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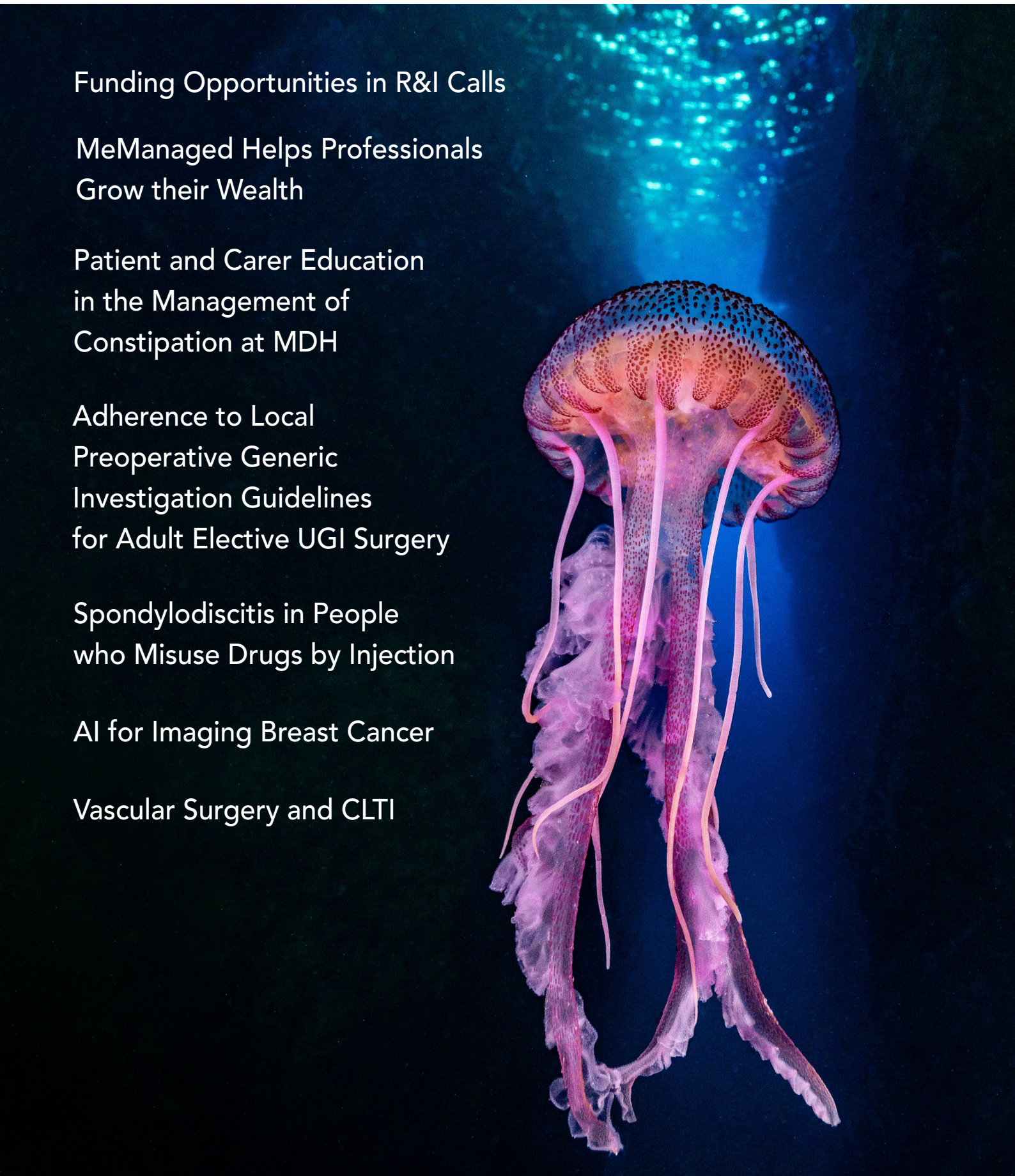
THE MEDICAL PROFESSIONALS' NETWORK



Funding Opportunities in R&I Calls

MeManaged Helps Professionals Grow their Wealth

Patient and Carer Education in the Management of Constipation at MDH

Adherence to Local Preoperative Generic Investigation Guidelines for Adult Elective UGI Surgery

Spondylodiscitis in People who Misuse Drugs by Injection

AI for Imaging Breast Cancer

Vascular Surgery and CLTI

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## CONTINUING MEDICAL EDUCATION

## Upcoming Webinars and Masterclasses 2023-2024

| Date | Session Title | Speaker | Type | Mode |
|---|---|---|---|---|
| 15th June 2023 | Men and GU Problems | Dr Donia Gamoudi | On Demand | Men's Health Masterclass |
| 21st June 2023 | Hepatitis C Virus Elimination Campaign | Dr Chris Barbara | On Demand | Stand Alone |
| **Summer Break** | | | | |
| 13th Sept 2023 | Men's Health - Opportunistic Screening in Men | Various | Live Webinar | Men's Health Masterclass |
| 27th Sept 2023 | Self Management 'Take Control' Programme Campaign | Dr Mariella Borg Buontempo | Live Webinar | Stand Alone |
| 11th Oct 2023 | Men's Health - Other Medical Issues | Various | Live Webinar | Men's Health Masterclass |
| 25th Oct 2023 | Management of Constipation in Adults and Children | Various | On Demand Live Webinar | Stand Alone |

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Malta Leadership Institute

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thesynapse THE MEDICAL PROFESSIONALS' NETWORK

GUEST EDITORIAL

HON. DR JO-ETIENNE ABELA
Minister for Active Ageing

# Vision for the Ageing Sector

My political career is only a shade over 18 months old; in April of last year I was thrust as the top man at the Active Ageing Ministry. As a medical doctor, it may be reflexive to get lost in the detail of medical care for older persons. However, having this attitude as a Minister can be deleterious. If we are to excel in end-user satisfaction, which is what really matters, we need to embark on a balancing act with the promotion of the healthcare aspect of older person medicine on one side and the pursuit of social reform on the other. In keeping with this, Government has recently launched a new version of the National Strategy for Active Ageing that will take us to 2030. Aside from the important pillars of social inclusion and addressing diversity and inequalities, the third pillar is healthy ageing and I shall focus on this aspect.

In the initial encounters with my heads of sections, I made it clear that we should follow the electoral manifesto but that we should not be constrained by it. Given the rising life expectancy, the soaring needs for long term care (LTC), the increasing expectations of users and family, and the relative lack of manpower, the sector is in dire need of long-term solutions rather than cosmetic touch-ups.

Awareness and appreciation for geriatric healthcare in our society needs to be improved. For this reason, the Ministry has embarked on a systematic year-long approach of inter-generational activities to bring young people closer to older ones. We believe that sustained social responsibility programmes will instill an understanding that ageing is a reality, and that working with older persons is rewarding and fulfilling. We have set in motion and/or refined such programmes over the past year - School Grannies, Adopt a Granny, University of the Third and Fourth age, recurring school visits, the Say-No-to-Stroke campaign and soon the NNANS-T heart failure campaign.

We need to attract manpower with conscience, with insight, with the stamina to be proactive. Of course, we want ambitious individuals that stay the course; we want to guarantee career progression. This vision will take years to reap results but it is heartening to see at the outset an incidental spike in geriatric HST interest. We are doing our best to set up fellowships and research projects to make the training experience worthwhile and progression easier. In order to achieve this, we are partnering up with the University of Malta, Malta Medicines Authority, Queen Mary University, University of the West of Scotland, National Alliance for Rare Diseases, Royal College of Physicians of Edinburgh and College Federation of Great Britain. This hubbub of activity is no mere visionary talk, the wheels are turning.

Compared to other affluent countries, Malta's life expectancy is high. We need to ensure that we are adding quality to the life years gained. I will not delve into the 27 different community services that the Ministry offers, clearly they are not enough because the waiting list is not getting smaller. This is despite our very high ratio of long-term beds, which is twice that of a similar population in the United Kingdom. Our commitment to transform our LTC facilities into safe, carbon-neutral and top-notch facilities remains undiminished but we aim to reduce the rate of need for these institutions.

We are just about to land onto 5 important beachheads to tackle this issue. **Firstly,** we expanded the services at our Day Hospital at St Vincent de Paule Long Term Facility. Sixteen clinics will offer the highest level of geriatric care in the country spanning from vascular and thoracic lung surgery to dermatology and cardiology. In particular, the geriatric gastro-enterology clinic will soon be integrated with a dedicated endoscopy unit that will feature minimally invasive trans-nasal endoscopy (a first in the Maltese national health service). Our ambition is to transform this into a state-of-the-art learning centre. **Secondly,** we set up a Frailty Hub that will provide a holisitic work-up for referred at-risk individuals. **Thirdly,** we are in the process of setting up an Intermediate Care Unit which will be tasked with a systematic approach to fast-track recovery. Ideally this should and will be co-ordinated with the acute services, whence most requests for LTC originate. **Fourthly,** we are in the process of acquiring knowledge to set up the Hospital-at-Home initiative. Again, this will be a multi-disciplinary enterprise aimed at providing quality care at home, saving on hospital admission and the de-conditioning and deterioration that comes with it. **In fifth place,** rehabilitation. This field of medicine is a pillar of geriatrics and we intend to pimp it with an after-burner; we just submitted a multi-million-euro proposal for an AI- and robot-assisted unit for EU-funding.

The future is bright. It is ours for the taking.


**ENTRESTO®**(sacubitril/valsartan)

**Presentation:** Each film-coated tablet of Entresto 24 mg/26 mg, 49 mg/51 mg and 97 mg/103 mg contains sacubitril and valsartan respectively (as sacubitril valsartan sodium salt complex).

**Indications:** In adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction.

**Dosage & administration:** The recommended starting dose of Entresto is one tablet of 49 mg/51 mg twice daily, doubled at 2-4 weeks to the target dose of one tablet of 97 mg/103 mg twice daily, as tolerated by the patient. In patients not currently taking an ACE inhibitor or an ARB, or taking low doses of these medicinal products, a starting dose of 24 mg/26 mg twice daily and slow dose titration (doubling every 3 - 4 weeks) are recommended. A starting dose of 24 mg/26 mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg, moderate or severe renal impairment (use with caution in severe renal impairment) and moderate hepatic impairment. Do not co-administer with an ACE inhibitor or an ARB. Do not start treatment for at least 36 hours after discontinuing ACE inhibitor therapy. Entresto may be administered with or without food. The tablets must be swallowed with a glass of water. Splitting or crushing of the tablets is not recommended.

**Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Concomitant use with ACE inhibitors. Do not administer until 36 hours after discontinuing ACE inhibitor therapy. Known history of angioedema related to previous ACE inhibitor or ARB therapy. Hereditary or idiopathic angioedema. Concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²). Severe hepatic impairment, biliary cirrhosis and cholestasis. Second and third trimester of pregn,inc:y

**Warnings/Precautions:** Dual blockade of the renin angiotensin-aldosterone system (RAAS): Combination with an ACE inhibitor is contraindicated due to the increased risk of angioedema. Sacubitril/valsartan must not be initiated until 36 hours after taking the last dose of ACE inhibitor therapy. If treatment with sacubitril/valsartan is stopped, ACE inhibitor therapy must not be initiated until 36 hours after the last dose of sacubitril/valsartan. Combination of Entresto with direct renin inhibitors such as aliskiren is not recommended. Entresto should not be co administered with another ARB containing medicinal product. Hypotension: Treatment should not be initiated unless SBP is ≥100 mmHg. Patients with SBP <100 mmHg were not studied. Cases of symptomatic hypotension have been reported in patients treated with sacubitril/valsartan during clinical studies, especially in patients ≥65 years old, patients with renal disease and patients with low SBP (<112 mmHg). Blood pressure should be monitored routinely when initiating or during dose titration with sacubitril/valsartan. If hypotension occurs, temporary down-titration or discontinuation of sacubitril/valsartan is recommended. Impaired or worsening renal function: Limited clinical experience in patients with severe renal impairment (estimated GFR <30 ml/min/1.73m²). There is no experience in patients with end-stage renal disease and use of sacubitril/valsartan is not recommended. Use of sacubitril/valsartan may be associated with decreased renal function, and down-titration should be considered in these patients. Impaired renal function: Patients with mild-moderate renal function are more at risk of developing hypotension while patients with severe renal impairment may be at a greater risk of hypotension. sacubitril/valsartan is not recommended in patients with end-stage renal disease. Hyperkalaemia: Treatment should not be initiated if the serum potassium level is >5.4 mmol/l. Monitoring of serum potassium is recommended, especially in patients who have risk factors such as renal impairment, diabetes mellitus or hypoaldosteronism or who are on a high potassium diet or on mineralocorticoid antagonists. If clinically significant hyperkalaemia occurs, consider adjustment of concomitant medicinal products or temporary down-titration or discontinuation. If serum potassium level is >5.4 mmol/l discontinuation should be considered. Angioedema: Angioedema has been reported with sacubitril/valsartan. If angioedema occurs, discontinue sacubitril/valsartan immediately and provide appropriate therapy and monitoring until complete and sustained resolution of signs and symptoms has occurred. It must not be re administered. Patients with a prior history of angioedema were not studied. As they may be at higher risk for angioedema, caution is recommended if Entresto is used in these patients. Black patients have an increased susceptibility to develop angioedema. Patients with renal artery stenosis: Caution is required and monitoring of renal function is recommended. Patients with NYHA functional classification Tu.: Caution should be exercised due to limited clinical experience in this population. Patients with hepatic impairment: There is limited clinical experience in patients with moderate hepatic impairment (Child Pugh B classification) or with AST/ALT values more than twice the upper limit of the normal range. Caution is therefore recommended in these patients. B- type natriuretic peptide (BNP): BNP is not a suitable biomarker of heart failure in patients treated with sacubitril/valsartan because it is a neprilysin substrate. Psychiatric disorders: Psychiatric events such as hallucinations, paranoia and sleep disorders, in context of psychotic events, have been associated with sacubitril/valsartan use. If a patient experiences such events, discontinuation of sacubitril/valsartan tre,itment should be considered

**Interactions:** Contraindicated with ACE inhibitors, 36 hours washout is required. Use with aliskiren contraindicated in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²). Should not be coadministered with another ARB. Use with caution when co-administering sacubitril/valsartan with statins or PDE5 inhibitors. No clinically relevant interaction was observed when simvastatin and sacubitril/valsartan were co-administered. Monitoring serum potassium is recommended if sacubitril/valsartan is co-administered with potassium-sparing diuretics or substances containing potassium (such as heparin). Monitoring renal function is recommended when initiating or modifying treatment in patients on sacubitril/valsartan who are taking NSAIDs concomitantly Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors or angiotensin II receptor antagonists including sacubitril/valsartan. Therefore, this combination is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended. Co-administration of sacubitril/valsartan and furosemide reduced $C_m$ and AUC of furosemide by 50% and 28%, respectively, with ;:educed urinary excretion of sodium. Co-administration of nitroglycerin and sacubitril/ valsartan was associated with a treatment difference of 5 bpm in heart rate compared to the administration of nitroglycerine alone, no dose adjustment is required. Co administration of sacubitril/valsartan with inhibitors of OATP1B1, OATP1B3, OAT3 (e.g. rifampicin, ciclosporin), OAT1 (e.g. tenofovir, cidofovir) or MRP2 (e.g. ritonavir) may increase the systemic exposure of LBQ657 or valsartan. Appropriate care should be exercised. Co-administration of sacubitril/valsartan with metformin reduced both $C_{max}$ and AUC of metformin by 23%. When initiating therapy with sacubitril/valsartan in patients receiving metformin, the clinical status of the patient should be evaluated.

**Fertility, pregnancy and lactation:** The use of sacubitril/valsartan is not recommended during the first trimester of pregnancy and is contraindicated during the second and third trimesters of pregnancy. It is not known whether sacubitril/valsartan is excreted in human milk, but components were excreted in the milk of rats. Entresto is not recommended during breastfeeding. A decision should be made whether to abstain from breast feeding or to discontinue Entresto while breast feeding, taking into account the importance of sacubitril/valsartan to the mother.

**Undesirable effects:** *Very common (≥1/10):* Hyperkalaemia, hypotension, renal impairment. *Common (≥1/100 to <1/10):* Anaemia, hypokalaemia, hypoglycaemia, dizziness, headache, syncope, vertigo, orthostatic hypotension, cough, diarrhoea, nausea, gastritis, renal failure, acute renal failure, fatigue, asthenia. *Uncommon (≥1/1,000 to <1/100):* Hypersensitivity, postural dizziness, pruritis, rash, angioedema.

**Packs sizes:** Entresto 24 mg/26 mg – x28 tablets; Entresto 49 mg/51 mg – x28 tablets; Entresto 97 mg/103 mg - x28 & x56 tablets.

**Legal classification:** POM.

**Marketing Authorisation Holder**: Novartis Europharm Ltd, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland.

**Marketing Authorisation Numbers**: Entresto 24 mg/26 mg film coated tablets EU/1/15/1058/001; Entresto 49 mg/51 mg film coated tablets EU/1/15/1058/002-004; Entresto 97 mg/103 mg film coated tablets EU/1/15/1058/005-007.

**Please refer to the Summary of Product Characteristics (SmPC) before prescribing.** Full Prescribing Information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel: +356 21222872.

**REFERENCES**: 1. Maddox TM, Januzzi JL Jr, Allen LA, et al. 2021 update to the 2017 ACC Expert Consensus Decision Pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021;77(6):772–810. 2. Claggett B, Packer M, McMurray JJV, et al; for the PARADIGM-HF Investigators. Estimating the long-term treatment benefits of sacubitril–valsartan. N Engl J Med. 2015;373(23):2289-2290. 3. Lewis EF, Claggett BL, McMurray JJV, et al. Health-related quality of life outcomes in PARADIGM-HF. Circ Heart Fail. 2017;10(8):e003430. 4. ENTRESTO Summary of product characteristics. European Medicines Agency website. http://www.ema.europa.eu. Accessed June 2021.

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Entresto® sacubitril/valsartan

# Issue Guide



# Authors

**Dr David Borg MD** graduated in 2021 and is currently working at Mater Dei Hospital as a foundation doctor. He is reading a Master's Degree in Advanced Surgical Practice at Cardiff University after showing interest in the surgical field. The co-authors are Dr Christina Cassar & Ms Rachel Abela.

**Dr Christina Cassar** MD graduated in 2021. She then began her Foundation Programme in Malta and has since completed rotations in rheumatology, geriatrics, general surgery, obstetrics & gynaecology, and is currently working in infectious disease. She looks forward to pursuing a career in general medicine.

**Dr Moses Camilleri** MD, MSc (Addiction) has worked in the field of addictions for 30 years and is certified by the International Society of Addiction Medicine (ISAM). He is particularly interested in infectious diseases in people who use drugs. Dr Camilleri is employed by Sedqa, caring for people with addiction disorders.

**Mr Ian Said** MD(Melit) MSc(Surg) FRCS is a consultant vascular and endovascular surgeon at Mater Dei Hospital. He has a special interest in surgical as well as minimally invasive management of lower limb ischaemia.

**Dr Madeleine Bonnici** MD BSc(Hons.) Nursing graduated in 2014 as a nurse and continued her studies to graduate as medical doctor in 2019. Dr. Bonnici is currently working as a BST in General Medicine at Mater Dei Hospital. The co-authors of the article are Dr Desiree Vella Brincat, Dr Nadia Abu Shamala, Dr Maria Xuereb Dingli and Mr Clifford Caruana.

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MAUVE STINGER JELLYFISH (PELAGIA NOCTILUCA)
Photo taken in the tunnel at the Inland Sea, Gozo
with a Sony A6400 camera with Inon z330 strobes.
10mm, 1/80s, ISO500, f5.6.
**Credits:** Lee Jellyman

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discretionary portfolio management

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# MeDirect Makes Investing Easily Accessible to Even the Busiest Professional

Many professionals struggle to find time for all the things they would like to do. Work and family schedules tend to leave little room for anything else. While financial planning is something most think about occasionally, the opportunity to sit down, map out and implement a proper investing strategy is too cumbersome for most. The result is that few professionals genuinely optimise their financial position, missing out on potential gains that could provide even greater financial security for them and their loved ones.

It is to help professionals tackle this issue that MeDirect, in partnership with BlackRock, the world's largest fund manager, has launched **MeManaged**. This is the first Discretionary Portfolio Management service launched in Malta which is available entirely online and is easily accessible with a minimum investment of just €100.

For those who may be unfamiliar with what a Discretionary Portfolio Management service is, it is a service which is normally reserved for high-net-worth individuals and only accessible through a personal relationship with a portfolio manager. In simple terms, the service allows the investor to create an actively managed portfolio where the day-to-day decisions are handed over to their portfolio manager. This means that once the investor has established clear financial goals and an investment strategy, the portfolio manager does all the work. As a result, the investor is free to go back to focusing on what they do best.

MeDirect's **MeManaged** product has transformed this service to make it easily accessible for everyone through its online banking and mobile application platforms. This ease of access complements MeDirect's client onboarding process which can also be completed entirely online. The initial strategy is established through an online questionnaire which takes a few minutes to complete and establishes the investor's financial goals and risk appetite. Investors are then assigned an investment strategy which is actively pursued by MeDirect's team of experts, in partnership with BlackRock. Investors receive a monthly report on the progress of their investment and can revise their strategy, should circumstances or goals change, by retaking the questionnaire.

In bringing this innovation to Malta, MeDirect is also being very transparent about any ongoing fees associated with **MeManaged.** The fact is that, apart from the ongoing fee relating to the costs of running the fund, the only charge applied is an annual management fee of 1.2 per cent of the market value of the portfolio (inclusive of VAT). This is something which is not always the case, especially in those investment products where charges are applied based on the number of transactions rather than on performance. Customers also need to keep in mind the efficiencies organisations, like BlackRock, can achieve through advanced market trading technology.

**MeManaged** also provides flexibility when it comes to additional investments, on top of the initial minimum €100 required. Investors have the opportunity to add a lump sum to their portfolio whenever they want to. On the other hand, should investors wish to top up their **MeManaged** account on a regular basis, they can do so with just €100 per month, or more should they want to. Consequently, customers can continue to build their portfolio and benefit from cost-averaging meaning that they are buying investment assets at regular intervals, and at different prices, thus providing some protection from market volatility.

Investors are also free to make withdrawals from their account, providing the minimum balance of €100 is maintained. Withdrawals do not attract any fees and hence give investors more flexibility in managing their money.

**MeManaged** is, therefore, an ideal solution for busy professionals who want to invest their hard-earned money efficiently but have neither the time nor the expertise to do so themselves or through a complicated process. With just €100, you can now have your own actively managed investment portfolio, accessible entirely online. For more information visit https://www.medirect.com.mt/invest/discretionary-portfolio-management/.

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## TWO DOSES A YEAR[1*]

*LEQVIO is dosed initially, again at 3 months, and then once every 6 months.[1]

## EFFECTIVE AND SUSTAINED LDL-C REDUCTION[1†]

†LDL-C reduction was maintained during each 6-month dosing interval.[1]

**Choose LEQVIO first for effective and sustained LDL-C reduction and as a strong complement to a maximally tolerated statin for your patients with ASCVD.[1]**

**LEQVIO®**

**PRESENTATION**: Leqvio 284 mg solution for injection in prefilled syringe. Each pre-filled syringe contains inclisiran sodium equivalent to 284 mg inclisiran in 1.5 ml solution. Each ml contains inclisiran sodium equivalent to 189 mg inclisiran.

**INDICATION**: Leqvio is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet: in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

**DOSAGE**: The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months. ♦*Missed doses*: If a planned dose is missed by less than 3 months, inclisiran should be administered and dosing continued according to the patient's original schedule. If a planned dose is missed by more than 3 months, a new dosing schedule should be started – inclisiran should be administered initially, again at 3 months, followed by every 6 months. ♦*Treatment transition from monoclonal antibody PCSK9 inhibitors*: Inclisiran can be administered immediately after the last dose of a monoclonal antibody PCSK9 inhibitor. To maintain LDL-C lowering it is recommended that inclisiran is administered within 2 weeks after the last dose of a monoclonal antibody PCSK9 inhibitor. ♦*Elderly, hepatic impairment, renal impairment*: no dose adjustment is necessary. Inclisiran should be used with caution in patients with hepatic and renal impairment. ♦*Paediatric population*: The safety and efficacy of inclisiran in children aged less than 18 years have not yet been established. ♦*Method of administration*: Inclisiran is intended for administration by a healthcare professional via subcutaneous route. Each pre-filled syringe is for single use only.

**CONTRAINDICATIONS**: Hypersensitivity to the active substance or to any of the excipients listed in the SmPC.

**WARNINGS/ PRECAUTIONS**: ♦*Haemodialysis*: The effect of haemodialysis on inclisiran pharmacokinetics has not been studied. Considering that inclisiran is eliminated renally, haemodialysis should not be performed for at least 72 hours after inclisiran dosing. ♦*Sodium content*: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

**INTERACTIONS**: Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. Therefore, inclisiran is not expected to have clinically significant interactions with other medicinal products. Based on the limited data available, clinically meaningful interactions with atorvastatin, rosuvastatin or other statins are not expected.

**PREGNANCY, LACTATION AND FERTILITY**: ♦There are no or limited amount of data from the use of inclisiran in pregnant women. As a precautionary measure, it is preferable to avoid the use of inclisiran during pregnancy. ♦It is unknown whether inclisiran is excreted in human milk. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from inclisiran therapy, taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. ♦No data on the effect of inclisiran on human fertility are available.

**ADVERSE REACTIONS**: *Common*: Adverse reactions at the injection site.

**LEGAL CATEGORY: POM PACK SIZES**: Pre-filled syringe: x1 pre-filled syringe. Pre-filled syringe with needle guard: x1 prefilled syringe with needle guard.

**MARKETING AUTHORISATION HOLDER**: Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland.

**MARKETING AUTHORISATION NUMBER**: EU/1/20/1494/001-2

Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta, P.O. Box 4, Marsa MRS 1000 Malta. Tel +356 21222872.

2022-MT-LEQ-24-MAR-2022

**References: 1.** Novartis Europharm Ltd. Leqvio Summary of Product Characteristics.

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DR IAN SAID

# Vascular Surgery and Chronic Limb Threatening Ischaemia (CLTI)

## INTRODUCTION

Vascular surgery is one of the youngest surgical specialities, having parted ways from the umbrella of general surgery in the 1990's. Over the past 30 years, advances in various techniques and technologies, have allowed vascular surgery as well as endovascular therapy to treat an increasingly broad and more complex range of arterial and venous pathologies.

The diagnosis and management of peripheral arterial disease (PAD) of the lower limbs causing chronic limb threatening ischaemia (CLTI - previously known as critical limb ischaemia) provides the biggest workload to most vascular units. CLTI is defined as peripheral arterial disease of the lower limbs in combination with rest pain, gangrene, or ulceration of over two weeks duration.

## HOW COMMON IS CLTI?

The incidence of PAD is on the increase worldwide, even more so in developing and low-income countries. The most recent data from WHO estimates the prevalence of PAD to be 5% in adults over 25 years of age. This is mirrored by the increase in CLTI, which has seen its worldwide incidence increase by 20% over a ten-year period (2010-2020).

## WHO GETS CTLI?

CTLI is associated with non-modifiable as well as modifiable risk factors, which are also synonymous with arterial diseases in other vascular beds (coronary and cerebrovascular). The former includes age, sex, ethnicity, socio-economic background, and genetic make-up.

Males and patients originating from a lower socio-economic class and lower income countries have an increased risk of developing CTLI. Patients with a family history of arterial disease are at an increased risk as well. Modifiable risk factors for CLTI include smoking, diabetes, hypertension, hypercholesterolaemia as well as obesity. Our increasingly aged population as well as the ever-increasing incidence of diabetes are the two main contributing factors for the swelling incidence of CLTI.

## MAKING THE DIAGNOSIS

Diagnosis of PAD is largely made thorough clinical examination. Whilst absent peripheral lower limb pulses are strongly suggestive of PAD, this should be supplemented by assessment using a handheld doppler device. This allows evaluation of the arterial waveforms over the dorsalis pedis and posterior tibial arteries at the ankles as well as obtaining an ankle-brachial pressure index (ABPI). To obtain an ABPI the highest occlusion pressure at the ankle is divided by the highest brachial artery occlusion pressure. A normal ABPI value should be 1. An ABPI of less than 0.9 has a sensitivity and specificity of around 90% in diagnosing PAD.

## WHY IS RECOGNISING CLTI IMPORTANT?

Patients diagnosed with PAD are subject to a higher incidence of cardiovascular morbidity and mortality when compared to an age and sex-matched population cohort without PAD. This is heightened in CLTI patients who have an estimated 1-year mortality in excess of 20%. This highlights the importance of risk factor modification as well as medical management in these patients.

A NORMAL ABPI VALUE SHOULD BE 1. AN ABPI OF LESS THAN 0.9 HAS A SENSITIVITY AND SPECIFICITY OF AROUND 90% IN DIAGNOSING PAD

The importance of smoking cessation cannot be overstated. According to figures by the Centers for Disease Control and Prevention, less than 10% of smokers are given evidence-based smoking cessation advice or counselling. Appropriate counselling and pharmacotherapy, when suitable, are associated with the highest abstinence rates. Even with adequate intervention and support, evidence shows that only 30% of patients will still be abstinent at 12 months. Locally, patients should be referred to our national quit line (23266116/ 80073333) for the best chances of success.

Tight glycaemic control for patients with non-insulin dependent and insulin-dependent diabetes is of utmost importance. This is shown to reduce foot complications in patients with diabetes and becomes even more crucial if there is associated PAD. Care for these patients should be overseen by a diabetologist. All patients with PAD, even more so patients who are diabetic, should be given lifestyle advice. Apart from smoking cessation, a balanced diet, regular exercise as well as maintaining a healthy weight are all crucial when it comes to decreasing morbidity and mortality.

## BEST MEDICAL THERAPY

Following risk factor modification, all patients with cardiovascular disease (coronary, cerebrovascular and PAD) should be started on best medical therapy consisting of an antiplatelet agent as well as a high dose statin.

The best studied and most widely used antiplatelet is aspirin. A meta-analysis of randomised controlled trials published in 2002[1] clearly demonstrated that aspirin decreases the risk of serious vascular events by 25% and decreases overall mortality by 15% when compared to placebo in patients with documented cardiovascular disease. Clopidogrel 75mg daily, performs better than aspirin in patients with PAD providing a further 22% relative risk reduction in serious vascular events (A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE)).[2] Dual antiplatelet therapy (aspirin + clopidogrel) does not improve outcomes and should not be used in PAD patients, unless in exceptional cases following specific interventions like implantation of drug eluting stents.

In this context, dual antiplatelet therapy is administered for 6 months.

A recent randomised controlled trial evaluated the combination of aspirin and low dose rivaroxaban vs aspirin monotherapy vs rivaroxaban monotherapy in patients with PAD or carotid disease.[3] Combining aspirin with low dose rivaroxaban (2.5mg bd) resulted in a significant reduction in major cardiovascular events as well as major adverse limb events when compared to aspirin monotherapy. This came at the cost of a slight increase in major bleeding observed with combination therapy. Unfortunately, we still do not have data comparing aspirin + rivaroxaban vs clopidogrel monotherapy.

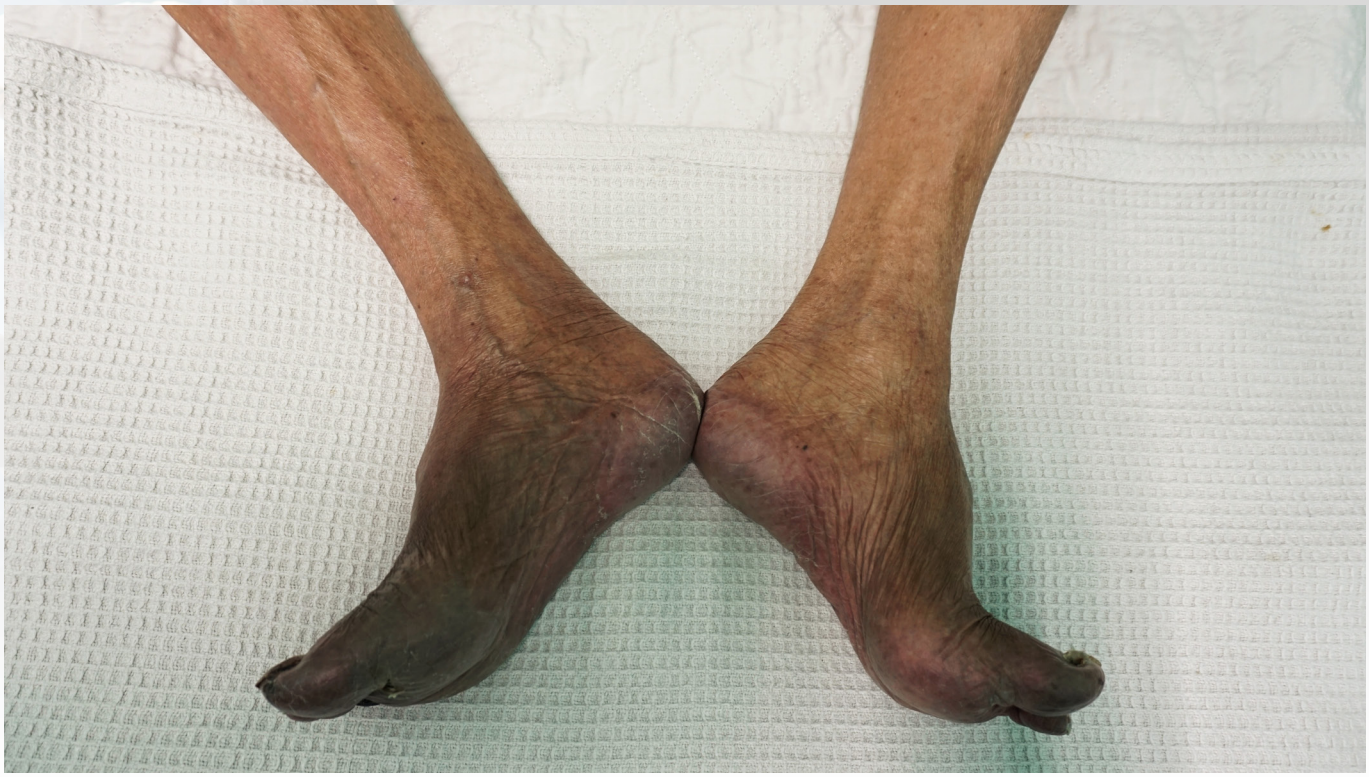
In PAD as well as CLTI, initiation of high dose statin therapy confers similar advantages to those offered by aspirin in terms of reducing serious cardiac events as well as overall mortality by 15%. This benefit is largely independent of the patient's total cholesterol and LDL levels prior to initiation of statin therapy. All patients who are diagnosed with arterial disease in any vascular bed should be on a high dose statin, whatever their starting level of total cholesterol and LDL, unless contraindicated.

## INTERVENTIONAL TREATMENT FOR CLTI

Following risk factor modification and initiation of best medical therapy, almost all patients presenting with CTLI are assessed for revascularisation, ideally by a multidisciplinary team. The initial investigation employed in assessing the suitability for revascularisation is Colour Duplex Ultrasonography (DUS). In experienced hands, DUS is the only imaging modality required for planning revascularisation in up to 80% of patients. Cross-sectional imaging (CT or MR angiography) becomes necessary if there is aorto-iliac vessel disease and is sometimes required if DUS is not diagnostic.

The technique employed to offer revascularisation must be individualised to each patient and in most instances, multiple techniques are required as patients with CLTI present with multilevel disease. With continual improvement in endovascular equipment and techniques, minimally invasive revascularisation

**PATIENTS DIAGNOSED WITH CLTI IN THE COMMUNITY SHOULD BE REFERRED URGENTLY TO THE VASCULAR UNIT AT MDH. THIS CAN BE DONE BY CONTACTING THE EMERGENCY ON-CALL VASCULAR SERVICE (PHONE: 7905 6653) WHICH IS AVAILABLE 24 HOURS PER DAY AND 7 DAYS A WEEK**



(angioplasty and stenting) is becoming the modality of choice in a larger number of CLTI patients. This enables vascular surgeons to offer revascularisation and attempt limb salvage in an increasingly frail and ageing population where open surgical revascularisation would carry prohibitive risks of morbidity and mortality.

Even after technically successful revascularisation, CLTI patients remain at high risk of limb loss and have increased all-cause mortality when compared to non-CLTI patients. This highlights the importance of aftercare in the community to ensure adherence to risk factor modification, best medical therapy, glycaemic control and adequate footcare and footwear.

## THE LOCAL SITUATION

The global trend of increasing prevalence of PAD and CLTI are also seen here in Malta. Over the five-year period prior to the COVID pandemic (2014 -2019), revascularisations done for CTLI and PAD at Mater Dei hospital increased steadily at a rate of 5% per year. Despite the increasing burden of CLTI, the incidence of major lower limb amputation in Malta has remained largely stable and is currently the lowest in the EU (11 per 100,000 population in males and 6 per 100,000 population in females).

To deal with the increasing number of CLTI patients, the multidisciplinary team at MDH is ever enlarging. The vascular surgeon is the primary carer for patients with CLTI whilst being strongly supported by interventional radiology, diabetology, vascular nurses, vascular sonographers, tissue viability nurses, podiatrists, occupational therapists, physiotherapists as well as orthotic specialists.

Patients diagnosed with CLTI in the community should be referred urgently to the vascular unit at MDH. This can be done by contacting the emergency on-call vascular service (Phone: 79056653) which is available 24 hours per day and 7 days a week. Alternatively, during weekdays, patients with CTLI or foot ulceration, can be referred to the urgent podiatry service at Mater Dei hospital which is supported by the vascular surgery team.

## CONCLUSION

Atherosclerotic diseases including CLTI are the commonest cause of mortality in the Western world. The diagnosis and management of CLTI, especially in our increasingly aged population, should have a central importance both in the community and in the tertiary setting, in order to ameliorate the significant morbidity and mortality of this disease.

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DR MADELEINE BONNICI, DR DESIREE VELLA BRINCAT, DR NADIA ABU SHAMALA,
DR MARIA XUEREB DINGLI, MR CLIFFORD CARUANA

# Adherence to Local Preoperative, Generic Investigation Guidelines for Adult Elective Upper Gastrointestinal Surgery

## ABSTRACT

Pre-operative assessment is essential in preparing patients for elective procedures as it risk-stratifies patients and optimises their conditions, reducing the rate of complications. Anaesthetists are key in this process as they are consulted about high-risk patients. They also release the guidelines for pre-operative assessments which are used in the POAC. Despite these guidelines being in place, there are still staff members who either do not use the guidelines or are unaware of their existence. This has cost implications and possibly leads to sub-standard assessments.

**Keywords:** Pre-operative, Guidelines, Investigations, Expenditure, Wastage.

## INTRODUCTION

Pre-operative assessment is an essential aspect in preparing patients for elective procedures. It allows us to risk-stratify patients, and optimise their associated medical or surgical conditions beforehand, thereby reducing the percentage of peri- and post-operative complications.

The pre-operative algorithmic guidelines were established by the Anaesthesia Department in 2017 in order to allow for a structured preoperative approach, hereafter referred as ACC/1/Guide/2017. The latter aims to standardise investigation bookings as well as referrals according to BMI, ASA score, age, nature of surgery and comorbidities. These were created in order to avoid unnecessary tests in healthy low risk patients. Studies have shown that in normal, healthy patients [ASA I patients] undergoing minor and intermediate surgery, there is a low likelihood of abnormal results and negative surgical outcomes. Therefore, blood tests should only be performed when specifically indicated according to the local guidelines. Moreover, additional and inappropriate blood tests result in unnecessary costs.[1]

The aim of this audit is to assess the adherence of preoperative generic investigations for adult elective surgery in concordance to local guidelines and the cost implications to clinical practice.

## ETHICS

Prior to the commencement of this audit, the data protection committee of Mater Dei Hospital and the Faculty of Medicine and Surgery were contacted for approval. The procurement of electronic data was obtained without the use of interviews, recordings or photographic documentation of the patients in question.

## METHODOLOGY

This retrospective study considered adult elective upper general intestinal surgery cases over a period of one year, from 25th January 2019 to 29th January 2020, of one Surgical firm at Mater Dei Hospital, Malta. The preoperative generic investigations were collected via iSoft. Exclusion criteria:

- Patients under 18 years of age
- Pregnant women
- Patients admitted for acute GI interventions
- Refusal to give informed consent.

The data collected included, as per ACC/1/Guide/2017:

- Age over or under 54
- BMI over or under 30
- Inability to climb two flights of steps
- ASA score
- Whether the procedure was classified as minor, intermediate or major surgery.

The investigations taken were documented, as reported on iSoft. These included:

- CBC
- Renal Profile
- HbA1C
- RBG
- INR
- APTT
- CRP
- ECG
- CXR
- Lung function test

The local preoperative guidelines as seen in Figure 1, were used to see whether the tests ordered were taken in accordance with the guidelines of Mater Dei Hospital.

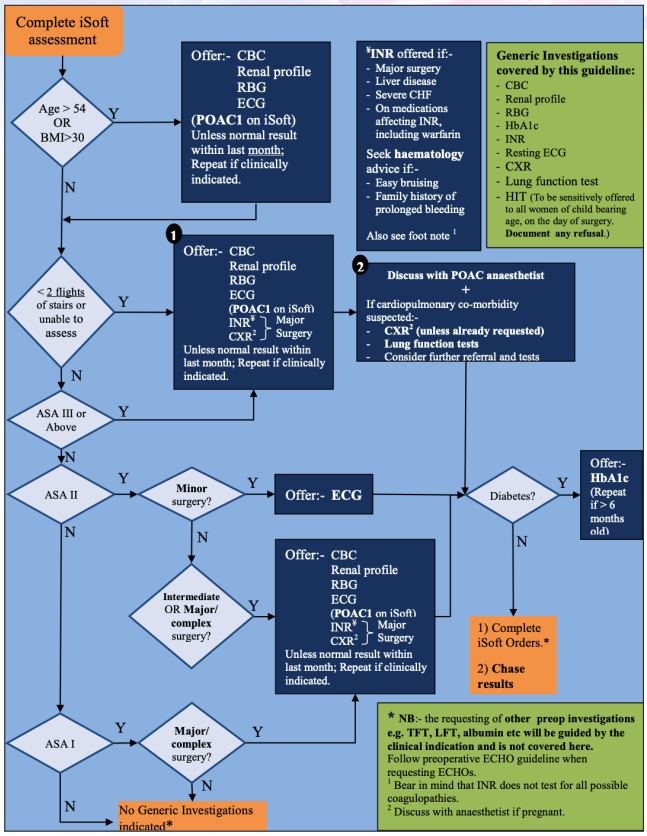


**Figure 1.** Preoperative, Generic Investigations for Adult Elective Surgery Guideline ACC/1/Guide/2017.[2]

**Table 2.** Total wasted cost per individual test in euros & the corresponding percentage waste.

| Test | Number of tests | Total cost | Wasted cost | % Waste | Taken when not indicated | Not taken even though indicated |
|---|---|---|---|---|---|---|
| **CBC** | 132 | 415.80 | 81.90 | 20% | 26 | 1 |
| **RP** | 132 | 110.88 | 21.84 | 20% | 26 | 2 |
| **HbA1C** | 13 | 40.56 | 21.84 | 54% | 7 | 11 |
| **RBG** | 81 | 27.54 | 5.78 | 21% | 17 | 42 |
| **ECG** | 133 | 1151.78 | 216.50 | 19% | 25 | 1 |
| **INR** | 132 | 1040.16 | 685.56 | 66% | 87 | 2 |
| **APTT** | 129 | 1270.65 | 1270.65 | 100% | 129 | 0 |
| **CXR** | 82 | 1910.60 | 1025.20 | 54% | 44 | 7 |
| **CRP** | 48 | 151.20 | 151.20 | 100% | 43 | 0 |
| **Lung function** | 15 | 284.30 | 25.62 | 9% | 1 | 1 |

The data was compiled by using the investigations ordered on the same or following date of the pre-operative assessment. The date was known due to the online POAC document found on iSOFT. The cost for each individual test was obtained from the Billings department of Mater Dei Hospital and the total costs were calculated using the data in Table 1. The costs exclude manpower.

**Table 1.** List of individual test costings

| Test | Cost (€) |
|---|---|
| CBC | 3.15 |
| Renal Profile | 0.84 |
| RBG | 0.34 |
| INR | 7.88 |
| APTT | 9.85 |
| CRP | 3.15 |
| HbA1C | 3.12 |
| ECG | 8.66 |
| CXR | 23.30 |
| Lung Function Test | 25.62 |

## RESULTS

A total of 133 patients were included in this audit. Table 2 shows that none of the patients were investigated according to the local guidelines. Figure 2 shows that 404 blood tests were taken when not indicated, while 63 blood tests were not taken, despite being indicated. Figure 3 reflects the percentage wasted cost.

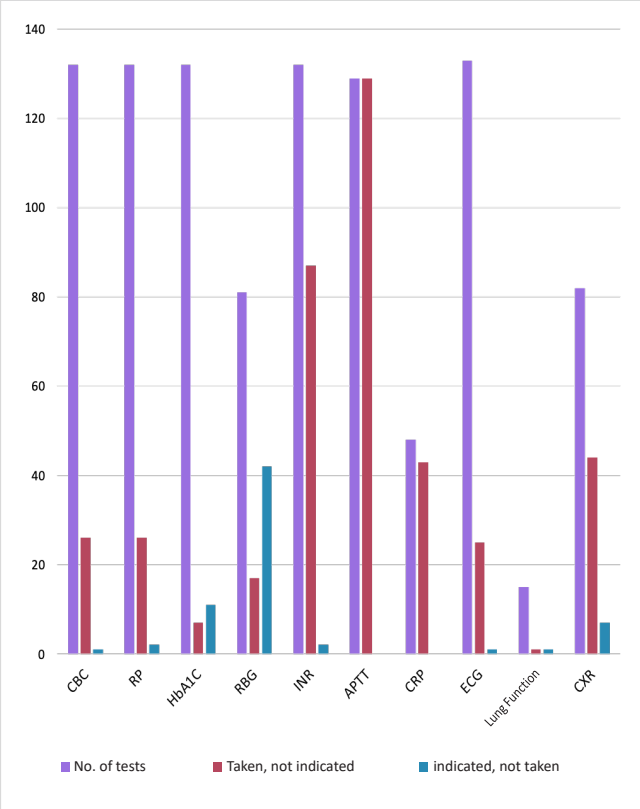


**Figure 2.** Preoperative Generic Investigation.

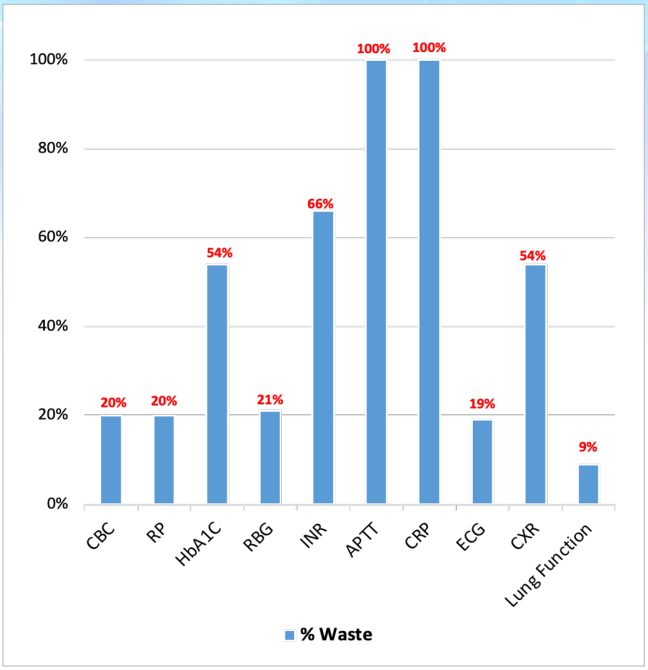


**Figure 3.** Percentage Wasted Cost.

## DISCUSSION

From the results extracted from this analysis, it is evident that there are a significant number of tests which are ordered without any indication or not according to guidelines. For instance, a patient having an ASA score of 1, undergoing minor or intermediate surgery does not require any generic investigations according to the guidelines, however, these were still taken. Hba1c blood tests were still repeated in diabetic patients, even though they were less than 6 months old and thus, not indicated, and HbA1C blood tests were taken in non-diabetic patients. Chest X-rays and INRs were ordered despite patients having only minor or intermediate surgeries. In addition, several CRP blood tests were ordered, even if not indicated in the ACC/1/Guide/2017. This is a nonspecific test indicating inflammation or autoimmune disease and particularly useful in post-operative patients to identify cases of infection. Therefore, their use in preoperative assessment should be questioned. APTT blood tests are not indicated in the ACC/1/Guide/2017. Despite this, it is common practice that APTT blood tests are ordered along with the INR. This highlights the lack of awareness of its omission in the guideline present amongst doctors. APTT blood tests are only indicated if patients have coagulopathy comorbidities.

Inappropriate testing leads to a significant amount of financial waste and misuse of resources. Notably, there are a number of tests which have a greater percentage of waste than others. Tests with a percentage waste of more than 50% included HbA1C, INR, APTT, CXR and CRP. APTT and CRP had a 100% total waste. However, given that each test price is different, the test that imposed the greatest unnecessary financial burden was that of the APTT blood test. This cost an additional 1270.65 euro which could have been invested into other medical resources. Overall, the total cost spent was €6,403.47 and the total wasted cost amounted to €3,506.09.

Also of concern is the fact that, with the exception of APTT and CRP, all the tests were not taken even when indicated for specific patients. This can directly impact the surgical outcome and the ensuing QoL of patients and their carers. More importantly such omission may lead to longer hospitalisation delays and complications for patients which would drastically increase the cost of patient care.

Of note here is that this audit relates solely to one surgical firm only.

## CONCLUSION

Out of all the 133 subjects, none of the investigations were carried out according to the guidelines. This evidently shows that the guidelines are not being followed during the preoperative assessment. This results in an unnecessary financial burden[3] on the healthcare system and, more importantly, creates an increased workload on health care professionals and lab technicians.

It is important to note that blood testing performed unnecessarily can cause both physical and psychological discomfort to patients, as well as increase occupational hazards to healthcare workers.

A qualitative study done by Brown et. al,[4] explored factors affecting conformity to available local guidelines. These included medico-legal concerns, a lack of awareness of guidelines, concerns about surgical delays or cancellations and lastly, the belief that other caring doctors might need the blood results taken.

This audit reinforces the requirement for frequent liaison of both anaesthetists and surgeons to ensure regular updates and increased awareness of current preoperative guidelines.[1]

## RECOMMENDATIONS

It is recommended that a similar audit is carried out across all surgical firms to obtain a more comprehensive view of the economics involved. Both over-investigations and under-investigations contribute to varying degrees of additional costs to our healthcare system. They may also lead to suboptimal surgical outcomes. It would also be beneficial if the guidelines and investigative costs[3] were made available in all allocated rooms in the POAC department. Moreover, it may be beneficial for the guidelines to be reviewed and updated accordingly given that they have last been published in 2017. An educational program could be included during the induction meetings of surgical placements where the appropriate preoperative investigations are explained to foundation year doctors. It would be also vital to inform the anaesthetists regarding such guidelines.


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## ABBREVIATIONS

**ASA** - American Society of Anaesthesiologist
**BMI** - Body Mass Index
**CBC** - Complete Blood Count
**HbA1C** - Glycated haemoglobin
**RBG** - Random Blood Glucose
**INR** - International normalised ratio
**APTT** - Activated partial thromboplastin time
**CRP** - C-reactive protein
**ECG** - Electrocardiogram
**CXR** - Chest X-ray
**POAC** - Pre-operative Assessment Clinic
**RP** - Renal profile

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**INDICATIONS**

Oral route: Disorders associated with progesterone deficiency, in particular: • Premenstrual syndrome • menstrual irregularities due to dysovulation or anovulation • Benign mastopathy • Perimenopause • Hormone replacement therapy for menopause (in addition to oestrogen therapy)

Vaginal route: • Progesterone support during ovarian insufficiency or complete ovarian failure in women lacking ovarian function (oocyte donation) • Supplementation of the luteal phase during in-vitro fertilisation (IVF) cycles • Supplementation of the luteal phase during spontaneous or induced cycles, in cases of sub-fertility or primary or secondary infertility, particularly due to dysovulation • In cases of threatened miscarriage or prevention of recurrent miscarriage due to luteal phase deficiency, until week 12 of pregnancy. For all other indications of progesterone, the vaginal route represents an alternative to the oral route in cases of: • Side effects caused by progesterone (drowsiness following absorption via the oral route).

**POSOLOGY** The dosage must not exceed 200 mg per dose, regardless of the indication and route of administration (oral or vaginal). Oral route: For progesterone deficiency, an average dose of 200-300 mg of micronised progesterone per day is recommended. • For luteal insufficiency (premenstrual syndrome, benign mastopathy, irregular menstruation and perimenopause), the usual therapeutic regimen is 200-300 mg per day. A single dose of 200 mg in the evening, upon going to bed, or 300 mg split over two doses Ten days per cycle, usually from day 17 to day 26, inclusive. • When used as a hormone replacement therapy for menopause: oestrogen therapy alone is not advised (due to the risk of endometrial hyperplasia). Instead, progesterone should be incorporated at a dose of 200 mg per day: Split over two 100 mg doses, or as a single 200-mg dose in the evening, upon going to bed, either from day 12 to day 14 of the month, or during the last two weeks of each treatment course. Following this treatment, all replacement therapies should be suspended for approximately one week, during which time it is normal to observe withdrawal bleeding. For these indications, the vaginal route should be used, at the same dosage as for the oral route, in the event of side effects caused by progesterone (drowsiness following oral absorption).

Vaginal route: • Progesterone replacement therapy in cases of ovarian insufficiency or complete ovarian failure in women lacking ovaries (oocyte donation). The therapeutic regimen (in addition to appropriate oestrogen therapy) is as follows: 100 mg of micronised progesterone per day on days 13 and 14 of the transfer cycle, then 200 mg of micronised progesterone per day on days 15 and 25 of the transfer cycle, split over one or two doses per day, then From day 26 of the cycle, and in cases of an incipient pregnancy, the dose may be increased up to a maximum of 600 mg per day, split over three doses. This dosage should be adhered to until day 60, or until week 12 of pregnancy at the latest. • Supplementation of the luteal phase during IVF cycles: The recommended dosage is 400-600 mg per day, over two to three doses per day, from the date of HCG injection until week 12 of pregnancy. • Supplementation of the luteal phase in cases of spontaneous or induced cycles, in subjects with sub-fertility or primary or secondary sterility, particularly due to dysovulation: the recommended dosage is 200-300 mg per day, over two doses, for ten days, from day 17 of the cycle. If menstruation does not resume and pregnancy is diagnosed, treatment should be quickly resumed until week 12 of pregnancy. • Threatened early miscarriage or repeated miscarriage due to luteal phase insufficiency: the recommended dosage is 200-400 mg per day, split over two doses, until week 12 of pregnancy. Method of administration Oral route It is recommended to use this medicinal product sometime after eating, preferably in the evenings upon going to bed. Vaginal route Each capsule should be inserted deep into the vagina.

**CONTRAINDICATIONS** This medicinal product is contraindicated in cases of severe liver impairment.

**SPECIAL WARNINGS AND PRECAUTIONS OF USE:** More than half of all early miscarriages are due to genetic disorders. Early miscarriages can also be caused by infectious phenomena or mechanical disorders. The administration of progesterone should therefore have the sole effect of delaying the release of a dead ovum (or interrupting a non-progressing pregnancy). • The use of progesterone should be reserved for cases of insufficient secretion by the corpus luteum. • Under the recommended conditions of use, this treatment is not contraceptive. • The use of UTROGESTAN 100 mg during pregnancy is restricted to the first trimester via the vaginal route. UTROGESTAN 100 mg is not a treatment for the threat of preterm birth. • Exceptional cases of cytolytic hepatitis and intrahepatic cholestasis of pregnancy have been reported in patients using micronised progesterone, during the second and third trimesters of pregnancy.

**FERTILITY, PREGNANCY AND LACTATION:** Several epidemiological studies in more than one thousand patients have found no association between progesterone and foetal malformation.

**EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:** It is important, particularly for those driving or using machines, to be aware of the risks of drowsiness and/or feelings of dizziness connected with the use of this medicinal product via the oral route.

**UNDESIRABLE EFFECTS:** Oral route: • Drowsiness or transient feelings of dizziness, occurring one to three hours after ingesting the product. In this event: Reduce the dosage of each dose, or adjust the timing of doses (e.g., for a dose of 200 mg per day, take the full 200 mg in a single dose in the evening, sometime after eating), or Adopt vaginal administration. • Shortened menstrual cycle or intercurrent bleeding: Delay the start of treatment until later in the cycle (e.g., start on day 19 of the cycle instead of day 17). These effects most commonly indicate an overdose. Vaginal route: No local intolerances (such as burning, pruritus or fatty discharge) have been observed during various clinical trials. No general side effects, including drowsiness or transient feelings of dizziness, have been reported during clinical studies, at the recommended dosages.

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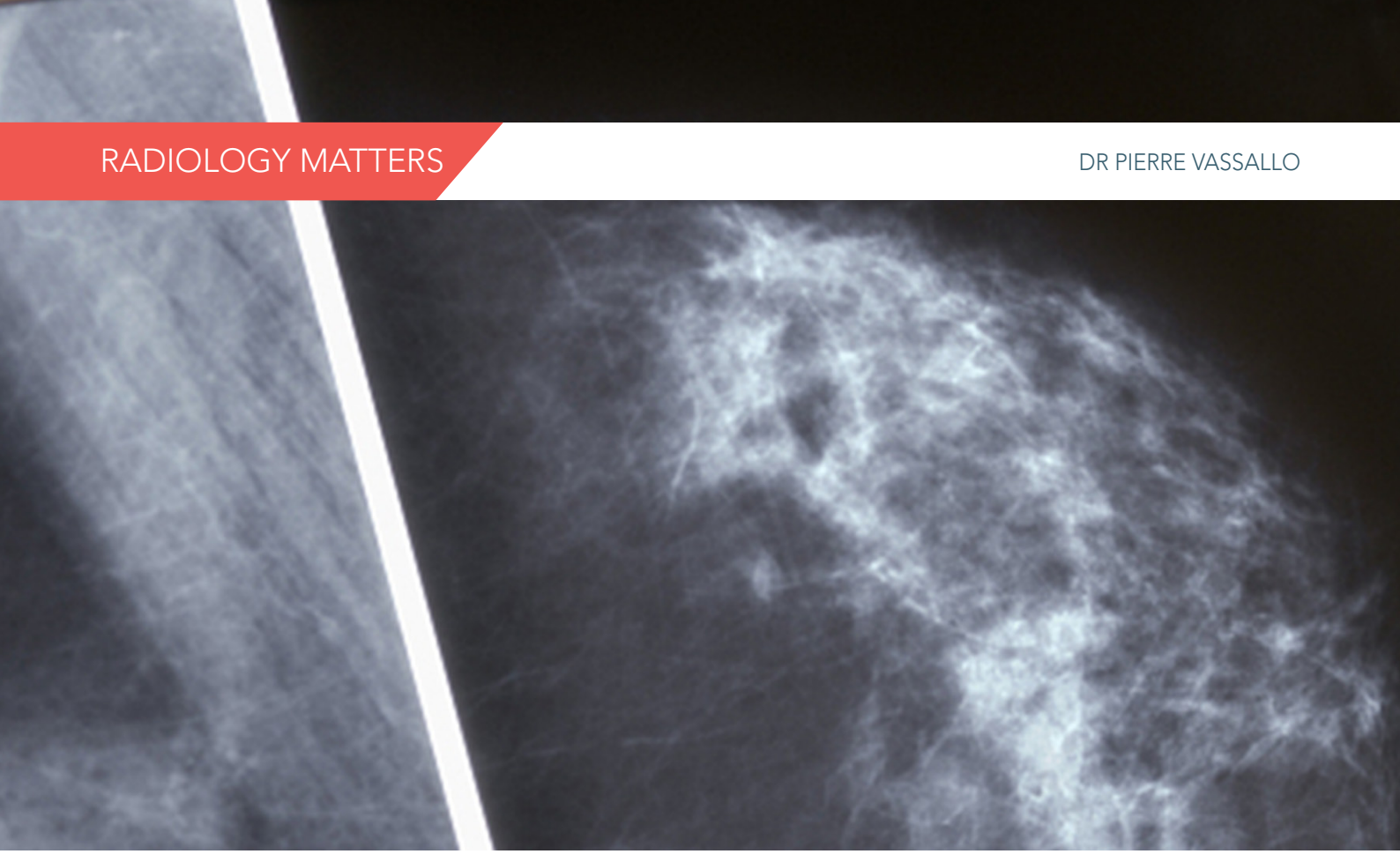


# Artificial Intelligence for Imaging Breast Cancer


## ABSTRACT

The incidence of breast cancer in women is high and has been increasing over the years. However, the mortality rate is decreasing as a result of improved early detection and treatment. These findings have driven worldwide efforts to increase breast cancer awareness and to deliver early cancer detection with improved treatment possibilities.

The achievements obtained for early detection would not have been possible without the massive strides in development of information technology and computational power. Where only 2D analogue images were available 20 years ago, today we consistently work with 3D imaging. These technologies however have resulted in an exponential increase in data volume that consistently challenges radiologists' capabilities.

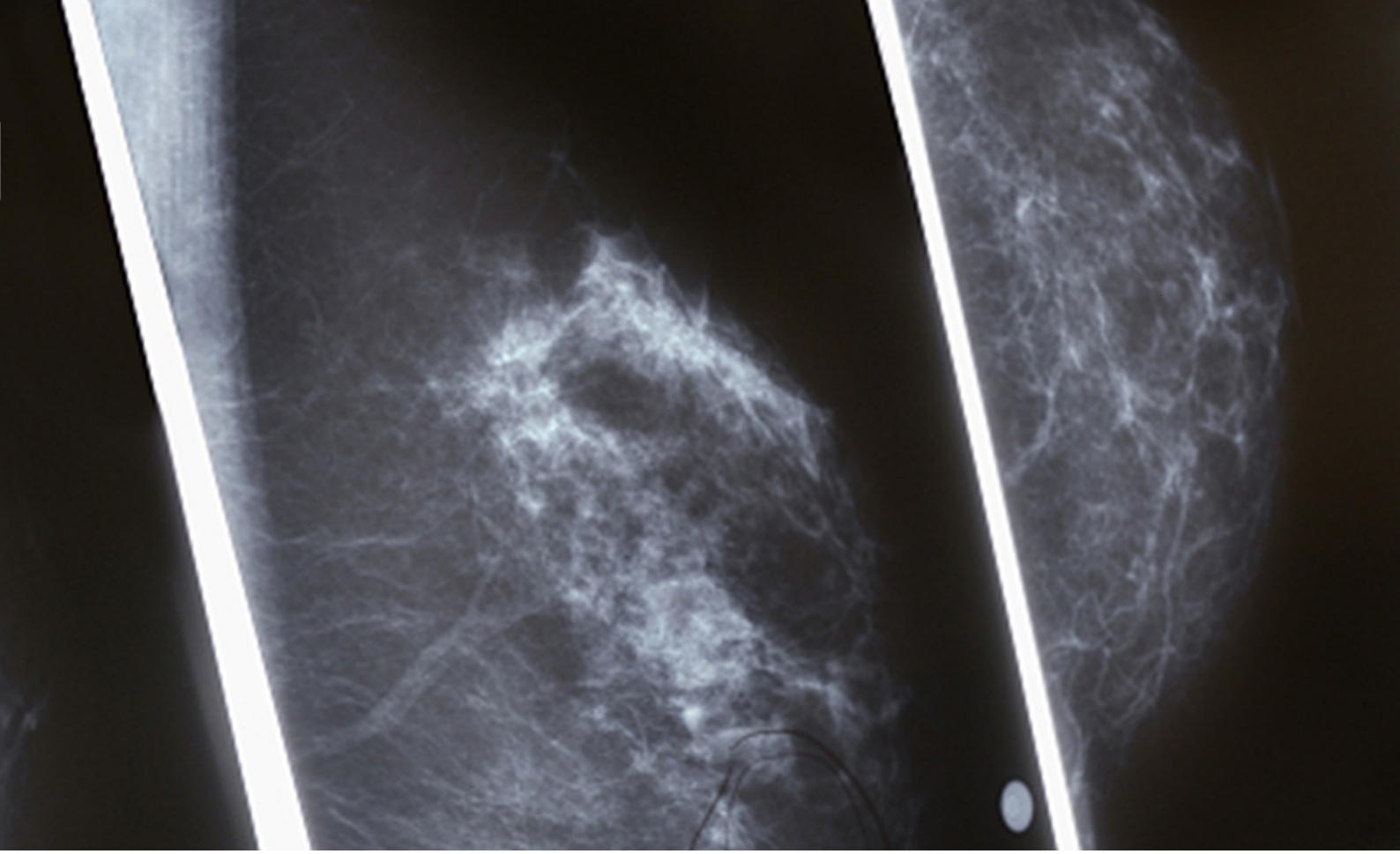
Artificial Intelligence promises to be a potential solution for the current imbalance between the demand on radiologists' time and the increasing volume of imaging data generated that needs to be reviewed.

Artificial Intelligence has further potentials for improving future practice workflows. Ongoing studies are working towards creating patient-specific screening and diagnostic workups, improving patient scheduling and protocol selection, radiation dose reduction, automated acquisition, improved image reconstruction to increase lesion visibility, a prioritised reading list (putting highly suspicious cases first and non-suspicious cases last), decreasing reading time, and prediction of breast cancer risk.

Recent studies have shown that artificial Intelligence can improve radiologists' cancer detection rates, reduce recall rates, and reduce reading times of high data volume exams such as 3D mammograms.


## BACKGROUND

The overall risk of a woman developing breast cancer is 1 in 8. Breast cancer is also the second leading cause of death from cancer in women. The chance that a woman will die from breast cancer is 1 in 39 (2.5%). However, breast cancer death rates have decreased steadily since 1989,



with an overall decline of 43% by 2020. This decline has been attributed to earlier detection and treatment of breast cancer through increased awareness, regular breast cancer screening and better treatment possibilities.[1]

The positive impact of breast cancer screening on decreasing mortality has led numerous technological developments aimed at improving early detection. These include improved technologies related to ultrasound (US) (improved image quality, 3D US and US elastography), mammography (3D mammography aka Digital Breast Tomosynthesis DBT and contrast enhanced mammography) and magnetic resonance imaging (MRI). Mammography is currently the mainstay for breast cancer screening, with 3D mammography clearly taking over from 2D Mammograms particularly for patients with dense breasts.[2,3] Currently over 80% of mammography machines in the United States are 3D units compared to only 30% in 2016.

Most of the challenges related to developing and perfecting the above technologies are now overcome. However, these technologies have resulted in an exponential increase in volume of images that need to be reviewed by the radiologist.[3] For example, for mammography, which is the mainstay for breast cancer screening, moving to 3D from 2D mammography means having to read 200-300 images instead of just 4. Comparison with past mammograms can detect subtle changes that may be the earliest signs of a developing breast cancer, but it also increases the number of images that need to be seen by 2 to 3-fold. This massively impacts the demand on the experienced breast radiologist's reading time.

## ARTIFICIAL INTELLIGENCE

Artificial Intelligence (AI) consists of a set of deep-learning enabled tools that could assist radiologists to achieve faster turnaround times and possibly to deliver more accurate results by prioritising cases and highlighting areas of concern (such as asymmetry, calcifications, architectural distortions and masses).[4] AI also has the potential to diminish radiologist fatigue, possibly mitigating radiologist shortages, by supporting the interpretation of large image datasets generated by 3D mammography. AI algorithms may also help reduce radiation dose and improve cancer visibility (conspicuity).[3]

**DENSE BREASTS HAVE 2.2X INCREASED RISK OF DEVELOPING CANCER COMPARED WITH AVERAGE DENSITY BREASTS**

Currently available AI solutions integrate with 2D mammography. They can detect asymmetries, masses, calcifications, and distortions within the breast. Abnormal areas can be depicted based on the level of suspicion using heat maps (red – high suspicion to blue – low suspicion) (Fig 1). Any abnormalities detected are also scored based on the likelihood of malignant disease (100% - highly suspicious and 0% - not suspicious) (Fig 2).

3D mammography-capable AI packages are currently in an advanced stage of development.[5] They work on the same principles of those based on 2D mammography but will be of greater benefit for screening the larger image volumes. When a 3D mammogram is performed, a synthetic 2D mammogram is generated from the data obtained; these can be used with currently available AI technologies. AI is also being implemented to generate an enhanced synthetic 2D mammogram which delivers better lesion conspicuity thereby reducing the likelihood of missed cancers.

Numerous research articles are reporting the use of AI in assessment of breast density. Dense breasts have 2.2x increased risk of developing cancer compared with average density breasts. However, inter-, and intra-observer variability in the interpretation of breast density is high. AI-assessed breast density can be standardised to eliminate observer bias.

The general consensus is that the best results are obtained when combining the experienced radiologist with AI. Clinical judgement is important in interpreting mammographic findings (Fig 3). Future AI interpretation algorithms will need to integrate electronic health records and prior mammograms done by the patient to improve specificity.

## CONCLUSION

At each step of the breast imaging process, from the decision to perform screening and image acquisition to the reporting of imaging findings and follow-up recommendations, there are multiple potential opportunities for AI to augment the benefits of 3D mammography. These will lead to improved practice efficiency and ultimately improved patient health outcomes of breast cancer screening and diagnostic evaluation.

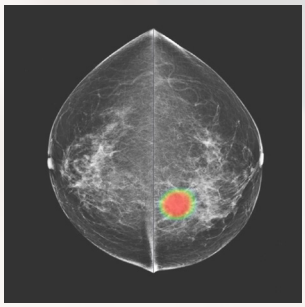


**Figure 1:** Deep learning technology can accurately analyse mammography images to detect lesions that could indicate breast cancer and provides location information for any detected lesions in the form of outlines and heatmaps (red - high, green - intermediate and blue - low level of suspicion for breast cancer). (Source: https://grand-challenge.org/aiforradiology/product/lunit-insight-mmg/).

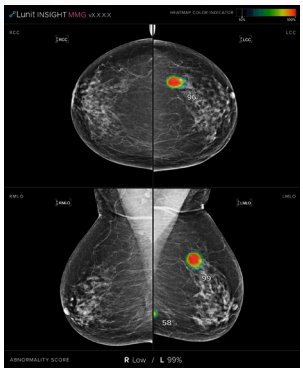
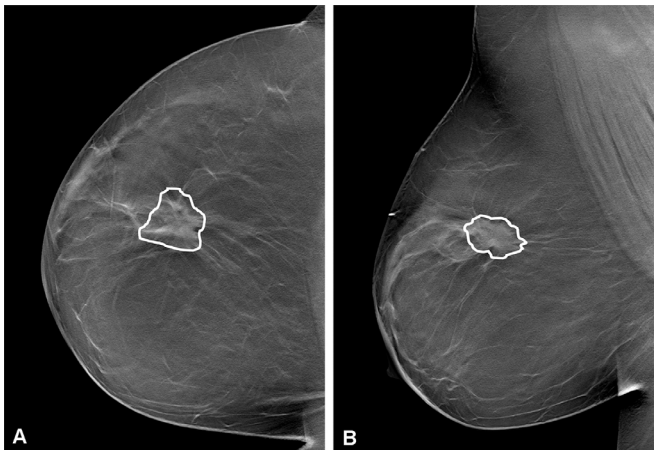


**Figure 2:** Same technology as in figure 1 showing percentage likelihood of malignancy (100% highly suspicious, 0% not suspicious). (Source: https://grand-challenge.org/aiforradiology/product/lunit-insight-mmg/).

**Figure 3:** Screening mammography in a 57-year-old woman with a history of excision of an area of atypical ductal hyperplasia with associated microcalcifications 10 months before. Craniocaudal (A) and mediolateral oblique (B) right breast screening DBT mammograms show a white outline around a suspicious architectural distortion. Using clinical judgment, these findings were deemed benign postsurgical changes. (Images obtained from NYU Langone Health internal cases.)[3]





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DR DAVID BORG, DR CHRISTINA CASSAR, MS RACHEL ABELA

# Patient and Carer Education in the Management of Constipation with a View of Reducing Unnecessary Admissions

## INTRODUCTION

Constipation is a significant health care issue, especially in high-risk groups such as the elderly, patients with psychiatric problems, institutionalised individuals and those with decreased mobility.[1] As indicated from this audit, in 2021, an estimated 2.5% of general surgery admissions were due to constipation.

A significant number of patients were being admitted to the inpatient service with a diagnosis of 'constipation' for which the majority had no neurological or anatomical cause. Thus, these patients would be defined as having 'functional constipation' (FC) as per Rome Criteria.[2] Additionally, different therapeutic regimens were noted to have been used in several primary health care facilities and elderly homes to treat constipation. Such regimens were not standardised and evidently, ineffective.

As a result of the lack of standardised management, there was inadequate use of health care resources giving rise to admissions. Treatment that could have occurred at primary health centres or else in the community was being given in hospital instead. Financial and hospital resources, patient discomfort, patient risk and inaccurate information relayed to the patient are all in play when it comes to unstandardised medical management.

## AIM

The aim of this audit was to investigate all cases of avoidable constipation from January 2021 to January 2022 and to assess if any standard was being followed for management of constipation at primary health level before being admitted to Mater Dei Hospital (MDH). The primary outcome of this audit will therefore attempt to improve patient and carer education in constipation management.

A standardised approach to improve the medical care of patients with functional constipation is described to decide when these patients need hospitalisation. Furthermore, a secondary outcome of this audit discusses the need of developing a standardised outpatient therapeutic approach for such patients to prevent recurrence. Before commencing this audit, approval from data protection department at MDH (Ref. MDH12/2020) was granted.

## THE RESEARCH QUESTION

The authors made use of the 'PICO' model'[3] to construct a research question in order to ensure that the appropriate outcomes are considered in relation to a clearly described patient cohort. The PICO model is made up of four elements:

- **Population:** Patients admitted to MDH with functional constipation. These may have been referred from primary health care, elderly homes, or else self-referred themselves from the community;
- **Intervention:** Medical management of constipation;
- **Comparison:** Comparing local management with standardised protocols used to categorise and treat constipation;
- **Outcomes:** In essence, the authors would like to determine whether the current strategy in admitting patients with functional constipation is an optimal method of using limited health care resources and also, whether current methods prove useful in preventing further recurrence.

## METHODOLOGY

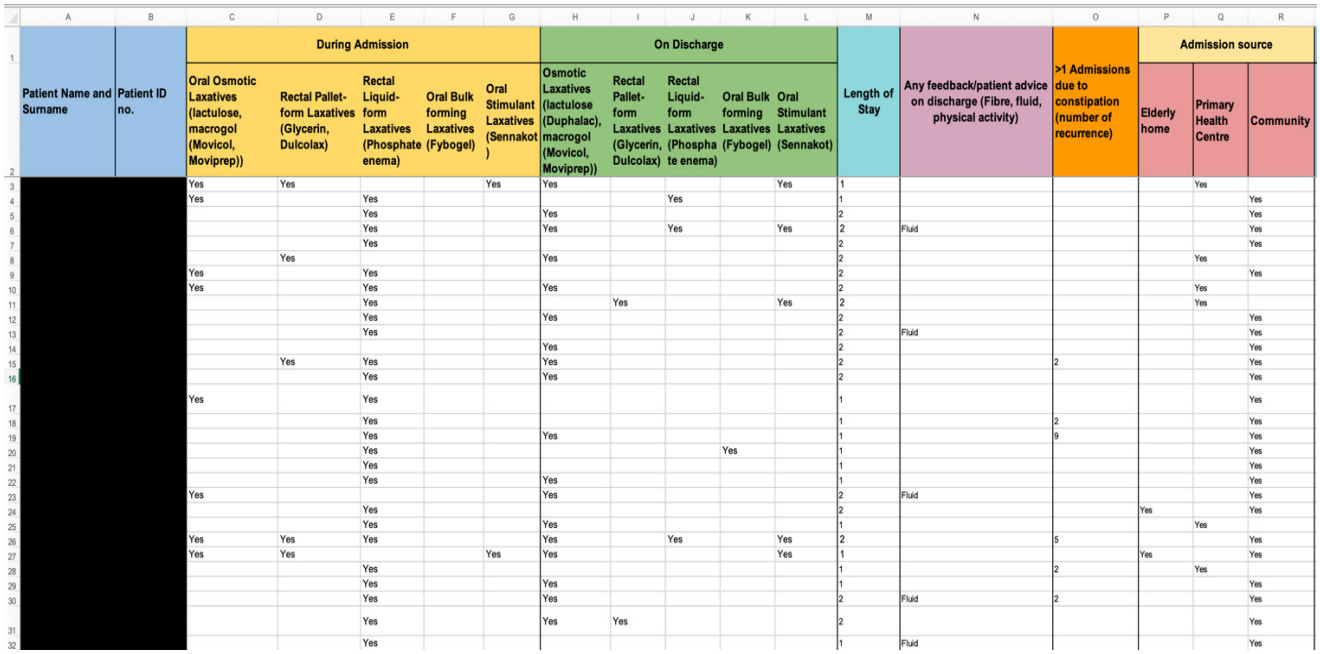
A literature search was conducted in specific databases to develop a standard for this audit i.e. NCBI and PubMed. Literature published between 2018 and 2022 was taken into consideration. It was decided that a retrospective method of assessment should be used to adequately conduct this audit.

The patients were recruited from the general surgery handover list which captures all emergency admissions at MDH. A set of inclusion and exclusion criteria was set up as shown in table 1 below.

**Table 1.** Population inclusion and exclusion criteria.

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| Patients admitted with constipation as primary cause of admission | Admissions requiring surgical escalation of treatment |
| Admission period between January 2021-January 2022 | Admissions requiring > 2-day length of stay due to unforeseen comorbidities e.g. undiagnosed oncology cases, thyroid function abnormalities |
| Patients ≥ 18 years of age | Patients with previous colorectal surgery, including colostomy and ileostomy cases |

Figure 1. Excel sheet used for data collection.



| Patient Name and Surname | Patient ID no. | During Admission | | | | | On Discharge | | | | | Length of Stay | Any feedback/patient advice on discharge (Fibre, fluid, physical activity) | >1 Admissions due to constipation (number of recurrence) | Admission source | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Oral Osmotic Laxatives (lactulose, macrogol (Movicol, Moviprep)) | Rectal Pallet-form Laxatives (Glycerin, Dulcolax) | Rectal Liquid-form Laxatives (Phosphate enema) | Oral Bulk forming Laxatives (Fybogel) | Oral Stimulant Laxatives (Sennakot) | Osmotic Laxatives (lactulose (Duphalac), macrogol (Movicol, Moviprep)) | Rectal Pallet-form Laxatives (Glycerin, Dulcolax) | Rectal Liquid-form Laxatives (Phosphate enema) | Oral Bulk forming Laxatives (Fybogel) | Oral Stimulant Laxatives (Sennakot) | | | | Elderly home | Primary Health Centre | Community |
| [redacted] | | Yes | Yes | | | Yes | Yes | | | | Yes | 1 | | | | Yes | |
| | | Yes | | Yes | | | | | Yes | | | 1 | | | | | Yes |
| | | | | Yes | | | Yes | | | | | 2 | | | | | Yes |
| | | | | Yes | | | Yes | | Yes | | Yes | 2 | Fluid | | | | Yes |
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| | | | | Yes | | | | | | Yes | | 1 | | | | | Yes |
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| | | | | Yes | | | Yes | | | | | 2 | Fluid | 2 | | | Yes |
| | | | | Yes | | | Yes | Yes | | | | 2 | | | | | Yes |
| | | | | Yes | | | | | | | | 1 | Fluid | | | | Yes |

An online excel form was developed to store and compare data. This data was only accessible by the authors of this paper. Patient and carer information was kept confidential throughout. Figure 1 is a screenshot-sample of the excel form used for data collection. Information compiled included the patients' source of admission, recurrences, treatment given during admission until patients open their bowels and any treatment prescribed on discharge to prevent recurrence.

## RESULTS

During data collection, a total of 174 patients were considered. After exclusion criteria, 145 patients were recruited for data assessment. Tables 2 and 3 represent the treatment which patients were prescribed to open their bowels on admission – laxatives prescribed from admission upon first time of recorded bowel motions, and upon discharge – laxatives prescribed to patients on discharge, respectively.

Table 2. Treatment during admission

| Treatment | Number of patients | Percentage out of 145 |
|---|---|---|
| Oral Osmotic Laxatives (Lactulose, Macrogols) | 27 | 18.6% |
| Suppositories (Glycerin, Bisacodyl) | 16 | 11.03% |
| Rectal Enemas (Phosphate enema) | 123 | 84.8% |
| Oral Bulk forming Laxatives (Fibre) | 1 | 0.7% |
| Oral Stimulant Laxatives (Senna) | 13 | 9% |

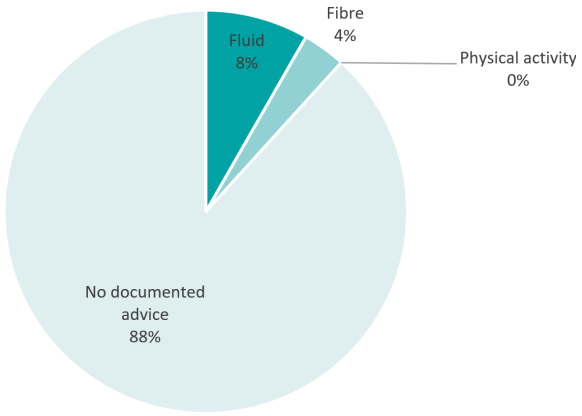
Table 3. Treatment on discharge

| Treatment | Number of patients | Percentage out of 145 |
|---|---|---|
| Oral Osmotic Laxatives (lactulose, macrogols) | 93 | 64.1% |
| Suppositories (Glycerin, Bisacodyl) | 4 | 2.8% |
| Rectal Enemas (Phosphate enema) | 7 | 4.8% |
| Oral Bulk forming Laxatives (Fibre) | 9 | 6.2% |
| Oral Stimulant Laxatives (Senna) | 24 | 16.6% |
| No treatment on discharge | 36 | 24.8% |

Figure 2 represents the feedback which patients were given upon discharge. Feedback was given in the form of written advice via a discharge letter. Apart from this, no brochures or leaflets discussing means to prevent constipation were given out on discharge. After data collection, any advice given to patients was analysed and compared to the standards set by the NHS. The standards include the following prevention strategies:

- Adequate hydration
- A mixture of soluble and insoluble fibre diet
- Physical activity

**Figure 2.** Patient advice on discharge as percentages.



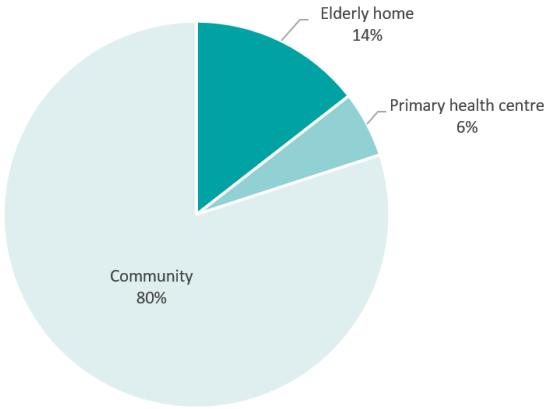

26.9% (39 patients) of the population had at least one re-admission due to functional constipation during the single year under scrutiny. It was ensured that during data collection, patients were only recruited on the datasheet once, in order to increase validity and reproducibility. The number of re-admissions for that particular patient was indicated in the datasheet in a separate column. Table 4 represents the number of re-admissions for the population audited until January 2022.

**Table 4.** Number of re-admissions as percentages.

| Number of re-admissions | Number of patients | Percentage from population |
|---|---|---|
| 2 | 21 | 14.5% |
| 3-5 | 12 | 8.3% |
| 6-10 | 3 | 2.1% |
| >10 | 3 | 2.1% |

44.8% of the population studied were admitted for two days, while the rest were admitted for a total of 1 day. Figure 3 represents the source of admission of the population as percentages.

**Figure 3.** Source of admission




## DISCUSSION

### *Management on admission*

On admission, a significant proportion of patients (84.8%) required phosphate enemas to open bowels. Other patients required suppositories or oral laxatives. It can be debated that these are medications that can be prescribed by GP's, bought, and administered safely at home, and if needed, with the assistance of community nurses.

Upon contacting primary health care centres, it was confirmed that no standard protocol for constipation management is used. Rectal laxatives are not administered in these centres and this is the primary reason that these patients are referred to MDH for a phosphate enema.

On contacting specific elderly homes, it was noted that not all homes administer phosphate enemas and the reason for this is a combination of inadequate resources and the home's requirement of a prescription from a medical doctor – who might not always be on site. In addition, it was noted that no standard protocol of constipation management was in use throughout these homes. This seems to be the main reason the delayed treatment of constipation and subsequent hospital admission.

This lack of adequate management resulted in 145 admissions (209 hospital bed days) at MDH simply for the administration of laxatives. This is suboptimal especially considering that rectal saline laxatives such as phosphate enemas can be safely administered outside of hospital.[4]

### *Management on discharge*

NHS recommendations[5] advise that constipation should not only be managed with medication, but also with diet and exercise. This signifies the importance of patient and carer education. Patients audited were found to be prescribed a wide range of laxatives, with no correlation or pattern, and only 12% of these patients were given advice on an adequate diet. There was no documented recommendation about the importance of physical exercise in preventing constipation.

Only 12% of patients were given documented advice on their diet, and 24.8% of patients were not even given treatment on discharge to prevent future constipation. This is significant and indicates the importance of patient education and a practical management regimen to be given upon discharge from MDH. Further unnecessary re-admissions could be prevented by not only prescribing laxatives but also by providing adequate information on diet, hydration and physical activity.

One cannot ignore the financial burden of such admissions. Patients with a diagnosis of constipation are generally admitted for a minimum of one day at hospital. MDH billing department gives the cost for a full day in a surgical ward, excluding investigation and treatment, to be Euro 256.23. Multiplying the number of bed days used by these admissions results in a cost of Euro 53,504 in a single year not including price of any routine and investigative tests incurred or any medication given. This is a hefty price to pay for management which may be provided outside of hospital. Patient/Carer education and standardisation of constipation management would greatly decrease these costs.

*Limitations of Audit*

- This audit has been based on clinician comments via handover documents and hospital online database. Despite taking into consideration any past medical or surgical patient history whilst undergoing inclusion/exclusion criteria, the audit has not considered patient's drug history. This may have contributed to functional constipation and would ultimately change the overall management to include treatment review, subsequently altering or omitting current medications which increase constipation.
- Prescriptions from public health centres were not analysed to confirm any possible issues faced by GPs which may have led to the decision to refer to ED. For example, a GP may not have been comfortable stepping up laxative doses to the maximum licensed doses in specific patients.
- When collecting data relating to discharge advice, it was not possible to correlate any lack of advice to the health status of the patient. For example, patients might have not been given advice on physical activity due to current mobility issues.

## CONCLUSION

The frequency of and the associated costs of ED visits and hospital admission for constipation are significant.[6] Management of constipation is most successful when multiple approaches are instituted and/or combined (adequate diet, exercise, and therapeutic medication). Similarly, the approach to medication often necessitates more than one agent/laxative, with the aim of titrating to optimal effect. Standard protocols for the management of common presentations such as constipation are recommended.

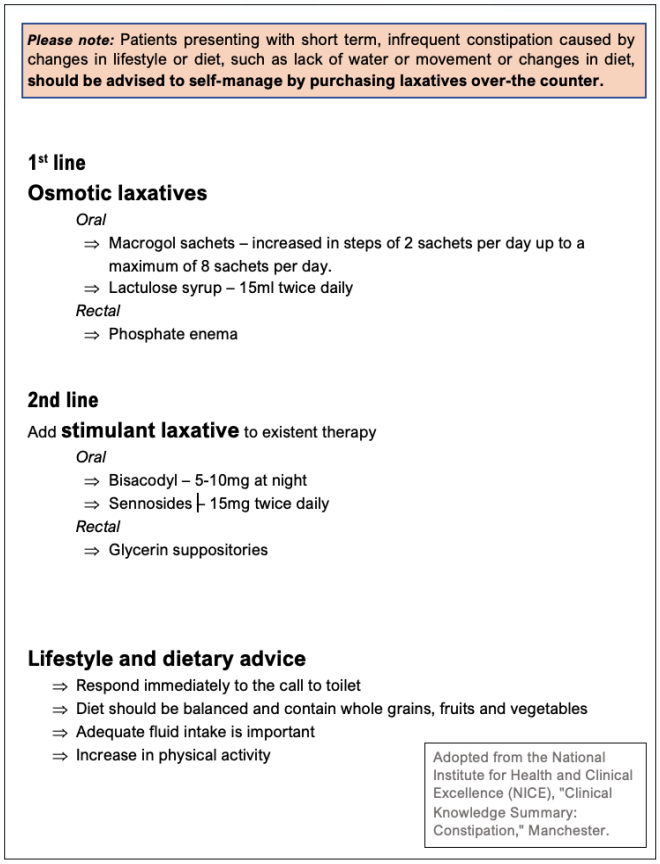
## GRADED RECOMMENDATIONS

*1. Carer education and a standardised approach*

A constipation management guideline has been compiled to standardise the management of patients presenting with constipation both at primary health centres and in elderly homes (Figure 4).

A copy of this audit along with the established management guidelines – which has been adapted from the NHS, will be promoted locally. Furthermore, brochures containing relative information will be sent to all local elderly homes.

Figure 4. Constipation management guidelines with QR code. Adapted from the National Institute for Health and Clinical Excellence (NICE), "Clinical Knowledge Summary: Constipation," Manchester.

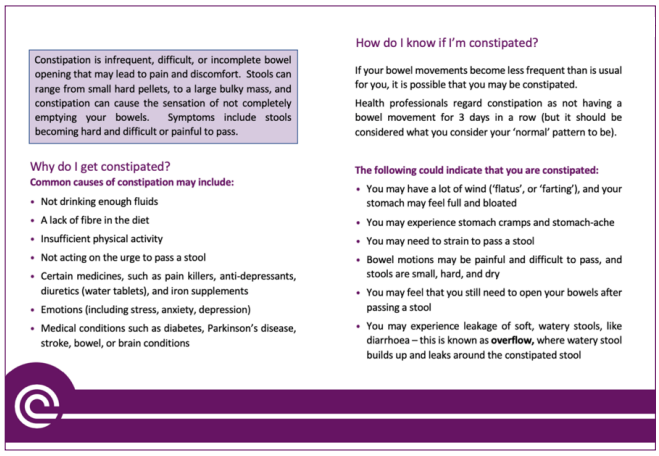


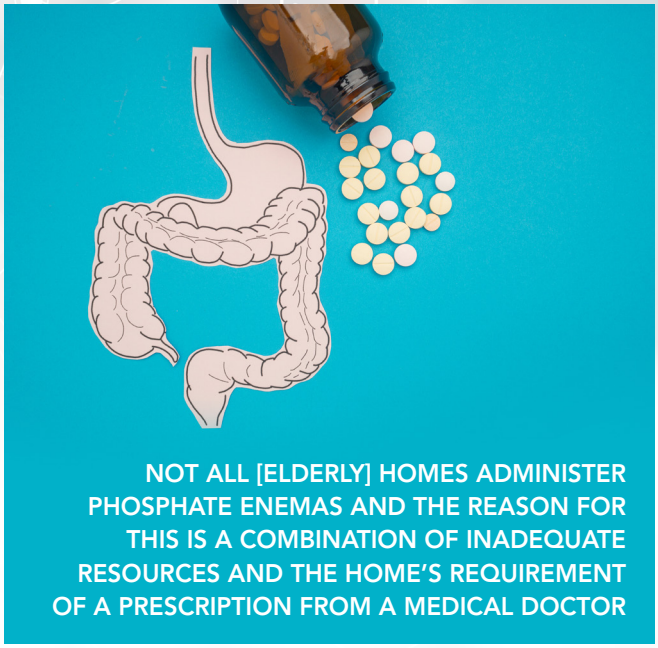
### *2. Patient education*

Figure 5 represents a brochure proposed by the authors of this paper as a form of patient education which will be sent to all local elderly homes. This brochure is pending approval by MDH's general surgery department. This brochure includes advice on diet, hydration, physical activity, and other recommendations to conservatively manage constipation. Furthermore, it signifies the stepwise approach of health care, reminding the patient to utilise primary health facilities adequately before choosing to present to the emergency department. This is pertinent since 80% of patients presented directly from the community to MDH ED.

This brochure, as approved, will be available to all doctors via MDH's online platform and will be circulated to doctors working in the general surgery department via email. It would be recommended that this brochure as well as the guidelines are printed and given to the patient along with the discharge letter.

**Figure 5.** Constipation leaflet with QR code. Adapted from the NHS website www.nhs.uk/conditions/constipation.


### *3. Local hospital improvements*

Considering the above results, it would be ideal to invest in carer education in this sector, especially in the administration of rectal laxatives, to decrease the number of unnecessary admissions. Furthermore, it would also be ideal to consider a specified outpatient constipation service to manage these admissions, further decreasing the number of patients presenting at the emergency department.

The above measures and recommendations are only indicated where functional constipation has been diagnosed and other causes needing further surgical intervention have been excluded. It is important to note that it is highly recommended to consider the patient in a holistic manner, along with their comorbidities and drug history, before attempting to prescribe laxatives.[7] Furthermore, prophylactic prescribing of laxatives along with drugs that may cause constipation is debatable but should always be considered.[8]

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DR MOSES CAMILLERI

# Spondylodiscitis in People who Misuse Drugs by Injection: A Case Series of Maltese patients

## INTRODUCTION

Spondylodiscitis is associated with significant morbidity and some mortality. This case series describes the diagnosis, management, and outcome of 11 patients who were diagnosed with spondylodiscitis over a period of 10 years. Information about the presentation, diagnosis and management of the patients was extracted from the summaries provided to patients on discharge from hospital. Access to such information was consented to by the patients. All patients were known to misuse drugs by injection and had been in contact with treatment services for a number of years before the onset of the infection. This case series highlights the possible deterioration in the quality of life of patients diagnosed with spondylodiscitis, especially if diagnosis and treatment are delayed. It also tries to impress the importance for health care professionals to facilitate and actively promote the engagement of patients who misuse drugs by injection with care and treatment services, if diagnosis and treatment of this condition are to be effective and result in less morbidity.

## CASE PRESENTATION AND DIAGNOSIS

The studied patients were diagnosed with spondylodiscitis over a 10-year period, between 2012 and 2021. The patients were in contact with services provided at the Substance Misuse Outpatient Unit (SMOPU), a community-based clinic in Malta providing comprehensive services to people with a substance use disorder. Doctors working at this clinic were asked to identify patients attending SMOPU who were referred or treated for spondylodiscitis. This case series refers to 13 episodes of spondylodiscitis in 11 different patients (Table 1).

Table 1. Yearly incidence of spondylodiscitis encountered by doctors at SMOPU over the years.

| Year | Number of cases |
|---|---|
| 2012 | 1 |
| 2013 | 1 |
| 2014 | 0 |
| 2015 | 1 |
| 2016 | 3 |
| 2017 | 0 |
| 2018 | 1 |
| 2019 | 0 |
| 2020 | 3 |
| 2021 | 3 |

The mean age of the patients in this case series was 36.5 years (range: 28 to 43 years). Four of the 11 patients were female.

Back pain was mentioned by all patients in their presenting complaint (Table 2) except in one patient with impaired level of consciousness at time of referral to hospital. Six patients were febrile at time of presentation. Complaints of a neurological nature were mentioned in less than half of the patients at time of presentation, in the form of paraesthesia and weakness of the limbs (five patients).

Table 2. Most common symptoms of patients with spondylodiscitis seen at SMOPU.

| Most common presenting complaints |
|---|
| Back pain |
| Fever |
| Neurological signs (paraesthesia and weakness of limbs) |

Two patients were referred to Mater Dei Hospital (MDH) with a diagnosis of spondylodiscitis, following magnetic resonance (MR) imaging of the vertebral column outside hospital. 10 patients who were referred to MDH had MR imaging done while in hospital as part of the various investigations to confirm the diagnosis. On one occasion, the MRI was taken solely after the patient was discharged. Four patients also had additional MR imaging done after discharge from hospital as part of the management plan at follow up. MR imaging showed that in this case series the lumbar level of the vertebral column was more often involved (Table 3).

Table 3. The specific vertebral column section affected by spondylodiscitis as identified by MRI.

| Part of vertebral column involved | MRIs taken |
|---|---|
| Cervical | 4 |
| Thoracic | 3 |
| Lumbar | 6 |

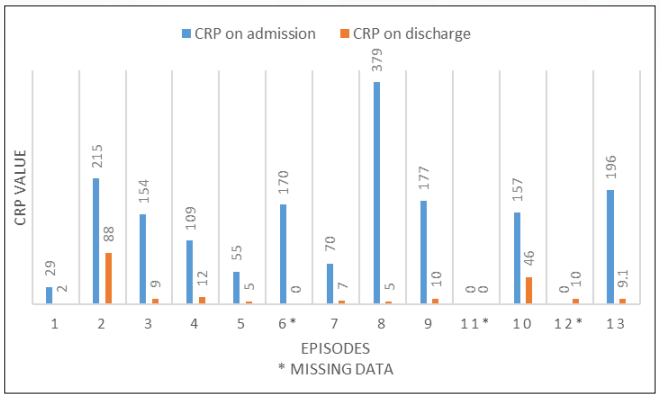
Most of the patients managed in this case series were admitted under the care of an infectious disease specialist. A minority of patients were admitted under other specialities (Table 4).

Table 4. Patients with spondylodiscitis referred to MDH were assigned to consultants with different specialisations.

| Speciality caring for patients | Admissions |
|---|---|
| Infectious disease | 9 |
| Orthopaedics | 2 |
| General medicine | 1 |
| Neurology | 1 |

Inflammatory markers in the form of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) where measured in most patients in order to follow the progress or otherwise of their condition. In this case series CRP was the investigation more often used. Figure 1 clearly shows the fall in CRP levels as patients responded to treatment.

Figure 1. CRP value over the treatment course.




10 out of 12 blood cultures grew *Staphylococcus aureus*, of which 2 were methicillin-resistant. In three cases no bacteria were grown on culture. Four patients underwent CT-guided aspiration in an effort to identify/confirm the infective organism. Of these, two had blood cultures. Seven patients had an echocardiogram done.

## MANAGEMENT

All patients were administered parenteral antibiotics. Parenteral administration of antibiotics lasted a few weeks. In 10 out of 13 treatment episodes an indwelling intravenous catheter was deemed necessary to facilitate this. All patients were changed to oral antibiotics before discharge from hospital. Multiple antibiotics, often administered concurrently with frequent changes made it extremely challenging to follow the order in which they were prescribed, since the primary source of information was the discharge summary. The following is a list of the various antibiotics mentioned in the patients' discharge summaries: Penicillins [flucloxacillin, piperacillin/tazobactam], Fluroquinolones [levofloxacin, ciprofloxacin], Glycopeptides [teicoplanin, vancomycin], Cephalosporins [ceftriaxone], Nitroimidazoles [metronidazole], Lincosamides [clindamycin], Carbapenems [meropenem], Sulfonamides [co-trimoxazole], and Tetracyclines [doxycycline]. Six patients required surgical intervention at the time of hospitalization as part of the management of spondylodiscitis.

## OUTCOME

Eight patients remain in contact with SMOPU at time of writing. One other patient passed away 12 months after the episode of spondylodiscitis, with the cause of death related to cardiac complications. These eight patients still in contact remain generally well, though some with less-than-optimal health, even as a consequence of the spondylodiscitis.

## DISCUSSION

Osteomyelitis of the vertebral bodies and infection of the intervertebral discs and surrounding tissues is a rare condition more often seen in an elderly population. An incidence of up to 6.5 per 100,000 in those over the age of 70 is described. Incidence is lower in the younger population at 0.4 to 2.4 per 100,000. Incidence is noted to be increasing.[1] Possible factors contributing to the increase include an ageing population, increased prevalence of chronic diseases and immunosuppressive therapies. Diabetes and drug injecting in people who use drugs are among the more common chronic diseases that predispose to osteomyelitis.[2] Osteomyelitis is more common in people who misuse drugs by injection as they tend to have multiple infected sites such as skin and soft tissue infections, abscesses, and foreign bodies such as broken needles at sites of injecting and an increased prevalence of dental and gum disease. Osteomyelitis of the vertebrae and intervertebral discs is a common site in people who inject drugs.[2]

With a mean age of patients in this case series being 36.5 years, this is by far a younger aged population compared to the age of patients usually developing spondylodiscitis. This is expected considering that the studied patients were people who misuse drugs by injection. This is also the more common age group of patients who access services provided by SMOPU. Patients developing this condition had been in contact with treatment services for an average of 14 years (range: 4 to 25 years). In this case series it is noted that the last two years included in the study were the two years when more patients were diagnosed with this condition (Table 1).

One patient in the case series was admitted to hospital and treated for spondylodiscitis on 3 separate occasions. The time between the first and second episode was of 13 months and 6 months between the second and third. In all 3 episodes the infection was at the level of the lumbar vertebrae, with the earlier episode involving the second lumbar vertebra and the latter episode 19 month later, the fifth. The patient was discharge from hospital when the health care providers considered it reasonable to

change to oral antibiotics. The patient claimed to have been compliant to oral antibiotics as advised at time of discharge from hospital. It is difficult to say whether the recurring spondylodiscitis was an exacerbation of previously unresolved infection or recurring in an individual successfully treated for the same condition but known to have persisted with drug injecting. Another two patients in the series required readmission for further care of spondylodiscitis, but it is assumed that management during the first admission was incomplete as the patients discharged themselves from hospital against medical advice.

Though less females than males were represented in this case series, the ratio female to male diagnosed with spondylodiscitis (1:1.8) is higher than the female to male ratio of patients making use of services at SMOPU, which stands roughly at 1:4. Females diagnosed with spondylodiscitis in this study were 4 years younger compared to males at time of diagnosis (females: 33.8 years, males: 37.8 years). The onset of spondylodiscitis after having established contact with SMOPU services is slightly shorter in females (12.6 years) compared with males (13.4 years). These gender disparities are an indication, also supported in the literature,[3] that females are likely to be involved in more risky behaviours than males and that they tend to develop complications secondary to drug use and injecting earlier than males.

Table 5. Gender differences in patients with spondylodiscitis noted in this study.

| Gender disparities |
|---|
| Proportionately more females infected |
| Females developing condition at a younger age |
| Females developing condition earlier following contact with services |

In this case series, nonspecific symptoms lingered for an average of 5 weeks (range: 1 to 16 weeks) until a diagnosis was made, and appropriate treatment started. Various factors are known to have contributed to the delay in diagnosis. Backpain in two of the patients was put down to pain of musculoskeletal origin with no further investigations recommended until the patients returned with deteriorating symptoms. One patient was involved in a motor vehicle accident and symptoms (neck pain and upper limb paraesthesia) attributed to a whiplash injury. Another patient complaining of severe neck pain and a history of cervical radiculopathy was referred back from hospital to primary care with no explanation for a spiking temperature. Some patients admitted having delayed presenting to care services as they did not think much of the symptoms they were suffering from.

All patients had MR imaging done at some stage in the course of the management. Some had more than one done (Table 6). This highlights the importance of this investigation in the diagnosis and further management at time of treatment and follow up.

Table 6. MRI investigations carried out during this review.

| Timing of magnetic resonance imaging | MRIs taken |
|---|---|
| Pre-hospital | 2 |
| In-patient | 10 |
| Post-discharge | 4 |
| Pre-hospital and in-patient | 1 |
| In-patient and post-discharge | 2 |
| Pre-hospital and post-discharge | 1 |

Another important investigation done in most patients in this case series is the serial estimation of inflammatory markers. Non-specific blood markers include an elevated white cell count, ESR and CRP. Elevated inflammatory markers, though not pathognomonic for this condition, have been recommended as a possible screening tool when the clinical presentation is indicative.[4]

In this case series antibiotics were withheld until culture and sensitivities were available to guide choice of antibiotics (Table 7). In three cases sampling did not culture any organisms. Literature describes this as happening in up to 40% of cases, rendering the choice of antibiotic less straight forward.[4,5]

Table 7. Biopsy and culture.

| Sampling type prior to start of antibiotics | Samples taken |
|---|---|
| Blood cultures | 12 |
| CT-guided biopsies | 4 |
| Blood cultures after CT-guided biopsies | 2 |

One patient had no specimens (neither blood nor material from site of infection) sent for cultures due to early discharge against medical advice. This patient was admitted to hospital 12 months later and diagnosed with infective endocarditis and a splenic abscess. It is reasonable to speculate whether the untreated episode of spondylodiscitis in this patient contributed to the development of the serious complications a year later. Two patients were diagnosed with infective endocarditis while in hospital being treated for spondylodiscitis. Both these patients had blood cultures which grew *Staphylococcus aureus*. Seven patients had an echocardiogram done while in hospital being treated for spondylodiscitis. Literature recommends transoesophageal echocardiography in all patients diagnosed with spondylodiscitis.[6]

Literature indicates that people who use drugs might not be compliant to antibiotic treatment if discharged too early form hospital.[7] This might explain the prolonged hospital stays. In this case series, patients' hospital stays when not discharged against medical advice (two patients), lasted a mean of 29.7 days (range 15 to 52 days). While the prolonged need for venous access is likely to determine the insertion of central catheters in most cases, one must keep in mind that peripheral venous access is particularly difficult in this population of patients, further making it more likely to resort to a central line insertion. None of the 10 patients requiring a central line were discharged from hospital while still on parenteral antibiotics and therefore there was no need to discharge with a central (or peripherally inserted) line. All patients were changed to oral antibiotics at time of discharge from hospital. The average duration of antibiotic treatment (both parenteral and oral) was of 10.5 weeks. Some centres abroad do resort to the practice of patients being discharged with indwelling central lines in an effort to reduce the duration of hospital stays. Such a practice requires an outpatient service that closely monitors and cares for such patients. Fear of relapse to intravenous use of drugs might present a dilemma in deciding who is more likely to benefit from earlier discharge while still on parenteral antibiotics. In people who inject drugs such intervention remains debatable. While prolonged hospital stays are expensive the aim should be to provide appropriate care to this vulnerable population.[2,7,8]

Two of the 6 patients requiring surgery required this urgently to decompress the spinal cord at the cervical level. Three patients, including the two who required an urgent intervention at the time of the initial hospitalization, required elective surgery at a later stage to restore spinal alignment and correct instability. Two patients in this case series required dental care while in hospital being treated for spondylodiscitis.

Cure in uncomplicated pyogenic spondylodiscitis is achieved in 86 to 91% of cases.[9] While the infection itself is treatable, up to a third of patients will suffer some physical sequela from this condition as was the case in this series of patients treated for spondylodiscitis.

## LIMITATIONS OF THIS STUDY

Asking doctors working at SMOPU to recall patients cared for or referred to further care with spondylodiscitis over a period of 10 years might have resulted in some patients being missed. Another limitation of this study is that information about diagnosis and management not mentioned in the discharge summaries provided to patients at time of discharge from hospital was not available to the author.

## CONCLUSION

Spondylodiscitis is an uncommon but serious disease seen at a younger age in people who inject drugs. It is worth remembering that patients who currently or recently injected drugs, should alert a health care professional to afford more time in their assessment if they are sickly and febrile. Early diagnosis and management by specialized treatment services usually results in a favourable outcome. Quality of life after an episode of spondylodiscitis does not always return to the premorbid state. It is important that people who use drugs who are treated for spondylodiscitis remain in contact with treatment services after discharge from hospital. This should help prevent hospital admissions or allow early intervention should there be a return to behaviours known to be risk factors for this and other serious diseases. Care services to people who use drugs must remain easy to access, even to enable the more vulnerable among them such as females, to establish and maintain contact.

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The Malta Council for Science and Technology (MCST) is offering exciting new opportunities in the field of Health Research and Innovation (R&I), offering Malta-based entities the possibility to collaborate with international counterparts.

- The **SINO-MALTA Science and Technology Cooperation**, administered in collaboration with the Ministry of Science and Technology (MOST) of the People's Republic of China, annually launches Joint Calls to support R&I projects between Maltese and Chinese researchers. The 2023 Joint Call has identified Health as one of its thematic areas, focusing on research on cancer, cellular therapy, drug development, traditional Chinese medicine and digital tools to support healthcare. Malta-based eligible entities can request up to € 200,000 per project proposal, with a total Call budget of €600,000.
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For more information and participation requirements, please visit **mcst.gov.mt/internationalisation** or contact **international.mcst@gov.mt**.

# Profile of Alzheimer's Disease in Women

MALTA PHARMACEUTICAL STUDENTS' ASSOCIATION

YLENIA XERRI

Alzheimer's disease (AD) is 1.5 to 3 times more frequent in women than in men. Women have higher life expectancies and age is the most important non-modifiable risk factor in developing AD. However, studies show that a potential leading cause of AD in women is oestrogen deprivation during menopause.

Oestrogen is produced by both men and women, but being the primary female sex hormone, oestrogen levels in women are higher. When women go through menopause, their bodies stop producing most of their oestrogen. Male sex hormone testosterone, per contra, is continuously produced by males throughout their lives. Within the brain cells, testosterone is transformed into oestrogen. This indicates that, compared to men their age, menopausal women have lower levels of oestrogen in their brains.

The fact that women are more likely to get Alzheimer's disease post-menopause indicates that it is related to the protective effect of oestrogen which is lost, as the hormone levels drop. Researchers found out that oestrogen aids in the increase of connections in the hippocampus, the area in the brain responsible for memory and certain types of learning, which are both affected by Alzheimer's disease.

Oestrogen can also affect the transmission of signals throughout the brain by chemicals such as serotonin, acetylcholine and dopamine. Certain AD symptoms have been attributed to issues with the cholinergic signalling pathway, which may be related to low oestrogen levels.

Amyloid-β and tau protein accumulation in the brain is a characteristic of Alzheimer's disease. Oestrogen may protect the brain from Alzheimer's disease by inhibiting some of the detrimental effects of the amyloid-β protein. Amyloid-β protein damages brain cells by increasing the production of free radicals. Increased oestrogen levels have been demonstrated to lower the number of free radicals that cells create. This explains why women appear to be more susceptible to Alzheimer's disease due to the abrupt decline in oestrogen levels that occurs after menopause.

Various clinical trials are being carried out to test whether oestrogenic replacement could refine the brain function or also delay the development of Alzheimer's disease. Until there is better evidence, the potential advantages of Hormonal Replacement Therapy (HRT) as a means of lowering Alzheimer's disease do not outweigh the potential risks of HRT, which includes an elevated risk of certain types of cancer, heart disease and stroke. Studies are continuously being carried out to yield conclusive evidence of why women get AD more than men do, with the purpose to design safer and more efficient antidotes.

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