Volume 4, Issue 1, 2020

# Malta Medical School Gazette

MMSG


University of Malta
Medical School

L-Università
ta' Malta

www.mmsjournals.org

MMSG

# Table of Contents

MMSG
EDITORIAL

# Editorial

## The MMJ-MMSG: a call to referees and authors

Simon Attard Montalto

The Malta Medical Journals, now comprising the Malta Medical Journal (MMJ) and the Malta Medical School Gazette (MMSG), remain the only strictly peer-reviewed journals that focus on medicine and medical issues in Malta. They offer local clinicians and colleagues the option to publish their research with reasonable odds in favour of acceptance, when compared with large international journals where the number of submitted manuscripts and refusal to publish are considerably greater. Admittedly, a publication in the MMJ-MMSG will reach a much smaller audience since, despite all the commendable efforts of the outgoing editor, Prof Victor Grech, the MMJ remains outside of PubMed and PubMed Central. Essentially, a substantial captive local population and, more importantly, a steady influx of high quality publications is a pre-requisite for acceptance onto PubMed and PubMed Central.[1] Little can be done about the former and, although the MMJ-MMSG do receive and publish quality work, this could be improved.

There is little doubt that significantly more quality publications are 'out there' – one only has to review the quality and wide-ranging research that is presented by disparate departments and several authors in fora such as the Malta Medical School Conferences (MMSC). Unfortunately, many local researchers appear to be satisfied with their work achieving the level of an oral or poster publication at conference, and do not follow this up with a formal, academically 'superior' publication.

**Cover Picture:**

'Valletta Skyline' (2019)'

*India Ink on paper*

**By** Ben Chetcuti

Dr Ben Chetcuti is a Maltese artist, currently completing psychiatry training in Glasgow. His artistic journey started in digital illustration during his time at medical school at the University of Malta. Since moving to Glasgow, Ben has become passionate about ink illustration and painting and now uses the medium to portray the nostalgic colours of the Maltese Islands

**Professor Simon Attard Montalto**
Editor, Malta Medical Journal and Medical School Gazette
Head, Department of Paediatrics,
The Medical School,
Msida, Malta
simon.attard-montalto@gov.mt

By rights, during the subsequent six months following a MMSC, one would expect the editorial board of the MMJ-MMSG to be inundated with submissions, yet this simply does not happen. This is a shame as, ultimately, prestige and longevity in one's research is garnered through a publication and not via a one-off presentation.

It is now pretty routine during many medical job interviews, to award credit for publications and, along the same lines, attainment of additional postgraduate degrees. These, by definition, involve some form of research and should, by default, generate material that is 'publishable'. Admittedly, the 'cream' is preferably sent to highly-cited journals, especially in the first instance. But surely (and we have all been there), this work is not always (usually doesn't!) accepted by the *Lancet, NJEM* or *Nature Genetics*, etc., and there is always valid data and results, sometimes 'spin-offs' from the core research, that would be eminently acceptable to the MMJ-MMSG. A gentle *caveat* in this regard: research and publications are important and do procure 'brownie points' at interview, but this should not be seen as a means to an end, and research should always be conducted properly, organised along accepted standards and contribute to knowledge. 'Research' simply with the aim of generating a publication, regardless of quality, is unacceptable, and will not skirt any hurdle supported by a peer-review process, including that of the MMJ-MMSG.

In case you are still in doubt, the MMJ-MMSG continues to welcome submissions of good quality research and papers. All those involved, in some form or another, in work relating to publications will know that this is a laborious and time-consuming exercise. This is not helped when manuscripts are submitted in sub-optimal or an incomplete state, or not in accordance with 'Instructions to Authors' and, as a minimum, will result in delays in publication if not an outright rejection of the article. ALL submitting authors MUST read and ADHERE to ALL the Instructions to Authors. Although it would seem 'obvious' that articles should be formatted as instructed, and the text, grammer, figures, tables, data, etc., are all double-checked, non-compliance in this regard remains a common problem. Indeed, the lead/senior author should ensure that all of the above has been completed before submission, particularly when manuscripts have been written by more junior and less experienced colleagues.

All submitted articles undergo editorial review and all, apart from guest editorials, are sent to expert referees for further review. The role of the referees cannot be understated: the entire peer-review process is propped up by these individuals who are generally busy people who undertake this lengthy process (a good review will take time, almost always no less than 30 minutes and, on occasion, several hours), for

no remuneration (although every three reviews will entitle referees employed by the Division of Health, Malta, to claim a merit award). Article reviews should, ideally, be returned within a period of six weeks, preferably using the Journal on-line portal. On the other hand, significant delays will hold up the manuscript and, if multiplied by several delayed articles, will delay the publication of the entire issue. Hence, as with other journals, referees are asked to declare whether they can complete in time and the editorial board would prefer a clear 'no' from the outset so that the manuscript in question can be passed on to a second referee. Problems trawling and maintaining quality refereeing is not unique to the MMJ-MMSG,[2] but is essential in ensuring 'a standard' as well as timely publication. On an international basis, this aspect of academic publication is reliant on collegiate support, no reward and little, if any, guidance, although some larger institutions do provide training.[3,4] Malta is no different and the MMJ-MMSG remains hugely dependant on good will of colleagues who offer their time and expertise 'gratis'.

The MMJ has come a long way from its origins as the St Luke's hospital based gazette in the 1980s. It is probably the oldest peer-reviewed journal in Malta that has been published, initially in paper format till 2014 and, like many other journals,[5] on-line since. It remains one of the key pillars that defines the Malta Medical School. The list of individuals who, in one way or another, have supported the MMJ/MMJ-MMSG is extensive, and I will not attempt to list these, given the inevitable risk of omission(s). The ultimate quality in the published product is the result of a multi-facetted effort, and is dependent on quality submissions, timely and in-depth manuscript review, and a dedicated and efficient production team. The latter incorporates a MMSJ-MMSG Board, editorial and secretarial team with most of the work being carried out at secretarial level. The Journals enjoy the continuing support from the Medical School: we expect Lecturers and members of the Faculty Board to contribute, particularly with accepting to referee submitted articles (greater support is required in this regard), and we continue to welcome quality submissions, both locally and from overseas.

***Sub-note:*** *Given the relevance to both, this editorial has been published in both the MMJ and MMSG.*

## References


1. Delamothe T, Smith R. PubMed Central: creating an Aladdin's cave of ideas. BMJ 2001; 322: 1-2.
2. Rose ME, Boshoff WH. The peer review system for academic papers is badly in need of repair. The Conversation, Feb 26, 2017.
3. http://theconversation.com/the-peer-review-system-for-academic-papers-is-badly-in-need-of-repair-72669
4. Bradley D, Huang W. Quality and value: How can we get the best out of peer review? Nature 2006. https://www.nature.com/nature/peerreview/debate/nature04995.html
5. Schroter S, Groves T. BMJ training for peer reviewers. BMJ 2004; 328: 658. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC381210
6. Delamothe T, Smith R. Revel in electronic and paper media. BMJ 2000; 321: 192.

MMSG
ORIGINAL ARTICLE

# The impact of COVID-19 on the Malta Medical School

Victor Grech, Simon Attard-Montalto

The novel coronavirus COVID-19 is currently pandemic and Malta has carried out numerous measures in a stepwise fashion to enforce a soft-lockdown, and from which it is slowly emerging. This paper outlines the history of Malta's Medical School, culminating in a state-of-the-art facility, and documents the School's (and Malta University's) adjustments in the wake of COVID-19. Changes span physical alterations carried at very short notice, drastic changes in teaching practices to comply with social distancing measures, transition to online learning and migration to on-line, hands-off and patient-free examinations.

**Victor Grech***
MD, PhD.
Department of Paediatrics
Mater Dei Hospital
Msida, Malta
victor.e.grech@gov.mt

**Simon Attard-Montalto**
MD
Department of Paediatrics
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

The novel coronavirus COVID-19 is currently pandemic. Malta has not been spared and, at an early stage, opted to carry out numerous measures implemented in a stepwise fashion but at short notice, to establish a national soft-lockdown. Medical Education and the Medical School have been directly affected by lockdown measures, and were constrained to introduce radical changes, again at very short notice. These measures included restructuring and relocation of their physical environment, drastic changes in teaching practices to comply with social distancing measures, transition to online learning and migration to on-line, hands-off and patient-free examinations. Malta's policy and approach to the pandemic has, to-date, ensured that the country has not had a significant hit in terms of the population's health and healthcare, with just 674 confirmed COVID-19 cases and just 9 deaths from a total population of circa 500,000. The economic impact has yet to be fully determined, but is likely to be significant with an estimated decrease in GDP of 2-6% for 2020. The country has emerged from the first phase of the pandemic, the National Public Health Emergency has been officially suspended and Malta is currently slowly emerging from its self-imposed lockdown.[1,2] The Medical School is likewise emerging from lockdown, and although some changes have been reversed, others are destined to remain long-term as part of the so-called 'New Normal'. This paper will outline the history of Malta's Medical School, culminating in a state-of-the-art facility complete with simulation training, and document the School's (and Malta University's) physical sacrifice in the wake of COVID-19.[3-4]

## History of Malta's Medical School

In 1592, the Hospitaller Order of the Knights of St. John founded the Collegium Melitense in Malta, a Jesuit college originally located in an old house in Valletta,[5-7] A purpose-built college was later constructed between 1595 and 1597 and this is now known as the Old University Building.[5-7] The Order's Sacra Infermeria was constructed in 1574 and despite this being one of Europe's best hospitals, no accompanying medical school existed until a century later when, in 1676, Grand Master Nicholas Cotoner founded the School of Anatomy and Surgery in the Sacra Infermeria itself.[5-7]

The University of Malta was founded in 1769 and the pre-existing School of Anatomy and Surgery was incorporated within the University in 1771, thus attaining academic status.[5-7] These events may have been prompted by Malta's worst-ever plague epidemic caused by Yersinia pestis, that was far worse than that experienced in the current COVID-19 pandemic.[8] Indeed the plague killed circa 11,300 from an estimated population of 60,000. The dead included 10 physicians and 16 surgeons, thereby significantly depleting the island's healthcare workforce at the time.

In 1676, students were required to study anatomy by attending lectures and cadaver dissection on patients dying in the Sacra Infermeria, initially within the hospital and later in a dissection room built in the hospital's graveyard.[5-7] The teaching of medicine and surgery has continued, uninterrupted, since then making Malta's Medical School almost three-and-a-half centuries old and, as declared by Sir Temi Zammit is the locus from which "the Maltese medical profession derived its origin, identity and vitality".[5]

The University inaugurated a larger campus on site at Tal-Qroqq in Msida in the late 1960s, but only the preclinical years (first and second years) of the Medical Course were located on campus.[7] By 1968, cohorts of Malta Medical students in their third to fifth year of clinical studies moved to a custom-built building within the grounds of St. Luke's Hospital in Gwardamanġa.[8]

Mater Dei Hospital in Msida opened in 2007, replacing St. Luke's Hospital as the country's acute general and teaching hospital. This public hospital was affiliated to the University of Malta, and offered all hospital and specialist services. The 250,000 square metre complex included over 800 beds and 25 operating theaters and cost over €580,000,000 to complete. The hospital is sited adjacent to the University of Malta, and incorporates the faculties of Health Sciences, the clinical years of Medicine and Surgery, and Dental Surgery in a purpose built Medical School wing. The Health Sciences Library, a branch library of the University of Malta Library, was located within this block, on the Hospital premises.[7]

## COVID-19 in Malta

The current COVID-19 (coronavirus) pandemic was initially identified in Wuhan, China, in December 2019,[9] and since then spread to virtually all countries in the world, resulting in over 13 million infections and well over half a million deaths. The pandemic is certainly not 'over'. Indeed, many countries particularly in Latin America and the East have yet to reach the peak of their first wave of infection, whilst others especially China, the Far East and Europe are recording up-surges and, in some cases, a second wave of infection, often coinciding with relaxation of lockdown measures. In medical terms, a second wave refers to a resurgence of infection in a different part of a population after an initial decrease.[10] Malta adopted an early and aggressive 'trace and isolate' policy that was well enforced and supported, and has fared well with 674 cases and 9 deaths recorded during the first wave of the pandemic.[2] The country is presently in a transition phase with a general return to "new normal", relaxation of lockdown and soon-to-reopen flight access. The resurgence of a second wave remains a possibility, and its magnitude, unknown.

## Malta's response

In order to address an expected strain on the healthcare system, in early March 2020, the hospital underwent extensive changes to accommodate the pandemic. Provision was made to increase capacity to ventilate 100 patients in five intensive care facilities as opposed to the former single 20-bed intensive care facility.[4] An additional 600 beds for COVID-19 patients were added, with escalation plans that utilised patient corridors, service corridors, the hospital foyer and the Medical School.[4] Indeed, the entire Medical School barring a few offices, were relocated twice, *en masse*, to first one and, when this was taken over by yet more 'beds-for-COVID', to a second more distant site on the University Campus. The Library was gutted, all books placed in storage and converted into a large 40–bedded ward, the Boardroom replaced with a store room and lecture rooms and offices changed into facilities for ward staff. The preparation and implementation of these changes were completed within just a few days, and translated into a radical metamorphosis as will be shown later in this paper.

## Social distancing, teaching and medical exams

A strong and relentless campaign was orchestrated by the Superintendent and Directorate of Public Health, the Ministry for Health and indeed, the Government of Malta for social distancing, staying at home, encouraging employers to provide telework facilities to all employees, the wearing of masks/visors, and maintaining personal hygiene measures, including regular washing of hands with soap etc.[1]

On-site education in all Schools, Higher Institutions and the University were stopped in March,[1] with transition to various remote teaching modalities for formal lectures and tutorials, with arguably the most popular being Zoom.[11] The Medical School with a mantra for hands-on clinical teaching, was particularly hard-hit and had to re-think at short notice. The inevitable reduction in hands-on teaching, bedside and patient contact, was unfortunate and, in a worse-case scenario, was epitomised by Morawo and colleagues:

> While live virtual learning has allowed for continued education, it presents its unique challenges. The impersonal nature of the virtual learning environment creates a propensity for detachment and disengagement. While the video function is turned off and the microphone is muted, a participant can completely disengage from virtual learning while still appearing to be present.[12]

Fortunately, the events that have led to this radical change in scenario and enforced *modus operandi* occurred close to the end of the scholastic year. Nevertheless, several student cohorts had yet to complete their clinical attachments especially in Medicine, Surgery, Obstetrics and Paediatrics, and many lectures and tutorials had yet to be delivered. Clinical attachments had to be suspended and are now being re-scheduled while lockdown is relaxed, whilst outstanding lectures/tutorials have been 'delivered' on-line using a plethora of platforms.

Clinical exams had to be altered, in some cases, with significant deviations (and, therefore, effort) from previous examinations, so as to exclude 'live' patients, increase simulation, and introduce social distancing and protective precautions. For example, in Paediatrics, although the Final Year Clinical Exam format was retained, the number of students examined during each session was halved, the examination period doubled and gaps between exam days tripled. These changes necessitated an 8-fold increase in the material (questions) that needed to be prepared to cover the entire examination. For written examinations, at the time of writing, the university has invested heavily for the June 2020 examinations in WISEflow, a "more than paperless" platform that constitutes a well proven cloud-based platform providing for digital examinations and assessments. It allows students to work on their own devices during exams, with or without proctoring (supervision).[13] This was a radical change and necessitated close liaison with (and considerably more work and support from) the University IT Department, rigorous and time-consuming training for all staff, and many more man-hours to set each examination paper. For various reasons, an unproctored format was chosen so that a degree of 'cheating' could not be eliminated, although several in-built measures within the system are designed to reduce this to a minimum. To date, and with credit to the IT Department and all

involved, numerous examinations have now been completed successfully using this platform.

## Malta Medical School and University

Both the Medical School as well as the University of Malta campus (which is just east of the hospital) have also sacrificed physical space to Malta's COVID-19 pandemic preparations. The University has been partially relieved of Gateway Building (figure 1 – red arrow) which is the building on campus closest to the hospital.[14]

Gateway now contain two wards that can take 42 patients. In addition, Medical Staff moved to temporary offices in Gateway in order make space at Medical School for a potential wave of patients.[15] Two thirds of the Medical School has been taken over (figure 1 – blue arrow). The library was gutted and converted into a 40 bed ward as can be seen in the engineering escalation plans (figure 2). Figures 3 and 4 show the work in progress and the final result. Figure 5 shows the plastic covered Medical School reception area, faced with a food trolley and extra beds (figure 6).

The adjacent board room was converted into a store room (figure 7) and the adjacent conference room was converted into a staff rest room (figure 8). The south corridor of Medical School along with the hospital's former VIP parking is now a COVID swabbing hub (figure 9). The larger lecture rooms have also been affected. The centre of the hospital housed 3 large overlying lecture halls and the ground floor has been split into two wards (figure 10). The benches are stacked outside, almost covering the hospital chapel entrance (figure 11).

**Figure 1** Map showing location of Mater Dei Hospital, just west of the University of Malta campus.

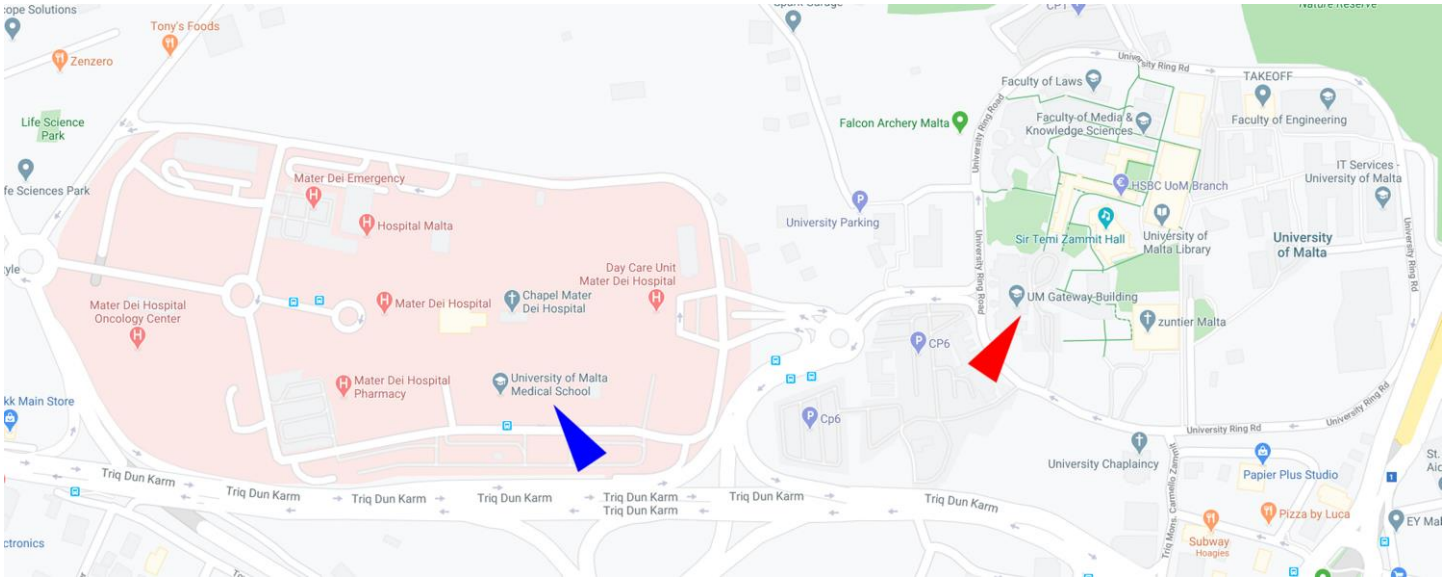


**Figure 2** Escalation plans as implemented for the Medical School Library.

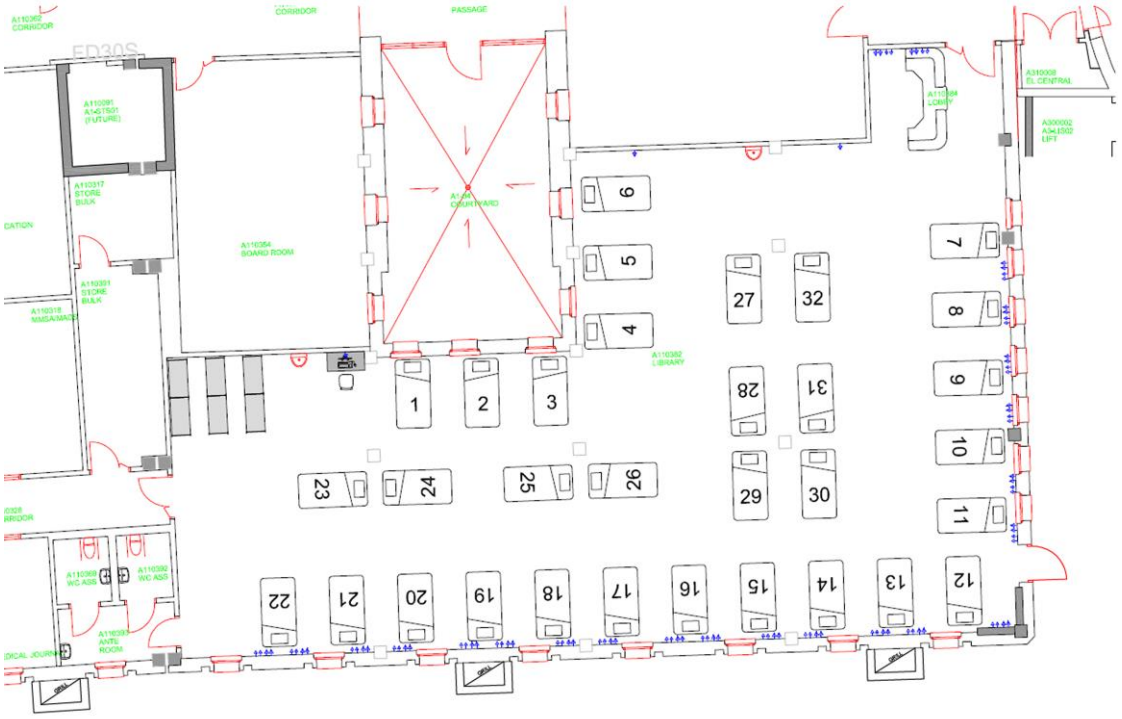



**Figure 3** The Medical School Library being gutted and converted into a ward.

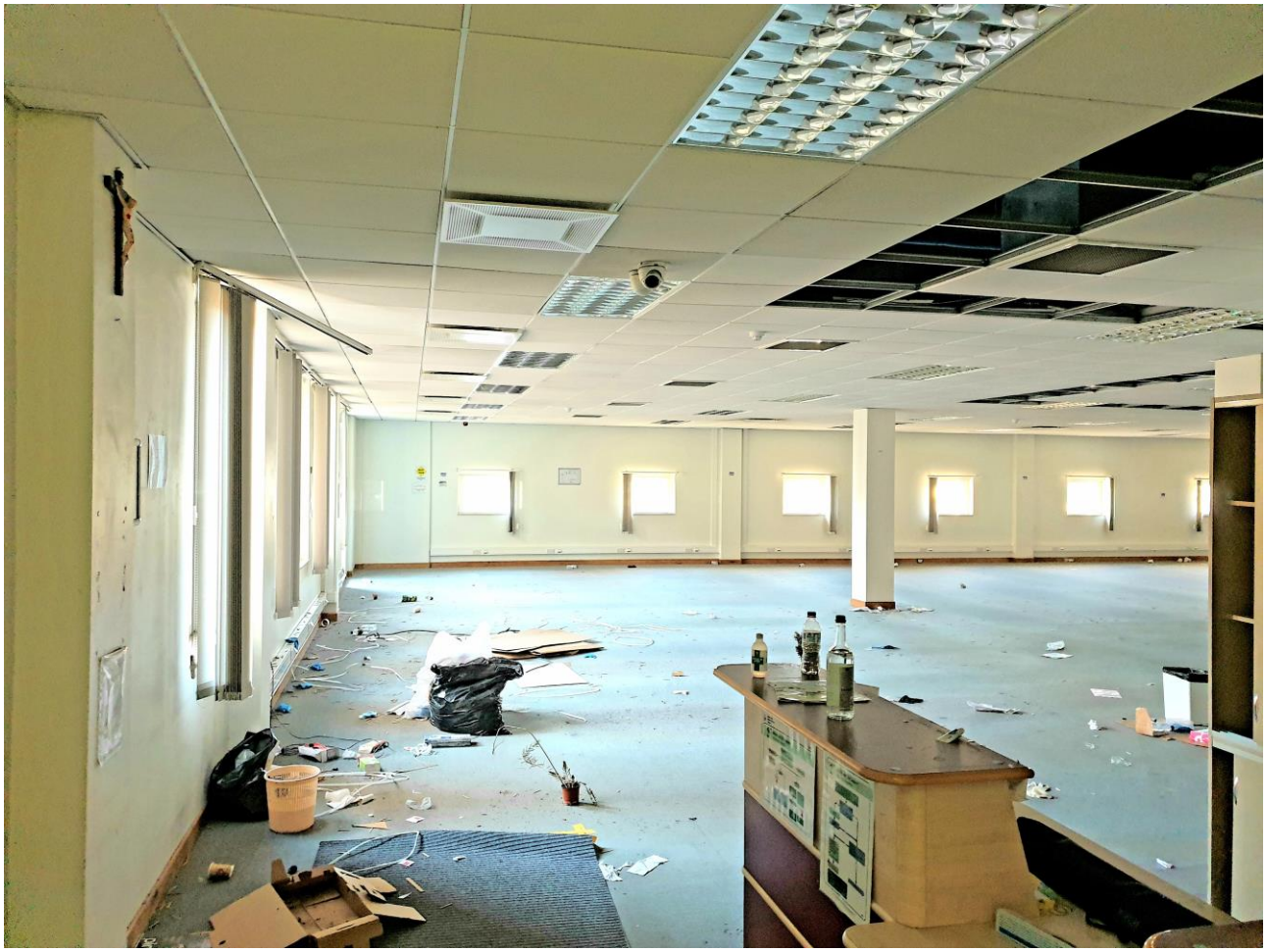


**Figure 4** The Medical School Library after conversion into a ward.

**Figure 5** The Medical School reception.

**Figure 6** The Medical School reception area complete with extra beds for the adjacent ward and a food trolley.

**Figure 7** The adjacent board room is now a store room.

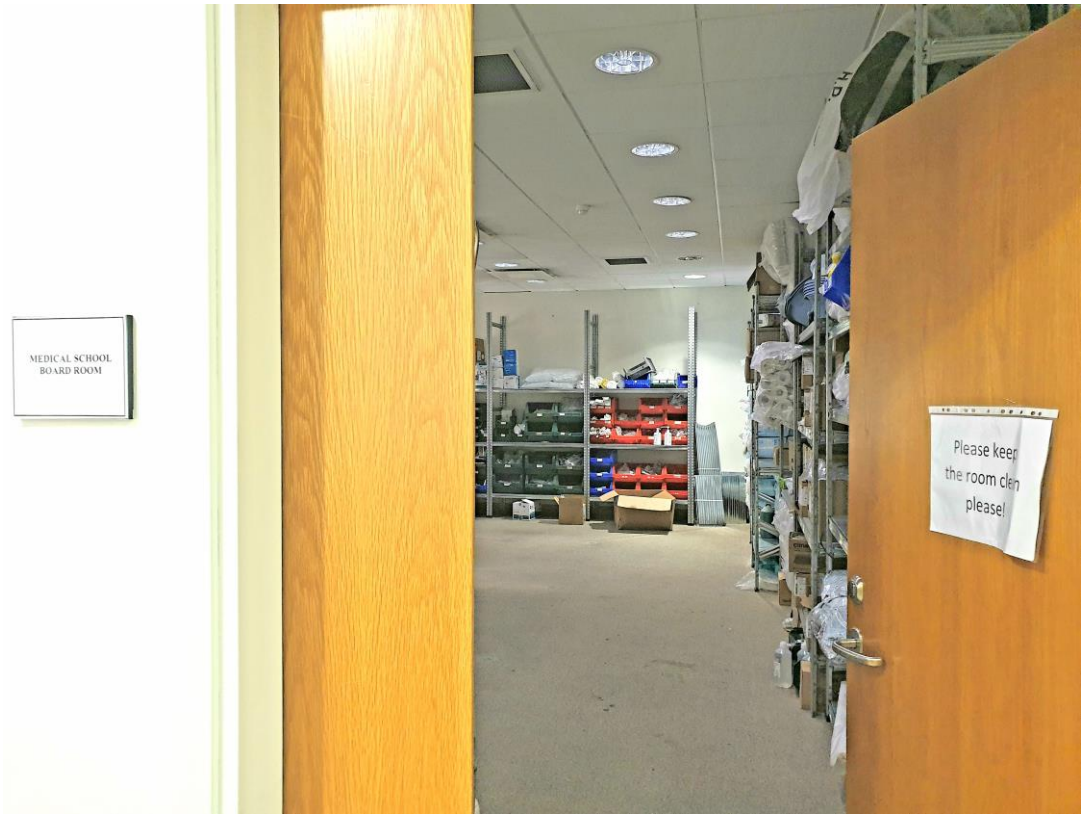


**Figure 8** The conference room is now a staff rest room.

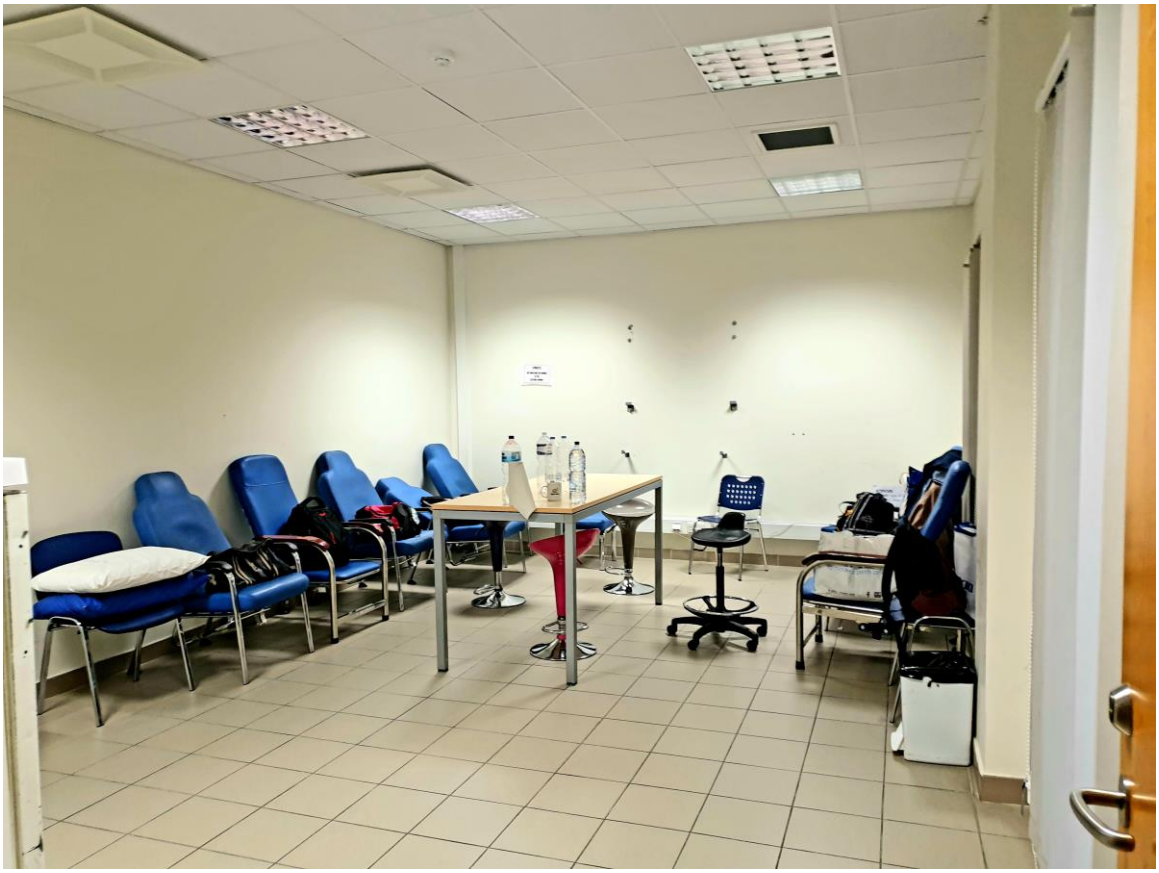


**Figure 9** The south corridor is now a COVID swabbing hub.

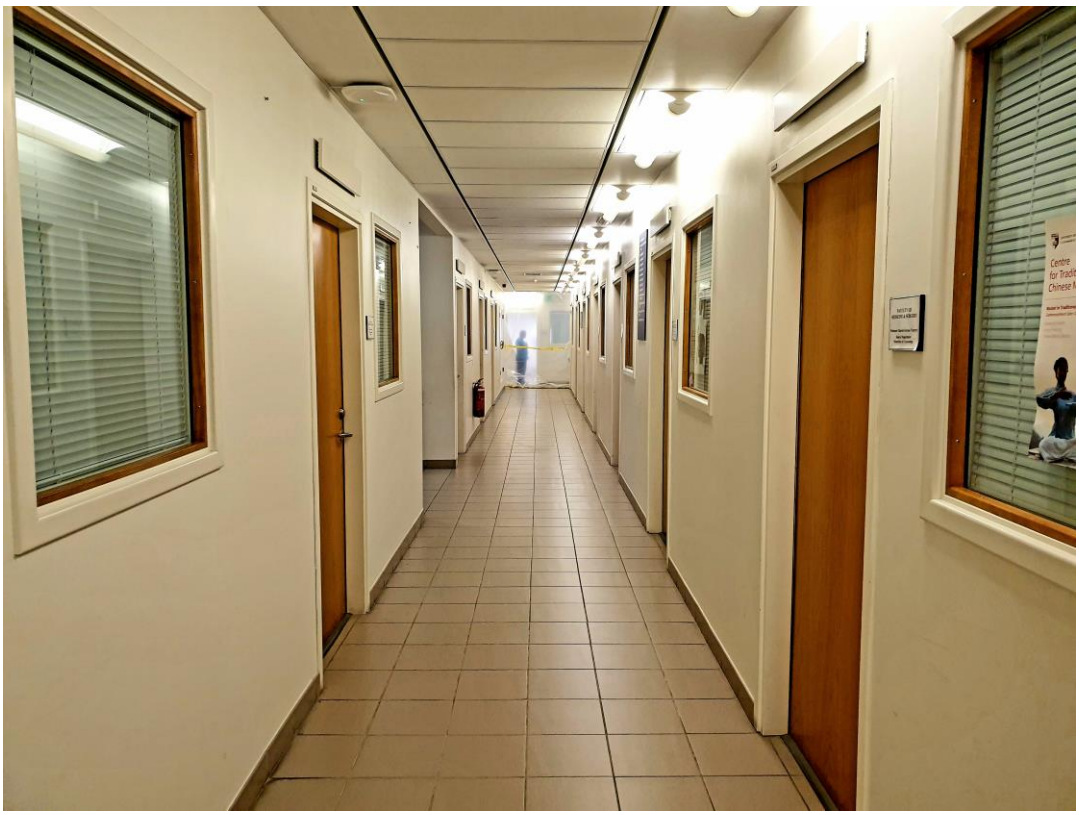


**Figure 10** Lecture halls converted to wards.

**Figure 11** The benches from figure 10 stacked in front of the Hospital Chapel.

## The future

Plans had already been laid for the Medical School and the Faculty of Health Sciences to move to a new building, an 8,000 square metre facility between University and Mater Dei Hospital (see figure 1). The space vacated from the existing facilities on the Hospital site will be converted into more wards and clinical areas to provide more services to patients.[15] There are certainly no plans to return the physical spaces to the Medical School as yet due to the possibility of the pandemic reappearing. The World Health Organisation has observed that past pandemics have been characterised by "waves of activity spread over months".[16] In addition, the hospital will remain prepared not only for an increase in cases in the short term, but also potential co-infected patients with seasonal influenza and COVID-19 next winter,[17] and hence increased bed requirements.

In the interim, the 'old' offices have been re-populated by Medical School Administrative and Teaching staff. The disruption to University and to Medical School has been monumental but the team has rallied magnificently and, despite the unforeseen and unchartered circumstances the work of the Medical School and examination processes have taken place without any hitches.[18]

## References


1. Cuschieri, S. COVID-19 panic, solidarity and equity—the Malta exemplary experience. J Public Health (Berl.) (2020). https://doi.org/10.1007/s10389-020-01308-w
2. Grech, Victor. COVID-19 in Malta, a Small Island Population. The Synapse. March 2020.
3. Grech, Victor. A Tale of Two Cities – Manchester and Malta's Grand Harbour. Tarxien: RE/MAX & Friends Foundation; 2019.
4. Grech V. Malta's healthcare escalation for COVID19. J Vis Comm Med – in press.
5. Zammit T. The Medical School of Malta. Proceedings of the Royal Society of Medicine. 1919;12(Suppl):133-142.
6. Cassar Paul. Grand Master Nicholas Cotoner and the foundation of the lectureship of anatomy and surgery 1676. Paper read on 19th December 1976 on the occasion of the Tercentenary Celebrations of the Foundation of the school of Anatomy and Surgery in the assembly hall of the University, tal-Qroqq. https://www.um.edu.mt/library/oar/bitstream/123456789/20899/1/grand%20master%20nicholas%20cotoner%20and%20the%20foundation%20of%20lectureship%20of%20anatomy%20and%20surgery.pdf
7. Savona-Ventura, C., & Borg Galea, C. (2007). Universitas Studiorum Melitensis – Medicinae Chirugiaeque Facultate: Roll of Honour. Malta: Faculty of Medicine & Medicine, University of Malta. https://www.um.edu.mt/library/oar/bitstream/123456789/34286/1/Savona%20Ventura%20-roll%20of%20honour.pdf
8. Grech V. COVID-19 and Malta's Black Plague epidemic of 1813. Hektoen. May 2020. https://hekint.org/2020/04/14/covid-19-and-maltas-black-plague-epidemic-of-1813/

9. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in Lancet. 2020 Jan 30;:]. Lancet. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5

10. Grech V. COVID-19 and potential global mortality - Revisited [published online ahead of print, 2020 Apr 30]. Early Hum Dev. 2020;144:105054. doi:10.1016/j.earlhumdev.2020.105054

11. Mahul-Mellier AL. Screams on a Zoom call: the theory of homeworking with kids meets reality [published online ahead of print, 2020 May 1]. Nature. 2020;10.1038/d41586-020-01296-7. doi:10.1038/d41586-020-01296-7

12. Morawo A, Sun C, Lowden M. Enhancing Engagement during Live Virtual Learning using Interactive Quizzes [published online ahead of print, 2020 May 21]. Med Educ. 2020;10.1111/medu.14253. doi:10.1111/medu.14253

13. Raaheim A, Mathiassen K, Moen V, Lona I, Gynnild V, Bunæs BR, Hasle ET. Digital assessment–how does it challenge local practices and national law? A Norwegian case study. European Journal of Higher Education. 2019;9(2):219-31.

14. Costa M. University lecture halls being converted into hospital facilities in case of COVID-19 second wave. Malta Today. 10th May 2020. https://www.maltatoday.com.mt/news/national/102240/university_lecture_halls_being_converted_into_hospital_facilities_in_case_of_covid19_second_wave#.XtuZCuplzIU University of Malta Newspoint. Faculty of Health Science: Move to Gateway. 17 Mar 2020. https://www.um.edu.mt/newspoint/notices/um/2020/03/fhs-gateway

15. Galea A. New 8,000 square metre medical school to be built at University of Malta. Malta Independent. 24 Nov 2019. https://www.independent.com.mt/articles/2019-11-24/local-news/New-8-000-square-metre-medical-school-to-be-built-at-University-of-Malta-6736216600

16. World Health Organisation. About pandemic phases. Accessed June 2020. http://www.euro.who.int/en/health-topics/communicable-diseases/influenza/data-and-statistics/pandemic-influenza/about-pandemic-phases

17. Ozaras R, Cirpin R, Duran A, et al. Influenza and COVID-19 Co-infection: Report of 6 cases and review of the Literature [published online ahead of print, 2020 Jun 4]. J Med Virol. 2020;10.1002/jmv.26125. doi:10.1002/jmv.26125

18. University of Malta. Assessments - June session 2020. https://www.um.edu.mt/services/coronavirus/assessments2020

MMSG
ORIGINAL ARTICLE

# Influenza vaccination survey in Maltese Healthcare workers in the COVID-19 era

Victor Grech, Charmaine Gauci, Stephen Agius, Simon Attard Montalto

## Introduction

Seasonal influenza globally infects 5%-15% annually, with a total of 3-5 million cases of severe illness and ≤500,000 deaths. Hospital-acquired influenza has a particularly high mortality, and healthcare workers are frequently the source of these infections. This study was carried out to ascertain last year's influenza vaccination uptake in Malta's government sector healthcare workers, and estimate the likely vaccine uptake rate in the coming winter season when COVID-19 is expected to be prevalent.

## Methods

A short, anonymous questionnaire was sent via the sector's standard email services (open 30/06-17/072020).

## Results

There were a total of 735 (7.6%) responses from a total workforce of 9,681. The proportion of Maltese healthcare workers who did not take the vaccine last year but who are likely to take the vaccine this winter halved from 41% to 21%. Doctors had the highest baseline uptake (23% refused vaccination in 2019) and the highest likely uptake next winter (6% likely to refuse vaccination in 2020). Analysis by age showed a likely increase in vaccine uptake with increasing age across almost all age brackets.

## Discussion

Influenza vaccination is advantageous and incurs a trivial burden. Clinicians, legislators and ethicists are increasingly aware of this aspect of healthcare, and increasingly mandate compulsory seasonal influenza vaccination for healthcare workers, where vaccine refusal can be taken to equate to maleficent practice. Education with regard to the low risk of side effects may increase voluntary uptake. Institutions are also responsible for ensuring employee vaccination, and this is even more the case for next winter in the setting of the potential co-circulation of novel COVID-19 with influenza.

**Victor Grech***
MD, PhD.
Department of Paediatrics
Mater Dei Hospital
Msida, Malta
victor.e.grech@gov.mt

**Charmaine Gauci**
M.D.(Melit.),M.Sc.,Ph.D.,F.R.S.P.H.,F.F.P.H.
Superintendent Public Health

**Stephen Agius**
B.Sc.(Hons)(Greenw.),M.B.A.(e-Business)
COO, Mater Dei Hospital
Msida, Malta

**Simon Attard-Montalto**
MD
Department of Paediatrics
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

Influenza-like illness is caused by over 200 different microorganisms (viruses and bacteria) with circa 10% caused by the influenza virus.[1] Seasonal influenza is a significant cause of morbidity and mortality and it is estimated that this virus annually infects 5% to 15% of the global population, resulting in 3-5 million cases of severe illness and up to half a million deaths.[2] Hospital-acquired influenza has a particularly high mortality, with an estimated median of 16%, rising up to 60% in high risk groups (e.g. transplant recipients and intensive care patients).[3,4] Healthcare workers who carry the virus have been frequently identified as sources of hospital-acquired outbreaks.[5]

The Centers for Disease Control strongly recommends annual influenza vaccination for all healthcare workers,[6] but vaccination rates remain poor,[7] despite models that show that a significant proportion of hospital-acquired burden of disease is vaccine preventable.[8]

The world is currently (2020) in the throes of the COVID-19 coronavirus pandemic,[9] and in the absence of an effective vaccine, next winter, this virus is likely to circulate in conjunction with seasonal influenza.[10] This study was carried out in order to ascertain last year's influenza vaccination uptake in Malta's government sector healthcare workers, and compare this with the projected uptake of the vaccine this coming winter.

## Methods

A short (6 tick boxes), anonymous questionnaire was sent out to all of Malta's government sector healthcare workers via the service's standard email services. The period for which the questionnaire was open was from 30th June to 17th July 2020. The questionnaire was hosted via Google forms and exported to bespoke Excel spreadsheets for analysis.

The questionnaire was sent to all healthcare workers in the main hospital (Mater Dei Hospital), District Primary Care Health Centres, St Vincent de Paul Long Term Care Facility, Mount Carmel Mental Health hospital, Karin Grech Rehabilitation Hospital and miscellaneous other smaller facilities.

The questions, formatted in tick boxes, covered sex, occupation (medical, nursing, allied profession and other, with the latter including support staff such as in administration, ward clerks, cleaners, etc.), place of work (as above), age bracket, whether the influenza vaccine was taken last winter (yes/no), and how likely was the respondent to take the vaccine this coming winter (2020-21) on a Likert scale of 1-5. For the latter question, it was assumed that scores 1 and 2 were "no" and 4 and 5 were "yes". A score of 3 was discarded.

Chi tests and chi tests for trend were used except for one two by two table with small values wherein a Fischer exact test was used. A p value $\leq 0.05$ was taken to represent a statistically significant result.

## Results

A total of 9,681 questionnaires were posted electronically, with just 735 (7.6%) responses. The response rate ranged from 0.3-0.9% from healthcare workers outside Mater Dei, improving to 11.9% from healthcare workers based at Mater Dei Hospital (table 1). For this reason, analysis for workplaces outside of Mater Dei Hospital were amalgamated.

**Table 1** Percentage response rates by workplace and occupation

| Workplace | Total | Responded % | Occupation | Total | Responded % |
|---|---|---|---|---|---|
| Health Centre | 1018 | 0.5 | Medical | 1472 | 12.3 |
| Karin Grech | 232 | 0.9 | Nursing | 2390 | 6.5 |
| Mater Dei | 5708 | 11.9 | Allied profession | 1705 | 14.4 |
| Mount Carmel | 723 | 0.4 | Other | 495 | 31.1 |
| Other | 200 | 21.5 | | | |
| SVPR | 1800 | 0.3 | | | |

**Table 2** Percentages who answered "no" to whether they took influenza vaccine last year (2019) and whether will take vaccine next year (20202), overall and by sex, workplace and profession

| % answer "no" | Overall | Females | Males | Mater Dei | Rest | Medical | Nursing | Allied profession | Other |
|---|---|---|---|---|---|---|---|---|---|
| Did not take | 41 | 42 | 39 | 41 | 43 | 23 | 42 | 47 | 49 |
| Will not take | 21 | 21 | 21 | 21 | 17 | 6 | 23 | 26 | 27 |
| chi | 65.7 | 50.2 | 16.2 | 57.1 | 9.2 | 17.0 | 20.9 | 16.1 | 14.8 |
| *p* | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.002 | <0.0001 | <0.0001 | <0.0001 | 0.0001 |

**Table 3** Percentages who answered "no" to whether they took the influenza vaccine last year and whether will take vaccine next year by age

| % answer "no" | Last winter | Coming winter |
|---|---|---|
| 18-24y | 21 | 4 |
| 25-34y | 39 | 20 |
| 35-44y | 47 | 23 |
| 45-54y | 51 | 30 |
| 55-64y | 33 | 17 |
| >64y | 25 | 0 |
| Chi for trend | 2.3 | 4.2 |
| *p* | 0.1 | 0.04 |

**Table 4** Statistical sub-analysis of age as per table 1.

| % answer "no" | 18-24y | 25-34y | 35-44y | 45-54y | 55-64y | >64y |
|---|---|---|---|---|---|---|
| Did not take | 21 | 39 | 47 | 51 | 33 | 25 |
| Will not take | 4 | 20 | 23 | 30 | 17 | 0 |
| chi | 8.2 | 17.0 | 17.4 | 16.7 | 7.9 | Fischer |
| *p* | 0.004 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.3 |

Replies were received from 14.4% of allied healthcare workers, 12.2% of doctors and from 6.5% of nursing staff. Overall, the proportion of Maltese healthcare workers who did not take the vaccine in 2019 but who replied that they were likely to do so this winter, halved from 41% to 21% (table 2). This increase in vaccine uptake was reflected in both sexes and at all workplaces (table 2). Although, there was an increase in the 'projected' vaccine uptake across all healthcare workers by profession, this improved from approximately 45% of nurses and allied healthcare workers who did not vaccinate against influenza in 2019, to 25% in 2020. Doctors had the highest baseline uptake with 77% vaccinated against influenza in 2019, and only 23% declining vaccination in 2019., This group also reported the highest likely uptake next winter, resulting in the steepest projected decline in vaccination refusal rate with just 6% likely to refuse vaccination (table 2).

Analysis by age showed a significant likely increase in vaccine uptake across almost all age brackets (tables 3 and 4).

## Discussion

It is encouraging to note that a higher proportion of healthcare workers intend to avail themselves of influenza vaccination next winter. This may be due, in part, to strong advice already being given in this regard by the Public Health Department The latter have announced that preparations are underway to develop a strategy to mitigate the impact of seasonal influenza come October, and that this may include the mandatory vaccination of vulnerable groups in order to minimise risks of a potential dual impact of seasonal influenza and COVID-19 on the country's healthcare system in winter 2020.[11] For this reason, in anticipation of expected demand, Malta has already ordered 200,000 vaccines, instead of the customary 100,000 usually ordered and given freely to vulnerable groups (for a population that approaches half a million).[11]

However, more can and should be done in order to raise the proportion of vaccinated workers as close to totality as possible. Clinicians, legislators and even ethicists are progressively more aware of this aspect of healthcare, and are increasingly mandating seasonal influenza vaccination for healthcare workers. Indeed, the Society for Healthcare Epidemiology has recommended that annual influenza vaccination should be a condition of employment for healthcare workers,[12] and this stance has been endorsed almost universally by professional bodies.[7] Ethicists have stated that:

> "given the mounting evidence for the efficacy of influenza vaccination in infection control […] the provision of health care by non-vaccinated health care workers is not merely suboptimal health care, but it is also at variance with generally accepted principles of health care ethics." [7]

Medical ethics upholds the twin principles of beneficence and non-maleficence. The former implies the promotion of patients' well-being and the latter can be summarised by the well known adage *primum non nocere*. Thus, "vaccination against influenza should be mandatory because practicing without vaccination is maleficent because it falls below the standard of medical care".[7]

## Vaccination efficacy in healthcare settings

Prospective trials have demonstrated that the influenza vaccination of healthcare workers reduces influenza morbidity and mortality in influenza-vulnerable populations. This is especially the case in the elderly and in care homes.[13-16] It has also been estimated that "Need to treat" vaccination numbers in order to prevent one healthcare-associated patient death from influenza are as low as 11.4 to 125.7.[13-16]

## Vaccination burden

The commonest reason for non-vaccination of healthcare workers is insufficient knowledge about the vaccine and its safety with irrational apprehension, and it has been shown that improved information about the vaccine improves voluntary vaccine uptake.[17] Our study partially supports this contention in that doctors were more likely to take the vaccine, both last year and with even greater likelihood next winter, and this may be due to greater knowledge in this group of healthcare workers. A ten year old study in Malta had shown that only 56.5% of healthcare workers availed themselves of free vaccination, and uptake depended mainly on their place of employment within the Health Service, whether they believed that vaccination caused actual influenza and whether they believed that vaccination was effective.[18] This type of analysis could not be done on this occasion as the number of responders outside of Mater Dei Hospital had to be amalgamated for statistical purposes.

There really is no excuse not to take the vaccine. Vaccine Adverse Event Reporting Systems have shown that medical contraindications are few, that side effects are mild and typically resolve within two days.[19-20]

### Influenza vaccination side effects.[20]

- Soreness, redness, and/or swelling at the vaccination site
- Headache
- Fever
- Nausea
- Muscle aches

The rate of true serious adverse effects (e.g. severe allergic reaction) is circa 1 in 300,000 doses and this is far lower than the risk of pneumonia and/or death following influenza infection.[20] Cost (in Malta) is not an issue as the vaccine is available for free for healthcare workers, or at a nominal price of circa €10 if taken privately. There is minimal inconvenience in vaccine administration as it is offered at the workplace as a quick intramuscular injection.

## Institutional Responsibility and the Influenza season 2020-21

Healthcare workers and their institutions accept professional responsibility for the care and well-being of their patients,[7] an accountability that is accompanied by the obligation to follow evidence-based practices.[21] Clearly, "institutions are obligated to enforce universal vaccination of their health care workers against seasonal influenza."[7]

In anticipation of increased influenza vaccine demand next season, manufacturers are ramping up production facilities. Indeed, a Reuters/Ipsos poll of 4,428 adults conducted between 13-19 May 2020 found that 60% of U.S. adults plan to take the vaccine, as opposed to the <50% uptake in this country.[22] Yet another survey between January and May showed willingness to take the vaccine increased from 34 to 65% and an increasing likelihood to take the vaccine at a pharmacy rather than a medical clinic or a healthcare center.[22] Demand for the vaccine is expected to be so heavy that options being considered are vaccine administration in parks, community centres and even home visits for vulnerable patients.[22] Heightened interest in influenza (and pneumococcal) vaccines is evident worldwide.[23]

This is partly driven not only by public health but also the possibility of "COVID-19 and flu, a perfect storm",[24] as well as by studies that show a potentially protective effect of the influenza vaccine on COVID-19 mortality in the elderly.[25]

## Conclusions

Healthcare worker influenza vaccination clearly benefits patients, the vaccination burden is minimal and it is unethical for these workers not to take the vaccine.[7] Institutions should strongly promote employee vaccination uptake with educational campaigns that target misconceptions and reinforce the contention that vaccination is integral to ethical, beneficent, and professionally competent care.[7] Making the vaccine mandatory may also be an option.

## References


1. Centers for Disease Control and Prevention FluView: A Weekly Influenza Surveillance Report Prepared by the Influenza Division. 24 April 2009. Retrieved 26 April 2009.
2. World Health Organization Media Center. Fact sheet N°211: influenza. 2003. Available at: http://www.who.int/mediacentre/factsheets/2003/fs211/en. Accessed May, 2020.
3. Salgado CD, Farr BM, Hall KK, Hayden FG. Influenza in the acute hospital setting [published correction appears in Lancet Infect Dis 2002 Jun;2(6):383]. Lancet Infect Dis. 2002;2(3):145-155. doi:10.1016/s1473-3099(02)00221-9
4. Evans ME, Hall KL, Berry SE. Influenza control in acute care hospitals. Am J Infect Control. 1997;25(4):357-362. doi:10.1016/s0196-6553(97)90029-8
5. Horcajada JP, Pumarola T, Martínez JA, et al. A nosocomial outbreak of influenza during a period without influenza epidemic activity. Eur Respir J. 2003;21(2):303-307. doi:10.1183/09031936.03.00040503
6. Centers for Disease Control and Prevention. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR Morb Mortal Wkly Rep. 2011;60(RR07):1–45.

7. Cortes-Penfield N. Mandatory influenza vaccination for health care workers as the new standard of care: a matter of patient safety and nonmaleficent practice. Am J Public Health. 2014;104(11):2060-2065. doi:10.2105/AJPH.2013.301514

8. van den Dool C, Bonten MJ, Hak E, Wallinga J. Modeling the effects of influenza vaccination of health care workers in hospital departments. Vaccine. 2009;27(44):6261-6267. doi:10.1016/j.vaccine.2009.07.104

9. Jiang S, Shi ZL. The First Disease X is Caused by a Highly Transmissible Acute Respiratory Syndrome Coronavirus [published online ahead of print, 2020 Feb 14]. Virol Sin. 2020;1-3. doi:10.1007/s12250-020-00206-5

10. Grech V, Borg M. Influenza vaccination in the COVID-19 era [published online ahead of print, 2020 Jun 18]. Early Hum Dev. 2020;148:105116. doi:10.1016/j.earlhumdev.2020.105116

11. Sansone K. Government targets 200,000 flu shots this year. MaltaToday. 9 June 2020. https://www.maltatoday.com.mt/news/national/102876/government_targets_200000_flu_shots_this_year#.XwgoUOosGUk

12. Talbot TR, Babcock H, Caplan AL, et al. Revised SHEA position paper: influenza vaccination of healthcare personnel. Infect Control Hosp Epidemiol. 2010;31(10):987-995. doi:10.1086/656558

13. Potter J, Stott DJ, Roberts MA, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. J Infect Dis. 1997;175(1):1-6. doi:10.1093/infdis/175.1.1

14. Carman WF, Elder AG, Wallace LA, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. Lancet. 2000;355(9198):93-97. doi:10.1016/S0140-6736(99)05190-9

15. Hayward AC, Harling R, Wetten S, et al. Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. BMJ. 2006;333(7581):1241. doi:10.1136/bmj.39010.581354.55

16. Lemaitre M, Meret T, Rothan-Tondeur M, et al. Effect of influenza vaccination of nursing home staff on mortality of residents: a cluster-randomized trial. J Am Geriatr Soc. 2009;57(9):1580-1586. doi:10.1111/j.1532-5415.2009.02402.x

17. Millner VS, Eichold BH 2nd, Franks RD, Johnson GD. Influenza vaccination acceptance and refusal rates among health care personnel. South Med J. 2010;103(10):993-998. doi:10.1097/SMJ.0b013e3181eda3d5

18. Spiteri G. Influenza vaccine coverage survey among high risk groups in Malta (University of Malta, unpublished Master's dissertation, 2009). Accessed May 2020. https://www.um.edu.mt/library/oar//handle/123456789/42629

19. Centers for Disease Control and Prevention. Guide to vaccine contraindications and precautions. 2008. Available at: http://www.cdc.gov/vaccines/recs/vac-admin/downloads/contraindications-guide-508.pdf. Accessed December 26, 2012.

20. Centers for Disease Control and Prevention. Seasonal influenza vaccine safety: a summary for clinicians. 2012. Available at: http://www.cdc.gov/flu/professionals/vaccination/vaccine_safety.htm. Accessed December 26, 2012.

21. Vellozzi C, Burwen DR, Dobardzic A, Ball R, Walton K, Haber P. Safety of trivalent inactivated influenza vaccines in adults: background for pandemic influenza vaccine safety monitoring. Vaccine. 2009;27(15):2114-2120. doi:10.1016/j.vaccine.2009.01.125

22. Reuters. Fears of coronavirus second wave prompt flu push at U.S. pharmacies, drugmakers. May 2017. https://www.reuters.com/article/us-health-coronavirus-flu-focus/fears-of-coronavirus-second-wave-prompt-flu-push-at-u-s-pharmacies-drugmakers-idUSKBN2321F0

23. Paguio JA, Yao JS, Dee EC. Silver lining of COVID-19: Heightened global interest in pneumococcal and influenza vaccines, an infodemiology study [published online ahead of print, 2020 Jun 25]. Vaccine. 2020;S0264-410X(20)30855-0. doi:10.1016/j.vaccine.2020.06.069

24. Belongia EA, Osterholm MT. COVID-19 and flu, a perfect storm. Science. 2020;368(6496):1163. doi:10.1126/science.abd2220

25. Zanettini C, Omar M, Dinalankara W, et al. Influenza Vaccination and COVID19 Mortality in the USA. Preprint. medRxiv. 2020;2020.06.24.20129817. Published 2020 Jun 26. doi:10.1101/2020.06.24.20129817

MMSG
ORIGINAL ARTICLE

# Complication, patency and incidence rates of first-time vascular dialysis access fashioned in Malta

Thomas Gatt, Adriana Grech, Kevin Cassar

## Background

The aim of the study was to assess first-time arteriovenous fistulae (AVFs) and grafts fashioned over a 5 year period in Malta, and analyse their patency and complication rates. The study also investigates compliance with Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for fistula incidence.

## Methods

Patients who underwent surgery between January 1st 2012 and December 31st 2016 were identified through the vascular surgery database at Mater Dei Hospital - Malta and followed up until 31st December 2017. Complications, interventions and patency duration were recorded from patient notes. Patency rates were calculated with Kaplan-Meier curves and log-rank test was used to compare significance between the curves.

## Results

A total of 258 vascular access (VA) procedures were analysed, only 242 of which were used for haemodialysis. The chance of a VA developing no complications was 38%, with stenosis and thrombosis rates of 36.8% and 24.8% respectively. There was no significant difference between the complication rates or intervention frequency when comparing different fistula types. Of the 207 patients who had AVFs created since January 2012, only 26.1% ($n$=54) had creation prior to initiation of haemodialysis. Primary patency survival rates for first-time AVFs were 58.7±7.1% at 1 year and 48.1±7.4% at 2 years. The assisted primary rates were 73.7±6.3% at 1 year and 67.6±6.9% at 2 years. The secondary patency rates were 76.4±6.1% (95% CI, 70.3%-82.5%) at 1 year and 70.8 ±6.9% at 2 years. There was no significant difference when comparing primary ($p$=0.539), assisted primary ($p$=0.634) or secondary patency ($p$=0.783) rates for the different AVF types.

## Conclusion:

In Malta, AVF incidence lags behind the European average of 66%, but patency rates compare favorably with most other countries.

**Thomas Gatt***
MD (Melit)
Vascular Surgery Unit
Mater Dei Hospital
Msida, Malta
thomas.p.gatt@gov.mt

**Adriana Grech**
MD (Melit)
Vascular Surgery Unit
Mater Dei Hospital
Msida, Malta

**Kevin Cassar**
MD (Malta), MMEd (Dundee), FRCS (Ed), MD (Abderdeen), FRCS (Gen Surg), FFSTEd
Vascular Surgery Unit
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

The number of patients receiving renal dialysis is steadily increasing, particularly in countries like Malta with a high prevalence of diabetes mellitus. Renal guidelines recommend the use of longer and more frequent haemodialysis (HD) sessions for which vascular access is required.[1] The aim of this study is to assess first-time arteriovenous fistulae (AVFs) and arteriovenous grafts (AVGs) fashioned over a 5 year period in Malta, and analyse their patency and complication rates. The study also investigates the time of fistula creation relative to haemodialysis start date, and compliance with Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines with regard to fistula incidence.[2]

## Materials and Methods

### Data Collection

All patients undergoing AVF or AVG creation surgery between January 1st 2012 and December 31st 2016 were identified through the vascular surgery database at Mater Dei Hospital, Malta. This hospital is the only centre in Malta were vascular access is fashioned surgically and is thus representative of the entire Maltese population. Vascular access procedures are performed by one vascular surgeon in Malta.

The vascular surgery history of this cohort was followed up until 31st December 2017. Complications, interventions and patency rates for all fistulae were recorded. For patients who passed away during the study period, records were reviewed till the date of death.

Data on patient age and gender, the type and site of fistula created, the date when created, number of days of patency, types of complications, types of interventions required, date of HD initiation and the date of death were collected.

Data for time of HD initiation was collected from records kept by the Mater Dei Hospital Renal Unit. The only digital records found available had only started being kept from January 2013 onwards. For earlier data, HD start date was taken as the date the patient was first registered to the renal unit on iSoft Clinical Manager. Dates from both sources were cross checked for accuracy.

Only patients above 18 years, who had a first-time AV fistula or graft created locally between the data collection period, were included in this study. Patients whose VA was not used for hemodialysis, were included in analysis of the fistula types created, however excluded from analysis of the complication and patency rates. This was done to eliminate bias from unused accesses.

### Definitions

Definitions of vascular terms were as per standardized definitions by Lee et al. [3] The term vascular access (VA) was used to define any AVF or AVG. When referring to AVFs, we were including brachiocephalic, radiocephalic, ulnarcephalic, snuffbox and transposed brachiobasilic, ulnar basilica and radiobasilic fistulae. AVGs were defined as any artificial prosthetic segment used to contact the artery and vein. [3]

Complications were classified as thrombosis, stenosis, complete occlusion, infection, steal syndrome, aneurysmal dilation and non-maturation.[3] Only complications documented in the patient's notes were recognized. In some cases a fistula or graft may have

developed a recurrence of the complication after it was initially treated, and in other cases, more than one complication may have co-existed.

The interventions carried out on a VA were classified as angioplasty, thrombectomy and any surgical revision of the fistula or graft. Again, many repeat interventions may have been carried out on the same fistula or graft.[3]

Patency was defined as described by Sidawy et al.[4] Primary patency was defined as time of access placement to the time of first angioplasty. Assisted primary patency was defined as time of access to the time of first thrombectomy. Secondary patency was defined as the time of access placement to access abandonment. Fistula incidence rates refer to the amount of people starting dialysis with a functioning fistula. Survival rates refer to the amount of fistulas which maintained their patency.

*Statistics*IBM SPSS Statistics 20.0 software was used to analyse the collected data. Comparison between categorical variables was with the chi-squared test. Patency rates were calculated with survival analysis curves (Kaplan Meir curves), and log-rank test was used to compare significance between the curves. A $p$ value of ≤0.05 was considered statically significant in all cases.

## Results

The sample assessed included a total of 258 patients, 70.2% ($n$=181) of which were male, while 29.8% ($n$=77) were female. The mean patient age at the time of fistula creation was 63 years (SD=12.7).

The different types of VA created are shown in Table 1. The most common VA type was brachiocephalic, accounting for 53.1% ($n$=137) of VAs. Radiocephalic ($n$=41), prosthetic grafts ($n$=35), transposed ($n$=27) and snuffbox ($n$=12), and ulnar cephalic ($n$=6) accounted for the rest. A total of 162 fistulas were sited on the left, while 96 were sited on the right.

**Table 1** Types of arteriovenous vascular access created

| | Number (%) | |
|---|---|---|
| Total | 258 | (100) |
| Brachiocephalic | 137 | (53.1) |
| Radiocephalic | 41 | (15.9) |
| At the wrist | 28 | (10.9) |
| At the forearm | 13 | (5.1) |
| Prosthetic graft | 35 | (13.6) |
| Arm Loop | 33 | (12.8) |
| Ulnar Artery to Axillary Vein | 1 | (0.4) |
| External Iliac to Profunda Vein | 1 | (0.4) |
| Snuffbox | 12 | (4.7) |
| Transposed | 27 | (10.5) |
| Brachiobasilic | 24 | (9.3) |
| Ulnarbasilic | 1 | (0.4) |
| Radiobasilic | 2 | (0.8) |
| Ulnarcephalic | 6 | (2.3) |

In cases were a prosthetic graft was fashioned, polytetrafluoroethylene (PTFE) was used in all cases. The majority of these grafts (12.8%, *n*=33) were arm loop fistulas.

### Patient Outcome

Of the 258 patients assessed for VA creation in the 5 year period, a total of 121 patients had died before the 31st December 2017 cut off. Mean number of days between date of fistula creation and death was 510 days.

The majority of patients (82.9%, *n*=214) remained dialyzing until death or until the cut off period. The rest were either transplanted successfully (8.1%, *n*=21), found to not require haemodialysis despite fistula creation (6.2%, *n*=16), stopped renal replacement therapy completely (1.6%, *n*=4) or reverted to peritoneal dialysis (0.8%, *n*=2). One person had left the country and was thus lost to follow-up.

### Complications

The breakdown of the different complications and their frequency, after excluding the 16 VAs which were never used for haemodialysis, are shown in Table 2. The chance of a VA not developing any complications was 38%, whilst the chances of stenosis or thrombosis at least once where 36.8% and 24.8% respectively. With regard to recurrent complications, the total number of stenotic events and thrombotic events were 138 and 102 respectively for 242 VAs.

**Table 2** Complication Rates

| | Number (%) | |
|---|---|---|
| **Total VAs [1]** | **242** | **(100)** |
| No Complications | 91 | (37.6) |
| Stenosis | 89 | (36.8) |
| Thrombosis | 60 | (24.8) |
| Occlusion | 30 | (12.4) |
| Aneurysm | 27 | (11.2) |
| Steal Syndrome | 16 | (6.6) |
| Infection | 6 | (2.5) |
| Non-maturation | 4 | (1.7) |
| Rupture | 3 | (1.2) |
| Other | 4 | (1.7) |

[1] *16VAs were excluded from the original sample, in view of them not ever having been used for dialysis*

**Table 3** Percentage of the most common complications according to each fistula type.

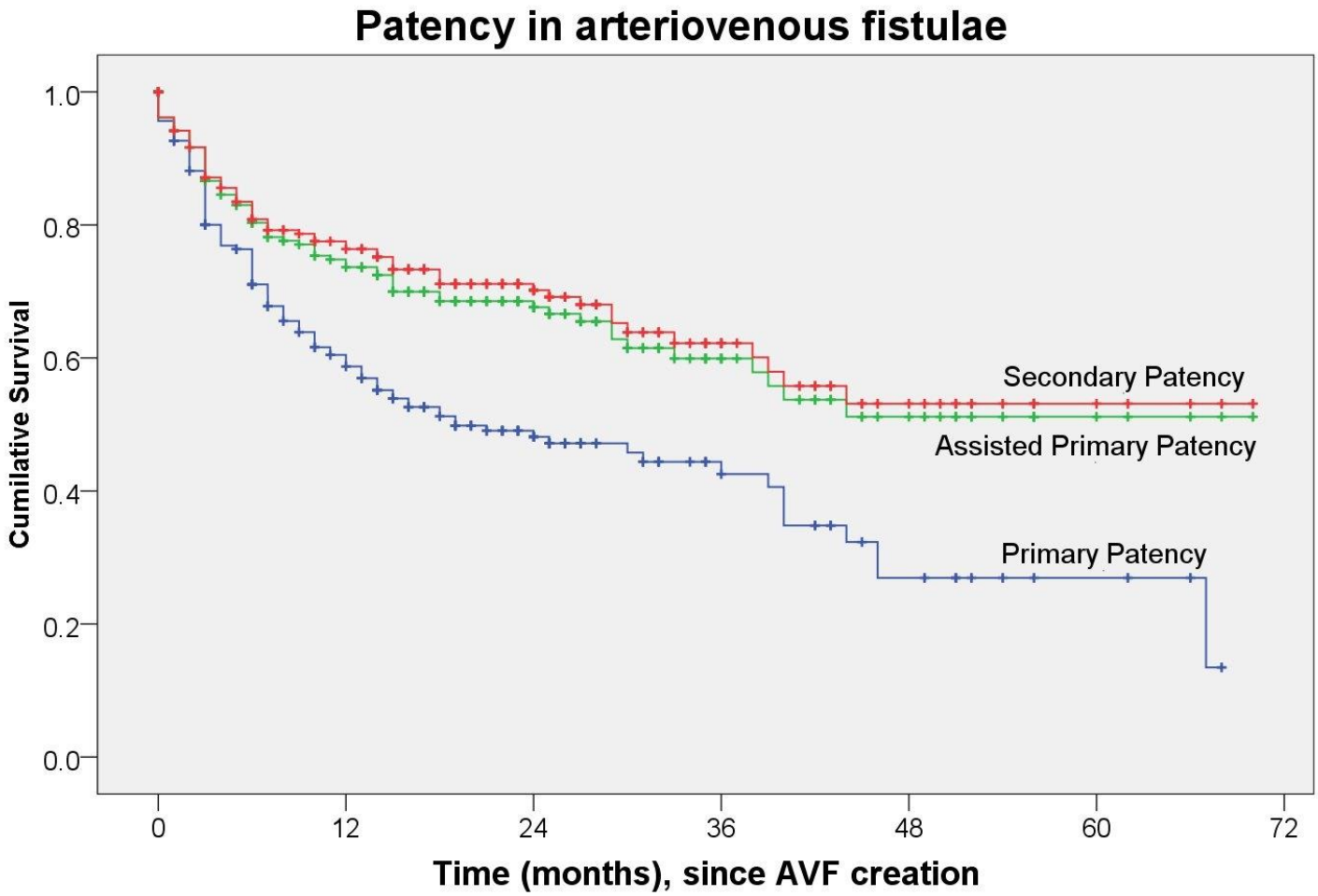
| Fistula Type | N of Fistulas | No Complications | | Thrombosis | | Stenosis | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| All | 242 | 91 | 37.6 | 60 | 24.8 | 89 | 36.8 |
| BC | 126 | 53 | 42.1 | 24 | 19.0 | 41 | 32.5 |
| RC | 39 | 15 | 38.5 | 8 | 20.5 | 13 | 33.3 |
| Graft | 35 | 4 | 11.4 | 24 | 68.6 | 19 | 54.3 |
| TP | 26 | 11 | 42.3 | 3 | 11.5 | 11 | 42.3 |
| SB | 11 | 4 | 36.4 | 1 | 9.1 | 5 | 45.5 |
| UC | 5 | 4 | 80.0 | 0 | 0.0 | 0 | 0.0 |

N, number; BC, brachiocephalic; RC, radiocephalic; SB, snuffbox; TP, transposed; UC, ulnarcephalic.

**Table 4** Frequency of required interventions by fistula type

| Fistula Type | Number of fistulas | Number of Interventions | | | |
|---|---|---|---|---|---|
| | | None | Thrombectomy | Angioplasty | Surgical Revision |
| Brachiocephalic | 126 | 60 | 6 | 38 | 39 |
| Radiocephalic | 39 | 19 | 2 | 11 | 12 |
| Graft | 35 | 6 | 25 | 20 | 12 |
| Transposed | 26 | 12 | 0 | 10 | 5 |
| Snuffbox | 11 | 5 | 0 | 5 | 1 |
| Ulnarcephalic | 5 | 4 | 0 | 1 | 1 |
| **Total** | **242** | **106** | **33** | **85** | **70** |

**Figure 1** Kaplan-Meier survival curves for patency rates of total AVFs, showing primary patency, assisted primary patency and secondary patency




No significant difference between having no complications ($p$=.507), or having thrombosis ($p$=.808), or stenosis ($p$=.513) was observed between the different AVF types (Table 3). However, a significant difference was observed between the rate of no complications ($p$<.001), thrombosis (p< .001) and stenosis ($p$=.020) for PTFE grafts when compared to the rest of the AVFs.

The frequency of interventions carried out according to VA type are shown in Table 4. Over the analysis period, a total of 85 angioplasties and 33 thrombectomies were carried out. Surgical revision of the VA was required 70 times. 43.8% ($n$=106) of the VAs created required no intervention. When looking at the various fistula types, only 16.6% of grafts required no intervention while 47.6% of brachiocepahlic, 48.7% of radiocephalic and, 46.1% of transposed fistulae required no intervention. When looking at the interventions carried out, we found that AVGs had an intervention rate of 0.27 per VA per year, when compared to AVFs with an intervention rate of 0.11 per VA per year.There was no significant difference between the different fistula types ($p$=.713) however there was significant difference in the rate of intervention between fistula and grafts ($p$<.001).

## AVF Incidence

Out of the 207 patients who had AVFs created since January 2012, only 26.1% (*n*=54) had AVF creation prior to initiation of HD. When calculating incident AVFs after May 2014, the end point of the local study by Caruana et al., the incident rate of AVFs was 28.6%, showing no significant difference (*p*=.584) and hence no significant improvement since the previous study.[5]

## Patency

The primary patency rates for first-time AVFs were 58.7% (95% CI, 51.7%-65.7%) at 1 year and 48.1% (95% CI, 40.7%-55.5%) at 2 years respectively. The assisted primary rates were 73.7% (95% CI, 67.4%-80.0%) at 1 year and 67.6% (95% CI, 60.7%-74.5%) at 2 years., while the secondary patency rates were 76.4% (95% CI, 70.3%-82.5%) at 1 year and 70.8 %(95% CI, 63.9%-77.7%) at 2 years. (Figure 1)

The patency rates according to the different type of VA are shown in Table 5. There was no significant difference when comparing primary patency (*p*=.539), assisted primary patency (*p*=.634) or secondary patency rates (*p*=.783) for the different types of fistulas (Figure 2).

The overall patency of AVGs was found to be lower at 17.1% (95%CI 4.6%-29.6%) primary patency, 17.1% (95%CI 4.6%-29.6%) assisted patency and 48.6% (95%CI 32.1%-65.1%) secondary patency. Comparing to the patency of AVFs (Figure 3.), there was a statistically significant difference between primary patency (*p*<0.001), assisted primary patency (*p*<0.001) and secondary patency (*p*=.010)

**Table 5** Patency Rates According to Different Type of VA

| VA Type | Overall | | | 1 Year | | | 2 Years | | |
|---|---|---|---|---|---|---|---|---|---|
| | P (%) | AP (%) | SP (%) | P (%) | AP (%) | SP (%) | P (%) | AP (%) | SP (%) |
| Grafts | 17.1 | 17.1 | 48.6 | 17.8 | 25.7 | 67.4 | 0 | 10.4 | 45.2 |
| All Fistulas | 47.8 | 66.2 | 68.6 | 59.7 | 74.3 | 76.9 | 48.9 | 68.1 | 70.8 |
| BC | 47.6 | 64.3 | 68.3 | 61 | 73.3 | 77.6 | 46.1 | 63.7 | 67.7 |
| RC | 48.7 | 61.5 | 61.5 | 58.4 | 71.5 | 71.5 | 53 | 68.8 | 68.8 |
| SB | 36.4 | 81.8 | 81.8 | 45.6 | 90.9 | 90.9 | 45.6 | 90.9 | 90.9 |
| TP | 46.2 | 73.1 | 73.1 | 58.4 | 75.1 | 75.1 | 49.3 | 75.1 | 75.1 |
| UC | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 |

*VA, Vascular Access; P, primary patency; AP, assisted primary patency; SP, secondary patency; BC, brachiocephalic; RC, radiocephalic; SB, snuffbox; TP, transposed; UC, ulnarcephalic.*

**Figure 2** Kaplan-Meier survival curves for secondary patency rates, according to the different types of fistulas

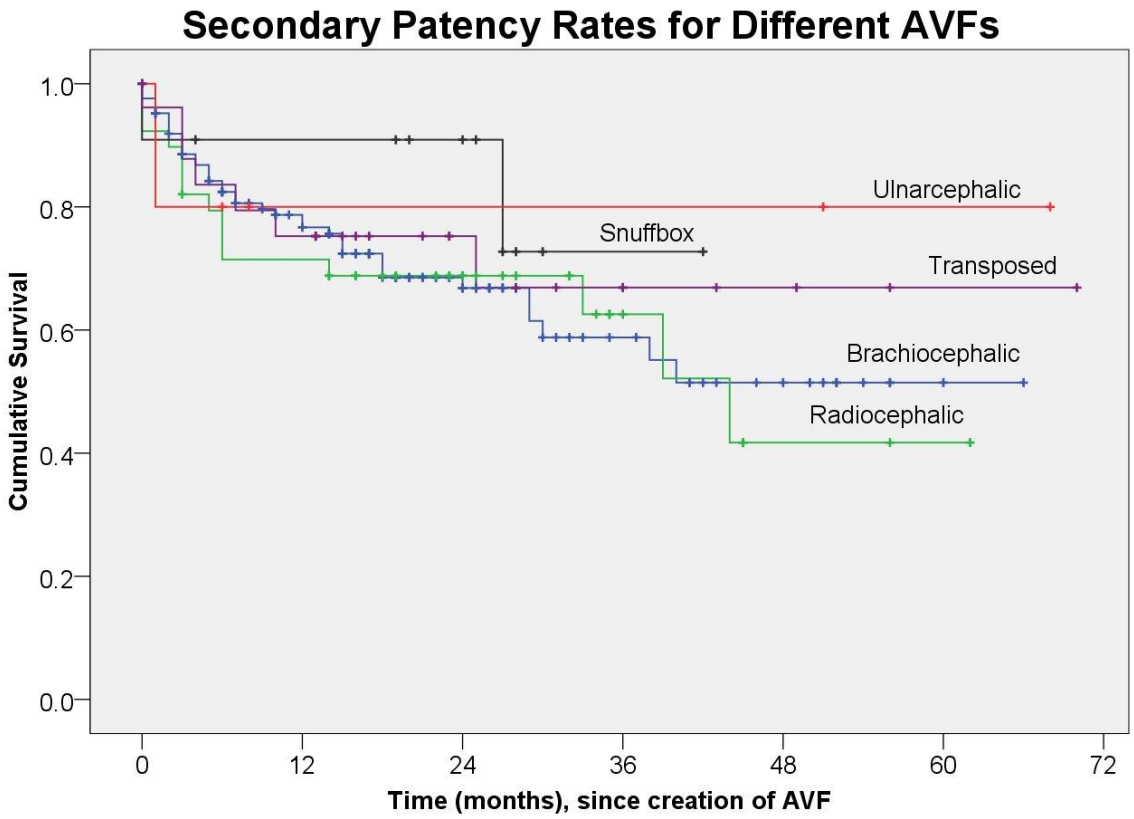
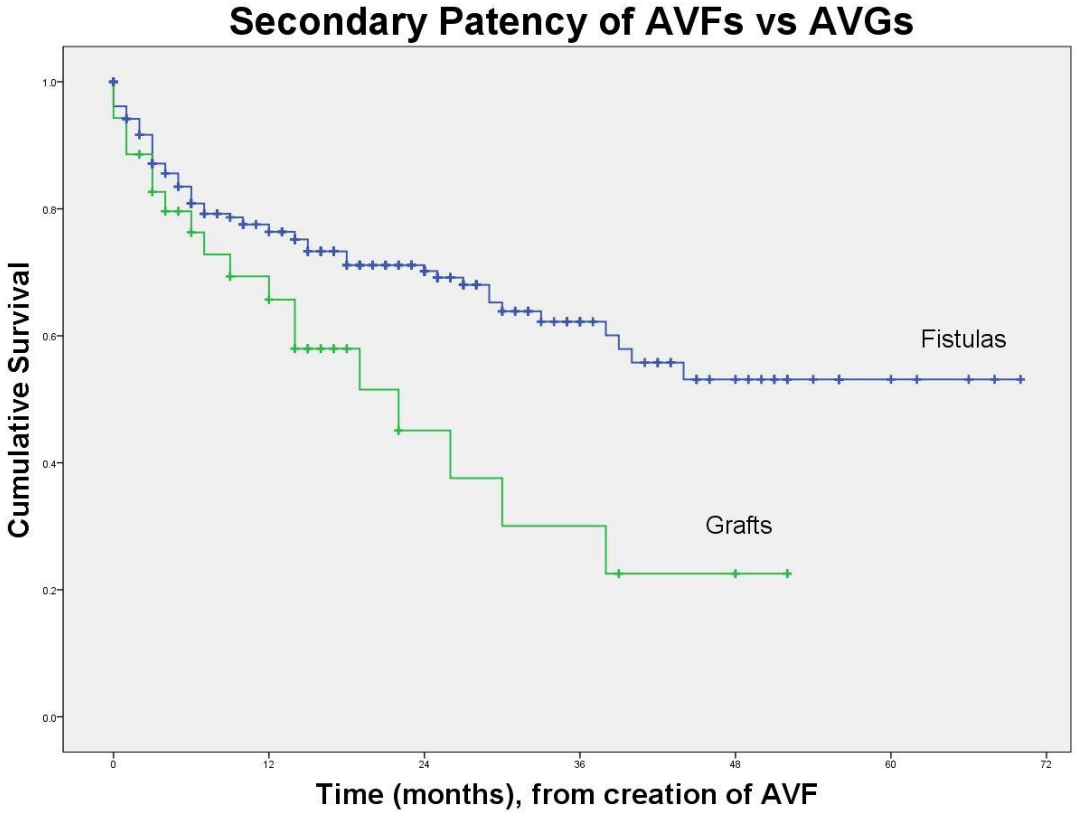



**Figure 3** Kaplan-Meier survival curves comparing the secondary patency between AVFs and AVGs



## Discussion

The patency rates of AVFs fashioned in Malta over a 5 year period are similar to those reported in international literature.[5-7] Al-Jaishi et al. who carried out a metaanalysis of 12,838 fistulas over a 12 year period, concluded that one may expect a primary patency rate of 60±4% (1 year) and 51±7% (2 years), and a secondary patency of 71±7% (1 year) and 64±9% (2 years).[6] These rates are very similar to patency rates achieved locally over the analysis period. In our study, the 1 year secondary patency rate of 76.4±6.1% is also similar to the 83.1% 1 year patency rate reported locally by Caruana et al. [5]

While McGrogan et al. had noted inferior primary and secondary patency rates of radiocephalic fistulas compared to brachiocephalic,[8] we found no significant difference between primary or secondary patency rates between the two ($p$=.812 and $p$=.765 respectively). Similarly we found no significant difference when comparing all the different fistula types.

There are varying patency rates reported when it comes to PTFE grafts. Our secondary patency rates of grafts are similar to those reported in studies by Ravari et al.[9] and Disbrow et al. [10] When it comes to primary patency rates, while our local rates do compare to some studies eg. 19.5% (1 year)[11], there are other studies which record considerably higher patency rates of 42-43% after a year.[12-13]

With transposed fistulas we noted similar patency rates at 1 and 2 year intervals, when compared to non-transposed fistulas. This differs to the study by Choi et al. which noted superiority of transposed patency rates after 2 years, despite similar rates after 1 year.[14]

With regards to snuffbox fistulas, we reported very satisfactory assisted and secondary patency rates up to 2 years follow up. Our 1 year secondary patency rates (90.9%) are in keeping with the 93±4% quoted in literature however we lag behind in primary patency (45.6%) when comparing to patency rates quoted from 65%-83%.[15-16] Despite this, it should be noted that our snuffbox fistula sample was relatively small (5.3%, $n$=11), and may therefore not be thoroughly representative. Snuffbox fistulas have the advantage of easier anastomosis due to closer proximity between artery and vein, as well as a reduced risk of steal in view of narrower artery caliber, which makes them an attractive option for fistula creation.[15]

Incidence of complications in fistulae were in keeping with reported incidence published by Stolic et al, with thrombosis 17-25% and stenosis 14-42%.[17] Although no difference in complication rates were noted between fistula types locally, it must be said that the ulnarcephalic and snuffbox fistula samples were small, and may not be fully representative. We did note that 43.8% of AVFs and AVGs created required some sort of intervention, be it surgical or endovascular. This highlights the high demand of stress placed on, not only the health service, but also on the physical and mental wellbeing of already vulnerable patients.

In 2006, the National Kidney Foundation (NFK) through the Kidney Disease Outcomes Quality Initiative (KDOQI) released updated guidelines which recommends incident fistula rates of 50% and at least 40% prevalent rates in patients undergoing haemodialysis. The Centers for Medicare & Medicaid Services (CMS) implemented a Fistula First Breakthrough Initiative (FFBI) in an attempt to

achieve these rates. In 2009, the target incidence rate was increase to 65%. In the study carried out by Caruana et al, which reviewed fistulae in Malta from October 2012 to May 2014 showed that only 25% of people had a functioning fistula before haemodialysis.[5] This is in keeping with our findings of 26.1% Even when analyzing our data from May 2014 onwards, the rate showed no significant improvement since the last local study carried out indicating that recommended targets are far from being reached.

When comparing this to countries across the world, we find that Malta lags behind the European average (66%) and most of the major countries such as Germany (72%), Japan (69%), Italy (61%), Spain (64%) and UK (37%). Our fistula incidence rates are comparable to Belgium (26%) and Canada (26%) while surpassing those of the USA (16%).[18] While the FFBI initiative had brought on a welcome improvement in fistula rates, it also led to increase in AVF failure rates and procedures required to salvage them.

In conclusion, we found that in Malta the AVF incidence lags behind the European average, but patency rates are comparable with most other countries. Efforts should be made for earlier referral to vascular surgeons and close liaison with the attending nephrologist to ensure the best possible patient-centered care.

## Summary Box

What is known about this subject?

- Need for arteriovenous fistulae and grafts are increasing with more frequent and longer haemodialysis sessions
- Fistula should be created prior to initiation of haemodialysis
- In Malta, incidence rates of fistulas prior to haemodialysis were at 25% in 2014

What are the new findings?

- Patency and complication rates of Maltese fistulas are comparable with European standards
- No increase in fistula incidence over the past 3 years since last local study
- We lag behind European counterparts in fistula incidence

## References


1. KDOQI Clinical Practice Guideline for Hemodialysis: 2015 Update [Internet]. National Kidney Foundation. 2015 [cited 16 July 2018]. Available from: https://www.kidney.org/professionals/guidelines/hemodialysis2015
2. 2006 Updates Clinical Practice Guidelines and Recommendations [Internet]. www.kidney.org. 2006 [cited 16 July 2018]. Available from: https://www.kidney.org/sites/default/files/docs/12-50-0210_jag_dcp_guidelines-hd_oct06_sectiona_ofc.pdf
3. Lee T, Mokrzycki M, Moist L, Maya I, Vazquez M, Lok C. Standardized Definitions for Hemodialysis Vascular Access. Seminars in Dialysis. 2011;24(5):515-524.

4. Sidawy A, Gray R, Besarab A, Henry M, Ascher E, Silva M et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses. Journal of Vascular Surgery. 2002;35(3):603-610.

5. Caruana L, Vella Baldacchino R, Sacco M, Cassar K. Autologous haemodialysis access in Malta. Malta Medical Journal. 2015;27(5):4-7.

6. Al-Jaishi A, Oliver M, Thomas S, Lok C, Zhang J, Garg A et al. Patency Rates of the Arteriovenous Fistula for Hemodialysis: A Systematic Review and Meta-analysis. American Journal of Kidney Diseases. 2014;63(3):464-478.

7. Kalman P, Pope M, Bhola C, Richardson R, Sniderman K. A practical approach to vascular access for hemodialysis and predictors of success. Journal of Vascular Surgery. 1999;30(4):727-733.

8. McGrogan D, Al Shakarchi J, Khawaja A, Nath J, Hodson J, Maxwell A et al. Arteriovenous fistula outcomes in the elderly. Journal of Vascular Surgery. 2015;62(6):1652-1657.

9. Ravari H, Kazemzade G, Modaghegh M, Khashayar P. Patency rate and complications of polytetrafluoroethylene grafts compared with polyurethane grafts for hemodialysis access. Upsala Journal of Medical Sciences. 2010;115(4):245-248.

10. Disbrow D, Cull D, Carsten C. Comparison of Arteriovenous Fistulas and Arteriovenous Grafts in Patients With Favorable Vascular Anatomy and Equivalent Access to Health Care: Is a Reappraisal of the Fistula First Initiative Indicated?. Journal of Vascular Surgery. 2013;58(2):549-550.

11. Kim W, Pyun W, Kang B. The Primary Patency of Percutaneous Transluminal Angioplasty in Hemodialysis Patients With Vascular Access Failure. Korean Circulation Journal. 2011;41(9):512.

12. Hodges T, Fillinger M, Zwolak R, Walsh D, Bech F, Cronenwett J. Longitudinal comparison of dialysis access methods: Risk factors for failure. Journal of Vascular Surgery. 1997;26(6):1009-1019.

13. Woo K, Doros G, Ng T, Farber A. Comparison of the efficacy of upper arm transposed arteriovenous fistulae and upper arm prosthetic grafts. Journal of Vascular Surgery. 2009;50(6):1405-1411.e2.

14. Choi H, Lal B, Cerveira J, Padberg F, Silva M, Hobson R et al. Durability and cumulative functional patency of transposed and nontransposed arteriovenous fistulas. Journal of Vascular Surgery. 2003;38(6):1206-1211.

15. Letachowicz K, Gołębiowski T, Kusztal M, Letachowicz W, Weyde W, Klinger M. The snuffbox fistula should be preferred over the wrist arteriovenous fistula. Journal of Vascular Surgery. 2016;63(2):436-440.

16. Wolowczyk L, Williams A, Donovan K, Gibbons C. The Snuffbox Arteriovenous Fistula for Vascular Access. European Journal of Vascular and Endovascular Surgery. 2000;19(1):70-76.

17. Stolic R. Most Important Chronic Complications of Arteriovenous Fistulas for Hemodialysis. Medical Principles and Practice. 2013;22(3):220-228.

18. Pisoni R, Young E, Dykstra D, Greenwood R, Hecking E, Gillespie B et al. Vascular access use in Europe and the United States: Results from the DOPPS. Kidney International. 2002;61(1):305-316.

MMSG
ORIGINAL ARTICLE

# The prevalence of parent reported food hypersensitivity at school entry in Malta

Mariella Porter, Stephen Fallows

Food hypersensitivity refers to an adverse reaction to food at a dose which is tolerated by the majority of individuals[1], which is further classified into allergic and non-allergic food-hypersensitivity.[2]

Research on food hypersensitivity in young children is minimal, with countries like Malta lacking research on this topic. The reported prevalence of food hypersensitivity worldwide for the paediatric population to date in the 21st century ranges from 1% in Denmark to 38.4% in Germany.[3-4] With regards to available research on food hypersensitivity for the age group 4 to 6 years, parent reported prevalence ranges from 4.2 to 11.8%[5-6], with the value going down to 2.5% when including research that reports a point prevalence based on food challenge and/or suggestive history and skin tests.[6]

The main food group causing food hypersensitivity worldwide in the paediatric population aged eighteen and under is reported to be cow's milk and milk products, with other food groups being country specific.[7]

This research aimed to provide local statistics in food hypersensitivity in the paediatric population, as the prevalence of such allergic and non-allergic food hypersensitivity (intolerance) to food in Malta was not previosuly documented. This research has found a 2.5%-point prevalence of food hypersensitivity in the 5-to 6yr-old population under study.

Milk and milk products followed by tree nuts have been identified as the main hypersensitivity causing food in this study.

The statistics and recommendations of this study provide an opportunity to the Maltese Healthcare system to start providing a holistic service which deals with food hypersensitivity.

**Mariella Porter**
B.Ed (Hons) Biology & Chemistry, MSc Human Nutrition
Department of Clinical Sciences & Nutrition
University of Chester,
Chester, UK
m.mariella.porter@gmail.com

**Stephen Fallows**
BSc Nutrition, PhD Food Policy
Department of Clinical Sciences & Nutrition
University of Chester,
Chester, UK

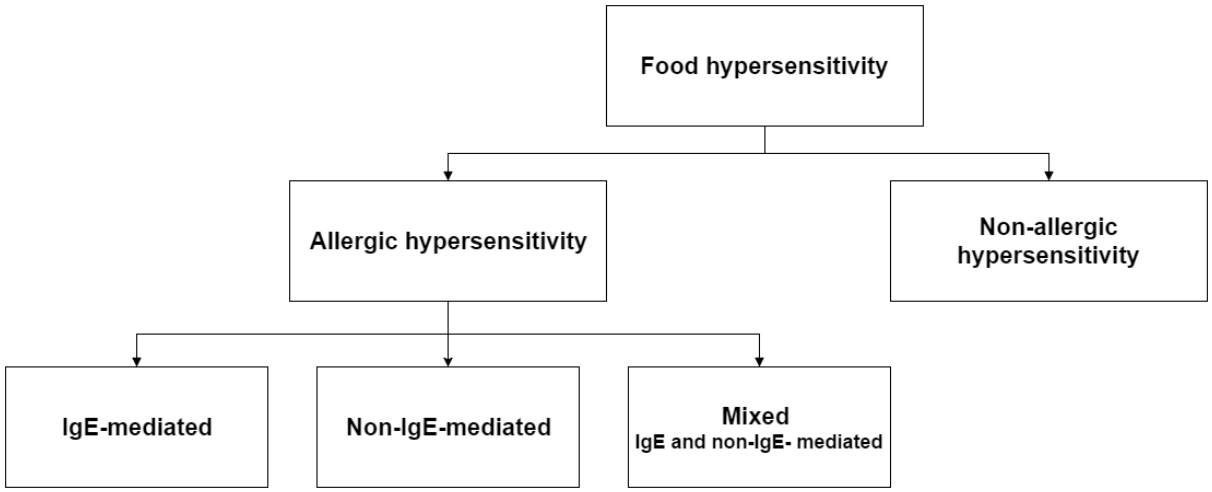
*Corresponding author

## Introduction

According to the nomenclature from the European Academy of Allergy and Clinical Immunology Task Force the term food hypersensitivity is the general term used to refer to any adverse reaction to food (figure 1).[1] This can be further classified into allergic and non-allergic food hypersensitivity[2], more commonly referred to as food intolerance. Madsen[7] also includes food aversion under the umbrella term of hypersensitivity, which is a psychological repulsion to food rather than a reaction to any chemical properties in the food itself.

Reported prevalence of food hypersensitivity depends on various factors, including the age bracket, methodology, food items considered, the country where the study is being conducted, and whether lifetime or point prevalence is researched.[8] Another influencing factor is the nomenclature used by various studies in this field. Whilst terms like 'allergy', 'perceived allergy' or 'food hypersensitivity' have specific scientific definitions, the general public often fails to distinguish between these terms.[9]

**Figure 1** Classification of food hypersensitivity. Adapted from Johansson et al.[1]




## Objectives

This research aimed to provide local statistics in food hypersensitivity in the paediatric population, by analysing the age group 5-to 6-year olds at compulsory school entry. The food which is reported to cause hypersensitivity locally has been analysed through this study and compared to the main causes of food induced hypersensitivities in other countries.

The term 'food hypersensitivity' has been used in this study in order to incorporate all reactions to food and to prevent having the participants misdiagnose non-allergic food hypersensitivity or aversion with the much - misused term 'food allergy'.

## Methods

Following approval by the Research Ethics Committee, Faculty of Life Sciences at the University of Chester; Research and

Development department at the Ministry of Education and Employment in Malta, and Secretariat for Maltese Catholic Education to carry out research in Maltese schools, between January and March 2015, every school in Malta which includes children aged 5-to 6 years (*N*=83) was invited to participate in this research study. Each school was provided with an electronic letter of invitation, together with a participant school information sheet. This included all state (*n*=50), church (*n*=22) and independent schools (*n*=11) on the island, with a total of 4,426 5-to 6-yr-olds in Year 1. Out of this total, 2,274 were boys (51.4%) and 2,152 girls (48.6%). The Heads of Schools who decided to participate in the study were asked to provide the number of Year (Grade) 1 students or equivalent (aged 5-to 6years), who have reported food hypersensitivity on the mandatory Health Information Sheet provided by the school at the beginning of the scholastic year.

The participant schools were then provided with letters of invitation, participant parent information sheets and questionnaires to be distributed to the parents who had reported food hypersensitivity. Figure 2 shows a flow chart for the methodology followed in this study.

**Figure 2** Study flow chart.

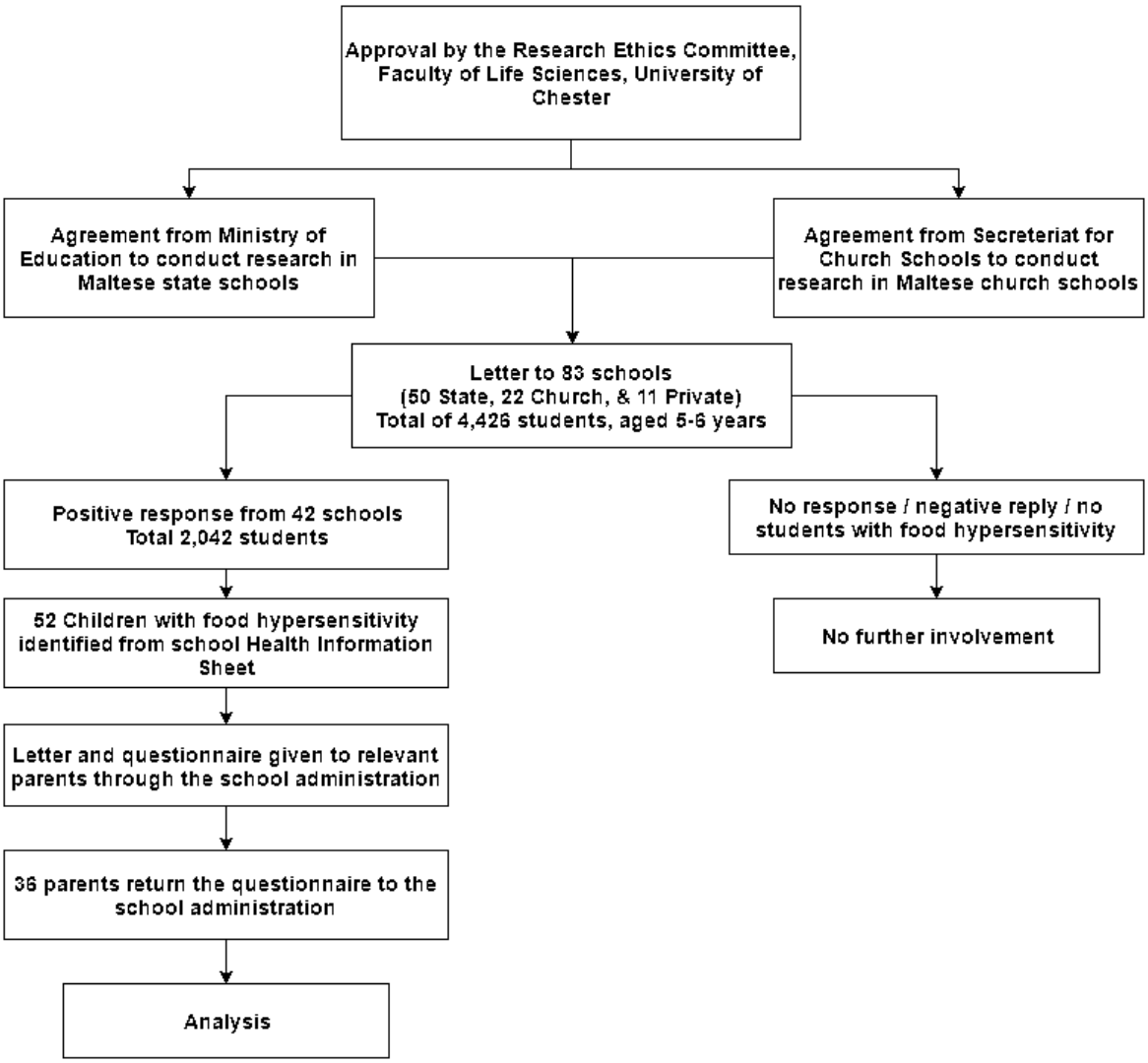
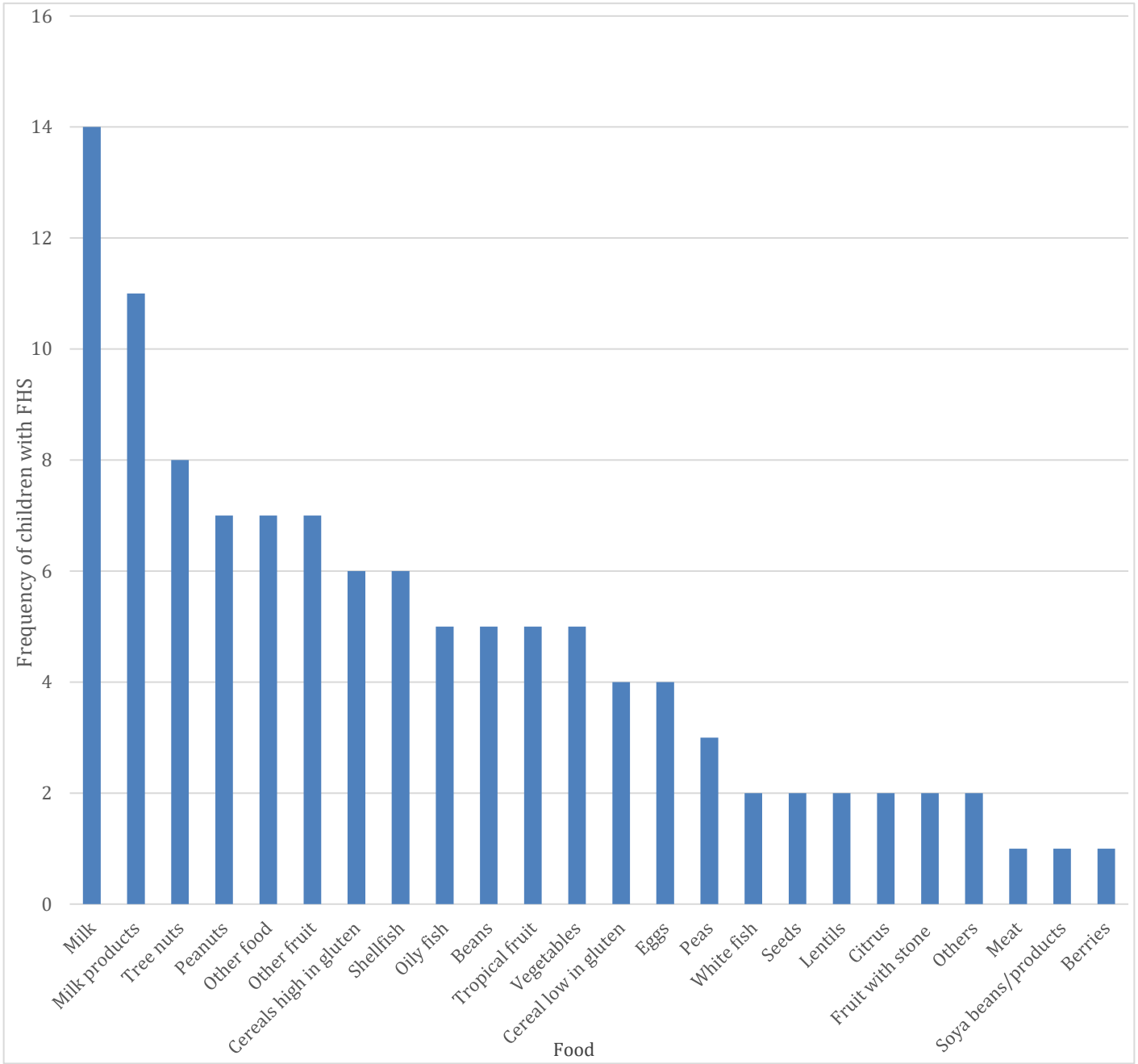


**Figure 3** Frequency of food causing hypersensitivity in the 5-to-6-yr-old group.




The questionnaire used for this study was validated by using past research on parent reported food induced hypersensitivity. All communication with parents including the questionnaires, was provided in both English and Maltese in order to facilitate understanding. This should have increased the rate of questionnaire content understanding.

All questionnaire data was entered into SPSS Version 22, where percentages were used to calculate the overall prevalence of food hypersensitivity in Malta, whilst frequencies were used to calculate the number of children showing hypersensitivity to each questioned food.

## Results

A total of 42 schools (50.6%) accepted to participate. This included 48% of the state,

59% of church and 45.5% of private schools. The cohort of students from participant schools was 2,042 tallying to 46.1% of the total Year 1 population in Malta for the scholastic year under study. School administration from the participating schools reported a total of 52 food hypersensitivity cases. This indicates a 2.5%-point prevalence for food hypersensitivity in the 5-to 6-yr-old population. Out of the 52 cases, 36 (69%) questionnaires were completed and returned by the parents. The sample of reported students with food hypersensitivity included

21 (58.3%) boys and 15 (41.7%) girls.

When it comes to the main food causing hypersensitivity in the 5-to 6-yr-old sample, milk and milk products were the main causes, affecting 14 (38.9%) and 11 (30.6%) participants respectively, followed by tree nuts affecting 8(22.2%). Peanuts, other fruit and the 'other food' category all showed a prevalence of 19.4%. The prevalence of food hypersensitivity for the various food included in this study is shown in Figure 3.

When asked how much of the food causing hypersensitivity can the child tolerate before a reaction is observed it resulted that 20 (55.6%) of the students could not have any of the food causing hypersensitivity.

**Table 1** Frequency and percentage of children showing different levels of reaction when exposed to the food causing hypersensitivity

| Level of reaction to food | Number of children | Percentage of children (%) |
|---|---|---|
| Swollen lips, face, eyes | 10 | 27.8 |
| Itchy or tingling mouth | 6 | 16.7 |
| Hives (allergic urticaria) or Itchy skin rash | 9 | 25 |
| Eyes symptoms | 1 | 2.8 |
| Atopic rash or worsening of atopic skin (infantile/atopic eczema) | 11 | 30.6 |
| Itching in the outer ear | 1 | 2.8 |
| Anal rash or itching | 5 | 13.9 |
| Hoarse voice, difficulty swallowing, swollen tongue | 4 | 11.1 |
| Difficult or noisy breathing, wheeze or persistent cough | 7 | 19.4 |
| Nausea or vomiting | 10 | 27.8 |
| Diarrhoea | 6 | 16.7 |
| Persistent dizziness / pale or floppy | 3 | 8.3 |
| Suddenly sleepy or collapse | 6 | 16.7 |
| Unconscious | 1 | 2.8 |
| Tummy Ache | 1 | 2.8 |
| Other swollen body parts | 1 | 2.8 |

Note: Percentage values do not add up to 100% due to the possibility to choose multiple responses from the questionnaire.

In order to obtain feedback on the level of reaction these children have to the hypersensitivity causing food, the parents were asked to mark the reactions observed when the child was exposed to the food. Table 1 shows the frequency of children showing different levels of reaction when exposed to the food causing hypersensitivity.

## Discussion

The 2.5 %-point prevalence of food hypersensitivity at school entry in Malta has been found to be equivalent to the prevalence in a study by Venter et al.[6] on the Isle of Wight, following food challenge and/or suggestive history. These two studies have various similarities in that both include a study on an island, both research the prevalence at school entry where the target population was approached via schools, and all the schools on each island were invited to participate. Other studies with similar prevalence include those in Tampere, Finland by Jarpenpaa et al.[10] and Kallio et al.[11], where a parent reported point prevalence of food hypersensitivity to basic food of 2.5% and 2.7% were reported respectively. Like the Maltese study, these researches were also carried out on first graders.

Whilst the prevalence in this study focused on a specific age group, the putative rather low food hypersensitivity prevalence in Malta is worth speculating. As an island in the middle of the Mediterranean where locals traditionally follow a Mediterranean diet, this diet could be offering protection against hypersensitivity. Yet with the relatively recent added incorporation of a vast range of international foods into the Maltese diet, the protective effect of the Mediterranean diet in Malta could still be questioned.

A hypothetical protective factor for a low rate of hypersensitivity in Malta could be the early introduction of certain food during weaning. Maltese research by Buttigieg, Townsend-Rocchiccioli and Ellul[12] on maternal awareness of health promotion in preschool children, has revealed early introduction of food. In fact, a study by Toit et al.[13] has shown how the rate of peanut allergy in Jewish 4-to 12-yr-olds living in Israel and consuming peanut through traditional snacks from the first weaning months is 0.12%, compared to 2.05% for Jewish children in the same age group living in London and exposed to peanuts at a later age.

Another hypothetical protective factor is genetics. Since Malta is an island the rate of immigration could be relatively low, resulting in a lower rate of introduction of genes from other populations possibly responsible for food induced hypersensitivity.[14] Hence whilst the Maltese paediatric population could be already exposed to environmental factors known for triggering food hypersensitivity, genetic susceptibility[15] together with the traditional early introduction of basic food[12] could be putative causes for the lower rate of hypersensitivity on the island when compared to international levels.

When it comes to the main food that causes hypersensitivity, similarly to most other European and non-European countries, cow's milk followed by milk products, were found to be the main cause of hypersensitivity in Malta. Yet when it comes to another Mediterranean country, Greece, eggs and 'other food' category were the main foods causing hypersensitivity in a 2007 study by Steinke et al. In Italy research by Caffarelli et al.[16] shows eggs as the second most prevalent food causing hypersensitivity whilst in Malta eggs were reported as the seventh food causing heightened reaction.

Hypersensitivity to peanuts and nuts in Malta is higher than that resulting from studies in Europe by Nwaru et al.[17] and Steinke et al.[5]. Since these food groups have been part of this country's culinary culture for years, their high hypersensitivity prevalence seems puzzling. What could be the cause of such a high prevalence is the increased promoted use of nuts and peanuts in the main dishes due to the introduction of dishes from other countries, which together with the traditional amounts used, could be exposing children from a younger age to a much higher level of these food groups.

Based on the hypothesis that early introduction of food allergens lowers the risk of food allergy, since the Maltese study by Buttigieg et al.[12] does not refer to peanuts and nuts as food groups introduced before 12 months, the late introduction of such food in Maltese children's diet could also be another factor for peanuts and nuts to be reported as top foods causing hypersensitivity.

## Conclusion

What makes this study unique in the field of food hypersensitivity is the small size of the island Malta, where all the schools in this country were invited to participate. In addition, half the schools in Malta have participated in this study and they were evenly distributed around the island. Besides, the number of invited participants and the cohort participating in the Maltese study are amongst the highest when compared to all reviewed research on prevalence of reported food hypersensitivity in the paediatric population. In addition, the prevalence for parent reported hypersensitivity was based on communication with school administration about the reported cases on the Health Information Sheet rather than on returned questionnaires. Hence it can be stated that the prevalence reported is a realistic outcome of the national food hypersensitivity prevalence in the age group studied.

The perceived food hypersensitivity in the age group under study can also be considered as a close measure of the demand for a hypersensitivity clinic in the paediatric population, which could be also applied to the whole Maltese population.[5]

A food hypersensitivity clinic should include a multidisciplinary approach which incorporates the clinical aspects which tests and analyses the hypersensitivity, the nutritional side which guides patients and their families with adjusting to a diet without the hypersensitivity causing food, and the psychological support to socially cope without the hypersensitivity causing food whilst dealing with possible anxiety especially resulting from IgE-mediated anaphylactic reaction risk.[8]

Whilst research in therapy that assists patients outgrow their food hypersensitivity is advancing, it would be beneficial to have local research in this field. This could include work on oral immunotherapy case studies followed by protocols which assist patients with allergies to outgrow their hypersensitivity.

As an outcome of this research, the Maltese Education division and all the participating schools have been provided with safety recommendations that not only will contribute to safeguarding the health of children with food hypersensitivity in Maltese schools, but will also provide the school management team, teachers and support assistants with the much needed strategies when faced with food hypersensitivity cases.

## Acknowledgements

We would like to thank the School Management Team, other school personnel and parents from each participating school, for their collaboration in this study.

## References

1. Johansson SG, Hourihane JO'B, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahtela T, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy. 2001; 56: 813-24.
2. Skypala IJ, Venter C. Food hypersensitivity. Diagnosing and managing food allergies and intolerance. Oxford: Wiley-Blackwell Press; 2009. 4-17, 85-96.
3. Osterballe M, Hansen TK, Mortz CG, Host A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. Pediat Allerg Imm. 2005; 16: 567-73.
4. Roehr CC, Edenharter G, Reimann S, Ehlers I, Worm M, Zuberbier T, et al. Food allergy and non-allergic food hypersensitivity in children and adolescents. Clin Exp Allergy. 2004; 34: 1534-41.
5. Steinke M, Fiocchi A, Kitchlechner V, Ballmer-Weber, B., Brockow, K., Hischenhuber C, et al. Perceived food allergy in children in 10 European nations. J. Allergy Clin Immunol. 2007; 143: 290-5.
6. Venter C, Pereira B, Grundy J, Clayton CB, Arshad SH, Dean T. Prevalence of sensitization reported and objectively assessed food hypersensitivity amongst six-year-old children: A population-based study. Pediat Allerg Imm. 2006; 17: 356-63.
7. Madsen C. Prevalence of food allergy: an overview. Proc Nutr Soc. 2005; 64: 413-7.
8. Jackson WF. Food allergy. Brussels: International Life Sciences Institute; 2003. 3-7.
9. Gupta RS, Springton EE, Smith, B, Pongracic J, Holl JL, Warrier MR. Parent report of physician diagnosis in pediatric food allergy. J. Allergy Clin. Immunol. 2013; 131: 150-156.
10. Jarpenpaa J, Paassilta M, Salmivesi S, Sannisto T, Niitty S, Korppi M. Stability of parent-reported food allergy in six and 7-year old children: the first 5 years of the Finnish allergy programme. Foundation Acta Paediatrica. 2014; 103: 1297-1300.
11. Kallio P, Salmivesi S, Kainulainen H, Paassilta M, Korppi M. Parent-reported food allergy requiring an avoidance diet in children starting elementary school. Acta Paediatr. 2011; 100: 1350-1353.
12. Buttigieg SC, Townsend-Rocchiccioli J, Ellul ML. Maternal awareness of health promotion, parental and preschool childhood obesity. Malta Med.J. 2012; 24: 9-15.
13. Toit GD, Katz Y, Sasieni P, Mesher, D, Maleki, SJ, Fischer HR, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. J. Allergy Clin. Immunol. 2008; 5: 984-91.
14. Hong X, Tsai H, Wang X. Genetics of food allergy. Curr Opin Pediatr. 2009; 21: 770-6.
15. Arrieta MC, Bistritz L, Meddings JB. Alterations in intestinal permeability. Gut. 2006; 55: 1512-20.
16. Caffarelli C, Coscia A, Ridolo E, Povesi Dascola C, Gelmetti C, et al. Parents' estimate of food allergy prevalence and management in Italian school-aged children. Paediatr Int. 2011; 53: 505-510.
17. Nwaru BI, Hickstein L, Panesar SS, Roberts G, Muraro A, Sheikh A. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. J. Allergy Clin. Immunol. 2014; 69: 992-1007.
18. Giovannini M, D'Auria E, Caffarelli C, Verduci E,Barberi S, Indinnimeo L, et al. Nutritional management and follow up of infants and children with food allergy: Italian Society of Pediatric Nutrition/Italian Society of Pediatric Allergy & Immunology Task Force Position Statement. Ital. J. Pediat. 2014; 40: 1-9

MMSG
ORIGINAL ARTICLE

# Local Experience of Transcutaneous Bilirubinometry – An Accurate Alternative to Serum Sampling?

Michelle-Marie Boffa, Mark Anthony Bailey, Helen Borg, Victor Grech

## BACKGROUND

Babies are frequently referred to the Paediatric Emergency Department from the Breastfeeding Clinic and Community Discharge Liaison Service with jaundice, as indicated by high transcutaneous bilirubin (TCB) readings measured using transcutaneous bilirubinometry. Serum bilirubin (SeB) testing is then performed in the Emergency Department and the decision for admission for phototherapy is based upon on the SeB. Strict correlation between these modes of bilirubin measurement would negate the need to verify TCB with SeB in cases where the bilirubin level is clearly above the cut–off value, thus reducing hospital waiting time, costs and time to starting treatment.

## OBJECTIVES

To establish whether TCB is a reliable screening test for neonatal jaundice that may require phototherapy based on the relationship between TCB and SeB levels in patients in Malta.

## METHOD

Neonates referred from the Breastfeeding Clinic to the Paediatric Emergency Department with raised TCB levels over five months (June-October 2017) were included. Data was obtained from the Breastfeeding Clinic, local delivery suite and iSOFT Clinical Database, and interpreted using in-built data analysis tools and custom-made data analysis spreadsheets on Microsoft Excel®.

## RESULTS

There was a significant difference between the two groups, with mean TCB being significantly greater than SeB (t=2.32, $p$=0.04), in fact TCB was greater than SeB in 18 out of 24 neonates. However, TCB occasionally also under-read bilirubin levels.

## CONCLUSIONS

These findings differ from results of similar studies conducted in other centres. Given the significant difference between TCB and SeB, it is recommended that, locally, TCB values continue to be cross-checked with SeB levels in the Emergency Department prior to establishing the need for phototherapy in neonatal jaundice.

**Michelle-Marie Boffa***
Department of Paediatrics,
Mater Dei Hospital
Msida, Malta
michelle-marie.boffa@gov.mt

**Mark Anthony Bailey**
Department of Paediatrics,
Mater Dei Hospital
Msida, Malta

**Helen Borg**
Department of Midwifery,
Mater Dei Hospital
Msida, Malta

**Victor Grech**
Department of Paediatrics,
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

Neonatal jaundice is common, occurring in over 50% of term neonates and over 80% of pre-terms.[1] Jaundice is the result of hyperbilirubinaemia, due to excess red blood cell breakdown or decreased excretion. It may be visually gauged, by looking for yellow discolouration at certain body sites such as the sclerae and the skin. However, this clinical method of detecting hyperbilirubinemia is subjective and should ideally be confirmed biochemically.[2]

In many cases, neonatal jaundice is transient and resolves spontaneously. However, in others hyperbilirubinaemia may be a significant cause of morbidity and mortality, with neurological complications such as hearing loss, kernicterus leading to cerebral palsy, and a mortality of 7-10%.[1-2] The aim of treatment is to reduce bilirubin levels before such complications occur.[3]

Bilirubinometers used to consist of 2-wavelength devices, i.e. 460nm and 520 nm, in order to generate a jaundice index. This method, however, required that a baseline bilirubin measurement be known.[3] Newer bilirubinometers, including those currently used locally (Philips BiliCheck®), utilise the entire visible spectrum (380 nm -760 nm) and have the advantage of not being affected by variables such as infant age, gestation or ethnicity, and do not require a baseline bilirubin level.[3]

Locally, babies are frequently referred to the Paediatric Emergency Department from the Breastfeeding Clinic and the Community Discharge Liaison Service because of high transcutaneous bilirubinometry (TCB) readings. Readings are obtained by applying the device to the sternum or forehead of the neonate. Elevated bilirubin levels are then verified in the Emergency Department using serum bilirubin (SeB) levels and the need for admission for phototherapy based on the latter.

This study was carried out to examine the association between TCB and SeB. A close association would negate the need for unnecessary venupuncture and would decrease the time from first medical contact to starting phototherapy, in patients in whom TCB levels are clearly elevated above accepted cut-off levels. Furthermore, it would also decrease hospital costs associated with SeB sampling and analysis.

## Method

This study was conducted at Mater Dei Hospital, Malta, the country's main hospital (928 in-patient and 86 day-care beds).[4] It included all neonates referred from the local Breastfeeding Clinic to the Paediatric Emergency Department with neonatal jaundice as indicated by a raised TCB level, measured using *Philips® BiliChek* monitoring device, over a five month period (June-October 2017). Data from this cohort was obtained directly from the Breastfeeding Clinic, with information regarding gestational age obtained from the local delivery suite in patients in whom this had not been documented by the Breastfeeding Clinic.

SeB was obtained from iSOFT Clinical Database for the remaining 24 neonates, the lab test used being the 'total bilirubin level' (BILT3 Cobas®).

## Statistical Analysis

Data was subsequently interpreted using data analysis tools in Microsoft Excel and custom-made spreadsheets with data analysis functions.

A contingency table was drawn up to determine the use of TCB as a screening test for SeB, based on whether or not phototherapy as predicted by TCB was actually required at respective SeB values, and data interpreted from this table to look at positive and negative predictive values of TCB.

TCB results >350 μmol $L^{-1}$ were also analysed separately from TCB <350 μmol $L^{-1}$ due to the fact that values >350 μmol $L^{-1}$ encompassed all readings above 350 μmol $L^{-1}$and could not be translated as a simple numerical figure for interpretation. Statistics were calculated for the 14 TCB values <350 μmol $L^{-1}$ and their respective SEB values, with a paired t-test to assess relationship. Of the TCB values <350μmol $L^{-1}$ the differences between TCB and respective SeB were calculated and statistics for these differences obtained, looking at under- and over-reading by the device.

The following were exclusion criteria for our study:

- Babies referred from the Breastfeeding Clinic to the Paediatric Emergency Department for jaundice on dates outside the study period
- Neonates born at <35 weeks gestational age
- Measurements before one day of age (before first 24 hours)

## Results

During the study-period, we looked at 25 neonates referred from the breastfeeding clinic in view of raised TCB levels, however, one was excluded from data interpretation in view of TCB level not having been documented prior to referral to Emergency Department. Results wherein TCB was indicated as >350 μmol $L^{-1}$ were analysed separately. For those <350 μmol $L^{-1}$, summary statistics for the two groups are shown in table 1.

**Table 1** Summary Statistics for TCB and SeB values in patients with TCB <350 μmol $L^{-1}$, showing 95% lower confidence intervals (LCI) and upper confidence intervals (UCI)

| Results | | LCI (95%) | UCI (95%) |
|---|---|---|---|
| Sensitivity | 94.7% | 71.9% | 99.7% |
| Specificity | 40.0% | 7.3% | 83.0% |
| Positive predictive value | 85.7% | 62.6% | 96.2% |
| Negative predictive value | 66.7% | 12.5% | 98.2% |
| Accuracy | 83.3% | 61.8% | 94.5% |
| Relative risk | 2.6 | | |
| Odd's ratio | 12.0 | | |

There was a significant difference between the two groups in that mean TCB was significantly greater than SeB (t=2.32, *p*=0.04), as shown in table 2 which gives the values for the t-test employed in this study.

**Table 2** Paired t-test for TCB and SeB values in patients with TCB <350 μmol $L^{-1}$

| | *TC* | *SeB* |
|---|---|---|
| Mean | 306.2143 | 288.5214 |
| Variance | 578.6429 | 1178.482 |
| Observations | 14 | 14 |
| Pearson Correlation | 0.572894 | |
| Hypothesized Mean Difference | 0 | |
| Df | 13 | |
| t Stat | 2.32469 | |
| P(T<=t) one-tail | 0.018463 | |
| t Critical one-tail | 1.770933 | |
| P(T<=t) two-tail | 0.036926 | |
| t Critical two-tail | 2.160369 | |

However, TCB occasionally also under-read bilirubin levels, and the differences are summarised in table 3 which compares the extent at of under- and over-reading of TCB.

**Table 3** Extent of under- and over-reading for TCB

| | Under | Over |
|---|---|---|
| Mean | -17.4 | 31.7 |
| Median | -17.8 | 33.7 |
| Standard Deviation | 10.4 | 19.2 |
| Min | -29.6 | 2.4 |
| Max | -4.6 | 67.7 |
| N | 4 | 10 |
| Confidence interval | 16.5 | 13.7 |

**Table 4** Further statistics for TCB and SeB values in patients with TCB <350 μmol $L^{-1}$

| | TC | Serum |
|---|---|---|
| Mean | 306.2 | 288.5 |
| Median | 306.5 | 286.9 |
| Standard Deviation | 24.1 | 34.3 |
| Min | 274.0 | 230.3 |
| Max | 340.0 | 350.1 |
| Confidence interval | 13.9 | 19.8 |

**Table 5** Contingency table indicating whether or not phototherapy was required based on values for TCB and SeB according to age-appropriate charts

| | SeB Yes | SeB No |
|---|---|---|
| TCB Yes | 18 | 3 |
| TCB No | 1 | 2 |

In fact, considering all neonates investigated, TCB levels were definitely greater than SeB in 18 cases, however, in two cases where both TCB and SeB were >350 we were unable to determine which was actually higher. In four cases TCB values were lower than SeB. Note that in stating that TCB over- or under-read results, we assume that SeB is the gold-standard method for analysing bilirubin levels.

Further statistics for TCB and SeB values <350 μmol $L^{-1}$ are seen in table 4, and the contingency table used to work out summary statistics is seen in table 5.

TCB, as a screening test for the need for phototherapy in the setting of neonatal jaundice, while sensitive (sensitivity=94.7%) was poorly specific (specificity=40.0%). In fact despite a positive predictive value of 85.7%, this method of gauging bilirubin levels has a negative predictive value of only 66.7%.

## Discussion

Contrary to results from similar studies conducted in other centres, there was a significant difference between the two groups in this study in that mean TCB was significantly greater than SeB. Of note is a study performed by the Medical University of South Carolina in the USA, published in 2015.[2] Here, the same bilirubinometer make was identical to that used in this study. Srinivas *et al.* report that given the good correlation between TCB and SEB in their study, TCB could reliably be used as a stand-alone screening test for neonatal jaundice.

The accuracy of TCB as a screening test for SeB was validated in many in-patient studies, with a correlation between BiliCheck® and high pressure liquid chromatography of 0.89 in one large, multicentre, hospital-based study. [3] Wickremasinghe et al (2011) noted a

decreased sensitivity and specificity of TCB in relation to SeB in an out-patient setting, with a tendency towards over-reading, and this was attributed to an increase in the incidence of hyperbilirubinaemia following hospital discharge, decreased moisture of neonatal skin and pigmentary differences.[5] This tendency of TCB to over-read SeB is similar to that seen in this study. Furthermore, Maisels *et al.,* (2011) noted an increase in false negatives picked up by TCB with increasing TCB levels.[6] Other out-patient based studies have shown a good correlation between TCB and SeB.[7]

This study shows that TCB is not a reliable screening test for SeB. Although our study showed a statistical difference between TCB and SeB ($t=2.32$, $P=0.04$), the limitations of our study include the following:

a. Since TCB measurement was unwitnessed, the method of device use might have been suboptimal in some instances
b. This study relied on TCB results collected by third-parties, however, although to our knowledge the majority of TCB levels of babies referred to the Paediatric Emergency Department in view of neonatal jaundice was documented, there might have been instances were no such record was kept, and the extent of under-documentation might have varied from individual to individual, with some midwives documenting results much more than others. This should not have been an issue if there were no differences in TCB measurement technique by different midwives and if each midwife had the same threshold for TCB measurement with a bilirubinometer.
c. Our data pool was small and the population size might have negatively affected reliability of results.
d. The results obtained are relevant for the bilirubinometer used in our study. These may or may not be able be applicable to other bilirubinometers
e. The following assumptions were made in our study, and these too might have affected results:
    - Transcutaenous bilirubinometry accuracy is independent of other variables including race, gestational age, post-natal age, general health and nutrition status
    - Values on transcutaneous bilirubinometry are independent of site of measurement
    - The transcutaneous bilirubinometer was adequately calibrated and functioning well
    - Proper technique was used in obtaining transcutaneous bilirubin readings
    - Transcutaneous and serum bilirubin readings were done in close chronological proximity, i.e. the time lag between transcutaneous bilirubinometer and serum sampling was not significant enough to affect results
    - Serum samples were kept in similar conditions until analysed in the laboratory, including avoiding exposure to sunlight
    - The serum test done locally is reliable and provides a true value for serum bilirubin

## Conclusion

Given the significant difference between TCB and SeB in our study, it is recommended that,

locally, baseline SeB levels continue to be checked prior to deciding on the need for phototherapy in neonatal jaundice unless a larger study concludes otherwise. It would be worth repeating this study at a later date using a larger cohort of patients, to conclude whether the results seen in our study were truly reliable, or whether they were seen by chance given the confounding factors of our study.

## Summary

**The facts:**

1. In Malta, patients are routinely referred from the breastfeeding clinic in view of elevated TCB
2. TCB gives a quick indication of SEB
3. TCB and SEB values are well-comparable according to previous studies
4. Using TCB values alone decreases on hospital waiting time and decreases time to start of treatment in hyperbilirubinaemia

**What's new?**

1. TCB does not appear to be a sensitive enough indicator of SEB in our local cohort
2. TCB over- and sometimes under-estimates SEB
3. TCB results as indicated from breastfeeding clinic referrals should continue to be verified with SEB in our local cohort to decide on treatment, unless a larger study proves otherwise

## References


1. Carolyn G. Scrafford, Luke C. et al. Incidence and Risk Factors for Neonatal Jaundice among Newborns in Southern Nepal. Trop Med Int Health 2013; 18(11): 1317–28.
2. R Keren, K Tremont, X Luan and A Cnaan. Visual assessment of jaundice in term and late preterm. Arch Dis Child Fetal Neonatal Ed 2009; 94: F317-F322.
3. G L Srinivas, C Dibattista Cuff, M D Ebeling, J T Mcelligott. Transcutaneous bilirubinometry is a reliably conservative method of assessing neonatal jaundice. J Matern Fetal Neonatal Med 2016; 29(16):2635-9.
4. F F Rubaltelli, G R Gourley, N Loskamp et al. Transcutaneous Bilirubin Measurement: A Multicenter Evaluation. Pediatrics 2001; 107(6):1264-71.
5. Malta Medical Students' Association. MMSA's Budget Recommendations in the Health Sector. Issuu (online) 2016.
6. A C Wickremasinghe, B S Karon, W J Cook. Accuracy of Neonatal Transcutaneous Bilirubin Measurement in the Outpatient Setting. Clin Pediatr (Phila) 2011; 50(12):1144-9.
7. M J Maisels, W D Engle, S Wainer, G L Jackson, S McManus, F Artinian. Transcutaneous bilirubin levels in an outpatient and office population. J Perinatol. 2011; 31(9):621-4.
8. T Kumra, S J Weaver,K Prather, L Garnepudi, E L Bartlett, M Crocetti. Correlation of Transcutaneous and Serum Bilirubin Measurements in the Outpatient Setting. Clin Pediatr (Phila) 2018; 57(2):231-4.

MMSG
ORIGINAL ARTICLE

# Perinatal Mental Health Screening Trial

Sarah Xuereb, Ethel Felice

## BACKGROUND

Pregnancy is a time of great joy and happiness but is also a time of great change, where the woman is at increased risk of onset and relapse of mental health disorders. However, unfortunately many patients go undiagnosed.

## METHOD

A trial for perinatal mental health screening was set up at Mater Dei Hospital. Mothers under the care of four consultant obstetricians were included in the study. All were asked a series of screening questions to assess necessity of referral to mental health services. If positive for one of the questions, a telephone consultation was carried out by one of the perinatal mental health midwives, giving them the necessary information about the mental health services available. The services offer a multidisciplinary approach with perinatal midwives, a specialised psychiatric team, social worker and psychologists.

## RESULTS

A total of 283 mothers were screened. 105 of which were positive for a screening question, requiring mental health services. 8 accepted an office session with the perinatal midwives, and 9 were followed-up up by psychiatric team in the perinatal mental health clinic.

## CONCLUSION

Previous data at Mater Dei Hospital stated that 3% of all mothers delivering in labour ward were being referred to the perinatal mental health clinic. During this trial 6% of the mothers screened were making use of the service. This points towards ~3% of mothers who would otherwise have been suffering in the dark, proving the necessity of a screening program.

**Sarah Xuereb***
MD
House Officer
Mater Dei Hospital
Msida, Malta
sarah.b.xuereb@gov.mt

**Ethel Felice**
M.D., B.C.Psych., M.Phil (Keele).,
M.Sc.(Perinatal Mental Health)
Consultant Psychiatrist
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

The perinatal period is a time of great change in a woman's life. It is considered to be a time of joy and happiness, however during this period the woman is at increased risk of onset and relapse of mental health disorders.[1]

One in five women experience a perinatal mental health disorder within the first year after the birth of their baby. However many of these women go undiagnosed.[2] Depression, stress and anxiety are among the most common mental health disorders experienced during pregnancy.[3] Studies have shown that mild to moderate perinatal distress can result in various complications such as preterm birth, low birthweight, child developmental delay, impaired mother-child bonding, and poor child mental health.[3]

Therefore perinatal mental health services have been set up and are concerned with the prevention, detection and treatment of perinatal mental health problems that complicate pregnancy and the postpartum year. However, studies have shown that up to three quarters of the women meeting DSM criteria for depression and anxiety are not recognised and only one in ten women requiring mental health services receive it.[1]

While health care system barriers are present which limit a woman's accessibility to mental health services, there are other significant barriers to consider. These include stigma, lack of understanding of whether symptoms are abnormal or a typical pregnancy experience, lack of support persons who understand their concerns, and fear that disclosing symptoms may lead others to think that they are incompetent mothers.[4]

## Materials and Methods

A trial for perinatal mental health screening at Mater Dei Hospital was set up in July 2018. This trial included all mothers under the care of four consultant obstetricians. All mothers involved in the trial were included in this prospective study, after obtaining appropriate ethics approval.

Screening was carried out by midwives during the booking visit by asking a series of five questions (including Whooley questions – questions 3 and 4):

1. Do you have a close family member (parent or sibling) with a history of bipolar disorder (manic depression) or any other serious mental illness?
2. Do you have a history of bipolar disorder (manic depression), puerperal psychosis, schizophrenia or other serious mental illness?
3. During the past month, have you often been bothered by feeling down, depressed or hopeless?
4. During the past month, have you often been bothered by having little interest or pleasure in doing things?
5. During the past month have you been feeling anxious or not being able to control worrying?

If the woman was found to be positive for one or more of these questions, the mother would be referred by the midwife for perinatal mental health services.

First a telephone consultation was carried out by the perinatal midwives discussing the perinatal mental health issues. An office consultation was always offered. During this office session the perinatal midwives would further evaluate her symptoms and score the

EPDS (Edinburgh Postnatal Scale) and ANRQ (Antenatal Risk Questionnaire) scores. Based on this evaluation, the perinatal midwife would decide whether a referral to the psychiatric perinatal mental health clinic is necessary.

The psychiatric perinatal mental health clinic involves a collaboration of a multidisciplinary team involving the psychiatric firm of doctors, an obstetrician and the perinatal midwives. The consultation would involve a thorough history and examination and an appropriate diagnosis is obtained. The necessary investigations and appropriate management are provided to the mother, involving psychiatric medications, psychology referral, or social work support.

## Results

A total of 283 mothers were screened from the 31st July to the 7th December. They had a mean age of 30.2 years and a mean gestation of 16 weeks.

From the 283 mothers, 105 were referred for perinatal mental health services. The majority of these mothers (46.67%) were referred due to anxiety. 43.80% were positive for the question regarding family psychiatric history; 34.28% were positive for personal psychiatric history; 29.52% were positive for low mood; and 20.95% were positive for anhedonia (refer to Figure 1).

The 105 mothers requiring referral all received a telephone consultation from the perinatal midwives and 8 of these accepted to come for an office session with the midwives, while 9 mothers were seen in the perinatal mental health clinic. 88 mothers did not agree to attend (refer to Figure 2).

**Figure 1** Reason for Referral to Perinatal Mental Health Services

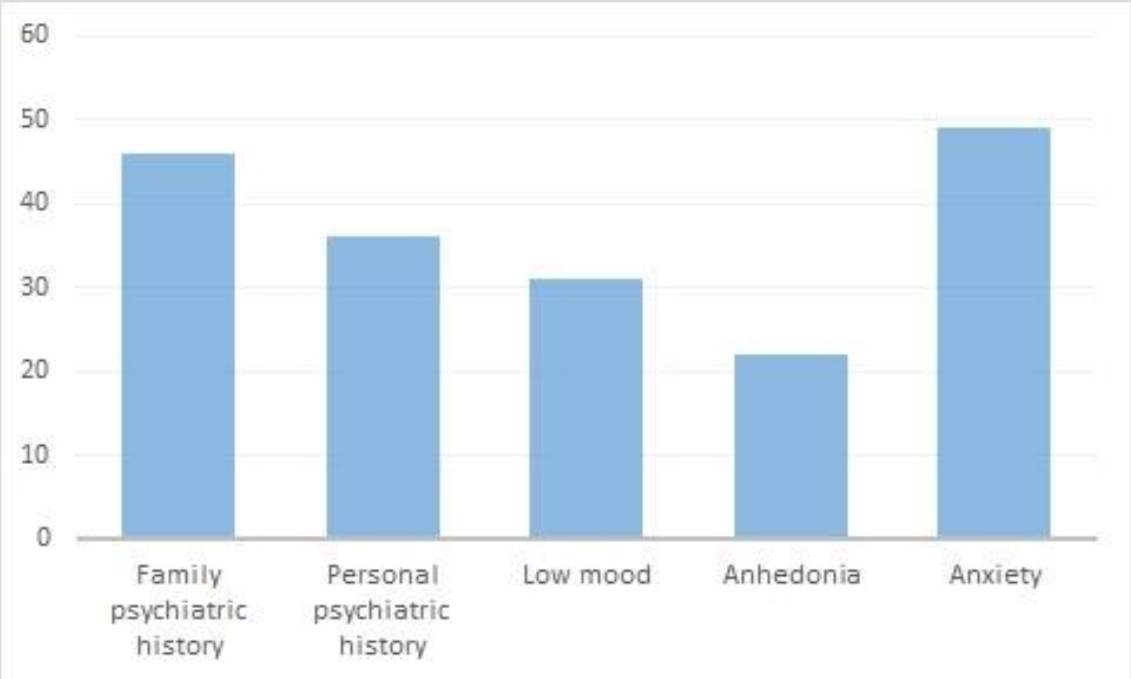
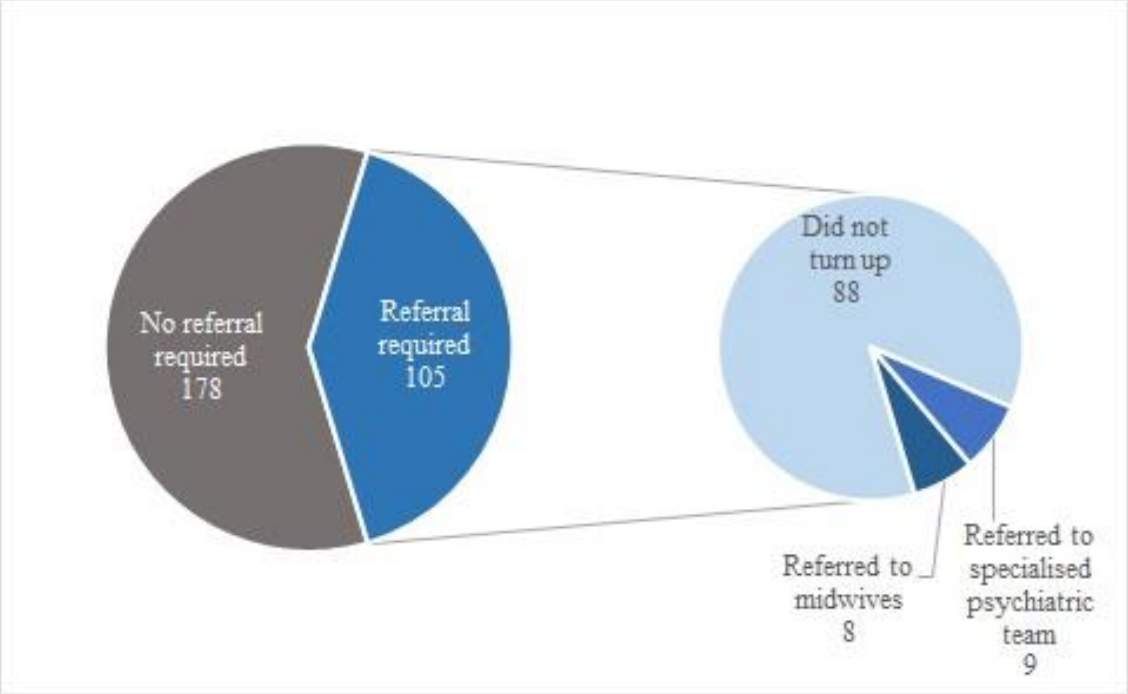


**Figure 2** Results of total patients screened during trial




Of the 9 mothers seen at the perinatal mental health clinic, 2 were diagnosed with anxiety, 1 diagnosed with depression, 2 diagnosed with both anxiety and depression, 1 had a somatisation disorder, 1 had a past history of OCD, 1 had adjustment disorder and 1 had no psychiatric diagnosis.

## Discussion

The American College of Obstetricians and Gynecologists (ACOG) recommends psychosocial screening of pregnant women at least once during the perinatal period, but screening in routine care is uncommonly done.[5]

The most validated and widely used self-report screening tool for depression during the perinatal period, is the Edinburgh Postnatal Depression Scale (EPDS). EPDS removes items related to physical symptoms of depression that may be affected by the perinatal period rather than by mood. It is not a diagnostic tool but a screening tool that asks about depressive symptoms in the past 7 days.[5] NICE guidelines recommend that healthcare professionals should ask the Whooley questions at a woman's first contact with primary care, then again at her booking visit, and again postnatally (at 4-6 weeks and 3-4 months). The Whooley questions will act merely as case-finding questions, which are then later followed up with the use of self-report measures, such as EPDS, for further assessment or monitoring.[6] During this trial a set of 5 questions were used as a case-finding measure (including the 2 Whooley questions). However the EPDS was only then carried out on those patients who agreed to an appointment with the perinatal midwives or at the clinic.

Perinatal mental health services were first set up at Mater Dei Hospital in November 2016. Data collected during 2017 states that 3% of all mothers delivering at Mater Dei Hospital were being referred and making use of the perinatal mental health service (although this

data was never formally published). Once must also keep in mind that this percentage includes both antenatal and postnatal mothers. During this trial, the number of women making use of the service was 6% from the total mothers screened. Therefore a 3% increase was identified despite the fact that postnatal mothers were not included in the trial. This refers to a significant number of mothers who otherwise would have been suffering in the dark. This data proves the importance and impact of perinatal mental health screening.

However, screening alone is insufficient to improve clinical outcomes and must be coupled with appropriate follow-up and treatment, when indicated. Therefore the increase in pick-up rate noted in our study, points towards a requirement for the growth of the perinatal mental health service, referring to more human resources, more clinics, etc.

The scarcity of human resources poses a major deterrent to routine screening. E-screening has the potential to increase efficiency of mental healthcare by reallocating limited human resources where they are most needed - in-depth follow-up assessment, referral, and treatment. It is a low-resource option that can be embedded in current prenatal and postpartum care across various settings and thus increases access to routine screening.[4]

Postnatal depression occurs in over 11% of women who experience major or minor depression six weeks postnatally. There is now considerable evidence to show that postnatal depression has a substantial impact on the mother and her partner, the family, mother-baby interactions, and the longer term emotional and cognitive development of the baby, especially when depression occurs in the first year of life.[6] Therefore a serious limitation of the trail was that screening was only carried out in the antenatal phase and therefore mental health disorders starting off in the postnatal stage were not picked up.

Another limitation of the study was that it was not identified why those 88 mothers who required referral to the service, refused to attend. Several factors may have come into play, including private psychiatric help, stigma, lack of social support and fear.

## Conclusion

Our study proves that the perinatal mental heath screening trial was successful at recognising mothers suffering from perinatal mental health conditions, with an increased pick-up rate of 3%. We recommend that an established perinatal mental health screening program is set up for all mothers delivering at Mater Dei Hospital. Screening would be carried out first by the using the case finding questions (as used in the trial) during the booking visit, and again postnatally (at 4-6 weeks). We also recommend an increase in the human resources at the clinic as the above refers to a significant increase in workload. The possibility of e-screening should also be considered.

## References


1. Centre of Perinatal Excellence. Mental Health Care in the Perinatal Period, Australian Clinical Practice Guideline, October 2017.
2. Johnson M, Schmeid V, Lupton SJ, Austin M-P, Matthey S.M, Kemp L, et al. Measuring perinatal mental health risk. Arch Womens Ment Health. 2012; 15(5): 375–386.
3. Kingston D, McDonald D, Tough S, Austin MP, Hegardoren K, Lasiuk G. 2014 Public views of acceptability of perinatal mental health screening and treatment preference: a population-based survey. BMC Pregnancy Childbirth. 2014; 14: 67.
4. Kingston D, McDonald S, Biringer A, Austin M-P, Hegadoren K, McDonald S, et al. 2014 Comparing the feasibility, acceptability, clinical- and cost-effectiveness of mental health e-screening to paper-based screening on the detection of depression, anxiety, and psychosocial risk in pregnancy women: a study protocol of a randomized, parallel-group, superiority trial. Trials. 2014; 15: 3.
5. Connelly CD, Baker-Ericzen MJ, Hazen AL, Landsverk J, McCue Horwitz S. 2010 A Model for Maternal Depression. J Womens Health (Larchmt). 2010 Sep; 19(9): 1747–1757.
6. Paulden M, Palmer S, Hewitt C, Gilbody S. 2009 Screening for postnatal depression in primary care: cost effectiveness analysis. BMJ 2009;339:b5203.

MMSG
ORIGINAL ARTICLE

# Epidemiological factors of cholera in Gozo, Malta in 1837

Joseph Galea, Liberato Camilleri

The second world cholera pandemic reached Malta in early June 1837. It arrived on the island of Gozo one month later. The Health Board of this island installed to combat cholera recorded all the cases reported up to the end of August of the same year on a special register. This manuscript register still exists at the Gozo Public Library. It contains the minutes of the Gozo cholera board meetings that took place during June, July and August 1837 and includes a list of cholera patients including their names, their village or town of abode, the dates of diagnosis, the dates of recovery or death and if they were treated in hospital or at home. Fifteen percent of patients had their age recorded. There were 740 cholera cases registered with a total mortality from the disease of 47%. Using statistical analysis the study showed that patients treated in hospital were more likely to die than if they were treated at home but there was no relation of death to gender or location of abode.

**Joseph Galea***
MD (Melit) MD (Sheffield) MA(Melit) LRCP MRCS (Edin) LRCPS(Glasgow) FRCS(Edin) FRCS (CTh) FETCS
Department of Surgery
University of Malta
Msida, Malta
joseph.f.galea@um.edu.mt

**Liberato Camilleri**
BEd (Melit) MSc (Melit) PhD (Lanc)
Department of Mathemetics,
University of Malta
Msida, Malta

*Corresponding author

The second world cholera pandemic raged throughout Europe and North America between 1829 and 1849. It affected Russia in 1830, the United Kingdom in 1831, Marseille in 1835 and Naples and Sicily in the spring of 1837. By the summer of the same year, it had reached the Maltese shores, having already massacred 62 million people worldwide. The first cases of cholera in Malta were reported at the Ospizio in Floriana on 9 June 1837. The Government, belatedly appointed Committees of Health to deal with the consequences of the epidemic, cholera hospitals were opened in the cities and villages, directives issued, and healthcare workers and priests mobilized. The malady wreaked havoc for 3 months attacking 8785 and killing 4252 individuals. Many Maltese doctors feared contagion and would not attend the cholera hospital; however other Maltese doctors and a few British army and navy doctors did not believe in the contagion theory of cholera and gave their services caring for the sick and the dying.[1]

The first cases of certified cholera in Malta appeared at the Old People's Hospital (Ospizio) in Floriana on 9 June 1837 and, in the first 10 days, 200 inmates died from the disease. On 19 June, Governor Henry Frederick Bouverie (1783-1852) appointed a Central Health Committee on nine Maltese and English members to supervise the reported cases and deal with the cholera epidemic. The committee included the physicians of the Naval and Military Hospitals and the Police.

The dreadful news arriving from the main island led the inhabitants of Rabat, Gozo to plead with the Lieutenant Governor of the island Major C.A. Bayley C.M.G. to form a Committee of Health for Gozo and to adopt the same measures taken in Malta. The Gozo Committee met for the first time on 21 June 1837. The minutes from its meetings are found in a manuscript located at the Gozo Public Library in Victoria, Gozo.[2]

The Gozo *Comitato* was made up of Magistrate Giovanni Battista Schembri (as President), Mr James Somerville, Dr Eduardo Dingli, the Reverend Pro-Vicar Canon Fr. Publius Gauci, Father Guardian Pelagio, Dr Michel'Angelo Mizzi, Dr Eduardo Mallia, Dr Giuseppe Cutajar and Giovanni Montanaro. Dr Fortunato Mizzi served as the Committee Secretary keeping the minutes of the meetings.[3] It was decided that the Committee should meet every day at the Lieutenant Governor's Office in Rabat and at any hour of the day if this became necessary. It also had to forward a report of its deliberations and activities to the Lieutenant Governor of Gozo.

During the first meeting, regulations similar to those enacted by the sister committee in Malta were proposed and accepted:

1. From then on, the dead were to be buried in cemeteries and not in churches, with the exception of those individuals who had a private tomb. The burial had to be under *sette palmi di terra* plus the necessary quantity of *calcina* (lime mortar), and conducted in the presence of a Police Sergeant who was responsible to ensure that the burial was carried according to the regulations. If anybody wanted to use their personal burial plot, permission was necessary from the Health Committee – in the knowledge that this burial might be prohibited or controlled in case of cholera or suspected cholera, depending on what the committee decides in each particular circumstance.
2. The Lieutenant Police Officer of Rabat (Gozo) and the Deputy Lieutenants of the various villages were obliged to inform the committee of all the suspected cases and

deaths that occur in the districts they were responsible for. The parishes were prohibited from moving or interning the cadavers without prior written permission from the Committee of Health.

3. Every morning the medical practitioners were to report any cases in their care – which report was to be given immediately in cases of death or suspected cholera.
4. All church burials were to be well sealed.
5. Due to the current circumstances, the *Magistrato del Mercato* was requested to pay special attention about the state and quality of fish, cured meat and other alimentary items that were being sold to the public and to perform frequently the obligatory inspection accompanied by one of the medics appointed by the Committee for Health.

The register of reported cases included the name, date of diagnosis, whether they were hospitalized or managed at home, and the date of death or recovery. They were recorded consecutively using the date of diagnosis (figure 1).

## Incidence and Demography of the Epidemic

### Incidence

The first cholera case in Gozo occurred on 6 July 1837 and, by 31 August, 743 patients had been registered. The cases of cholera peaked between the 20-27 July 1837 and the register stops abruptly when the Committee was dissolved on 31 August (figure 2) during which period 743 cases of cholera had been recorded. In the beginning of 1837, the population of Gozo was recorded at 16 534 [4] giving an infection incidence of 4.5% of the Gozitan population.

Most patients were treated at home, but after the fifth week of the epidemic, the number of patients treated at home was the same as those treated in hospital. Both home and hospital treated patients peaked in the 3rd week (figure 3).

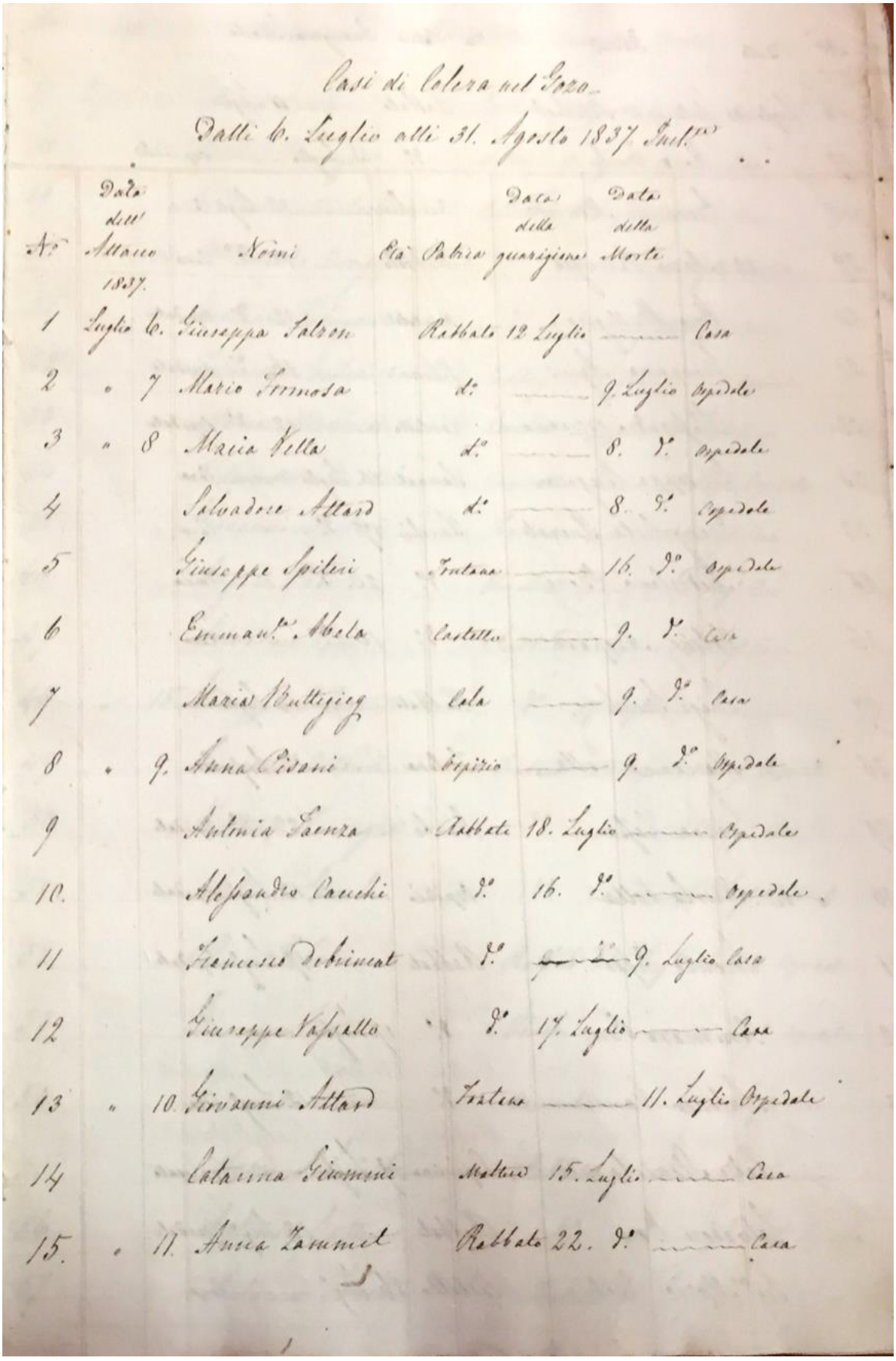
### Gender

Up to 31 August the number of females afflicted was 392 (53%) and that of males was 351 (47%). The female population of Gozo was 8377 (affliction rate of 4.7%) and the male population was 8157 (affliction rate of 4.3%). Females after correction for the population were affected more than males.

### Age

The age was not recorded in all patients, but using the data available in the register, it appears that the larger majority of infected cases were adults aged 21-60 years. (figure 4).

**Figure 1** The first 15 consecutive patients on the list of patients afflicted with cholera.



Casi di Colera nel Forzo

Dalli 6. Luglio alli 31. Agosto 1837 Inclusive

| N.° | Data dell'Attacco 1837. | | Nomi | Età | Patria | Data della guarigione | Data della Morte | |
|---|---|---|---|---|---|---|---|---|
| 1 | Luglio | 6. | Giuseppa Falzon | | Rabbato | 12 Luglio | ——— | Casa |
| 2 | " | 7 | Mario Formosa | | d.° | ——— | 9. Luglio | Ospedale |
| 3 | " | 8 | Maria Vella | | d.° | ——— | 8. d.° | Ospedale |
| 4 | | | Salvadore Attard | | d.° | ——— | 8. d.° | Ospedale |
| 5 | | | Giuseppe Spiteri | | Fontana | ——— | 16. d.° | Ospedale |
| 6 | | | Emmanu.l Abela | | Castello | ——— | 9. d.° | Casa |
| 7 | | | Maria Buttigieg | | Cola | ——— | 9. d.° | Casa |
| 8 | " | 9. | Anna Cesari | | Ospizio | ——— | 9. d.° | Ospedale |
| 9 | | | Antonia Farrugia | | Rabbato | 18. Luglio | ——— | Ospedale |
| 10. | | | Alessandro Caruchi | | d.° | 16. d.° | ——— | Ospedale |
| 11 | | | Francesco Debrincat | | d.° | ——— | 9. Luglio | Casa |
| 12 | | | Giuseppe Vassallo | | d.° | 17. Luglio | ——— | Casa |
| 13 | " | 10. | Giovanni Attard | | Fontana | ——— | 11. Luglio | Ospedale |
| 14 | | | Catarina Giommi | | Malta | 15. Luglio | ——— | Casa |
| 15. | " | 11. | Anna Zammit | | Rabbato | 22. d.° | ——— | Casa |

**Figure 2** Cases of cholera diagnosed in July and August of 1837.

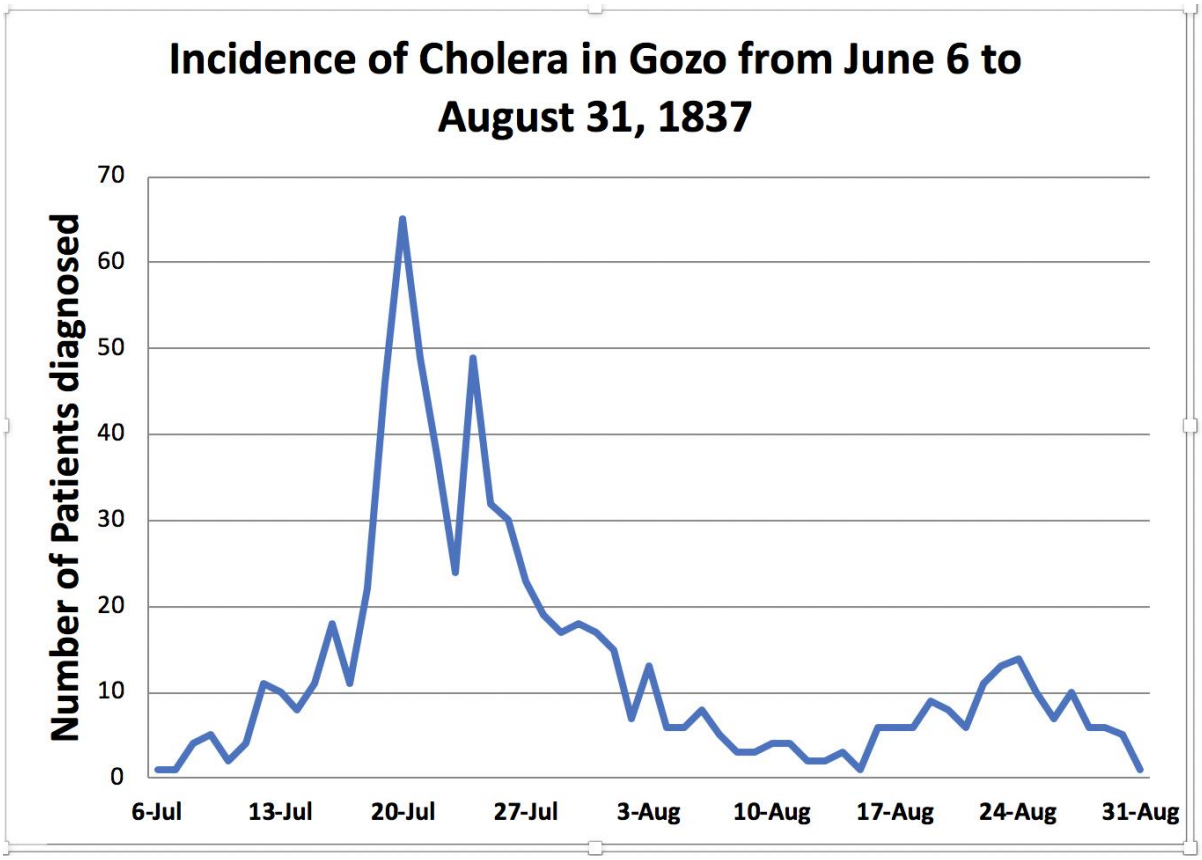



**Figure 3** The number of patients treated at home and in hospital during the cholera epidemic in Gozo.

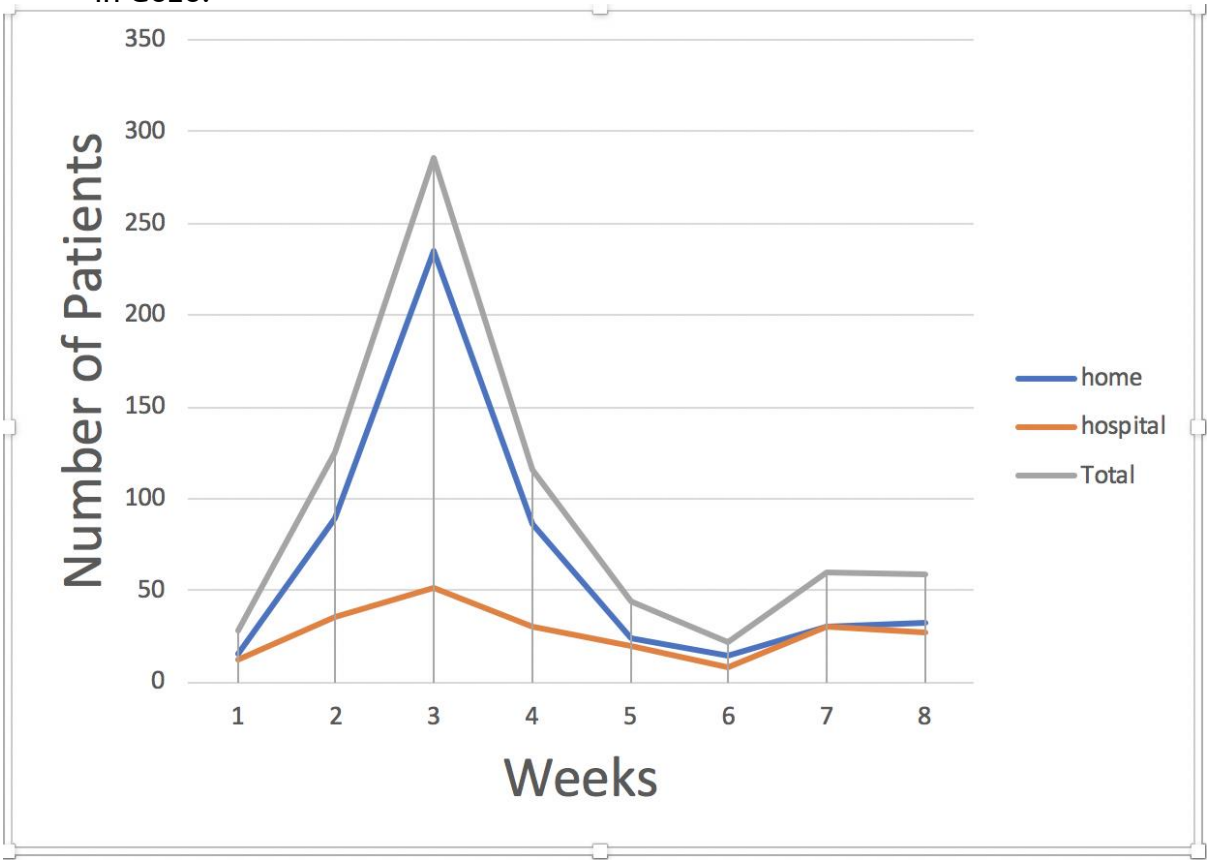


**Figure 4** The frequency of cholera patients for different age groups (*n*=96).

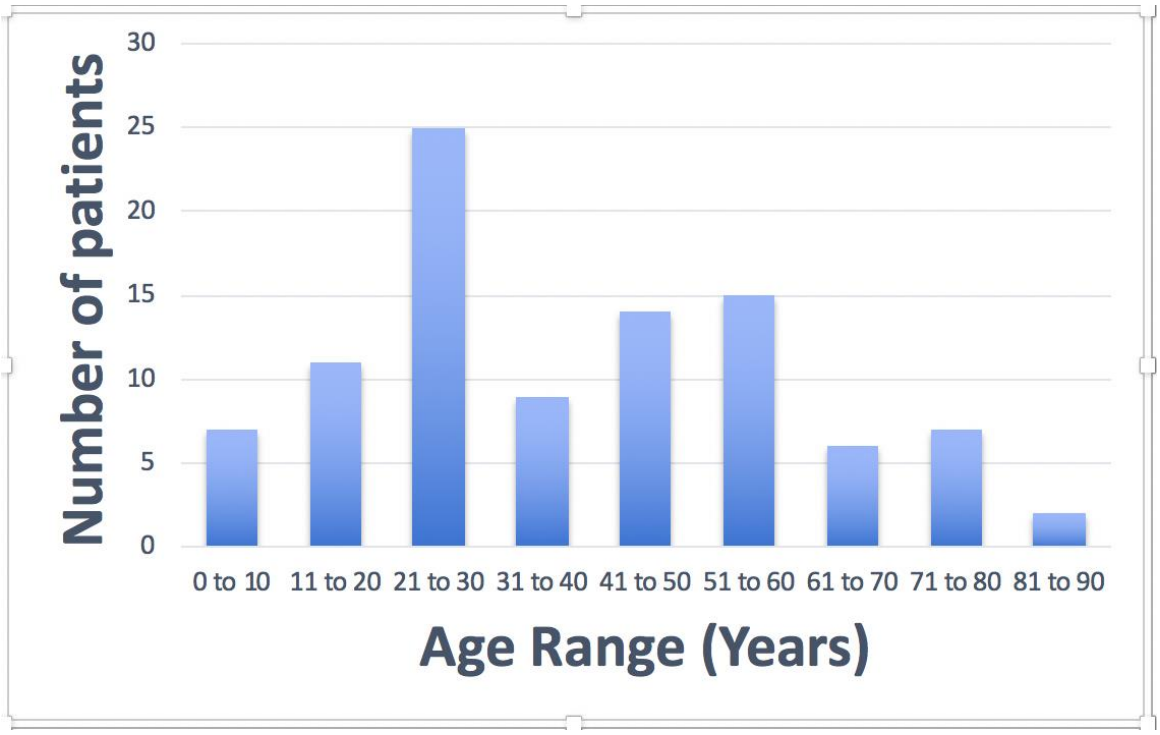



**Table 1** Location of Habitation of Cholera patients in Gozo for July and August 1837

| **Districts of Gozo** | **Cholera Cases** | **Population 1842 census[5]** |
|---|---|---|
| Rabat, Castello, Kercem and area* | 380 | 4904 (7.7)§ |
| Xagħra | 180 | 1720 (10.4) |
| Xewkija | 77 | 1391 (5.5) |
| Sannat and Munxar | 39 | 899 (4.3) |
| Żebbug and Għasri | 9 | 720 (1.25) |
| Nadur, Qala, Għajnsielem | 20 | 3295 (0.61) |
| Għarb | 4 | 1413 (0.28) |
| Ospizio and Ospedali civili | 15 | - |
| Others | 3 | - |

*Belliegħa (17), Għajn Qatet (7), Ħammimiet (1), Wied Sara (1), Wara s-Sur (1), Għammiesa (3) Għajn Tuta (2) Mandraġġ (1), Lunzjata (4), Ħamrija (8) u Fontana (41)

§ These percentages are only indicative because the cholera epidemic occurred 5 years earlier.

## Distribution in Towns and Villages

The distribution of cholera cases in Gozo shows the majority of patients to come from Rabat and its surrounding territories, Xagħra and Xewkija. The incidence of cholera in Għarb, Nadur, Qala, Għajnsielem was comparatively low. No information of population size by village for 1837 is available, however information is available from the first national census in 1842. Although the population size was different in 1842 compared to 1837, the 1842 population distribution provides a reasonable picture of regional habitations sizes which would have changed little in a five-year period of the mid-19$^{th}$ century. While the infection incidence per district cannot be worked accurately, an approximate indication is therefore possible using the 1842 census data. The highest incidence thus appeared to have occurred in Xagħra (at about 10.4%) followed by Rabat, Xewkija and Sannat (7.7%, 5.5%, and 4.3% respectively). Għarb has the lowest incidence (about 0.28%) but Nadur-Qala-Għajnsielem and Żebbuġ-Għasri also show a relatively low incidence (0.61% and 1.25% respectively) (table 1).

## Mortality from the Disease

Of all the infected cases, 345 (46.5%) patients succumbed to the disease while 395 (53.5%) survived up to end of August. Data from other sources show that the mortality rate for the three summer months (July- September) was 359 of 804 patients (44.6%).[6] The mortality rate registered in Gozo was therefore less than that registered in Malta, which stood at 3893 of 7981 (48.8%) infected individuals. Possible contributions to a better outcome of cholera patients in Gozo compared to Malta include the timely preparations taken by the Lieutenant Governor and the Committee before the epidemic attacked Gozo and cleaner air and water in Gozo.

## Mortality in Relation to the Place of Treatment (Home vs Hospital)

The duration of the illness, i.e. whether it ended in recovery or death, was also recorded in the register. The data from the registry shows that the mean duration of illness for survivors was 7.8 days (n= 393, SD 4.05, SEM 0.20) and for the deceased was 2.5 (n= 346, SD 2.08, SEM 0.11). During their treatment 71.4% of the cholera patients remained at home, while the remaining 28.6% of the patients were sent for management to hospital. The crosstab shows a larger percentage of cholera patients treated in hospital who eventually died (64.0%) when compared to those who were treated at home (39.5%). This percentage difference is significant (Table 2).

The survival plot (figure 5) shows that the survival probability for the cholera patients in hospital is lower than their counterparts who stayed at home. The Log-Rank test shows that the survival distributions of the two groups of cholera patients whose convalescence period was at home or in hospital differ significantly since the p-value (approximately 0) is less than the 0.05 level of significance.

## Residence Locality

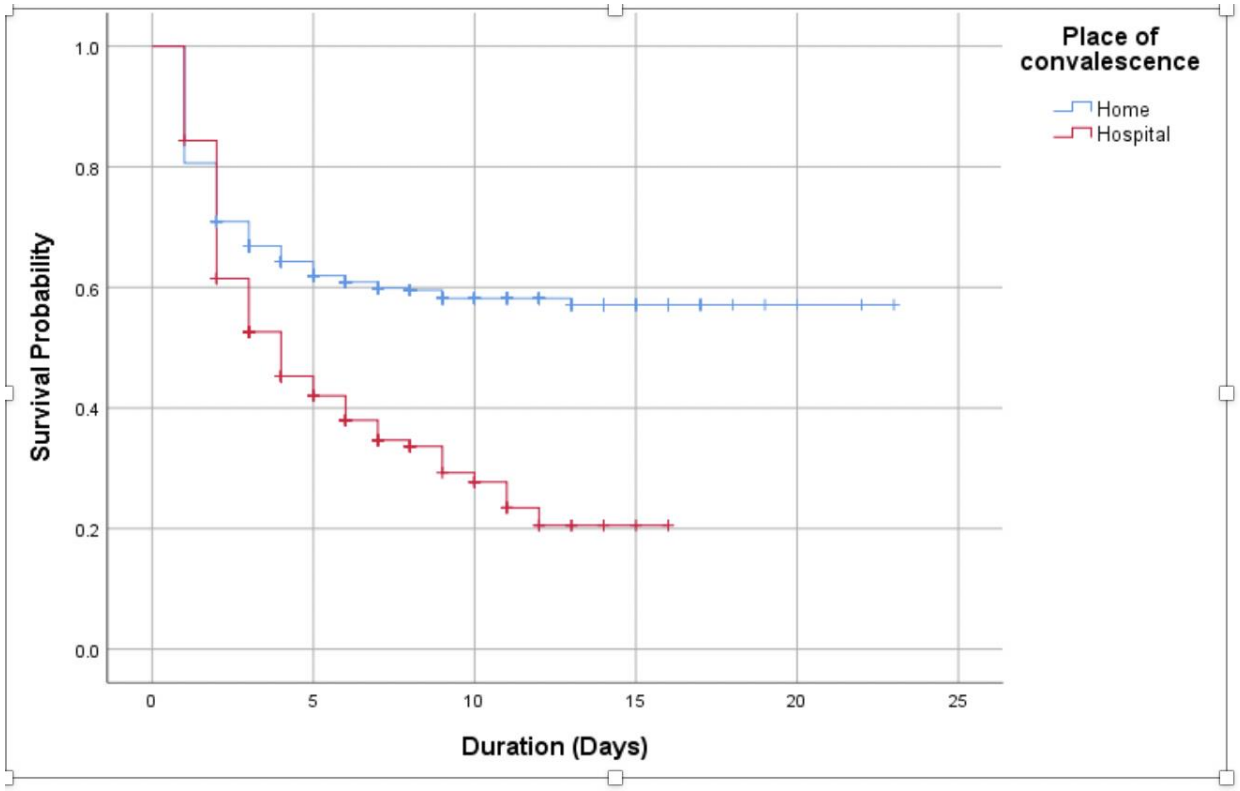
The crosstab shows larger numbers of cholera patients from Rabat, Xaghra, Xewkija and Kercem compared to other Gozitan towns. 46.6% of all cholera patients eventually died. The crosstab also shows that the percentages of patients who died vary marginally between the residence localities and percentage differences are not significant since the p-value (0.255) exceeds the 0.05 level of significance (Table 3).

**Table 2** Percentage of cholera patients who died or survived, grouped by place of treatment.

| | | | Status | | Total |
|---|---|---|---|---|---|
| | | | Die | Survive | |
| Place of Treatment | Home | Count | 208 | 318 | 526 |
| | | Percentage | 39.5% | 60.5% | 100.0% |
| | Hospital | Count | 135 | 76 | 211 |
| | | Percentage | 64.0% | 36.0% | 100.0% |
| Total | | Count | 343 | 394 | 737 |
| | | Percentage | 46.5% | 53.5% | 100.0% |

$X^2(1) = 36.145$, $p<0.001$

**Figure 5** Survival probabilities of cholera patients treated at home/hospital by convalescence duration




**Overall Comparisons**

| | Chi-Square | df | P-value |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 32.534 | 1 | .000 |

**Table 3** Percentage of cholera patients who died or survived, grouped by residence locality

| | | | Status | | Total |
|---|---|---|---|---|---|
| | | | Die | Survive | |
| Locality | Rabat/ Fontana/ Lunzjata | Count | 148 | 177 | 325 |
| | | Percentage | 45.5% | 54.5% | 100.0% |
| | Xaghra | Count | 82 | 98 | 180 |
| | | Percentage | 45.6% | 54.4% | 100.0% |
| | Xewkija | Count | 41 | 35 | 76 |
| | | Percentage | 53.9% | 46.1% | 100.0% |
| | Kercem | Count | 21 | 39 | 60 |
| | | Percentage | 35.0% | 65.0% | 100.0% |
| | Munxar/Sannat | Count | 18 | 20 | 38 |
| | | Percentage | 47.4% | 52.6% | 100.0% |
| | Zebbug/Ghasri | Count | 5 | 4 | 9 |
| | | Percentage | 55.6% | 44.4% | 100.0% |
| | Qala/ Ghajnsielem/ Nadur/ Mgarr | Count | 14 | 6 | 20 |
| | | Percentage | 70.0% | 30.0% | 100.0% |
| | Gharb/ S.Lucija/ S.Lawrenz | Count | 3 | 4 | 7 |
| | | Percentage | 42.9% | 57.1% | 100.0% |
| | Ospedale/ Ospizio | Count | 13 | 12 | 25 |
| | | Percentage | 52.0% | 48.0% | 100.0% |
| Total | | Count | 345 | 395 | 740 |
| | | Percentage | 46.6% | 53.4% | 100.0% |

$X^2(8) = 10.151$, $p=0.255$

The survival plot (figure 6) shows the survival probabilities of cholera patients residing in each village by convalescence duration. The Log-Rank test shows that these survival distributions do not differ significantly since the p-value (0.052) exceeds the 0.05 level of significance.

### Gender

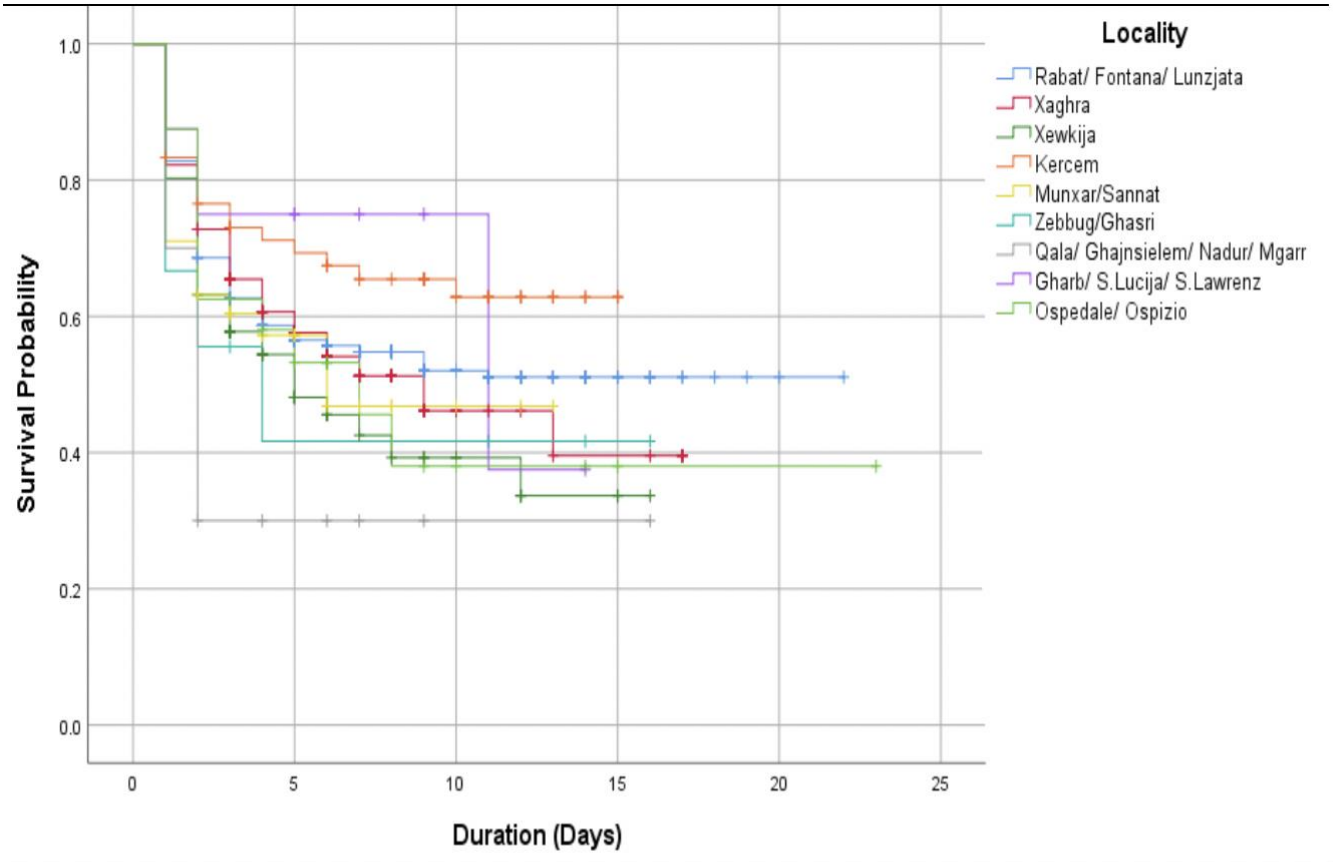
The crosstab (table 4) shows that the proportion of male patients who died of cholera (45.4%) is similar to the proportion of female patients (47.7%) and the difference is not significant since the p-value (0.538) exceeds the 0.05 level of significance.

The survival plot (figure 7) shows the survival probabilities of male and female cholera patients by convalescence duration. The Log-Rank test shows that these survival probabilities do not differ significantly since the p-value (0.713) exceeds the 0.05 level of significance.

## Cox Regression Model

When these three predictors (Gender, Residence locality and Place of convalescence) were analyzed collectively through a Cox regression model, only place of treatment was found to be significant (table 5).

**Figure 6** Survival probabilities of cholera patients in each village by convalescence duration.




**Overall Comparisons**

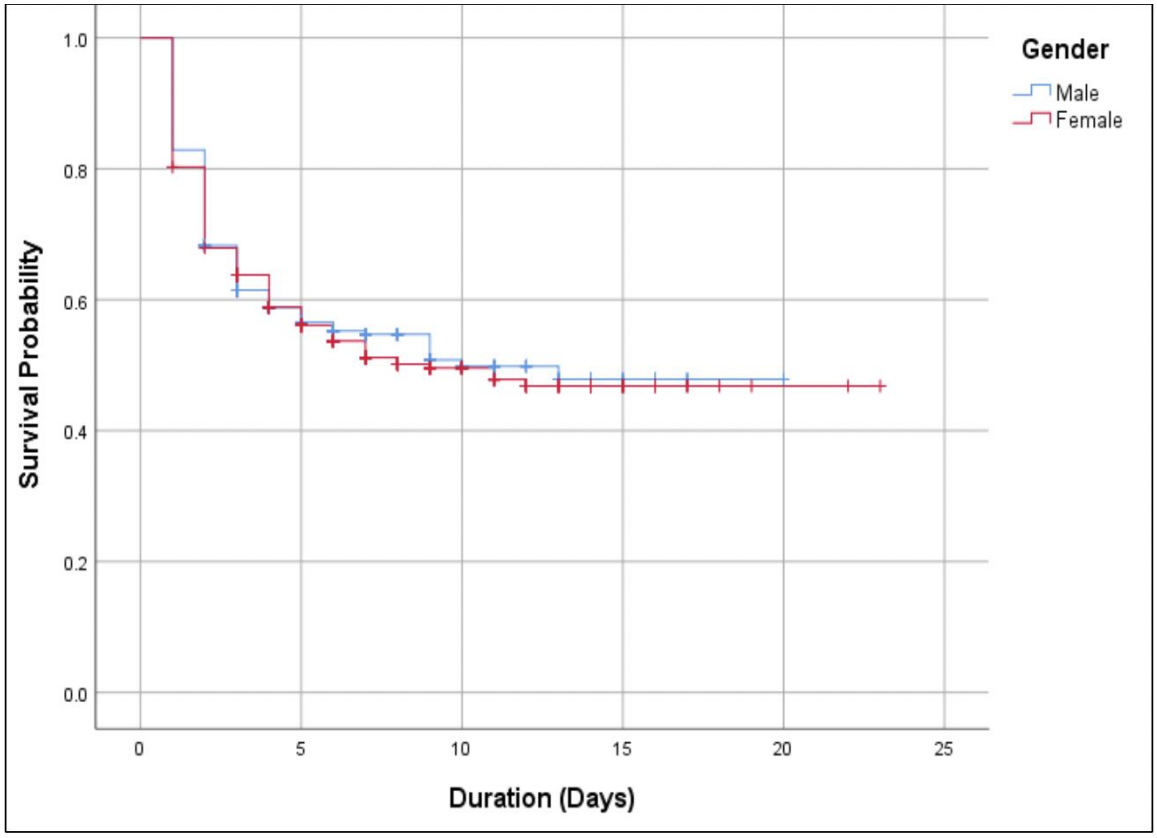
| | Chi-Square | df | P-value |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 15.364 | 8 | 0.052 |

**Table 4** Percentage of cholera patients who died or survived, grouped by gender

| | | | Status | | Total |
|---|---|---|---|---|---|
| | | | Die | Survive | |
| Gender | Male | Count | 159 | 191 | 350 |
| | | Percentage | 45.4% | 54.6% | 100.0% |
| | Female | Count | 186 | 204 | 390 |
| | | Percentage | 47.7% | 52.3% | 100.0% |
| Total | | Count | 345 | 395 | 740 |
| | | Percentage | 46.6% | 53.4% | 100.0% |

$X^2(1) = 0.380$, $p=0.538$

**Figure 7** Survival probabilities of male and female cholera patients by convalescence duration.




**Overall Comparisons**

| | Chi-Square | df | P-value |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 0.135 | 1 | 0.713 |

**Table 5** Cox regression analysis of the three predictors

| | Wald | df | P-value |
|---|---|---|---|
| **Gender** | 0.027 | 1 | 0.868 |
| **Residence locality** | 11.938 | 8 | 0.154 |
| **Place of treatment** | 26.440 | 1 | 0.000 |

## Discussion

The finding of a register of cholera patients diagnosed during the summer months of 1837 in Gozo, an island making part of the Maltese archipelago, sheds important light on various aspects of the cholera epidemic in this island. The epidemic reached the shores of Gozo four weeks after its appearance in Malta and the register provided the name and gender of the patients, the town or location where they lived and the date of admission followed by the date of discharge or death. It also informs us if the patient was treated at home or at the cholera hospital. The age of the patients was recorded in only 15% of patients. There is no information if patients were treated partly at home and partly in hospital. Some patients were transferred to the cholera hospital from the Ospizio or the Civil Hospital.

The census available closest to 1837 was that from the survey of 1842. Although this is 5 years after the affliction the population mobility of the time was very low and there would not have been any significant variation. The use of the 1842 census data to work out the incidence of disease necessitated a district/town selection similar to that given by the census. This showed the highest incidence of disease to be in Xagħra (10.4%) and the lowest to be in Għarb (0.28%). The mortality rate from cholera was 47% which is very similar to results from other places during the 18th century cholera epidemics[7,8] and to untreated cholera patients today[9].

The survival from cholera was significantly better if a patient was treated at home rather than in hospital. This could have occurred because sicker patients would have been taken to hospital rather than managed at home or patients were taken to hospital when their condition had deteriorated. The district/village designation was free from the fixation to the areas of the 1842 census in table 3 and allowed us to use purely geographic allocations e.g. pooling the village of Għarb with its hamlets of San Lawrenz and Santa Luċija. There was no significant differences in survival probabilities between the different towns and villages, and between males and females. The survival probabilities of cholera patients was not related to the age of the patient since age readings were only recorded for 15% of patients, which was not deemed to be a good representation.

In conclusion, using the Cox regression methodology this study has shown that the patients' gender and the resident locality were not significant predictors of mortality rate. However, the place of treatment was shown to be a significant predictor of mortality because cholera patients treated in hospital were more likely to die than those treated at home.

## References


1. Galea J. Doctors during the 1837 Cholera Epidemic in Malta: Unearthing the truth. Malta Medical Journal, 2018;30(1):32-41.
2. Galea J. The Gozo Committee of Health Minutes during the Cholera Epidemic of 1837. Gozo Observer (University of Malta Publication) 2019; (40):3-12.
3. Mizzi F. Minutes of the Comitato di Salute del Gozo. 1837. Manuscript, National Library, Victoria Gozo Malta. U VII-246.
4. Government of Malta. Malta Blue Book 1836. Chapter 13. (Internet). Valletta, Malta: 1836 (accessed 1 May 2019). Available from: https://nso.gov.mt/en/nso/Historical_Statistics/Malta_Blue_Books/ Documents/1836_chapter13.pdf.
5. Bezzina J. Religion and Politics in a Crown Colony – The Gozo Malta Story 1798-1864. Population Distribution. Valletta: Bugelli Publications; 1985. Appendix 6 342 p.
6. Galea J. Living and Dying in Malta During the Horrible Summer of 1837. Journal of Community Health (Internet). 2019, Nov. DOI: 10.1007/s10900-019-00769-9.(cited 2020 Feb 20).
7. Dean ME. Selective suppression by the medical establishment of unwelcome research findings: The cholera treatment evaluation by the General Board of Health, London 1854. JLL Bulletin: Commentaries on the history of treatment evaluation. 2015. (cited 2020 Feb 20). Available from: (https://www.jameslindlibrary.org/articles/selective-suppression-by-the-medical-establishment-of-unwelcome-research-findings-the-cholera-treatment-evaluation-by-the-general-board-of-health-london-1854/).
8. Phelps M, Perner ML, Pitzer VE, Andreasen V, Jensen PKM, Simonsen L. Cholera Epidemics of the Past Offer New Insights Into an Old Enemy. J Infect Dis. 2018;217(4):641–649. doi:10.1093/infdis/jix602.
9. Sack DA, Sack RB, Nair GB, Siddique AK (2004). Cholera. Lancet 363:223-233.

MMSG
ORIGINAL ARTICLE

# Incidence and prevalence of smoking amongst local medical students

Matthew Pizzuto, Brendan Caruana Montaldo, Tamara Muscat, Matthew Seychell

## Background

Smoking is a detrimental addiction associated with various diseases. Locally, in 2016, 20.9% of females and 30.2% of males were smokers.

## Method

The methodology used was in the form of a cross sectional retrospective study with 717 questionnaires being distributed to medical students via electronic social media. The questionnaires were based on the MONICA 1998 questionnaire. It enquired about demographics, clinical year of studies and cigarette smoking habits.

## Results

65% of questionnaires were received. From the cohort of students who answered the questionnaire, 68.5% (CI 64.2–72.7%) admitted to having never smoked, 10.8% (CI 8.0–13.6) are current active smokers, 16% (CI 12.7–19.3) are social smokers, 3.7% (CI 2–5.4) were ex-smokers and 1% (CI 1–1.9) vape. Amongst active smokers, 67% smoked 0-5 cigarettes daily. Most social smokers also smoke 0-5. 63.3% of students admitted to unsuccessfully quitting smoking. Ex-smokers stated that health, hypocrisy and sports were important reasons for them quitting smoking. In the non-smoking cohort, health and odour ranked highly as reasons for never having started smoking. Students who vaped admitted to doing so multiple times daily.

Although stress and coping mechanisms were chief reasons why students declared that they smoked, long term smoking increases anxiety and stress. Doctors who smoke are less likely to encourage their patients to quit smoking[10]. Social smokers are students who do not smoke daily and only during stressful situations or social events. Moreover, they frequently smoke more when surrounded by friends, especially whilst drinking alcohol[16]. A significant portion of students are social smokers; most smoke 0-5 cigarettes (97.3%) (CI 94–100). A chi-square test of independence was performed to examine the relation between this study and a similar unpublished study conducted locally in 2008. The relation between these studies was not significant (p-value 0.83). Prevalence of student smoking is the same as it was a decade ago.

## Conclusion

Smoking is still common amongst medical students in Malta in 2019. In view of the current local problem and considering that local practices have failed to reduce smoking; counselling should be offered on campus, more emphasis should be placed during the medical student years on the deleterious effects of tobacco [25]

**Matthew Pizzuto***
M.D. (Melit) 2018, BSc (Hons) Nursing
Mater Dei Hospital
Msida, Malta
matthew.a.pizzuto@gov.mt

**Brendan Caruana Montaldo**
M.D. (Melit) 1988, Dip. ABIM (Chicago, USA) 1994, ABIM (Pulm Dis) (Pennsylvania, USA), 1996 ABIM (Critical Care) (Illinois, Chicago, USA).
Consultant Respiratory Physician
Mater Dei Hospital
Msida, Malta

**Tamara Muscat**
University of Malta
Msida, Malta

**Matthew Seychell**
M.D. (Melit) 2018
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

Healthcare professionals play an important role in tobacco prevention[1]. They educate the community by their actions and campaigns against tobacco smoking whilst also influencing key national stake holders. Physicians occupy a unique role in prescribing and leading teams in smoking cessation clinics both in hospital and in the community[1]. Patients who smoke often turn towards their physicians for advice. Physicians' actions (whether s/he is a smoker) have direct implications on the likelihood whether their patients will stop smoking or not. Present medical students will graduate to be doctors in a few years' time and smoking clinicians are less likely to discourage their patients to quit smoking.[2]

Unfortunately, smoking is still prevalent in the national and international medical student population groups and a superior knowledge does not seem to correlate with a lower rate of smoking amongst more senior medical students.[3]

Smoking in medical students is prevalent worldwide and is perceived as an international phenomenon.[4] Medical students continue to smoke despite direct exposure both to the teaching of the harmful effects of cigarettes, as well as to the experience of patients suffering from the effects of continued smoking. Prevalence of smoking amongst medical students, as well as the rationale for the behaviour of medical students with regards to tobacco use has been studied the world over and is the subject of a number of meta-analyses.[4]

In the European region, tobacco is responsible for 16% of adult deaths in 2016 (over 7million deaths). Smoking is attributed to cause 12% of all deaths in the Maltese population.[5] Prevalence of smoking in Malta will drop to 25% in males and 16% in females by 2025.[6]

The incidence of lung cancer in Malta has increased from 118/100,000 in 2006 to 136/100,000 in 2015 in men and from 28/100,000 in 2006 to 54/100,000 in women in 2015 according to the Trading Economics (an article about smoking prevalence in Malta published in 2016)[7]. 20.9% of all women and 30.2% of all men were smokers in 2016.The total number of deaths attributed to lung cancer in men has risen from 107 in 2004 to 142 in 2014, whilst in the women, it has risen from 16 in 2004 to 28 in 2014. Although the fatalities attributed to lung cancer amongst men were higher than amongst women, a statistical downward trend was seen in the male population, in contrast to a slow uptrend being seen amongst women.[5]

## Methods

All medical students enrolled in the five years of the curriculum of the single medical school in Malta (University of Malta Medical School) in the academic year 2018/2019, either for first or repeated times, were eligible for participation in the study. 465 of 717 eligible students participated in the survey with a response rate of 65% (CI 69.3; 60.7).

This was a cross sectional point prevalence study design, utilising a self-reporting questionnaire. The questionnaire was anonymous, confidential and self-reported. It was formulated in English. The questionnaire was based on the MONICA (Monitoring of Trends and Determinants of Cardiovascular Diseases) study questionnaire but further clarification was sought and supplemental questions were added.

The questionnaire consisted of 17 items that covered 5 areas; demographical data,

prevalence of cigarette and tobacco use, smoking habits and attitudes to abstention from smoking and vaping habits.

The questionnaires were all individually sent between February and March 2019. Students were briefed about the survey, where the reason, anonymity and voluntary participation were stressed. The commonest reason for not participating was failure to open the questionnaire (confirmed by the feedback obtained by the platform of social media).Social media was chosen for the dissemination of questionnaires since less students had been attending lectures and it was thought to be a superior method of data collection. The obtained data were processed by Microsoft Excel 2010.

## Results

From the 465 students who filled in the questionnaire, most respondents (60%) were females. 68% of all female medical students filled in the questionnaire whilst only 58% of all male medical students filled in the questionnaire. 55% of the cohort was made up of clinical students whilst 45% were pre-clinicals. The responses received showed a significant difference in responses filled between pre-clinical year students and clinical year ones (p-value 0.0036). Pre-clinical students were likelier to answer the questionnaire, figure 1.

The age of the participants varied but the majority were between 21 and 24 years old (45.5%), closely followed by 17 and 20 years old (45%), 25 to 28 years old (7.6%) and the remainder were over 29 years. The social background of the students was not recorded in this study.

From the cohort of students who answered the questionnaire, 68.5% (CI 64.2–72.7%) admitted to having never smoked, 10.8% (CI 8.0–13.6) are current active smokers, 16% (CI 12.7–19.3) are social smokers, 3.7% (CI 2–5.4) were ex-smokers and 1% (CI 1–1.9) vape. Figures 2A and 2B below show the student tendencies in the pre-clinical and clinical cohort.

**Figure 1** Distribution of medical students by clinical year

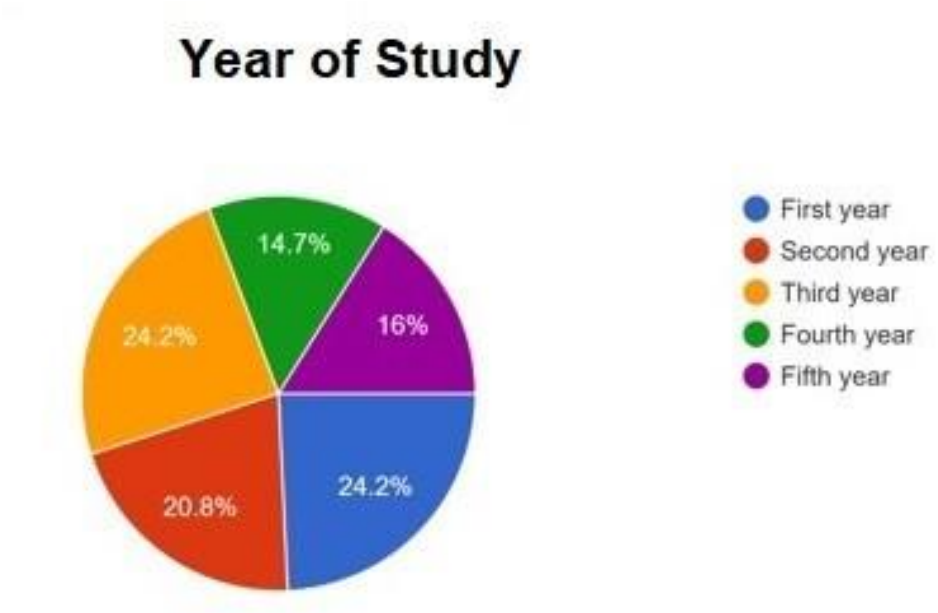
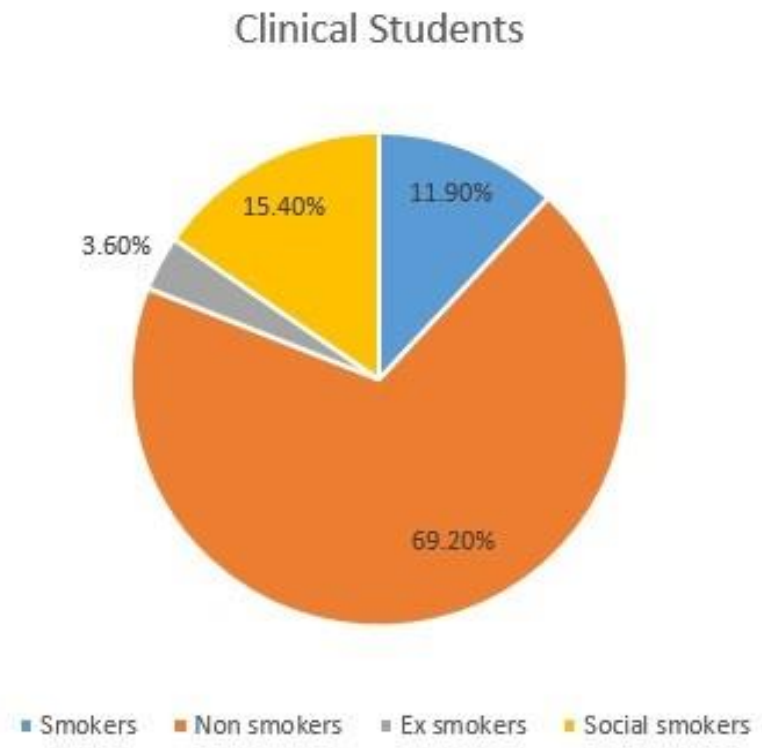
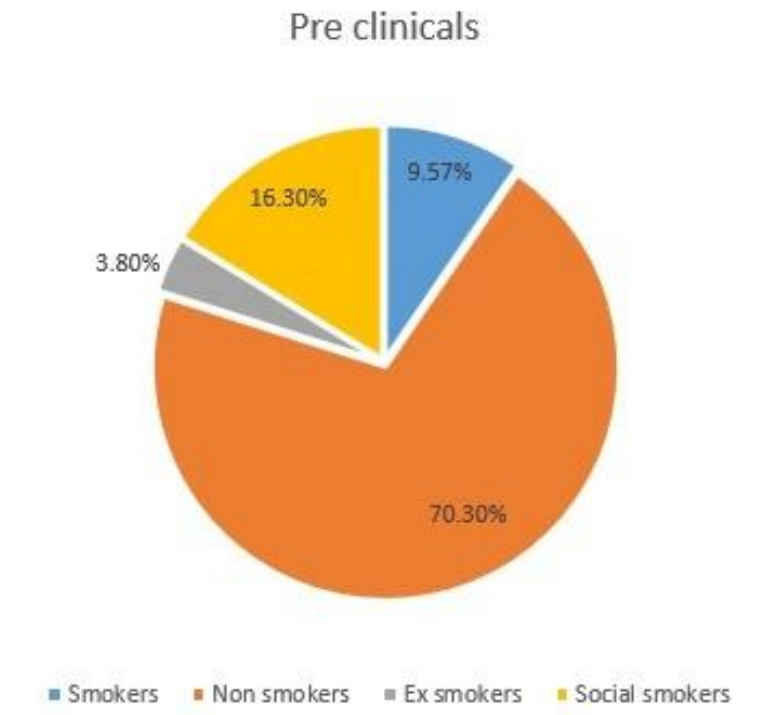


**Figure 2a & 2b** Pre-clinical and clinical medical student's smoking tendencies



Most medical student smokers were males (55%) (CI 41–69). The most common reasons that smokers gave as to why they smoke can be found in Figure 3 below. 55% of smokers admitted to smoking during stressful situations, 33.3% use smoking as a coping mechanism, 13.7% smoke due to outside peer pressure whilst 7.8% smoke to aid their weight loss.

The vast majority of the smoking cohort, admitted to smoking 0-5 cigarettes per day (67%), whilst a further 17.6% smoked 6-10 cigarettes a day. The remaining 15.7% smoked between 11-20 cigarettes per day. 63.3% of the students admitted to having unsuccessful attempts to quit smoking in the past whilst the remaining 36.7% have never even attempted to stop smoking.

**Figure 3** Reasons why smokers start and continue smoking

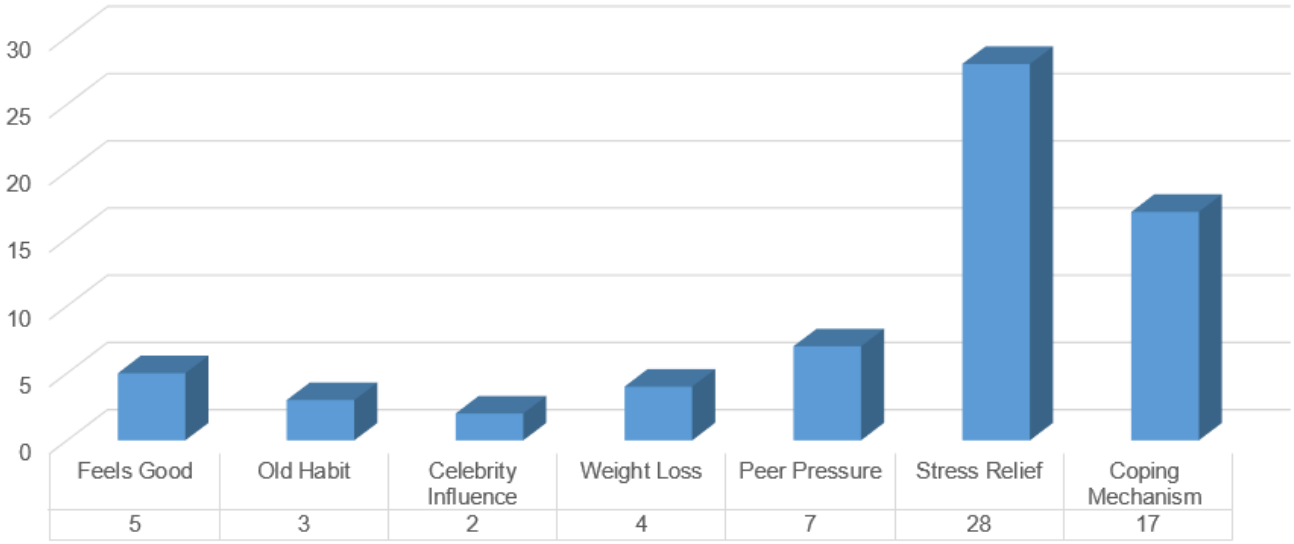
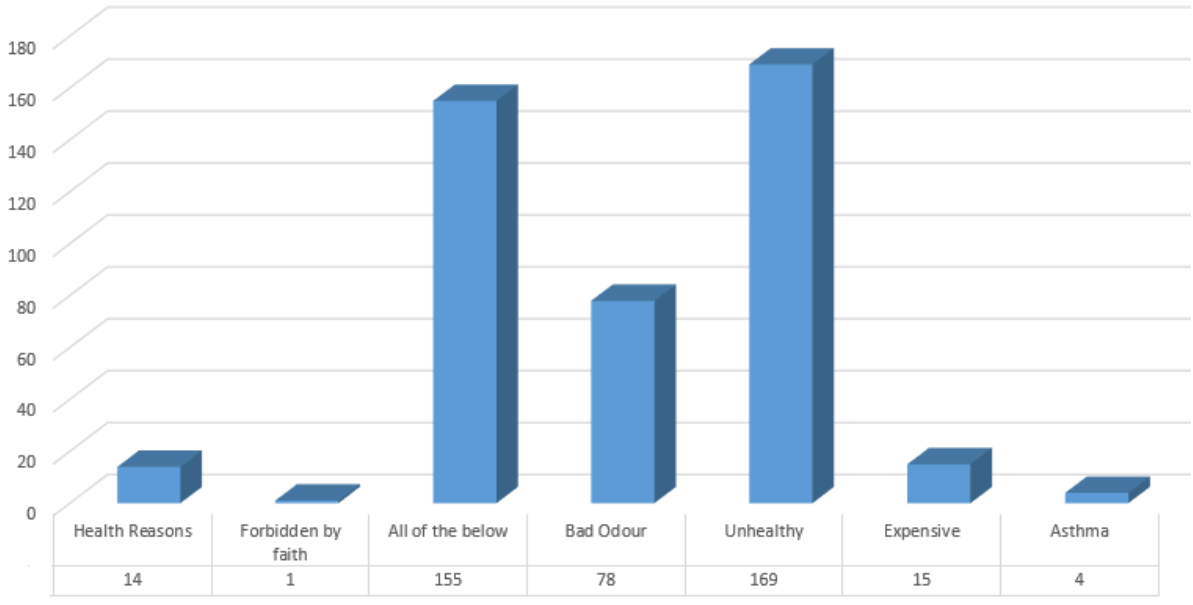



**Figure 4** Full list of reasons why medical students do not smoke

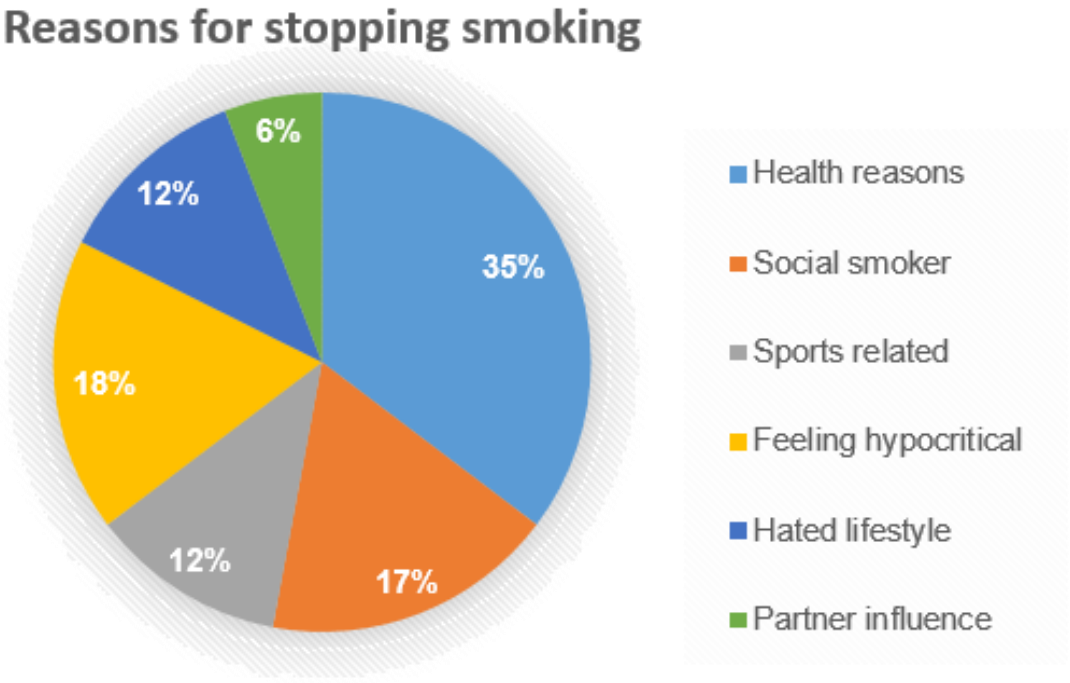


From the cohort of 465 students, 318 students admitted to never smoking; with unhealthy addiction ranking first as the main reason why students never smoked (53.1%). A good proportion of students (48.7%) attributed several factors and reasons as to why they never started smoking. The list of reasons can be found in Figure 4 above.

Some smokers do acknowledge the harm done by tobacco smoking and in fact, 64% admitted to trying to stop smoking but did not manage. Ex-smokers were also asked as to why they had stopped smoking and below one can find the list of reasons given by the 17 students below in Figure 5.

A minority of students (74) admitted to social smoking. Social smokers are students who do not smoke daily and only during stressful situations or social events. Moreover, they frequently smoke more when surrounded by friends, especially whilst drinking alcohol.[16] Most of them were already smoking before entering university (66.2%) whilst the remaining 33.8% started to smoke after they entered University. Most social smokers stated that they smoked 0-5 cigarettes (97.3%) whilst the other 2.3% smoked between 6-10 cigarettes a day. A slight majority (51.4%) admitted to having tried quitting smoking in the past whilst the other 48.6% stated that they never tried to stop smoking.

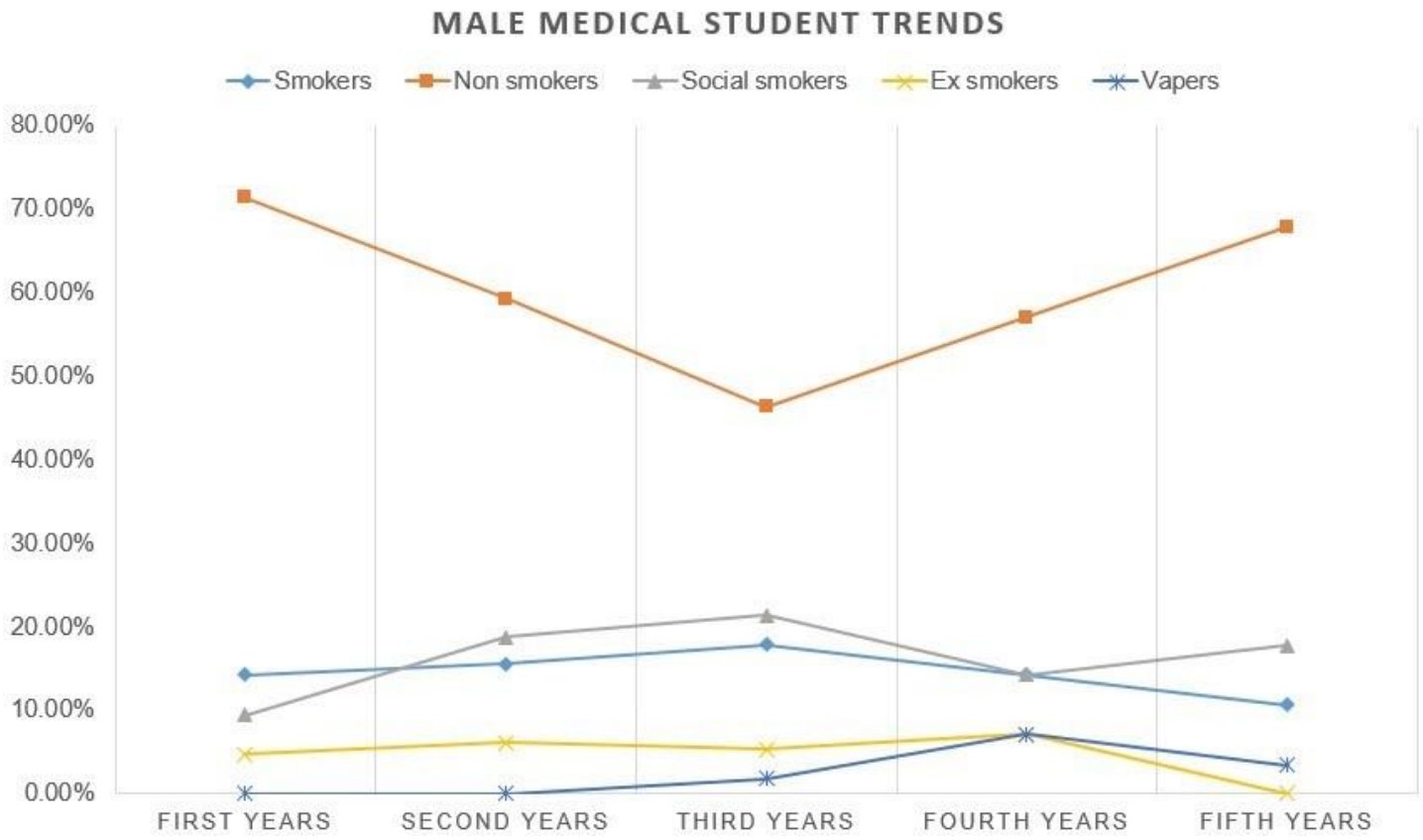
**Figure 5** Reasons why medical students stopped smoking



A very small percentage of the students admitted to vaping (5 in total) and all of them started after they entered University. 3 of the 4 participants admitted to vaping more than 5 episodes per day whilst the other student vapes once a day. 80% of the students admitted to never having a wish to stop vaping whilst the other student admitted to trying unsuccessfully to quit vaping.

From the 2018-2019 medical students at the University of Malta, there were 113 first year medical students (71 females and 42 males). From the first year medical student's male cohort, 71.4% were non-smokers, 14.3% were smokers and 9.5% were social smokers. Comparatively, 67.9% of male fifth year clinical students were non-smokers, 10.7% were smokers and 17.8% were social smokers. Overall, there is a rising trend in number of students smoking from the first years (23.8%; combined value of smokers and social smokers) when compared against the fifth years medical students (28.5%). This is illustrated in Figure 6 below.

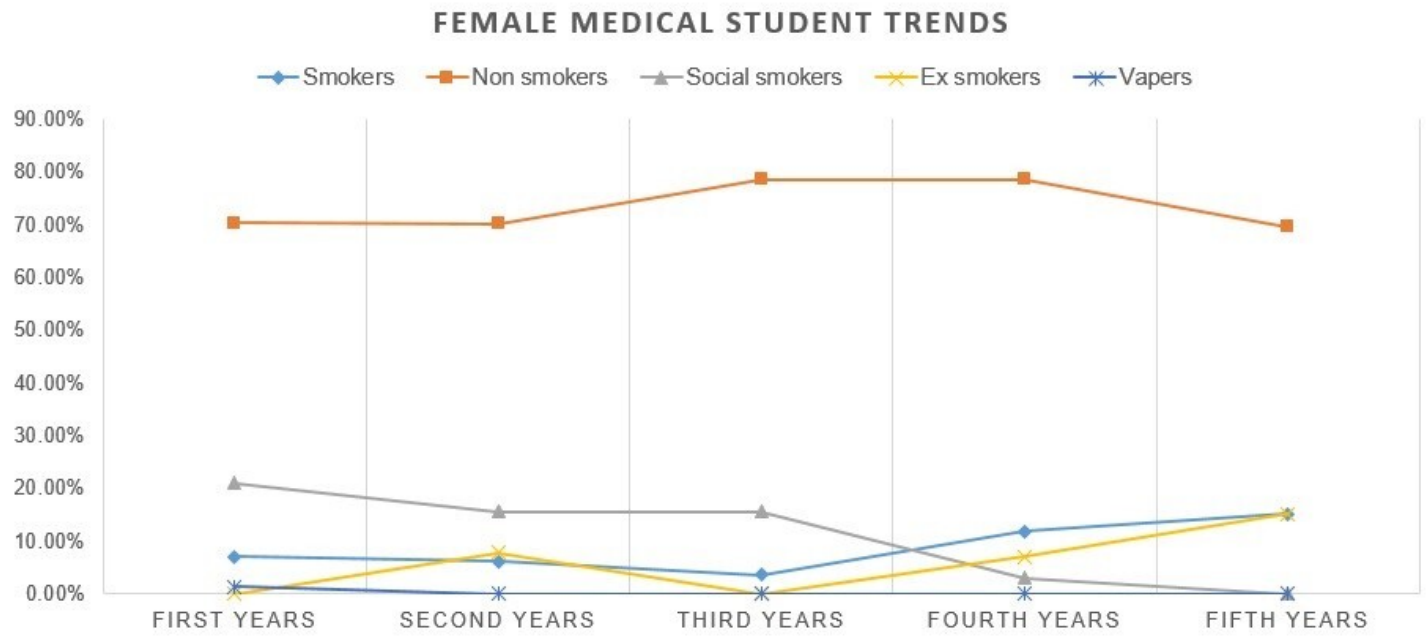
**Figure 6** Prevalence of smoking amongst the male medical student cohort



From the female cohort, there were 70.4% who were non-smokers in the first years which decreased to 69.6% in fifth year medical students. There was 7% of the cohort who were smokers in first year, but that figure rises in fifth year medical students (15.2%). 21.1% of female first year medical students were social smokers whilst 15.2% of fifth year medical students were social smokers. Overall, the number of smokers (social and regular smokers) increased from 28.1% in the first years to 30.4% in fifth years. This is also illustrated in Figure 7 below.

In summary, the pre-clinical cohort was made up of 9.6% active smokers, 16.7% social smokers, 3.8% ex-smokers, 68.9% non-smokers and 0.5% who admitted to vaping whilst the clinical cohort was made up of 11.9% active smokers, 15.5% of social smokers, 3.6% of ex-smokers, 68% non-smokers and 1.6% who admitted to vaping.

**Figure 7** Prevalence of smoking amongst the female medical student cohort




## Discussion

The aim of this research was to study smoking behaviour amongst Maltese medical students. The null hypothesis was that the local medical student population would smoke the same compared to the general population. Two separate Chi squared tests for males and females were performed comparing this sample to the Maltese population in 2016. With a p-value of <0.0005 in males and a p-value of <0.0005 in females, the null hypothesis is rejected. Therefore both male and female medical students would smoke less than the general population, accepting the alternate hypothesis.

Since unskilled or unemployed workers were more likely to smoke[8].This would suggest that the fact that they are in training for a health-

related profession would make them less likely to start smoking.[8-9]

Stress relief and smoking as a coping mechanism rank high amongst the reasons as to why students state that they start and continue to smoke. Many smokers have reported and stated that smoking helps them cope with stress and increased their ability to concentrate. However, this appeared to be since when they go for a prolonged period without smoking, they experience nicotine withdrawal symptoms which are relieved by smoking. Long-term smokers who stopped smoking have indeed reported lower levels of stress than when they were smoking and no reduction in ability to concentrate [10-11].

It is also commonly thought that smokers with mental health problems are using cigarettes to 'self-medicate' or treat their psychological symptoms[12]. According to a joint report issued in 2013 by the Royal College of Physicians and Psychiatry[13], neither nicotine nor smoking improved psychological symptoms and people with serious mental health disorders who stop smoking do not experience a worsening of mental health. Indeed, these patients do indeed fare better and there is a marked improvement in their mental health disorder and improvement in their quality of life. Smokers who stop show reduced levels of stress and mood disorder than those who continue. They also report higher levels of happiness and life satisfaction than those who continue[10].

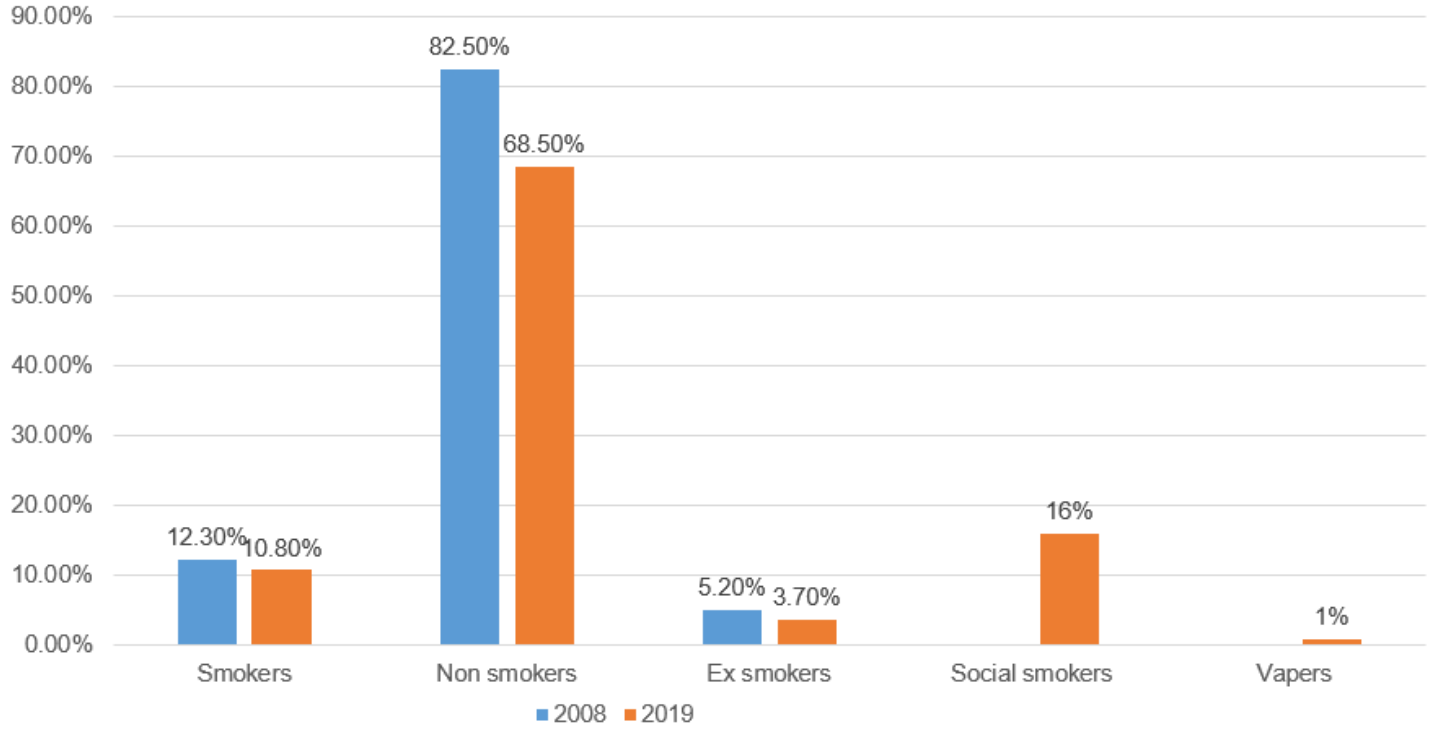
The percentage of active smokers amongst local medical students remains considerably high. The literature suggests that medical students who smoke may become doctors who may not be as effective as other non-smoking doctors in advising and succeeding in getting their patients to quit smoking by failing to be proactive in promoting smoking cessation and not motivating their patients to quit. [14 15 16].

In 2005, international smoking rates amongst medical students were highly variable, ranging from 4% in America to 58% in Japan. A 10.8% smoking rate amongst Maltese medical students is a comparatively low rate when taking into account those in a number of European countries, including Slovakia (21%), Germany (24%), Spain (37%) and Greece (41%); all in 2005. However, Malta followed a general international trend in seeing the medical student population of a country enjoying a lower smoking rate than the national rate of that country[4]. However, some countries (such as Slovakia) are seeing a trend in increasing rates of medical student smoking[17].

Moreover, results from this study were compared to a similar local unpublished study done in 2008[18]. This study conducted locally in 2007-2008 had a cohort of 288 medical students (145 pre-clinical and 143 clinical students) and showed that the prevalence of smoking was that of 12.3%. The study did not explore the possibility of social smokers. An important note, social smokers might label themselves as non-smokers due to them not perceiving social smoking as smoking; in fact, half of social smokers do not believe that they are smokers[19]. This might have resulted in social smokers identifying themselves as non-smokers in the above- mentioned questionnaire. Comparison to the current study can be found in Figure 8 below.

The study done in 2008 was compared to this study and there was no significant difference in the findings in smokers, non-smokers or ex-smokers (p-value 0.83).

**Figure 8** Comparing the unpublished study results of 2008 with the current study




Since smoking is a known detrimental addiction, several people do try and quit smoking. Social stigma against female smokers still exists, however literature has suggested that females are less likely to quit than males[20]. This was not reflected in this study since 71% of the female smoking cohort has tried to quit smoking in the past compared to the much lower 42.3% of the equivalent male cohort. However the latter statistics were also shown to be true in a local 2008 study whereas 78% of ex-smokers were females.

The total prevalence of smokers (social and regular smokers) was noted to have increased from first year to fifth year in both males and females.

Another interesting emerging phenomenon is that of social smoking. Social smokers are students who smoke more frequently when surrounded by fellow friends, especially whilst drinking alcohol[21 22]. Social smoking tended to start before university. Social smoking usually started when an individual gets exposed to cigarettes during events and parties and this is usually around the mid-teens. Furthermore, females tended to be more of social smokers in this study[23]. This result is echoed by a 2015 US survey[24] which enquired as to what were the reasons for women to smoke and the majority (62.4%) of them admitted to being social smokers[24].

Social smokers smoked less during the week than active smokers, a result which was found also in this study[21]. Social smokers are less dependent on smoking and are more readily able to quit smoking if the need arises (due to health risks) [25]. The US Department in 1994[26] also noted that the less cigarettes smoked during adolescence, the higher the likelihood that they will not be smoking within 5 years' time.

Another important aspect that should be addressed is the fact that 57.5% of students who do not smoke cite 'Unhealthy and Health reasons' as being their motivator for abstention suggests that there is an

appreciation amongst medical students for the deleterious effects of tobacco products. Despite this, there may still be a role for further emphasis on tobacco and smoking cessation in the curriculum - cessation both for future patients as well as for the students themselves.[27]

The statistics produced in a similar local study done more than a decade ago and the current statistics do not differ by much. That is, despite the number of local awareness campaigns having improved tremendously, both on a University level via the increased number of campaigns done by the Malta Medical Students' Association and on a national level done by several NGOs. The Malta Medical Students' Association, has a standing committee on public health that regularly organises anti-smoking and health awareness campaigns for the general public, showing that there is an interest among local medical students to take up the role of smoking cessation advisors.

Ideally, we may be able to decrease smoking amongst medical students by having anti-smoking programs made available to medical students while in training.[28] This is not currently available at the University of Malta Medical School. Some improvements have been made since 2008; smoking is prohibited on most areas of the local hospital grounds. Challenging local health beliefs remains a formidable task.[29]

This study raises a number of important questions; whether medical students smoke more or less than their non-medic counterparts at the University of Malta, whether medical students report their smoking status and patterns accurately, and whether they would be responsive to a more aggressive anti-smoking attitude in the course curriculum. A repeat of this study in the future may take these issues into account and monitor whether there have been any changes in smoking prevalence to match any national trends. The current trend indicates that current methods and awareness campaigns are not producing statistically significant results in reducing the number of active smokers within the medical student cohort.

## Conclusion

In conclusion, our study confirms that smoking amongst local medical students is as prevalent as it was a decade ago. This study furthers the knowledge on local medical student's smoking habits, tendencies and adds habits and tendencies of social smoking and vaping as well. Females were more likely to be social smokers than males whilst males were more likely to be active smokers. Females were also less likely to smoke in general. Females were more likely to have tried stopping smoking. A small group of students admitted to vaping as well. Smoking is still a major issue amongst local medical students and current practises to stop students smoking have not yielded any benefits.

The above data should enable better development of antismoking campaigns and groups to be formed and be more effective. We recommend that greater emphasis is placed upon the deleterious effects of tobacco during the medical course as well as opportunities for free smoking cessation counselling sessions to be made available to students. (Khan et al., 2005) These conclusions reflect and consolidate the studies in which there needs to be a better framework and structure towards combating smoking amongst medical students as well as smoking cessation programmes readily available for those who wish to quit (Khan et al., 2005). Moreover, smoking should be banned from all

hospital grounds and premises in order to further decrease smoking areas available and hence decrease smoking. The relevant health and education authorities would do well to recognize and tackle this issue so that all future doctors can become role models for their patients.

## Summary Box

- Healthcare providers are the most important link in convincing patients to stop smoking.
- Most people start smoking in their teens, however they usually enter medical school at the age of 18 by which time they may already be established smokers.
- Smoking in medical students is less prevalent than in the general population.
- Mortality from lung cancer continues to increase locally.

## Learning points

- Smoking in medical students is less than the national average.
- Smoking amongst medical students has remained virtually unchanged compared to a prior audit done a decade previously.
- Female medical students were more likely to be social smokers and more likely to try to quit.
- Medical students have started to vape similar to the general population.

## References


1. Chapman S. The role of doctors in promoting smoking cessation. BMJ (Clinical research ed.). 1993 307(6903), 518–519.
2. Pipe A, Sorensen M, Reid R. Physician smoking status, attitudes toward smoking, and cessation advice to patients: An international survey. Patient Education and Counseling. 2009 74, (1) 118-123.
3. Sreeramareddy CT, Ramakrishnareddy N, Rahman M.

   Prevalence of tobacco use and perceptions of student health professionals about cessation training: results from Global Health Professions Students Survey. BMJ Open 2008;8:e017477.
4. Smith DR, Leggat PA. An international review of tobacco smoking among medical students. J Postgrad Med 2007, 53: 55-62.
5. England K. & Gauci D. Smoking and lung cancer mortality in Malta. The Synapse, 2015, 14(4), 24-25
6. Elizondo L, Lebedeva E, Graen L, Mauer-Stender K, Fedkina N, Rakovac I. European Tobacco Use Trends Report 2019.
7. Malta - Smoking prevalence, males (% of adults). Trading Economics 2016.

Retrieved from: https://tradingeconomics.com/malta/smoking-prevalence-males-percent-of-adults-wb-data.html on 10th July 2019.

8. Sant Portanier C. Cigarette Smoking across Three Maltese Generations Malta Medical Journal 2004 Vol 6 issue 1 31-35.
9. Sebo, P., Bouvier Gallacchi, M., Goehring, C. et al. Use of tobacco and alcohol by Swiss primary care physicians: a cross-sectional survey. BMC Public Health 2007, 7, 5.
10. Shahab L, West R. Differences in happiness between smokers, ex-smokers and never smokers: cross-sectional findings from a national household survey. Drug and Alcohol Dependence, 2012, 38–44.
11. West R, & Shiffman S. Smoking cessation (3rd ed.). Abingdon: Health Press. 2016.
12. Do YK, Bautista MA. Medical students' tobacco use and attitudes towards tobacco control Medical Education 2013, 47, (6)607.
13. Smoking and mental health. A joint report by the Royal College of Physicians and the Royal College of Psychiatrists 2013.
14. Josseran L, King G, Gilbert P Smoking by French general practitioners: behaviour, attitudes and practice. The European Journal of Public Health 2005,15(1):33-38.
15. Toriola A, Myllykangas M and Barengo N. Smoking behaviour and attitudes regarding the role of physicians in tobacco control among medical students in Kuopio, Finland in 2006 CVD Prevention and Control, Volume 3, Issue 2, 2008, Pages 53-60.
16. Robert West. Tobacco smoking: Health impact, prevalence, correlates and interventions, Psychology & Health, 2017, 2:8, 1018-1036.
17. Baška T, Bašková M. Increasing trends of tobacco use in medical students in Slovakia. Cent Eur J Publ Health 2007, 15 (1):29–32).
18. Caruana Montaldo B. Prevelance of Smoking amongst medical students. Unpublished. 2008
19. Levinson AH, Campo S, Gascoigne J, Jolly O, Zakharyan A, Tran ZV. Smoking, But Not Smokers: Identity Among College Students Who Smoke Cigarettes. Nicotine & Tobacco Research 2007, 9(8); 845–852
20. Smith PH, Bessette AJ, Weinberger AH, Sheffer CE, McKee SA. Sex/gender differences in smoking cessation: A review. Prev Med Nov; 2016, 92:135-140.
21. Moran S, Wechsler H, Rigotti N. Social smoking among US college students. Pediatrics Oct; 2004, 114(4):1028-34.
22. Waters K, Harris K, Hall S, Nazir N, Waigandt A. Characteristics of Social Smoking among College Students. J Am Coll Health. 2006 Nov–Dec; 55(3): 133–139.
23. Li X, Holahan CK, Holahan CJ. Sociodemographic and Psychological Characteristics of Very Light Smoking among Women in Emerging Adulthood, National Survey of Drug Use and Health. Prev Chronic Dis 2011, 12:140547.
24. MacGill M. Young women increasingly attracted to social smoking. MedicalNewsToday 2015 Retrieved from: https://www.medicalnewstoday.com/articles/296993.php on 26th June 2019
25. Rollins S, Malmstadt Schumacher JR, Ling PM. Exploring the phenomenon of social smoking — why do so many young adults socially smoke? Paper presented at: National Conference on Tobacco or Health; November 20, 2002; San Francisco, CA.
26. US Department of Health and Human Services. Preventing Tobacco Use Among Young People: A Report of the Surgeon General. Atlanta, GA: US Dept of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1994.
27. Chatkin J, Chatkin G. Learning about smoking during medical school: are we still missing opportunities? Int J Tuberc Lung Dis. Apr; 2009, 13(4):429-37.

28. Khan FM, Husain SJ, Laeeq A, Awais A, Hussain SF, Khan JA. Smoking prevalence, knowledge and attitudes among medical students in Karachi, Pakistan. East Mediterr Health J 2005;11:952-8.

29. Cauchi D, Mamo J. Smoking Health Professional Student: An Attitudinal Challenge for Health Promotion? International Journal of Environmental Research and Public Health 2012, 9(7)2550.

MMSG
REVIEW ARTICLE

# The role of the general practitioner in palliative care: a review

Marilyn Harney

Family medicine and palliative care are two specialities that share several important principles and have the needs of the 'whole person' at their core. For this reason, the general practitioner can provide an invaluable role in palliative care through the early identification of palliative care needs, care coordination and end-of-life decisions. Two online databases were used to search for scientific papers focusing on the role of family doctors in this growing speciality. These features, together with the challenges and barriers encountered by family doctors, are explored and discussed in detail in this review.

**Marilyn Harney**
MD MMCFD MRCGP(INT)
Department of Primary Health Care,
Ministry of Health, Malta
harneymarilyn@gmail.com

## Introduction

Family medicine and palliative care are two specialities that share several important principles. **Family medicine** is the speciality that is responsible for providing comprehensive and continuing care to all individuals seeking medical advice, irrespective of gender, age and illness. Family doctors are often the initial point of contact for people in the health system, and aside from diagnosis and treatment their responsibilities include health promotion, disease prevention, palliation and patient empowerment.[1] An important characteristic of family medicine is the focus on the 'person', treating individuals as a 'whole' and seeing them in the context of their family, community and culture. Family doctors also have the privilege of building a unique relationship with their patients which further improves the quality of care provided. **Palliative care** is the speciality that focuses on prevention and relief of suffering as a way of improving the quality of life of patients who are facing a life-threatening illness with a limited prognosis (not restricted solely to malignancy), by addressing the physical, psychosocial and spiritual needs, as well as providing support to their families.[2] This care is usually provided by a multi-disciplinary team.

Both family medicine and palliative care have the needs of the 'whole person' at their core, and two of their most marked characteristics are prevention and continuity of care. Taking into consideration these similarities, and with the reality of an ever-increasing ageing population and the burden posed by malignancy and other chronic conditions on the health of populations in developed countries[3], the family doctor can provide an invaluable role in palliative care, the various features of which will be discussed in this review.

The terms 'general practitioner' and 'family doctor' are used interchangeably in the text.

## Method

A search for scientific papers related to the various aspects of the role of the general practitioner in palliative care was done using two online databases, namely PubMed/MEDLINE and Google Scholar.

The keywords used in the search included: 'family medicine', 'primary care', 'palliative medicine', 'palliative care', 'general practitioner' and 'primary palliative care'.

The titles and abstracts of the papers in the literature search results were reviewed and assessed for quality and relevance to the topic in question. Further papers were selected through citation searching, and eventually a final set of papers to be included in the review was chosen.

## Identification of palliative care needs

In everyday practice, palliative care is often started during the terminal phase of a life-threatening illness. Palliative care improves the quality of life of patients and their families by means of **early identification** of needs, followed by assessment and management[2], therefore identifying and dealing with issues early on, during routine visits by the family doctor, would be ideal. A number of tools have been developed to aid doctors in this process. These tools help in identifying patients' needs at an early stage during the course of an illness, and thus developing a proactive palliative care plan. Family doctors are often patients' initial and main medical contact point, and they also build a unique relationship with their patients over time. In view of this, the family doctor is in a distinctive position to use the consultation as an opportunity to start a discussion about this sensitive topic, which

patients often find difficult to bring up themselves.

Deciding when a palliative approach should be started is difficult, especially in the case of non-malignant diseases.[4] The following is a summary of the tools which have been developed over the years for this purpose, and which are particularly adapt to be used in family medicine.

- **The 'surprise question'** was initially suggested for use by doctors as a rough initial indication in patients with advanced disease or progressive life-limiting conditions – *'Would I be surprised if the patient were to die in the next few months, weeks, days?'*.[5] The answer to this, based on the family doctor's intuition (derived from clinical, social and other factors that provide an overall picture of deterioration[5]), if in the negative should initiate thinking of possible measures to improve the patient's quality of life both at present and in the future, taking into consideration the likely deterioration in the condition. This question was however found to be of limited use in practice since doctors tend to overestimate the survival of their patients[6], but is of benefit when incorporated in other tools. A recent study published in 2018 explored the value of adding a second question when the surprise question above is answered in the negative. The second surprise question *'Would I be surprised if this patient is still alive after 12 months?'* was found to be helpful by general practitioners (GPs) and appeared to contribute to more extensive and anticipatory palliative care planning.[7]
- **RADPAC (RADboud indicators for PAlliative Care needs)** is another tool that can be used by family doctors to identify patients who would benefit from a palliative care approach.[6] It presents a set of indicators for patients with congestive heart failure, chronic obstructive pulmonary disease and malignancy. It is disease-specific, focusing on physical aspects, and lacks consideration of the psychosocial and spiritual domains. This tool does not include the 'surprise question'. Family doctors trained in the use of this tool have been found to be more sensitive in identifying palliative patients and providing a multidimensional palliative care approach.[8]
- **Gold Standards Framework – Prognostic Indicator Guide (PIG)** was developed in the UK and incorporates the 'surprise question' with a set of general and specific clinical indicators for decline in organ failure, dementia and frailty trajectories.[5]
- **Supportive and Palliative Care Indicators Tool (SPICT)** is based on a combination of general indicators and disease-specific assessment criteria. It was developed in Scotland[9] and the 'surprise question' is not part of this tool as the authors feel it can delay appropriate early palliative care intervention.[10]
- **NECPAL CCOMS-ICO (NECPAL: Necesidades Paliativas)** tool was developed in Spain, is based on PIG and SPICT**,** but has been adapted to a Latin-Mediterranean clinical and cultural context. Of particular note are the inclusion of the request of the patient or family for palliative support as one of the criteria, as well as psychosocial domain, frailty and any progression of functional and nutritional decline.[11]

- **Early identification tool for palliative care patients** was developed in North America. It incorporates the use of the 'surprise question' together with a set of general indicators for decline and parameters for advanced stages of illness.[12]
- **The 'quick guide'** was developed in London and provides simple guidance for daily clinical practice. It makes use of the 'surprise question' together with a set of general indicators of decline, hospital admissions, weight loss, comorbidities and burden of illness.[12]

A comparison of the four main identification tools available is illustrated in Table 1. SPICT appears to be the most validated, accessible and comprehensive tool available to general practitioners; it is also straightforward, making it easy to use irrespective of the level of experience of the physician in palliative care.[13]

**Table 1** Comparison of tools available for identification of palliative care needs

| | RADPAC | GSF - PIG | SPICT | NECPAL |
|---|---|---|---|---|
| **Primary care** | ✓ | ✓ | ✓ | ✓ |
| **Secondary care** | | | ✓ | ✓ |
| **Surprise question** | | ✓ | | ✓ |
| **Patient choice/request** | | | ✓ | ✓ |
| **Target patient group** | | | | |
| - Cancer | ✓ | ✓ | ✓ | ✓ |
| - COPD | ✓ | ✓ | ✓ | ✓ |
| - Heart failure | ✓ | ✓ | ✓ | ✓ |
| - Others* | | ✓ | ✓ | ✓ |
| **General indicators** | | | | |
| - Age | | ✓ | | |
| - Functional status | ✓ | ✓ | ✓ | ✓ |
| - Weight loss | ✓ | | ✓ | ✓ |
| - Hospital admissions | ✓ | ✓ | ✓ | ✓ |
| - Other | ✓ | | ✓ | ✓ |
| **Specific indicators for:** | | | | |
| - Cancer | ✓ | ✓ | ✓ | ✓ |
| - COPD | ✓ | ✓ | ✓ | ✓ |
| - Heart disease | ✓ | ✓ | ✓ | ✓ |
| - Kidney disease | | ✓ | ✓ | ✓ |
| - Liver disease | | | ✓ | ✓ |
| - Neurological disease (inc. MND, PD, MS) | | ✓ | ✓ | ✓ |
| - Dementia/Frailty | | ✓ | ✓ | ✓ |

**RADPAC**: RADboud indicators for PAlliative Care needs; **GSF-PIG**: Gold Standards Framework – Prognostic Indicator Guide; **SPICT**: Supportive and Palliative Care Indicators Tool; **NECPAL**: Necesidades Paliativas; **COPD**: Chronic Obstructive Pulmonary Disease; **MND**: Motor Neurone Disease; **PD**: Parkinson Disease; **MS**: Multiple Sclerosis; *Others: Kidney disease, Neurological disease, Frailty/Dementia/Stroke

**Shaded rows** indicate features common to all the four tools.

Even though these tools are available, studies in Europe have shown that these are rarely used in the identification of palliative care needs, and currently this practice is largely based on the family doctor's clinical judgement, information received from the hospital[12], observation of increase in patient dependency and information from family members.[14]

## Coordinating care

Family doctors will often have a coordinating role in palliative care.[15] This includes the important management of symptom complexity: dealing with the psychosocial and spiritual symptoms for which specific skills need to be developed[15], in addition to the physical symptoms. GPs are capable of delivering satisfactory symptom control[15] but there is room for improvement in this aspect especially when dealing with pain management.[16] Non-acute issues might need to be gently explored by the family doctor, as the patients and families often do not readily discuss these in an attempt not to bother the doctor, and as they often believe the doctor's role is more focused on dealing with acute problems. On the other hand, family doctors might also avoid such discussions about palliative care needs because they are uncomfortable approaching the subject and because of fear of taking away the patient's hope.[17]

Upon identification of the palliative care needs, the family doctor can plan and coordinate care by involving other professionals as required and facilitating use of services in the community which might be beneficial, such as loan of equipment. Collaborating with specialist teams in palliative care results in improved outcomes for patients.[15,18]

Ensuring continuity of care is an important feature, especially by liaising with hospital doctors and the specialist palliative care team, as well as the family.[19] Family doctors tend to be involved more during the early stage of diagnosis/referral and the terminal stage of care, leaving a "vacuum" in the middle of the disease trajectory which if not addressed possibly leads to sub-optimal treatment and unnecessary admissions to hospital.[20] Indeed, doctors in primary care have an important role to play and should be there for patients throughout the whole course of the illness.[21] Communication between specialists and GPs during and after hospital admissions is important for doctors to be aware of any changes or developments, and to emphasize the valuable role the family doctor has in the holistic management of the patient in the community.[22]

The family doctor needs to be sensitive to the 'unspoken needs' of patients and their families, patiently being there for them and providing them with the time and space to talk about their fears and concerns, while acknowledging that this might be a difficult and challenging journey for them. Providing emotional support to family members and helping them deal with anticipatory grief is another important role, which should also be extended to the relatives after the patient's death as they go through the bereavement process.[23]

Good communication between the family doctor and the patient is of utmost importance. A number of issues might affect this, including when patients are unwilling to know their diagnosis or prognosis and when relatives put pressure not to fully disclose information to the patient.[24] There should be frequent reassessment of patients' ideas regarding disclosure of information, and care

should be tailored accordingly.[25] A high level of communication skills is needed in dealing with these situations.[24]

Family doctors can influence and prevent hospital admissions at the end of life by carefully anticipating possible scenarios, discussing them with patients and relatives, planning and giving advice accordingly.[26] Relatives and caregivers need to feel supported by the family doctor, especially through the doctor being accessible during emergencies while being able to take decisions and shoulder responsibility.[26] Hospital referrals may also be affected by patient and family factors, such as requests for referral by patients who feel 'safer' in a hospital environment, or relatives feeling that they cannot provide the necessary care at home. Improving holistic community palliative care by early referral, communicating with patients and supporting caregivers, are important aspects which help to reduce admissions to hospital and decrease the number of hospital deaths at the end of life.[27-28]

## End-of-life decisions

Family doctors are often faced with challenging end-of-life issues, which include informing patients about their diagnosis and prognosis, discussing their preferred place of care, withholding or withdrawing treatment and symptom control.[24,29] The family doctor, as well as the patient might be reluctant to start discussions about such issues, however doctors should use their privileged position to initiate and facilitate these sensitive discussions while helping patients prepare for death.[24] The question 'How long have I got?' is commonly asked and might be difficult for the doctor to answer, especially in view of uncertainty and fear of over- or underestimating the length of survival, which might in turn be a source of distress for relatives or carers.[24,30] Prognostic indices such as the Palliative Prognostic Score may help family doctors reach a more accurate prediction.[30] Discussions about prognosis can also be challenging for the doctor when the patients and/or relatives are in denial and fail to accept that the end-of-life is near, and this might make it more stressful for the GP to make decisions regarding the palliative care needs of the patient.[24] Even though most patients (approximately 75%) would prefer to die at home, the majority die in hospitals or nursing homes, with only about 30% dying at home.[31] Carers of patients who died in their 'preferred place' were significantly more satisfied with the care provided by their family doctor.[16]

Withholding and withdrawing treatment and intensification of analgesia are options that most GPs would consider in their management of palliative patients, and discussion of these issues with patients was found to be related to doctors having received some form of training in palliative care.[32-34] This is in contrast to palliative sedation, which GPs were in general uneasy with, as they felt abuse of this could result in euthanasia.[35-37] Euthanasia and physician-assisted dying is a very broad subject and constantly changing especially in view of developments and changes to legislation. Studies have shown that the majority of GPs in the UK, Malta, Italy, Belgium, Australia and New Zealand would be reluctant to perform euthanasia, even if this is legal. [35, 38-41] This is in contrast to the situation in the Netherlands where euthanasia is legal, and the majority of these procedures are performed by GPs.[42] Having been exposed to training in palliative care and working with palliative patients was found to significantly affect doctors' views resulting in a lower chance of considering

euthanasia.[32,38,39] This could possibly be due to doctors feeling more confident in effectively managing symptoms and keeping patients comfortable at the end of life.

Since 2012, a hospital trust in the UK has developed a two-day course for healthcare professionals called 'Transforming End of Life Care'. This was found to be useful by participants, including family doctors, and was noted to be a source of increased self-rated confidence, competence and knowledge in end-of-life care.[43] Similar initiatives in other countries might prove to be beneficial, especially for GPs to gain skills in dealing with this often challenging period in their patients' lives.

There is a lack of legal and moral guidance for GPs when it comes to end-of-life decisions[35] and developing guidelines or protocols in this regard would facilitate this difficult process for doctors.

## Challenges and barriers faced by family doctors

Family doctors might feel that they are not knowledgeable enough when dealing with palliative care patients.[15,24,44-46] This might stem from the fact that exposure to such patients is infrequent, and therefore they would feel less comfortable prescribing certain medications such as high doses of opiates, or using certain equipment such as a syringe driver, which are otherwise not commonly used in everyday practice.[45]

Family doctors may have to deal with feelings of helplessness and might also struggle emotionally when dealing with patients with a terminal illness, whom they have known for a long time, as well as their relatives.[15,23,24,44] This exposure to painful emotions highlights the possible lack of coping skills of doctors when faced with death and suffering. Several studies have shown that family doctors provide excellent educational support and are involved in pain management, but tend to lack in providing emotional, social and spiritual support to patients.[15,20,47]

The multidisciplinary team is a key characteristic of palliative care, and the fact that many family doctors usually work alone might be a challenge in delivering this care.[23] Liaising with specialist palliative care services available is important, and if possible having discussions with the team about individual patient care and issues would be ideal. In the absence of specialist palliative services, such as in rural areas, the GP is seen to take more the role of leading and managing palliative patients.[48] This might indicate that simply referring patients to specialist palliative services is resulting in family doctors being less involved and experienced in the care of their palliative patients.

Dealing with palliative care patients is often demanding, and family doctors would often be required to be available out-of-hours, dealing with emergencies as they arise and carrying out home visits.[24,44,49] Guidelines are lacking in palliative care, and in this always-evolving speciality family doctors need to keep up-to-date with new knowledge and advances, which might be a challenge for busy practitioners.[23,44,49]

There appears to be a big demand for improved and extended medical training in palliative care as shown by a number of studies with doctors in different countries, including Australia, Belgium, Sweden, Italy, Malta, Denmark and Switzerland.[15,32,33] Incorporating palliative care as part of the post-graduate family medicine specialization programme has been found to be an effective way of teaching, as well as causing a positive change in

attitudes towards end-of-life care.[50] Palliative care is incorporated in most GP vocational training programmes worldwide, however studies have found that lack of time and patient exposure were common barriers to providing effective training, and it was suggested that training should focus more on specific needs which were relevant for GP trainees, including addressing ethical issues, using a syringe driver, managing dying patients in the community and self-care.[51,52] GP trainees' confidence in palliative care was found to improve after their rotation which they found useful in terms of developing communication skills and improving knowledge of managing symptoms at the end-of-life.[15,53] A study in Canada however showed that most of the trainees were discouraged from incorporating palliative care in their everyday practice as after seeing it being carried out by specialised physicians the trainees did not feel confident in their ability to manage such patients independently.[53] This highlights that training should be modified to address the particular needs of the trainees and focus on improving their confidence in areas which they can eventually put into practice, by involving them in the care of patients being managed by specialist teams and giving them the opportunity to learn by experience.[15] The Primary Palliative Toolkit developed in 2015 also highlights the need for promotion of palliative care training.[45] A number of learning opportunities are available for doctors, including conferences, e-learning modules and courses. The European Certificate in Essential Palliative Care is an 8-week distance learning course, aimed at healthcare professionals, and is available in the UK, Ireland and Malta. It has been found to improve confidence in the management of palliative care patients, which confidence is sustained over time.[54] A study by Reed et al. demonstrates evidence of improved confidence in management of symptom control, communication skills and a holistic approach towards patients in candidates who had completed this course.[54]

## Conclusion

In high-income countries, about 70% of deaths are due to advanced cancer and other chronic conditions[11] and the increase in demands on the service is one of the main reasons why the role of family doctors in palliative care is becoming more important.

Several adjectives can be used to describe the family doctor's role in palliative care, including 'team leader', 'guide', 'supporter', 'coordinator', 'interpreter', 'co-morbidity manager' and 'gatekeeper'.[46] The GP should be the key person to manage and coordinate care, and this role can be improved by facilitating communication with specialists and providing training opportunities.[46]

Palliative care is considered to be one of the best parts of the job of a family doctor, and acting as a 'reference point' by simply explaining what is going on is particularly reassuring for patients.[16,44] When given appropriate training in the important skills of communication, leadership and empathy, the family doctor can feel empowered to provide an invaluable service to patients and families during this very delicate period in their lives.

In his General Practice textbook, John Murtagh brilliantly summarizes the role of the family doctor as follows:

'The GP is the ideal person to manage palliative care for a variety of reasons—availability, knowledge of the patient and family, and the relevant psychosocial influences. A key feature is the ability to provide the patient with independence and dignity by managing

palliative care at home. Someone has to take the responsibility for leadership of the team and the most appropriate professional is a trusted family doctor.'[55]


## Acknowledgement

I am sincerely grateful to Dr Jurgen Abela for many insightful discussions about the topic which inspired the writing of this article.


## References


1. WONCA Europe: The European Definition of General Practice/Family Medicine [Internet]. 2011 [cited 2018 Mar 09]. Available from: www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202011%20with%20revised%20wonca%20tree.pdf
2. World Health Organization: Definition of Palliative Care [Internet]. 2018 [cited 2018 Mar 09]. Available from: http://www.who.int/cancer/palliative/definition/en/
3. World Health Organization: Global Health Observatory Data: Causes of death, by WHO region [Internet]. 2015 [cited 2018 Mar 09]. Available from: www.who.int/gho/mortality_burden_disease/causes_death/region/en/
4. Beernaert K, Deliens L, De Vleminck A, Devroey D, Pardon K, Van den Block L et al. Early identification of palliative care needs by family physicians: A qualitative study of barriers and facilitators from the perspective of family physicians, community nurses, and patients. Palliat Med [Internet]. 2014 [cited 2018 Mar 19]; 28(6):480-490. Available from: http://journals.sagepub.com/doi/abs/10.1177/0269216314522318
5. Thomas K. Prognostic Indicator Guidance (PIG). 4th ed. The Gold Standards Framework Centre in End of Life Care [Internet]. 2011 [cited 2018 Mar 19]. Available from: http://www.goldstandardsframework.org.uk/
6. Thoonsen B, Engels Y, van Rijswijk E, Verhagen S, van Weel C, Groot M et al. Early identification of palliative care patients in general practice: development of RADboud indicators for Palliative Care Needs (RADPAC). Br J Gen Pract [Internet]. 2012 [cited 2018 Mar 19]; 62(602) 625-631. Available from: http://bjgp.org/content/62/602/e625.long
7. Weijers F, Veldhoven C, Verhagen C, Vissers K and Engels Y. Adding a second surprise question triggers general practitioners to increase the thoroughness of palliative care planning: results of a pilot RCT with cage vignettes. BMC Palliat Care [Internet]. 2018 [cited 2018 Nov 02]; 17:64. Available from: https://doi.org/10.1186/s12904-018-0312-6
8. Thoonsen B, Gerritzen SHM, Vissers KCP, Verhagen S, van Weel C, Groot M et al. Training general practitioners contributes to the identification of palliative patients and to multidimensional care provision: secondary outcomes of an RCT. BMJ Support Palliat Care [Internet]. 2016 [cited 2018 Mar 19]; 9:e18. Available from: https://doi.org/10.1136/bmjspcare-2015-001031
9. Maas EAT, Murray SA, Engels Y, et al. What tools are available to identify patients with palliative care needs in primary care: a systematic literature review and survey of European practice. BMJ Support Palliat Care [Internet]. 2013 [cited 2018 Mar 19]; 3:444-451. Available from: http://spcare.bmj.com/content/3/4/444
10. The University of Edinburgh – Using SPICT [Internet]; c2013-2018 [cited 2018 Nov 11] Available from: https://www.spict.org.uk/using-spict/
11. Gómez-Batiste X, Martínez-Muñoz M, Blay C, Amblas J, Vila L, Costa X, Espaulella J, Espinosa J. Recommendations for the comprehensive and integrated care of persons with Advanced chronic conditions and life-limited prognosis in Health and social services: NECPAL-CCOMS-ICO© 3.0. 2016 [cited 2018 Mar 19]. Available from: http://ico.gencat.cat/web/.content/minisite/ico/professionals/documents/qualy/arxius/NECPALCCOMS-3.0-ENG-DEFINITIVE.pdf

12. Maas EAT, Murray SA, Engels Y. What tools are available to identify patients with palliative care needs in primary care: a systematic literature review and survey of European practice. BMJ Support Palliat Care [Internet]. 2013 [cited 2018 Mar 19]; 3:444-451. Available from: http://spcare.bmj.com/content/3/4/444

13. Walsh R, Mitchell G, Francis L, van Driel M. What diagnostic tools exist for the early identification of Palliative Care patients in General Practice? A systematic review. J Palliat Care [Internet]. 2015 [cited 2018 Nov 02]; 31(2) 118-123. Available from: https://journals.sagepub.com/doi/abs/10.1177/082585971503100208

14. Claessen SJ, Francke AL, Engels Y, Deliens L. How do GPs identify a need for palliative care in their patients? An interview study. BMC Fam Pract [Internet]. 2013 [cited 2018 Mar 21]; 14:42. Available from: https://doi:10.1186/1471-2296-14-42

15. Mitchell GK. How well do general practitioners deliver palliative care? A systematic review. Palliat Med [Internet]. 2002 [cited 2018 Apr 21]; 16: 457-464. Available from: http://journals.sagepub.com/doi/pdf/10.1191/0269216302pm573oa

16. Hanratty, B. Palliative care provided by GPs: the carer's viewpoint. Br J Gen Pract [Internet]. 2000 [cited 2018 Apr 21]; 50: 653-654. Available from: http://bjgp.org/content/bjgp/50/457/653.full.pdfhttp://bjgp.org/content/bjgp/50/457/653.full.pdf

17. Beernaert K, Deliens L, De Vleminck A, Devroey D, Pardon K, Van den Block L et al. Early identification of palliative care needs by family physicians: A qualitative study of barriers and facilitators from the perspective of family physicians, community nurses, and patients. Palliat Med [Internet]. 2014 [cited 2018 Apr 21]; 28(6):480-490. Available from: http://journals.sagepub.com/doi/abs/10.1177/0269216314522318

18. Schneider N, Mitchell GK, Murray SA. Palliative care in urgent need of recognition and development in general practice: the example of Germany. BMC Fam Prac [Internet]. 2010 [cited 2018 Apr 21]; 11:66. Available from: http://www.biomedcentral.com/1471-2296/11/66

19. Brotzman GL and Robertson RG. Role of the primary care physician after diagnosis of cancer. J Prim Care [Internet]. 1998 [cited 2018 Apr 21]; 25(2):401-406. Available from: https://doi.org/10.1016/S0095-4543(05)70072-5

20. Hickner J, Kent, S, Naragon P, Hunt L. Physicians' and Patients' Views of Cancer Care by Family Physicians: A Report From the American Academy of Family Physicians National Research Network. J Family Med [Internet]. 2007 [cited 2018 May 02]; 39 (2):126-31. Available from: https://pdfs.semanticscholar.org/1d17/30ba836a0b071a6e6c2245e27f28546bdeab.pdf

21. Beernaert K, Van den Block L, Van Thienen K, Devroey D, Pardon K, Deliens L. Family physicians' role in palliative care throughout the care continuum: stakeholder perspectives. J Family Prac [Internet]. 2015 [cited 2018 May 02]; 32(6): 694-700. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26373666

22. Mitchell GK, Reymond EJ, and McGrath BP. Palliative care: promoting general practice participation. Med J Australia [Internet]. 2004 [cited 2018 May 02]; 180(5):207-8. Available from: https://www.mja.com.au/system/files/issues/180_05_010304/mit10648_fm.pdf

23. Ramanayake R, Dilanka G, Premasiri L. Palliative care; role of family physicians. J Family Med Prim Care [Internet]. 2016 [cited 2018 May 02]; 5:234-7. Available from: http://www.jfmpc.com/text.asp?2016/5/2/234/192356

24. Slort W, Schweitzer BPM, Blankenstein AH, Abarshi EA, Riphagen Il, Echteld MA et al. Perceived barriers and facilitators for general practitioner–patient communication in palliative care: A systematic review. Palliat Med [Internet]. 2011 [cited 2018 May 02]; 25(6) 613–629. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21273221

25. Michiels E, Deschepper R, Bilsen J, Mortier F, Deliens L. Information disclosure to terminally ill patients and their relatives: self-reported practice of Belgian clinical specialists and general practitioners. Palliat Med [Internet]. 2009 [cited 2018 May 12];23(4) 345–353. Available from: https://doi.org/10.1177/0269216308102043

26. Reyniers T, Houttekier D, Pasman HR, Stichele RV, Cohen J, Deliens L. The Family Physician's Perceived Role in Preventing and Guiding Hospital Admissions at the End of Life: A Focus Group Study. Ann Fam Med [Internet]. 2014 [cited 2018 May 21]; 12(5): 441-446. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25354408

27. Reyniers T, Deliens L, Pasman HRW, Vander Stichele R, Sijnave B, Houttekier D. Appropriateness and avoidability of terminal hospital admissions: Results of a survey among family physicians. Palliat Med [Internet]. 2016 [cited 2018 May 21]; 31(5): 456-464. Available from: http://journals.sagepub.com/doi/abs/10.1177/0269216316659211

28. Murray S, Boyd K, Sheikh A, Thomas K, Higginson IJ. Developing primary palliative care - People with terminal conditions should be able to die at home with dignity. BMJ [Internet]. 2004 [cited 2018 May 21]; 329:1056–7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC526105/

29. Abela J. Practical aspects of Palliative Care. JMCFD [Internet]. 2013 [cited 2018 May 25]; 02(02): 18-19. Available from: https://www.um.edu.mt/library/oar/bitstream/handle/123456789/4461/Practical%20aspects%20of%20palliative%20care.pdf?sequence=1&isAllowed=y

30. Cachia E. Why palliative care? Encountering challenging issues. MMJ [Internet]. 2007 [cited 2020 Feb 16]; 4:6-10. Available from: https://www.um.edu.mt/umms/mmj/showpdfbf24.html?article=190

31. Davies E and Higginson IJ. World Health Organization Regional Office for Europe. Palliative Care: The Solid Facts. [Internet]. Copenhagen 2004 [cited 2018 May 25]. Available from: www.euro.who.int/__data/assets/pdf_file/0003/98418/E82931.pdf?ua=1

32. Abela J, Mallia P. Training in palliative medicine and Maltese doctors: a cross-sectional survey. JMCFD [Internet]. 2016 [cited 2018 May 25]; 05(02): 13-19. Available from: https://www.um.edu.mt/library/oar//handle/123456789/19025

33. LÖfmark R, Mortier F, Nilstun T, Bosshard F, Cartwright C, Van Der Heide A, Onwuteaka-Philipsen B. Palliative Care Training: A Survey of Physicians in Australia and Europe. J Palliat Care [Internet]. 2006 [cited 2020 Feb 16]; 22(2):105–110. Available from: https://doi.org/10.1177/082585970602200207

34. Hinkka H, Kosunen E, Metsänoja R, Lammi UK, Kellokumpu-Lehtinen P. Factors affecting physicians' decisions to forgo life-sustaining treatments in terminal care. J Med Ethics [Internet]. 2002 Apr [cited 2020 Feb 16]; 28(2):109-14. Available from: https://doi.org/10.1136/jme.28.2.109

35. Abela J. GPs and End of Life Decisions: Views and Experiences. MMJ [Internet]. 2015 [cited 2018 May 25]; 27(02): 31-36. Available from: https://pdfs.semanticscholar.org/60e5/52a54a622d7304ac02531931bcefa86a8344.pdf

36. Seale C. End-of-life decisions in the UK involving medical practitioners. Palliat Med [Internet]. 2009 [cited 2020 Feb 16]; 23(3): 198–204. Available from: https://doi.org/10.1177/0269216308102042

37. Berghe PV, Mullie A, Desmet M, Huysmans GT, Jones DA, Gastmans C, MacKellar C. Assisted Dying: The Current Situation in Flanders: Euthanasia Embedded in Palliative Care. Eur J Palliat Care [Internet]. 2017 [cited 2020 Feb 16]; 20(6): 266-272. Available from: www.palliatief.be/accounts/143/attachments/Publicaties/ejpc_20_6_vdb_am_md_gh.pdf

38. Porter K, Warburton KG. Physicians' views on current legislation around euthanasia and assisted suicide: Results of surveys commissioned by the Royal College of Physicians. Future Healthc J [Internet] 2018 Feb [cited 2020 Feb 16]; 5(1):30-34. Available from: https://doi.org/10.7861/futurehosp.5-1-30

39. Young J, Egan R, Walker S, Graham-DeMello A, Jackson C. The euthanasia debate: synthesising the evidence on New Zealander's attitudes. Kōtuitui [Internet]. 2019 [cited 2020 Feb 16]; 14(1):1-21. Available from: https://doi.org/10.1080/1177083X.2018.1532915

40. Peretti-Watel P, Bendiane M K, Pegliasco H, Lapiana JM, Favre R, Galinier A. Doctors' opinions on euthanasia, end of life care, and doctor-patient communication: telephone survey in France. BMJ [Internet]. 2003 [cited 2020 Feb 16]; 327:595. Available from: https://www.bmj.com/content/327/7415/595

41. Sercu M, Pype P, Christiaens T. Are general practitioners prepared to end life on request in a country where euthanasia is legalised? J Med Ethics [Internet]. 2012 [cited 2020 Feb 16]; 38:274-280. Available from: https://jme.bmj.com/content/38/5/274

42. Kouwenhoven PSC, van Thiel GJM, van der Heide A, Rietjens JAC, van Delden JJM. Developments in euthanasia practice in the Netherlands: Balancing professional responsibility and the patient's autonomy. Eur J Gen Pract [Internet]. 2019 [cited 2020 Feb 16]; 25(1):44-48. Available from: https://doi.org/10.1080/13814788.2018.1517154

43. Selman L, Robinson V, Klass L. Improving confidence and competence of healthcare professionals in end-of-life care: an evaluation of the 'Transforming End of Life Care' course at an acute hospital trust. BMJ Support Palliat Care [Internet]. 2016 [cited 2020 Feb 16]; 6:231-236. Available from: https://spcare.bmj.com/content/6/2/231

44. Groot MM, Vernooij-Dassen MJF, Crul BJP, Grol RPT. General practitioners (GPs) and palliative care: perceived tasks and barriers in daily practice. Palliat Med [Internet]. 2005 [cited 2018 May 30]; 19: 111-118. Available from: http://journals.sagepub.com/doi/abs/10.1191/0269216305pm937oa?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

45. Murray SA, Firth A, Schneider N, Van den Eynden B, Gomez-Batiste X, Brogaard T et al. Promoting palliative care in the community: Production of the primary palliative care toolkit by the European Association of Palliative Care Taskforce in primary palliative care. Palliat Med [Internet]. 2015 [cited 2018 May 30]; 29(02): 101-111. Available from: http://journals.sagepub.com/doi/abs/10.1177/0269216314545006?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

46. Easley J, Miedema B, O'Brien MA, Carroll J, Manca D, Webster F et al. The role of family physicians in cancer care: perspectives of primary and specialty care providers. Oncology [Internet]. 2017 [cited 2018 Jun 06]; 24(02): 75-80. Available from: www.current-oncology.com/index.php/oncology/article/view/3447

47. Giezendanner S, Jung C, Banderet HR, Otte IC, Gudat H, Haller DM, Elger BS, Zemp E, Bally K. General Practitioners' Attitudes towards Essential Competencies in End-of-Life Care: A Cross-Sectional Survey. PloS one [Internet]. 2017 [cited 2020 Feb 16]; 12(2), e0170168. Available from: https://doi.org/10.1371/journal.pone.0170168

48. Ankuda CK, Jetty A, Bazemore A, Petterson S. Provision of Palliative Care Services by Family Physicians Is Common. J Am Board Fam Med [Internet] 2017 [cited 2018 May 30]; 30:255–25. Available from: http://www.jabfm.org/content/30/2/255.full.pdf+html

49. Yuen KJ, Behrndt MM, Jacklyn C, Mitchell GK. Palliative care at home: general practitioners working with palliative care teams. Med J Australia [Internet]. 2003 [cited 2018 May 30]; 179(6 Suppl):S38-40. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12964936

50. Singer Y and Carmel S. Teaching end-of-life care to family medicine residents–what do they learn? Med Teacher [Internet]. 2009 [cited 2018 May 30]; 31:2, e47-e50. Available from: https://doi.org/10.1080/01421590802331420

51. Abela J, Mallia P. An evaluation of palliative care education in the specialist training programme in family medicine. MMJ [Internet]. 2010 [cited 2018 May 30]; 22(04): 26-33. Available from: www.um.edu.mt/umms/mmj/PDF/306.pdf

52. Bryce C, Kam-Magruder J, Jackson J, Ledford CJ, Unwin BK. Palliative Care Education in the Family Medicine Clerkship: A CERA Study. PRiMER [Internet]. 2018 [cited 2020 Feb 16];2:20. Available from: https://doi.org/10.22454/PRiMER.2018.457651

53. Mahtani R, Kurahashi AM, Buchman S, Webster F, Husain A, Goldman R. Are family medicine residents adequately trained to deliver palliative care? Can Fam Physician [Internet]. 2015 [cited 2018 May 30]; 61(12):e577-82. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4677961/

54. Reed E, Todd J, Lawton S, Grant R, Sadler C, Berg J, Lucas C, Watson M. A multi-professional educational intervention to improve and sustain respondents' confidence to deliver palliative care: A mixed-methods study. Palliat Med [Internet]. 2017 [cited 2018 Sep 12]; 32(2): 571-580. Available from: https://doi.org/10.1177/0269216317709973

55. Murtagh John. Murtagh's General Practice. 6th ed. Australia: McGraw-Hill Education; c2015. Chapter 11, Palliative Care.

MMSG
REVIEW ARTICLE

# Traditional counter-stimulation practices in a Central Mediterranean Island population

Charles Savona-Ventura

A review of the medical folklore of the Maltese Islands identifies the use of counter-irritation practices dating to the prehistoric period. These practices are very much reminiscent of those in contemporary Traditional Chinese Medicine. Because of the distances involved, it is unlikely that direct cultural intercourse took place and it is suggested that these similarities were the result of isolated parallel development of ideas based on observation and experimentation

**Charles Savona-Ventura**
MD, DScMed, ACOG, FRCOG, FRCPI, FRCPE
Centre for Traditional Chinese Medicine,
University of Malta,
Msida, Malta
charles.savona-ventura@um.edu.mt

## Introduction

The Maltese Islands are a small group of very small islands sited in the Central Mediterranean just 93 kilometres south of Sicily and 290km from the Northern African mainland. Gibraltar is 1836km to the west and Alexandria is 1519km to the east. This central position within the Mediterranean Sea made the islands an important meeting place for the various Mediterranean cultures throughout the ages, merging and amalgamating European traditions with cultures derived from the Eastern Mediterranean lands and the Maghreb region of North Africa. The presence of man on the Maltese Islands has been archaeologically documented since the Palaeolithic or Old Stone Age Period dating to before 15,000 years ago [or BP – Before present]. However, evidence of a definite cultural presence on the islands potentially affecting medical practice can be dated to the Ghar Dalam Phase of the Neolithic Period, about 7,000 BP. Much of the evidence relating to medical interventions comes from the archaeological skeletal record, where evidence of surgical interventions were carried out to correct fractures and to expel adverse humours through trephining.[1] One statuette excavated from one of the Copper Age Temple complexes dating to about 6,000-4,500 BP suggests that counter-stimulation of some form or other may have been applied in the management of pregnancy conditions. Counter-stimulation continued to be used as a form of medical therapy right through the millennia up to the beginning of the twentieth century. Counter-stimulation or counter-irritation has been defined by the US Food and Drug Administration as 'An externally applied substance that causes irritation or mild inflammation of the skin for the purpose of relieving pain in muscles, joints and viscera distal to the site of application. They differ from the anaesthetics, analgesics, and antipruritic agents, however, in that the pain relief they produce results from stimulation—rather than depression—of the cutaneous sensory receptors and occurs in structures of the body other than the skin areas to which they are applied as for example, in joints, muscles, tendons and certain viscera.'[2] The irritation can be produced by a variety of methods, e.g. cupping, acupuncture, heat applications, and the application of cataplasms, poultices and sinapisms.

## Prehistoric evidence

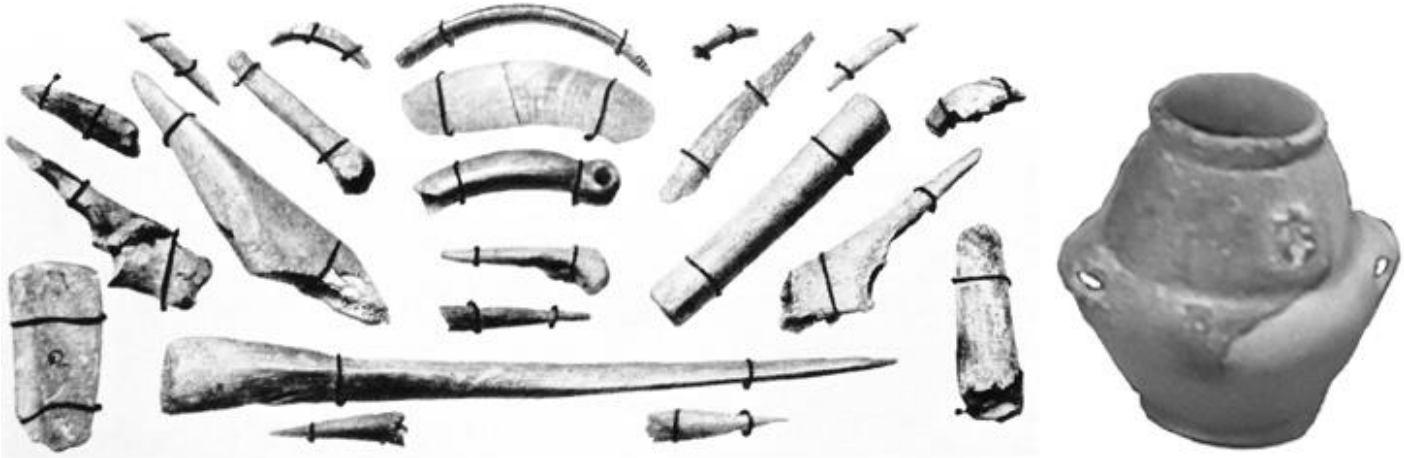
The medical practices prevalent within the Maltese population during the prehistoric phase of history (i.e. before written records were kept) can only be gleaned by reviewing the archaeological record and offering interpretations for the artefacts. A clay statuette (Figure 1), excavated from Tarxien Temples complex dated to 4,500-5,150 BP, depicts a definitely pregnant form with clearly defined external genitalia to which the figure is pointing to and clearly defined incisions on the back, probably representing the lunar months of pregnancy. Two other similar figures were excavated from the Mnajdra Temple complex dated 5,600-5,800 BP, and the Hal Saflieni Hypogeum complex dated 5,000-5,300 BP. The Tarxien Temple model is particularly different from the other two statuettes in that it has a number of shell fragments obviously purposefully impacted in various parts of the body within the clay before firing. It can be suggested that this model actually indicates pressure points where counter-stimulation may be applied during pregnancy.[3] The various bone implements excavated from various Temple Period sites in Malta may themselves have been also used to supplement the counter-

stimulation procedure. These are similar to the sharp-ended bone needles and bian blades unearthed from the Neolithic archaeological sites in China. The small earthenware cup measuring 7.3 cm high excavated from Hal Saflieni Hypogeum may have possibly been used as a cupping vessel (Figure 2).[4]

Counter-stimulation in the form of cupping, where cups are applied to the skin under suction, was used during the prehistoric period in Ancient Egypt. The Ebers Papyrus dated to about 3,550 BP refers to cupping for removing foreign noxious matter from the body. Archaeological depictions of cupping utensils have been described in the ancient medical instruments drawing on the wall of the temple Kom Ombo in Egypt.[5] The practice remained widespread throughout the Mediterranean region in the subsequent centuries.[6]

**Figure 1** Clay statuette from Tarxien Temples, 4,500-5,100 BP

**Figure 2** Bone implements including needles and earthenware cup from Temple Period sites in Malta



## Evidence from the Classical Period

Archaeological evidence of cupping [*fintusi* in the Maltese vernacular] probably combined with venesection is seen on one of the tomb slabs at the necropolis sited outside the capital city of the island of Malta in use during the Classical period 1,200-1,700 BP (Figure 3). The tomb slab served the purpose of sealing up one of the tombs in the catacomb complex. The slab depicts a series of fourteen surgical instruments in common use during the Roman Period. The tool series includes two cups known to have been used to assist the process of venesection.[7] Similar-shaped cups have been depicted on other tomb slabs and found in various archaeological sites in Europe. The practice of cupping with or without associated venesection remained an integral part of Maltese traditional practice right up to the twentieth century.

**Figure 3** Tomb slab depicting surgical instruments from Malta [bleeding cups shown one above the other on the right] and 2nd century cupping kit excavated from doctor's grave at Bingen am Rhein in Germany

Cupping, combined with venesection, became the mainstay management to restore health equilibrium during the Classical Period between the 8th century BCE (Before Common Era) and the 6th century AD (Anno Domini or ACE = After Common Era). In European culture, the rationalization of medical practice was developed by the Greek physician Galen of Pergamum [born 129; died 216 AD]. He adopted the writings and conceptions of the Greek philosophers Plato and Aristotle as well as the writing of the physician Hippocrates. Galen proposed that human health required equilibrium between four main bodily fluids or humours – blood, yellow bile, black bile, and phlegm. Disease was caused by an imbalance of these humours and treatment regimens were directed to restore this balance. Treatment regimens aiming to restore the humours were varied but commonly included venesection, cupping and purging with emetics or laxatives.

## The Medieval and Early Modern Period

Galen's concepts were to dominate medical theory and practice in Europe from the Middle Ages right through to the 18th century. Cupping or the application of *fintusi* involved the application of vacuumed glass cups in specific regions over the body, usually but not restricted to the back. In traditional Maltese practice, cupping was generally used to alleviate muscular pains, lumbago and sciatica, fever, mental disease and for a number of other non-specific illnesses.[7] The methodology in general use in Malta involved a heat source which was usually a small piece of cloth lightly soaked in spirit or a small piece of candle placed on a coin. After setting up and lighting the heat source, a cup in the form of a normal table tumble or a specifically designed cup was applied over the heat source. The burning process removed the oxygen contained in the cup extinguishing the heat source and causing a vacuum effect.[8] The mechanism of action of cupping, especially in regard to the relief of pain, is difficult to explain but may be assumed to work by acting as a method of counter-stimulation based on distraction in one location with the goal of lessening discomfort and/or inflammation in another.

Venesection also remained an important management option in a large variety of diseases right up to the beginning of the 20th century, and was carried out by direct lancing of a vein, or by using scarficators that made multiple incisions on the skin to cause multiple bleeding points, or by the application of leeches.[9] Venesection in small repeated quantities was regularly used in the management of fevers; while in the presence of wounds, the procedure was believed to reduce the inflammatory reaction by helping the absorption of extravasated blood from the tissues. The procedure was also used to prevent the development of eclampsia in pregnancy, cerebral stroke, and in the management of severe headache, pulmonary oedema, mental disease and gastric symptomatology. Venesection was generally performed on the jugular or brachial veins, rarely from the veins of the leg. It was sometimes combined with cupping to help extract a larger volume of blood. Leeches were also applied to reduce superficial inflammation at wound sites especially after plastic surgery such as rhinoplasty.[10] This concept has been re-adopted in modern medicine using the anticoagulant injected by the leech to help with improving the circulation after plastic surgery.[11]

A prescription from 16th century Malta clearly demonstrates the use of the various

therapeutic options to attempt cure disease by balancing the humours. A teenage child suffering from kidney problems received a "constrictive cataplasm ….. to harden and warm … the kidneys". He was also prescribed *pillule foetidae* and *opopanax* to evacuate "the cold rather crude and even bilious mood". Further prescriptions in the form of *pillulae aggregativae* were also prescribed to aggregate the humours prior to dispelling them with the assistance of the prescription *Jera pigra Galieni* which was supposed to "purge the stomach and cleanse the blood".[12]

Another method of counter-stimulation used in traditional Maltese medicine was the application of cataplasms, poultices and sinapisms. These substances were supposed to cause irritation or mild inflammation wherever they were applied and thus act as a counter-irritant. A medical dressing made of a soft heated mass of meal or clay was spread on a cloth and applied to the skin to treat inflamed areas or improve the circulation at the site and manage local pain. They were also used to decrease swelling. The dressing was potentially made out of clay, linseed flour, bread, yeast or mustard. Charcoal was occasionally added with dressing made using clay, linseed flour or bread.[13] The first list of pharmacological agents mentioned in the historical record in Malta dates to 1345 when these items had a 10 percent tax imposed upon their importation. The 19 products listed in the *Capitula Sagati* of 1345 included mainly items of botanical origin but included *bolu* (medicinal clay) imported for medicinal use.[14]

The 16th century prescriptions from Malta clearly demonstrate the use of the various therapeutic cataplasms used to manage cases of trauma. One case had a cataplasm of *quinque farinarum* applied, while the patient further had two lotions of *fusco* and *Aegypciaco* applied to his wounds. He also received oil and honeyed extracts of oil of roses that were attributed with sedative properties. A second case involving trauma was prescribed an *unguenti digestive* made from turpentine, basil, aloe, tincture and eggs applied to an open wound.[12] These methods continued to be used in Malta right through to the 20th century.[13]

## Conclusion

The application of counter-stimulation techniques in this Central Mediterranean relatively isolated community, appears to emulate the physical methods used in modern Traditional Chinese Medicine. The long-distance separation from China [China to Malta is 7,775 km to the east] makes it highly unlikely that any direct cultural intercourse took place between the two populations during the prehistoric or classical periods. In later centuries, indirect contact may have helped introduce the methods to the European region. However, it is more likely that the similarities reflect parallel cultural development in isolation without the need for direct contact between the cultures. This isolated parallel development of ideas is most likely to occur in the promotion of medical cultural concepts that are based on observation and experimentation.

The progress in medical knowledge, especially that related to the pathophysiology of disease and the development of a wide array of pharmacological armamentarium has, in the western world, relegated all forms of traditional medicine to the 'thrash heap'. Their mode of action, if any, is not understood and, therefore, they are deemed 'unworthy' to be investigated using the standard rigors of clinical and scientific research. Any attempt to investigate these physical methods is often

not taken seriously and any results from animal and clinical studies are generally ignored.

With the increasing costs associated with medical care, especially in communities with an aging population, it becomes imperative that cheaper forms of sustainable medical management be investigated and, if proved efficacious, adopted for general use. These methods do appear to have a general effect on the physiology of the individual. To cite one example from studies in an animal model involving Sprague–Dawley and Wistar rat breeds, cognitive function in vascular dementia was improved through the use of acupuncture possibly by effects of antioxidative stress reactions, anti-apoptosis and metabolism enhancement.[15] The time is ripe to put aside preconceived prejudices and adopt an integrative outlook towards clinical research and practice. Western doctors are ready to accept the concept of investigating and using tibial nerve stimulation in the management of intractable urgency incontinence, but would turn a deaf ear to stimulation of lower limb peripheral somatic nerves using acupuncture.[16] In the words of Isaac Asimov: 'Your assumptions are your windows on the world. Scrub them off every once in a while, or the light won't come in".

## References


1. Savona-Ventura C. Medical Mythology in Stone Age Malta. In: Mifsud A, Savona-Ventura C (editors): Facets of Maltese Prehistory. Prehistoric Society of Malta: Malta; 1999, pp. 107-116.
2. National Archives and Records Administration. *Federal Register* 1979 Dec 4; 44(Reg. 9): 234.
3. Cassar P. Medical history of Malta. Wellcome Historical Medical Library: London; 1965, p. 4.
4. Evans JD. The Prehistoric antiquities of the Maltese Islands. University of London: London; 1971, p.62.
5. Savona-Ventura C. Ancient Egyptian Medicine. Lulu: U.S.A.; 2017, p. 21.
6. Mehta P, Dhapte V. Cupping therapy: A prudent remedy for a plethora of medical ailments. *J Tradit Complement Med* 2015 Jul; 5(3):127–134.
7. Cassar P. Surgical instruments on a tomb slab in Roman Malta. *Medical History* 1974; 18:89-93.
8. Lanfranco GG. Medicina popolari ta' l-imghoddi fil-Gzejjer Maltin. Klabb Kotba Maltin: Malta; 2001, pp. 125, 166.
9. Savona-Ventura C, Sawyer RT, Schembri PJ. The Medicinal Use of Leeches in Malta. *Malta Medical Journal* 2002; 14(1):48-52.
10. Savona-Ventura C. Contemporary Medicine in Malta [1798-1979]. P.E.G. Ltd: Malta; 2004, pp. 471-479.
11. Savona-Ventura C. Invertebrates in the medical service of man: Part I – The Biotherapeutic Worms. Part II – The Insect Surgeons. Part III – The Research Assistants. *The Synapse – The Medical Professional's Network* 2007-08; Jan:14,18 Mar:16-17 May: 16,28 Feb: 12,20.
12. Fiorini S. A prescription list of 1546. *Maltese Medical Journal* 1988/89; 1(1): 19-31.
13. Galizia S. Il Ctieb ta l'Infermier – Lezionijiet mghotia lil infermieri ta li Sptar. Government Printing press: Malta; 1904, pp. 84-100.
14. Fiorini S. Kura u Servizzi tas-Sahha f'Malta sa nofs is-seklu XVI. In: Cortis T (editor): Oqsma tal-kultura Maltija. Ministry of Education: Malta; 1991, pp. 233-4.
15. Zhang ZY, Liu Z, Deng HH, Chen Q. Effects of acupuncture on vascular dementia (VD) animal models: a systematic review and meta-analysis. *BMC Complement Altern Med.* 2018 Nov; 18(1): 302.
16. Stewart F, Gameiro LF, El Dib R, Gameiro MO, Kapoor A, Amaro JL. Electrical stimulation with non-implanted electrodes for overactive bladder in adults. *Cochrane Database Syst Rev* 2016 Dec; 12:CD010098.

MMSG
CASE REPORT

# Retropharyngeal abscess with atlanto-axial subluxation

Veronica Said-Pullicino, Andre Stefan Gatt, David Pace

We describe a case of a 4-year-old boy who presented with fever, neck pain and bilateral non-suppurative cervical lymphadenopathy. Torticollis, painful limitation of neck movements and nuchal tenderness were present. CT scan revealed a retropharyngeal abscess and rotatory subluxation of the atlanto-axial joint, consistent with Grisel's syndrome. This is an important differential in children with fever and torticollis as if unrecognized, may potentially lead to serious neurological deficits from cervical cord compression.

**Veronica Said-Pullicino***
MD, MRCPCH
Higher Specialist Trainee
Department of Child & Adolescent Health,
Mater Dei Hospital,
Msida, Malta
veronica.said-pullicino@gov.mt

**Andre Stefan Gatt**
MD, MRCS, FRCR
Consultant Pediatric Radiologist
Mater Dei Hospital,
Msida, Malta

**David Pace**
MD, Pg Dip PID (Oxf), FRCPCH, PhD
Consultant Infectious Disease Pediatrician
Postgraduate Training Coordinator in Pediatrics and Neonatology
Mater Dei Hospital,
Msida, Malta

*Corresponding author

## Case report

A 4-year old Caucasian boy with no significant past medical history, who was on holiday in Malta, was referred for evaluation of a 1 week history of cough and rhinorrhea followed by 8 hours of fever of up to 38.2˚C, neck pain and odynophagia that limited his oral intake. There was no history of vomiting, photophobia, rashes or trauma to the neck. On examination, the child looked generally well and was not lethargic. He had a temperature of 38.2˚C, a heart rate of 135 beats/minute, was normotensive, not tachypnoeic and had satisfactory oxygen saturations in air. He had bilateral non-suppurative cervical lymphadenopathy with torticollis to the right, together with painful limitation of neck movements and nuchal tenderness. Mouth opening was significantly limited due to pain. There was no drooling or stridor, and no neurological deficit was present. ENT examination revealed pharyngitis with no pus or membrane.

**Figure 1A** CT scan in bone window: rotatory subluxation of the atlanto-axial joint – the left lateral facet of C1 is anteriorly displaced relative to its corresponding facet on C2. The soft tissue window demonstrates the poorly enhancing inflammatory phlegmon (1.7cm x 1.2cm) in the left retropharyngeal space.

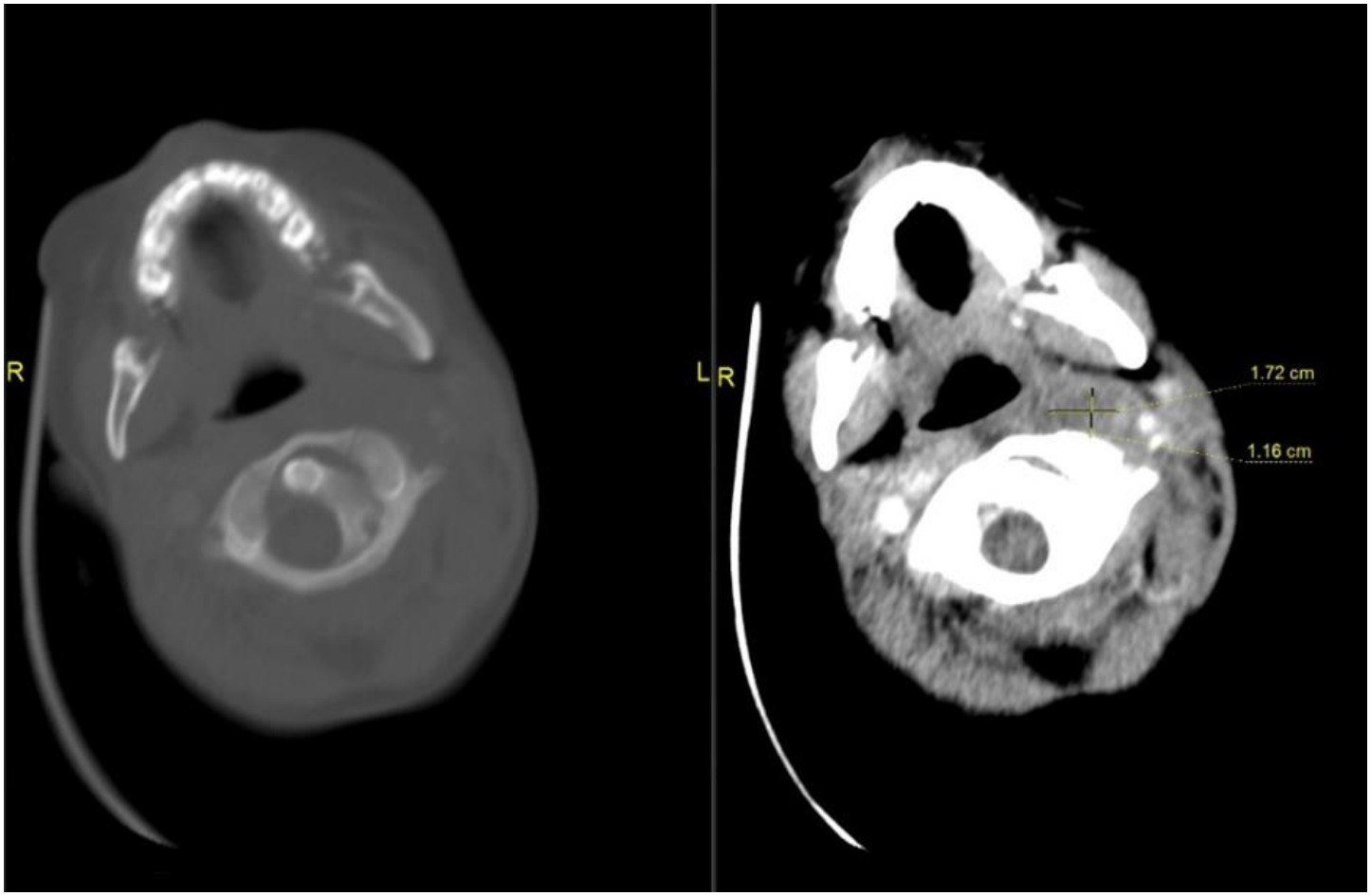
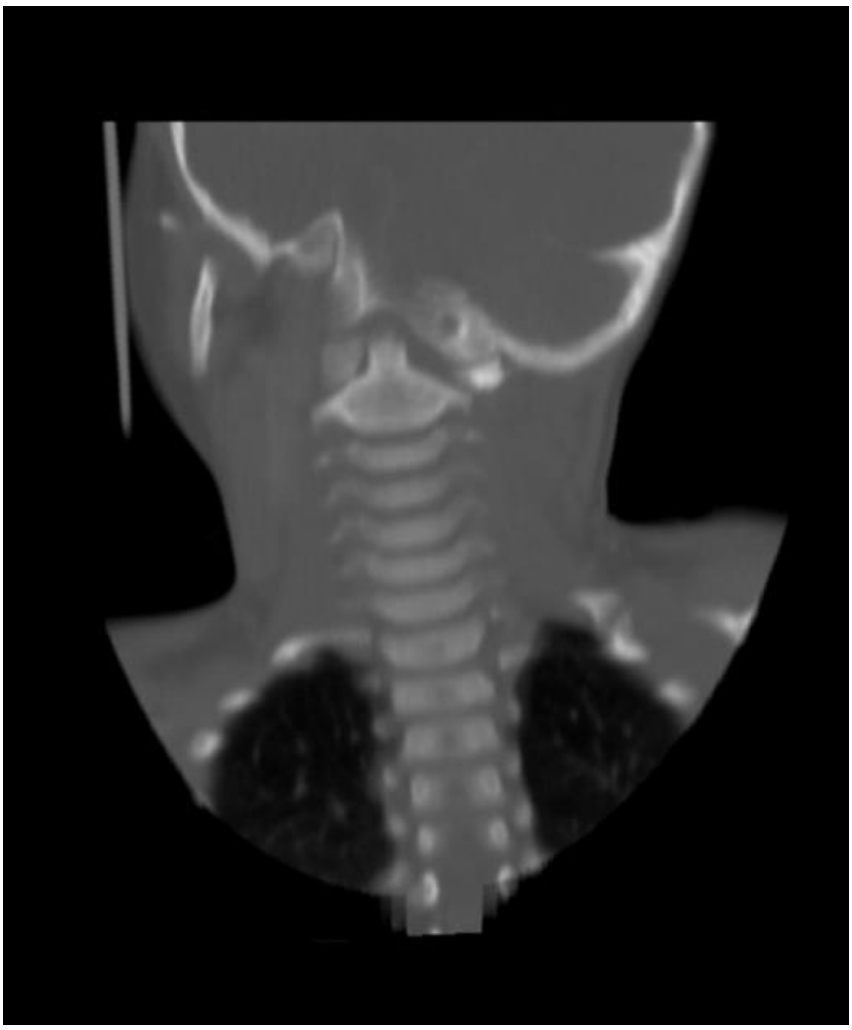


**Figure 1B** Coronal CT scan in bone window demonstrates marked asymmetry of the lateral masses of C1 relative to C2 and the remainder of the cervical spine.



He was initially started on maintenance intravenous fluids due to decreased oral intake, together with analgesia as required. Notable laboratory results included an elevated neutrophil count of $18.3x10^9$/L and a C-reactive protein that reached 241mg/L. Blood cultures were negative. An ultrasound of the neck showed multiple prominent lymph nodes in the left submandibular region and along the left cervical chain, the largest measuring 8mm in short axis dimension, together with increased internal vascularity in keeping with inflammatory changes. The thyroid, parotid and submandibular glands were normal. In view of persistent fever, torticollis and raised inflammatory markers, a computed tomography (CT) scan of the neck was performed and this revealed a left - sided retropharyngeal abscess measuring 1.7cm x 1.2cm, with an associated rotatory subluxation of the atlanto-axial joint (Figure 1A and 1B) consistent with Grisel's syndrome. Surgical drainage was not required due to clinical improvements. His C-reactive protein and temperature normalised on intravenous cefotaxime and clindamycin and his neck movements improved. No interventions on the cervical spine were necessary since the atlas was not significantly shifted anteriorly. After 10 days of intravenous antibiotics he was discharged and was advised to use a soft collar as he was flying back home.

Recovery was uneventful following a further 2 weeks of high dose oral co-amoxiclav. The torticollis resolved within one month and there was full range of cervical movements. Follow up ultrasound scans of his neck showed resolution of the inflammatory changes.

## Discussion

A retropharyngeal abscess is a deep infection that forms in a potential space between fascial layers posterior to the pharynx. It is an uncommon but serious infection that presents mostly in the pediatric population. It should be considered in children presenting with neck pain and restricted neck movements, fever, cervical lymphadenopathy, odynophagia and dysphagia. Neck swelling may also be present. Despite the life-threatening airway compromise that may result from respiratory distress and stridor, these are rarely the presenting features.[1-2] Infections of the head and neck may lead to lymphadenitis, cellulitis and eventually suppurative adenitis of the retropharyngeal lymph nodes with abscess formation.[3]

Retropharyngeal abscess is often a polymicrobial infection. Predominant bacterial species responsible are *Streptococcus pyogenes* (Group A streptococcus), *Staphylococcus aureus* including methicillin-resistant *S. aureus* (MRSA), *Haemophilus influenzae* and oral anaerobes. A beta-lactamase-resistant penicillin together with an agent having anaerobic cover will provide appropriate antibiotic cover. Early commencement of appropriate high dose systemic antibimicrobial treatment may stop the progression of mature abscess formation from cellulitis or from an organised phlegmon.[2,4] Most patients with a retropharyngeal abscess generally respond to a course of appropriate intravenous antibiotics and do not require any surgical intervention.[1] McClay et al. describe how 91% of the pediatric patients in their study who had radiographic evidence of a deep neck abscess and had no severe symptoms, responded to intravenous antimicrobial treatment alone.[5]

Prompt diagnosis and treatment of retropharyngeal abscesses is imperative so as to avoid complications that may be potentially fatal. Infection may spread to the bloodstream, to other deep neck spaces or to adjacent structures, leading to mediastinitis, aspiration pneumonia if the abscess ruptures into the airway and internal jugular vein thrombosis amongst others.[6]

Rarely a retropharyngeal abscess may be associated with non-traumatic fixed rotary atlanto-axial subluxation, a condition known as Grisel's syndrome. This should be suspected if there is concurrent torticollis with neck stiffness and possibly pain on neck movement, in a child with a history of fever with recent infection or surgery in the head and neck.[7]

Atlanto-axial subluxation refers to a loss of stability between the atlas (C1) and axis (C2). This results in abnormal articulation between the vertebrae and may progress to dislocation. The presentation may range from minor axial neck pain to death. Approximately 50% of patients present with restricted neck movements and/or neck pain, 70% with numbness and/or weakness and 90% with pyramidal signs. They may also present with sphincter disturbances, lower cranial nerve pathology and respiratory compromise.[8]

Grisel's syndrome commonly affects children, with 68% of cases occurring in those under 12 years of age and 90% occurring in those under 21 years of age. Radiological evaluation with CT scan of the neck is the gold standard for diagnosis of Grisel's syndrome. An increased

atlanto-odontoid distance (>5mm in children) may be found in lateral projections.[9-10]

The etiology is uncertain and though several theories have been proposed to explain the pathogenesis of the inflammatory subluxation, this continues to be debated.[9] The two-hit hypothesis proposed by Battiata and Pazos (2004) gives a hypothetical explanation for the aetiology. It states that atlanto-axial subluxation results from a pre-existing cervical ligamentous laxity, seen commonly in the pediatric population, worsened by inflammatory mediators from the retropharyngeal space that are transported to the soft tissues of the atlanto-axial space via the pharyngovertebral plexus, that lead to cervical muscle spasm.[9-10] Although the etiopathogensis of Grisel's syndrome has not been proven, a history of pharyngitis, adenotonsillitis, peritonsillar abscess, otitis media, upper respiratory tract infection, certain genetic disorders and head and neck surgery have been reported as risk factors.

Many acute cases can be treated conservatively with bed rest, antimicrobials, anti-inflammatory agents, immobilization and may also require simple traction, however some acute cases and most of the chronic cases with symptoms persisting more than one month, require surgical intervention. This may include skeletal traction or bone fusion. In pediatrics, whenever possible, conservative treatment is preferred.[7]

## Conclusion

Grisel's syndrome is an uncommon but important differential in children with fever and torticollis. Prognosis highly depends on early intervention as delay in diagnosis may be dramatic. Clinicians should be aware of acute non-traumatic torticollis after recent head and neck surgery or recent local infection, as, if unrecognized, it may potentially progress and lead to painful and long-lasting deformity of the neck or serious neurological deficits from cervical cord compression, including death.[7,9]

## References


1. Grisaru-Soen G, Komisar O, Aizenstein O, Soudack M, Schwartz D, Paret G. Retropharyngeal and parapharyngeal abscess in children - epidemiology, clinical features and treatment. Int J Pediatr Otorhinolaryngol. 2010;74(9):1016-20.
2. Tebruegge M, Curtis N. Infections related to the upper and middle airways. In: Long SS, Pickering LK, Prober CG, editors. Principles and Practice of Pediatric Infectious Diseases. 3rd ed. New York: Elsevier Saunders; 2012. p.205.
3. Goldstein NA, Hammersclag MR. Peritonsillar, retropharyngeal, and parapharyngeal abscesses. In: Feigin RD, Cherry JD, Demmler-Harrison GJ, Kaplan SL, editors. Textbook of Pediatric Infectious Disease. 6th ed. Philadelphia: Elsevier Saunders; 2009. p.177.
4. Brook I. Microbiology and management of peritonsillar, retropharyngeal, and parapharyngeal abscesses. J Oral Maxillofac Surg. 2004;62(12):1545.
5. McClay JE, Murray AD, Booth T. Intravenous Antibiotic Therapy for Deep Neck Abscesses Defined by Computed Tomography. Arch Otolaryngol Head Neck Surg. 2003;129(11):1207-1212.
6. Yellon RF. Head and neck space infections. In: Bluestone CD, Simons JP, Healy GB, editors. Pediatric Otalrynology. 5th ed. Philadelphia: Elsevier Saunders; 2014. p.1769.

7. Bucak A, Ulu S, Aycicek A, Kacar E, Miman MC. Grisel's Syndrome: A Rare Complication following Adenotonsillectomy. Case Reports in Otolaryngology. vol. 2014, Article ID 703021, 4 pages. [Internet]. 2014 [cited 5th January 2018]. Available from: https://doi.org/10.1155/2014/703021.

8. Yang SY, Boniello AJ, Poorman CE, Chang AL, Wang S, Passias PG. A Review of the Diagnosis and Treatment of Atlantoaxial Dislocations. Global Spine J. 2014;4:197–210.

9. Lee SH. Grisel Syndrome: Pathophysiological Evidence from Magnetic Resonance Imagine Findings. Ann Rehabil Med. 2013;37(5):713-6.

10. Battiata AP, Pazos G. Grisel's syndrome: the two-hit hypothesis-a case report and literature review. Ear Nose Throat J. 2004;83:553-5.

MMSG
CASE REPORT

# Primary localised laryngeal amyloidosis - an atypical presentation

Justine Borg, Gerd Xuereb, Kurt Apap, Charles Borg

Primary localised laryngeal amyloidosis is a rare disease that classically presents with dysphonia. We present a case of a 38-year-old woman who presented with a history of early morning haemoptysis, progressively worsening hoarseness and intermittent dysphagia. A bulky left false vocal cord was seen on examination. A computed tomography scan of the neck and trunk revealed thickening of the left side of the larynx with associated asymmetry. Direct laryngoscopy showed a round, well-circumscribed lesion on the left false vocal cord and histological examination of the lesion confirmed the presence of amyloid.

Systemic disease was ruled out and the patient was treated with endoscopic excision of the mass through carbon dioxide laser technology. The patient's symptoms improved and the patient is being followed up yearly to exclude disease recurrence. The report highlights the presentation, diagnosis and appropriate management of localised laryngeal amyloidosis.

**Justine Borg***
University of Malta
Msida, Malta
justineborg97@gmail.com

**Gerd Xuereb**
MD (Melit.)
Mater Dei Hospital
Msida, Malta

**Kurt Apap**
MD (Melit.)
Mater Dei Hospital
Msida, Malta

**Charles Borg**
MD, D.SPEC, ORL
Mater Dei Hospital
Msida, Malta

*Corresponding author

## Introduction

Dysphonia, dysphagia and haemoptysis are common complaints in the ENT clinic, however localised amyloidosis causing this symptomatology is rare. This report describes the management of a patient with a benign disorder presenting with worrying symptoms.

Amyloidosis is a rare condition that progresses relatively slowly and constitutes a variety of heterogeneous disorders defined by abnormal deposits of extracellular fibrillar proteins. The deposition of amyloid in various organs and tissues around the body invariably causes organ dysfunction over time.[1]

Localized amyloidosis can be demonstrated in a single organ in the absence of systemic involvement and is typically benign in nature when isolated to an individual area in the head and neck region. Amyloid can be deposited at any laryngeal site however the true vocal cord is believed to be the most commonly affected.[2]

## Case Presentation

A 38-year-old previously healthy woman presented to the Ear, Nose and Throat (ENT) department with a one-week history of early morning haemoptysis. The patient also complained of a six-month history of progressively worsening hoarseness and a shorter history of intermittent dysphagia. The patient, who previously smoked 20 cigarettes a day, initially attributed her hoarseness to smoking. The patient quit smoking in the three months before presentation, to no effect. Indirect laryngoscopy showed a bulky left false vocal cord. History and examination were otherwise unremarkable.

A computed tomography (CT) scan of the neck and trunk revealed thickening of the left side of the larynx with associated asymmetry (Figure 1, Figure 2). The thickening was characterised by loss of fat plane between the left side of the larynx and the thyroid cartilage anteriorly. A 7mm nodule straddling the longus colli muscles was observed, which was most likely in keeping with a Thornwaldt cyst. No abnormal enhancing of soft tissue and no loco-regional lymphadenopathy was noted. The base of tongue, parotid and submandibular glands appeared normal. No features of concern were observed elsewhere

Direct laryngoscopy revealed a round, well-circumscribed lesion on the left false vocal cord (Figure 3). The true vocal cord was visible underneath. Multiple biopsies were taken and sent for histology.

Histological examination of the left false vocal cord lesion showed the presence of amyloid. This was demonstrated by the staining of amorphous material with Congo red that displayed apple-green birefringence when viewed under high-intensity cross-polarised light. Amyloid deposits were present throughout. Vascular proliferation of stroma, which was covered by normal looking respiratory epithelium was also observed. Mild chronic inflammation with no evidence of atypia was noted.

Immunohistochemical staining of the amyloid deposits was performed using monospecific antibodies reactive with serum Amyloid A protein (SAA), apolipoprotein A1 (apoA1), Transthyretin (TTR) and with kappa and lambda immunoglobulin light chains. The amyloid stained with antibodies to lambda light chains. This confirmed amyloid of AL type (lambda subtype).

**Figure 1** A CT scan of the neck showing thickening of the left side of the larynx. The arrow points towards the mass on the left false vocal cord.

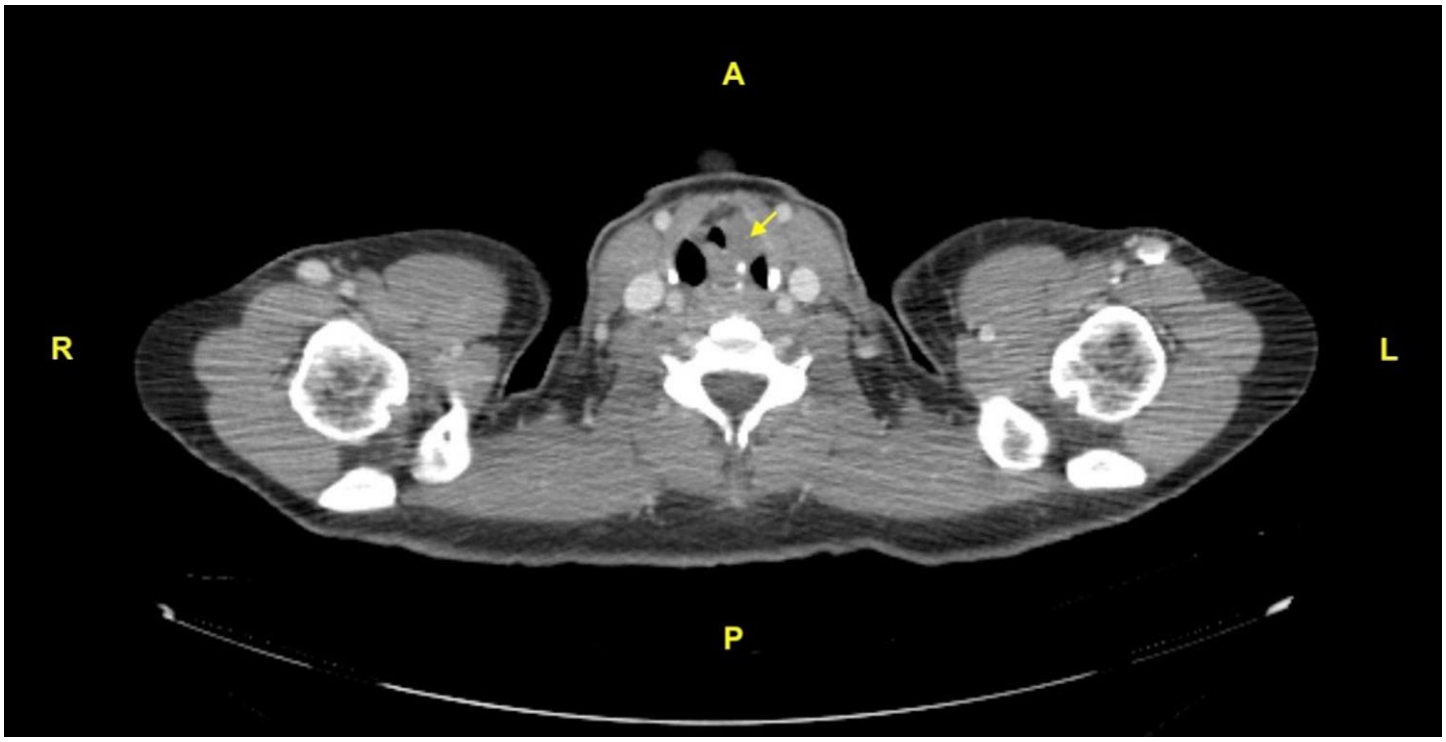
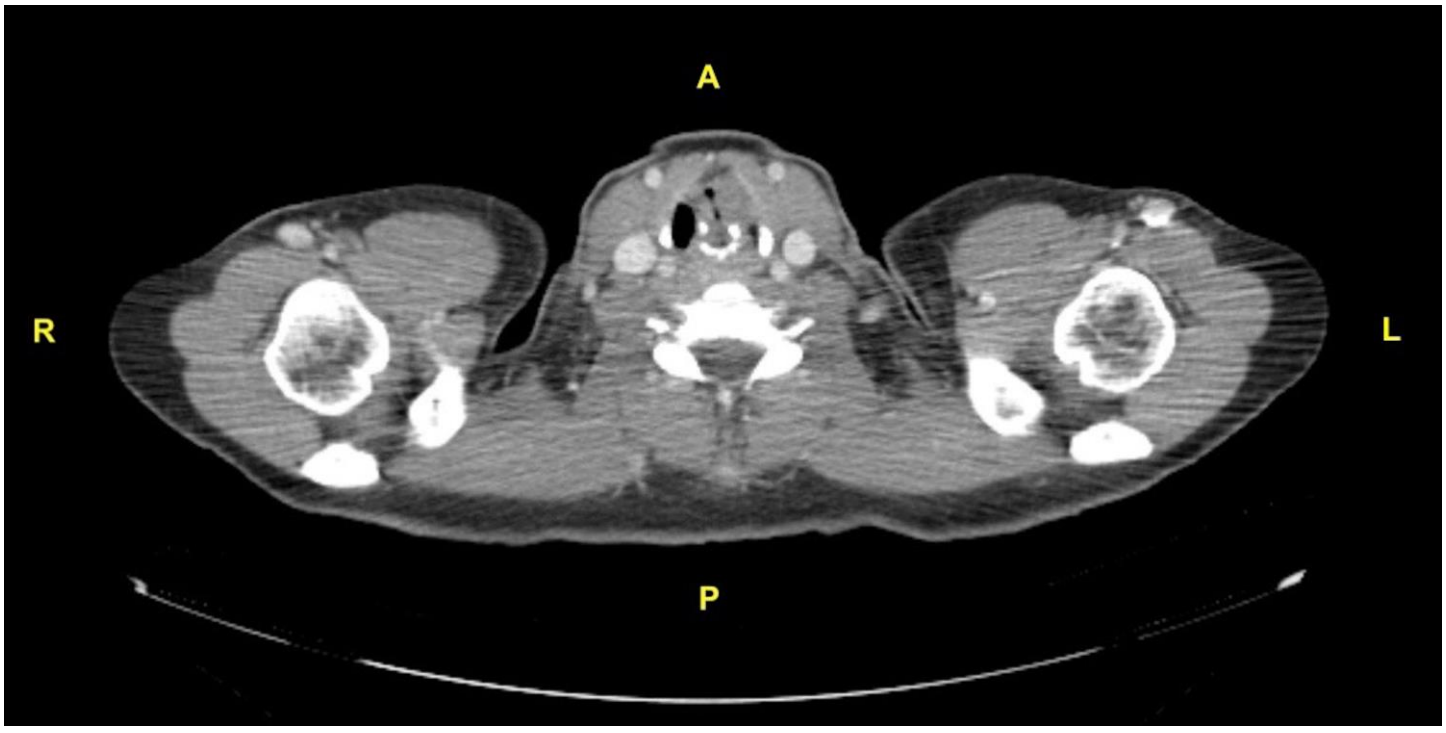


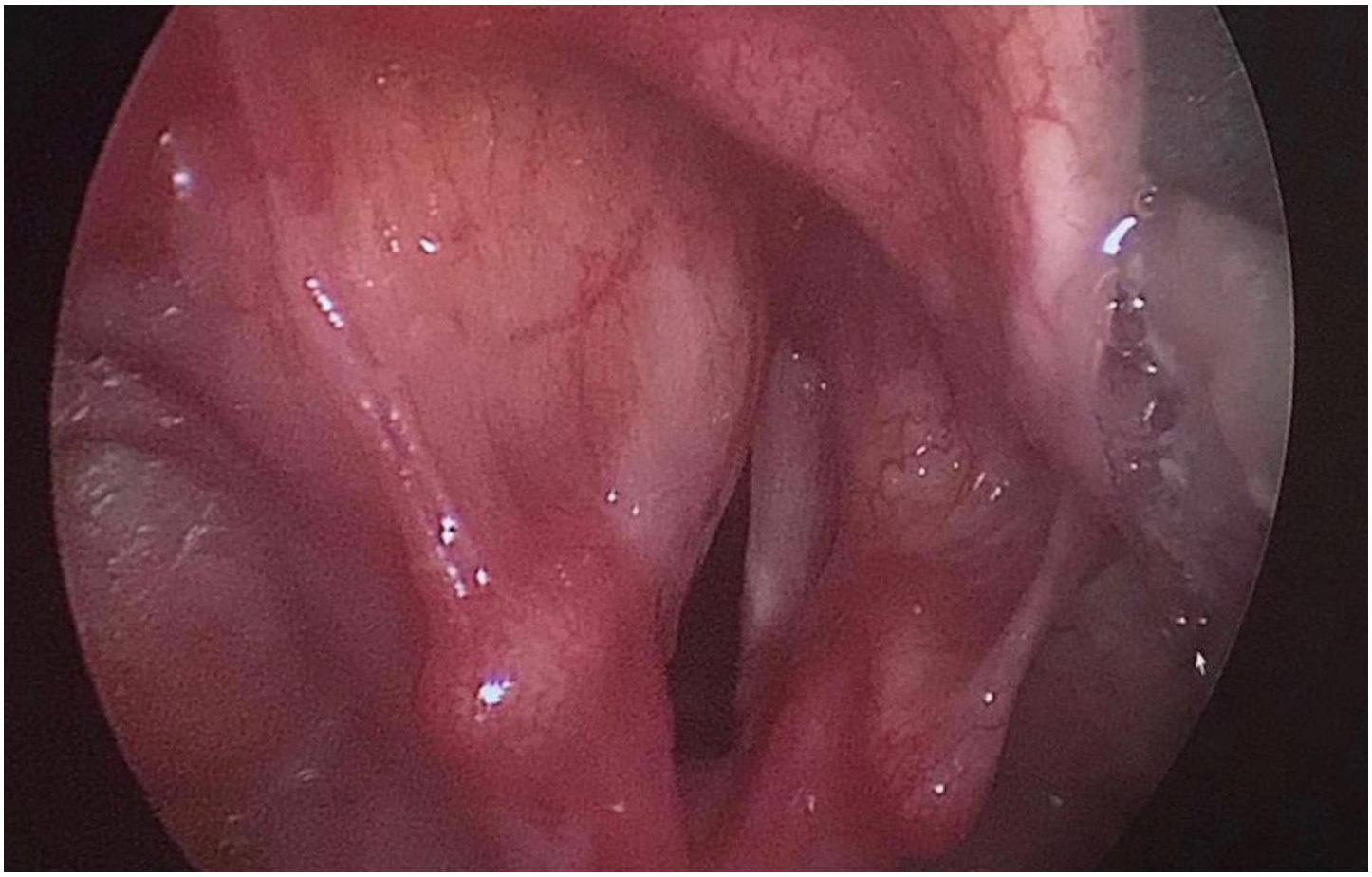

**Figure 2** A CT scan of the neck showing thickening of the left side of the larynx with associated asymmetry



Serum Protein Electrophoresis showed no indication of an increase in free light chains, however an elevated kappa/lambda ratio was observed. A full blood count, renal profile, liver profile, serum paraproteins, CRP, serum albumin and NT-proBNP were within normal limits. An electrocardiogram (ECG) and an echocardiogram were normal with no evidence of cardiac amyloidosis. A bone marrow biopsy excluded an underlying plasma cell dyscrasia as there was no evidence of plasma cell clone. A CT scan of the thorax showed no thoracic involvement. Serum Amyloid P (SAP) scintigraphy was unremarkable. These investigations ruled out systemic amyloidosis.

The patient was diagnosed with localised laryngeal amyloidosis affecting the left false vocal cord. She was treated with endoscopic excision of the mass using carbon dioxide laser technology. The patient had an initial good response to treatment, however later complained about the development of a gravelly quality to her voice. Endoscopy showed a 0.5cm cyst overlying the left false vocal cord and was treated with a further two laser procedures. As a consequence to laser therapy, a granuloma was seen on follow up but this healed spontaneously. The symptoms resolved following the third laser procedure and the patient is being followed up once yearly.

**Figure 3** Direct laryngoscopy showing thickening of the left false vocal cord.



## Discussion

Primary localised amyloidosis of the larynx is very rare accounting for only 1% of benign laryngeal tumours.[3] It is characterised by the deposition of monoclonal light chains of the AL type.[4] Two theories have been described to give an explanation for the development of localised laryngeal amyloidosis. The first theory proposes that amyloid light chains are produced by plasma cell clones while the other theory is centred around the body's inability to remove light chain proteins leading to localized deposits.[5]

Amyloidosis typically presents non-specifically in patients aged 50 to 70 years old and has a preponderance for males over females with a ratio of 3:1.[5] In this case, our 38 year old female patient, presented with a sole nodule on the left false vocal cord. Other sites such as the orbits, the eyes and the salivary glands can also be affected. Submucosal deposits may be present in the oral cavity, stomatopharynx, nasopharynx, bronchotracheal tree and lungs as well as the nose, nasopharynx and paranasal cavities.[6]

Our patient presented with atypical symptoms. The most common presenting complaint in patients suffering from laryngeal amyloidosis is worsening hoarseness.[3] Symptoms such as cough and dyspnoea are also frequently observed, however dysphagia and haemoptysis are rarely reported.[3] Keeping in mind that laryngeal cancer can present similarly, a high index of clinical suspicion together with the appropriate investigations are needed to rule out the possibility of laryngeal cancer.[1]

Systemic involvement should be excluded and therefore causes of systemic disease such as rheumatic disease and tuberculosis must be ruled out. Typically, systemic amyloidosis involves the kidneys, affecting approximately 70% of patients, with nephrotic range proteinuria leading to renal failure in 50% of patients. It also affects the heart causing cardiomyopathy in around 60% of patients, manifesting as a thick-walled heart, low voltage ECG and pleural and pericardial effusions. Other forms of systemic involvement include cholestatic hepatopathy, peripheral and autonomic neuropathy, purpura and soft tissue infiltration, of which macroglossia is pathognomonic.[7]

Plasma cell dyscrasias, which include, Waldenström macroglobulinemia and multiple myeloma can also lead to amyloidosis and should therefore be looked for.[5] The build-up of abnormal amyloid protein leads to organ dysfunction. Therefore, in contrast to localised amyloidosis, systemic amyloidosis which affects various body organs, normally carries a very poor prognosis. Confirming the extent of amyloidosis guides management and serves to reassure the patient.[1]

The treatment of choice for localised laryngeal amyloidosis is surgery, ideally aided by laser technology. First line therapy involves endoscopic excision of the mass using carbon dioxide laser.[8] Spontaneous remission leaving no evidence of disease is possible however disease recurrence is a much more common outcome and therefore long-term follow up is advised for a minimum of 5 years.[3]

## Key Messages

1. Primary localised laryngeal amyloidosis is a rare phenomenon that normally presents with hoarseness. However, physicians should be aware that it can also present with dysphagia and haemoptysis.
2. Hoarseness should not always be attributed to smoking and should be investigated to

rule out underlying pathology. Laryngeal amyloidosis should be considered as part of the differential diagnosis in patients presenting with persistent dysphonia.

3. Localised amyloidosis has a very high rate of recurrence and complications secondary to laser treatment may arise. Long-term follow up for a minimum of 5 years is therefore advised.
4. Localised laryngeal amyloidosis can present very similarly to laryngeal cancer. Physicians should have a reasonable degree of suspicion for both diagnoses and should confirm the diagnosis with a biopsy.
5. Localised and systemic amyloidosis have very different clinical outcomes, prognosis and management. Systemic involvement should therefore always be ruled out.

## References


1. Yiotakis I, Georgolios A, Charalabopoulos A, Hatzipantelis P, Golias C, Charalabopoulos K, et al. Primary localized laryngeal amyloidosis presenting with hoarseness and dysphagia: a case report. Journal of medical case reports. 2009 Sep 16,;3(1):9049.
2. Raymond AK, Sneige N, Batsakis JG. Amyloidosis in the Upper Aerodigestive Tracts. Annals of Otology, Rhinology & Laryngology. 1992 Sep;101(9):794-6.
3. Biewend ML, Menke DM, Calamia KT. The spectrum of localized amyloidosis: A case series of 20 patients and review of the literature. Amyloid. 2006;13(3):135-42.
4. Lewis JE, Olsen KD, Kurtin PJ, Kyle RA. Laryngeal Amyloidosis: A Clinicopathologic and Immunohistochemical Review. Otolaryngology–Head and Neck Surgery. 1992 Apr;106(4):372-7.
5. Behnoud F, Baghbanian N. Isolated laryngeal amyloidosis. Iranian journal of otorhinolaryngology. 2013;25(70):49-52.
6. Lachmann HJ, Hawkins PN. Amyloidosis and the lung. Chronic Respiratory Disease. 2006 Nov;3(4):203-14.
7. Merlini G, Seldin DC, Gertz MA. Amyloidosis: Pathogenesis and New Therapeutic Options. Journal of Clinical Oncology. 2011 May 10,;29(14):1924-33.
8. Siddachari RC, Chaukar DA, Pramesh CS, Naresh KN, de Souza CE, Dcruz AK. Laryngeal Amyloidosis. The Journal of otolaryngology. 2005 Feb;34(1):60.