also regular cooperation with the specialized rheumatology nurses, as they sometimes start patients on specific therapies, which are part of either a study or a study inclusion criteria. To ensure smooth study participation, timing for inclusion or study visits is often combined and coordinated to take advantage of these other visits.

What other aspects of research do you encounter?

Studies can vary widely in our participation, as we do studies for PIs, we support other researchers such as PhDs and we also coordinate studies sponsored by pharmaceutical companies. In each the tasks to be carried out can vary as for a PhD I might only prepare some tubes for blood draws, whilst for a pharma study the entire clinical evaluation is part of my responsibilities. To manage all these tasks requires that I keep a close eye on current and future regulations, such as the new European Clinical Trial Regulation to ensure any study I do, is up to date. In addition, I also keep my clinical skills up to date, to ensure I can do all the evaluations required by a new potential study. So my work brings me into contact with all aspects of clinical research

Answers 'pain: From toothache to suicide?'

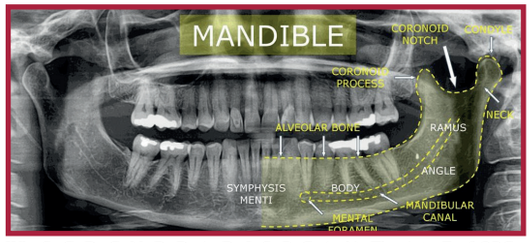
Mert Uluç

Answer options Q1
A. caries: Cavity in the 48, probably reaching the nerve.
B. Periodontitis: A radiolucency around the crown (pericoronal) of the 48 indicates vertical bone loss.
C. Temporomandibular Joint (TMJ) disorder: The TMJ has a sharp angle, indicating overuse of the lower jaw.
D. No notable findings.

Answer options Q2
A. Overuse of the jaws
B. A blood vessel
C. A lack of sleep
D. Multiple sclerosis
E. Tumor
F. Idiopathic

Answer options Q3
A. Carbamazepine (anti-epileptic)
B. Sumatriptan (selective 5HT1-agonist)
C. Verapamil (calciumantagonist)
D. Morphine (opioid)

Correct answers: 1D, 2B-D-E-F, 3A



Wk, S. C. D. C. N. B. D. A. B. J. S. P. C. (z.d.). The A to Z of OPGs. Sarah Constantine MBBS, FRANZCR Dental Radiologist. ppt download. https://slideplayer.com/slide/13121786/

EXPLANATION

Answer Q1: There are no (peri)odontogenic pathologies. The TMJ is not visible. The ascending branch of the mandible (ramus) has 2 processes, namely, the condylar process (dorsal) and the coronoid process (ventral). The condylar process is part of the TMJ and is not visible on the OPT of the patient. The coronoid process, deceitfully referred to in option C, forms the insertion of the temporal muscle. Furthermore, overuse of the jaws is not noticeable by 'the angle of the TMJ' but rather by the formation of small irregular bumps on the angle of the mandible, which are absent.

Answer Q2: Generally, trigeminal neuralgia is caused by either direct pressure to the nerve or demyelinating disease. Three categories can be made[1]:
- Idiopathic
- Classic: Due to neurovascular compression at the trigeminal root entry zone.
- Secondary: Due to underlying diseases such as a tumor or multiple sclerosis.

Answer Q3: Carbamazepine may be effective due to its ability to block voltage-gated sodium channels, thus inhibiting action potentials, reducing synapse transmission, and stabilizing the membrane potential in hyperexcitable neurons.[1, 2]

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Answers 'Neurological abnormalities in a young patient'

Matthijs J. van Ee, Dr. Carl A.J. Puylaert and Prof. Dr. Mario Maas

Answer options Q1
A. Plaques
B. Ischemia
C. Dawson's fingers
D. Granulomas

Answer options Q2
A. No abnormalities
B. This is an axial post-contrast T1 image showing a lesion with open ring enhancement in the left frontal lobe
C. This is an axial FLAIR image showing T2-hyperintense juxtacortical lesions
D. This is an axial FLAIR image showing T2-hyperintense lesions in the periventricular white matter

Answer Q3
Multiple Sclerosis. There is dissemination in place and time, so the radiologic McDonald criteria for MS diagnosis are met.

Correct answers: 1C, 2B

EXPLANATION

In this case, the diagnosis is multiple sclerosis (MS). MS is a demyelinating disease of unknown exact etiology, that affects the brain and spinal cord. MS leads to damage to the insulating myelin sheath that surrounds nerve fibers. Consequentially, signals traveling along these nerves are disrupted leading to a wide range of neurological symptoms, such as vision problems, fatigue, and stiffness.

In this typical case of MS, the sagittal FLAIR MRI image shows multiple ovoid lesions in the periventricular white matter. This sign is called Dawson's fingers and represents areas of white matter demyelination.[1]
The second MRI image is a post-contrast T1 image showing open ring enhancement in the left frontal lobe. This finding is suggestive of an active demyelinating lesion. Open ring enhancement refers to the presence of contrast enhancement around part of the edge of a lesion, forming an incomplete ring.[2] After the initial phase of active demyelination, older lesions do not show enhancement anymore on post-contrast images.

The McDonald Criteria is a set of criteria for the diagnosis of MS. The radiologic criteria for lesions on MRI require what is called dissemination in time and space. Dissemination in space refers to lesions in at least two out of four specific regions of the central nervous system (periventricular, juxtacortical, infratentorial, and spinal cord)
Dissemination in time refers to the progression of this disease, which the presence of new T2-hyperintense lesions can establish compared to a previous MRI or the simultaneous presence of enhancing and non-enhancing lesions (as in this patient). The current MRI images show both dissemination in place and time, thus fulfilling the radiologic criteria for MS diagnosis.

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