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**Editorial**

# Another Asymptomatic Epidemic?

Pierre Ellul

In this edition of the MMSG, in the manuscript by Coppini et al, we read about the presence of oesophageal varices in patients with Child-A cirrhosis. In this study group the main cause for cirrhosis was Non-alcoholic steato-hepatitis (NASH) (28.9%), closely followed by alcohol at 25.8%.

Alcohol related liver disease can be preventable through education programmes. The significant improvement and introduction of Hepatitis C antiviral agents and vaccination programmes for hepatitis B will eventually result in a reduced prevalence of endstage liver disease secondary to chronic viral hepatitis. Non-alcoholic fatty liver disease (NAFLD) is becoming the most prevalent liver disease in western countries. NAFLD is strongly related to metabolic syndrome and insulin resistance seems to play a crucial role.NAFLD is defined by the presence of liver fat accumulation exceeding 5% of hepatocytes in the absence of significant alcohol intake (20 g per day for men and 10 g per day for women), viral infection, or any other specific aetiology of liver disease.[1]

NAFLD encompasses a histological spectrum ranging from simple steatosis to NASH. Various stages of fibrosis can exist, ranging from absent (stage F0) to cirrhosis (stage F4). Simple steatosis can progress to NASH and clinically significant fibrosis and thus progressive liver disease and hepatocellular carcinoma.[2]

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More than 50% of adults in the 27 European Union (EU) countries are considered to be overweight (36.4%) or obese (15.5%). Obesity presents greater health risks than being overweight. The prevalence of obesity varies among these EU countries, from less than 10% in Romania, Switzerland and Italy to over 20% in the United Kingdom, Ireland and Malta. NAFLD also has reached epidemic proportions among populations typically considered at low risk, such as China (15%) and Japan (14%).

In an Italian study, NAFLD prevalence was 26%. In a multi-centre European study it was 30.4% and in a southern European study 33% of patients had a high probability of having the disease.[3-5] A study in Greece revealed evidence of NAFLD in 31% and of NASH in 40% of autopsied cases of ischaemic heart disease or traffic accident death.[6] Two major European studies reported NAFLD prevalence rates of 42.6-69.5% in patients with type 2 diabetes.[7-8]

Moving on to mortality, data from the Danish National Registry of Patients revealed NAFLD-associated age-adjusted standardized mortality ratios (SMR) (After adjustment for sex, diabetes and cirrhosis at the baseline) were 2.3 (95% CI 2.1-2.6) for all causes, 19.7 (95% CI 15.3- 25.0) for hepatobiliary disease, and 2.1 (95% CI 1.8-2.5) for cardiovascular disease.[9]

In a cohort of Swedish NAFLD patients, the age, sex, and calendar-period adjusted mortality ratio was 1.69 (95% CI 1.24-2.25) for NAFLD compared to the general population.[10]

With regards to the economic burden, a German study demonstrated that the average annual overall health-care costs were significantly higher at baseline and at follow-up measurements for individuals with evidence of NAFLD.[11]

Based on data from the USA adult liver transplantation databases, since 2004 NASH is the second leading cause for liver transplantation. In the USA, NAFLD and NASH related cirrhosis is anticipated to become the leading cause for chronic liver disease and transplantation within the next 1-2 decades.[12]

What can we do about it? In the absence of a universal protocol and effective therapy to treat these patients, general lifestyle interventions including dietary changes and increased physical activity remains the main treatment modality for this group of patients.[13]

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**Original Article**

# The need for gastroscopy in early cirrhotics – a retrospective analytical study

Jessica Coppini, Nicholas-Paul Delicata, James Pocock

**Abstract**

The aim of this study was to predict which Child-A cirrhotic patients would not have oesophageal varices at endoscopy.

This is a retrospective study that reviewed 59 Child-A cirrhotic patients under the care of a gastroenterology firm. All gastroscopy reports (97 episodes in total) undergone by these patients were analysed. Patients were classified into 3 groups namely absent varices (AV) group: no oesophageal varices seen at endoscopy, small varices (SV) group: small oesophageal varices seen, banded varices (BV) group: moderate/large oesophageal varices requiring banding. In this study the varices were graded as per UK guidelines that is small varices being ones which collapse to inflation of the oesophagus with air, moderate varices do not collapse and large varices occlude the lumen.[1] Patient demographics, a platelet count and spleen size on imaging at the time of endoscopy were also noted. Statistical differences between the 3 groups were then analysed using ANOVA.

Our results showed that most of the patients were middle aged males. Furthermore, there was a statistically significant difference in platelet count and spleen size between the three groups (*p* values: 0.008 and 0.035 respectively). A noteworthy finding was that none of the patients who required banding had a normal spleen size (spleen < 12 cm). Having said this, due to considerable overlap between the three groups, further recommendations could not be proposed.

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**Keywords**

gastroscopy, varices, spleen, portal hypertension, cirrhosis

## Background

Despite recent advances, oesophageal variceal bleeding in cirrhosis is still associated with 10-20% mortality at 6 weeks.[1] Furthermore, in 35-90% of patients rebleeding occurs after spontaneous haemostasis (approximately 40% of rebleeding episodes occurring within the first 5 days).[2] Once cirrhosis is diagnosed a gastroscopy is recommended to check for oesophageal varices in most cases.[3] If oesophageal varices are present, treatment is required to prevent variceal bleeding (primary prophylaxis of variceal haemorrhage).[4] The recommended treatment is with non-selective beta blockers (NSBB) for patients with small varices and either NSBB or variceal banding if medium to large varices are present.[1] Splenomegaly and consumptive thrombocytopenia are recognized complications of significant portal hypertension secondary to cirrhosis[5] and potential indices for indirect diagnosis of oesophageal varices.[6]

## Aim

Oesophageal varices are a major complication of portal hypertension and occur in 30-70% of cirrhotics.[7] Is it possible to predict which cirrhotic patients will have oesophageal varices requiring treatment before performing a gastroscopy?

## Method

This is a retrospective study looking at all the gastroscopy reports of Child-A cirrhotic patients under the care of a single gastroenterology/hepatology firm performed in 2015 (see table 1 for population demographics). The diagnosis of cirrhosis was in most cases based on imaging studies as shear wave elastography has only recently been introduced locally. The aetiology of liver cirrhosis included autoimmune liver conditions, alcoholic liver disease, chronic viral

hepatitis and non-alcoholic steatohepatitis. Once a patient was recruited their previous endoscopies were also retrieved and matched with their Child-

Pugh score at the time (see table 2). Platelet counts and spleen size as measured on imaging (US/CT/MRI) within three months of endoscopy were also recorded. For the purposes of the study a normal sized spleen is one which is less than 12 cm. During data collection whenever splenomegaly was noted on imaging but no precise measurement was given, a spleen size of 12 cm was allocated. Conversely a normal spleen with no precise measurement was given a value of 11 cm.[8] The gastroscopy report was used to determine whether varices were present. If present and banding was performed this was also recorded. Once oesophageal banding was performed further endoscopies to control variceal size were excluded from the study since the question of prediction is no longer relevant in these patients. Patients with a previous splenectomy or who were suffering from myeloproliferative conditions (which often effects spleen size and platelet counts) were excluded from the study. Patients with early hepatocellular carcinoma (within the Milan transplant criteria)[9] were not excluded from the study as it was felt that early cancer would not contribute significantly to portal hypertension. ANOVA statistical analysis was used to measure significant differences between groups regarding platelet count and spleen size.

## Results

A total number of 59 patients undergoing 97 gastroscopies (episodes) between 2008 and 2015 were included in the study. The cases were divided into 3 groups; absent varices (AV) group: no varices seen at endoscopy, small varices (SV) group: small varices not requiring banding and banded varices (BV) group: medium–large varices requiring banding at endoscopy. Figure 1 illustrates the number of episodes in each group.

### *Age Distribution*

75.3% (*n*=73) of episodes were in patients between 50 -69 years of age (Figure 2)

### *Gender distribution*

71.1% (*n*=69) of episodes studied involved males (figure 3). This gender distribution was similar throughout the three groups.

***Table 1:*** *Population Demographics*

| VARIABLE | MEAN (± SD) OR NUMBER (%) |
|---|---|
| **Age (years)** | 60.8±9.3 |
| **Gender (male)** | 69 (71.1%) |
| **Gender (female)** | 28 (28.9%) |
| **Aetiology of cirrhosis** | |
| **AICAH** | 2 (2.1%) |
| **AIH** | 1 (1.0%) |
| **ALD** | 25 (25.8%) |
| **Cryptogenic** | 10 (10.3%) |
| **HBV** | 8 (8.2%) |
| **HCV** | 15 (15.5%) |
| **HCV/HBV** | 1 (1.0%) |
| **NASH** | 28 (28.9%) |
| **PBC** | 1 (1.0%) |
| **PCLD** | 2 (2.1%) |
| **PSC** | 2 (2.1%) |
| **Schistosomiasis** | 1 (1.0%) |
| **Wilson's** | 1 (1.0%) |
| **No varices on endoscopy** | 42 (43.3%) |
| **Varices on endoscopy** | 55 (56.7%) |
| **Grade of varices** | |
| **Small varices** | 29 (52.7%) |
| **Moderate varices** | 21 (38.2%) |
| **Large varices** | 5 (9.1%) |
| **Treatment of varices** | |
| **Varices not banded** | 28 (50.9%) |
| **Varices banded x1** | 24 (43.6%) |
| **Varices banded x2** | 3 (5.5%) |
| **Spleen size (cm)** | 13.3±2.3 |
| **Splenomegaly** | 87 (89.6%) |
| **Child score 5** | 83 (85.6%) |
| **Child score 6** | 14 (14.4%) |
| **Platelet count x$10^9$/L** | 147.8±65.5 |
| **Platelet count <150 x$10^9$/L** | 48 (50.5%) |
| **HCC comorbid patients** | 12 (12.4%) |

***Table 2:*** *Child-Pugh classification used in the study*

| CHILD SCORE | 1 | 2 | 3 |
|---|---|---|---|
| **Encephalopathy** | Absent | Mild (1,2) | Severe (3,4) |
| **Ascites** | Absent | Easy to Rx | Difficult to Rx |
| **Bilirubin** | <4 | 34-51 | >51 |
| **Albumin** | >35 | 28-35 | <28 |
| **INR** | <1.3 | 1.3-1.5 | >1.5 |

**CHILD GRADE**
Child A: 5-6
Child B: 7-9
Child C: 10-15

***Figure 1:*** *The 97 episodes were divided into 3 groups depending on gastroscopy findings- absent varices (AV) group, small varices (SV) group and banded varices (BV) group*

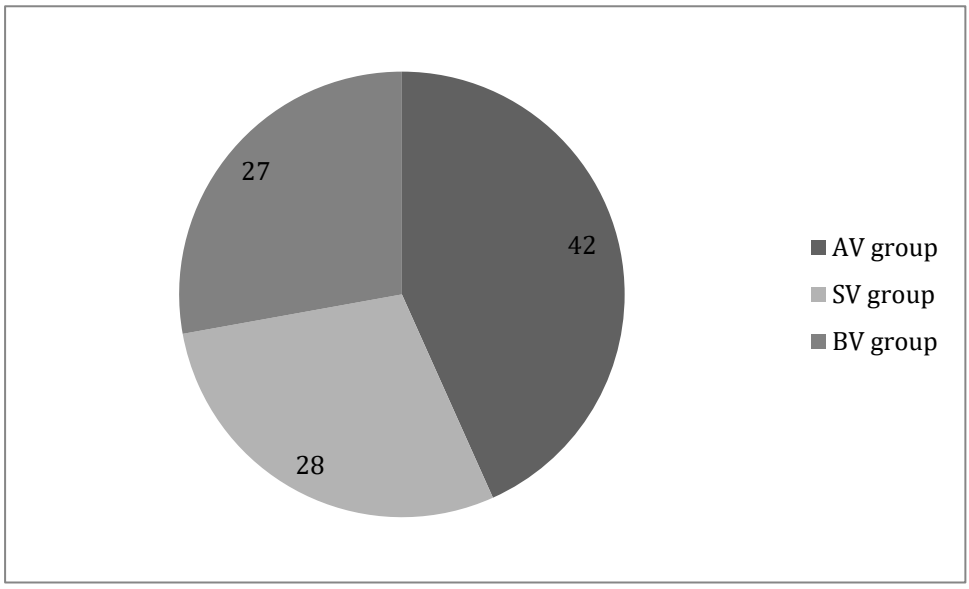


***Figure 2:*** *Age distribution. N=97*

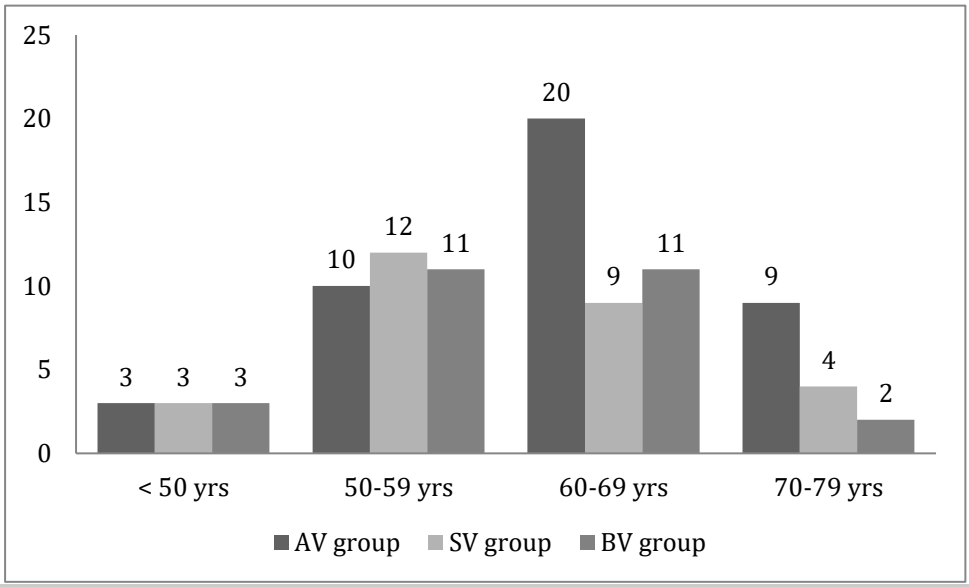

***Figure 3:*** *Gender distribution. N=97*

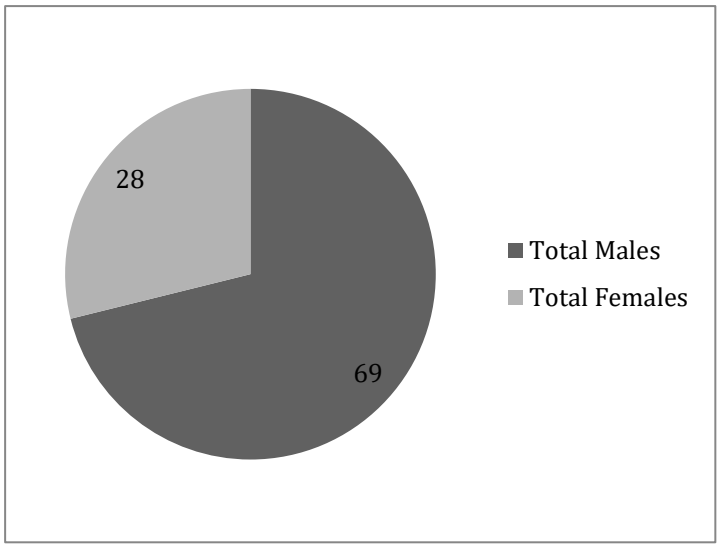


***Figure 4:*** *Proportion of the total population with spleen size <12cm vs proportion with splenomegaly. N= 97*

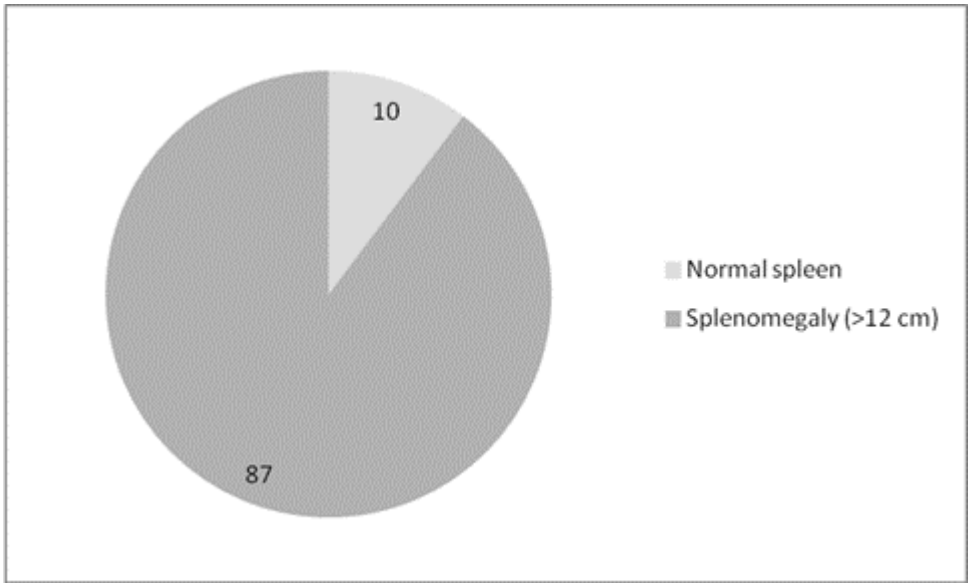


***Table 3:*** *Spleen size across the three groups; absent varices (AV) group, small varices (SV) group and banded varices (BV) group*

| GROUP | Normal Spleen | Spleen >12cm | % Splenomegaly |
|---|---|---|---|
| **AV group** | 2 | 40 | 95.2% |
| **SV group** | 8 | 20 | 71.4% |
| **BV group** | 0 | 27 | 100% |

***Table 4:*** *ANOVA results comparing spleen size between the groups*

| | AV group | SV group | BV group |
|---|---|---|---|
| **Mean** | 12.8 | 12.9 | 14.2 |
| **95% confidence interval for Mean** | 12.09-13.48 | 12.06-13.76 | 13.31-15.04 |
| **Standard deviation** | 1.64 | 2.85 | 2.4 |
| **High** | 16.5 | 19 | 20.2 |
| **Low** | 8 | 4.4 | 12 |
| **Median** | 12 | 12 | 13 |
| **Absolute Average deviation from Median** | 1.05 | 2.02 | 1.99 |

***Table 5:*** *Platelet count across the three groups*

| GROUP | Platelets ($10^9$/L) <150 | Platelets ($10^9$/L) >150 | % with thrombocytopenia |
|---|---|---|---|
| **AV** | 16 | 26 | 38.1% |
| **SV** | 13 | 15 | 46.4% |
| **BV** | 18 | 9 | 66.7% |

***Table 6:*** *ANOVA results comparing platelet count across the three groups*

| | AV group | SV group | BV group |
|---|---|---|---|
| **Mean** | 169 | 143 | 120 |
| **95% confidence interval for Mean** | 150-188 | 119-167 | 96-144 |
| **Standard deviation** | 72 | 58 | 52 |
| **High** | 380 | 321 | 243 |
| **Low** | 70 | 37 | 48 |
| **Median** | 158 | 141 | 119 |
| **Absolute Average deviation from Median** | 47.4 | 43.5 | 45 |

**Spleen size (cm)**

89.6% (*n*=87) of the population studied had a spleen size >12cm as seen in figure 4. Interestingly 23.8% (*n*=10) of AV group patients had spleens larger than 14 cm. On the other hand, none of the patients in BV group had a normal sized spleen (<12 cm) (table 3).

Statistical analysis using ANOVA showed that spleen size difference between the 3 groups was statistically significant (*p*= 0.035) (table 4).

***Platelet count: Units x$10^9$/L***

In BV group, 66.7% (*n*=18) of patients had a platelet count <150 x$10^9$/L whereas in AV group 61.9% (*n*=26) of patients had a platelet count > 150 x$10^9$/L (table 5).

Statistical analysis using ANOVA showed that platelet count differences between the 3 groups was statistically significant (*p*=0.008) (table 6).

**Discussion**

Several recent studies have explored possible non-invasive predictors of the presence and/or severity of oesophageal varices in cirrhotics including such indices as spleen size, platelet count, spleen stiffness, liver stiffness, liver volume and

serum albumin level.[10-11,5] Spleen size and platelet count are indices which are readily available after initial workup of patients with chronic liver disease and were thus selected in this study for further evaluation. Studies have shown that as cirrhosis progresses spleen size tends to increase and platelet count tends to decrease.[6] The aim of this study was to assess whether one could predict which patients would have oesophageal varices requiring treatment before performing endoscopy and therefore which patients can safely avoid such invasive monitoring.

In this study 66.7% of BV group had platelet counts below 150 $x10^9$/L as opposed to 38.1% of AV group patients and this result was statistically significant. There was still however considerable overlap between the 2 groups such that 33.3% (*n*=9) of BV group patients had platelet counts above 150 $x10^9$/L. Platelet counts on their own therefore cannot be used to predict the presence of varices in cirrhotic patients. In the case of spleen size the differences between groups were again statistically different and the overlap between the groups was less marked. A possible inference from the results obtained would be that with spleen size of <12 cm varices requiring banding would not be found. However, only 10.3% (*n*=10) of the population studied had a spleen size within normal limits, and out of these, 8 episodes had small oesophageal varices (SV group) which would still require treatment with non-selective beta blockers.

In recently published guidelines [2] recommendations were made for which cirrhotic patients could safely avoid screening at endoscopy. These guidelines stated that patients with a liver stiffness <20 kPa and with a platelet count >150 $x10^9$/L have a very low risk of having varices requiring treatment, and can avoid screening endoscopy. Liver stiffness measurement was not considered in this study as this modality has only recently been introduced in Malta and is subject to numerous variables such as obesity, elevated ALT levels and liver venous or biliary congestion.[12]

The main limitation of our study was that the diagnosis of cirrhosis was based on imaging studies rather than liver biopsies. Liver biopsies are considered invasive and often avoided clinically. In future, similar studies should also include liver stiffness measurements in the diagnosis of cirrhosis. Another limitation of our study was that patients with different aetiologies of cirrhosis were recruited. Considering cirrhotic patients with a single aetiology may produce more robust conclusions. Furthermore, when collecting data on spleen size US, CT and MRI modalities were referenced depending on which imaging study was performed closest to the date of endoscopy. More accurate measurements would have been obtained had all spleen size measurements been calculated using MRI[13] however since data was collected retrospectively this was not possible. At the start of the study several inclusion and exclusion criteria were laid out before selecting the population to be studied to improve validity of the results obtained. One limitation of the study however was that not all variables that may affect spleen size and platelet count were taken into consideration.

In conclusion, despite the relatively small size of our study the results were statistically significant and it is unlikely that more patients would have resulted in a different outcome. Having said this, the study did not yield any new recommendations to alter existing clinical practice.

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**Original Article**

# Is it giant cell arteritis? a retrospective audit on temporal artery biopsy for giant cell arteritis

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**Abstract**

Background: Giant cell arteritis (GCA) is the commonest of the vasculitides and should form part of the differential diagnosis of a new-onset headache in patients over 50 years with elevated inflammatory markers. Temporal artery biopsy (TAB) is the gold standard for its diagnoses.

Aim: The aim of this audit was to determine whether patients referred for a TAB between 2010 and 2015 at Mater Dei Hospital qualified for a diagnosis of GCA and the significance of the TAB result in affecting management of GCA by correlating the clinical profile and biochemical criteria according to the guidelines based on the American College of Rheumatology (ACR) criteria.

Results: The percentage of positive TABs in our cohort of 170 patients was 23%. The ESR (sensitivity - 100%) was shown to be a significant factor associated with a positive TAB when compared to CRP (sensitivity 90%). 79.5% of positive TAB results were patients aged between 70-89 years of age, proving age is also a significant factor. New onset headache was the most common complaint (66%). Only 45.9% of patients were started on steroids prior to TAB despite the clinical suspicion of GCA. This increased to 54.1% of patients on steroids after TAB was performed, pending a histology result.

Conclusion: Our findings, which are similar to comparing studies, question the practicality of TAB in the clinical diagnosis of GCA. Clinical symptoms, raised ESR and increasing age proved to be significant factors contributing to the clinical diagnosis and management of GCA. Non-invasive ultrasonography can further confirm the diagnosis and is to replace TAB in the near future.

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**Keywords**

Giant cell arteritis, Temporal artery biopsy, New-onset headache, ESR, Age

## Introduction

Giant cell arteritis (GCA), also known as temporal arteritis, is a chronic systemic vasculitis of unknown aetiology, usually occurring in older people, affecting medium and large arteries, leading to a variety of complications if not promptly treated. GCA predominantly affects branches of the external carotid artery. Histopathologically, it is a granulomatous inflammation of the affected vessels with eventual arterial luminal narrowing and distal ischaemia.[1]

GCA is the commonest of all the vasculitides and should form part of the differential diagnosis of new-onset headache in patients over 50 years of age

with elevated inflammatory markers. The reported incidence of GCA is between 7 and 29/100,000 in Europe for people aged more than 50 years. [2] The condition is a common cause of acute blindness, with visual loss occurring in up to one-fifth of patients, thus making it a medical emergency requiring prompt initiation of treatment. Moreover, it is one of the commonest indications for long-term glucocorticoid use in the community.[3-5]

GCA is often managed both in the community by general practitioners and in secondary care by rheumatologists, ophthalmologists and other specialists thus further emphasizing the importance of formulating guidelines in order to ensure proper quality care. Temporal artery biopsy is currently the gold standard for diagnosis of GCA.[6]

**Guidelines**

The guidelines used for this audit as a standard for comparing our data were the British Society of Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) guidelines for the management of GCA based on the American College of Rheumatology (ACR), published in 1990.

The ACR classification criteria for diagnosing GCA is if at least three of five of the criteria listed below are present:

1. Age at disease onset ≥50 years: development of symptoms or findings beginning at the age of 50 years.
2. New onset headache
3. Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries
4. Elevated ESR: ESR ≥50 mm/h according to the Westergren method
5. Abnormal artery biopsy: biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells.

**Aim**

The aim of this audit was to determine:

1) Whether patients referred for a temporal artery biopsy between 2010 and 2015 qualified for a diagnosis of GCA
2) The significance of a temporal artery biopsy result in affecting management of giant cell arteritis by correlating the clinical profile and biochemical criteria associated with a positive histology obtained from a temporal artery biopsy

**Methodology**

Permission was obtained from the Chairperson of Surgery and the Data Protection Unit in Mater Dei Hospital prior to data collection. The time period for patients included in this audit was between 2010 and 2015.

Patients who underwent temporal artery biopsy in the Mater Dei Hospital Surgical Theatres were included in the study. iSOFT clinical Manager and discharge letters were used for data collection. A proforma was used for data collection. Patient demographics, clinical indication for temporal artery biopsy, histological results, ESR and CRP were collected for the patients.

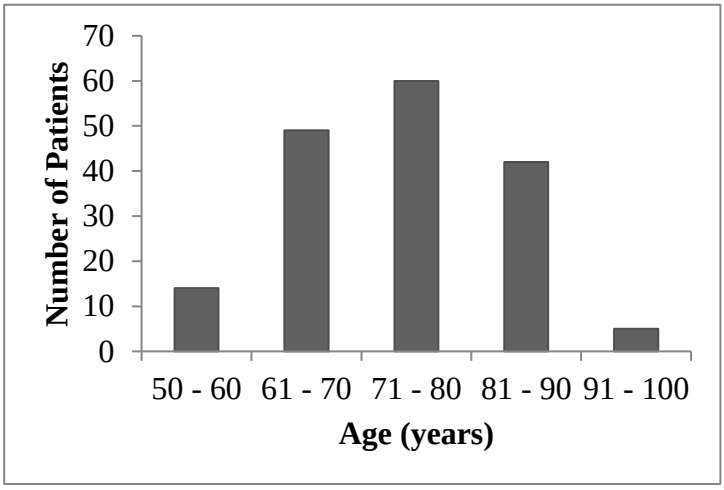
The data collected was then compared to the BSR and BHPR guidelines for the management of Giant Cell Arteritis, based on the American College of Rheumatology 1990 criteria.

**Results**

A total of 201 patients were identified from the Surgical Theatre Logbooks. 170 patients (55 males vs. 115 females) were included in the audit after patients without availability of ESR, CRP or temporal artery biopsy results were excluded. The mean age of the patients was 74.34 years (range 55 to 97 years).

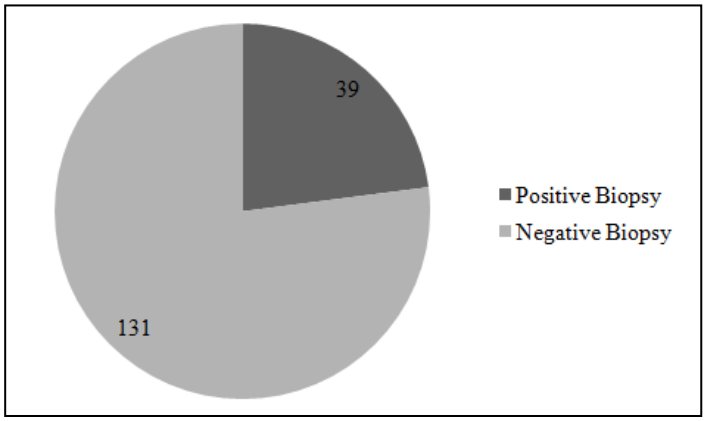
Figure 1 shows the age distribution of the patients included in the audit.

***Figure 1**: Age Distribution*



As shown in Figure 2, 131 (77%) patients had a negative TAB result compared to 39 (23%) patients with a positive TAB result. The average length of the branch of temporal artery sent for histology was 8.3mm. The length ranged from 2mm to 21mm. 145 (85% of the total population studied) patients had a TAB specimen of 5mm or longer. 111 (76.55%) of patients with a TAB biopsy of >5mm was negative for a temporal artery diagnosis, whilst 34 (23.45%) of patients with a TAB biopsy <5mm was positive for a temporal artery diagnosis. 25 (15% of the total population) had a TAB specimen less than 5mm, with 20 of the patients having a negative TAB and 5 patients with a specimen less than 5mm had a positive TAB result.

***Figure 2:*** *Temporal artery biopsy result*




The average ESR result was 72.60mm/hr. Figure 3 shows the distribution of the ESR results in the patients included.

***Figure 3****: ESR Distribution*

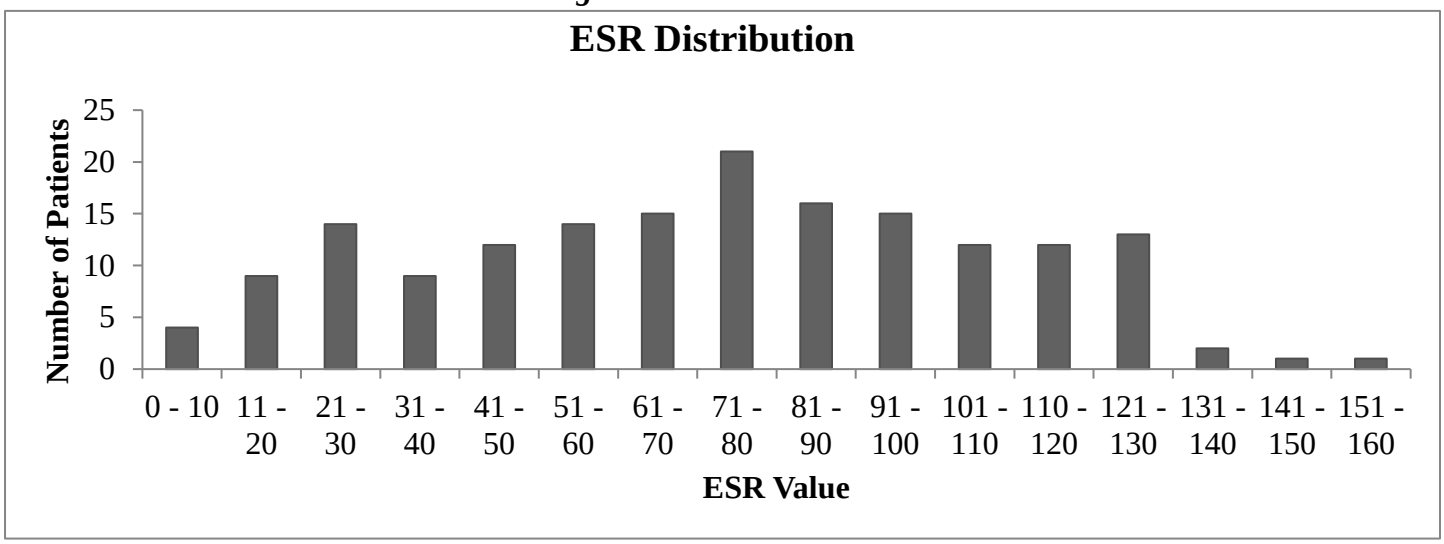



***Figure 4****: CRP Distribution*

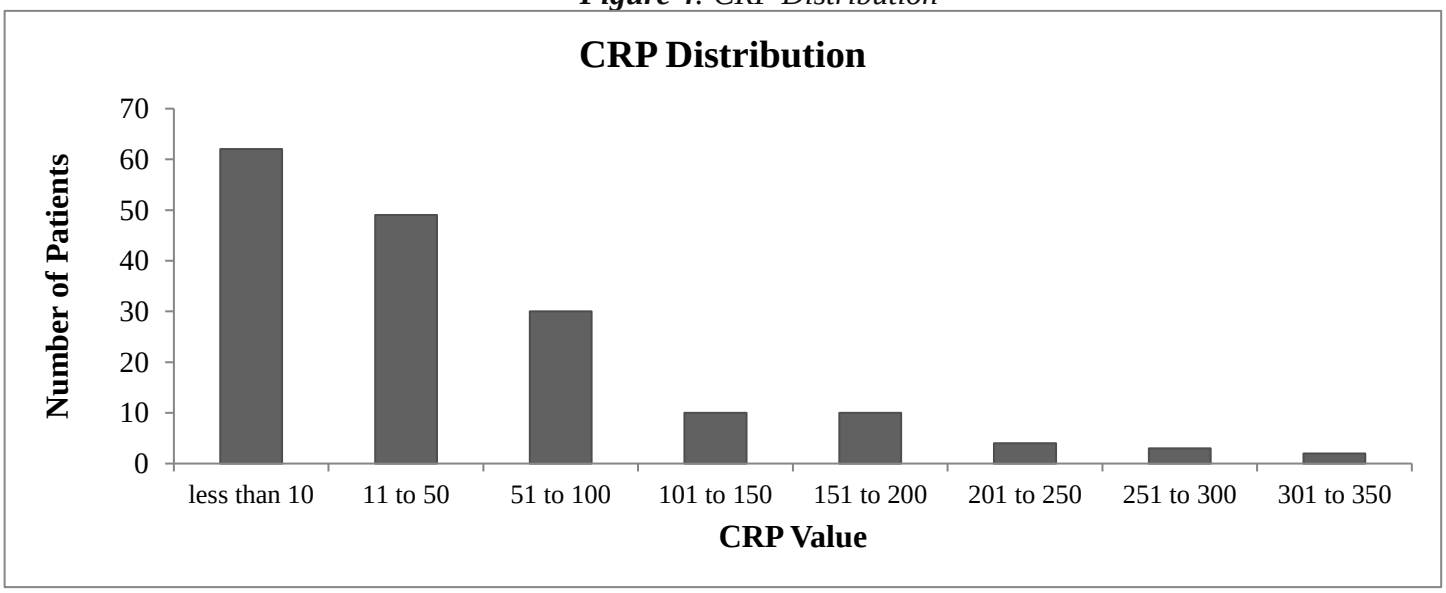


***Figure 5**: Patients' Symptoms*

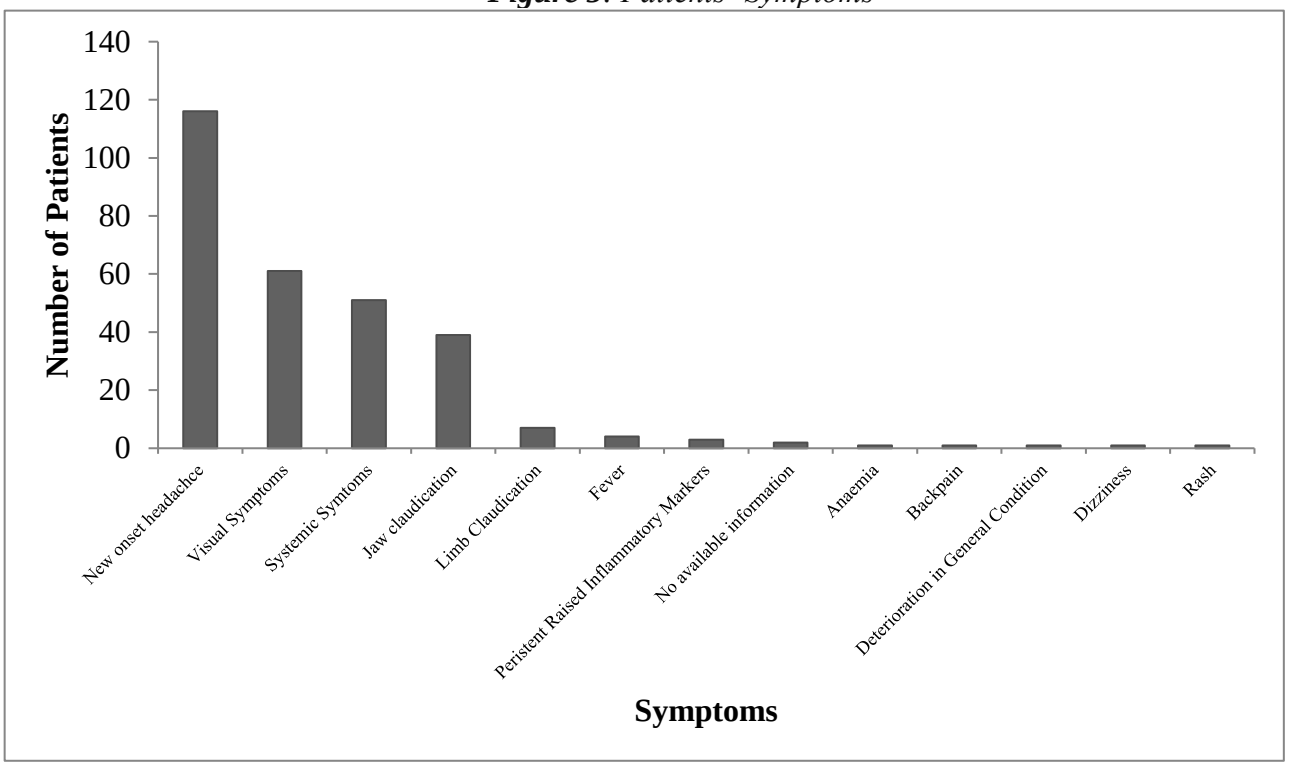



***Table 1**: Sensitivity, Specificity, PPV and NPV results*

| Parameter | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|
| ESR value >10 | 100.00% | 3.05% | 23.49% | 100.00% |
| ESR value >100 | 25.64% | 78.81% | 23.26% | 77.17% |
| CRP >6 | 90.00% | 35.88% | 30.00% | 92.16% |
| CRP >100 | 41.03% | 90.08% | 55.17% | 83.69% |
| ESR and CRP positive | 94.81% | 21.76% | 26.26% | 93.44% |
| Headache present | 64.86% | 30.00% | 20.87% | 75.00% |
| Jaw Claudication | 21.62% | 86.05% | 30.77% | 79.29% |
| Visual Symptoms | 36.84% | 64.12% | 22.95% | 77.78% |
| Headache, jaw, visual symptoms present | 25.00% | 79.41% | 30.00% | 75.00% |
| Symptoms and inflammatory markers >50 | 100.00% | 76.47% | 42.86% | 100.00% |

The average CRP result was 54.42 (range 6 to 320). The distribution of the CRP result is shown in Figure 4.

The most common symptom for which TAB was performed was for new onset headaches (60% of patients). Figure 5 shows the different symptoms reported by patients undergoing TAB procedure.

Sensitivity and specificity rates for TAB positive results were calculated in relation to variables. Positive predictive value (PPV) and negative predictive values (NPV) were also calculated for different parameters (Table 1).

Steroids administration to patients following the TAB procedure was recorded. 78 (45.9%) patients had steroids prescribed prior to the TAB procedure whilst 76 (44.7%) patients did not have steroids prescribed prior to the TAB procedure. No information was found for 16 (9.4%) patients. Following the TAB histopathological result, steroids were stopped in 49 (28.90%) patients. Steroids were continued in 92 (54.10%) patients.

**Discussion**

In our cohort of 170 patients undergoing temporal artery biopsy, patients with an ESR >10 had a positive TAB with a sensitivity of a 100%. A CRP value less than 6 was sensitive in 90% of cases with a positive TAB. This shows that ESR is an

important significant factor associated with a positive histological diagnosis of GCA when compared to CRP.

Positive TAB results were seen in 39 patients, 79.5% of which were patients aged between 70-89 years of age. Such a result shows that age is a significant factor associated with a positive TAB result. These results mirror a similar study outcome by Saedon *et al*. The authors in this study concluded that ESR and age are the two important significant factors associated with a positive histological diagnosis of GCA.[7] This was compared to a previous study by Kernani *et al*. which showed that elevated CRP provided a sensitivity of 87% for a positive TAB when compared to an elevated ESR which had a sensitivity of 86%.[8] Our audit suggests that ESR still has an important role in the work-up of GCA and may be superior to CRP in predicting a positive TAB.

A variety of symptoms were reported by the patients undergoing a TAB, with new onset headache being the most common complaint in 66% of patients. A positive TAB with new onset headache was reported in 25 patients (14.71%) of the patient population. The sensitivity was 64.86%, however a negative predictive value of 75% was seen, indicating that there is a 75% chance of having a positive TAB without a headache. A sensitivity of only 25% was seen in patients who reported headaches, jaw claudication and visual symptoms collectively, with a negative predictive value of 75% of more seen both in the cohort of patients who reported the triad of symptoms, or in those patients who had individual symptoms. This shows that there was at least a 75% chance of having a positive TAB without any of these symptoms.

In our study, the average length of the branch of temporal artery sent for histology was 8.3mm with a range from 2mm to 21mm. 85% of TAB specimen had a biopsy length of 5mm or more; 76.55% of which had a negative TAB whilst 23.45% had a positive TAB. The other 20 cases had a biopsy length of less than 5mm, 80% of which had a negative TAB with 20% having a positive TAB. This shows that TAB length did not significantly correlate with a positive histology result. This is in conflict with previous studies. Mahr*et al*. identified 5mm as the TAB length for diagnostic sensitivity[9] whilst Ypsilantis *et al*. identified that 7mm is the cut-off length with the highest positive predictive value for a positive biopsy.[10] Moreover, Su *et al*. recommend a length of at least 12.5mm to allow for artery contraction following tissue fixation.[11]

Recent guidelines by the British Society for Rheumatology and British Health Professionals in Rheumatology for the management of GCA recommend that high-dose glucocorticosteroid therapy should be initiated immediately when clinical suspicion of GCA is raised.[2] In our study, only 45.9% of patients were started on steroids prior to TAB despite the clinical suspicion of GCA. This increased to 54.1% of patients on steroids after TAB was performed with a pending histology result.

The percentage of positive TABs in our cohort was 23%. Similarly, Saedon *et al*.'s study involving 153 patients found a positive TAB in 29% of patients [7] whilst Mahr*et al*,'s study included 1520 patients with only 15% resulting in a positive TAB.[9] These findings question the practicality of TAB in the clinical diagnosis of GCA in view of the low percentage of positive biopsies seen in our study and similar results in other studies with a high proportion of patients with negative biopsies in our study still being treated as GCA, based on clinical symptoms and inflammatory markers.

The role of TAB is starting to be replaced by colour duplex ultrasonography which is a new, noninvasive method to diagnose GCA whilst reducing the chances of false-negative biopsies due to skip lesions.[12] Other imaging modalities such as positron emission tomography and three tesla-magnetic resonance imaging are also being used in other centres.[13-14]

**Limitations**

This audit was done retrospectively based on observational data. Therefore, it is limited by possible inconsistent record keeping. This might have influenced the data regarding the initiation of steroid treatment prior to TAB for a presumptive diagnosis of GCA and steroid treatment pending biopsy result. Another limitation to this audit was the level of specialization of the surgeon performing the TAB. Despite this, similar clinical and biochemical criteria associated with a positive TAB were found in other studies.

**Conclusion**

From this study, it is evident that it would be

practical to reduce the number of TAB performed if there was sufficient clinical suspicion of GCA to commence treatment. Clinical symptoms as well as a raised ESR, are significant factors contributing to the clinical diagnosis of GCA. Diagnosis can be further confirmed by ultrasonography as a non-invasive methodology to replace TAB in the near future.

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**Original Article**

# The effect of a hospital oxygen therapy guideline on the prescription of oxygen therapy

Rachelle Asciak, Caroline Gouder, Maria Ciantar, Julia Tua, Valerie Anne Fenech, Stephen Montefort

**Abstract**

Aim: To assess the effect of a hospital oxygen therapy guideline on oxygen prescription and administration at the emergency Department (ED) and medical wards of Mater Dei Hospital, Malta.

Methods: Patients admitted to medical wards through the ED with conditions most likely to require oxygen therapy were recruited over 2 months in 2011. Data was collected on oxygen therapy prescription and administration. A hospital guideline on oxygen therapy was introduced and disseminated in 2015, following which data was collected again and compared to the 2011 data. A *p* value <0.05 was deemed to be statistically significant.

Results: 248 and 293 patients were recruited in 2011 and 2015 respectively. Oxygen therapy was indicated in 34.3% and 31.4% of patients respectively ($p$=0.47). Oxygen saturation on air was not documented in 14.1% (2011) and 4.4% (2015) ($p$<0.01).

In patients in whom oxygen therapy was indicated, correct documentation (including delivery device and flow rate) of oxygen therapy administered at ED improved from 23.5% to 73.9% ($p$<0.01), and correct oxygen therapy prescription in the management plan improved from 34.1% to 76.1% ($p$<0.01).

In the medical wards, correct oxygen therapy administration according to prescription improved from 7.1% to 48.9% ($p$<0.01).

56.8% of patients in whom oxygen therapy was not indicated were prescribed oxygen anyway in 2011, improving to 27.1% after the guideline ($p$<0.05).

Conclusion: Oxygen saturation, oxygen therapy prescription and documentation at the ED and oxygen therapy administration in the medical wards improved significantly at Mater Dei hospital, Malta, after a hospital guideline was introduced.

**Key words**

Oxygen, Oxygen prescription, Guideline, Oxygen therapy in hospital

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## Introduction

Oxygen therapy can be life saving, and oxygen is one of the most commonly prescribed drugs in Internal Medicine wards. Both hypoxia and hyperoxia can be harmful, and so great care must be taken to prescribe oxygen therapy correctly and only when it is indicated.

## Aim

The aim was to document the effect of a local hospital oxygen therapy guideline on the prescription, documentation and administration of

supplemental oxygen within the emergency department and medical wards in Mater Dei Hospital, Malta.

## Method

Patients admitted to medical wards through the emergency department, with conditions likely to require oxygen therapy were recruited in 2011.[1] Data was collected on oxygen therapy documented to have been administered at the emergency department, oxygen therapy prescribed for patients being admitted to medical wards and whether this was indicated or not based on oxygen saturation measurements documented, and actual administration of oxygen therapy once the patients reached the medical wards. The data was compared to the standards established by the British Thoracic Society (BTS) guideline for emergency oxygen use in adult patients.[2] Oxygen was said to be indicated if oxygen saturation from pulse oximetry ($SpO_2$) or oxygen saturation from arterial blood gas result ($SaO_2$) on air was <94% (or <88% in patients with, or at risk of, type two respiratory failure). Where both $SaO_2$ and $SpO_2$ were available on air, the lower value was used.

In July 2015, a local hospital oxygen therapy guideline was issued on the local hospital intranet and disseminated among all hospital employees. A further email was sent out in August 2015 specifically to emergency department doctors and doctors in the Internal medicine department. This email included a short summary of the pitfalls identified in oxygen therapy documentation and prescription as identified from our data collection in 2011, informed the doctors of the new guideline available, with the guideline attached to the email, and informed doctors that oxygen therapy would be audited.

The guideline contained information on the different types of oxygen delivery devices available in the hospital, and when each one is indicated, a flow chart on the use of oxygen therapy in emergencies, information on pulse oximetry measurements and documentation of the readings, oxygen therapy prescription and documentation, the risks of hyperoxaemia, conditions at risk of hypercapnic respiratory failure, and oxygen therapy administration and monitoring to ensure that the oxygen saturation is within the target range identified for each patient.

Data was then collected again in September 2015 using the same proforma used in 2011. Results were compared to those obtained in 2011,[1] before the guideline was issued. The Z-test was used to compare the proportions in the two populations and assess the statistical significance of results, and a $p$ value of $<0.05$ was deemed to be statistically significant.

The patients were prospectively and randomly selected adult patients, over the age of 16 years, who were admitted to Mater Dei Hospital with medical conditions most likely to require oxygen treatment. These included cardiovascular and respiratory conditions, cerebrovascular attacks and transient ischaemic attacks, loss of consciousness, deterioration in general condition and confusion. Data was collected from the emergency department sheets, documented results of $SpO_2$ measurements by pulse oximetry, and documented arterial blood gases (ABGs) including $SaO_2$. Details of oxygen delivery and written instructions about oxygen prescription, if at all present, were noted. Within the first 24 hours following admission the patients were then followed up at the wards to document the oxygen prescription on the treatment chart, and to see if oxygen treatment was being administered as prescribed.

Patients being admitted to the intensive care unit were excluded.

'Complete' documentation was said to be present when oxygen therapy documentation or prescription contained full details including the oxygen delivery device (normal standard oxygen mask, Venturi mask, nasal prongs, or non-rebreather mask), and flow rate (not deemed to be necessary for Venturi masks as long as the percentage of oxygen concentration was specified, e.g. 28% Venturi mask).

## Results

### *Documentation of oxygen saturation*

There were 14.1% ($n$=35) of patients in 2011 who had no documentation of $SpO_2$ or $SaO_2$ on air so it was not possible to tell whether oxygen therapy was indicated or not in these cases. This improved to 4.4% ($n$=13) of patients in 2015 ($p$<0.01).

### *Oxygen therapy in patients in whom oxygen therapy was indicated*

Table 1 shows the results obtained in the

group of patients in whom supplemental oxygen therapy was indicated. The results obtained before and after the guideline was introduced were compared. Oxygen therapy was indicated in 34.3% (*n*=85) in 2011, and 31.4% of patients (*n*=92) in 2015 (*p*=0.478, i.e. no statistically significant difference between the sizes of the two populations in whom oxygen therapy was indicated). In these patients, the correct documentation of oxygen therapy administered at the emergency department, i.e. including the delivery device used and the flow rate (where indicated), improved from 23.5% to 73.9% after the guideline was introduced (*p*<0.01). Correct oxygen therapy prescription in the management plan for these patients also improved from 34.1% to 76.1% (*p*<0.01). Oxygen therapy prescription in the treatment charts currently used in medical wards was 51.8% before the guideline and 58.7% after the introduction of the guideline (*p*=0.352).

In the medical wards, there was correct oxygen therapy administration according to prescription in 48.9% after the guideline, as compared to 7.1% before the guideline (*p*<0.01).

***Table 1:*** *showing the results of oxygen therapy prescription, documentation and administration before (2011) and after (2015) the publication of the local hospital oxygen therapy guideline in patients in whom oxygen therapy was indicated, i.e. $SpO_2$ or $SaO_2$ <94%, or <88% in patients with, or at risk of, type two respiratory failure.*

| **In patients in whom oxygen therapy *was* indicated** | | | | | | |
|---|---|---|---|---|---|---|
| **Year of data collection** | **No. of patients in whom $O_2$* was indicated** | **$O_2$ administered at the ED** and documented correctly**** | **$O_2$ prescribed correctly in management plan** | **Correct *** $O_2$ prescription documented in treatment chart** | **$O_2$ administered in ward** | |
| | | | | | **Correctly as prescribed** | **Incorrectly or not given at all** |
| 2011 (before guideline) | 85 | 23.5% (*n*=20) | 34.1% (*n*=29) | 51.8% (*n*=44) | 7.1% (*n*=6) | 92.9% (*n*=79) |
| 2015 (after guideline) | 92 | 73.9% (*n*=68) | 76.1% (*n*=70) | 58.7% (*n*=54) | 48.9% (*n*=45****) | 48.9% (*n*=45****) |
| | | *p*<0.01 | *p*<0.01 | *p*=0.352 | *p*<0.01 | *p*<0.01 |

*$0_2$ = supplemental oxygen therapy
**ED = emergency department
***Correct = including both the delivery device *and* the flow rate (not deemed to be necessary for Venturi masks if the concentration of oxygen is specified)
****1 patient refused $0_2$, and another patient had oxygen therapy prescribed only as required (PRN)

***Table 2:*** *showing the results of oxygen therapy documentation, prescription and administration before (2011) and after (2015) the publication of the local hospital oxygen therapy guideline in patients in whom oxygen therapy was not indicated, i.e. $SpO_2$ or $SaO_2$ >94% on air, or >88% in patients with, or at risk of, type two respiratory failure (Y = yes, N = no)*

| **In patients in whom oxygen therapy was *not* indicated (*n*=132 in 2011, *n*=170 in 2015)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Year of data collection** | **Received oxygen therapy at the ED** | | **Prescribed oxygen therapy in management plan** | | | **Received oxygen therapy in ward** | |
| | **Y** | **N (or not documented)** | **Y** | **N** | **PRN*** | **Y** | **N** |
| 2011 (before guideline) | 23.5% (*n*=31) | 76.5% (*n*=101) | 56.8% (*n*=75) | 37.1% (*n*=49) | 6.1% (*n*= 8) | 47.0% (*n*=62) | 53.0% (*n*=70) |
| 2015 (after guideline) | 27.1% (*n*=46) | 72.9% (*n*=124) | 27.1% (*n*=46) | 67.1% (*n*=114) | 5.9% (*n*=10) | 33.5% (*n*=57) | 66.5% (*n*=113) |
| | *p*=0.478 | *p*=0.478 | *p*<0.01 | *p*<0.01 | *p*=0.952 | *p*<0.01 | *p*=0.018 |

*PRN = oxygen therapy prescribed only as required
**ED = emergency department

***Oxygen therapy in patients in whom oxygen therapy was not indicated***

Table 2 shows the results obtained in the group of patients in whom supplemental oxygen therapy was not indicated. The results obtained before and after the guideline was introduced were compared. There was no difference in the number of patients who were documented to have received oxygen therapy at the emergency department before and after the guideline (*p*=0.478). However, fewer of these patients were prescribed continuous oxygen in their management plans, that is 56.8% before the guideline compared to 27.1% after the guideline (*p*<0.01). Also, fewer of these patients actually received oxygen therapy once in the wards, 47.0% before the guideline, compared to 33.5% after the guideline (*p*<0.01).

**Discussion**

Oxygen therapy is frequently used. Both hypoxia and hyperoxia can be harmful, and so oxygen therapy requires an adequate, detailed prescription like any other prescribed medication. Hypoxia can cause sudden cardiorespiratory arrest and irreversible damage to vital organs. On the other hand, the effects of hyperoxia are controversial. Possible adverse effects of hyperoxia include the production of reactive oxygen species, leading to oxidative stress and resultant cellular necrosis and apoptosis; coronary artery vasoconstriction[3] with consequent reduced coronary blood flow potentially increasing infarct size; and life-threatening hypercapnoea in patients at risk of type two respiratory failure, especially in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) – nearly half of acute exacerbations of COPD are associated with hypercapnia. This increases the need for mechanical ventilation and risk of death.[4] In a randomized controlled trial, mortality was shown to increase with the delivery of high concentration oxygen in acute exacerbation of COPD (9% mortality) when compared with controlled oxygen therapy (4% mortality).[5] Randomized controlled trials have also shown that high concentrations of oxygen increase the risk of hypercapnia also in conditions not typically associated with type two respiratory failure, including asthma and pneumonia.[6-7] Excess oxygen therapy also causes patient discomfort, and increases healthcare costs.

In this audit, the documentation of oxygen saturation on air at the emergency department,

documentation of oxygen therapy given at the emergency department, prescription of oxygen therapy when indicated for inpatients, and actual administration of oxygen therapy according to prescription once the patients got to the wards, were identified as areas needing improvement. Inadequacy of oxygen prescription is common not just in Malta. In a multicentre nationwide audit in Portuguese Internal Medicine wards, only 11.6% of oxygen prescriptions stated all the required parameters.[8] An audit in the UK revealed that oxygen therapy prescription was accurate for only 7% of patients, and the most common omission was the oxygen flow rate.[9] Another audit in New Zealand revealed that 75% of oxygen therapy prescriptions were inadequate.[10]

In Mater Dei Hospital, Malta, after the local hospital guideline on oxygen therapy in adults was published, there were improvements in the documentation of oxygen saturation on air at the emergency department, documentation of oxygen therapy being given at the emergency department, the prescription of oxygen therapy in management plans of patients when oxygen therapy was indicated, and also improvement in the administration of oxygen therapy in the medical wards for patients in whom oxygen therapy was indicated. Also, fewer patients received oxygen therapy when it was not indicated.

The British Thoracic Society (BTS) emergency oxygen audits[11] showed similar improvements in oxygen therapy prescription and administration after the publication of the BTS guideline on emergency oxygen use. Prior to the guideline, oxygen was commonly used without prescription, and even if oxygen therapy was prescribed, it was rarely administered according to prescription. However, after the guideline was introduced, the proportion of patients with a prescription for oxygen therapy increased from 32% to 56%, compared to this audit's results of 34.1% before the local hospital guideline, increasing to 76.1% after the hospital guideline was introduced. In the BTS emergency oxygen audits, the proportion of patients receiving oxygen therapy via the correct oxygen delivery system increased from 47% to 59% after the guideline was published. In this audit, oxygen therapy administration according to prescription improved from 7.1% to 48.9% after the local guideline publication.

There was no statistically significant change in the number of patients who received oxygen therapy at the Emergency department when it was not actually indicated. We postulate that this may be a reflection of the fact that patients are in the early stages of care, and would still be in the process of being worked up, with the underlying diagnosis not yet evident, and the arterial blood gas measurements not yet available.

The local hospital guideline significantly improved oxygen therapy use in Mater Dei hospital. This is certainly positive and encouraging. However, although there was an improvement in the number of patients receiving oxygen therapy when indicated, there were still 48.9% of patients in whom oxygen was indicated who did not receive oxygen therapy at all, or received it incorrectly (i.e. not according to prescription). One reason for this may be that the hospital guideline was disseminated on the local hospital intranet to all hospital employees including doctors and nurses just once, while a separate email was then also sent out to all emergency and medicine department doctors personally, with the guideline itself attached to the email, and some further information about the guideline. Given that within the hospital, doctors are responsible for oxygen therapy prescription, while nurses usually administer the oxygen therapy, the fact that the dissemination of the guideline was focused more on the doctors may be one of the reasons why oxygen therapy administration still needs further improvement. Also, the local hospital guideline did not significantly increase the documentation of oxygen therapy prescription in the standard treatment chart currently in use in the medical wards. These treatment charts are for general drug prescription and do not include a specific area for oxygen therapy prescription. Treatment charts including a specific area for documentation of oxygen therapy prescription and oxygen saturation target range are being designed for use at Mater Dei hospital, and may help to further improve oxygen therapy prescription, and facilitate better administration of oxygen therapy by nurses in the wards.

Since there was a time lapse between the first data collection in 2011 before the introduction of the guideline, and the second data collection after the introduction of the guideline in 2015, another limitation of the audit was that the guideline itself might not be the only reason for the improvement in oxygen therapy prescription and documentation.

Another possible reason may be that trainee doctors in both departments may have been exposed to lectures including information on oxygen prescription too.

## Conclusion

Documentation of oxygen therapy administered at the emergency department, prescription of oxygen therapy for patients being admitted to medical wards, and actual administration of oxygen therapy at Mater Dei Hospital needed to be improved.

The local hospital guideline, which was introduced in 2015, provided information and guidance on all these points.

Data collected after the guideline was introduced showed a significant improvement in the documentation of oxygen therapy given at the emergency department, correct prescription of oxygen therapy prescribed including essential details such as delivery device and flow rate where required, and correct administration of oxygen therapy according to prescription in the medical wards.

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**Original Article**

# An overview of patient cases which have problems with discharge from Mater Dei Hospital

Matthew Formosa, Cynthia Farrugia Jones

**Abstract**

Patients which have problems for discharge can be commonly found within the confines of Mater Dei Hospital. These patients pose a considerable burden both economically as well as in terms of opportunity cost. The management of these patients is complex and multifaceted. All patient cases residing within the medical wards and had issues preventing discharge from hospital during the months of August and September 2016 were analysed so as to identify common factors between cases. Most patients were between 81-90 years old, female and partially dependent in their Activities of Daily Living. 94% of these cases presented as emergency cases. Interestingly, 52% of all cases were started on psychiatric medication whilst awaiting long term care. The most popular drug which was started in this instance was Haloperidol (Serenace) 0.5mg. Majority of patients and their relatives were unaware of the available supporting services. Hence from this we can recommend that better marketing of available domiciliary services could decrease the problem and more education on psychiatric problems of the elderly especially in institutionalizations would be of benefit.

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**Keywords**

Psychiatry, Geriatric Medicine, Long-Term Care

## Introduction

Within Mater Dei Hospital, there are a number of patients who exist in a state of metaphorical "limbo". These patients lack the degree of health which would enable them to be discharged back home safely and in good conscious. However, they are not able to take care of themselves and thus require long term care. Whilst long term is being sourced, these patients reside at Mater Dei hospital, and occupy a bed which is normally required for more acute patients. These patients are collectively and colloquially known as "social cases". Mater Dei Hospital, in Msida, is Malta's main Acute General teaching hospital. A study of these patients was carried out over the months of August and September 2016, and this sought to elucidate more information about the common factors which exist within this population, as well as to see whether these patients developed psychiatric problems or required psychiatric medication as a reaction to their long stay?

## Aim

To identify common factors amongst cases with problems to be discharged, to identify if these patients were started on psychiatric medication whilst residing in Mater Dei and to optimise the treatment of these patients.

## Method

The criteria used to define the population were that the patient had been an inpatient for more than 30 days and that the patient had been flagged for long term care. Fifty seven patients (n=57) met the criteria when the entire patient list from Medical wards 1 through 9 and Day-Care was analysed. Thus the files were obtained and the data charted.

## Results

Patients were distributed evenly from all-over Malta. The majority of patients lie within the 81-90 age group with the 91-100 group being the second largest group. Only 2% of patients were under 60. The vast majority (82%) were female. 50% of patients were taken care of by their families whilst 41% of patients lived alone. Only 9% lived with their spouse. Most patients (65%) lived in terraced houses. Very few patients made use of support services prior to their admission to Mater Dei Hospital. Most patients were partially dependent as identified by the Barthel Index. Very few patients (4%) had discernible risk factors such as smoking and drinking alcohol. The length of stay of most patients was 30 to 50 days and 70 to 100 days (Fig. 1). The vast majority of patients (92%) were admitted as emergency cases. A number of patients had a stay well beyond 200 days. Interestingly, 52% of all patients were started on psychiatric medication. Moreover, most patients were admitted with a complaint of acute confusion or lethargy and dehydration (Fig. 3).

## Discussion

Geographically, as expected, larger concentrations of patients were seen to be originating from the more traditional, heavily populated districts within the central and harbour regions. Fewer patients were seen to be originating from the peripheries of the island and this finding, tallies with observed housing patterns and trends[1]. This also correlates with the fact that most patients lived in terraced houses (65%). Interestingly, a number of patients were referred from homes from the elderly when the home could no longer care for the individual. However, the fact that a fairly even distribution was observed could reflect the limited sample size. Vis-a-vis age, this pattern reflects the life expectancy of the Maltese population which in 2015 was 79 for men and 83 for women. This is especially significant when view in tandem with the patient's gender, which showed that the overwhelming majority of patients were female. It is with interest that one views the home situation of these social cases. Very few lived with their spouse and most lived alone which indicates that the spouse had died, and again, this is in keeping with the expected life expectancies. Moreover, a number of patients were taken care of by their families and were only brought to hospital when the burden of care grew too great. The vast majority of patients did not make use of domiciliary services nor had any idea that they existed. Of the patients' who did use them, home nursing was the most popular option and this was used mainly for washing purposes or stoma changes. One could postulate that better marketing of these services would enable patients to stay longer in the community.

***Figure 1:*** *The length of stay of patients at Mater Dei Hospital at the time of data collection*

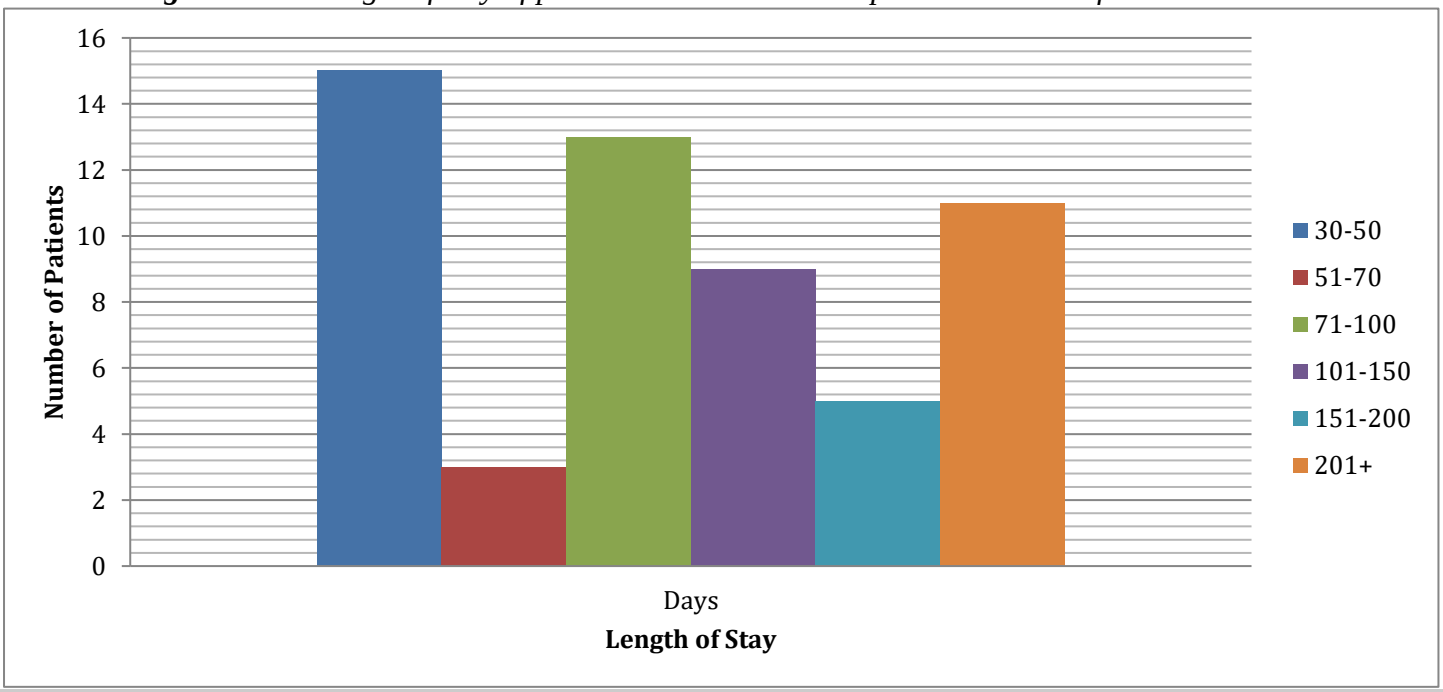


***Figure. 2:*** *A breakdown of the psychiatric medication started in patients who were admitted*

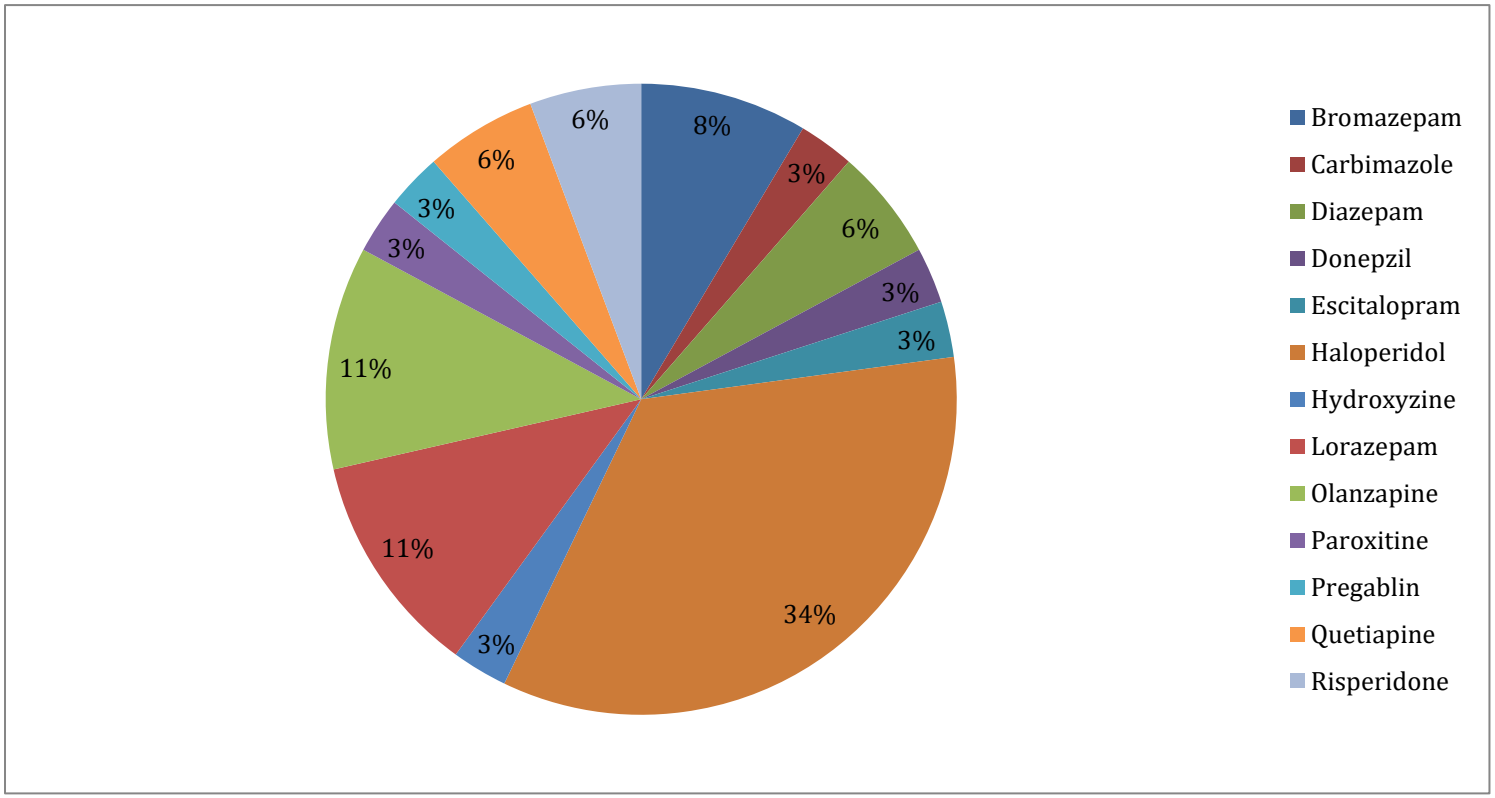
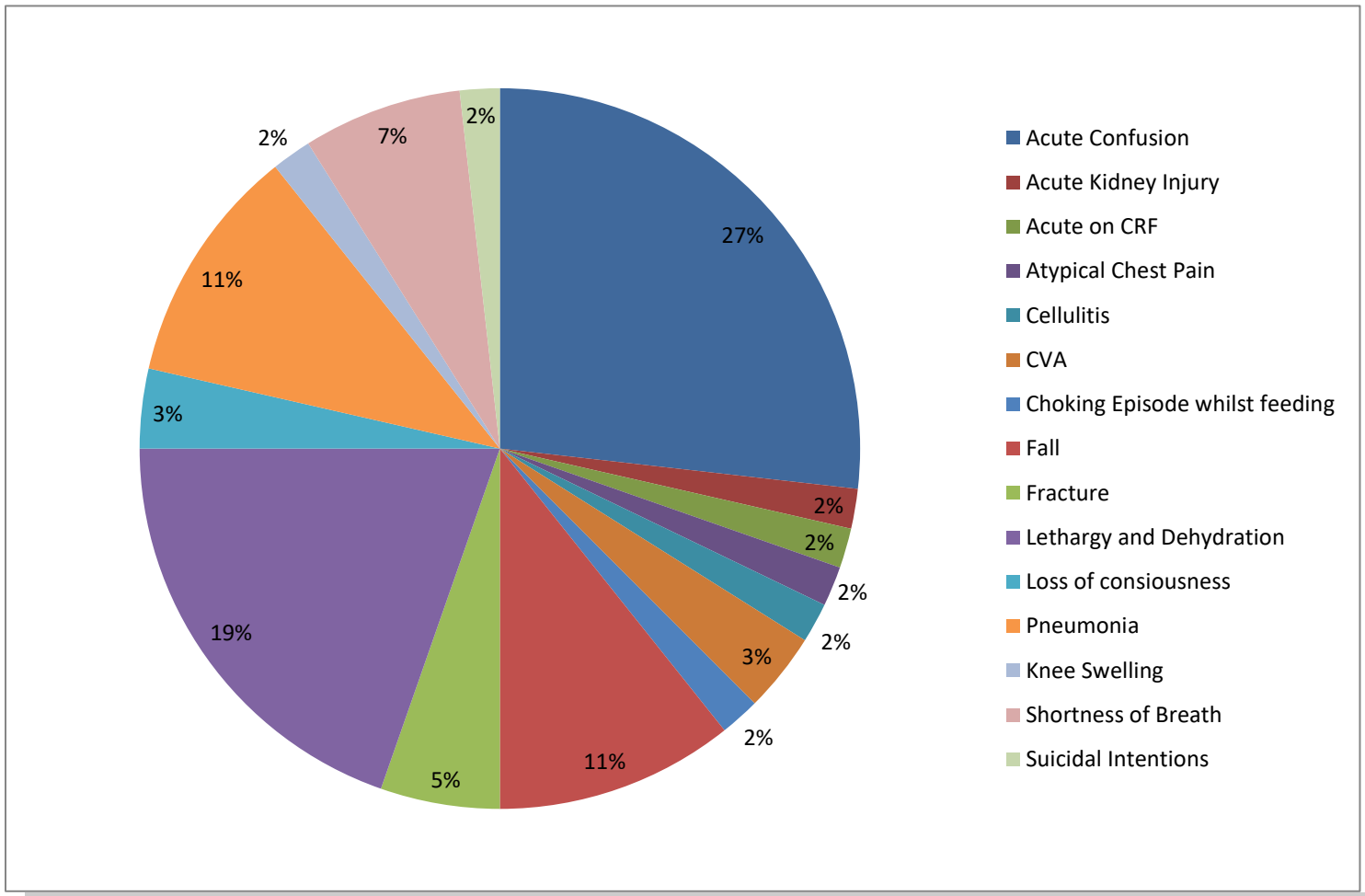



***Figure 3:*** *The admitting complaint with which patients were admitted to Mater Dei Hospital*



The length of stay of these patients is quite long with a large number of patients requiring extended periods of care. This reflects the saturated state of the system but it also highlights an area for improvement and where investment is needed. Most patients were admitted as an emergency and this reflects the frailty of these patients health. However, the fact that confusion and lethargy were the most common reasons for admission is a cause for concern, since this indicates that there is deterioration in general condition as opposed to new onset pathology. Finally, 52% of patients were started on psychiatric medication during their stay in Mater Dei Hospital. The picture reflects that intention behind these was sedation as evidenced by the drugs chosen, namely Haloperidol, Lorazepam, Bromazepam and Olanzapine (Fig. 2). The use of haloperidol follows the NICE guidelines which state that in a person with delirium is considered to be a risk to themselves or other, and that verbal and non-verbal de-escalation techniques have failed, one should consider giving short-term haloperidol, or if contra-indicated, olanzapine.

## Limitations

A larger sampler size would add more weight to the results.

## Recommendations

Greater investment within long term care is required since this is impinging on the health care system. Moreover, increased marketing of the available domiciliary services would support patients within the community for a longer time and thus decrease the burden on secondary care. Moreover, better marketing could change the prevailing mentality that exists within the community. Furthermore, optimising the said services to patients' needs and requests would increase their uptake. Community physiotherapy and occupational therapy would again decrease the chance of patients becoming wards of the hospital. Finally, most psychiatric medications in this population are started by members of the Department of Medicine. It would be beneficial if psychiatric input was obtained in these decisions. Moreover, continued medical education, provided by the Psychiatry Department, in this area, would be beneficial to all concerned.

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**Original Article**

# A study to assess the utilization of the influenza vaccine amongst doctors and nurses in the medical wards at Mater Dei Hospital

Annelise Aquilina, Stephanie Anastasi, Christopher Zammit

**Abstract**

Introduction: Seasonal influenza may be associated with a high morbidity and mortality rate. Efforts at promoting effective influenza vaccination in the general population and amongst health-care workers have been of increasing importance over recent years.

Aim: To assess use of influenza vaccine amongst doctors and nurses working in the medical wards at Mater Dei Hospital.

Method: Data was collected using questionnaires supplied to nurses on the wards and posted online to doctors.

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Results: A total of 130 questionnaires were completed. Results showed underutilization of the vaccine, with only 34% of respondents taking the vaccine in 2015. 43% of doctors (*n*=76) and 20% of nurses (*n*=54) confirmed taking the vaccine. 44% of senior doctors (HST level and above; *n*=27), were compliant with the vaccination; 43% of the junior doctors (*n*=49) took the vaccine, of which foundation-year doctors formed the larger portion (FY 55%; BST 19%). In the case of nurses, 25% of the 8 senior nurses took the vaccine, and 19% of the 46 staff nurses were compliant. The commonest reasons for non-compliance to vaccination included doubt about its beneficial effects and fear of side effects. The most effective method for promoting the influenza vaccine included nurses handing out the vaccine on site

Conclusion: The influenza vaccination coverage-rate in Malta amongst health-care workers during the 2015-2016 season was estimated to be 33.8%. The audit was limited by its small sample size and selection bias. Improved education about the beneficial effects of the vaccine is recommended in order to improve outcomes.

**Keywords**

Influenza, vaccine, immunization, health-care workers

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## Introduction

Influenza, is an acute infectious disease caused by an RNA virus which attacks the respiratory system. It is one of the most common causes of human respiratory tract infections and holds a high morbidity and significant mortality rates. The 1918 pandemic killed about 50 million people all over the world.[1] Influenza outbreaks usually occur in annual cycles, mainly during the winter months. Symptoms can be mild to severe and include: high fever, coryza, sore throat, cough, myalgia, headache and generalized lethargy and

malaise. Disease severity is greatest in the elderly, infants, and immunocompromised patients. Transmission occurs mainly via air-borne droplets of respiratory tract secretions as well as by direct contact.

The most effective measure against the influenza virus has been shown to be the prevention of infection by vaccination with inactivated or live attenuated virus. Studies in young and healthy individuals have shown 70% to 90% effectiveness in preventing influenza, with lower rates seen in the elderly population.[2] Continuous viral antigenic drift causes new variant strains of influenza to emerge, rendering previously effective vaccines ineffective after a few years and hence annual re-vaccination is recommended.

The aim of this audit was to establish the vaccination rate amongst doctors and nurses in Malta during Autumn 2015, with the purpose of initiating the necessary changes in order to improve the vaccination rate amongst health care workers, both for their own protection and for the protection of patients. The risk of exposure to influenza virus is higher in health care workers than the general population, due to their increased contact with infected patients during routine clinical practice.

## Method

Questionnaires were supplied to doctors and nurses working in the medical wards at Mater Dei Hospital. Nurses received a paper version of the questionnaire by hand whilst doctors received a link to an electronic version of the identical questionnaire via email or through social media.

The wards included in the audit included the respiratory wards (M3 and M6), cardiac medical ward, neuro-medical ward, the acute medical admission wards (MAU1, MAU2 and MAU3) and the medical wards M1 and M2.

The questionnaire was centered around the influenza vaccine which was distributed during the month of Autumn 2015. It included questions which addressed whether or not the vaccine was taken and the main reasons which affect health care workers in their decision to take the vaccine. The best method for publicizing the influenza vaccine was also addressed. The questionnaire is included in Appendix 1.

## Results

### *Demographic details*

A total of 130 questionnaires were completed. Out of the respondents, 44 (33.8%) were male and 86 (66.2%) were female. 87 respondents (66.9%) were aged between 20 and 30 years, while 43 (33%) were above the age of 30. In total, 76 doctors and 54 nurses replied to the questionnaire. The response rate among nurses was 54%. It is not possible to estimate the response rate among doctors as the number of doctors contacted is unknown.

### *Percentage of respondents who took the vaccine in 2015*

A total of 44 (33.8%) respondents took the vaccine in 2015, out of which 33 were doctors, and 11 were nurses (refer to table 1). It was noted that 20.3% of nurses who replied to the questionnaire took the vaccine during Autumn 2015, compared to the 43.4% of doctors who took the vaccine during the same time frame. There was a significant difference in the uptake of the vaccine between doctors and nurses ($p$=0.0063; using N-1 Chi Squared test with 95% confidence interval).

***Table 1:*** *Vaccine uptake in 2015*

| | Took the vaccine (%) | Did not take vaccine (%) |
|---|---|---|
| Doctors | 33 (43.4%) | 43 (56.6%) |
| Nurses | 11 (20.3%) | 43 (79.7%) |
| Total | 44 (33.8%) | 86 (66.2%) |

### *Respondents who took the vaccine according to grade*

Compliance to the influenza vaccine was highest amongst the junior doctors (FY1/FY2) at 54%, and amongst the more senior staff; Consultant/RS, HST and Senior Staff nurses; 44% and 25% respectively. The lowest compliance rates were amongst the middle grade doctors (BST = 18%) and more junior staff nurses (19%). Refer to table 2 and figure 1 below.

***Figure 1**: Percentage of Health care workers who took the vaccine according to Grade*

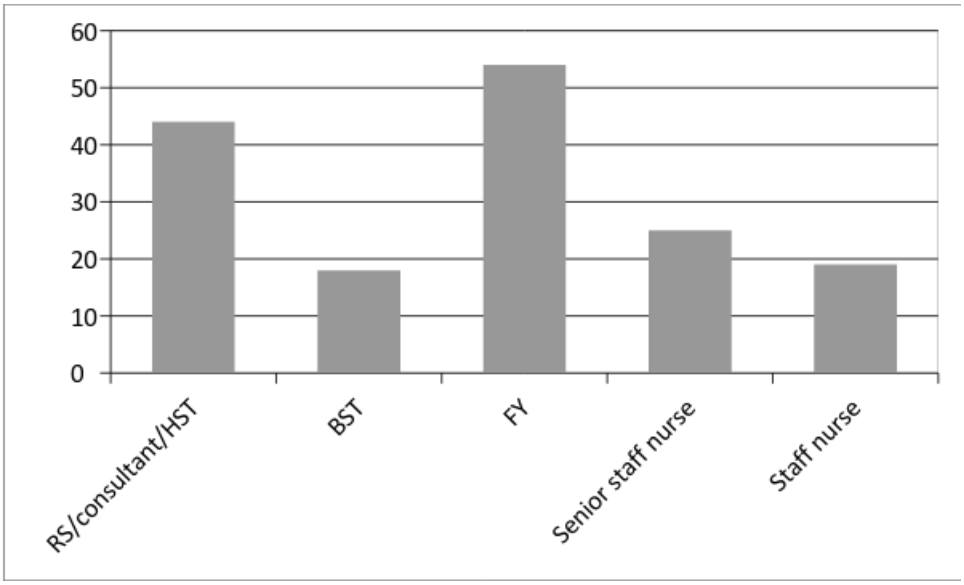



***Table 2**: Percentage of Health care workers who took the vaccine according to Grade*

| Grade | Number of respondents | Number who took vaccine | Percentage who took vaccine |
|---|---|---|---|
| **RS/consultant/HST** | 27 | 12 | 44% |
| **BST** | 16 | 3 | 18% |
| **FY1/2** | 33 | 18 | 54% |
| **Senior staff nurse** | 8 | 2 | 25% |
| **Staff nurse** | 46 | 9 | 19% |

***Figure 2**: Reasons why respondents took the vaccine. Vertical axis represents number*

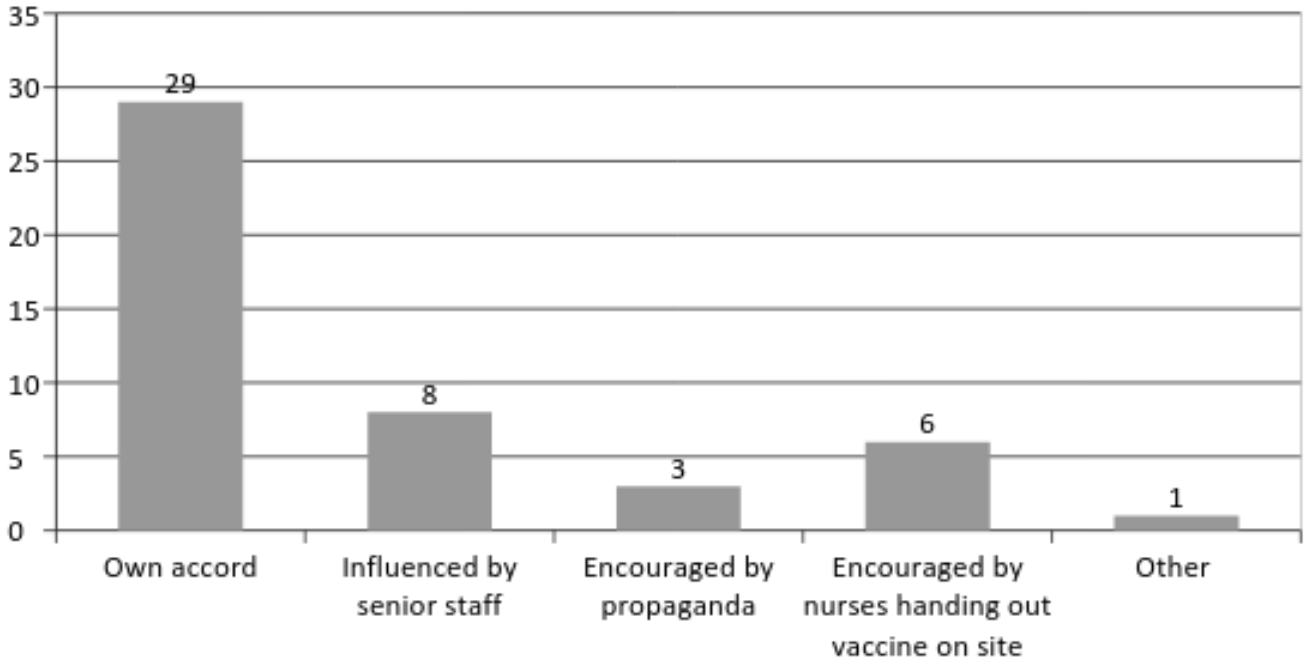


***Figure 3**: Reasons why respondents did not take the vaccine. Vertical axis represents number*

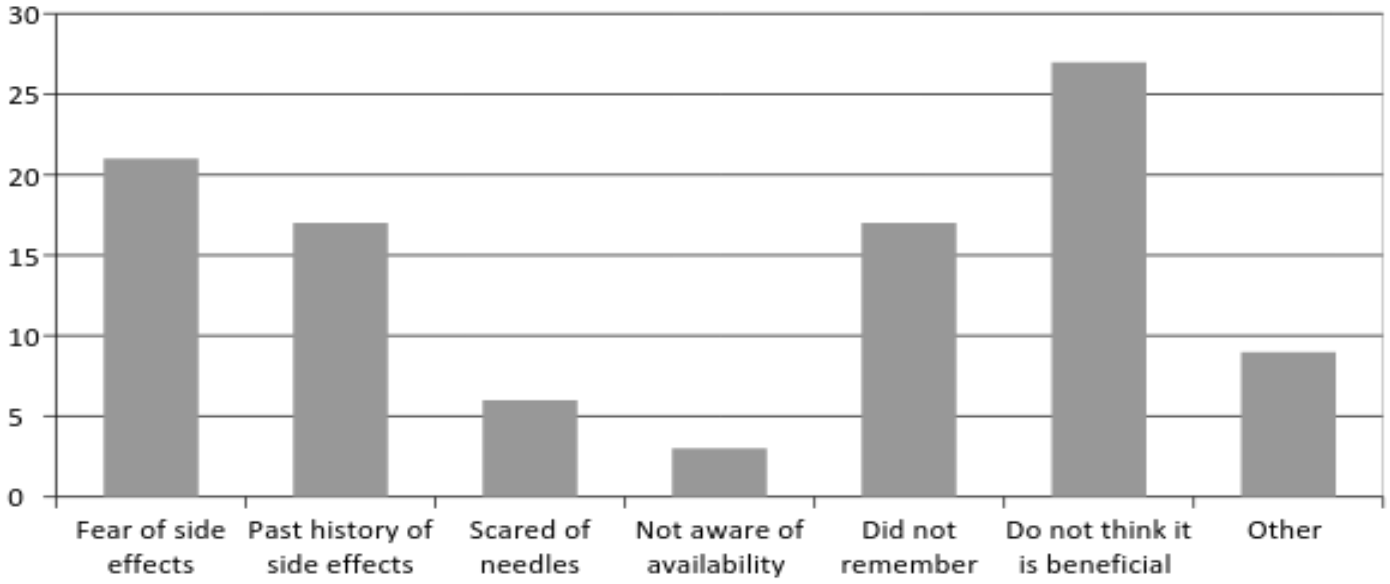



***Table 3**: Percentage of respondents who thought the vaccine is not beneficial*

| Grade | Number of respondents thinking vaccine is not beneficial | Total of respondents at that grade | Percentage compared to total of grade |
|---|---|---|---|
| RS/Consultant/HST | 3 | 15 | 20% |
| BST | 4 | 13 | 30.8% |
| FY | 3 | 15 | 20% |
| Senior staff nurse | 1 | 6 | 16.7% |
| Staff nurse | 14 | 37 | 37.8% |

***Figure 4:** Percentage of respondents who thought the vaccine is not beneficial*

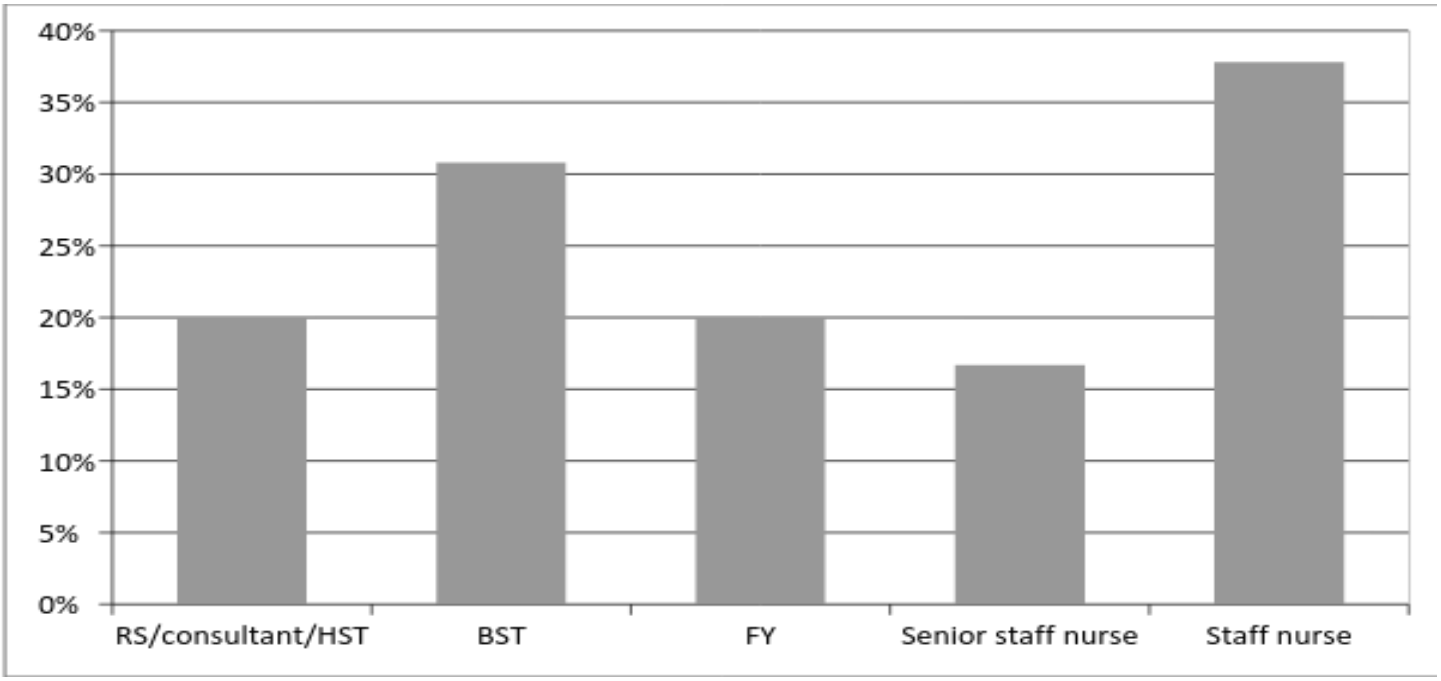
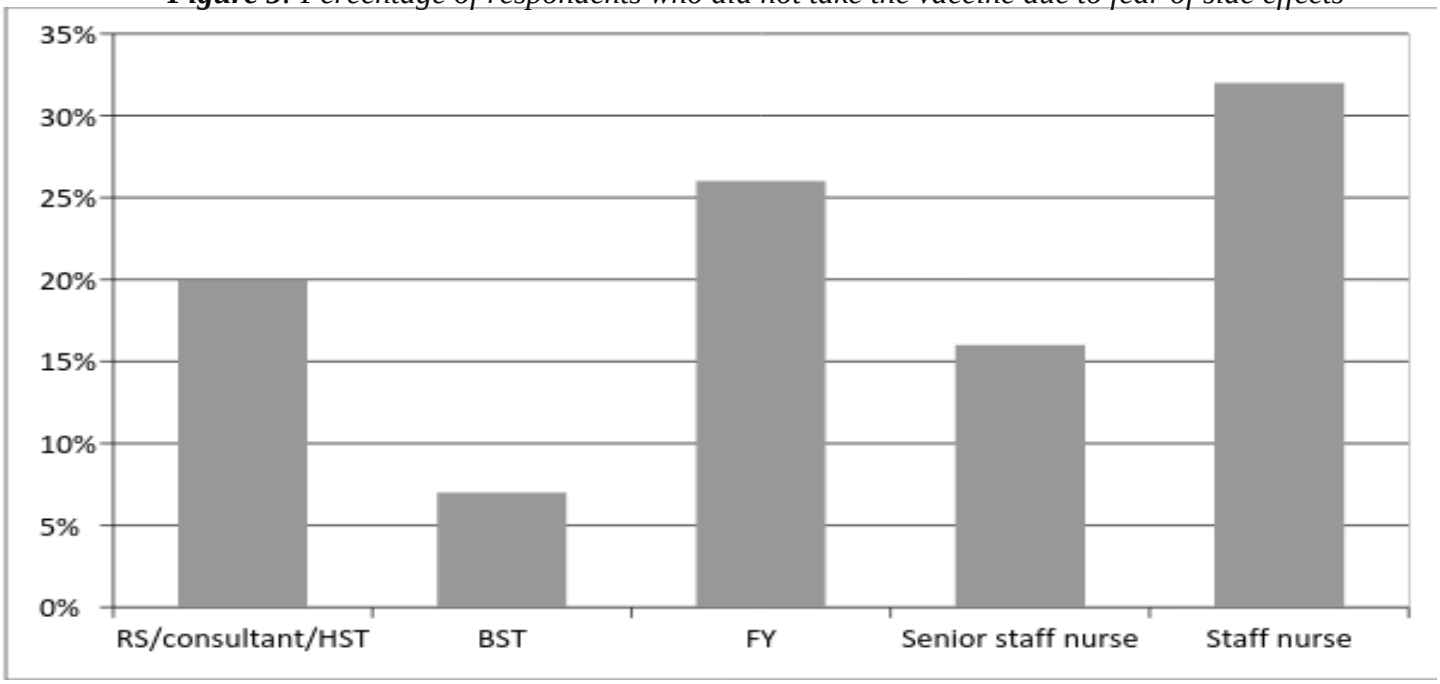


***Table 4**: Percentage of respondents who did not take the vaccine due to fear of side effects*

| Grade | Number of respondents who had a fear of side effects | Total of respondents at that grade who did not take the vaccine | Percentage compared to total of grade |
|---|---|---|---|
| RS/Consultant/HST | 3 | 15 | 20% |
| BST | 1 | 13 | 7% |
| FY | 4 | 15 | 26% |
| Senior staff nurse | 1 | 6 | 16% |
| Staff nurse | 12 | 37 | 32% |

***Figure 5**: Percentage of respondents who did not take the vaccine due to fear of side effects*




***Reasons why respondents took the vaccine***

There were five different reasons for taking the vaccine. Of the respondents who took the vaccine, 66% took it of their own accord (*n*=29); 18% were influenced by senior staff (*n*=8); 7% were encouraged by propaganda (*n*=3); 14% were encouraged by nurses handing out vaccine on site (*n*=6). There was a significantly small proportion of health care staff who admitted to taking the vaccine due to external influence (i.e. infection control propaganda or senior influence) at *p*=0.003 using "N-1" Chi Squared test at 95% confidence intervals.

***Reasons why respondents did not take the vaccine***

Of the 86 respondents who did not take the vaccine, 24% said it was due to the fear of side effects (*n*=21), while 20% reported a past history of side effects (*n*=17). 7% reported a fear of needles (*n*=6), 3.4% were not aware of its availability (*n*=3), and 19.7% did not remember to take it (*n*=17). 31.4% did not think the vaccine is beneficial (*n*=27). The larger proportion of this group including staff nurses (37.8%) and the BST middle grade doctors (30.8%). See Table 3 and Fig 3.

***Reported side effects***

Seventeen respondents reported past history of side effects. These included: pain (11%, *n*=2), erythema (17.6%, *n*=3), nausea/vomiting (5.8%, *n*=1), diarrhea (5.8%, *n*=1), upper respiratory tract symptoms (76.4%, *n*=13), allergy (5.8%, *n*=1) and other (5.8%, *n*=1, not specified).

***Respondents planning on taking the vaccine in Autumn 2016***

Seventy one respondents (54.6%) would like

to take the vaccine in 2016, while 59 respondents (45.4%) were not keen on taking the vaccine in 2016. 75% of respondents who were planning on taking the vaccine in 2016 were doctors. 74.1% of respondents who were not planning on taking the vaccine in 2016 were nurses.

***Effective ways of promoting the influenza vaccine***

5 methods of promoting the influenza vaccine were looked into. These included posters at MDH, nurses handing out the vaccine on site, KURA notice, email memos and word of mouth. The overall preferred method was that of nurses handing out the vaccine on site, with a total of 59 respondents (45%) choosing this method.

In addition, nurses also recommended promotional posters at MDH as a useful incentive. Doctors found on-site distribution of the vaccine to be the most effective way to encourage compliance to the vaccination. Both groups seem to give little importance to notices on KURA.

***Table 5**: Respondents' opinions on best ways of promoting the vaccine*

| | Posters at MDH | Nurses handing out the vaccine on site | KURA notice | Email memos | Word of mouth |
|---|---|---|---|---|---|
| **Doctors** | 10 | 41 | 3 | 7 | 15 |
| **Nurses** | 21 | 18 | 2 | 3 | 10 |
| **Total** | 31 | 59 | 5 | 10 | 25 |

**Discussion**

Our study population included a total of 130 subjects. Out of the respondents, 33.8% took the vaccine while 66.2% did not take the vaccine during the distribution period of 2015, representing a relative underutilization of the vaccine, especially amongst nurses. Professional category is a significant and independent predictor of vaccination and this has been reported in a meta-analysis, which showed that being a physician increased the chances of being vaccinated whilst being a nurse was associated with lower vaccination rates.[3] Our results also showed that there was a higher vaccination compliance amongst Senior staff nurses and RS/Consultant/HST when compared to general staff nurses and middle grade/junior doctors. The number of years of healthcare service has been shown to be another significant determinant in vaccination uptake, with a lower adherence in healthcare workers with less than 5 working-years experience.[4] In our audit, the junior doctors seemed to have a higher compliance rate to the vaccine, when compared to the middle grades and general staff nurses.

In December 2009, the EU Council of Ministers agreed to take action in order to mitigate the impact of seasonal influenza by encouraging vaccination amongst the elderly or people with chronic conditions, pregnant women and in health care workers. The main objective was to increase the vaccination coverage rates to a minimum of 75% amongst this group of at-risk people. The European Centre for Disease prevention and Control (ECDC) issued a technical report on the influenza immunization situation in Europe during the 2011-2012 and the 2012-2013 influenza season.[5]

Evidence from the report illustrated that vaccination coverage rates in most EU countries remains lower than that targeted by national governments in the Council Recommendation. A wide range of coverage rates amongst healthcare workers has been reported by the ECDC in 13 EU countries, varying from 9.5% to 75% with a median of 28.6%.[5] The highest vaccination rate was reported by the United Kingdom, Romania, Lithuania and the Netherlands. The ability to monitor vaccination coverage rates is a key component of any vaccination program and aids in identifying gaps and weaknesses.

Influenza vaccination coverage rates in the United States in the general adult population has been quoted by the Centre for Disease Control and Prevention as having ranged between 40.4% in 2009 and 41.7% in 2016 (CDC, 2016). Among Health Care Personnel the coverage rates were quoted as 77.3% during the 2014-15 season and 79.0% (CDC, 2015) during the 2015-16 season (CDC, 2016b).[6-8] This is a much higher percentage than that found in our audit. Similarly, the percentage of health care workers taking the vaccine in the United States was higher in physicians than in nurses or other health care workers.

66% of those who took the vaccination in Autumn 2015, took it of their own accord. Only 44% of those who took the vaccine appeared to have been encouraged by senior staff or infection control propaganda. It is of prime importance to establish whether this stark difference is due to the This could be a combination of lack of promotional encouragement and lack of interest or disregard by health care staff. However other determinants could not have specified in our audit; such as knowledge and awareness of the risk of exposure to seasonal influenza within the hospital setting as well as responsibility towards patients regarding the risk of influenza transmission.

Misconceptions about the severity of influenza and lack of knowledge on the benefits of the vaccine play a role in the refusal of the vaccine. In our audit, the main reasons reported for not taking the vaccine were that subjects did not think of it as beneficial and the fear of possible side effects. This was especially true amongst general staff nurses and the middle grade BST doctors.

The main barriers to vaccination as described by the ECDC include a low perception of risk particularly in healthcare settings, fear of possible or perceived side effects from vaccination, questions about the effectiveness of the vaccine, issues of cost, availability and convenience, misleading reports in the mainstream media, and a general lack of accurate information about the influenza and vaccination.[5]

The commonest reported side effect was that of upper respiratory tract symptoms. According to the CDC, the influenza vaccine does not cause influenza since the vaccination is made from the inactivated virus, or in the case of the recombinant vaccine, with no virus at all. Mild, short lasting side effects of the influenza vaccine do however exist: low grade fever; pain and/or erythema located to the injection site; myalgia. Out of the 17 respondents who reported not taking the vaccination in view of side effects, 76.5% stated these side effects were in the form of upper respiratory tract symptoms. As reported by the CDC, there is no correlation between influenza-like symptoms and the influenza vaccine.[6-8]

It appears that any increase in the uptake of the influenza vaccination in our local hospital would primarily require investing in educational programs tailored for our health care workers. Such programs should emphasize the significant morbidity and mortality associated with influenza, the proven effectiveness of the vaccine in the prevention of such morbidity and mortality, as well as the paucity of severe side effects to be expected.

In response to whether subjects were interested in taking the vaccine during the distribution period in 2017, 55% of respondents claimed to be planning on taking the vaccine. This was a significant improvement from the original 33.8%, who took it during 2015. This encouraging finding requires re-enforcement by means of ongoing education that would then reach its culmination during the distribution phase of the vaccine.

According to our results, the most effective way of promoting the influenza vaccine was through the infection control nurses freely handing out the vaccine on site. This likely makes the vaccine readily available and reduces the effort involved in seeking out the vaccine. Equally important and effective methods seem to be promotional posters distributed at Mater Dei Hospital. These audit results provide important information on where to focus promotional resources to encourage compliance.

The main limitation of this audit was the small sample size. A re-audit with a larger sample size may help provide a better representation of the hospital cohort. Our audit results depended exclusively on respondents returning the questionnaires to us, therefore allowing for significant selection bias. Although there was an apparent low compliance rate amongst health care workers at Mater Dei Hospital, this may still have been an over-representation - the respondents who completed and returned the questionnaire, are more to have taken the vaccine. The actual compliance to the vaccination may indeed be lower.

## Conclusion

The data which was collected has shown that there is still relative underutilization of the influenza vaccine among doctors and nurses, despite persistent efforts at promoting its use and despite its availability to health care workers. Further education about the benefits versus side effects of the influenza vaccine is suggested, with promotional posters and increased availability via on-site distribution of the vaccine to all health care workers at Mater Dei Hospital.

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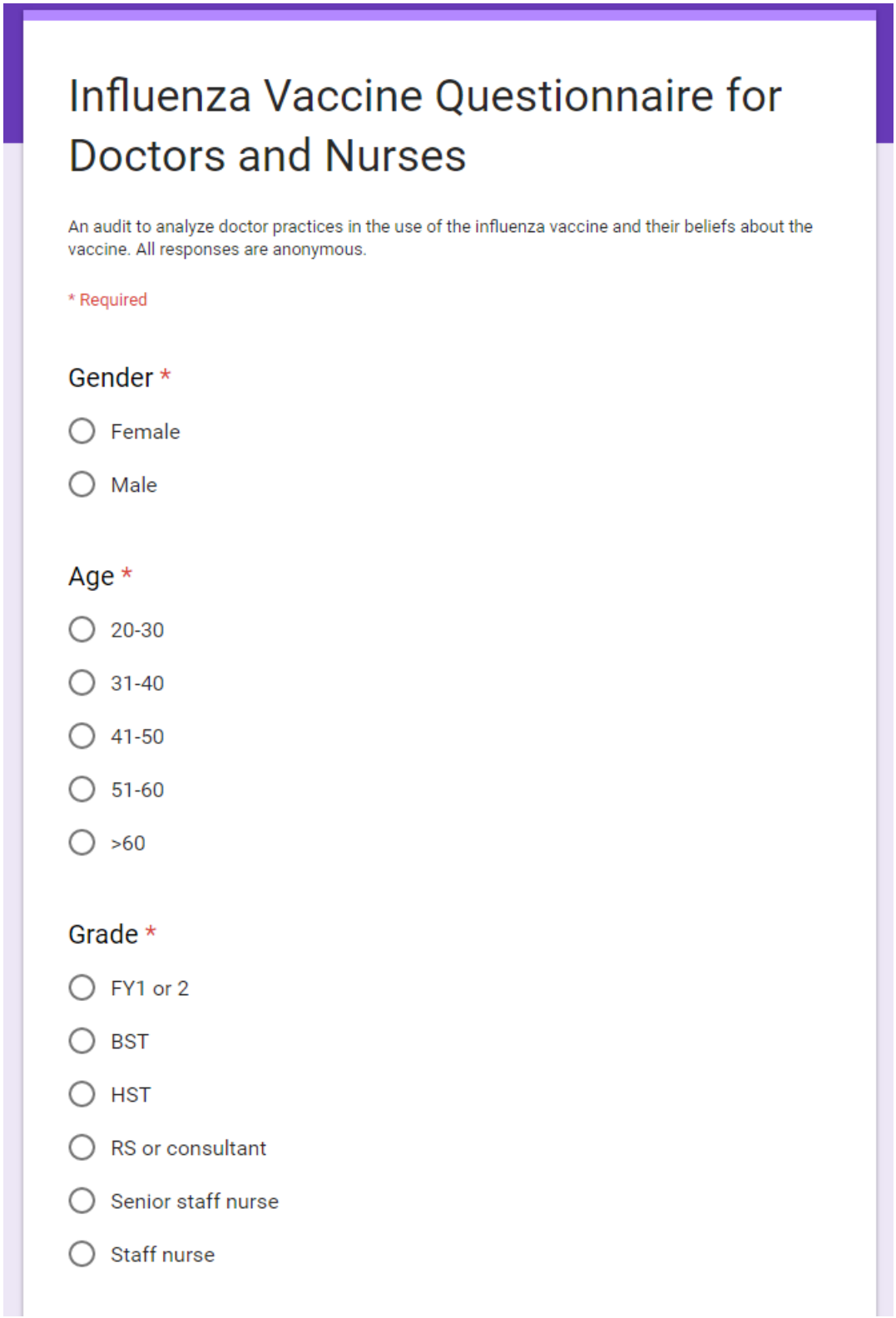
***Appendix 1:*** *Questionnaire (screen shots of the electronic version). Note that the paper version was an exact copy of the electronic version*



# Influenza Vaccine Questionnaire for Doctors and Nurses

An audit to analyze doctor practices in the use of the influenza vaccine and their beliefs about the vaccine. All responses are anonymous.

* Required

Gender *

- ○ Female
- ○ Male

Age *

- ○ 20-30
- ○ 31-40
- ○ 41-50
- ○ 51-60
- ○ >60

Grade *

- ○ FY1 or 2
- ○ BST
- ○ HST
- ○ RS or consultant
- ○ Senior staff nurse
- ○ Staff nurse

Did you take the influenza vaccine in October/November 2015? *

- ○ Yes
- ○ No

Did you decide to take the vaccine due to any of the below? *

- ☐ I take it every year of my own accord
- ☐ Influenced by senior member of staff or other colleagues
- ☐ Encouraged by propaganda at MDH/KURA/email notices
- ☐ Encouraged by nurses handing out the vaccine on site
- ☐ N/A
- ☐ Other: _____

Did you decide not to take the vaccine due to any of the below? *

- ☐ Fear of side effects
- ☐ Past history of side effects
- ☐ Scared of needles
- ☐ Not aware of availability (influenza vaccine is free for health care staff)
- ☐ Did not remember
- ☐ Do not think it is beneficial
- ☐ N/A
- ☐ Other: _____

If your answer to the above question was 'past history of side effects', which side effects did you experience? *

- [ ] Pain
- [ ] Erythema
- [ ] Nausea
- [ ] Vomiting
- [ ] Diarrhoea
- [ ] Upper respiratory tract symptoms
- [ ] Allergy
- [ ] N/A
- [ ] Other: _____

If you took the vaccine, where did you take it? *

- ○ MDH
- ○ Health centre
- ○ Privately
- ○ N/A

Are you planning on taking the influenza vaccine in October/November 2016? *

- ○ Yes
- ○ No

Did you suffer from influenza in winter 2016? *

- ○ Yes
- ○ No

If you suffered from influenza in 2016, did you experience any of the symptoms below? *

- ☐ Fever
- ☐ Muscle aches
- ☐ Headahce
- ☐ Fatigue/lethargy
- ☐ Cough
- ☐ Sore throat
- ☐ Nasal congestion
- ☐ N/A
- ☐ Other: _____

Was the influenza confirmed by a respiratory screen? *

- ○ Yes
- ○ No
- ○ N/A

How many days did you take off work in view of the influenza? *

- None
- 1-2
- 3-5
- >5
- N/A

What do you think is th most effective way of publicizing the influenza vaccine? *

- Posters at MDH
- Nurses handing out he vaccine on site
- KURA notice
- Email memos
- Word of mouth

SUBMIT

Never submit passwords through Google Forms.

**Original Article**

# Maternal factors and the male to female birth ratio in Malta

Victor Grech, Miriam Gatt, Julian Mamo, Neville Calleja

**Abstract**

Introduction: The sex ratio at birth is commonly calculated as the total male live births divided by all live births, and is represented as M/F. A multitude of factors influence M/F, especially stress, which increases male foetal losses during pregnancy.

This study was carried out in order to ascertain whether any maternal or perinatal relevant factors influenced M/F in Malta.

Methods: National Obstetric Information System data was used for the period 2012-2015. Non-Maltese mothers were excluded. Factors analysed were maternal age, marital status, education, body mass index, regularity of menses, utilisation of assisted reproductive technology, previous diabetes mellitus, previous miscarriages, abortions, ectopic pregnancies, vaginal deliveries, caesarean sections, livebirths, early and late neonatal deaths, stillbirths and premature deliveries. Intra-partum conditions included infection, cardiovascular disorders and all forms of diabetes mellitus.

Results: This study analysed 14498 births. None of the above mentioned variables was significantly linked to the M/F ratio.

Discussion: Our dataset failed to find any variables that influenced M/F, including stressing variables. However our study may have been underpowered due to the small numbers of births and the relative rarity of the various conditions. Alternatively, in Malta, such variables may produce little or no stress due to hitherto unknown mitigating factor/s.

**Key words**

Sex Ratio, Infant, Newborn, Malta

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## Introduction

The sex ratio at birth is commonly defined as male divided by total births and is conventionally referred to as M/F. A multitude of factors have been shown to influence this ratio,[1-2] most notably stress, which appears to be linked to an increase in male foetal losses during pregnancy.[3] It is very difficult to access any given country's periconceptual and pregnancy data at sufficiently detailed level in order to perform an analysis of factors that might conceivably influence M/F.

In Malta, data on all births is collected by the National Obstetric Information System (NOIS) at the Directorate for Health Information and Research and access to anonymised data was possible.

This study was carried out in order to ascertain whether any relevant variables influenced M/F in Malta and if so, to perform a multivariate analysis (logistic regression with binary outcome male or female) so as to determine which model best fits any putative discernible influence on M/F.

## Methods

NOIS data was deemed suitably complete for the period January 2012- December 2015 (Dr. Miriam Gatt – personal communication) and therefore analysis was restricted to births in this period. Furthermore, a shorter time period was deemed more appropriate so as to avoid time-series issues. All non-Maltese mothers were excluded.

Variables deemed relevant to this analysis

were maternal age, marital status, education, body mass index, regularity of menses, utilisation of assisted reproductive technology, previous history of diabetes mellitus, miscarriages, abortions, ectopic pregnancies, vaginal deliveries, caesarian sections, livebirths, early and late neonatal deaths, stillbirths and premature deliveries. The following conditions in the pregnancy itself were also factored in: infection, cardiovascular disorders and all forms of diabetes mellitus

The data was analysed in the Statistical Package for the Social Science (SPSS) version 20. The null hypothesis was that none of the above variables significantly influenced M/F. Each variable was first tested in order to ascertain whether it was linked to M/F. The chi-squared test of association and the unpaired t-test was used depending on the nature of the individual variables. A p value of $\leq 0.05$ was taken to represent a statistically significant result.

## Results

This study analysed all 14498 births to mothers of Maltese Nationality during this period. None of the above mentioned variables was significantly linked to M/F ratio on univariate analysis. For this reason, multivariate analysis was not indicated.

## Discussion

It is well known that stress at population level is strongly linked to changes in M/F. The ultimate cause is postulated to be one of evolutionary biology and is known as the Trivers–Willard hypothesis.[4] This suggests that in polygynous species (wherein males have multiple mating opportunities with several females), female mammals (including humans) are able to adjust M/F in response to their periconceptual and intrapregnancy conditions. This is because under poor environmental conditions, a male pregnancy (which yields a larger baby) is more difficult to carry to term. If the baby survives to birth, a frail male may not survive infancy and childhood. Should he manage, he would compete poorly for mating privileges with more robust males. A female baby who survives to reproductive age is likely to become pregnant. On the other hand, in good conditions, a male baby is likelier to propagate his mother's genes as he has more mating opportunities than a female who is limited by pregnancy and lactation. Hence, under poor conditions, males are likelier to be spontaneously aborted than females,[3] a process which appears to cull the frailer males.[5]

Our dataset failed to find any variables that influenced M/F, including variables that prima facie appear to be reasonable proxies for poor condition as defined above. These include, for example, single mothers and lack of support during pregnancy. However, such influences may be small and our study may have been underpowered due to the relatively small available number of births. Alternatively, in Malta, such variables may produce little or no stress due to mitigating factor/s that were untestable as unavailable.

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**Review Article**

# Diffusion MRI: From basic principles to clinical applications

Claude J Bajada, Geoff J M Parker, Matthew A Lambon Ralph, Lauren L Cloutman

**Abstract**

Diffusion MRI (dMRI) is widely used by clinicians and radiologists to diagnose neurological disorders, in particular stroke. The most commonly encountered diffusion technique in the clinic is simple diffusion weighted imaging and apparent diffusion coefficient (ADC) mapping. However, dMRI can tap into a wealth of data that is usually overlooked by clinicians.

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While most of this 'additional' information is primarily used in a research setting, it is beginning to permeate the clinic.

Despite the widespread use of dMRI, clinicians who do not have radiological training may not feel comfortable with the basic principles that underlie this modality. This paper's aim is to make the fundamentals of the technique accessible to doctors and allied health practitioners who have an interest in dMRI and who use it clinically. It progresses to discuss how these measures can be used.

**Keywords**

diffusion MRI, diffusion tensor imaging, radiology, tractography

## Introduction

Diffusion Magnetic Resonance Imaging (dMRI) is a well-established tool that is routinely used in clinical practice to identify an acute cerebral infarction and is increasingly used as an aid to tumour characterisation. Tractography (an extension of dMRI) has been used to identify the location of white matter tracts in pre-surgical planning. Other less widespread uses include the differentiation of intra-cranial cysts, the assessment of diffuse axonal injury and the assessment of demyelinating disorders.

In light of the increasing interest in diffusion imaging within the clinical community, this paper explains the basic principles of diffusion MR in order to give the reader a better appreciation of why dMRI can be used in the above conditions.

The review is split into three main sections. The first describes the physical process of diffusion, explains how it is measured using MRI, and describes the different measurements obtained from dMRI. The second describes how to use the obtained measurements to reconstruct the white matter tracts; tractography. The final section discusses different clinical applications of dMRI.

## Basic principles

### *Diffusion*

Water diffuses according to an apparently random, passive movement of molecules that collide and interact with one another. In a container (such as glass or vase) water molecules diffuse uniformly in all orientations (known as 'isotropic' diffusion) and without restriction. However, the brain is not structureless. In neural tissue the diffusion of tissue water is hindered by cell membranes and myelin sheaths.[1] In white matter, axons are often lined up in parallel, which hinders diffusion particularly perpendicular to the fibres, with greater diffusion in parallel with the fibre orientation (known as 'anisotropic' diffusion).[2] In grey matter, where the barriers are not highly ordered, this hindered diffusion is relatively more isotropic than in white matter.

### *Diffusion MRI*

Water is an abundant source of hydrogen nuclei (protons), which are detectable by an MRI scanner. All hydrogen nuclei possess a quantum mechanical property known as spin, which determines their intrinsic magnetic moment; each proton can be considered loosely as a tiny bar magnet. If a container of water is put into a scanner, the magnetic moments of the protons on average align with the main magnetic field. If a 90 degree radio frequency (RF) pulse is turned on, the proton magnetic moments rotate into the plane perpendicular to the field (known as the transverse plane) and precess (rotate round their own axes) in synchrony (in-phase) with each other.

This is the source of the MR signal. After a period of time, the protons dephase (precess at different rates so moving out of phase) which causes signal to be lost gradually. Indeed, the time it takes for protons to dephase is called the $T_2$* relaxation time.

In a standard spin echo MRI, a 180 degree pulse rephases (realigns) the protons and causes reappearance of signal as an 'echo' (see http://www.drcmr.dk/BlochSimulator/ for a good simulation of the process). Not all signal is recovered in the echo; with the amount of signal remaining dependent of the intrinsic $T_2$ relaxation time. The application of diffusion gradients causes additional dephasing and signal loss.

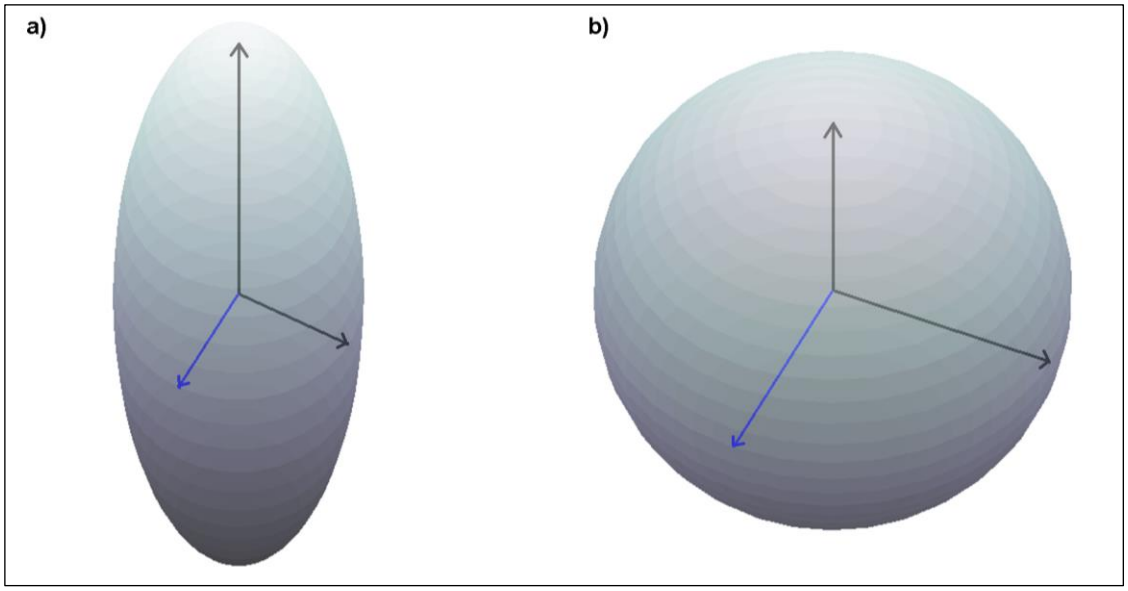
When a scanner is configured to detect diffusion, if a proton does not diffuse (i.e., stays in the same place), the signal is regained on application of the 180 degree pulse. If the proton diffuses, signal is lost.[3-5] Hence, image intensities in a diffusion weighted image are hypointense in regions where there is diffusion and relatively hyperintense where there is little diffusion.

## The Diffusion MRI Measures

Multiple diffusion weighted images are typically acquired in a scanning session. Each diffusion weighted image (DWI) contains information about water diffusing in one specific orientation. Thus, to estimate the dominant orientation along which water is diffusing in every voxel, the information from all the orientations, sampled by the various individual diffusion-weighted images, is combined. By doing this, one can measure the amount of diffusion in each voxel and the orientation of that diffusion. This can be described mathematically by using a tensor. In this application, a tensor can be thought of as a sphere or ellipsoid that best describes the amount of diffusion and level of anisotropy in the voxel. For example, a voxel in which there is a large amount of isotropic diffusion can be modelled by a large sphere while a voxel where diffusion occurs preferentially along a white matter tract (anisotropic diffusion) can be modelled by an elipsoid that has its main axis parallel to the orientation of diffusion (Figure 1).

Tensors describe both the level of isotropy and the magnitude of diffusion in any orientation in every voxel of the brain. These metrics are derived by 'decomposing' the tensor into three eigenvectors (orientation) and three eigenvalues (magnitude).[6]

***Figure 1***: *Ellipsoids depicting an anisotropic (a) and isotropic (b) tensor. The arrows represent the eigenvectors. The length of each of those vectors is called its eigenvalue. Note that all vectors are at 90 degrees to each other.*




***Apparent Diffusion Coefficient***

The Apparent Diffusion Coefficient (ADC) is a measure of the amount of diffusion occurring in a given voxel of the brain. A measured diffusion coefficient differs from the true diffusion coefficient of a substance depending on the conditions in which it is measured and the type of medium within which diffusion occurs hence the term apparent diffusion coefficient is used. ADC is calculated from one or more diffusion weighted image in combination with an image with no diffusion weighting. Since the DWI still has $T_2$ weighting it is not a pure measure of diffusion. If a tissue has a long $T_2$, then it will appear bright on a DWI despite there being relatively unrestricted diffusion ($T_2$ shine through). The ADC map is a pure, mathematically calculated, measure of diffusion and hence not affected by $T_2$ weighting. If a single diffusion weighted image is used in the generation of the ADC value then the ADC will be dependent on the orientation of the diffusion sensitisation within that image. The ADC values along the six main orientations (xx, yy, zz, xy, xz and yz) are the values that form the diffusion tensor matrix.

***Mean diffusivity***

The mean diffusivity (MD) is a measure of the average amount of diffusion that occurs in a voxel irrespective of whether the diffusion is isotropic or anisotropic. It is rotationally invariant since it is the average ADC in three orthogonal directions (xx, yy and zz) of the diffusion tensor. There are two ways to calculate an MD map. The first approach requires a minimum of three diffusion sensitised images in orthogonal orientations to be produced, hence a full tensor of six directions does not need to be estimated. However, if a full tensor is estimated then MD is the average of the three eigenvalues of the tensor. Both these approaches give identical results (apart from measurement error). MD maps are clinically often referred to as (rotationally invariant) ADC maps. MD is affected by the cellularity of a voxel, and the presence or absence of oedema or necrosis.[7]

***Longitudinal diffusivity***

Longitudinal or axial diffusivity (AD) is a more specific measure of diffusion. While MD is the average amount of diffusion in all directions, AD is the measure of diffusion occurring along the principal eigenvector of the diffusion tensor and is therefore another term for the principal eigenvalue. A decrease in AD is often associated with a disruption of white matter integrity. For example, in axonal injury, damage and debris could impede diffusion in the principal orientation.

***Radial diffusivity***

Radial diffusivity RD is a measure of the

amount of diffusion occurring perpendicular to the principle eigenvector. RD is often interpreted in an inverse fashion to AD; that is an increase in RD is associated with possible white matter integrity damage such as demyelination or axonal injury, as barriers to the radial diffusion of water, such as myelin and axon membranes are damaged or destroyed.[8] RA and AD together make up MD.

***Fractional anisotropy***

Fractional anisotropy (FA) is a measure of the level of orientational anisotropy of water diffusion in each voxel. FA varies between zero (if all eigenvalues are equal - a totally isotropic voxel) and 1 (if only one eigenvalue is non-zero). FA is frequently considered to be related to white matter integrity as axonal damage is expected to lead to increased diffusivity in directions radial to the axis of axons and fibre bundles. DTI studies often investigate the change in FA in differing neurological conditions with the assumption that a decrease in FA is caused by damaged white matter.[9] The use of FA and MD can give complementary information that enriches ones understanding of the underlying structure of the brain. However, these metrics do not directly measure microstructure and any interpretation as such must be made with caution

***Advanced measures***

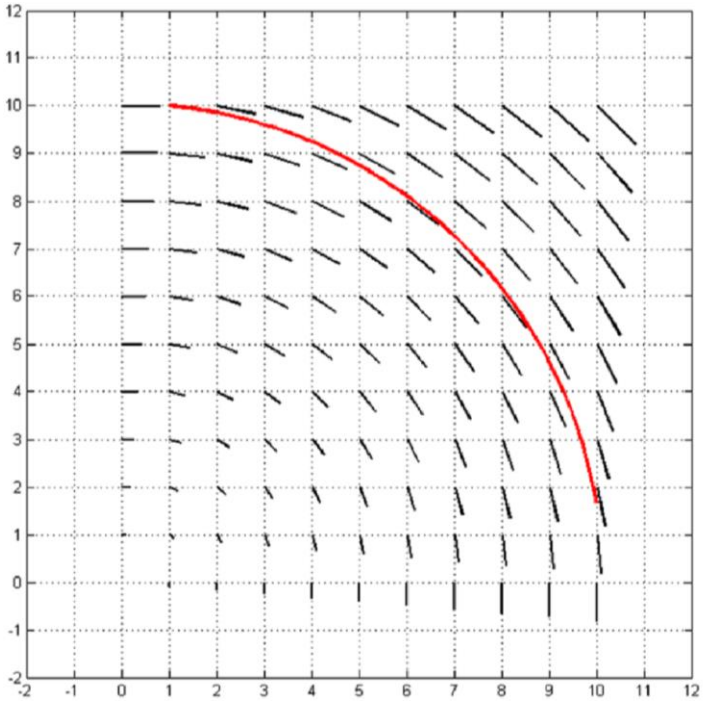
The tensor is not the only mathematical way to describe diffusion in voxels. In fact, many more complicated and arguably more precise methods of modelling diffusion exist.[10] As an introductory text, however, it is beyond the scope of this review to go into details. The measures described above are still the most commonly used, but it is important to be aware that diffusion MRI has the potential to give even more information than is discussed here.

**The Reconstruction of White Matter Tracts**

Tractography is a computational method that allows the virtual reconstruction of white matter tracts [11]. This paper will focus on a brief discussion of the most straightforward type of tractography, deterministic streamline tractography using tensors. A short reference to more advanced tractography algorithms will be given at the end of this section.

In tractography, each voxel can be modelled with a tensor and the principal orientation (eigenvector) is determined. An algorithm builds up a stepwise streamline from a seed (starting) voxel going through the most likely pathway through each voxel (see Figure 2).[12]

***Figure 2****: in this deterministic approach, you can see that each voxel has one direction associated with it. A streamline (red) can thus be propagated from the seed voxel (1,10) and a 'tract' generated.*



Tractography has the advantage over gross dissection and tracer studies that it is non-invasive and that it is easily repeatable on the same individual. The same process can be carried out by different individuals and using different algorithms to ensure that a consistent result is obtained. It is the only method that is available to investigate human white matter tracts in-vivo. It is with this in mind that one must assess its limitations.

Data obtained from dMRI is determined by the diffusion of water. Algorithms infer white matter tracts from the way water diffuses around them, therefore some of the tracts obtained may be false tracts (false positive) while sometimes the algorithm may not reconstruct a tract that is really present (false negative). This can also occur because diffusion data contain noise, which results in errors in the tractography process. Errors can also occur in voxels that have more than one fibre population within them, since it can be difficult to determine configuration of the fibres that caused the observed diffusion (for example, the points at which two or more fibre bundles cross or diverge). Since deterministic tractography only uses the principal fibre direction for propagation, it is liable to rather large errors in these ambiguous or noisy voxels.[13] Also, since the algorithm does not allow for quantification of errors in the tract, confidence in the resultant tracts is unknown[14]. Such algorithms are poorly suited to deal with configurations such as crossing and kissing fibres because deterministic tractography computes the most likely streamline between two parts of the brain, without allowing for any form of branching or divergence.[14] Other, more advanced, methods to perform tractography exist and have been developed to tackle some of the issues discussed. These include using advanced non-Gaussian approaches to model intra-voxel diffusion such as constrained spherical deconvolution[15] and using probabilistic algorithms to perform the tractography.[13-14] While an in-depth discussion of these techniques is beyond the scope of this short primer, the interested reader is referred to[13-14] for more information.

Tractography is still being validated by comparing outputs with invasive dissection of tracts. Although to date there has been a high degree of agreement between dissection and diffusion tractography studies it is still not recommended for routine clinical use. [16-18]

## Clinical Applications

### *Stroke*

Within a few minutes of an acute ischaemic event, cytotoxic oedema accumulates within the infarct which translates into a lower MD. There are two common approaches that are used to identify these regions of reduced diffusion that imply an area of infarction in an acute stroke: MD measurement and assessment of the DWI signal (which also contains $T_2$ information).

In stroke, hindered diffusion is relatively hyperintense in a diffusion weighted image. In the MD map, on the other hand, each voxel contains the value of the MD, hence an area with hindered diffusion has a low MD and looks dark. Diffusion MRI can be used to accurately diagnose hyperacute stroke. This is in contrast to CT or conventional MRI where a stroke lesion may take hours to appear. Diffusion MRI is often used alongside perfusion techniques to assess a diffusion-perfusion mismatch.[19]

### *Tumours*

MRI is a standard tool in the diagnosis and follow-up for tumours. MD mapping is increasingly being investigated as a marker for tumour cellularity and thus tumour grade, where a decrease in MD corresponds to higher cellularity.[20] It has also been investigated as a possible method for differentiating between brain mass effect and oedema from tumour and its infiltration, however results have been mixed.[21-22] These findings are yet to be validated for routine clinical use.

### *Multiple Sclerosis*

The most commonly used MRI sequence in multiple sclerosis (MS) is the fluid attenuated inversion recovery sequence (FLAIR). However, demyelinating disorders such as MS also have an impact on diffusion measures. The two most commonly used measures are FA and MD. FA generally decreases while MD typically increases in MS lesions, with subtle alterations in the normal appearing white and grey matter also being detectable.[23]

RD and AD (more detailed measures of diffusion in white matter tracts than MD, see above) can help in differentiating between pure demyelination and axonal injury that includes inflammation.[8,24] Demyelination alone increases RD

with no impact on AD while axonal damage and inflammation can decrease both measures.

These measures are not reliable in areas of complex white matter architecture such as in regions with complex fibre structure (e.g., crossing fibres).

### *Diffuse Axonal Injury*

In traumatic brain injury (TBI) patients, dMRI has been investigated for diagnosis of axonal injury. When axons are damaged, their configuration is no longer as highly structured as in the healthy brain due to damage to membranes, alterations to the myelin sheath, replacement of axons and/or infiltration by other cell types, and the accumulation of cellular debris. Each of these factors can cause a decrease in FA. It has been suggested that a decrease in FA may be a biomarker for a poor cognitive prognosis in TBI.[24-25]

It is important to note that, while in many cases a decrease in FA is caused by damage to axons in certain areas such as when there are two populations of fibres going in different directions, damage to one fibre population can lead to a paradoxical overall increase in FA rather than a decrease. This is due to the initial presence of two separate fibre populations with different orientations leading to an average low FA as there is not one single dominant diffusion orientation. If one population is damaged or removed, the other population becomes dominant, with a subsequent higher average axonal orientation consistency and therefore higher FA.

### *Intra-cranial Cysts*

Diffusion imaging can be used to differentiate epidermoid from arachnoid cysts. MD or DWI are the usual measures of choice. Since an arachnoid cyst is filled with cerebrospinal fluid (CSF), the MD will be very high (due to unrestricted diffusion) while DWI will be hypointense. The inverse pattern is seen in epidermoid cysts.[26]

### *Surgical Planning*

Tractography is a promising technique for pre-surgical planning. Surgeons can reconstruct tracts of interest prior to the surgery in order to know where (or where not) to target their intervention.[27] While the images rendered by tractography algorithms look convincing, the limitations described above make it not recommended for routine clinical use outside a research setting.[18]

## Conclusion

Many clinicians utilise diffusion imaging in their practice. This brief review summarised the basic principles of the modality and has introduced some of the ways in which this MR modality is currently being used. It is hoped that this primer will prove invaluable to anyone wanting to improve their interpretation of dMRI images and those who are interested in using these techniques for research or clinical application.

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**Review Article**

# Lipodystrophy: focus on HIV Lipodystrophy

Miriam Giordano Imbroll, Manuel Fenech, Mark Gruppetta

**Abstract**

Lipodystrophy is a rare condition which can be inherited or acquired, localised or generalised. It is characterised by abnormal adipose tissue distribution and in some cases underlying metabolic derangement, including diabetes mellitus, hypertriglyceridemia, hepatic steatosis, polycystic ovaries and acanthosis nigricans. Today, most cases of lipodystrophy are associated with human immunodeficiency virus (HIV).

This article gives a review of the possible mechanisms associated with HIV lipodystrophy, namely HIV infection itself, genetic susceptibility to HIV lipodystrophy and effects of treatment with highly active antiretroviral therapy (HAART). Treating HIV lipodystrophy is challenging. The various treatment options currently available for treating lipodystrophy are reviewed.

**Key Terms**

lipodystrophy, human immunodeficiency virus (HIV), highly active antiretroviral therapy (HAART), protease inhibitors (PI), Nucleoside reverse transcriptase inhibitors (NRTI)

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## Introduction

Lipodystrophy is a rare disorder. In recent years it is most often seen in association with human immunodeficiency virus (HIV). Recognising this syndrome is of importance because it has a psychological impact due to body shape changes and also because of the underlying metabolic abnormalities, which are linked with increased morbidity and mortality.

Lipodystrophy is characterised by generalised or partial loss of adipose tissue. There are different extents of adipose tissue loss, with some having loss from discrete areas (localised lipodystrophy), others from the limbs (partial lipodystrophy) whilst others having loss from most of the body (generalised lipodystrophy).[1] In localised lipodystrophy, usually there are only cosmetic implications. However, in the partial and generalised forms, an association with severe metabolic derangement exists, including diabetes mellitus, hypertriglyceridemia, hepatic steatosis, polycystic ovaries and acanthosis nigricans.

Lipodystrophy can be inherited (monogenetic), or acquired (autoimmune or idiopathic), in patients who do not have a clear inheritance pattern. Therefore lipodystrophy can be classified into the following 4 main categories: congenital generalised lipodystrophy (CGL), familial partial lipodystrophy (FPL), acquired generalised lipodystrophy (AGL) and acquired

partial lipodystrophy (APL). Lipodystrophy in patients receiving highly active antiretroviral therapy (HAART) has become the most common form of lipodystrophy .[1-2]

**Presentation and diagnosis**

HIV-associated lipodystrophy refers to both lipohypertrophy, where there is abnormal fat accumulation usually in the dorsocervical fat pad, neck, breasts and around abdominal viscera [3], and lipoatrophy with loss of subcutaneous fat around the face, arms, legs and buttocks. Facial fat loss can be very severe and psychologically disturbing to patients, as it carries a social stigma. This may limit compliance to HAART. In fact lipodystrophy has also been associated with lower reported quality of life.[4] Patients report reduced satisfaction with their body image, self-esteem, problems with social relationships, less confidence about their health and embarrassment due to body changes. Many patients also develop hypertriglyceridemia and some also develop impaired glucose tolerance and insulin resistance.[1]

The diagnosis is mainly clinical, but additional tests for glucose intolerance, serum lipids, liver function and hyperuricaemia are indicated.[1] Some tools that are used to help make a diagnosis are: anthropometry, bioelectrical impedance analysis (BIA), imaging techniques such as dual-energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI) and computed tomography (CT). Both CT and MRI demonstrate accumulation of intra abdominal visceral fat and minimal subcutaneous fat.[3,5-6]

**Pathogenesis**

Lipodystrophy has a multi-factorial aetiology, including HIV infection itself, genetic susceptibility and effects of HAART. HIV infection itself may contribute to fat redistribution by infecting macrophages in adipose tissue, which release pro-inflammatory cytokines and enhance local inflammation.[7] This is supported by increased tumour necrosis factor-alpha (TNF-α) expression observed in HAART-naive HIV-infected patients, a pro-inflammatory cytokine that initiates adipocyte apoptosis.[2,7].In a study by Castilhos et al[8] genetic variability in the adiponectin receptor, which is a circulating petptide secreted by mature adipocytes that acts as a regulator of glucose and lipid metabolism, appears to be associated with different anthropometric and metabolic phenotypes in HIV infected patients on HAART.

HIV type 1 (HIV-1) protease inhibitors (PI) are a class of drugs used in HIV[9]. They inhibit viral replication by selectively binding to viral proteases, therefore blocking proteolytic cleavage of protein precursors necessary for the production of infectious viral particles. Nucleoside reverse transcriptase inhibitors (NRTIs), another class of drugs used in patients infected with HIV[9], block the reverse transcriptase enzyme, which controls the replication of HIV genetic material. Both these drugs are particularly implicated in HAART-induced lipodystrophy.

One mechanism thought to be implicated in the pathogenesis of PI-induced lipodystrophy is the down-regulation of peroxisome proliferator-activated receptor gamma (PPAR-ϒ), (a nuclear-receptor which regulates adipocyte differentiation and maintenance) by the up-regulation of the Wingless-related integration site (wnt)/β-catenin signalling pathway.[10] One of the functions of this pathway is to inhibit adipogenic gene expression.[11] Another effect of PI is the down-regulation of essential adipogenesis transcription factors like CCAAT-enhancer-binding proteins (C/EBP)-α, which have major adipogenic function.[9] This down-regulation creates reactive oxygen species, which may induce insulin resistance by inhibiting glucose transporter 4 (GLUT-4), together with impaired leptin and adiponectin production. PIs share similar sequence homology with 2 proteins involved in lipid metabolism, namely cytoplasmic retinoic acid-binding protein type 1 (CRABP-1) and low-density lipoprotein receptor-related protein (LDLR-RP). Inhibition of the former leads to decreased fat storage and adipocyte apoptosis with subsequent release of lipids into the blood and the latter induces hyperlipidaemia by inhibiting hepatic and endothelial removal of chylomicrons and triglycerides from the circulation.[12-14]

NRTIs, especially zidovudine and stavudine, are thought to inhibit mitochondrial polymerase-ϒ and cause mitochondrial dysfunction, ultimately leading to apoptosis and loss of fat cells. This in turn causes insulin resistance and secondary dyslipidaemia.[6,15]

Since PI and NRTI are usually prescribed simultaneously, it is difficult to predict which drug is responsible for which phenotypic appearance, although it is likely that PI induce peripheral

lipoatrophy and metabolic abnormalities whereas NRTIs may be responsible for the lipohypertrophy with accumulation of fat in the neck region.[1] Newer HIV drugs are less likely to cause the condition: old NRTIs such as zalcitabine, didanosin, stavudine and zidovudine are more prone to lipodystrophy than the newer NRTIs lamivudine, abacavir and tenofovir.[6,16] The older agents have been phased out in most developed countries but are still in use in low-resource settings.

**Epidemiology**

The global prevalence of lipodystrophy among HIV patients ranges considerably and studies quote very differing rates (1-84%).[6] Gender influences mode of presentation: women tend to be more likely to report fat accumulation in the abdomen and breasts, whereas men are more likely to notice the loss of fat from the face and other extremities.[17]

Risk factors for HIV-induced lipodystrophy include the duration of antiretroviral therapy (particularly receiving treatment for 2 years or more), female sex, obesity, higher triglyceride level, white race, older age and low CD4 count.[18]

**Management**

Treatment can be challenging. First and foremost, it should be targeted at managing the underlying metabolic derangements of glucose and lipids aggressively.[1] Diet and exercise have been proven to improve insulin sensitivity but no controlled clinical trials have been conducted to guide treatment for the metabolic complications in patients with lipodystrophy.

Management of severe lipodystrophy needs to involve modifying the treatment regimen, especially if an older drug is being administered. If this is not possible, using a lower dose of the drug will need to be considered. In a meta-analysis of trials comparing doses of stavudine which is an older NRTI (40mg vs 30mg) in high income countries, there was strong evidence that the lower 30 mg dose of stavudine was associated with lower rates of side-effects including lipodystrophy, and similar efficacy in suppressing HIV viral load, compared to the 40 mg dose.[19] These findings informed the WHO recommendations for lower dose stavudine in 2007 and the subsequent discontinuation of stavudine due to severe side-effects in 2009.[20] In a study HIV-infected adults were switched from stavudine/didanosine to the newer agents tenofovir/lamivudine. There was an increase in limb fat mass and total fat mass, as measured by DEXA 48 weeks after the regimen change.[21] Thus the newer NRTI agents are recommended.

No controlled clinical trials have been conducted to guide drug therapy for metabolic complications. For severe hypertriglyceridemia, fibrates and fish oil should be used and may be combined with a statin.[1] Metformin remains the first-line treatment for diabetes and insulin resistance, when tolerated. Studies of thiazolidinedione treatment for HIV lipodystrophy have shown conflicting results. A meta-analysis has shown that pioglitazone may be safer than rosiglitazone but any benefits on improved fat deposition in lipodystrophic regions were small.[22] In many patients with diabetes, insulin therapy is needed and since patients usually require high doses of insulin, highly concentrated insulin such as U-500 insulin should be used, due to the difficulty in injecting a large volume of insulin whilst having no subcutaneous fat in the abdomen or thighs. GLP-1 analogues may also be considered in selected patients.[23]

Tesamorelin, a synthetic form of growth hormone-releasing hormone, which was approved by the Food and Drug Administration (FDA) in 2010, seems to have some role in decreasing visceral adipose tissue.[24-25]

Leptin therapy (Metreleptin) was approved by the FDA in 2014 for treating generalised lipodystrophy with or without metabolic complications but not associated with HIV.[26-27] In patients with lipodystrophy a state of leptin deficiency occurs due to lack of adipocytes. Leptin regulates appetite by allowing negative feedback via the hypothalamus. Patients with leptin deficiency lose this regulation causing hyperphagia. However due to the lack of adipocytes, which usually store the excess food ingested, this fat is deposited in abnormal places, leading to the typical appearance in patients with lipodystrophy. Leptin therapy was found to improve the overall clinical picture of the metabolic syndrome; namely the hyperglycaemia and insulin resistance, the hyperlipidaemia and hepatosteatosis.

Plastic surgery procedures, namely liposuction and lipectomy did not yield very positive cosmetic results, as lipohypertrophy usually recurs. For lipoatrophy, free flaps, lipotransfer (transplantation

of fat harvested during liposuction of the dorsocervical fat pad), and commercial fillers such as Poly-L-lactic acid (Sculptra®) have been approved by the FDA as treatment for facial lipoatrophy in HIV-positive patients.[3,28]

In addition to the physical consequences of lipodystrophy, an important component to clinical management is the evaluation of the impact of lipodystrophy on emotional well-being and quality of life.[4]

## Prognosis

There might be some regression of HIV-associated lipodystrophy on stopping the implicated PI or NRTI therapy. To date, there has been no studies determining the morbidity and mortality from the body morphologic changes of HIV associated lipodystrophy per se. However the excess morbidity and mortality is attributed to atherosclerotic cardiovascular disease secondary to insulin resistance, hyperglycaemia and hyperlipidaemia.

## Conclusion

HAART is the gold standard treatment for HIV/AIDS care and treatment, however adverse treatment related outcomes, including lipodystrophy are relatively more common in low and middle-income counties, due to the use of older drugs. This has considerable implications in view of the increased risk of metabolic disease, quality of life and drug adherence. With early detection of HIV and longer lifespans of infected individuals, the length of HAART exposure and the burden of related metabolic complications are also expected to rise. More evidence based interventional studies are needed in this respect to reduce the burden of HIV and lipodystrophy.

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# Case report - Rectal Diverticuli

Daniela Zammit, John Bonello, Martina Muscat,
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**Case Report**

A 56 year old gentleman presented with a long-standing history of constipation and new onset rectal bleeding. The patient underwent a Computed Tomography (CT) Colonography (Figure A) which showed multiple rectal diverticuli and mildly enlarged mesorectal lymph nodes. A flexible sigmoidoscopy was performed and demonstrated the presence of four rectal diverticuli (Figure B).

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Rectal diverticuli occur in only about 2% of patients with concomitant colonic diverticular disease.[1-2] The low incidence of this condition has been explained by the uniform disposition of the longitudinal muscle fibres in the rectum (in contrast to the colon) and the lower intraluminal pressure generated in the rectum compared to the colon. They are normally found on the rectal lateral wall due to the support provided by the taenia omentalis and libera, anteriorly, and the taenia mesocolica posteriorly.[3] Rectal diverticula are true diverticuli as they involve all layers of the rectal wall.[3]

Most patients are asymptomatic. The finding is usually incidental.[4] Patients may present with symptoms secondary to faecal impaction or due to complicated disease such as abscess, rectal prolapse, rectal stenosis, recto-vesical fistula and rectal mass.[5-6]

The cause for their formation is yet unknown. Possible risk factors include congenital anomalies such as primary muscle atrophy and absence of the coccyx,[6] longstanding constipation and rectal trauma.[4] Iatrogenic causes can occur secondary to stapled haemorrhoidoplexy or stapled transanal haemorrhoid resection.[7] Surgery is reserved for complicated disease.[8]

***Keywords***

Rectum; Diverticuli; Colonography; Endoscopy.

***Figure A:*** *CT Colonography – Rectal diverticuli*

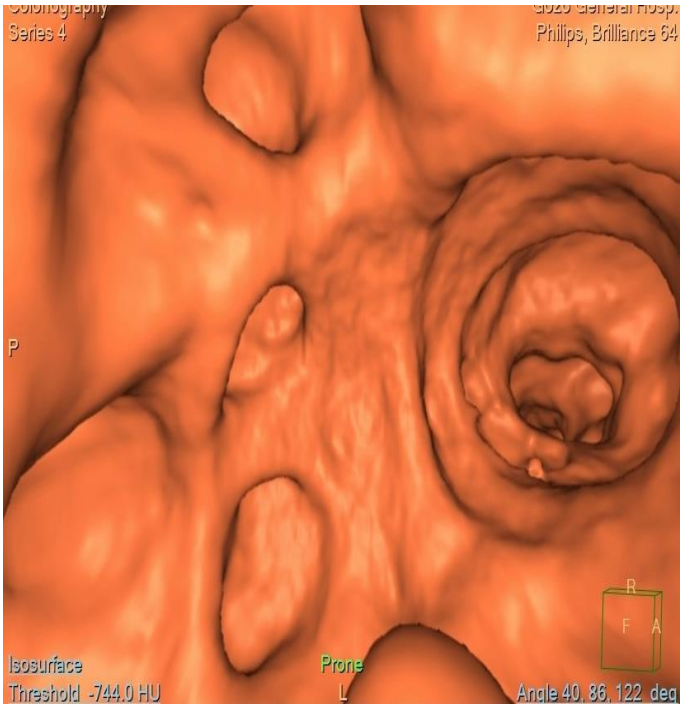
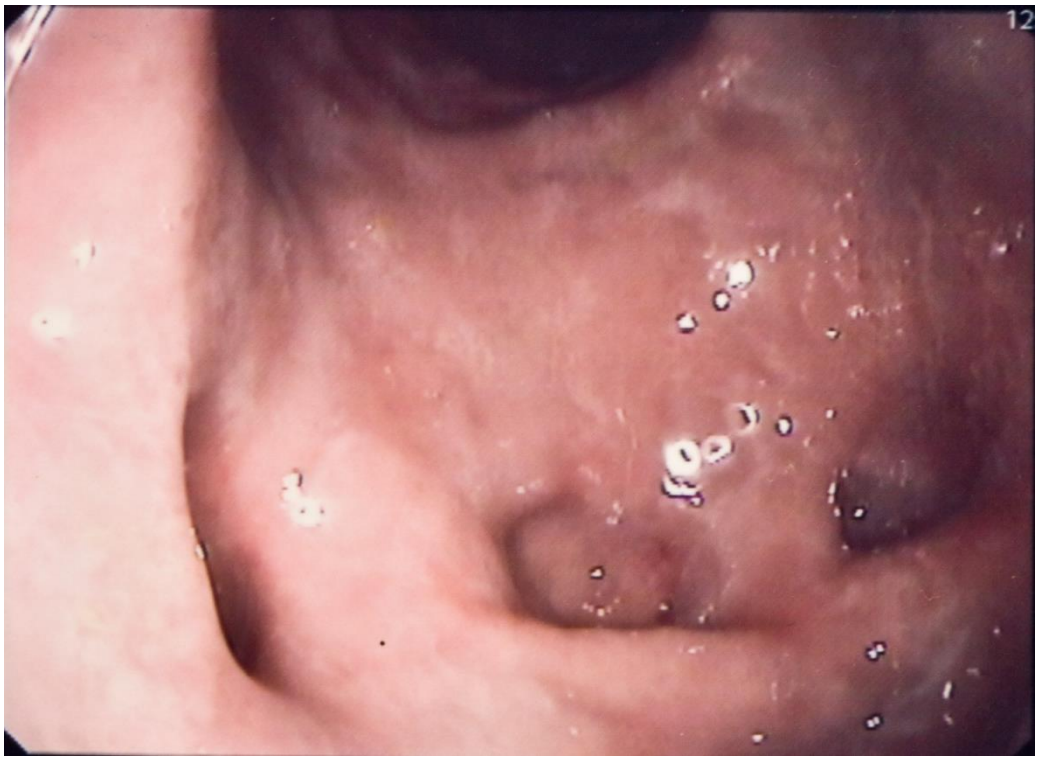



***Figure B:*** *Flexible Sigmoidoscopy – Rectal diverticuli*



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