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thesynapse

THE MEDICAL PROFESSIONALS' NETWORK

READING THE SCREEN:

Re-Thinking CME through Screen-Based Learning Initiatives

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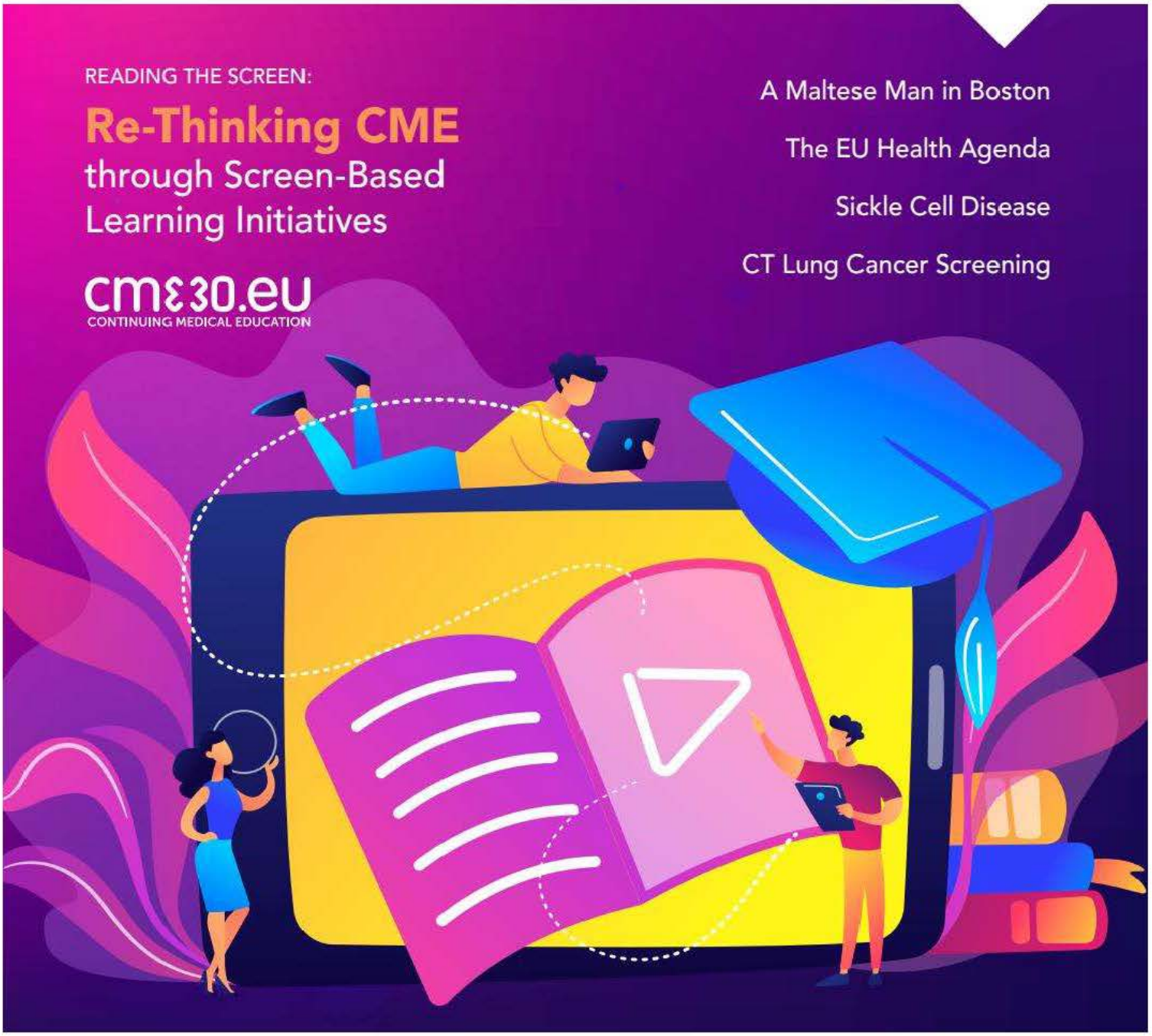
CONTINUING MEDICAL EDUCATION

A Maltese Man in Boston

The EU Health Agenda

Sickle Cell Disease

CT Lung Cancer Screening



Actifed*

Actifed* oral solutions provide symptomatic relief of upper respiratory tract disorders [1-6]

Actifed* DM COUGH LINCTUS

- relieves dry cough and nasal congestion [2,5]

Actifed* SYRUP

- clears blocked and runny noses [1,4]

Actifed* EXPECTORANT

- clears chesty cough and nasal congestion [3,6]

Dosage	
children aged 2 to 5 years [1-3]	2.5ml every 4-6hrs as required
children aged 6 to 11 years [1-3]	5ml every 4-6hrs as required
adults (including the elderly) and children aged 12 years and over [4-6]	10ml every 4-6hrs as required

OTC legal status applies for oral solutions in adults and children aged 12 years and over.

ACTIFED ABRIDGED PRESCRIBING INFORMATION: Please refer to full Summary of Product Characteristics (SPC) before prescribing. **TRADE NAME: ACTIFED. ACTIVE INGREDIENT:** Actifed **DM** Cough Linctus: Each 5ml contains Dextromethorphan Hydrobromide 10mg, Pseudoephedrine Hydrochloride 30mg and Triprolidine Hydrochloride 1.25mg; Actifed Syrup: Each 5ml contains Pseudoephedrine Hydrochloride 30mg and Triprolidine Hydrochloride 1.25mg; Actifed Expectorant: Each 5ml contains Triprolidine Hydrochloride 1.25mg, Pseudoephedrine Hydrochloride 30mg and Guaiphenesin 100mg. **PHARMACEUTICAL FORM:** Oral Solution **INDICATIONS:** Symptomatic relief of upper respiratory tract disorders which are benefited by a combination of: Actifed **DM** Linctus: a nasal decongestant, an anti-histamine and an antitussive; Actifed Syrup: a nasal decongestant, and an anti-histamine; Actifed Expectorant: a nasal decongestant, an anti-histamine and an expectorant. **DOSAGE:** please refer to full **SPC**. Actifed **DM** Cough Linctus, Actifed Syrup and Actifed Expectorant are authorised for use without the need of a medical prescription in Adults and Children over 12 years. In Children between 2-11 years of age, these products are authorised for use only against a medical prescription as recommended by your doctor. **CONTRAINDICATIONS:** Previous intolerance to any of the active substances; use of **MAOI**'s in the preceding two weeks; severe hypertension or heart disease; concomitant use of pseudoephedrine can cause a rise in blood pressure. **PRECAUTIONS:** May cause drowsiness; avoid the concomitant use of alcohol or other centrally active sedatives; use with caution in patients with liver impairment or moderate to severe renal impairment. **INTERACTIONS:** Sympathomimetics; **MAOI's. ADVERSE EVENTS:** Central nervous system depression or excitation with drowsiness being reported most frequently; sleep disturbance and rarely hallucinations have also been reported; skin rashes, tachycardia, dryness of mouth, nose and throat and urinary retention have occasionally been reported especially in men with prostatic enlargement. **PREGNANCY AND LACTATION:** Administration should only be considered if the expected benefits to the mother outweigh the potential risks to foetus or child. **PRESENTATION: DM**Cough Linctus, Expectorant, Syrup: Amber glass bottle x 100ml.**Marketing** Authorisation Holder: GlaxoSmithKline(Ireland) Ltd. **Marketing** Authorisation Number: **MA** 192/02001-6. Legal category: **POM – Actifed DM** Cough Linctus, Actifed Syrup, Actifed Expectorant in Children between 2-11 years. **OTC – Actifed DM** Cough Linctus, Actifed Syrup, Actifed Expectorant in Adults and Children over 12 years. Date of preparation: October 2019.

For the latest product information, please refer to the full SPC or contact us at GSK Malta (phone: +35621238131).

Suspected adverse events should be reported to GSK Malta through: gskpro.com/en-mt (Phone: +35621238131, Address: GSK Malta, 1 (1st floor), de la Cruz Avenue, Qormi, Malta). Cases may also be reported through medicinesauthority.gov.mt/adrportal (Malta Medicines Authority)

References: 1. Actifed Syrup SPC (Nov 2018); 2. Actifed DM Cough Linctus SPC (Nov 2018); 3. Actifed Expectorant SPC (Mar 2019); 4. Actifed Syrup SPC OTC (Nov 2018); 5. Actifed DM Cough Linctus SPC OTC (Nov 2018); 6. Actifed Expectorant SPC OTC (Mar 2019)

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Issue Guide

TheSynapse

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MMSA

MPSA

MADS

The magazine is distributed free of charge to all Maltese doctors, pharmacists & dentists, as well as students of the aforementioned professions, with a print run of 3500 copies.

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More cooperation needed in EU Healthcare

Smaller Member States are Key

DENIS HORGAN BCL LLM MSC PHD
Executive Director • European Alliance for Personalised Medicine Brussels, Belgium

It is well known that EU Member States have competency for their own healthcare systems under the Treaties, but it is equally true that, in today's fast-moving health-related environment, there are disadvantages for European patients if Member States act in isolation.

Two obvious examples are frustrated attempts to improve EU-wide cooperation on health technology assessment and the much-reported current failings of the cross-border healthcare directive.[1,2] More willingness to collaborate would not only improve the lot of patients and citizens, but also attract investment, allowing Europe to become a hub of innovation, able to provide services to its own economy for its continued prosperity.

Unfortunately, there are currently key gaps in stakeholder involvement, standardisation, interoperable infrastructure, European-level policy making, funding, data and research, and healthcare systems.[3] On a scientific level, barriers exist since molecular data is complex to translate into information for clinical practice, for example, because of the heterogeneity of disease subtypes. And at the level of regulation, urgent policy actions are needed - backed by investment and relevant training - to remedy the research-to-market gap in the EU that threatens to condemn the bloc to trailing global competitors.[4]

The EU faces choices if it wants to pursue innovation and bridge the gap between research and the market place.

AREAS OF EU INFLUENCE

It is the EU that can encourage the constructive pooling of resources in research. It is the EU that can remove bottlenecks by creating an internal market for skills, patents, venture capital, innovation procurement and standard setting, to foster ideas which are quickly implemented on the market.

Within a strategic framework, it is the EU that can provide the coordination, via policy interventions and instruments, that permits more efficient and beneficial research activity to take place at an EU level, to make sure things dovetail well.

There have been some moves to take up the challenge with Member States and multi-stakeholder collaboration beginning to drive policy, regulatory, research and innovation activities. Subsequent moves are building on these leads.[5]

SMALLER MEMBER STATES TO THE FORE

Smaller Member States are starting to collaborate regionally in health-related areas, such as electronic health record and prescription exchange, cross-border agreements, and banding together in groups in an effort to lower medicine prices.[6] Smaller states have been active in shaping health policy at European level and can now act as vital policy entrepreneurs pursuing normative policy agendas. This has been demonstrated by, for example, Slovenia and its major role in promoting cancer policy development at EU level.[7]

Due to the EU's structure, more and more often smaller Member States are acting as rotating presidencies, and while they take the broader EU view given their six-month task, it has also become clear that Europe's health policies need to recognise and tackle the inherent health system vulnerabilities faced, specifically, by smaller countries (by region) and in the regions of the larger ones.[6] Many challenges remain for the EU's smaller states, especially in the health arena, and these include – but are not exclusive to – a lack of interest by industry to place medical goods on such small markets due to high or inefficient unit costs of production, a lack of competition between providers which means high prices for medicines and medical supplies due to small volumes of consumption and, meanwhile, the administrative burden of regulation does little to help patient access and lower prices in these countries. In essence,

European health policy needs to become better attuned to the specific challenges facing the health systems in smaller states and regions.[8]

EU NEXT STEPS IN HEALTHCARE

Let us be clear, Europe has attributes - including in smaller Member States and regions - that give it the chance of being highly competitive in a world fighting for leadership in this promising sector. It boasts cohesive and predominantly social health systems, working to a high standard with the same values in comparable structures and under similar pressures, adhering to similar legislation and other influences.[9] Its scientific and technology capabilities in genomics and in many broader fields are globally respected and envied. Public funding support is available for health research, and major national and multinational programmes have demonstrably delivered successful results. And there is some health data infrastructure.[10]

With adequate investment and political will, the chances are good for successful cross-border collaboration, for enhancement of the data infrastructure, and even for that most elusive element of Europe's skill-set – translating its knowledge capital into innovation. The merits of collaboration by Member States at EU level have been repeatedly extolled – now we need more of it. Closer collaboration on reference networks and data banks; wider access to information; institutionalised cross fertilisation between providers, payers, and regulators; and enhanced common understanding on health technology assessment are just some of the most obvious needs to integrate innovation into healthcare.[11] Going forward, it will be important for everyone in the policymaking and regulatory frameworks to have a clear view of the impact they have on the development and introduction of innovation into healthcare.

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THE MEDICAL PROFESSIONALS' NETWORK

For your weekly dose of continuing medical education

Providing you with relevant information

NOT JUST AN AESTHETIC CHANGE

January 2020 saw the launch of a complete restructure of TheSynapse online services. This was the result of a yearlong exercise where we wanted to position TheSynapse to an even greater professional level to what it has been for the past 23 years.

TheSynapse network now has two distinct and interlinked portals:

1. TheSynapse.net is dedicated to providing users with news and resources from many sources. To put it in a nutshell, we scan and filter news items and publish succinct, relevant and timely news.
2. **CME30.EU** is a brand new video-based eLearning platform using one of the best reviewed eLearning engines in the world. **CME30.eu** continues to affirm TheSynapse as top content provider in the Maltese islands. Each peer-reviewed and accredited session or masterclass provides relevant CME content which is further subdivided into sections which makes it easy for the busy medical professional to assimilate knowledge. Each session is followed by a set of MCQs following which one can obtain a certificate of participation which may be used for accreditation purposes.

Both the Malta College of Family Doctors and the Medical Association of Malta provide accreditation of these sessions.

CME30.EU offers the opportunity to each and every medical professional to keep up to date by participating in CME sessions, delivered by some of the best local peers. This can be done in one's own space at one's own pace.

CME30.EU complements other forms of CME. An interesting feature is found in myCME, by clicking on myAccount (top right of landing page). This shows all CME credits gained through **CME30.EU** but also gives the opportunity to record CME done through other sources simply by filling in the required information and uploading a copy of certificate of participation when available. At the end of any period, one may request a report on CME which may be passed on to the relevant CME accreditors as may be required.

Behind any great service there is a great team. Indeed, TheSynapse is made up of a great team each with diverse expertise and skills but with a common passion to work selflessly and with dedication to deliver an outstanding service.

The work involved was and still is gargantuan but greatly satisfying. TheSynapse team welcomes anyone who is interested to join in consolidating **CME30.EU** as an effective resource for medical professionals. In particular, TheSynapse welcomes colleagues who are interested in participating as peer reviewers to ensure its value remains up to internationally recognised standards.

Change does not necessary mean improvement but there can be no improvement without change!

ASTHMA MASTERCLASS

Asthma is a chronic condition responsible for significant morbidity whose prevalence is increasing worldwide. Treatment options for asthma are numerous and along the years significant advances have been made in these treatment options. The high and increasing prevalence of asthma along with the recent advances in asthma management highlighted the need of this Asthma Masterclass with the aim of keeping healthcare professionals updated with the latest information and guidelines on this highly relevant condition.

The Asthma Masterclass consists of three sessions delivered by key opinion leaders in Asthma Management.

ASTHMA DIAGNOSIS AND INVESTIGATIONS

Prof Stephen Montefort

Lead consultant respiratory physician at Mater Dei Hospital. Head of Department and Deputy Dean of the Malta Medical School

ASTHMA MANAGEMENT GUIDELINES

Dr David Bilocca

Specialist in Respiratory Medicine. Dr Bilocca leads the endobronchial ultrasound service at Mater Dei Hospital

SEVERE ASTHMA: CASE PRESENTATIONS AND MANAGEMENT OF ASTHMA Q AND A

Dr Caroline Gouder

Specialist in Respiratory Medicine at Mater Dei Hospital

After watching each session, participants are invited to attempt a short set of Multiple Choice Questions and download a certificate of participation which may be used for accreditation purposes.

Each of the three sessions is accredited as follows:

ACCREDITATION

Medical Association of Malta as representative of UEMS
0.5 Credits

Malta College of Family Doctors
0.5 Credits

In this issue we meet **Prof. Sandro Galea**, a Maltese export to the US who has contributed much to the medical field. A physician, epidemiologist and author, Prof. Galea is the dean at the Boston University School of Public Health, US.

A Maltese Man in Boston

YOU HAIL FROM MALTA. FROM WHERE EXACTLY?

I was born in Sliema, and raised in St. Venera, close to Hamrun.

TELL ME SOMETHING ABOUT YOUR FAMILY.

My parents were both teachers when we lived in Malta. This made the teachers strikes of the 1980s, and the broader political unrest of those years, very much part of our daily life. I remember teachers holding lessons in their homes during the strike, the knock of police at the door, and worrying about my father, who was often out at protests. These conditions would play a role in my family's decision to leave Malta for Canada. They also shaped my thinking about how a country's political dynamic shapes the physical and mental health of citizens. I saw the toll political instability took on my parents, the injuries suffered by protestors, and the how polarization could take hold even in a place as small as Malta, undermining quality of life. The fact that my first exposure to these challenges was witnessing their effect on my family is perhaps why the link between politics and health has remained core to my thinking to this day.

WHY DID YOU OPT TO GO TO THE UNIVERSITY OF TORONTO MEDICAL SCHOOL?

As far back as I can remember, I have always wanted to make people better, healthier. When I was younger, the most direct way of doing so seemed to be becoming a doctor. The University of Toronto was attractive for the quality of its program and for its proximity to where my family was living at the time, hence allowing me to honor my family's wish to have me remain relatively close by - a fairly common wish for immigrant families.

AT 48 YEARS OF AGE, YOU SEEM TO POP OUT OF A FICTION BOOK. YOU WORKED IN NEW GUINEA, THE PHILIPPINES AND ALSO WITH DOCTORS WITHOUT BORDERS IN SOMALIA. YOU HAVE PUBLISHED A STAGGERING 800 SCIENTIFIC JOURNAL PAPERS AND 18 BOOKS. YOUR WORK HAS BEEN CITED MORE THAN 50,000 TIMES AND YOU HAVE BEEN INVITED TO PRESENT YOUR WORK IN 30 COUNTRIES. DO YOU CONSIDER YOURSELF TO BE A STORYTELLER? WHO IS BLIND WILLIE JOHNSON?

I think storytelling is necessary if we want to effect change that leads to a healthier world. We all tell ourselves a story about health. At the moment, the story in the United States is roughly this: to stay healthy, we must make good choices about what we eat, how much exercise we get, whether or not we engage in risky behaviour, etc. When we get unhealthy, it is generally because we have failed to make these good choices. We go to the doctor, who prescribes us medicine which makes us better. We then pay an astronomical fee for this treatment.

This story is wrong. The story we should be telling is that our health is shaped by the social, economic, and environmental conditions in which we live - by the food we eat, the water we drink, the air we breathe, our education level, neighbourhood safety, etc. Doctors and medicines treat us when we are sick, but these conditions decide whether or not we get sick to begin with. We should spend as much on improving them as we currently spend on treatment. The first step to doing so is changing our story about health.

This means talking about people like the blues singer Blind Willie Johnson. He was born in Texas in 1897. He lost his sight early, grew up poor and black in the American South, and eventually made his living playing music on street corners. One day his house burned down. With nowhere to go, he slept in the damp ruins, until he died from malaria after reportedly being turned away from the hospital because he was poor or because he was black (it is unclear which). Yet it was not really malaria that killed him. It was the conditions of his life - poverty, racism, injustice - which truly made him sick. We need to talk about these conditions when we tell the story of health.

WHY STUDY EPIDEMIOLOGY?

Epidemiology is centrally concerned with the causes of disease in populations. By pointing towards the roots of what makes us sick or keeps us well, it helps us prevent disease from occurring. Its focus on populations reminds us that health is ultimately a collective concern. And it provides a scientific foundation for the practical steps we must take towards a healthier world. When epidemiology tells us, for example, that income inequality undermines health, this finding has political implications, opening the door to the high-level, structural changes that can improve our health.

YOU SEEM TO PREFER EQUITY TO EFFICIENCY. WHAT ARE YOUR ALLEGIANCES?

A core tenet of public health is that we are not healthy until we are ALL healthy. In the last century, life expectancy in the US rose from 47 to about 79, yet the lives of the poorest Americans are now 10 to 15 years shorter than those of the richest. Such health inequities persist despite the efficiency and technological promise of our age. Equity, the closing of such gaps, should be at the heart of our approach to health. I am not sure I "prefer" equity to efficiency. I think both are very important and we should work hard not to sacrifice one for the other as much as possible.

YOU SEEM FIXATED WITH THE IDEA OF PEOPLE DYING HEALTHY ... WHAT IS THE 'HEALTHIEST GOLDFISH'?

There is a story I often tell about a pet goldfish. Its owner wants it be healthy and live a long life. So, she feeds the goldfish nutritious food. She encourages the goldfish to exercise. She makes sure it receives special goldfish medication when it gets sick. Then one day, she wakes up and the goldfish is dead. Why? She forgot to change its water. The story is a metaphor for the conditions that shape health. Place, politics, the environment, the economy, community networks - these are the "water" of our daily lives. When we neglect these conditions, then, like the goldfish, we will get sick, regardless of the medicine we can access or our personal choices about health. When we improve these conditions, when we keep our "water" clean, we create a world where we can be healthy throughout life, rather than a world of constant sickness mediated by expensive drugs and treatments. This is the world we should invest in creating, a world where we can "die healthy," rather than spend our money in a futile effort to live forever while ignoring the core drivers of health.

IN WHAT SEEMS TO STEM FROM ONE OF PROF. EDWARD DE BONO'S BOOKS, YOU EVEN ADVOCATE BUYING A/CS BY HOSPITALS FOR INSTALLATION IN POOR PEOPLE'S HOMES TO CURB ACUTE ASTHMA ATTACKS, AND SUBSEQUENT HOSPITAL ADMISSIONS, IN TROPICAL CLIMATES. CAN YOU EXPLAIN FURTHER IN VIEW OF THE CURRENT HEALTHCARE PAYMENT MODELS WHICH WE USE?

We need to address poor health at the level of causes, while remaining pragmatic about changes we can make to improve health quickly in the near-term, prioritizing the goal of prevention over treatment. Ideally, we would prevent disease among the economically disadvantaged by creating an economy where income inequality, and the poor health it generates, is no longer endemic. This is a long-term goal. In the meantime, if we can prevent disease through smaller adjustments, such as installing A/Cs, we should do so. We should constantly aim for the best, without ever making it the enemy of the good.

YOU HAVE BEEN NAMED ONE OF *TIME MAGAZINE*'S EPIDEMIOLOGY INNOVATORS IN 2006 AND THOMSON REUTERS LISTED YOU AS ONE OF THE 'WORLD'S MOST INFLUENTIAL SCIENTIFIC MINDS' FOR THE SOCIAL SCIENCES IN 2015. WHAT DRIVES YOU TO DO ALL THIS?

I am driven by what, I think, drives us all: a desire to build a healthier world for ourselves and for future generations. Each day I work with talented, committed young people who are driven by a desire to do right by the world. I also have children who constantly inspire me with their instinctive embrace of creating a fairer, more just world. We owe it to the rising generation to be no less committed than they are to building this world, where all can live healthy.

YOUR LATEST BOOK, *TEACHING PUBLIC HEALTH*, HAS BEEN PUBLISHED BY JOHNS HOPKINS UNIVERSITY PRESS IN AUGUST 2019. WHY SHOULD ONE READ IT?

I edited the book in partnership with Lisa Sullivan, Associate Dean for Education at the Boston University School of Public Health. Our aim was to address how public health education can respond to emerging trends in our field and create the best possible experience for students in the classroom and through curricula. The book features contributions from leading public health thinkers and teachers, and will, we hope, be useful to anyone interested in the future of public health.

WILL YOU RETURN TO YOUR ROOTS, MALTA?

My years in Malta were formative. They shaped who I am and much of how I see the world. I cannot imagine ever straying too far from their influence.

WHAT ADVICE WOULD YOU GIVE TO THE RECENTLY APPOINTED PRIME MINISTER, DR ROBERT ABELA?

I would advise him to stand for health. This means investing in creating structures that generate health, such as housing, education, public parks and places to exercise, and other factors that contribute to the "water" in which we live. Health is a public good sustained by collective investment, and politics is, at core, about how we allocate resources within a society. A leader who makes the resources necessary for health more accessible - particularly to people who have been historically marginalized or overlooked - is positioned to create truly transformative change.

HAVE YOU EVER READ THE SYNAPSE?

I confess I have never actually read it, but I look forward to doing so!

Augmentin® ES

600 mg/42.9 mg/5 ml

Amoxicillin/Clavulanate Potassium

Powder for oral suspension

- Provides extended antibacterial coverage to include the most penicillin-resistant strains.[1]
- Recommended by leading Guidelines as first line treatment in AOM.[2,3]
- Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis.[4]
- Indicated for children <40 kg and older than 3 months; dosed at 90/6.4 mg/kg/day in 2 divided doses.[4]

Spreading infectious energy!

Abridged Prescribing Information: *Please refer to the full Summary of Product Characteristics (SPC) before prescribing.* **TRADE NAMES:** Augmentin ES. **ACTIVE INGREDIENTS:** Amoxicillin (as trihydrate) and potassium clavulanate. **PHARMACEUTICAL FORM:** 600mg/42.9mg/5ml powder for oral suspension. **INDICATIONS:** Treatment of acute otitis media & community acquired pneumonia in children aged at least 3 months and less than 40kg body weight, caused or thought likely to be caused by penicillin-resistant *S.treptococcus pneumoniae.* **POSOLOGY:** 90/6.4mg/kg/day in 2 divided doses. Oral use. Administer with a meal. **CONTRAINDICATIONS:** Hypersensitivity to active substances/penicillins/excipients. History of: severe immediate hypersensitivity reaction to another beta-lactam agent, jaundice/hepatic impairment due to amoxicillin/clavulanic acid. **PRECAUTIONS:** Enquiry of previous hypersensitivity reactions to beta-lactams. Switch to an amoxicillin-only preparation (to be considered for infections proven due to amoxicillin susceptible organism). Convulsions may occur in patients receiving high doses or impaired renal function. Should be avoided if infectious mononucleosis is suspected. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Overgrowth of non-susceptible organisms with prolonged use. Occurrence of a feverish generalised erythema associated with pustula at treatment initiation may be symptom of AGEP (reaction requires discontinuation, contraindicates subsequent administration of amoxicillin). Caution in patients with hepatic impairment. Hepatic events may be associated with prolonged treatment. Antibiotic-associated colitis. Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Appropriate monitoring when anticoagulants are prescribed concomitantly. Creatinine clearance less than 30 ml/min (not recommended). Possibility of amoxicillin crystalluria. Potential of incorrect diagnostic test results during treatment *(refer to full SPC for details)*. Contains 2.72mg of aspartame (E951) per ml (source of phenylalanine). Contains maltodextrin (glucose). *Refer to the SPC for full details of precautions.* **PREGNANCY/ FERTILITY/LACTATION:** Pregnancy: Use should be avoided unless considered essential by the physician. Lactation: benefit/risk assessment to be considered. **UNDESIRABLE EFFECTS:** Common (≥1/100 to <1/10): mucocutaneous candidosis, diarrhoea, nausea, vomiting. Refer to the SPC for full list of undesirable effects. **LOCAL PRESENTATION:** 100ml glass bottle with plastic measuring spoon. **MARKETING AUTHORISATION NUMBER:** AA1051/00101. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline Bulgaria EOOD. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** November 2017. In order to ensure that this product information reects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131) *REPORTING ADVERSE EVENTS (AEs):* If you become aware of any AEs, medication errors and/ or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Ltd, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). Alternatively, any suspected AEs and medication errors can be reported via the Medicines Authority Adverse Drug Reactions reporting website: www.medicinesauthority.gov.mt/adrportal

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Prepared: June 2018 Job No: MLT_GIB/AES/0001/18

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DR STEPHEN MIFSUD

The EU Health Agenda

2019 - 2024

BACKGROUND

On 2 July 2019, Dr Ursula von der Leyen, who is a physician, was proposed by the European Council as the candidate for the office of President of the European Commission. She was elected by the European Parliament on 16 July. At the beginning of September 2019, President von der Leyen presented the political guidelines for the next European agenda 2019 – 2024, headed by the theme ***'A Union that strives for more, my agenda for Europe'***. Furthermore, on 10 September 2019, the President-elect of the European Commission sent mission letters to all Commissioner designates, in which the respective portfolios of the commissioners designate were elaborated. The one sent to the Commissioner-designate for Health Stella Kyriakides, together with the political guidelines provide a glimpse of the Health Agenda of the Commission for the period 2019 – 2024.

The von der Leyen Commission came in office on 1 December 2019, following a positive vote in the European Parliament on 27 November 2019.

The 2014 – 2019 Commission led by President Juncker was guided by the political guidelines[1] headed by the theme '***A New Start for Europe: My Agenda for Jobs, Growth, Fairness and Democratic Change'***. Throughout its mandate the Juncker Commission focused on the following ten priorities:

1. A New Boost for Jobs, Growth and Investment
2. A Connected Digital Single Market
3. A Resilient Energy Union with a Forward-Looking Climate Change Policy
4. A Deeper and Fairer Internal Market with a Strengthened Industrial Base
5. A Deeper and Fairer Economic and Monetary Union
6. A Balanced and Progressive Trade Policy to Harness Globalisation
7. An Area of Justice and Fundamental Rights Based on Mutual Trust
8. A New Policy on Migration
9. A Stronger Global Actor
10. A Union of Democratic Change

All Commission initiatives within this period which were also guided by the principle '***big on big things and small on small things'*** had to be framed within the above 10 points. As voiced in Eurobarometer surveys, health is a big thing for EU citizens; however, unfortunately health policy was sidelined during the Juncker Presidency. In the field of public health, the Commission only adopted one legal proposal for a regulation on Health Technology Assessment[2] and one Recommendation on vaccination.[3] The former relates to the advancement of Europe in the area of permanent cooperation on Health Technology Assessments. The latter addresses vaccine hesitancy, coordination on vaccine procurement, research and innovation, as well as EU cooperation on vaccine-preventable diseases. The recommendation was adopted by the Council in December 2018, whilst negotiations on the regulation on Health Technology Assessment are still ongoing within the Council of Ministers and within the European Parliament.

THE VON DER LEYEN COMMISSION

The Von der Leyen Commission will focus on the following six priorities:

1. A European Green Deal
2. An Economy that Works for People
3. A Europe Fit for the Digital Age
4. Protecting our European Way of Life
5. A Stronger Europe in the World
6. A New Push for European Democracy

The von der Leyen Commission is structured in hierarchical layers. A system of Executive Vice Presidents and Vice Presidents has been introduced. Consequently, the health Sector will fall under the Responsibility of the Executive Vice President Frans Timmermans who will coordinate the work on the *European Green Deal* and of

the Vice President Margaritis Schinas who has been tasked with *Protecting our European Way of Life*. The Executive Vice President Valdis Dombrovskis will lead the Commission's *An economy that works for people*, under which Europe's social pillar falls.

Digital health which was high on the EU agenda under the Juncker Commission, under the Connected Digital Single Market priority, will remain a priority under the van der Leyen Commission under the *Europe fit for the digital age* strategy. This work will be led by Executive Vice-President Margrethe Vestager. The Internal Market and Services Commissioner, Thierry Breton will also promote the Digital Single Market. Digital health is also given prominence in the mandate letter sent to the Health Commissioner Stella Kyriakides,

The health Commissioner's portfolio falls within the first and second priorities listed within the political guidelines, i.e. *European Green Deal* when it comes to the 'Farm to Fork Strategy' and *An Economy that Works for People* in which the implementation of the European Pillar of social rights is being prioritized.

The pillar of social rights[4] includes 20 points, which includes one on health, which is however very broad and practically encompasses the entire spectrum of health services. In fact principle 16 states that *'Everyone has the right to timely access to affordable, preventive and curative health care of good quality'*. It should be borne in mind that the delivery and management of healthcare services are exclusive Member State competences, thus direct EU action in this field is rather limited. Notwithstanding this, the EU may play a significant role as elaborated below.

The political guidelines for the next European agenda 2019 – 2024 make a specific reference to the adoption of a European plan to fight Cancer with the aim to support Member States in improving cancer control and care. This plan should propose actions to strengthen our approach at every key stage of the disease: prevention, diagnosis, treatment, life as a cancer survivor and palliative care. There should be a close link with the research mission on cancer in the future Horizon Europe programme. The Cancer plan will only be adopted in late 2020. On the 'World Cancer Day' that is 4 February 2020, Commissioner Kyriakides will announce the start of a comprehensive consultation process, with stakeholders.

These political guidelines for the next European agenda 2019 – 2024 are further supplemented by the mission letter which was sent to Stella Kyriakides. Through this letter, President designate von der Leyen has requested that the Commissioner Designate for health:

- Finds ways to help **ensure Europe has the supply of affordable medicines** to meet its needs. In doing so, she should **support the European pharmaceutical industry to ensure that it remains an innovator and world leader.**
- Implements effectively the new regulatory framework on **medical devices** to protect patients and ensure it addresses new and emerging challenges.
- Makes the most of the potential of **e-health** to provide high-quality healthcare and reduce inequalities.
- Works on **the creation of a European Health Data Space** to promote health-data exchange and support research on new preventive strategies, as well as on treatments, medicines, medical devices and outcomes, whilst ensuring that citizens have control over their own personal data.
- Focuses on the full implementation of the European One Health Action Plan against **Antimicrobial Resistance** and work with the EU's international partners to advocate for a global agreement on the use of **and access to antimicrobials.**
- Prioritizes communication on **vaccination**, explaining the benefits and combating the myths, misconceptions and scepticism that surround the issue.

The European Cancer Plan is also mentioned in the mission letter.

ACCESSIBILITY AND AFFORDABILITY MATTERS

Currently the EU is facing problems related to availability, accessibility and affordability of pharmaceuticals and medical devices. Affordability has been explicitly referred to within the mission letter, yet it should be recalled that both affordability and accessibility are linked to the pricing and reimbursement policies of the respective Member State which is of the Member State competence. In fact, article 168(7) of the Treaty of the European Union explicitly states that "Union action shall respect the responsibilities of the Member States for the definition of their health policy and for the organisation and delivery of health services and medical care. The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them." Any EU action in this regard would have to maneuver within the limits of its competence. Having said that, the pharmaceutical market must comply with EU internal market provisions and with EU competition rules amongst others. The placing on the market of pharmaceuticals and medical devices is regulated at EU level. Consequently, EU legislation sets the requirements the industry must comply with to place

and retain products on the EU market. However, there is no obligation of the industry to place products on each Member State market, nor to maintain the products in the respective markets of the Member States. These decisions are taken by the industry and are usually market-driven.

It should be recalled that the EU grants various incentives to pharmaceutical companies. These range from financial incentives at research and development stage to supplementary protection certificates and market exclusivity once a product has been placed on the market. The EU therefore has leverage on the industry and may impose conditions linking these incentives to access at an affordable price.

During the last few years Member States have also grouped together in different regional groups to tackle these common challenges related to access and affordability together. The Valletta Declaration, BENELUXA and the Visigrad groups are the main groups.

Shortages and the excessive pricing of innovative medicines were also on the agenda of the Employment, Social Policy, Health and Consumer Protection Council held on 9 December 2019. Many Member States shared the view that structural cooperation and coordination on pharmaceutical policy at an EU-level is essential to tackle current and future challenges within the pharmaceutical system. In this regard a large group of Member States, in particular those forming part of the Valletta Declaration and BENELUXA, invited the Council to prepare a draft EU working agenda 2020-2024 on pharmaceutical policy, addressing key priorities and concerns, in cooperation with the Commission. The proposed agenda should include priorities, actions, timetables, responsible parties and desired outcomes, while respecting the existing division of competences between the national and EU-level.

There are various reasons for shortages. These include manufacturing problems such as global shortages of an active pharmaceutical ingredient, increasing demand for the specific product, quality problems, uncontrolled market withdrawals, the increasing concentration outside Europe of the manufacturing and logistics chains (with their associated vulnerability, in particular of older medicines) and the fragmentation caused by subcontracting chains. Consequently, there is no one single solution to address these shortages and a multifaceted approach is required. The Commission is in the preparatory phase to propose legislation to incentivize the development of medicinal products which are not financially attractive to develop and to manufacture. This proposal will probably include within the scope the development of antimicrobials, vaccines and also cheap essential drugs of which many EU Member States are facing shortages.

A European Health Data Space was also mentioned in the mission letter of the Health Commissioner. This could speed up the current work on the cross-border exchange of health data and could draw inspiration from the eHealth Digital Service Infrastructure. This includes e-prescriptions and patient summaries, the clinical consultations on rare disease patients under the European Reference Networks, and the emerging collaboration on putting together more than 1 million sequenced genomes, as well as other research infrastructures which showcase benefits of health-data sharing. The European Health Data Space could be backed up by European and national legislation or other instruments that implement the data protection rules, data security and related ethical principles, in particular on the secondary use of health and social data.

On another note, on 11 October 2019, the Commission published its Evaluation of the Union legislation on blood, tissues and cells.[5] The evaluation concluded that many of the EU requirements within the legislation in force no longer reflect the best practice and guidance issued by authoritative expert bodies in the field, including the Council of Europe or the European Centre for Disease Prevention and Control. Amongst others, the report concluded that the current framework is inefficient, when it comes to technical updates and that that there is a lack of a robust oversight of the blood tissues and cells sectors. The report also concluded that there are shortcomings related to vigilance, inspections and authorizations and insufficient measures in place to protect blood tissue and cells donors. In response to this report it is highly likely that the Commission adopts legislative proposals to amend the current legislative framework, in order to address the deficiencies highlighted within the report.

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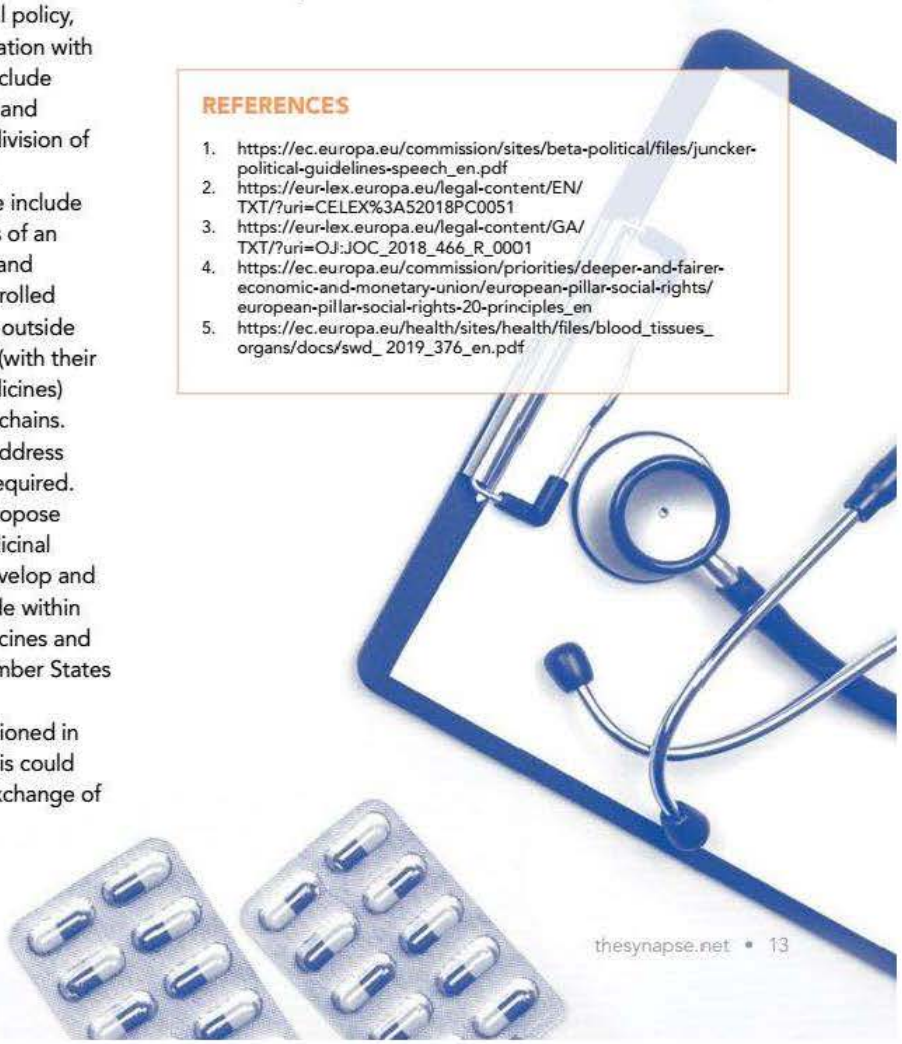

Saint James Hospital Group
teams up with TheSynapse

JEAN CLAUDE MUSCAT • CEO – CENTRAL SERVICES SAINT JAMES HOSPITAL GROUP

I have known Dr Wilfred Galea since when, at the young age of nineteen I used to meet doctors in order to promote the services being offered by Saint James in Zabbar. This was the early nineties.

Over the last thirty years, what was acceptable practice in terms of healthcare standards is unthinkable now, let alone acceptable. The public hospital moved to a new modern facility, the number of consultants working in the private sector has mushroomed and today patients have a far broader choice of specialists to choose from as compared to those days. Access to training and development has also improved significantly ensuring that the quality of our medical professionals remains very high and local healthcare standards are now at par, or even better, than some of our European counterparts.

The healthcare scene has gone through a revolutionary process indeed, and of which we, as Saint James Hospital Group, form an integral part. Saint James Hospital developed from a converted house in Żabbar into becoming Malta's leading private healthcare provider with two first class hospitals, one in Sliema and the recently opened one in Tal-Barrani, Limits of Żejtun, the latter replacing the Żabbar hospital. The Saint James Hospital Group also encompasses a specialised ophthalmic centre of excellence in Birkirkara, the operation of a leading private laboratory, an import and medical distribution company, and an out-patient clinic in Burmarrad.

In 2005, the Saint James Hospital Group also took the ambitious decision to explore the international markets, namely Libya and Hungary. We were successful in setting up healthcare facilities in both Tripoli and Budapest, both of which are still active although unfortunately the Libya operation suffers the consequences of political instability in the region.

This development was an evolving process during which we encountered numerous challenges of every sort, then and now, as is common with any other business I suppose. In our desire to develop and improve, we faced financial, recruitment, innovation, management and clinical challenges. Some complex, others less so. Today's ever-changing business realities require us to be able to react in a timely manner in order to always be ahead in the clinical field as the world of medicine continues to evolve and technology paves the way to new and exciting horizons.

This all comes at a cost, and prices for services in private hospitals have increased significantly over the years as a direct consequence of this. This is where private medical insurances also play a pivotal role. This sector also evolved from having one predominant player to a wide range of insurance providers offering various products and services to their clients nowadays. It is to my view that this service should be

better supported by Government in the form of, for example, tax rebates in order to encourage more demand, directly resulting in lessened pressures on the national health system, fewer waiting lists and an improved service for those who truly cannot afford private healthcare. Naturally, even more challenging is the fact that private hospital operators continue to operate against a completely free government service that seems to defy financial logic. It remains to be seen whether such unique and recurrent expenditures will be sustainable in the long run.

Going back to the private healthcare sector, we feel the need to set up channels through which private family doctors have more accessibility to the Saint James Hospital services such that referrals and feedback on patients referred is received in a complete and timely manner allowing the referring doctors to safely manage the follow up and care of their patients.

Dr Galea remains one of those medical practitioners who has been relentless in pursuing his dream to provide added value to the medical profession. I have followed the development of TheSynapse internet portal and magazine from conceptual stage to implementation. Their quality and the value of the contribution from the respective members is unique and guarantees their excellent standard.

Dr Galea and TheSynapse team are now taking this to the next level by introducing an e-learning site, CME30.eu, which is a unique and fantastic tool for doctors to have access to Continuing Medical Education and earn CME points. Medical education is an area which is very close to our Group values and is one of the pillars in which we continue to invest in and promote further. We are therefore very happy to announce that as part of this ongoing interest, Saint James Hospital Group has partnered with TheSynapse and CME30.eu in order to support ongoing medical education for the medical profession.

We believe that together we can achieve more, and this key partnership will be duly beneficial for all parties involved, particularly the medical profession itself in making continued medical education more accessible to one and all.

Helping people with MDD* rediscover the love for life

Treatment with Bupropion led to greater improvement in fatigue scores (p<0.01) in Bupropion remitters (-1.56) as compared to SSRI* remitters (-1.43) in MDD patients at study end point. This improvement was evident from week 4.[1]

Wellbutrin XR should not be used together with other Bupropion containing medicinal products.[2]
Wellbutrin XR tablets should be swallowed whole and not crushed or chewed.[2]

WELLBUTRIN XR ABRIDGED PRESCRIBING INFORMATION
Please refer to full Summary of Product Characteristics (SmPC) before prescribing
TRADE NAME: Wellbutrin XR modified release tablets. **ACTIVE INGREDIENT:** Bupropion Hydrochloride, 150mg/300mg. **PHARMACEUTICAL FORM:** Modified release tablet. **INDICATIONS:** Treatment of major depressive episodes. POSOLOGY: Should be swallowed whole with or without food. Tablets should not be cut, crushed or chewed as this may lead to increased risk of adverse effects including seizures. *Adults:* Recommended starting dose is 150 mg, once daily. If no improvement is seen after 4 weeks, dose may be increased to 300 mg, once daily. There should be interval of at least 24 hours between successive doses. Patients should be treated for a sufficient period of at least 6 months. Full antidepressant effect may not be evident until after several weeks of treatment. Insomnia may be reduced by avoiding dosing at bed time. *Children and Adolescents (less than 18 years of age):* not indicated. *Discontinuing therapy:* a tapering off period may be considered. *Refer to full SPC for full Posology details.* **CONTRAINDICATIONS:** Hypersensitivity to Bupropion or any of the excipients; co-administration with other medicinal products containing Bupropion (incidence of seizures is dose-dependent); current seizure disorder or history of seizures; known CNS tumour; patients undergoing withdrawal from alcohol or any medicinal product known to be associated with risk of seizures on withdrawal; severe hepatic cirrhosis; current or previous diagnosis of bulimia or anorexia nervosa; concomitant use with MAOI's. **PRECAUTIONS:** *Seizures:* Recommended dose should not be exceeded; Caution in patients with predisposing risk factors for seizures such as concomitant administration of medicinal products known to lower the seizure threshold (e.g. antipsychotics, antidepressants, antimalarials, tramadol, theophylline, systemic steroids, quinolones, sedating antihistamines), alcohol abuse, history of head trauma, diabetes treated with hypoglycaemics or insulin, use of stimulants or anorectic products; should be discontinued in patients who experience a seizure during treatment; *Interactions:* Bupropion inhibits metabolism by cytochrome P450 2D6; Caution is advised when medicinal products metabolised by P450 2D6 are administered concurrently; Use of Wellbutrin XR, which is an inhibitor of CYP2D6, should whenever possible be avoided during tamoxifen treatment; *Neuropsychiatry: Suicide/suicidal thoughts or clinical worsening:* Careful monitoring should be carried out during first weeks of treatment, during dose changes and in patients who have history of suicide-related events prior to treatment; close supervision should accompany drug therapy in particular those at high risk especially in early treatment and following dose changes; Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medicinal product, in patients who experience the emergence of suicidal ideation/behaviour, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms; increased risk of suicidal behaviour with antidepressants in patients less than 25 years old compared to placebo. *Neuropsychiatric symptoms including mania and bipolar disorder:* Neuropsychiatric symptoms have been reported. In particular, psychotic and manic symptomatology has been observed, mainly in patients with a known history of psychiatric illness. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. Caution in patients receiving ECT therapy concomitantly. *Hypersensitivity:* should be discontinued promptly if patients experience hypersensitivity reactions during treatment; *Cardiovascular Disease:* caution in patients with cardiovascular disease due to limited clinical experience. Bupropion was generally well tolerated in studies for smoking cessation in patients with ischaemic cardiovascular disease. Monitor blood pressure especially in patients with pre-existing hypertension; consider discontinuation if a clinically significant increase in blood pressure is observed; Concomitant use with a nicotine transdermal system may result in elevations of blood pressure. *Other:* Treatment with antidepressants is associated with increased risk of suicidal thinking and behaviour in children & adolescents with major depressive disorder and other psychiatric disorders. Use with caution in patients with mild to moderate hepatic impairment. Patients with renal impairment should be closely monitored. Older people: Greater sensitivity in some older individuals cannot be ruled out. Bupropion interferes with the assay used in some rapid urine drug screens which can result in false positive readings. WELLBUTRIN XR is intended for oral use only. **PREGNANCY/FERTILITY/LACTATION:** *Pregnancy:* should not be used during pregnancy unless clinical condition requires treatment with bupropion and alternative treatments are not an option. *Lactation:* Bupropion and its metabolites are excreted in human breast milk. Fertility: no data on effect on human fertility. **UNDESIRABLE EFFECTS:** *Very Common* (≥1/10): Insomnia; headache; dry mouth; gastrointestinal disturbance including nausea and vomiting; *Common* (≥1/100, <1/10): Hypersensitivity reactions such as urticaria; anorexia; agitation, anxiety; tremor, dizziness, taste disorders; visual disturbance; tinnitus; increased blood pressure (sometimes severe), flushing; abdominal pain, constipation; rash, pruritus, sweating; fever, chest pain and asthenia. *Refer to the SPC for a full list of undesirable effects.* **LOCAL PRESENTATIONS:** 150mg (x30 tablets); 300mg (x30 tablets). **MARKETING AUTHORISATION NUMBER:** MA192/02301-2. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline (Ireland) Limited. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** January 2019.

For the latest product information, please refer to the full SPC available from: gskpro.com/en-mt/products or contact us at GSK Malta (phone: +35621238131).

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Job No: PM-MT-BPR-ADVR-190002
Prepared: April 2019

References:

* **MDD:** Major Depressive Disorder; **SSRI:** Selective Serotonin Reuptake Inhibitor; Post-hoc analysis of subjects with remitted MDD on data pooled from six double blind, randomized trials comparing ≤ 300mg/day bupropion (n=169) with SSRIs (Sertraline, Paroxetine or Escitalopram) (n=324).
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Wellbutrin® bupropion hydrochloride XR
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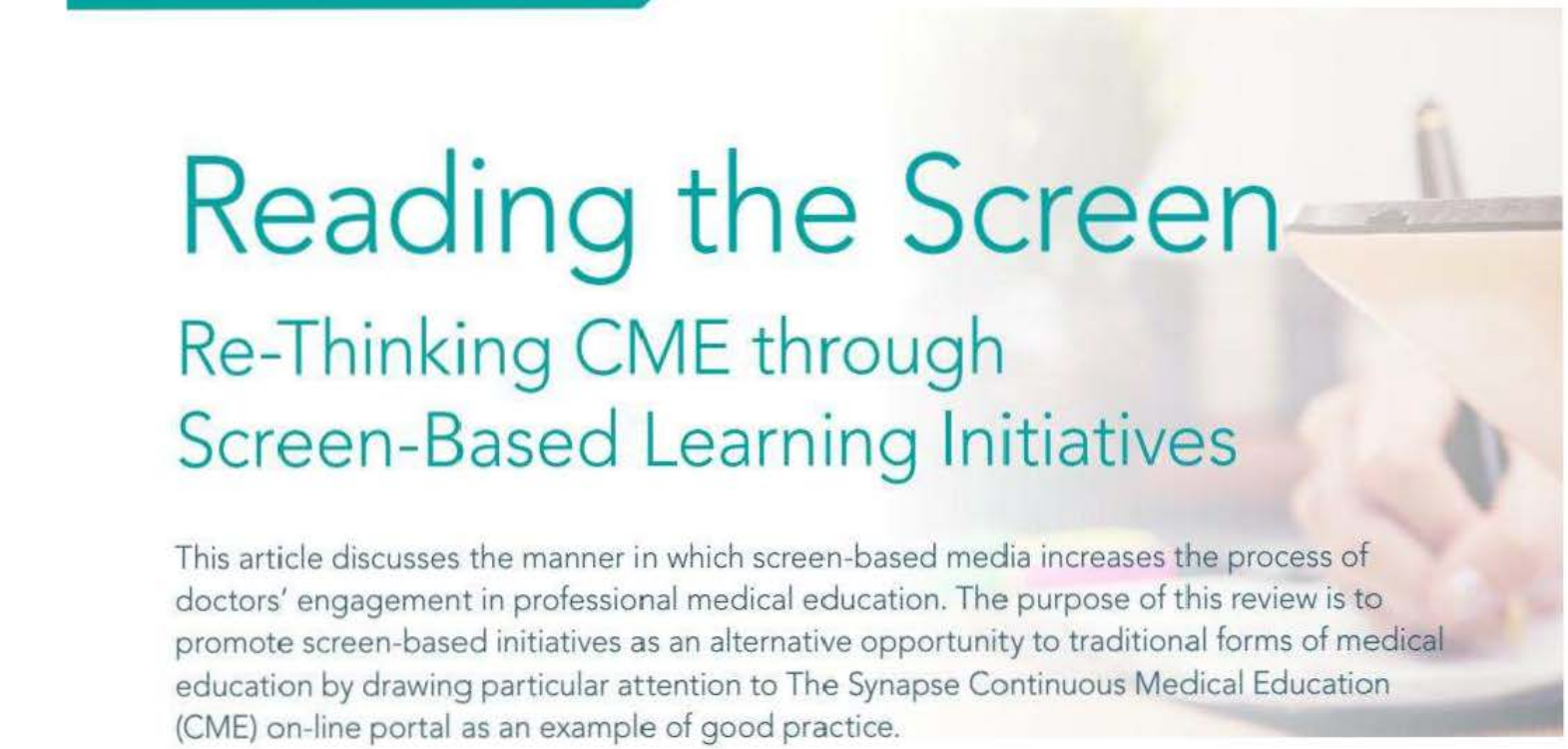
IAN ATTARD

Reading the Screen

Re-Thinking CME through Screen-Based Learning Initiatives



This article discusses the manner in which screen-based media increases the process of doctors' engagement in professional medical education. The purpose of this review is to promote screen-based initiatives as an alternative opportunity to traditional forms of medical education by drawing particular attention to The Synapse Continuous Medical Education (CME) on-line portal as an example of good practice.

1. INTRODUCTION

To date a lot of resources have been invested in order to help people become better achievers in education. Generally, learning initiatives focus on developing strategies on how people can achieve higher grades in education notwithstanding the internal and external challenges that people face in order to learn. Initiatives include strategies that focus on improving classroom participation, individual attention, and new methods to help people improve learning performance.

This review is written from the perspective of a media practitioner-lecturer, also a Doctorate student in education, who in the past years introduced various media-based initiatives to facilitate learning of Higher Education (HE) students during their studies.

2. WHY CME?

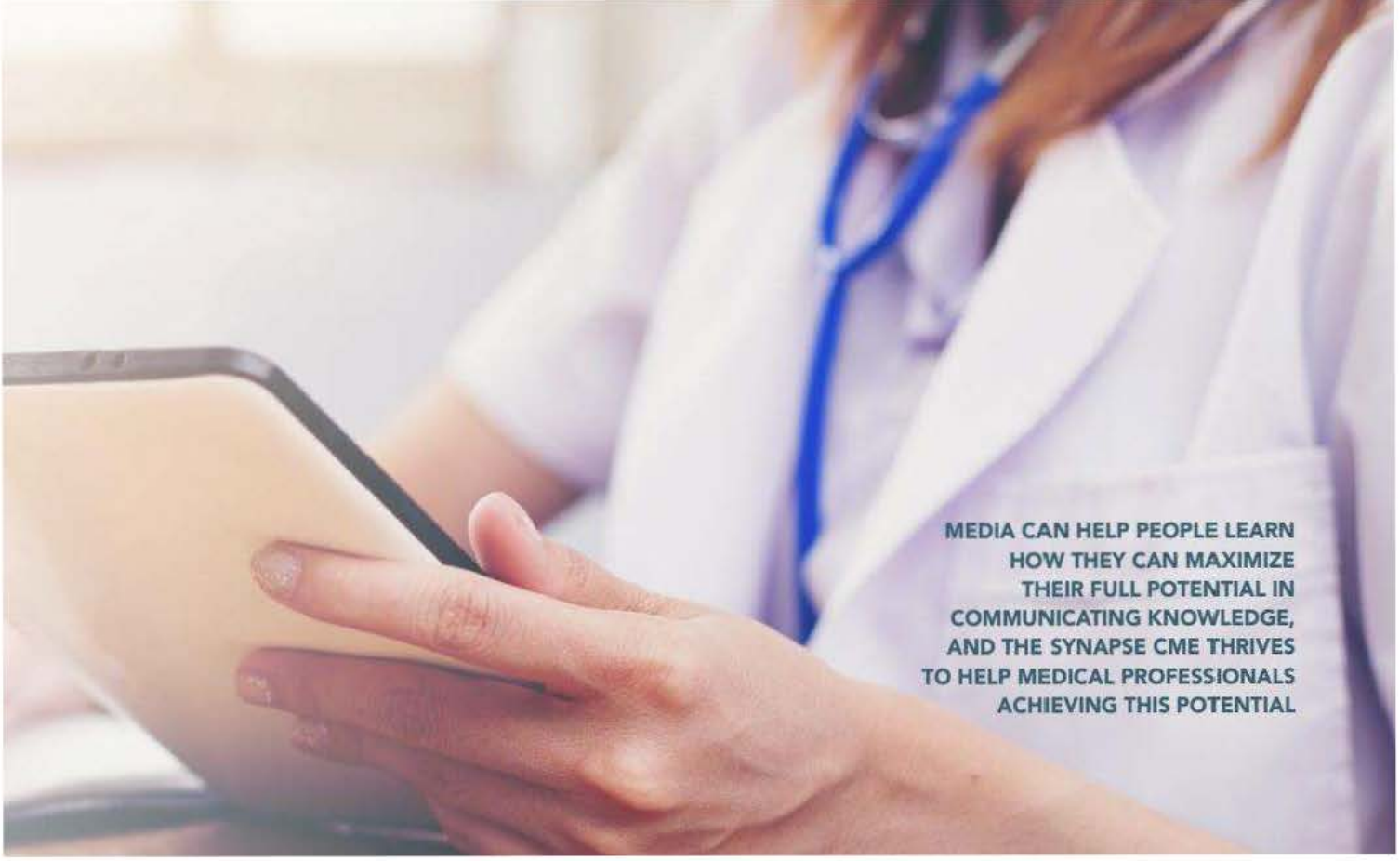
The busy lifestyles of medical professionals continuously shape the ways CME is evolving in its modes of delivery. In the US, the Accreditation Council of Continuous Medical Education (ACCME) reports that CME is critical in the lives of medical and health care professionals.[1] Since ACCME's last report in 2018 there has been a steep growth in demand for new and alternative CME initiatives, with almost 180,000 accredited activities for medical and health care professionals around the world seeking to keep updated in latest medical developments. This echoes also in Europe with most of the European countries believing that CME should be mandatory for medical professionals.[2]

This report draws attention to The Synapse CME as a smart and a flexible form of CME initiative for all medical professionals who are seeking to keep up-to-date with the latest medical developments. The article focuses primarily on how The Synapse CME breaks away from traditional learning approaches providing countless alternative learning spaces for the busy health care professionals using latest screen-based technologies.

2.A. ALTERNATIVE LEARNING SPACES

Many mainstream education systems around the world encourage people to experience education through one-size fits all learning processes. For example, in Malta exams can be considered as a dominant form of evaluating education achievement in which the 'daily' learning processes directly tie into the examination requirements and not the personal. Many projects have been developed aiming to help people become better achievers in education. However, the majority of such projects focus on how people can achieve higher grades in education.

Conversely, an educational reform in Finland has thought us that educational processes that encourage people to identify with phenomenological cases can be very effective. According to Irmeli Hallinen, the now retired lead of curriculum development in Finland, teaching should not stop at teaching subjects in isolation and training students in recalling information, but should aim to push for transversal skills and to provide value in education by involving people in phenomenological cases to motivate



MEDIA CAN HELP PEOPLE LEARN HOW THEY CAN MAXIMIZE THEIR FULL POTENTIAL IN COMMUNICATING KNOWLEDGE, AND THE SYNAPSE CME THRIVES TO HELP MEDICAL PROFESSIONALS ACHIEVING THIS POTENTIAL

learning based on real-life professional contexts. Hallinen states that the ability to secure knowledge in isolated specific subjects is not enough in today's society and she asserts that nowadays people must be able to apply their skills and knowledge to a multitude of real-life contexts.

The Synapse follows such an approach and provides screen-based professional medical courses to people through contemporary real-life medical cases. This approach can be considered as an alternative educational method purposely designed to help people value professional medical education based on their own individual professional identities, experiences and motivations. The Synapse creates motivating learning experiences for medical professionals with a view to communicate knowledge using screen-based media as a catalyst of transversal competences. The literacy consultant Debbie Miller states that learning by 'case' should be defined by the principles of action and practice that are accessible within the world that a person is familiar with so as to maximise learning opportunities. Miller asks '... is thinking valued and made visible? Is there student input? How will I know they understand?'[3] Learning by 'case' can be considered as a stepping-stone towards making medical education more effective using 'tailor-made' screen-based methods of education suitable for today's busy life-styles of health care professionals Moreover, in establishing unique creative methods to engage people in CME, one needs to consider the relationship between screen-based media and education.

2.B. SCREEN-BASED LEARNING

The implications of using screen-based media as a learning tool should be analysed through its potential to facilitate learning by encouraging reading, writing, interpretation and induction of knowledge dialogue between peers. Professor Sarah Pink, an international interdisciplinary scholar in visual methodologies, argues that media can be considered not solely as a means of communication but also as means to help democratizing and maximising learning potentials for various situations. Media can help people learn how they can maximize their full potential in communicating knowledge,[4] and the Synapse CME thrives to help medical professionals achieving this potential.

However, it also is very important to identify how The Synapse assists medical professionals value their educational experiences. In this respect one should understand that changes are continuously taking place in the medical field worldwide. Creativity is one of these changes. It is a tool that impacts the educational world at large. For Sir Ken Robinson, Professor Emeritus at the University of Warwick, creativity is a key factor to engage people with mixed learning priorities to learn and to make this world more dynamic. He states that the "... world is suffering from a crisis of human resources."[5] If creativity is key to improve education and human resources, how can we make sure we formulate a sustainable professional education route that combats such a crisis? Robinson stresses the importance of how education should empower people to understand the world around them, by making more effective use of the world they exist in. This type of

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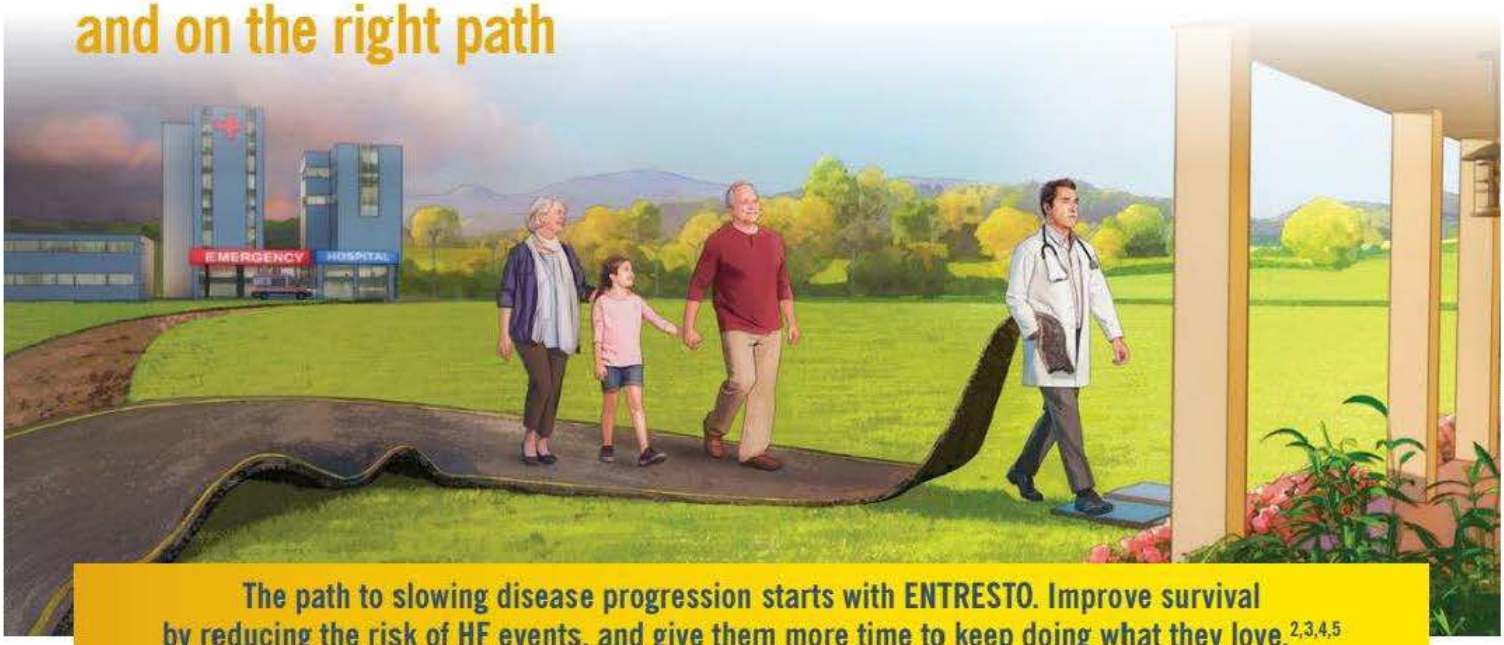

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- The target dose is 97/103 mg twice daily[1]
- Stop using an ACE inhibitor for 1.5 days (36 hours) before starting ENTRESTO[1]

ENTRESTO is available in 3 dosage strengths[1]

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Before your NYHA Class II patients with HFrEF leave your office, take action with ENTRESTO—and keep them on the right path.

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. 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 pregnancy. 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. Entresto must not be initiated until 36 hours after taking the last dose of ACE inhibitor therapy. If treatment with Entresto is stopped, ACE inhibitor therapy must not be initiated until 36 hours after the last dose of Entresto. Combination of Entresto with direct renin inhibitors such as aliskiren is not recommended. Entresto should not be co administered with another ARB containing 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 Entresto 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 Entresto. If hypotension occurs, temporary down-titration or discontinuation of Entresto 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 Entresto is not recommended. Use of Entresto 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. Entresto is not recommended in patients with end-stage renal disease. Hyperkalaemia: Entresto 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 of Entresto. If serum potassium level is >5.4 mmol/l discontinuation should be considered. Angioedema: Angioedema has been reported with Entresto. If angioedema occurs, discontinue Entresto immediately and provide appropriate therapy and monitoring until complete and sustained resolution of signs and symptoms has occurred. Entresto 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 IV: 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 Entresto because it is a neprilysin substrate. 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 co-administered with another ARB. Use with caution when co-administering Entresto with statins or PDE5 inhibitors. No clinically relevant drug-drug interaction was observed when simvastatin and Entresto were co-administered. Monitoring serum potassium is recommended if Entresto 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 Entresto who are taking NSAIDs concomitantly. Interactions between Entresto and lithium have not been investigated. Therefore, this combination is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended. Co-administration of Entresto and furosemide reduced Cmax and AUC of furosemide by 50% and 28%, respectively, with reduced urinary excretion of sodium. Co-administration of nitroglycerin and Entresto was associated with a treatment difference of 5 bpm in heart rate compared to the administration of nitroglycerin alone, no dose adjustment is required. Co administration of Entresto 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 Entresto with metformin reduced both Cmax and AUC of metformin by 23%. When initiating therapy with Entresto in patients receiving metformin, the clinical status of the patient should be evaluated. Fertility, pregnancy and lactation: The use of Entresto 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 Entresto 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 Entresto 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. 2018-MT-ENT-30-APR-2018

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educational empowerment is at the core of The Synapse modus operandi in which empowerment of learning is achieved by embracing more effectively the medical professionals' own experiential resources such as memory, talent and emotion. Quoting Robinson, this leads to "... fulfilled individuals and active, compassionate citizens."[5]

CME also has a very important role in helping professionals thrive in their own sustainable future. In order to achieve sustainability, it is important to promote educational endeavors with creativity at their core. This should be done by first examining current educational parameters, and secondly search for creative solutions that can facilitate life-long learning for the benefit of, not only the present, but also for the longer term in a professional's life experience.

Sarah Pink states that the screen has potential to engage people with '... a reflexive and experiential process through which understanding, knowing and academic knowledge are produced... Exploration of and reflection on new routes to knowledge.'[4] In keeping with this, can screen-based CME qualify as a 'new route' of knowledge with same 'parity of esteem' as other traditional learning routes? For Pink this is possible, '... innovative methods have been developed to provide routes into understanding other people's lives, experiences, values, social worlds and more to go beyond the classic observation approach.'[4]

In fact The Synapse works in tandem with participatory methods, and it periodically organizes think-tanks on professional medical education and training. Initial thoughts about such learning initiatives might sound as structure-less and without a determined bearing as Pasi Sahlberg, a Finnish school reform and educational practices expert, critically argues. Sahlberg poses a question whether non-written work should be considered as academic, and of a high standard. His view is that although public opinion is a necessity in one's academic work, it needs to be rigorously structured and to follow a 'critical pathology'. Thus, if peoples' works need to be taken seriously by the public, works need to follow such a pathology.

'Critical pathology' in education raises a discussion about which type of direction fits best learning and assessment methods that clearly speak out 'good professional education practice'. However, should 'critical pathology' just reduce to the distinguishing factors between creative methodologies and academic principles? In order to arrive to such conclusions on education standards, I argue that it is imperative to put the medical professional at the centre of what defines 'good education', keeping in mind the social and 'political' factors that impact directly a person's ability to show acquired learning.

In response to the above observations, the medical professional learning cases adopted in The Synapse CME set out to stimulate various educational objectives. One of the main aims is to enable medical professionals to re-create 'knowledge' through contemporary 'real-life cases' using a digital screen-based medium. The Synapse

CME focuses on professional medical education as a 'case' that briefs the users about the learning outcomes that are expected to be achieved in a given syllabus and to give directions on how they can be achieved through the interventions of screen-based initiatives. In this type of learning environment professionals are encouraged to explore and identify with professional medical education through their own medical experiences.

3. CONCLUSIONS

In this article I argued that The Synapse CME is a screen-based educational initiative that provides medical professionals with a platform to explore new ways of how to express knowledge by acquiring transversal competences that are relevant today. It has been identified how The Synapse builds on theoretical resources and academic discussions, and provides an alternative learning framework for medical professionals in various fields.

The above review of topics that emanate from this article informs the professional reader on how The Synapse CME thrives to be a responsive-type of learning initiative that can be considered as an 'equally' effective, alternative and an attractive professional medical education platform. This augurs well that The Synapse will further design, develop and invest in its learning strategies that are fit for the contemporary medical professional to instill added value in professional medical educational achievement.

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enough already.

It's time to prevent migraine with Aimovig®.

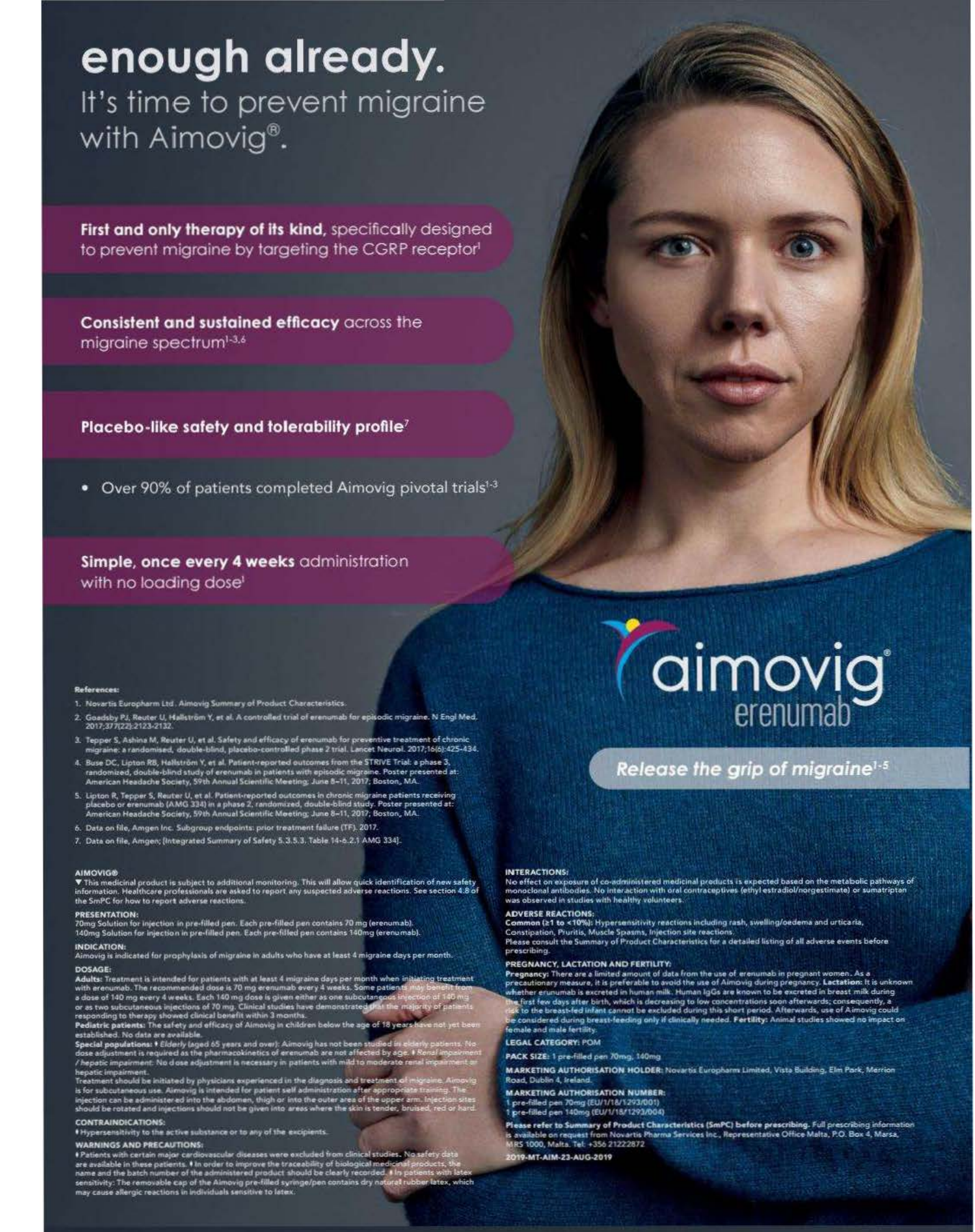
First and only therapy of its kind, specifically designed to prevent migraine by targeting the CGRP receptor[1]

Consistent and sustained efficacy across the migraine spectrum[1-3,6]

Placebo-like safety and tolerability profile[7]

- Over 90% of patients completed Aimovig pivotal trials[1-3]

Simple, once every 4 weeks administration with no loading dose[1]



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Release the grip of migraine[1-5]

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AIMOVIG®
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

PRESENTATION:
70mg Solution for injection in pre-filled pen. Each pre-filled pen contains 70 mg (erenumab).
140mg Solution for injection in pre-filled pen. Each pre-filled pen contains 140mg (erenumab).

INDICATION:
Aimovig is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month.

DOSAGE:
Adults: Treatment is intended for patients with at least 4 migraine days per month when initiating treatment with erenumab. The recommended dose is 70 mg erenumab every 4 weeks. Some patients may benefit from a dose of 140 mg every 4 weeks. Each 140 mg dose is given either as one subcutaneous injection of 140 mg or as two subcutaneous injections of 70 mg. Clinical studies have demonstrated that the majority of patients responding to therapy showed clinical benefit within 3 months.
Pediatric patients: The safety and efficacy of Aimovig in children below the age of 18 years have not yet been established. No data are available.
Special populations: ♦ *Elderly* (aged 65 years and over): Aimovig has not been studied in elderly patients. No dose adjustment is required as the pharmacokinetics of erenumab are not affected by age. ♦ *Renal impairment / hepatic impairment:* No dose adjustment is necessary in patients with mild to moderate renal impairment or hepatic impairment.
Treatment should be initiated by physicians experienced in the diagnosis and treatment of migraine. Aimovig is for subcutaneous use. Aimovig is intended for patient self administration after appropriate training. The injection can be administered into the abdomen, thigh or into the outer area of the upper arm. Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard.

CONTRAINDICATIONS:
♦ Hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS:
♦ Patients with certain major cardiovascular diseases were excluded from clinical studies. No safety data are available in these patients. ♦ In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. ♦ In patients with latex sensitivity: The removable cap of the Aimovig pre-filled syringe/pen contains dry natural rubber latex, which may cause allergic reactions in individuals sensitive to latex.

INTERACTIONS:
No effect on exposure of co-administered medicinal products is expected based on the metabolic pathways of monoclonal antibodies. No interaction with oral contraceptives (ethyl estradiol/norgestimate) or sumatriptan was observed in studies with healthy volunteers.

ADVERSE REACTIONS:
Common (≥1 to <10%): Hypersensitivity reactions including rash, swelling/oedema and urticaria, Constipation, Pruritis, Muscle Spasms, Injection site reactions.
Please consult the Summary of Product Characteristics for a detailed listing of all adverse events before prescribing.

PREGNANCY, LACTATION AND FERTILITY:
Pregnancy: There are a limited amount of data from the use of erenumab in pregnant women. As a precautionary measure, it is preferable to avoid the use of Aimovig during pregnancy. **Lactation:** It is unknown whether erunumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. Afterwards, use of Aimovig could be considered during breast-feeding only if clinically needed. **Fertility:** Animal studies showed no impact on female and male fertility.

LEGAL CATEGORY: POM

PACK SIZE: 1 pre-filled pen 70mg, 140mg

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

MARKETING AUTHORISATION NUMBER:
1 pre-filled pen 70mg (EU/1/18/1293/001)
1 pre-filled pen 140mg (EU/1/18/1293/004)

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

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DR LAURA GRECH AND PROF. JOSEPH BORG

Sickle Cell Disease

INTRODUCTION

Sickle cell disease (SCD) is the most common monogenic disorder and its prevalence is high throughout large areas in sub-Saharan Africa, the Mediterranean basin, the Middle East and India because of the remarkable level of protection that the sickle cell trait provides against malaria.[1] This stems from a selection pressure, in fact high frequencies of the variant gene correspond to areas of high malarial transmission. It is estimated that approximately 300,000 babies per year are born with sickle cell anaemia.[2]

SCD is an inherited haemoglobinopathy caused by a single amino acid substitution at the sixth residue of the beta (β)-globin subunit (p.Glu6Val) resulting in the production of the characteristic haemoglobin S (HbS).[3,4] Under deoxygenation conditions (when Hb is not bound to oxygen), the haemoglobin tetramers, that include the two-mutant sickle β-globin subunits (HbS), can polymerize causing the erythrocyte to undertake a crescent or sickle cell shape (figure 1). These sickle cell shaped RBCs are rigid and dysfunctional, and also play a central role in acute and chronic clinical manifestations of SCD.

Figure 1: Demonstration of how sickle shaped RBCs give rise to vaso-occlusion events.[5]

The increased adhesiveness of the sickle cells causes microvascular obstructions in capillaries giving rise to blockage of blood flow with ischaemic/reperfusion injury.[6]

INHERITANCE OF SCD

SCD is inherited as an autosomal codominant trait[4]. The most clinically relevant genotype is when the HbS mutation is inherited in homozygous fashion, that is when an individual inherits both the HbS alleles. This is also known as homozygous haemoglobin SS disease (HbSS). The HbS mutation can also be inherited in heterozygous form with other mutations. The most common double heterozygous mutation is an S mutation coupled with a thalassaemia or with haemoglobin C (HbC).[7] These forms have the same characteristic clinical feature as HbSS but severity can vary, in fact when inherited with HbC the severity is milder than when inherited with thalassaemia. The phenotypic variability can also be due to an increase in foetal haemoglobin (HbF) levels. Subjects suffering from SCD with high HbF show a milder phenotype. On the other hand, if a person is heterozygous for the HbS allele the individual is said to be suffering from sickle cell trait (HbAS) and it is generally clinically benign.[8]

PATHOPHYSIOLOGY OF HOMOZYGOUS SCD

SCD is a multisystem disorder that affects nearly every organ in the body as shown in figure 2. Vaso-occlusion, haemolytic anaemia and vasculopathy are the hallmark of SCD while hypercoagulability and inflammation are also involved in organ damage.

In SCD the essential pathophysiological occurrence is the HbS polymerization which gives rise to:

i. **Changes in Erythrocyte morphology** – When compared to HbA (normal haemoglobin) the HbS has reduced oxygen affinity which aggravates HbS polymerization.[9] HbS polymerization correlates exponentially with the concentration of HbS within the erythrocyte. As the polymer fibres extend, the

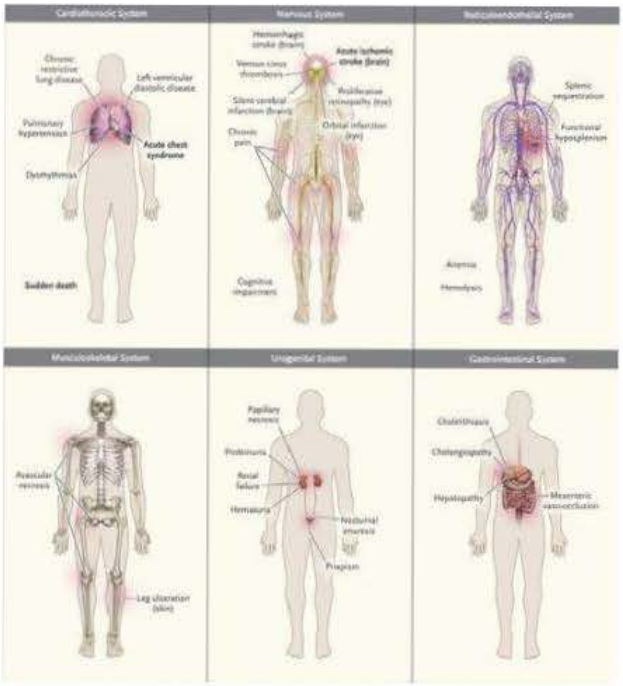

Figure 2: Common Clinical Complications of SCD.[1]

erythrocytes are deformed and this interferes with their flexibility and flow properties giving rise to vaso-occlusion.[10]

ii. **Altered erythrocyte membrane –** HbS polymerization directly or indirectly alters the typical lipid bilayer and proteins of the erythrocyte membrane. This leads to early erythrocyte apoptosis due to reduced cellular hydration, increased haemolysis and abnormal interactions with other blood cells.[11]

iii. **Haemolysis –** Sickle erythrocytes are highly unstable with a lifespan that is reduced by >75%. Principally, haemolysis occurs via extravascular phagocytosis by macrophages, but about one-third occurs through intravascular haemolysis.[12]

iv. **Oxidative stress –** Haemolysis gives rise to oxidative stress which enhance HbS auto-oxidation contributing to the damage of the cell membrane, premature erythrocyte ageing and haemolysis.[13]

v. **Free plasma Hb and haem –** Extracellular haemoglobin and haem in plasma promotes oxidative stress of blood vessels and blood cells. Superoxide is produced by the continuous auto-oxidation of extracellular haemoglobin. The superoxide dismutases into hydrogen peroxide which promotes further vasoconstriction.[13]

vi. **Innate immune system activation –** Neutrophils are activated by haem to release DNA as neutrophil extracellular traps which increase platelet activation and thrombosis and promote pulmonary vaso-occlusion.[14]

CLINICAL FEATURES OF HOMOZYGOUS SCD

In homozygous SCD clinical features are that of severe haemolytic anaemia punctuated by crises. The clinical expression of homozygous SCD is very variable; some patients develop severe crises even as infants and may die in early childhood or as young adults. Crises may be:

Painful Vaso-occlusive Crises

In early infancy, childhood and adulthood patients with SCD may experience intense pain which usually accounts for the majority of hospitalisations. This pain which is described as one of the most unbearable forms of pain that affects human beings is caused by factors such as infection, acidosis, dehydration or deoxygenation. Pain occurs due to stimulation of nociceptive nerve fibres caused by microvascular occlusion. The microcirculation is obstructed by sickle-shaped RBCs which restrict the flow of the blood to the organ and results in ischaemia, oedema, pain, necrosis and organ damage.[15] Infarcts can occur in a variety of organs such as the bone, the lungs and the spleen but the most serious vaso-occlusive crises are those that occur in the brain or spinal cord. In children the 'hand-foot' syndrome (painful dactylitis caused by infarcts of the small bones) is frequently the first presentation of the disease and may lead to digits of varying lengths. Resolution of pain is unpredictable. Acute pain might lead to chronic pain.[2]

Visceral Sequestration Crises

The visceral sequestration crises are caused by sickling within organs and pooling of blood, often with a severe exacerbation of anaemia. After puberty, the most common cause of death is acute sickle chest syndrome which presents with dyspnoea, falling arterial PO_2, chest pain and pulmonary infiltrates on chest X-ray. Splenic sequestration is typically seen in infants; these present with an enlarged spleen, decrease in haemoglobin and abdominal pain. Patients must be monitored at regular intervals and treatment is with transfusion. Since attacks tend to be recurrent, splenectomy is often needed.[16]

Aplastic Crises

In SCD, aplastic crises can occur either as a result of infection with parvovirus or from folate deficiency. The virus affects erythropoiesis by invading progenitors of RBCs in the bone marrow and destroying them, thus preventing new RBCs from being made. In SCD the life span of RBCs is reduced to about 10–20 days. This results in a sudden fall in haemoglobin which usually requires transfusion.[17]

Other clinical features include ulcers of the lower legs as a result of vascular stasis and local ischaemia. In infancy and early childhood, the spleen is enlarged but as a result of infarcts, later on in life is often reduced in size. Other clinical complications include pulmonary hypertension, retinopathy, priapism and chronic damage to the liver.

DIAGNOSIS OF HOMOZYGOUS SCD

Diagnosis of SCD involves the combination of blood counts and quantitative studies of haemoglobin fractions.

Blood Counts and Blood Films

In SCD the blood count and the erythrocyte indices depend on the presence or absence of confounding conditions such as iron or folic acid deficiency and coincidence of beta or alpha thalassaemia. In patients homozygous for SCD the haemoglobin is usually 6-9g/dL while if SCD is inherited together with alpha thalassaemia or beta thalassaemia the haemoglobin will be between 8-10g/dL. Figure 3 shows a blood picture with sickle cells, target cells, Howell-Jolly bodies (due to splenic atrophy), nucleated RBCs and polychromatophilic cells.

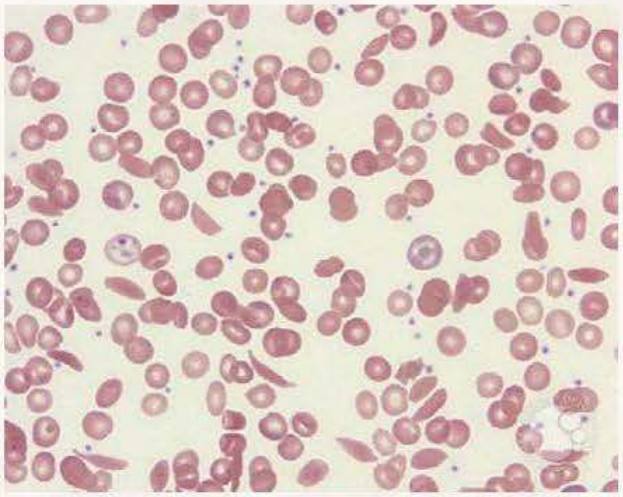

Figure 3: Peripheral smear from a patient with sickle cell disease illustrates the spectrum of RBC findings in this disorder including sickle cells, polychromatophilic RBCs, target cells and Howell-Jolly bodies.[18]

Detection of HbS and Measurement of Haemoglobin Fractions

In SCD, from neonatal life through early adult life, there is a slow but continual fall in HbF, whereas an increase in HbA_2 level is seen until ages 1-2 years. The haemoglobin fractions present at one year of age are sufficiently stable to be relied on for diagnosis. In untreated SCD, more than 80% of the hemolysate is always HbS, except in infancy when the γ to β globin gene switching is incomplete. HbS can be detected by isoelectric focusing, haemoglobin electrophoresis or high-performance liquid chromatography. Since sickling haemoglobins are insoluble and precipitate in high-molarity phosphate buffer when reduced with sodium dithionite they can be detected chemically. The definitive test for SCD is DNA-based methods for the detection of HbS.[19]

TREATMENT

The only treatments approved for SCD are hydroxyurea (hydroxycarbamide, HU). Hydroxyurea which is a ribonucleotide reductase inhibitor acts in a number of ways, by (i) increasing foetal haemoglobin, (ii) modulating endothelial activation, and (iii) help to reduce chronic inflammation by reducing neutrophil counts.[8] RBC exchange transfusion is usually used when HU therapy is not well-tolerated or not effective, such as in pregnancy and in SCD patients with acute or recurrent cerebrovascular disease. This can lead to iron overload or alloimmunization.[20] The only curative option is bone marrow transplantation but it is a risky and costly treatment.

An improved understanding of both the pathogenesis and the pathophysiology of sickle cell-related organ damage based on mouse models for SCD has allowed new therapeutic options to be identified. These include agents that target SCD vasculopathy and sickle cell endothelial adhesive events. On the other hand, while various clinical trials on lentiviral gene therapy in SCD are currently ongoing.

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DR PIERRE VASSALLO

CT Lung Cancer Screening

The much-awaited results from the Dutch-Belgian Randomized Lung Cancer Screening (NELSON) trial were published online on January 29 in the New England Journal of Medicine.[1] The study shows that CT lung cancer screening can significantly reduce the likelihood of high-risk smokers dying from lung cancer.

EPIDEMIOLOGY

Lung cancer (both small cell and non-small cell) is the second most common cancer in both men and women (not counting skin cancer). In men, prostate cancer is more common, while in women breast cancer is more common.

Lung cancer mainly occurs in older people. Most people diagnosed with lung cancer are 65 years or older; a very small number of people diagnosed are younger than 45 years. The average age of people when first diagnosed is about 70 years.[2]

Lung cancer is by far the leading cause of cancer death among both men and women, making up almost 25% of all cancer deaths. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.[2]

On a positive note, the number of new lung cancer cases continues to decrease, partly because people are quitting smoking. Also, the number of deaths from lung cancer continues to drop due to people stopping smoking and advances in early detection and treatment. Early detection can only be achieved through routine screening of individuals at high-risk for lung cancer.[2]

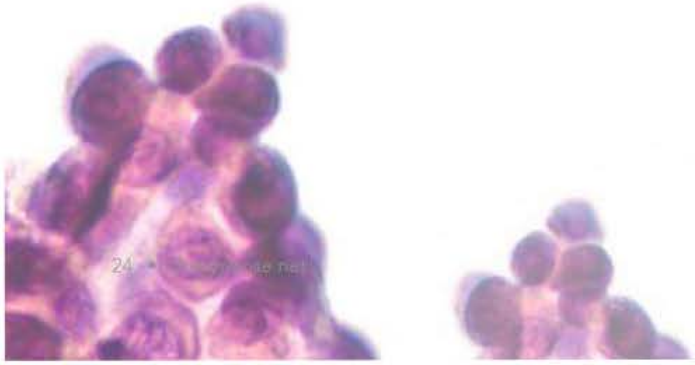
EFFORTS AT EARLY DETECTION OF LUNG CANCER

The large-scale randomized controlled NELSON trial referred to above has investigated the potential benefits of CT lung screening among 15,792 individuals in the Netherlands and Belgium between the ages of 50 and 74 years, who had a high risk of lung cancer. Risk was estimated based on a current smoking history of 20 pack-years or more or having quit smoking 10 years or less before screening.

Participants were randomly assigned to either the CT lung cancer screening protocol or no screening. The four-round screening protocol included a baseline CT exam followed by a CT exam at one, three, and five and a half years after the initial exam.

Analysis of results of the NELSON study showed that screening led to a statistically significant reduction in total lung cancer deaths by 24% for men and 33% for women, compared with no screening.

The study showed that CT lung cancer screening increased the likelihood of detecting lung cancer in the early stages: the proportion of cancers detected in stage IA or IB was 58.6% with CT lung screening and only 13.5% for the control group.



The same study also indicated that the screening interval can be readily increased from one year to two years without any impact on death rate. It was also noted that an increased risk in the screened population was only evident after two years from the start of screening; this further confirmed that a bi-yearly CT scan is adequate as a screening method for lung cancer.

Further observations from this study included that women fare better than men with treatment of early lung cancer and that the best criterion for assessing tumour growth is to measure tumour volume and not diameters.

LUNG CANCER DIAGNOSIS

On CT scan, lung cancer presents mostly as a solid mass. Irregular borders are more indicative of a primary lung tumour, whilst smooth margins are more commonly seen with metastases from an extrapulmonary source. However, benign nodules may also exhibit smooth margins (Fig 1).

Subsolid (not completely solid) pulmonary nodules, comprising pure ground-glass nodules (Fig 2) and part-solid (Fig 3) nodules, have a high risk of indolent malignancy; indolent malignancy refers to a slow growing type of cancer. Lung Imaging Reporting and Data System (Lung-RADS) nodule management guidelines are used to classify nodules based on their likelihood of being malignant (Fig 4). These guidelines have been set based on expert opinion but lack independent validation. In fact, subsolid nodules classified as Lung-RADS categories 2 and 3 have a higher risk of malignancy than reported.[3]

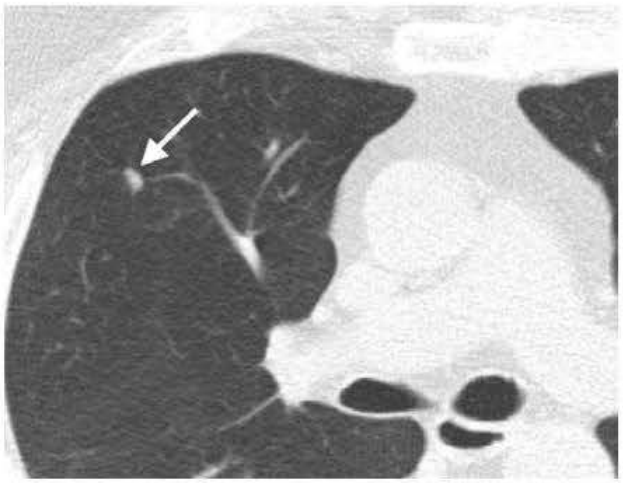


Figure 1. CT scan in 60-year-old man undergoing low-dose lung cancer screening. Scan shows a 6-mm solid nodule with irregular margins along the right minor fissure. This nodule was stable over 2 years of follow-up and most likely represents an intrapulmonary lymph node.

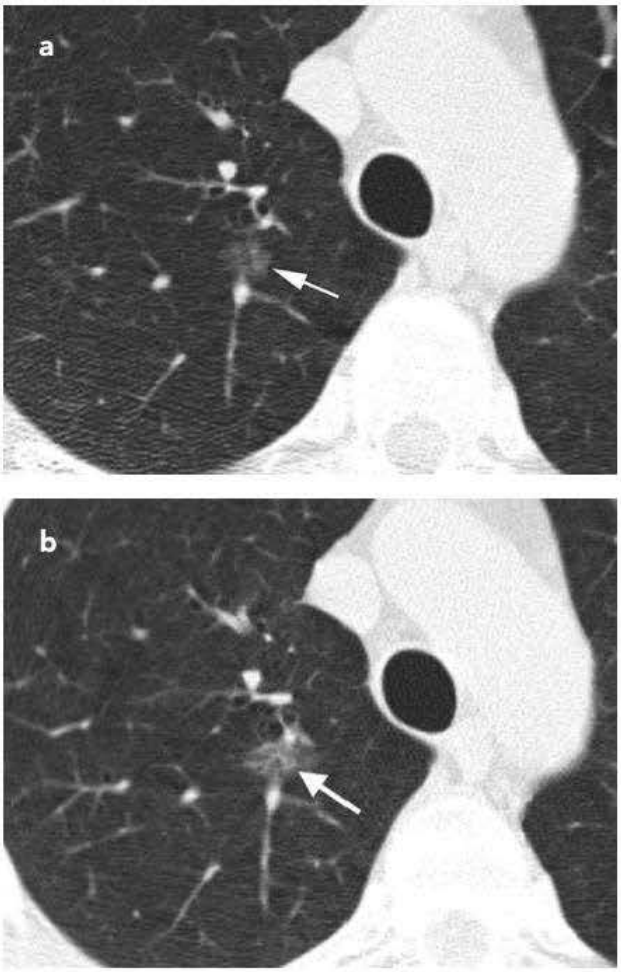


Figure 2. CT scans in a 57-year-old man undergoing low-dose lung cancer screening. (a) Baseline scan shows a right upper lobe pure ground-glass nodule measuring 11 mm (arrow). Nodule was classified as Lung-RADS category 2. (b) CT scans obtained at second annual follow-up show that this nodule grew to 15 mm (arrow). Malignancy was subsequently diagnosed.

Equivocal lung lesions that are either very small or indeterminate by their morphological appearance need to be followed up with CT. A change in size of the relevant lesion is best assessed by measuring lesion volume and not diameter. Increasing lesion size should lead to biopsy.

Enlarged or heterogeneous mediastinal or hilar lymph nodes or those showing increasing size should also raise the level of suspicion in favour of malignant disease.

IMPORTANCE OF EARLY DIAGNOSIS

Currently, the only way to improve outcome of lung cancer treatment is through early detection. Surgical excision is the most effective treatment for lung cancer

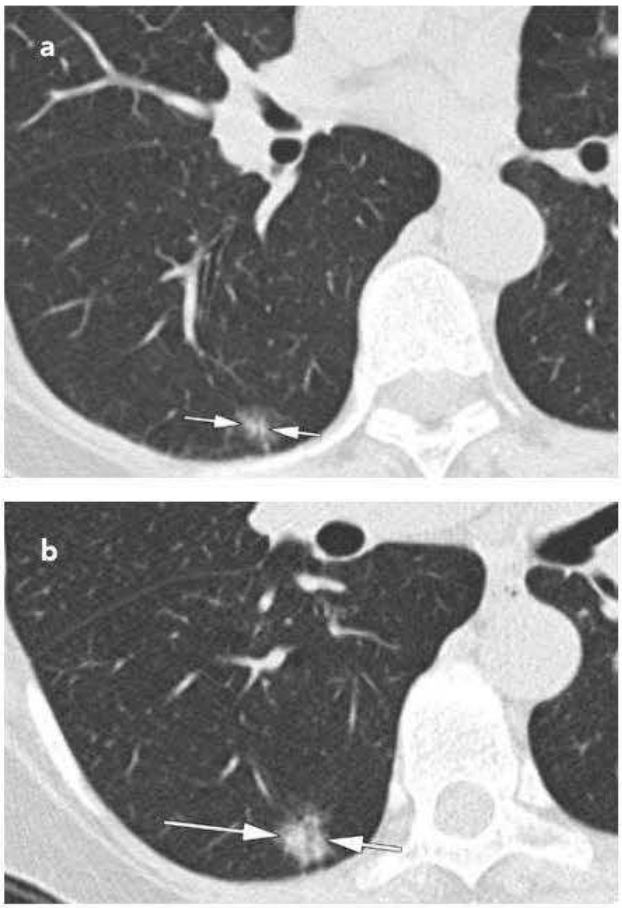


Figure 3. CT scans in a 60-year-old woman undergoing low-dose lung cancer screening CT. (a) Baseline scan shows a right lower lobe part-solid nodule measuring 11 mm with 5-mm solid component (arrows). Nodule was classified as Lung-RADS category 3. (b) Scan obtained at second annual follow-up shows that nodule grew to 17 mm with 7 mm solid component (arrows). Malignancy was subsequently diagnosed.

and it is only possible in the early stages of the disease. In addition, smaller cancers need less extensive surgery and consequently lead to lower morbidity. CT lung cancer screening is the best tool for detection of asymptomatic cancers and the results of the NELSON study are clearly supporting this view.

Lung nodule morphology and changing morphology are important criteria that guide management; these criteria are best assessed with CT. One study which remeasured more than 400 subsolid nodules from the National Lung Screening Trial (NLST) data at baseline and follow-up imaging showed that the malignancy risks for these lesions were higher than previously reported.[3] Larger subsolid lesions are also more likely to be malignant based on the same study.

CONCLUSION

Lung cancer is common and has a higher death rate than most cancers. Low-dose lung CT scans have a high accuracy for detection of lung cancers and impact significantly on the disease outcome and on the patient's quality of life. Bi-yearly screening of high risk individuals is therefore highly recommended.

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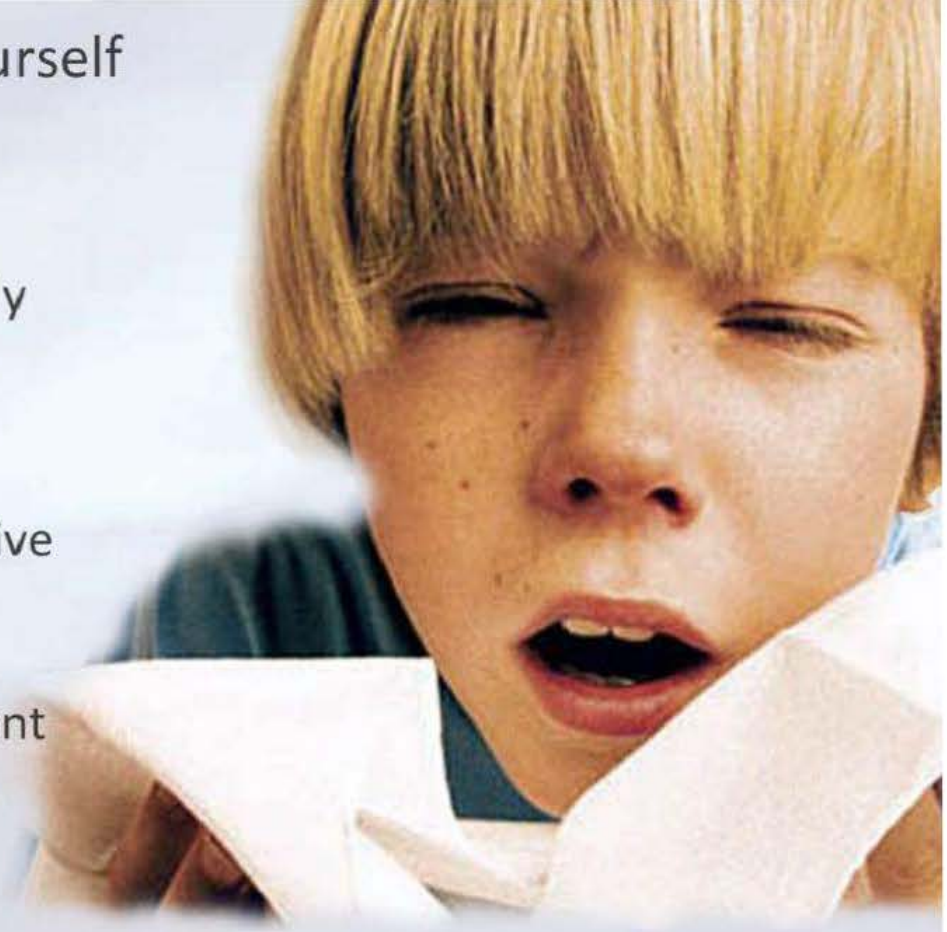
Be Safe.. Protect Yourself



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#loveyourheart

Heart disease is Malta's number one killer and affects women and men equally.

This is why it is important to screen for heart disease, since early detection may prevent future complications.

What is a heart scan?

Calcium deposition in the lining of the coronary arteries is one of the earliest manifestations of heart disease, indicating the presence of fatty material in the arteries (atheroma).

When diagnosed and managed early, the risk of a heart attack and other types of cardiovascular disease (such as stroke and poor circulation) can be greatly reduced. A heart scan is a low dose CT technique designed to detect and quantify the presence of calcium deposits in the lining of the heart's coronary arteries.

Sophisticated software will then highlight the calcium deposits, and provide a score based on your age and gender. The score is used by a doctor to estimate the risk of cardiovascular disease over the next few years.

Importantly the scan is very rapid (less than 10 minutes) and does not require injection of contrast.

Who should consider a heart scan?

Typically, the test is most useful in men between 40 to 60 and women between 50 to 70.

Risk factors for heart disease include:

- age
- gender
- family history of the disease
- tobacco smoking
- high blood cholesterol
- high blood pressure
- physical inactivity
- obesity
- diabetes

Therefore anyone with the above risk factors should undertake regular screening.

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