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## British Journal of Medical Practitioners

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#### Reaching a Personalized Medicine Era: The Dream of the Drug Market

Juan S. Barajas-Gamboa, Patrick Francois Tarquino, John Elkin Pedraza and Daniel Gonzalez-Nuñez

#### Abstract

Personalized medicine, the study of the influence of a patient's genetic makeup on their disease susceptibility, prognosis, or treatment response (efficacy and safety), is actually in the spotlight. This field is expected to allow us to have effective and safe medication to targeted patients with appropriate genotypes.

Keywords: Personalized Medicine, Pharmacogenetics, Clinical Outcomes, Human Genomics, Drug Response

In the last few decades, the practice of medicine has seen swift changes, as well as its visualisation in the near future. It was designed and focused on serving the community and helping people in need. However, it is not a secret that there is a huge business around this labour and the economic interest of a diverse industry in the field. <sup>1,2</sup>

Not intending to generalise, many have observed in daily practice a comparable trend with modern society. A phenomenon including both patients and health personnel, where there is a demand for health services, a growing supply, and a considerable revenue. Basic market economics, right? <sup>3</sup>

Not that simple.

It would be the triumph of basic sciences to explain each disease under a biological substrate, minimising the involvement of other factors. A definitive targeting of biological research would be the key to unlocking knowledge. What is certain is that this approach has transformed pharmacotherapy, treatment alternatives and prognosis. $^{2,3,4}$ 

Early physicians had little to nil information on what today we call aetiology, pathophysiology and therefore treatment. Patients were rarely relieved due to human intervention. Trepanations were frequently performed in the Classical and Renaissance periods and although having modern indications (decompressive craniotomy), its uses and technique were at best questionable. Belief and verbally transmitted understanding of a handful of medicinal plants whose effect were known empirically were standards of care.<sup>5</sup>

These times have changed, the pharmaceutical industry is a pillar of the economies in many countries, and the number of transactions and cash flow that they move are beyond the wildest dreams of the first physicians. Born each year, thousands

of new pharmaceutical companies develop and market new drugs and medical supplies.  $^{1,\,6}$ 

As advocated by experts, pharmaceutical and medical supply companies are considered one the safest businesses nowadays, with everyone being a potential consumer/patient. It is the race for continuous development of new drugs to its current rate that guarantees soon we will have more drugs and procedures available. The drug industry may be easily overloaded by an oversupply of organic compounds and procedures to patients. <sup>2, 4, 6</sup>

This pharmaceutical industry thriving is widening its horizon. Personalised medicine, the study of the influence of a patient's genetic makeup on their disease susceptibility, prognosis, or treatment response (efficacy and safety), is actually in the spotlight. This can be assessed in different ways, being preventive and/or therapeutic. <sup>7</sup>

In the preventive field, preconception screening studies have been unravelling genetic disorders, as recommended by different guidelines such as those of the American College of Medical Genetics, which are designed for individuals with known genetic conditions or high-risk patients who wish to become pregnant. <sup>8</sup>

In the therapeutic filed, pharmacogenomics can aid in the identification of alterations of Single Nucleotide Polymorphism (SNPs) that affect the function or expression of proteins associated with pharmacokinetics or pharmacodynamics of different drugs. In recent years the research community has doubled efforts in personalising certain therapies. Hormonal therapy in breast cancer has been from the beginning a receptor-guided therapy, especially with ER (Oestrogen Receptor) therapy. Initial clinical results of trials conducted so

far have allowed to establish single therapies regimens with Tamoxifen or combined with Arimidex. <sup>9</sup>

Another model of the advances in this arena is reflected in the new alternatives for prostate cancer. This hormone-dependent tumour has demonstrated recurrent alterations in the androgen receptor and its pathway. In specific patients the disease can be found in Castration-Resistant Prostate Cancer (CRPC), a lethal clinical state in which the tumour has developed resistance to androgen deprivation therapy. This clinical scenario is commonly established in advanced or metastatic prostate cancer patients. The genomic landscape of localised prostate cancer has been well defined, describing putative pathogenic BRCA2 germ line mutations as well as somatic and germ line DNA repair alterations found such as BRCA1, CDK12, FANCA, and RAD51B. Furthermore, the research advances described above can allow clinicians to determine treatment, therefore achieving better outcomes. <sup>10</sup>

It is unquestionable that personalising treatment will improve clinical outcomes for patients in the near future and help achieve a more effective use of available health care resources. The next challenge for scientists and researchers is to demonstrate with strong evidence the clinical and cost-effectiveness to support the use of personalised medicine and its implementation in different health care systems around the world. <sup>2, 3, 5</sup>

In conclusion, individual patient variability currently studied in drug efficacy and drug safety has represented a major objective in current clinical practices. Years of research results have converged in progresses in pharmacogenetics and human genomics that have dramatically accelerated the discovery of genetic variations that potentially determine variability in drug response, providing better clinical outcomes for patients. The future in this field is expected to allow us to have effective and safe medications to targeted patients with appropriate genotypes.

#### **Competing Interests**

None declared

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# Psychiatric aspects in endocrinolgical disorders: Identifying depressive and anxiety in endocrine patients attending outpatient department - A Study from General Hospital in Kashmir (India)

Sheikh Shoib, Javid Ahmad, Aatif Rashid, Hamid Shah, Raheel Mushtaq and Manzoor Malik

#### Abstract

**Background:** Psychiatric disorders like depression and anxiety is frequently associated with function of hypothalamic-pituitary-thyroidal axis. Psychiatric disorders frequently mimic the symptoms of endocrinological disorders. With this background, we studied the depression and anxiety in different endocrinogical disorders.

Objective: The aim of the study was to assess the depression and anxiety in patients suffering from endocrinological disorders.

Method: We conducted a cross-sectional study for a period of one and half year in patients attending the Department of Medicine, Government Medical College Hospital Srinagar. General description, demographic data were recorded using the semi structured interview scale. A total of 152 cases of different endocrinological disorders were taken up for the study for one year, while Hospital Anxiety and Depression scale (HADS) was used for purpose of screening anxiety and depressive disorders in patients suffering from different endocrinogical disorders. Descriptive statistics and unadjusted 3×2×2 test chi square was conducted to determine prevalence.

Results: Out of total 152 subjects, 71 were males (46.72%)), and 81 were females (53.28%) and mean age of the patients was  $35.85 \pm 9.475$ . The mean HADS score for anxiety alone, depression alone and anxiety/depression patients were 13.42, 15.7 and 25.62 respectively. On the basis of HADS screening, 96(63.157%) patients had varying degree of psychiatric co morbidity. 27 had anxiety alone, 30 had depression alone where 39 patients had anxiety and depression both.

Conclusion: The findings of our study suggest that depression and anxiety is highly prevalent in diabetic patients and is largely unrecognized in the primary care setting. Most of the clinicians do not suspect this important co morbidity of endocrinological disorders in the beginning resulting in delayed diagnosis.

Keywords: Anxiety, depression, endocrinological disorder

#### Introduction

Endocrine disorders are frequently accompanied by psychological disturbances. Conversely, psychiatric disorders, to significant extent demonstrate consistent pattern of endocrine dysfunctions. [1] Endocrinopathies manifests as myriad of psychiatric symptoms, as hormones affect a variety of organ systems function. The presence of psychiatric symptoms in patients with primary endocrine disorders provides a new insight for exploring link between hormones and affective function.[2] Disturbance of hypothalamic-pituitary-thyroidal axis is of considerable interest in psychiatry and is known to be associated with a number of psychiatric abnormalities.[3] Thus, the main focus of psychoneuroendocrinology is on identifying changes in basal levels of pituitary and end-organ hormones in patients with psychiatric disorders. Psychiatric symptoms may be the first manifestations of endocrine disease, but often are not recognized as such. Patient may experience a worsening of the psychiatric condition and an emergence of physical symptoms with the progression of the disorder.[4] Psychiatric manifestations of endocrine dysfunction include mood

disturbances, anxiety, cognitive dysfunction, dementia, delirium, and psychosis. While dealing with treatment-resistant psychiatric disorder, endocrinopathies should also be considered as a possible cause in management. Psychotropics medicine may worsen the psychiatric symptoms and improves only once the underlying endocrine disturbance is corrected. [5]The lifetime prevalence of depression and anxiety is 11.8% to 36.8% and 5.0% to 41.2% respectively in the group with previously known thyroid disorder. [6,7]. The occurrence of major depression in DM is mostly estimated around 12% (ranging from 8-18%). 15-35 % of individuals with DM report milder types depression. [8]. Depressive symptom is seen in almost half of patients with Cushing's syndrome and these experience moderate to severe symptoms. Some patients with Cushing's syndrome also experience psychotic symptoms [9]. Patients suffering from Addison's disease may be misdiagnosed with major depressive disorder, personality disorder, dementia, or somatoform disorders [4, 10]. Women with hyperandrogenic syndromes are at an increased risk for mood disorders, and the rate of depression among women with PCOS has been reported

to be as high as 50 percent. Central 5-HT, system dysregulation that causes depression might simultaneously affect peripheral insulin sensitivity, or vice versa, possibly via behavioral or neuroendocrinological pathways, or both. [10]

Hollinrake 2007 showed prevalence of depression has shown it to be four times that of women without PCOS. Hollinrake screened patients with PCOS for depression and found total prevalence of depressive disorders which included women diagnosed with depression before the study, was 35% in the PCOS group[11]. No specific psychiatric symptoms have been consistently associated with acromegaly or gigantism or with elevated GH levels. Adjustment disorder may occur from changes in physical appearance and from living with a chronic illness [11]. Sheehan's syndrome (SS) refers to the occurrence of varying degree of hypopituitarism after parturition (1). It is a rare cause of hypopituitarism in developed countries owing to advances in obstetric care and its frequency is decreasing worldwide. Reports of psychoses in patients with Sheehan's syndrome are rare. [13] Psychiatric disturbances are commonly observed during the course of endocrine disorders .The underlying cause can be hyper- or hyposecretion of hormones, secondary to the pathogenic mechanisms. medical or surgical treatment of endocrine diseases, or due to genetic aberrations[14]. Psychiatric disorders frequently mimic the symptoms of endocrinological disorders. In view of sizable number of patients seeking treatment from our department present with comorbid endocrinolgical disorders, we planned the present study to investigate psychiatric morbidity preferably anxiety and depression pattern among endocrinolgical disorders patients. With this background, we studied the depression and anxiety in different endocrinogical disorders.

#### Methods

The present study was conducted in the SMHS Hospital of Government medical college Srinagar and the study sample was drawn from patients attending the endocrinogical OPD in the Department of Medicine at Government Medical College Hospital Srinagar (SMHS). The study was conducted over a period of one and half year, from April 2011 to September 2012 in patients attending the Department of Medicine Government Medical College Hospital Srinagar enrolling 152 cases of Endocrinological disorders. All patients were first examined by Consultant endocrinologist. The patients were then selected using simple random sampling choosing every alternate patient. General information including age, sex, residence, economic status, past history of thyroid disorders, family history of psychiatric disorders was included. An endocrinology specialist first examined the patients, while a psychiatrist administers Hospital Anxiety and Depression scale (HADS). Hospital Anxiety and Depression scale (HADS) was used for purpose of screening anxiety and depressive disorders in patients suffering from different endocrinogical disorders. Hospital Anxiety and Depression scale (HADS) is used for purpose of screening anxiety and depressive disorders in patient suffering from chronic somatic disease. HADS contain 14 items

and consist of two subscales: anxiety and depression with seven question each. Each question is rated on four point scale (0 to 3) giving maximum total score of 21 each for anxiety and depression. Score of 11 or more is considered a case of psychological morbidity, while as score of 8-10 represents borderline and 0-7 as normal. The forward backward procedure was applied to translate HADS from English to Urdu by a medical person and professional translator. [15]

The participating physicians subjected select patient of chronic Endocrinological disorders to HADS Questionnaire and recorded scores both for anxiety and for depression.

The patients were subjected to inclusion and exclusion criteria as given below:

#### Inclusion criteria

- All endocrinological disorders.
- Both sexes will be included.
- Age > 15 yrs.
- Those who will give consent.

#### Exclusion criteria

- Those who don't consent.
- If diagnoses is not clear.
- Age less than 15 years.
- Presence of pregnancy or a history of pregnancy in the last six months.
- Those who are on steroids or drugs known to interfere with thyroid function

General description, demographic data and psychiatric history was be recorded using the semi structured interview which was pretested

Statistical methods: Statistical analyses were performed using the SPSS, version 16.0 for Windows. A secure computerized database was established and maintained throughout the study. Patient names were replaced with unique identifying numbers. Descriptive statics were used to generate a profiles of each illness group based on presence of depression only, anxiety only and those with both anxiety and depression. To determine whether there were any significant differences between each illness group in the prevalence of depression and anxiety disorders, an unadjusted 3×2×2 test chi square was conducted. Data were analyzed by the Pearson chi-squared test and t test. P<0.05 was considered as the significance level in the evaluations.

Consent: Informed consent was obtained from each patient; those who were considered incapable of consenting were allowed to participate with consent of their closest family member or custodian. All patients were informed about the nature of the research within the hospital and willingly gave their consent to participate. Information sheets and preliminary interviews made it clear that the choice to consent or otherwise would have no bearing on the treatment offered. The project ensured the anonymity of the subjects by replacing patient names with unique identifying numbers before the statistical procedures began.

Table 1: Age and sex distribution

		Sex		Total	Total			
		Male		Female				
Age group	< 25	14	20%	7	9%	21	14%	
	25 – 35	20	28%	17	21%	37	24%	
	35 – 45	17	24%	23	28%	40	26%	
	45 – 55	11	16%	19	24%	30	20%	
	55 & above	9	13%	15	19%	24	16%	
Total		71	100%	81	100%	152	100%	
Mean ± SD		51.4± 13.7		56.4± 13.1		54.1± 13.6		

Table 2: Demographic Characteristics of the Studied Patients

Characteristic		N	%
DII:	Rural	98	64.47
Dwelling	Urban	54	35.52
	Unmarried	28	18.4
Marital status	Married	103	67.7
	Widowed	21	13.8
	Household	61	40.1
	Unskilled	29	19
Occupation	Semiskilled	39	25.6
	Skilled	23	15.1
	Professional	8	5.26
	Nuclear	79	51.97
Family type	Joint	28	18.4
	Extended	45	29.6
	Illiterate	82	53.9
	Primary	22	14.4
I :	Secondary	16	10.5
Literacy status	Matric	13	8.55
	Graduate	11	7.23
	Postgraduate/Professional	8	5.26
	< 5000	45	29.6
Family Income(Rs)	5000 to 10000	85	55.92
	≥ 10000	22	14.4
	Lower	32	21
Socioeconomic status	Upper lower	11	7.23
( Kuppuswamy	Middle	84	55.2
Scale)	Upper middle	19	12.5
	Upper	6	3.94

Table 3: Result of HADS Scoring

Variable	Total (n=96)	Anxiety alone	Depression Alone	Anxiety depression both	p value
Male	37(38.54%)	8(29.6%)	18(60 %)	11(28.2%)	-
Female	59(61.4%)	19( 70.3%)	12( 40%)	28(71.7 %)	-
Age (Years)	54.1± 13.6	51.4± 13.7	56.4± 13.1	54.1± 13.1	< 0.005
Mean HADS Score	-	13.42±3.4	15.73±3.3	25.62±4.3	< 0.005

Table 4: Types of endocrinological disorders

Endocrinological disorders	Number of patients(N=152)	Psychiatric comorbidity	percentage
Thyroid disorders	62 (40.7%)	43	69.35
Diabetes mellitus	47(30.92%)	32	68.05
PCOD	28(18.4%)	16	57.1
Cushings syndrome	5(3.289%)	2	40
Acromegally	2(1.31%)	0	0
Addisions disease	1(0.65%)	0	0
Sheehan's syndrome	3(1.97%)	2	66.6
Miscellaneous	4(2.63%)	1	25

Table-5 Psychiatric Co-morbidity across Socio-demography of the Patients

		Present		Absent	t	
		n	%	N	%	p value
DII:	Rural	59	60.02	39	39.7	.0.005 (C:-)
Dwelling	Urban	37	68.5	17	31.4	<0.005 (Sig)
	Unmarried	8	28.5	20	71.4	
Marital status	Married	72	69.9	31	30	>0.005 (NS)
	Widowed	16	76.1	5	23.8	
	Household	57	93.4	4	6.55	
	Unskilled	14	48.2	15	51.7	
Occupation	Semiskilled	9	39.1	30	76.9	>0.005 (NS)
	Skilled	14	60.8	9	39.1	
	Professional	2	25	6	75	
	Nuclear	45	56.9	34	43.0	
Family type	Joint	22	78.5	6	21.4	>0.005 (NS)
	Extended	29	64.4	23	51.1	
Literacy status	Illiterate	70	85.2	12	14.6	>0.005 (NS)
Literacy status	Literate	26	36.1	46	63.8	>0.00) (N3)
	< 5000	17	37.7	28	62.2	
Family Income(Rs)	5000 to 10000	65	76.4	20	23.5	>0.005 (NS)
	≥ 10000	14	63.6	8	36.3	
	Lower	18	50	18	50	
	Upper lower	7	63.6	4	36.3	
Socioeconomic status	Middle	59	70.2	25	29.7	>0.005 (NS)
	Upper middle	10	52.6	9	47.3	
	Upper	2	33.3	4	66.6	

#### Results

A total of 152 patients from the endocrinological departments of Govt. Medical College, Srinagar hospitals were taken up for study. They were evaluated in detail with regard to sociodemographic profile regard to presence of psychiatric comorbidity by HADS and the results have been presented below in the tabulated form .Only patients who consented for complete interview and respond to all HADS questions were considered in final analyses.

Out of total 152 subjects 71 were males (46.72%)), and 81 were females (53.28%) (Table 1). Most of cases belong to 35-45 year age group (26.3%) followed by age group 25-35 years (24.3%) and 67.7% were married and 18.4% were unmarried. More than half (51.97%) of the study subjects were from nuclear families and 82 (53.9%) were illiterate and majority 84(55.4%) belonging to middle class family. The sociodemographic profile of the studied patients is shown in Table-2.

Out of 152 patients with endocrine disorders, 56(37%) patients elicited HADS score of 10 or less indicating absent or doubtful association anxiety or depression. 96 (63.15%) patients were found positive to HADS Questionnaire with anxiety/depression score of 11 or more. The mean HADS score for anxiety alone, depression alone and anxiety/depression patients were 13.42, 15.7 and 25.62 respectively. On the basis of HADS screening, 96(63.157%) patients had varying degree of psychiatric co morbidity. 27 (28.12%) had anxiety alone, 30(43.47%) had depression alone where 39(40.62%) as patients had anxiety and depression both.(Table 3) The breakdown of total number of different Endocrinological disorders is given in table. Maximum psychiatric comorbidity is found in thyroid patients (69.35%) followed by diabetic patients (68.05) (Table 4).

#### Discussion

This study is the first to offer data on psychiatric morbidity among endocrine patients in the Kashmiri population. 63.15% (96) patients were found positive to HADS questionnaire with anxiety/depression score of 11 or more in our study. The results of this study suggest patient suffering from endocrinological disorders are likely to have a co-morbid psychiatric disorder. [5, 16]. Depressive disorders and anxiety disorders are the commonest psychiatric disorders in endocrinogical patients. [3].

Numerous studies have shown a high correlation between depression and endocrinological disorders and this study supports these findings, with 43.47 %( 30) of the participants having depressive symptoms on the HADS. [3, 16] 40.62% (39) respondents had both depressive symptoms and an anxiety disorder. 28.12% (27) participants were diagnosed with an anxiety disorder, which is slightly higher than the lifetime prevalence of anxiety disorder in men [16]. Our findings of a high proportion of respondents with endocrinological disorders (45.7%) Female were more in number than their male counterparts 59(61.4%) vs. 37(38.54%) and the majority of men presenting with endocrinological disorders were between the ages of 35 and 45 years has also been reported in a previous studies. [4, 8].

The findings of our study suggest that psychiatric disorders are highly prevalent in endocrinological disorders and is largely unrecognized in the primary care setting. Endocrine disorders of different kinds, irrespective of treatment have been associated with Psychological distress. Psychological wellbeing of endocrine disorders may provide new insights in clinical endocrinology. Further psychological disorders comorbid with endocrinological disorders adds to their disability as well as cost

to the individual and the society.[17] Most of the clinicians do not suspect this important association of endocrinological disorders in the beginning resulting in delayed diagnosis. Thus, the high prevalence of anxiety and depression in endocrinological disorders in our study supports a case for screening for these disorders in endocrinological clinics. Furthermore, recognition and treatment of these comorbidities could improve patient outcomes.

Future studies should focus on replicating or refuting these findings in larger samples as well as in testing interventions aimed at targeting psychological morbidities in this patient group. Under-recognition of psychiatric morbidity is not an uncommon phenomenon, and has been found in similar local studies of psychiatric morbidity in other medical illnesses[8]. Thus, more attention should be paid to recognizing psychiatric morbidities in this group of patients. The reasons for increase in the frequency of psychiatric disorders are multi-factorial. Having chronic illness leads to psychological stress.

The major limitation of our study was relatively small sample size. Another limitation of our study is its crossectional design, which does not allow us to determine direction of causality in the relationship between endocrinological disorders and depression/anxiety. More community based studies are required to assess the magnitude of the problem and to lay down principles to help such patients. In order to clarify the temporal relationship prospective studies with a bigger sample size are essential in the future. As far as we are aware, this is a first of its kind study in kashmir. Endocrinological disorders accounts for a huge proportion of referrals to psychiatric clinics and misery is added upon an already devastating metabolic disease. To add the cost associated with psychiatric morbidity accounts individual and to the society are substantial. Thus, the high prevalence of anxiety and depression in endocrinological disorders in our study supports a case for screening for these disorders in Endocrinological clinics. Furthermore, recognition and treatment of these comorbidities could improve patient outcomes.

#### **Competing Interests**

None declared

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#### Perioperative hypertensive crisis - the anaesthetic implications. A Review of Literature

Mohamed A. Daabiss, MD

#### Abstract

Hypertensive emergencies involve a series of clinical presentations where uncontrolled blood pressure (BP) leads to progressive end-organ dysfunction affecting the neurological, cardiovascular, renal, or other organ systems. In these situations, the BP should be controlled over minutes to hours. Many causes are involved in severe elevation of blood pressure; inadequate treatment of hypertension, renal diseases, head trauma and pre-eclampsia. Intraoperative hypertension is also common and has many causes. It is usually successfully controlled by anaesthetists. However, there is a lack of agreement concerning treatment plans and appropriate therapeutic goals, making common management protocols difficult. A wide range of pharmacological alternatives are available to control blood pressure and reduce the risk of complications in these patients. This article reviews the perioperative hypertensive crisis and the common strategies used in management. Perioperative hypertension commonly occurs in patients undergoing surgery. Accurate adjustment of treatment and monitoring of patient's response to therapy are essential to safe and effective management of perioperative hypertension.

Keywords: Hypertension, crisis, perioperative, anaesthesia.

Abbreviations: blood pressure (BP), mean arterial pressure (MAP)

#### Introduction

Hypertension is the most common risk factor for perioperative cardiovascular emergencies. Acute episodes of hypertension may arise due to the aggravation of a pre-existing chronic hypertensive condition or as de novo phenomena<sup>1</sup>.

Emergency, anaesthesia, intensive care and surgery are among the clinical settings where proper recognition and management of acute hypertensive episodes is of great importance. Many surgical events may induce sympathetic activity, leading to sudden elevations in BP<sup>2</sup>.

The long term end-organ effects add to patient morbidity and mortality. Ensuring cardiovascular stability and pre-optimization of BP allows safe manipulation of physiology and pharmacology during anaesthesia<sup>2</sup>. Different medications are available for the management of hypertensive emergencies. The greatest challenge is the acute care setting where the need for proper and sustained control of BP exists.

#### Definition

Acute severe elevations in BP have several terms. The syndrome characterized by a sudden increase in systolic and diastolic BPs (equal to or greater than 180/120 mmHg) associated with acute end-organ damage that requires immediate management otherwise it might be life-threatening was defined as malignant hypertension<sup>3</sup>. The international blood pressure control

guidelines removed this term and replaced it with hypertensive emergency or crisis<sup>4</sup>.

Criteria for hypertensive emergencies (crises) include: dissecting aortic aneurysm, acute left ventricular failure with pulmonary oedema, acute myocardial ischemia, eclampsia, acute renal failure, symptomatic microangiopathic haemolytic anemia and hypertensive encephalopathy<sup>5</sup>.

While they suggest 'hypertensive urgency' for patients with severe hypertension without acute end-organ damage<sup>3</sup>. The difference between hypertensive emergencies and urgencies depends on the existence of acute organ damage, rather than the absolute level of blood pressure<sup>5</sup>.

#### Causes of hypertensive crises

Cessation of antihypertensive medications is one of the main causes. Other common causes are autonomic hyperactivity, collagen-vascular diseases, drug use (stimulants, e.g. amphetamines and cocaine), glomerulonephritis, head trauma, pre-eclampsia and eclampsia, and renovascular hypertension<sup>6</sup>.

Signs and symptoms of hypertensive crisisinclude severe chest pain, severe headache accompanied by confusion and blurred vision, nausea and vomiting, severe anxiety, shortness of breath, seizures and unresponsiveness.

#### Pathogenesis

Humoral vasoconstrictors released in the hypertensive crises episodes result in a sudden increase in systemic vascular resistance. Endothelial injury accompanies severe elevations of BP resulting in fibrinoid necrosis of the arterioles with the deposition of platelets and fibrin, and a breakdown of the normal autoregulatory function. The resulting ischemia speeds the further release of vasoactive substances completing a vicious cycle<sup>7</sup>.

#### Perioperative hypertension

At least 25% of hypertensive patients who undergo noncardiac surgery develop myocardial ischemia associated with the induction of anaesthesia or during the intraoperative or early post-anaesthesia period<sup>8</sup>. Previous history of diastolic hypertension greater than 110 mmHg is a common predictor of perioperative hypertension. The level of risk depends on the severity of hypertension<sup>9</sup>.

Sympathetic activation during the induction of anaesthesia increases the BP by 20 to 30 mmHg and the heart rate by 15 to 20 beats per minute in normotensive individuals<sup>8</sup>. These responses may be more obvious in patients with untreated hypertension in whom the systolic BP can increase by 90 mmHg and heart rate by 40 beats per minute.

Intraoperative hypertension is associated with acute pain induced sympathetic stimulation besides certain types of surgical procedures like carotid surgery, intrathoracic surgery and abdominal aortic surgery. Paix et al, analysed 70 incidents of intraoperative hypertension and reported that drugs were the precipitating cause (inadvertent vasopressor administration by the anaesthetist or surgeon, intravenous adrenaline with local anaesthetic and failure to deliver a volatile agent or nitrous oxide) in 59% of the cases. Light anaesthesia and excessive surgical stimulation represented 21% of incidents, while equipment related causes (ventilation problems e.g. stuck valve, hypoventilation, soda lime exhaustion and endobronchial intubation) were 13% of incidents. Awareness under general anaesthesia, myocardial infarction and pulmonary oedema represented 7% of incidents<sup>10</sup>.

In the early postanaesthesia period, hypertension often starts within 10 to 20 minutes after surgery and may persist for 4 hours. Besides pain induced sympathetic stimulation, hypoxia, intravascular volume overload from excessive intraoperative fluid therapy and hypothermia can promote postoperative hypertension. If untreated, patients are at high risk for myocardial ischemia, cerebrovascular accidents and bleeding<sup>11</sup>. Hypertension might happen 24 to 48 hours postoperative due to fluid mobilisation from the extravascular space, besides cessation of antihypertensive medication in the early postoperative period<sup>12</sup>.

The absolute level of BP is as important as the rate of increase. For example, patients with chronic hypertension may tolerate systolic BPs (SBP) of 200 mm Hg without developing hypertensive encephalopathy, while pregnant

women and children may develop encephalopathy with diastolic BPs of 100 mm Hg<sup>13</sup>.

#### Preoperative general considerations for hypertensive patients

During preoperative assessment we have to review associated medical problems such as ischaemic heart disease, cerebrovascular disease and renal failure. This can assess the risk for anaesthesia and so the hypertensive end-organ damage. Some patients with hypertension are asymptomatic and accidentally discovered during preoperative assessment. Incidental hypertension may suggest long standing hypertensive disease<sup>1</sup>. Idiopathic hypertension comprises about ninety percent of hypertensive patients<sup>6</sup>.

#### Management of perioperative hypertension crises

The treatment plan of perioperative hypertension differs from treatment of chronic hypertension. Hypertensive patients undergoing elective surgery are at risk for increased perioperative hypertensive attacks. Postponement of elective surgery is recommended in chronic hypertensive patients if the diastolic BP is  $\geq 110$  mm Hg until the BP is controlled <sup>14</sup>. We have to determine if it is a hypertensive emergency or urgency, besides the underlying causes of the patient's BP elevation.

The most appropriate medication for management of hypertensive emergency should have a rapid onset of action, a short duration of action, be rapidly titratable, allow for dosage adjustment, have a low incidence of toxicity, be well tolerated and have few contraindications<sup>2,15</sup>. A parenteral antihypertensive agent is preferred due to rapid onset of action and ease of titration<sup>5</sup>.

The goal of therapy is to halt the vascular damage and reverse the pathological process, not to normalise the BP. Guidelines by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP for treating hypertensive emergencies include starting intervention with reducing systolic BP by 10 to 15%, up to 25% within the first hour. Followed

by gradual reduction of the absolute BP to 160/110 mmHg over the following two to six hours<sup>5,16</sup>.

Hypertension that occurs with tracheal intubation, surgical incision and emergence from anaesthesia is best treated with short-acting -blockers, calcium channel blockers, vasodilators, or angiotensin-converting enzyme inhibitors. Postoperative hypertension is best managed by correction of precipitating factors (pain, hypothermia, hypervolemia, hypoxia and hypercarbia)<sup>17</sup>.

Unintentional hypotension and associated organ hypoperfusion happens with aggressive attempts to lower BP since the homeostatic mechanisms depend on higher blood pressure for adequate organ perfusion. While inadequate lowering of BP may result in increased morbidity and mortality. However, the alteration between overshooting BP and severe hypotensive states and using vasopressors to get the normotensive levels may

damage end-organs and the vasculature - precise control of BP in a hypertensive crisis is a challenge<sup>18</sup>.

Since chronic hypertension shifts cerebral and renal perfusion autoregulation to a higher level, the brain and kidneys are prone to hypoperfusion with rapid decrease in blood pressure. So control of blood pressure to baseline levels should take 24 to 48 hours<sup>5</sup>.

In cases of aortic dissection, the systolic BP should be reduced to less than 120 mmHg within twenty minutes. In ischemic stroke, BP must be lowered to less than 185/110 before administration of thrombolytic therapy<sup>19</sup>. Gentle volume expansion with intravenous saline solution will maintain organ perfusion and prevent sudden drop in BP with using antihypertensive medications<sup>5</sup>. Preoperative hypertension is a hypertensive urgency, not an emergency, as it rarely involves end-organ damage with adequate time to reduce the BP<sup>18</sup>. Longer acting oral medications such as Labetalol and Clonidine may be more suitable <sup>20</sup>.

### Common antihypertensive medications used in hypertensive crises

Sodium Nitroprusside is a combined venous and arterial vasodilator which decreases both afterload and preload. The onset of action is within seconds and duration of action lasts for one to two minutes, so continuous BP measurement is recommended. If the infusion is stopped, the BP rises immediately and returns to the pretreatment level within one to ten minutes. Prolonged intravenous administration with infusion rates more than 2 mcg/Kg/min may result in cyanide poisoning. Thus, infusion rates greater than 10 mcg/Kg/min should not be continued for prolonged periods<sup>21</sup>.

Labetalol, an alpha- and beta-blocking agent has proven to be beneficial to treat patients with hypertensive emergencies. Labetalol is preferred in patients with acute dissection and patients with end-stage renal disease. The onset of action is five minutes and lasts for four to six hours. The rapid fall in BP results from a decrease in peripheral vascular resistance and a slight fall in cardiac output<sup>22</sup>. A reasonable administration protocol is to give an initial intravenous bolus of Labetalol 0.25 mg/Kg, followed by boluses (0.5 mg/Kg) every 15 minutes until BP control or a total dose 3.25 mg/Kg. Once an adequate BP level is achieved, we can start oral therapy with gradual weaning from parenteral agents<sup>22</sup>.

Fenoldopam, a peripheral dopamine-1-receptor agonist, induces peripheral vasodilation; administered by intravenous infusion. Duration of action from 30 to 60 minutes. Gradual decrease in blood pressure to pretreatment values occurs without rebound once the infusion is stopped because of short elimination half-life. A starting dose of 0.1 g/kg/min, titrated by 0.05 to 0.1 g/kg/min up to 1.6 g/kg/min. Fenoldopam provides rapid decline in blood pressure with reflex tachycardia so beware in patients at risk of myocardial ischemia<sup>23</sup>.

Clevidipine, a dihydropyridine calcium channel blocker, produces rapid and precise BP reduction. It has a short half-life of about one to two minutes with potent arterial vasodilation without affecting venous capacitance, myocardial contractility or causing reflex tachycardia<sup>24</sup>. Start intravenous infusion of Clevidipine at 1-2 mg/h; titrate the dose at short intervals (90s) initially by doubling the dose. Systolic pressure decreases by at least 15% from baseline within 6 minutes post-infusion<sup>24</sup>. A 1-2 mg/h increase in infusion rate produces an additional 2-4 mmHg reduction in SBP<sup>14</sup>. Clevidipine is an ideal agent to manage acute severe hypertension moreover safe for patients with hepatic and renal dysfunction<sup>2</sup>.

#### Rational approach to the management of hypertensive crises

#### Neurological emergencies

Subarachnoid haemorrhage, acute intracerebral haemorrhage, hypertensive encephalopathy, and acute ischemic stroke require rapid BP reduction. In hypertensive encephalopathy, reduce the mean arterial pressure (MAP) 25% over 8 hours. Labetalol, Nicardipine and Esmolol are the preferred medications; Nitroprusside and Hydralazine should be avoided<sup>25</sup>.

For acute ischemic stroke, the preferred medications are Labetalol and Nicardipine. The target BP is < 185/110 mm Hg especially if the patient is receiving fibrinolysis<sup>25</sup>.

In acute intracerebral haemorrhage, Labetalol, Nicardipine and Esmolol are preferred; avoid Nitroprusside and Hydralazine. If signs of increased intracranial pressure (ICP) exist, keep SBP < 180 mm Hg, while maintain SBP < 160 mm Hg in patients without increased ICP for the first 24 hours after onset of symptoms<sup>25</sup>. Early intensive BP control is recommended to reduce hematoma growth<sup>26,27</sup>.

In subarachnoid haemorrhage, Nicardipine, Labetalol and Esmolol are also the preferred agents; while Nitroprusside and Hydralazine should be avoided. Maintain the SBP < 160 mm Hg until the aneurysm is treated or cerebral vasospasm happens<sup>25</sup>.

#### Cardiovascular emergencies

Rapid BP reduction is also indicated in cardiovascular emergencies such as aortic dissection, acute heart failure, and acute coronary syndrome. Labetalol, Nicardipine, Nitroprusside (with beta-blocker), Esmolol, and Morphine are preferred in aortic dissection. Beta-blockers should be avoided if there is aortic valvular regurgitation or suspected cardiac tamponade. Keep the SBP < 110 mmHg unless signs of end-organ hypoperfusion exists<sup>28</sup>.

In acute coronary syndrome if the BP is >160/100 mm Hg, Nitroglycerin and beta blockers are used to lower the BP by 20-30% of baseline but, thrombolytics are avoided if the BP is >185/100 mm Hg<sup>28</sup>. In acute heart failure use intravenous Nitroglycerin and intravenous Enalaprilat. Give vasodilators (besides diuretics) when SBP is 140 mm Hg<sup>28</sup>.

#### Cocaine toxicity/Pheochromocytoma

Diazepam, Phentolamine and Nitroglycerin/Nitroprusside are the preferred drugs. In cocaine toxicity, tachycardia and hypertension rarely require specific treatment. Phentolamine is proper for cocaine-associated acute coronary syndromes. In pheochromocytoma, beta blockers can be added after alpha blockade for BP control<sup>29</sup>.

#### Pre-eclampsia/eclampsia

The proper medications are Hydralazine, Nifedipine and Labetalol however avoid Nitroprusside, Esmolol and angiotensin-converting enzyme inhibitors. The BP should be <160/110 mm Hg in the antepartum period and during delivery. The BP should be maintained below 150/100 mm Hg if the platelet count is less than 100,000 cells mm<sup>3</sup>. Intravenous Magnesium Sulphate should also be used to prevent seizures<sup>30</sup>.

#### Perioperative hypertension

Nitroprusside, Nitroglycerin and Esmolol are used. Target the perioperative BP to within 20% of the patient's baseline pressure. Perioperative beta blockers are best to use in patients undergoing vascular procedures or at risk of cardiac complications<sup>28</sup>.

#### **CONCLUSION**

Perioperative hypertension commonly occurs in patients undergoing surgery. The permitted value is based on the patient's preoperative BP. It is approximately 10% above that baseline however more reduction in BP may be warranted for patients at high risk of bleeding or with severe cardiac problems. Accurate adjustment of treatment and monitoring of patient's response to therapy are essential to safe and effective management of perioperative hypertension.

#### Competing Interests

None declared

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#### On the rise worlwide: Bed Bugs and Cimicosis

#### Sibylle Rahlenbeck, Jochen Utikal and Stephen Doggett

#### Abstract

After they became rare in developed nations over some 30-50 years ago, bed bugs have dramatically increased in incidenceand rapidly spread worldwide over the last two decades. Insecticide resistance along with an increase in travel and trade are thought to be the main contributing factors for the resurgence of this public health pest. Bed bugs are not only a hoteliers' nightmare, but they have also conquered many a private home.

Keywords: bed bugs, inseciticides, bullae, hygiene, cimicosis

#### Introduction

Bed bugs belong to the family Cimicidae and there are two species involved in the modern resurgence; the Common bed bug, Cimex lectularius and the Tropical bed bug, Cimex hemipterus. They are wingless insects with an oval-flat shape that allows them to hide in narrow cracks and crevices. The adults are dark brown, 4-5mm long, becoming to around 10mm when fully blood-engorged. There are five smaller juvenile stages (nymphs) that are similar in appearance, although lighter in colour. All nymphs require a blood meal to moult to the next stage, and both adults also bloodfeed for nutrition, and egg development in the case of the female. Bed bugs are solely haematophagous ectoparasites. After feeding they return to a harbourage and do not remain on the host. The main hosts are humans, but pets, bats, and birds may act as secondary hosts.

#### Epidemiology

In the past, bed bugs were particularly an affliction of the poor. However, in the early part of the modern resurgence it was the tourist areas and the hospitality sector that were initially impacted. Today, bed bugs have conquered quite diverse locations, ranging from hospitals, hotels and homes, to trains, cruise ships, and even airplanes. Most commonly, bed bugs travel in comfort as stowaways in luggage, although they can be transferred via furnishing and other belongings, as well by spreading to adjoining properties. Unfortunately, exact figures on the occurrence of bed bugs are unknown, as there are no mandatory reporting requirements. Additionally, due to the stigma associated with bed bugs, many infestations are simply not reported. During the day, the largely nocturnal bed bugs will crawl deep into crevices of bed frames and mattresses (Fig.1), or behind wallpaper, and floor moldings. Here they

tend to lay their eggs, often several hundred during the female lifetime. Live bed bugs, shed nymphal skins, and dark excrement spots indicate an active infestation. At night they are attracted by carbon dioxide, heat and other host odours to a victim, from which they may take a blood meal every 3-5 days. The adult bugs can survive long periods of starvation, up to five months at 22°C or even longer at cooler temperatures. When a host is found, they insert their mouthparts into the skin, blood feeding for 5-10 minutes. When bed bugs are in large numbers, often lines of bites occur on the unfortunate victim and this sign is almost a sure indication of the presence of the insect. The bites tend to occur along the arms and legs, down the back and across the shoulders.<sup>4,5</sup>

There has been long speculation whether bed bugs can transmit diseases, and in fact more than 40 different pathogens have been implicated. This has included Hepatitis B and C viruses, Human Immunodeficiency Virus (HIV), and *Coxiella burnetii* (Q fever). Recently, research has indicated that bed bugs are capable of transmitting the agent of Chagas Disease, *Trypanosoma cruzi*, in the laboratory. However, to date there is not one piece of evidence that bed bugs have transmitted any pathogen to humans. <sup>4,6</sup>

#### Clinical Features

During the act of feeding, saliva is injected which contains a variety of anticoagulants as well as other proteins whose function has yet to be determined. Contrary to popular belief, there is no evidence that bed bugs inject an anaesthetic. One protein, Nitrophorin, is involved in the transport of nitric oxide into the wound. This results in local vasodilation that increases blood supply to the feeding insect. The same protein can also induce a sensitivity to the bite.<sup>6</sup>

Table 1. Bed bug infes	Table 1. Bed bug infestation							
Bites on the body	Wheals, 4-6cm in diameter, lines of bites							
	Any exposed body part							
	Often intense itching							
	Occasional central haemorrhage							
Bed Sheet, mattress	Small blood spots							
(clothing)	Droppings (black dots)							
	Shed nymphal skins							
	Eggs, small (~1mm in length), white, oblong, glued to the substrate							
Space	Pungent smell (mostly commonly noticed when an insect is squashed, or during the control program)							

	Bite preference	Pattern	Itching	Notes
Bed Bugs	Any exposed parts	In small infestations, bites will be random. In larger	Often intense, especially	Often associated with
Ö	of the body, arms,	infestations, bite can occur in lines along the limbs	in the morning, but can	travel or used furniture
	legs, face, torso	and across the shoulder. Large wheals (up to 6cm	be variable between	
		across) may form, even some 14 days after the bite	individuals	
Fleas	Exposed parts of	Random, usually not grouped or in lines	During the day	Usually associated with
	the body,			pets
	especially the legs			
Mosquitoes	Exposed skin,	Random	Variable between	Most commonly
	particularly legs		individuals	outdoors
	and arms			
Ticks	Potentially	Erythema migrans with Lyme disease. Localised	Low / no	Those who work or
	anywhere on the	macules/papules at the bite site may occur		recreate in native forests
	body			are at greatest risk.
Itch Mites	Forearms, inter	Skin rashes, subcutaneous courses	At night	Most common in the
(Scabies, Sarcoptes	digital, genital area			elderly and infirmed
scabiei)				
Harvest mites	Skin surfaces	Red macules and wheals	Severe itching	Often occurs in gardens
(Trombidiosis)	under tight			or meadows, most active
	clothing			during summer and
				autumn
Cheyletiellosis	Arms and trunk,	Polymorphic rash	Variable	Tends to be associated
	contact points			with pets
	with pets			
Bird mites	All over	Macular rash	Variable itching	Most commonly in
				homes as a result of
				birds roosting in roof
				cavities
Head Lice	In the hair of the	Bar-shaped scratch effects with lichenification and	Night and day,	Most common in school
(Pediculosis)	head	hyper-pigmentation (Vagabond's disease)	generally mild itching	aged children
Spiders, e.g. long-	Arms, face	Necrotic lesion at bite site	Immediate severe pain,	Uncommon
legged sac spiders			no itching	

The diagnosis of Cimicosis is via the clinical appearance of the bite reaction and confirmation of an actual bed bug infestation (Table 1).<sup>3,5</sup> The most commonly affected body parts are those that are left uncovered during sleep (Fig. 2,3,4), notably the arms, shoulders and legs. In young children, the face and even the eyelids can be bitten. Rarely, however, armpits are bitten, which are often preferred by other insects and ticks (Table 2).

The degree of the bite reaction often depends on the level of prior exposure. With low level sensitization, individuals may develop a 1-2 cm wheal, with a small central haemorrhagic point. This haemorrhagic point can be recognized easily by diascopy. In contrast, a highly sensitized person will react

immediately and may develop a wheal up to 15cm across (6 inches). If many bed bugs are present, an urticarial rash may develop as a result of the large number of bites and subsequent trauma to the area from scratching. On rare occasions, vesicles and bullae (Fig. 5) may form on the arms and legs. In the course of Cimicosis, papules that are extremely itchy may develop and can persist for several days to weeks. Due to the strong pruritus eczematous lesions, bacterial infections may occur, although this is extremely rare. There are case reports of systemic reactions such as anaphylaxis and asthma, although these are uncommon.

Figure 1: Typical appearance of bed bugs



**Figure 2:** Bites on the back, note the lines of bites common in moderate to large infestations



Figure 3: Bed bug bites on the arm, typical formation



Through repeated exposure, some individuals may develop a tolerance to the bites. The clinical symptoms are then largely inapparent with small punctures at the bite site. Small blood spots are then the only clues that an infestation may be present.

#### Differential Diagnosis

Since reactions to stings and bites of various arthropods are non-specific, bed bug bites are commonly misdiagnosed. Single

biting midges may appear very similar morphologically (Table 2).

Consideration of where the bites are on the body can assist in the differential diagnosis. For bed bugs, lines of bites are very common in moderate to large infestations and this clinical picture is virtually unique amongst blood sucking arthropods. For the most part, the identification of the actual pest is required to confirm the diagnosis. Histologically, bed bug bites

Figure 4: Bed bug bites on the torso and arm



Figure 5: Bullae due to bed bug bites



**Figure 6:** Bed bugs, their droppings and eggs underneath a mattress



resemble perivascular eosinophilic infiltrates through the superficial and deep dermis, with minimal spongiosis.

Other possible diagnostic confounders can be various allergic reactions and other medical conditions such as urticaria, chickenpox, prurigo subacuta, and erythema multiforme. These do not show a central haemorrhagic point in the lesion which allows a correct diagnosis. However, in young children the diagnosis can sometimes be difficult.

#### Treatment

The treatment of Cimicosis is symptomatic. Local lesions can be treated with antipruritics e.g. Polidocanol 2-4% in Lotio alba (aqueous lotion) and topical antiseptic. Spirit of menthol may also be helpful. Local treatment with antihistamines is controversial. In severe reactions topical glucocorticoids such as Betamethasone may be required. In severe itching, the use of oral antihistamines is recommended. With infected bites, antibiotic therapy may be required. Uncomplicated bed bug bites tend to stop itching within 1-2 weeks, although temporary scarring from the bite may remain for several months.

#### Management

Treatment of patients with bed bug bites ultimately comes down to removing the source of the irritant, namely the eradication of the active infestation. Bed bugs have a typical pungent odor. This can be used to detect bed bugs through specially trained sniffer dogs that can rapidly locate the insects. Due to insecticide resistance, bed bugs are very difficult to control with traditional insecticides alone, and non-chemical means of eradication must be employed to reduce the overall insect biomass. Bed bug control should be undertaken by professionals trained in bed bug management, and the process may take some weeks to achieve.

#### Prevention

When travelling (1) always inspect the bed and surrounds for bed bugs hiding beneath the mattress and/or in seams of the bedding. Also, look for blood stains or small black dots (Figure 6, Table 1). (2) If present, request another room. (3) Always keep your luggage on the desktop or the luggage rack. A good preventative is to seal luggage in plastic or garbage bags during travelling, even when in transit. (4) When returning home, all clothing should be washed in at temperatures exceeding 60°C or frozen for one week with delicate fabrics. If there is no choice, then repellents containing N, N-Diethyl-meta-toluamide (DEET) should reduce the biting rate, but will not completely prevent all bed bug bites. <sup>10,11</sup>

Bed bugs can enter homes via an array of additional ways, particularly from objects bought second hand at flea markets or thrift stores, for example wooden frames, vintage clothes, furniture and the like. These should be heat-treated for a minimum of 10-20 minutes to kill bugs and their eggs.

#### Competing Interests

None declared

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#### Striae distensae: What's new at the horizon?

#### Mohammad Abid Keen

#### Abstract

Striae distensae, commonly known as stretch marks, are benign skin lesions associated with considerable cosmetic morbidity. Despite considerable investigations into their origins, the pathogenesis of striae distensae remains unknown. Currently, there is no treatment which consistently improves the appearance of striae. With a high incidence and unsatisfactory treatments, stretch marks remain an important target of research for an optimum consensus of treatment. The aim of present article is to appraise the readers with various newer treatment options in the management of this difficult condition.

Keywords: Striae distensae, stretch marks, cosmetic

#### Introduction

Striae distensae, or stretch marks, are linear scars in the dermis which arise from rapid stretching of the skin over weakened connective tissue. It is a common skin condition that rarely causes any significant medical problems but is often a significant source of distress to those affected. Striae distensae were described as a clinical entity hundreds of years ago, and the first histological descriptions appeared in the medical literature in 1889.1 With a high incidence and unsatisfactory treatments, stretch marks remain an important target of research for an optimum consensus of treatment. These appear initially as red, and later, as white lines on the skin, representing scars of the dermis, and are characterized by linear bundles of collagen lying parallel to the surface of the skin, as well as eventual loss of collagen and elastin. The estimated prevalence of striae distensae range from 50 to 80%.<sup>2,3</sup> The anatomical sites affected vary, with areas commonly affected including the abdomen, breasts, thighs and buttocks.<sup>4</sup> The three maturation stages of striae include the acute stage (striae rubra) characterized by raised, erythematous striae, the sub-acute stage characterized by purpuric striae, and the chronic stage (striae alba), characterized by white or hypo-pigmented, atrophied striae.5 Although stretch marks are only harmful in extreme cases, even mild stretch marks can cause distress to the bearer<sup>6</sup> (Table 1).

#### Aetiology

Striae may result from a number of causes, including, but not limited to, rapid changes in weight, adolescent growth spurts, corticosteroid use or Cushing Syndrome, and generally appear on the buttocks, thighs, knees, calves, or lumbosacral area. In addition, approximately 90% of all pregnant women develop stretch marks either on their breasts and/or abdomen by the third trimester. Genetic predisposition is also presumed, since striae distensae have been reported in monozygotic

twins. 9,10 There is decreased expression of collagen and fibronectin genes in affected tissue. 11 The role of genetic factors is further emphasised by the fact that they are common in inherited defects of connective tissue, as in Marfan's syndrome. 12,13 Obesity and rapid increase or decrease in weight have been shown to be associated with the development of SD. 14 Young male weight lifters develop striae on their shoulders. 15 Striae distensae also occurs in cachetic states, such as tuberculosis, typhoid and after intense slimming diets. 16 Rare etiologies include human immunodeficiency virus positive patients receiving the protease inhibitor indinavir and chronic liver disease. 13,15 A case of idiopathic striae was also reported. 17

Rosenthal<sup>18</sup> proposed four aetiological mechanisms of striae formation: insufficient development of tegument, including elastic properties deficiency; rapid stretching of the skin; endocrinal changes; and other causes, possibly toxic.

#### Pathogenesis

The pathogenesis of striae is unknown but probably relates to changes in the components of extracellular matrix, including fibrillin, elastin and collagen. There has been emphasis on the effects of skin stretching in the pathogenesis of striae because the lesions are perpendicular to the direction of skin tension. A possible role of glucocorticoids in the pathogenesis of striae has been suggested because of an increase in the levels of steroid hormones and other metabolites found in patients exhibiting striae. There are studies suggesting the role of fibroblasts in the pathogenesis of striae. Compared to normal fibroblasts, expression of fibronectin and both type I and type III procollagen were found to be significantly reduced in fibroblasts from striae, suggesting that there exists a fundamental aberration of fibroblast metabolism in striae distensae.

Table 1: Histological comparisons between striae rubrae and striae albae

Epidermis	Oedema	Epidermal atrophy
	Increased melanocytes	Loss of rete ridges
		Decreased melanocytes
Papillary dermis	Dilatation of blood vessels	No vascular reaction
Reticular dermis	Structural alteration of collagen fibres	Densely packed collagen parallel to skin surface.
	Reduced and reorganized elastic fibres	Thick elastic fibres in dermis
	Fine elastic fibres in dermis	
Inflammatory cells	Lymphocytes and fibroblasts	Eosinophills

Table 2: Visual scoring systems for the assessment of striae distensae

Davey method	Used for evaluating striae rubrae and albae.
	Divide the abdomen into quadrants using midline vertical and horizontal lines.
	Each quadrant given a score (0 no SD; 1 moderate number of SD; 2 many SD).
	Score given out of 8.
Atwal score	Used for evaluating striae rubrae and albae.
	Six sites chosen (abdomen, hips, breasts, thigh/buttocks).
	Each site given a maximum score of six.
	Total score out of 24.
	Score 0–3 for the presence of striae (0 no SD; 1 < 5 SD; 2 5–10 SD; 3 > 10 SD).
	Score 0–3 for the presence of erythema (0 no erythema; 1 light red/pink; 2 dark red; 3 purple).

#### Pathological aspects

The earliest pathological changes are subclinical to be detected by electron microscopy only. These changes include mast cell degranulation and the presence of activated macrophages in association with mid-dermal elastolysis.<sup>23</sup> When the lesions become become clinically visible, collagen bundles start showing structural alterations, fibroblasts become prominent, and mast cells are absent.<sup>23</sup> On light microscopic examination, Inflammatory changes are conspicuous in the early stage, with dermal oedema and perivascular lymphocytic cuffing.<sup>24</sup> In later stages, there is epidermal atrophy, loss of rete ridges and other appendages including hair follicles are absent.<sup>25</sup>

#### Evaluation of striae distensae

Approaches to evaluating SD severity visually include the Davey <sup>26</sup> and Atwal scores, <sup>27</sup> although these have not been validated specifically for SD. An objective evaluation of SD may be carried out using skin topography, imaging devices including three-dimensional (3D) cameras, reflectance confocal microscopy and epiluminescence colorimetry. <sup>28,29,30</sup>

#### Management

Striae distensae (striae alba) is a very challenging cosmetic problem for dermatologists to treat. Various modalities of treatment have been tried. Although therapeutic strategies are numerous, there is no treatment which consistently improves the appearance of striae and is safe for all skin types.<sup>31</sup> Weight loss by diet alone or a combination of diet and exercise do not change the degree of striae distensae.<sup>32</sup>

#### Topical treatments

*Topical tretinoin* (0.1%) ameliorates striae and the improvement may persist for almost a year after discontinuation of

therapy.<sup>33</sup> More recently, tretinoin has been shown to improve the clinical appearance of stretch marks during the active stage (striae rubra), although with not much effect during the mature stage (striae alba).<sup>34</sup> Some of the studies have proven the inefficacy of the vitamin A derivative in the treatment of SD, but most of the patients included in these early studies presented with old lesions that had evolved into whitish atrophic scars.<sup>35</sup> A study comparing topical 20% glycolic acid and 0.05% tretinoin versus 20% glycolic acid and 10% L-ascorbic acid, found that both regimens improved the appearance of striae alba.<sup>36</sup>

Hydrant Creams: 1) Trofolastin (a cream containing Centella asiatica extract, vitamin E, and collagen-elastin hydrolysates). The exact mechanism of action was identified as the stimulation of fibroblastic activity <sup>37</sup> and an antagonistic effect against glucocorticoids. <sup>38</sup> 2) Verum (a cream containing vitamin E, panthenol, hyaluronic acid, elastin and menthol). The results suggest that the product may show the benefit of massage alone. <sup>39</sup> 3) Alphastria (a cream composed of hyaluronic acid, allantoin, vitamin A, vitamin E, and dexpanthenol). Only one study was conducted, which concluded that the product markedly lowered the incidence of stretch mark development after pregnancy. <sup>40</sup>

Glycolic acid (GA): The exact mechanism of action of GA in the management of striae distensae is still unknown because, although GA is reported to stimulate collagen production by fibroblasts and to increase their proliferation in vivo and in vitro, which may be useful for the treatment of stretch marks. 41,42 A study comparing topical 20% glycolic acid and 0.05% tretinoin versus 20% glycolic acid and 10% L-ascorbic acid, found that both regimens improved the appearance of striae alba. 43

Trichloroacetic acid (TCA; 10–35%): It has been used for many years as a treatment option for striae distensae and is repeated at monthly intervals with reported improvement in texture and color of marks.<sup>44</sup>

Other topical products: Several oils have been used in the prevention of SD. A non-randomized, comparative study investigated the effect of almond oil in the prevention of SD in which they noted significant differences in the frequency of SD between the groups (almond oil and massage 20%, almond oil alone 38.8%, control 41.2%).<sup>45</sup>

Overall, there is limited evidence for the efficacy of topical therapy for the treatment of SD.

#### Microdermabrasion

Microdermabrasion may improve many skin problems including acne scars, skin texture irregularities, mottled pigmentation and fine wrinkles. Karimipour et al reported that microdermabrasion induces epidermal signal transduction pathways associated with remodelling of the dermal matrix. However, studies documenting the efficacy of rnicrodermabrasion in treatment of striae are lacking. Published in 1999, a book on microdermasion written by a French dermatologist, Francois Mahuzier, and translated to English, has a chapter "Microdermabrasion of stretch marks". The author states that 10-20 sessions of microdermabrasion at an interval of not less than 1 month, each session resulting in bleeding points, provide satisfactory results. The author concludes that, "microdermabrasion is the only effective treatment of stretch marks today."

#### Lasers

Lasers have recently become a popular therapeutic alternative to ameliorate and improve the appearance of stretch marks. Most commonly used lasers used include pulsed-dye laser (PDL), short- pulse carbon dioxide and erbium-substituted yttrium aluminium garnet (YAG), neodymium- doped YAG (Nd:YAG), diode, and Fraxel.

Pulsed dye laser: The dilated blood vessels render the striae rubrae a good candidate for PDL.<sup>48</sup> The 585- nm pulsed dye laser has a moderate beneficial effect in the treatment of striae rubra.<sup>49</sup> To evaluate the effectiveness of the 585-nm flashlamp-pumped pulse dye laser in treating cutaneous striae, 39 striae were treated with four treatment protocols.<sup>50</sup>Subjectively, striae appeared to return toward the appearance of normal skin with all protocols. Objectively, shadow profilometry revealed that all treatment protocols reduced skin shadowing in striae. Laser treatment of SD should be avoided or used with great caution in darker skin types (IV–VI), because of the possibility of pigmentary alterations after treatment.<sup>51</sup>

Excimer laser: Studies have shown temporary repigmentation and improvement of leukoderma in SD with excimer laser,

although it failed to show any improvement in skin atrophy.<sup>52,53</sup> To evaluate the true efficacy of the 308-nm excimer laser for darkening striae alba, 10 subjects were treated using the excimer laser on the white lines of striae, while the normal skin near to and between the lines was covered with zinc oxide cream. The results of this study showed the weakly positive effect of the 308-nm excimer laser in the repigmentation of striae alba.<sup>54</sup>

Copper Bromide laser: copper-bromide laser (577-511 nm) has been used for stretch marks. A clinical study was conducted in 15 Italian women with stretch marks, treated with the CuBr laser (577-511 nm) and followed-up for 2 years. <sup>55</sup> The results of the study concluded that the copper-bromide laser was effective in decreasing the size of the SD and there were some pathogenic considerations that justified the use of this laser.

1,450-nm Diode Laser: The non-ablative 1,450-nm diode laser has been shown to improve atrophic scars and may be expected to improve striae. To evaluate the efficacy of the 1,450-nm diode laser in the treatment of striae rubra and striae alba in Asian patients with skin types 4-6, striae on one half of the body in 11 patients were treated with the 1,450-nm diode laser with cryogen cooling spray with the other half serving as a control. So None of the patients showed any noticeable improvement in the striae on the treated side compared to baseline and to the control areas. The study concluded that the non-ablative 1,450-nm diode laser is not useful in the treatment of striae in patients with skin types 4, 5, and 6.

1,064-nm Nd:YAG Laser: A study was aimed to verify the efficacy of this laser in the treatment of immature striae in which 20 patients with striae rubra were treated using the 1,064-nm long-pulsed Nd:YAG laser.<sup>57</sup> A higher number of patients (55%) considered the results excellent when compared to the same assessment made by the doctor (40%).

Intense Pulsed Light: In order to assess the efficacy of IPL in the treatment of striae distensae, a prospective study was carried out in 15 women, all of them having late stage striae distensae of the abdomen. <sup>58</sup> All the study subjects showed clinical and microscopical improvement after IPL. It seems to be a promising method of treatment for this common problem with minimal side-effects, a wide safety margin and no downtime.

Fractional Photothermolysis: To determine the efficacy of fractional photothermolysis in striae distensae, 22 women with striae distensae were treated with two sessions each of fractional photothermolysis at a pulse energy of 30 mJ, a density level of 6, and eight passes at intervals of 4 weeks and response to treatment was assessed by comparing pre- and post-treatment clinical photography and skin biopsy samples.<sup>59</sup> Six of the 22 patients (27%) showed good to excellent clinical improvement from baseline, whereas the other 16 (63%) showed various degrees of improvement. This study concluded that Fractional

photothermolysis may be effective in treating striae distensae, without significant side effects.

Ablative 10,600-nm carbon dioxide fractitional laser: Ablative 10,600-nm carbon dioxide fractional laser systems (CO<sub>2</sub> FS) have been used successfully for the treatment of various types of scars. To assess the therapeutic efficacy of CO2 FS for the treatment of striae distensae, 27 women with striae distensae were treated in a single session with a CO2 FS and clinical improvement was assessed by comparing pre- and posttreatment clinical photographs and participant satisfaction rates. 60 The evaluation of clinical results 3 months after treatment showed that two of the 27 participants (7.4%) had grade clinical 4 improvement, 14 (51.9%) had grade 3 improvement, nine (33.3%) had grade 2 improvement, and two (7.4%) had grade 1 improvement. None of the participants showed worsening of their striae distensae. To assess and compare the efficacy and safety of nonablative fractional photothermolysis and ablative CO(2) fractional laser resurfacing in the treatment of striae distensae, 24 ethnic South Korean patients with varying degrees of atrophic striae alba in the abdomen were enrolled in a randomized blind split study and were treated with 1,550 nm fractional Er:Glass laser and ablative fractional CO(2) laser resurfacing.<sup>61</sup> These results of the study support the use of nonablative fractional laser and ablative CO(2) fractional laser as effective and safe treatment modalities for striae distensae of Asian skin with neither treatment showing any greater clinical improvement than the other treatment.

UVB/UVA1 Combined Therapy: Besides lasers, light sources emitting ultraviolet B (UVB) irradiation have been shown to repigment striae distensae. A study was conducted on 9 patients with mature striae alba who received 10 treatment sessions, and biopsies were taken at the baseline and end of the study.<sup>62</sup> At the end of the study, all patients reported some form of hyperpigmentation that was transient and did not affect any surrounding tissues. No changes were seen on biopsy to indicate an effective remodelling collagen effect of the device, although it needs further assessment. Another study was conducted to analyse the histologic and ultrastuctural changes seen after UVB laser- or light source-induced repigmentation of striae distensae in which analyses of biopsied skin after treatment with both the UVB laser and light source showed increased melanin content, hypertrophy of melanocytes, and an increase in the number of melanocytes in all patients.63

Radiofrequency devices: RF devices are based on the principle of heat generation that occurs in response to poor electrical conductance according to Ohm's law (heat generation is directly correlated with tissue resistance). The heat that is generated is sufficient to cause thermal damage to the surrounding connective tissue,<sup>64</sup> which is responsible for the partial denaturation of pre-existing elastic fibers and collagen bundles.<sup>65</sup> Initial collagen denaturation within thermally modified deep tissue is thought to represent the mechanism for immediate tissue contraction; subsequent neocollagenesis

further tightens the dermal tissue and reduces striae. <sup>66</sup> The efficacy and safety of combination therapy with fractionated microneedle radiofrequency (RF) and fractional carbon dioxide (CO2) laser in the treatment of striae distensae has been evaluated revealing that this combination therapy is a safe treatment protocol with a positive therapeutic effect on striae distensae. <sup>67</sup> A recent study evaluating the effectiveness of a RF device in combination with PDL subjected 37 Asian patients with darker skin tone with SD to a baseline treatment with a RF device and PDL. <sup>68</sup> All histological evaluations demonstrated an increase in the amount of collagen fibers, and six of the nine specimens showed an increase in the number of elastic fibers. TriPollar RF device appears to be a promising alternative for the treatment of striae distensae in skin phototypes IV-V. <sup>69</sup>

#### Needling therapy:

To evaluate the effectiveness and safety of a disk microneedle therapy system (DTS) in the treatment of striae distensae, 16 Korean volunteers with striae distensae alba or rubra were enrolled which received three treatments using a DTS at 4-week intervals. Marked to excellent improvement was noted in seven (43.8%) patients, with minimal to moderate improvement in the remaining nine. This study revealed that Disk microneedle therapy system (DTS) can be effectively and safely used in the treatment of striae distensae without any significant side effects. Another study assessed and compared the efficacy and safety of needling therapy versus CO2 fractional laser in treatment of striae and the results supported the use of microneedle therapy over CO2 lasers for striae treatment.

#### Platelet-rich plasma:

Platelet-rich plasma has these wound-healing properties, affecting endothelial cells, erythrocytes, and collagen,<sup>72</sup> which potentially aids in the healing of the localized chronic inflammation believed to be a factor in the aetiology of striae distensae. Platelet-rich plasma is well tolerated by the patients and is a safe and cost effective treatment option for striae distensae.

Platelet-rich plasma alone is more effective than microdermabrasion alone in the treatment of striae distensae, but it is better to use the combination of both for more and rapid efficacy.<sup>73</sup>

The plasma fractional radiofrequency and transepidermal delivery of platelet-rich plasma using ultrasound has also been found to be useful in the treatment of striae distensae.<sup>74</sup>

Since thermal damage from intradermal RF has characteristics similar to those of many wounds, combination treatment with intradermal RF and autologous PRP would eventuate in enhanced localized collagen neogenesis and redistribution. In one of the studies, three sessions of intradermal RF were used combined with autologous PRP administered once every four

weeks.<sup>75</sup> All of the participants showed satisfactory changes and no patient was reported to show no improvement.

#### Transepidermal retinoic acid:

Transepidermal retinoic acid delivery using ablative fractional radiofrequency associated with acoustic pressure ultrasound has also been used for the treatment of stretch marks.<sup>76</sup>

#### Conclusion

Striae distensae are an extremely common, therapeutically challenging form of dermal scarring. Adequate scientific knowledge and the evidence behind both preventative and therapeutic agents are vital in order to understand striae and to offer patients the best therapeutic options. The treatment of this cosmetically distressing condition has been disappointing and there is no widely accepted surgical procedure for improving the appearance of stretch marks. Laser therapy has been advocated as a treatment for striae distensae.

#### **Competing Interests**

None declared

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## A Registry Comparison of ESC and NICE guidelines 95 in the assessment of stable angina in a UK district hospital

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#### Abstract

Background: National Institute for Clinical Excellence (NICE) and European Society of Cardiology (ESC) have developed guidance and risk-stratification tables to assist physicians in assessing the pre-test probability of coronary artery disease (CAD) in patients with stable chest pain. We hypothesised that NICE clinical guideline 95 overestimates prevalence of CAD and that using ESC guidelines instead may enable more targeted, cost-effective use of investigations.

Methods and results: Clinic records of 1968 patients who attended Tunbridge Wells Hospital's Rapid Access Chest Pain Clinic between July 2005 and December 2012 were reviewed. A comparison was made between the pre-test probability of CAD in these patients and the actual incidence of CAD.

In patient groups where NICE guidelines' pre-test probability of CAD was 61–90%, 31-60%, 10-29% and <10%, actual incidence of CAD was 31% (95% CI 27.6 – 34.5), 4.4% (3.0–6.5), 2.5% (1.2-5.0) and 0.28% (0.1–1.6) respectively.

Where ESC guidelines pre-test probability of CAD was >85%, 66-85%, 15-65% and <15%, actual incidence of CAD was 73.4% (63.7–82.7), 58.5% (51.1–65.5), 6.4% (5.3–7.8) and 0.76% (0.2–2.7) respectively.

Conclusion: Strict adherence to NICE guidelines overestimates the pre-test probability of CAD in our cohort. ESC guidelines offer a more conservative estimate and their use may reduce the number of coronary angiograms performed, resulting in more cost-effective practice. £322,545.88 was spent on investigations when hypothetically applying ESC guidelines to our cohort, compared with £943,865.22 spent when applying NICE guidelines. However, strict use of ESC guidelines may risk missing other diagnoses of chest pain.

Keywords: angina pectoris, coronary artery disease, chest pain, risk, pre-test probability

Abbreviations: NICE - national institute for clinical excellence, ESC - European Society of Cardiology, CAD - coronary artery disease,

RACPC - rapid access chest pain clinic

#### Introduction

Chest pain accounts for 1% of all GP consultations, but in only 8%-18% of cases is it an indicator of underlying ischemic heart disease.¹ Given the potential diagnostic uncertainty associated with chest pain at initial presentation, specialist evaluation of patients in a Rapid Access Chest Pain Clinic (RACPC) is of value and represents an important process in the evaluation of symptoms. These clinics were established with the aim of providing rapid outpatient assessment of patients with suspected cardiac disease in order to permit earlier provision of appropriate treatment and investigations where required.

Stable chest pain typically presents as angina, a triad of dull central chest pain, brought on with exertion and relieved by rest or GTN spray. The aetiology is usually stable atherosclerotic plaque disease which is associated with low mortality and can be treated with oral anti-anginals, as demonstrated by meta-analyses and the landmark COURAGE study. <sup>2, 3</sup>

NICE Clinical Guideline 95 (NICE CG95) suggests that choice of initial investigation for stable chest pain should be guided by a patient's pre-test probability of having CAD. Calculations of the pre-test probability take into consideration a patient's age, gender, cardiac risk factors and symptoms. Patients are defined as high risk of cardiac disease if they have diabetes, smoke or have hyperlipidaemia (total cholesterol >6.47mmol/litre). Patients with none of the above are considered low risk. Symptoms are defined as "typical angina" if the pain is: 1) constricting discomfort in the front of the chest or in the neck, shoulders, jaw or arms; 2) is precipitated by physical exertion and 3) is relieved by rest or GTN spray within approximately five minutes. Pain is defined as "atypical angina" if only two of the above criteria are met and defined as "non-anginal" if one or none of the above criteria are met.

NICE pre-test probabilities of CAD (Table 1), are based on a version of Diamond and Forrester's pre-test probabilities published in 1979, modified using data from Duke's cohort study, published in 1993.<sup>4, 5, 6</sup> Recent studies suggest that these

NICE pre-test probabilities may overestimate the prevalence of CAD in a primary care population and may risk over investigating patients.<sup>7, 8</sup> In addition to having financial implications, this may cause patients undue anxiety and unnecessarily put them at risk of complications.

ESC guidelines utilise an updated, validated model of the Diamond-Forrester model by Genders et al. to create pre test probabilities of CAD (Table 2), based on patient's age, gender and typicality of symptoms. <sup>9, 10</sup>

We hypothesised that strict adherence to NICE guidelines results in over-estimation of the pre-test probability of CAD and therefore over-investigation of patients presenting with stable chest pain. ESC guidelines may offer more accurate pre-test probabilities of CAD and allow a more targeted and cost-effective use of investigations.

#### Methodology

Clinic records of all patients who attended the RACPC at Tunbridge Wells Hospital between July 2005 and December 2012 were reviewed. This service is run by a cardiology specialist. Patient demographics, cardiac risk factors and information regarding the nature of patient symptoms were collected prospectively and completed at the time of the patient's RACPC appointment. Results of cardiac investigations were collected from paper and computerised records, and included diagnoses of significant CAD made following invasive coronary angiogram. These results were compared with patients' pre-test probabilities of CAD calculated using both NICE and the ESC's calculation methods. Outcome and readmissions were obtained from electronic records from the Maidstone and Tunbridge Wells NHS Trust computer records retrospectively.

#### Results

#### Study population

A total of 1968 records were reviewed. 59% (n = 1162) of patients were male and 41% (n = 806) were female. Their mean age was 60 years. At initial assessment, 69.8% patients (n=1373) had non-anginal chest pain, 19.5% (n=383) had atypical angina and 10.8% (n=212) had typical angina, based on the NICE guideline definitions of chest pain.

97.2% (n= 1912) patients underwent further investigation; 15% (n=256) of these were subsequently diagnosed as having significant CAD, accounting for their symptoms. The 2.8% (n=56) of patients who did not undergo investigation either chose not to, were unable to, were lost to follow up, or were diagnosed as having a non-cardiac cause of their symptoms at the initial RACPC appointment.

## NICE CG95 pre test probabilities compared against cohort data

The average discrepancy between the pre-test probability and actual incidence of CAD in cohort patients was 28% (range 20% - 88%). In 48% of cells in the NICE CG95 pre-test

probability table (Table 1) the pre-test probability of CAD was overestimated by 30% or more (Table 3). A marked discrepancy between pre-test probability and actual incidence of CAD was found between "high risk" and "very low risk" patients. On average, high risk patients had an overestimated pre-test probability of 34.3 – 40.9% per cell compared with low risk patients whose pre-test probability was only overestimated by 6.5% (Table 3).

The cells highlighted in dark red in table 3 represent high risk patients whose pre-test probability was of 61-90+%, according to NICE CG95. In our cohort, only 31.2% (n=214, 95% CI 27.6-34.5) of high risk patients in this category were diagnosed with CAD. On average, actual incidence of CAD compared with pre-test probability was overestimated by 34.4% - 40.9% in each cell.

The pink cells in table 3 represent medium risk patients with a pre-test probability of CAD of 30-60%, according to NICE CG95. In our cohort, only 4.4% (n=24, 95% CI 3.0 – 6.5) of medium risk patients had a positive angiogram (Table 4). The average overestimate of actual incidence against pre-test probability was 35.9%.

The cells highlighted in blue in table 3 represent low risk patients with a pre-test probability of CAD of 10-29%, according to NICE CG95. In our cohort, only 2.5% (n=7, 95% CI 1.2-5.0) of low risk patients were diagnosed with CAD (Table 4). On average, the pre-test probability of CAD exceeded the found incidence of CAD by 18.6% (Table 3).

The white cells in table 3 represent very low risk patients with pre-test probability of CAD <10% according to NICE CG95. In our cohort, only 0.28% (n= 1, 95% CI 0.1-1.6) of patients were diagnosed with CAD. Average overestimation in this group was 6.5% in each cell.

### ESC guidelines pre test probabilities compared against cohort data

The average discrepancy between pre-test probability of CAD, according to the ESC's risk stratification table, and actual incidence of CAD in cohort patients was 20.7%. In 28% of cells, the pre-test probability of CAD exceeded the found incidence of CAD by 30% or more (Table 5).

The cells highlighted in dark red in table 5 represent very high risk patients with a pre-test probability of CAD greater than 85%, according to ESC guidelines (Table 5). 73.4% (n= 58, 95% CI 63.7 – 82.7) of cohort patients in this high-risk category were diagnosed with CAD (Table 6). On average, incidence of CAD in each cell has been overestimated by 13% in this category.

The cells highlighted in pale pink in table 5 represent high risk patients, with a pre-test probability of CAD of 66-85%, according to ESC guidelines. 58.5% (n=103, 95% CI 51.1-65.5) of cohort patients in this high-medium risk category were diagnosed with CAD (Table 6). On average, the pre-test

Table 1: NICE Clinical Guideline 95 pre-test probabilities table.

	Non-anginal Chest pain					Atypical Angina				Typical Angina					
	M	en		Wo	men	M	Men		Women		Men			Wom	nen
Age	Lo	Hi		Lo	Hi	Lo	Hi		Lo	Hi	Lo	Hi		Lo	Hi
35	3	35		1	19	8	59		2	39	30	88		10	78
45	9	47		2	22	21	70		5	43	51	92		20	79
55	23	59		4	25	45	79		10	47	80	95		38	82
65	49	69		9	29	71	86		20	51	93	97		56	84
>70	-	-		61-90	61-90	>90	>90		61-90	61-90	>90	>90		61-90	>90

Each cell represents the percentage risk of each group of patients having CAD, based on their typicality of symptoms, gender, age and cardiac risk factors (lo, low and hi, high)<sup>4</sup>

Table 2: ESC guidelines clinical pre-test probabilities in patients with stable chest pain symptoms

	Typical angina			Atypical angina			Non-anginal pain		
Age	Men	Women		Men	Women		Men	Women	
30–39	59	28		29	10		18	5	
40–49	69	37		38	14		25	8	
50-59	77	47		49	20		34	12	
60–69	84	58		59	28		44	17	
70–79	89	68		69	37		54	24	
>80 93	93	76		78	47		65	32	

Each cell represents likelihood of each group of patients having CAD, based on typicality of symptoms, age and gender.9

Table 3: NICE guidelines 95 pre test probabilities compared against cohort data

	Non-ai	nginal Ch	nest p	ain		Atypical Angina			Typical Angina							
	Men			Wome	n	Men			Wome	n		Men			Wome	n
Age	Lo	Hi		Lo	Hi	Lo	Hi		Lo	Hi		Lo	Hi		Lo	Hi
35	0	0		0	0	0	0		0	0		-	-		-	-
45	1	1		0	2	0	30		0	14		75	67		-	-
55	2	4		0	0	18	7		0	13		100	64		0	100
65	0	2		0	2	26	36		12	10		83	75		50	67
>70	7	12		3	4	35	31		19	14		86	59		44	55

Each cell represents the proportion (%) of cohort patients from each group who were diagnosed with CAD. We have colour-coded cells to represent the NICE estimated pre-test probability of CAD in each group. Red cells represent 61-90+% probability, pink cells represents 30-60% probability, blue cells represent 10-29% probability and white cells represents <10% probability of CAD according to NICE Guidelines. "—" marks a cell where pre-test probabilities of CAD could not be calculated for cohort patients.

Table 4: A comparison of NICE pre-test probabilities and cohort patient data.

Risk	Total number	Number with CAD	Percentage CAD (95% CI)
61-90+%	691	214	31.0% (27.6- 34.5)
30-60%	544	24	4.4% (3.0 – 6.5)
10-29%	284	7	2.5% (1.2 – 5.0)
<10%	347	1	0.28% (0.1-1.6)
NA	102	9	8.8% (4.7-15.9)

The risk of CAD as predicted by NICE guidelines 95 on the left compared with the actual number of cohort patients in each category and the proportion of those patients diagnosed with significant CAD.

Table 5: A comparison of ESC pre-test probabilities with cohort patient data.

	Typical angina			pical angina	Non-anginal pain		
Age	Men	Women	Men	Women	Men	Women	
30–39	-	-	0	0	0	0	
40–49	71.4	-	22.2	7.7	0.9	1	
50–59	73.3	60	10.6	8.0	3.3	0	
60–69	78.0	57.1	32.9	11.1	1.0	0.9	
70–79	72.7	43.8	36.4	15.6	8.8	2.6	
>80 93	83.3	75	23.6	20	4.5	7.7	

Each cell shows the proportion (%) of cohort patients from each group diagnosed with CAD. Each cell is colour coded to correspond with the ESC estimated pre-test probability. Dark red cells represent >85% probability, pale pink cells represent 66-85% probability, pale blue cells represent 15-65% probability and white cells represent <15% probability.

Table 6: A comparison of ESC pre-test probabilities and cohort patient data

Risk	Total number	Number with CAD	Percentage CAD (95% CI)
>85%	78	58	74.4% (63.7-82.7)
66-85%	176	103	58.5% (51.1-65.5)
15-65%	1451	93	6.4% (5.3-7.8)
<15%	263	2	0.76% (0.2 -2.7)

The risk of CAD as predicted by ESC guidelines on the left compared with the actual number of cohort patients in each category and the proportion of those patients diagnosed with significant CAD.

probability of CAD exceeded the found incidence of CAD in each cell by 17.7% (Table 5).

The cells highlighted in pale blue in table 5 represent medium risk patients with a pre-test probability of CAD of 15-65%, according to ESC guidelines. 6.4% (n=93, CI 5.3 –7.8) of cohort patients in this risk category were diagnosed with CAD (Table 6). On average, the pre-test probability of CAD exceeded the found incidence of CAD by 24.1% in each cell (Table 5).

The cells highlighted in white in table 5 represent patients whose pre-test probability of CAD was less than 15% according to ESC guidelines. Only 0.76% (n=2, 95% CI 0.2 –2.7) of cohort patients in this risk category were diagnosed with CAD (Table 6). On average, pre-test probability of CAD exceeded found incidence of CAD in each cell by 6.2% (Table 5).

#### Discussion

Only 15% of a total of 1968 patients referred to RACPC were diagnosed with significant CAD. The majority (70%) of referred patients had "non-anginal" chest pain and low pre-test probabilities of CAD, reflecting the importance ascribed by General Practitioners of ruling out ischemic heart disease as the underlying cause for chest pain, even in low risk patients. This may not be surprising given the large media attention to heart disease and sustained campaigns for early warning signs of heart attack in the British media. It is therefore of great public interest for cardiac disease to be identified.

### NICE CG95 pre test probabilities compared against cohort data

Comparing cohort data to the pre-test probabilities of CAD outlined in NICE CG95, NICE have overestimated the number of patients likely to have CAD in the majority of groups. Strict adherence to NICE CG95 therefore carries the risk of over-investigating patients. NICE recommend CT calcium scoring as the first line investigation for patients with a low (10-29%) pre-test probability of CAD. 284 patients fall into this category and only 7 patients were shown to have CAD. This means that 40.5 patients need to be treated in order to identify 1 positive patient (NNT= 40.5).

In patients with a medium (30-60%) pre-test probability of CAD, NICE recommends functional imaging as the first line diagnostic investigation. In our cohort 544 patients would undergo functional imaging, but only 24 of these patients would be diagnosed with CAD, NNT=22.7.

Finally, in patient groups with a high (61-90%) pre-test probability of CAD, NICE recommends invasive coronary angiography as the first line diagnostic investigation. In our cohort of 1968 patients, 691 patients had a high pre-test probability of CAD, and 214 had significant coronary artery disease on angiography, NNT= 3.2.

Although invasive coronary angiography is considered the gold standard investigation for diagnosing CAD, and permits simultaneous therapeutic intervention, the procedure is not without risk, particularly in elderly patients and those with renal impairment. Furthermore, invasive angiography is expensive and is costed by the East Kent Hospitals University NHS Foundation Trust at £1166.02 per procedure (private correspondence).

NICE CG95 offers no guidance on managing patients who have a <10% pre-test probability of CAD. 347 of our cohort patients fell into this very low risk category and only 1 was diagnosed with CAD. Therefore, NICE CG95, if strictly adhered to, would have missed one diagnosis of CAD in our patient cohort.

#### ESC pre test probabilities compared against cohort data

ESC guidelines tend to offer more conservative estimates of pretest probability of CAD compared with NICE guidelines. Using the ESC's risk stratification table, almost all patients, except those with over 85% pre-test probability and those with less than 15% pre test probability, would be investigated for chest pain. This is due to their claim that non-invasive, image-based diagnostic methods for CAD have typical sensitivities and specificities of around 85%, so that roughly 15% of these investigations could be yielding false results. Hence, due to these inaccuracies, in patients with pre-test probabilities of CAD below 15% or above 85%, ESC state that performing no test at all could provide fewer incorrect diagnoses.<sup>9</sup>

In our patient cohort, 79 patients had very high (>85%) pretest probability of CAD, but only 58 patients (73%) were diagnosed with CAD. For this patient risk group, ESC guidelines suggest that further investigation may not be necessary and that a diagnosis of CAD may be assumed. Thus, applying ESC guidelines to our cohort could result in 21 patients being incorrectly diagnosed with stable angina, and more serious causes of chest pain, for example pulmonary emboli or gastric ulceration, may be missed. However, in practice, it is likely that many patients in this very high pre-test probability category would have undergone angiography, because patients who have "severe symptoms" or who are

clinically thought to have "high risk coronary anatomy" should be offered an invasive angiography with or without pressure wire studies. The vagueness of the guidelines allows interventionists to interpret this in the clinical context.

In ESC guidelines, invasive coronary angiography is not specifically recommended as a first line investigation for stable angina, regardless of the pre-test probability of CAD. In patients with a high (66-85%) pre-test probability of CAD, ESC guidelines recommend non-invasive functional imaging first line. Of the 176 patients who fell into this category, only 102 (58.0%) patients were ultimately diagnosed with CAD.

In patients with medium (15-65%) pre-test probability of CAD, ESC guidelines advise exercise ECG testing (or non-invasive imaging for ischemia if local expertise is available) as first line diagnostic investigations. Of the 1451 patients which fell into this category, only 93 were diagnosed with CAD, NNT= 15.6. Fortunately, exercise ECG testing would not expose the patient to potentially harmful radiation or medication, but their poor diagnostic power may result in the need for further investigations, despite a negative result.

In patients with low risk of CAD (<15%) ESC guidelines suggest making an assumption that the patient does not have CAD and advocates conducting no further investigations. In our cohort, 263 patients fell into this low risk category, two (0.8%) of which were diagnosed with CAD.

The ESC guidelines appear to have higher specificity than the NICE guidelines, and only two patients would have been missed had ESC guidelines been adhered to, compared to one patient missed if NICE guidance was used. Thus, although highly sensitive, ESC guidelines when applied to our cohort have lower sensitivity than NICE guidelines.

#### Comparison of number of investigations

Following ESC guidance for our cohort of patients would have resulted in fewer diagnostic invasive angiograms being performed than if NICE guidance had been followed. ESC guidance only recommends invasive angiography if first line, non-invasive investigations generate positive results. Overall, however, ESC guidance would result in a greater number of overall investigations being performed.

In total, NICE advises that all 691 of our high risk cohort patients should undergo invasive angiography as a first line investigation. 544 with medium risk should undergo functional testing first and 24 of these patients (assuming an angiogram would follow a positive result) would go on to have invasive angiography. 284 low risk patients should undergo CT calcium scoring first, of which 7 would go on to have functional imaging and angiography if the above logic is followed. This generates a total of 1557 investigations; 722 angiograms, 551 functional imaging investigations and 284 cardiac CT scans.

In comparison, using ESC guidance, 176 of our high risk patients would have functional imaging investigations, 103

patients with positive results would then undergo invasive angiography. 1451 patients would receive exercise ECGs, of which 93 with positive results would undergo functional imaging and invasive angiography. This generates a total of 1916 investigations; 196 angiograms, 269 functional imaging investigations and 1451 exercise ECGs.

If we assume that stress echocardiograms are used as "functional imaging" we can estimate costs for our cohort when applying each set of guidelines. Costs for each investigation are supplied by East Kent Hospitals University NHS Foundation Trust and are as follows: Outpatient elective coronary angiograms are costed at £1,166.02; stress echocardiograms are costed at £132.30; exercise ECGs at £40.26 and CTs of one area at £102.47 (private correspondence). If we were to apply NICE guidelines to our cohort, £841,866.44 would be spent on angiograms, £72,897.30 would be spent on stress echocardiograms and £29,101.48 on CT scans. This is a total of £943,865.22 on investigations.

If we were to apply ESC guidelines to our cohort, £228,539.92 would be spent on coronary angiograms, £35,588.7 would be spent on stress echocardiography and £58,417.26 would be spent on exercise ECGs. A total of £322,545.88 would be spent on investigations. Overall, this is £621,319.34 cheaper than applying NICE guidelines.

#### Limitations of study

This study is based on data from a single site and may not be nationally representative. The final diagnosis was made clinically by an experienced interventional cardiologist, which introduces subjectivity and the risk of interpreter bias. Not all patients underwent the gold standard of invasive coronary angiography to demonstrate the presence of CAD. However, all patients were seen and fully assessed by a cardiologist and 97% underwent investigations if deemed necessary. This study has all the limitations of a registry study. In addition, costs for investigations may vary throughout the country, and indeed the world, with varying expertise available.

#### Conclusion

In conclusion, strict adherence to NICE CG95 over-estimates the pre-test probability of CAD in our local population group. This is consistent with previous studies conducted in South London where there is a larger Afro-Caribbean population, as well as with studies conducted in the North of England. Adherence to ESC guidelines in place of NICE guidelines may enable a more targeted and cost-effective use of investigations. Strict application of the ESC guidelines to the study cohort would have resulted in investigations costing an estimated £322,545.88, compared to £943,865.22 if NICE guidelines were applied. However, conducting fewer investigations carries greater risk of misdiagnosis, and using ESC guidelines in isolation introduces the possibility of assuming CAD in patients without conducting investigations to confirm this.

It is advisable that local cardiology departments audit their stable chest pain guidelines to ensure that the interpretation of pre-test probabilities is in keeping with the local population. Unfortunately there is no ideal policy and local protocols should reflect the local population.

#### **Competing Interests**

None declared

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## A survey of Foundation doctors' attitudes towards psychiatry before and after their first clinical working year

M Aamer Sarfraz, India Merrony and Carol Atkins

#### Abstract

Recruitment into psychiatry has always been relatively difficult because medical graduates perceive it to be unattractive due to stigma and possible systemic professional bias. In the United Kingdom, recruitment into psychiatry has reached a crisis point and a number of posts remain unfilled. This has impact on current and future mental health services. Notwithstanding government policies, to ensure a stable psychiatric workforce for the future, there is an urgent need to motivate current and future cohorts of young doctors to take up psychiatry as a career. This cannot be done without establishing the reasons behind this negative trend among those choosing future medical careers. There is some evidence to suggest that clinical experience in psychiatry positively changes attitudes towards choosing it as specialty for training. We carried out a survey among first year Foundation doctors to examine their perception of psychiatry as a future career and ascertain whether their clinical experience changed their attitudes towards this specialty.

Keywords: recruitment, psychiatry, career, choice

#### Background

Global recruitment in psychiatry has been falling for several decades because medical students and graduates have been finding it consistently unattractive <sup>1,2</sup>. An analysis of the career choices of newly qualified doctors in the United Kingdom (U.K.) found the same trend from 1974 to 2009; psychiatry was the first career choice for only 3-5% of medical graduates annually<sup>3</sup>. In the U.K., lack of recruitment into psychiatry had reached a crisis point by 2003 when 15% of all unfilled consultants posts in England were in psychiatry and the Royal College of Psychiatrists was finding recruitment into specialist psychiatry posts increasingly difficult<sup>4,5</sup>. In 2012, only 78% of the Core Training year one (CT1) posts in psychiatry were filled; a serious shortfall which was overcome by overseas recruitment up until changes in immigration rules.

The factors that seem to dissuade medical students from taking up psychiatry as a future career may include: stigma, bad prognosis of psychiatric disorders, poor scientific base of psychiatry, 'bad-mouthing' from medical colleagues, lack of respect among peers & public, threats of violence from patients and lack of resources<sup>1-5</sup>. However, there is evidence to suggest that many students' attitudes towards career choice changed in a positive direction after working in psychiatry due to the perceived 'job satisfaction', 'life-style', 'training available' and 'multidisciplinary approach'<sup>3</sup>.

Psychiatry has previously been ranked higher in career choice at the end of students' clinical year<sup>6</sup>. To ensure a stable psychiatric workforce for the future, there is an obvious need to motivate current and future cohorts of young doctors to take up psychiatry as a career. Das & Chandrasena (1988) found that attitudes changed positively towards mental health following clinical placement in this specialty<sup>7</sup>. It is also known that medical students' attitudes to psychiatry and career intentions can be improved by their experiences of teaching<sup>8</sup>. Students were found to develop more positive attitudes when encouraged by senior psychiatrists, had direct involvement in patient care, or saw patients respond well to treatment. Improvement in attitudes during the placement was also related to an increased intention to pursue psychiatry as a career.

Previous research into attitude to psychiatry as a specialty and career choice seems to have produced conflicting results and most of it was carried out among medical students. Since career choices in the U.K. are actually made in the first clinical year following graduation, we carried out a survey among a recent cohort of foundation year one (FY1) doctors in the South East England before and after their first clinical year.

#### Method

Our study sample consisted of all FY1 doctors (n=101) in one region of South East England. They participated in the study at the beginning and then at the end of their first clinical year. We used a 20-item questionnaire devised by Das &

Chandrasena(1988) to ascertain their perceptions and attitudes towards psychiatry before they commenced their first clinical placement. The questionnaire was sent to them via their Medical Education Managers (MEMS). It was handed out to the FY1 doctors as part of their induction pack for completion along with a study information sheet.

At the end of their first year of working, the participants were asked to complete an amended version of the questionnaire. This included two additional questions which ascertained whether the doctor had an opportunity to work in a psychiatric post, or had any experience of psychiatry in practice (such as taster days or cases in A&E). These amended questionnaires were sent to the foundation doctors electronically via their MEMS for completion.

The data was collected and entered into a spreadsheet to prepare descriptive statistics. Comparisons for before and after exposure to psychiatry, and between the psychiatry and non-psychiatry groups were made using the chi-square test. As the data was binary, a latent class model was developed using LatentGOLD software<sup>9</sup> to explore the associations between different items in the questionnaire. Responses from the questionnaires were coded as: responses which agree with a positive attitude to psychiatry or disagree with a negative attitude were coded as +1; those not sure were coded as 0; and responses which agree with a negative attitude to psychiatry or disagree with a positive attitude were coded as -1.

#### Results

A 100% (n=101) response rate was obtained for the first set of questionnaires completed at the beginning of the year. However, there was a significant drop in the number of questionnaires completed at the end of the year - a 53.5% response rate (n=54) generally but 61.1% (22 out of 36) for those FY1 doctors who had the opportunity or access to a post in psychiatry within their clinical year.

## <u>Initial cohort at beginning of the clinical year vs. those with no exposure to psychiatry at the end</u>

Table 1 shows the group means for each questionnaire item, for the whole cohort at the beginning of the year compared to those with no exposure to psychiatry by the end of the year.

Those FY1 trainees who had not worked in psychiatry during the year were significantly more positive (p = < 0.05) for psychiatry's future, psychiatrist being better at patient communication and not over-medicating their patients. However, they remained significantly less convinced as compared to the whole cohort about psychiatry's intellectual attraction or taking it up as a future career.

### <u>Initial cohort at beginning of the year vs. those with exposure to psychiatry at the end</u>

Table 2 shows the group means for each questionnaire item, for the whole cohort at the beginning of the year compared to those with exposure to psychiatry at the end of the year. After a psychiatry placement, significant positive differences (p=<0.05) were observed in their responses to medical staff's view of psychiatry, future of psychiatry and place of Electro Convulsive Therapy (ECT) in modern medicine. While there was a positive trend in most responses in favour of psychiatry, trainees remained negative about psychiatry's status, its scientific base, curriculum & training and taking up psychiatry as a future career.

#### Those exposed to psychiatry vs. those not exposed to psychiatry

Table 3 compares responses between FY1 doctors exposed to psychiatry during the clinical year and those who were not.

Those exposed to psychiatry agreed more often that non-psychiatric medical staffs were critical of psychiatry compared to the group not exposed to psychiatry. They also had comparatively negative responses for psychiatrists not abusing legal powers and to have the legal power to treat someone against their will. Trainees exposed to psychiatry also felt significantly (p=<0.05) positive towards psychiatry being intellectually comprehensive and adopting it as a career. However, they were less enthusiastic about psychiatrists treating patients against their will and psychiatry being the expanding frontier of medicine.

#### Discussion

In this study, we have ascertained attitudes of a regional cohort of FY1 doctors towards psychiatry as a specialty and as a career choice. Our findings are similar to previous research carried out among medical students, which found that there were generally negative attitudes towards psychiatry as a specialty and career choice but fairly positive attitudes towards the role of psychiatry in medicine and in society in general<sup>1-5,10</sup>. Like others, we also found that personal experience of psychiatry placement can improve trainees' view of psychiatry as a specialty and as a future career <sup>3,11</sup>.

It was interesting to find out that after a year in clinical practice but without any experience of psychiatry, trainees' attitudes towards psychiatry as a specialty had been positive. It is difficult to know the exact reason but we can speculate that this respect for the specialty may have developed when they experienced limitations of the other specialties in medicine and/or perhaps due to the positive professional encounters with psychiatrists at the Accident & Emergency (A&E) or with psychiatric liaison teams during ward consultations. As opposed to previous research<sup>11</sup>, it was heartening to note that the group with no exposure to psychiatry agreed that non-psychiatric medical staff were not critical of psychiatry; a possible sign of reduced stigma for psychiatry within the medical profession.

Despite exposure to psychiatry, FY1 doctors' attitudes to psychiatry's status, scientific base, curriculum & training and career choice remained somewhat negative. Similar results were found by Lyons et al<sup>11</sup> when they assessed students' attitudes towards psychiatry after a clerkship in the specialty. There was a significant decrease in negative & stigmatising views towards

<u>Table 1:</u> All FY1 doctors before training placements started (initial cohort) versus FY1 doctors without a psychiatric post after FY1 training

	Before	After	Difference	L	U	p-value
Within medicine, psychiatry has a high status	-0.686	-0.591	0.095	-0.169	0.359	0.476
I may consider pursuing a career in psychiatry in the future	-0.539	-0.136	0.403	0.046	0.760	0.028
Psychiatry is attractive because it is intellectually comprehensive	-0.500	0.273	0.773	0.436	1.000	0.000
Most non-psychiatric medical staff are not critical of psychiatry	-0.431	-0.500	-0.069	-0.442	0.305	0.717
Physicians do not have time to deal with patients emotional problems	-0.294	0.273	0.567	0.142	0.991	0.009
Psychiatrists understand and communicate better than other physicians	-0.127	0.364	0.491	0.090	0.892	0.017
Psychiatrists don't overanalyse human behaviour	0.147	0.364	0.217	-0.200	0.633	0.306
Expressing an interest in psychiatry is not seen as odd	0.157	-0.136	-0.293	-0.727	0.141	0.184
Hospitalised patients are not given too much medication	0.167	0.591	0.424	0.116	0.732	0.007
Psychiatrists don't make less money on average than other physicians	0.255	0.045	0.209	-0.537	0.118	0.208
Psychiatry is a rapidly expanding frontier of medicine	0.363	0.727	0.365	0.033	0.696	0.032
Psychiatric curriculum and training are not too easy	0.520	0.682	0.162	-0.112	0.436	0.243
Psychiatrists are not fuzzy thinkers	0.578	0.818	0.240	-0.082	0.561	0.142
Psychiatrists should have the legal power to treat patients against their will	0.608	0.955	0.347	0.051	0.642	0.022
A placement in psychiatry can change one's negative views of psychiatry	0.618	0.864	0.246	-0.066	0.558	0.121
Psychiatry is scientific and precise	0.627	0.818	0.191	-0.098	0.480	0.194
There is a place for ECT in modern medicine	0.755	0.727	-0.028	-0.239	0.184	0.797
Psychiatric consultations are often helpful	0.853	0.864	0.011	-0.210	0.231	0.924
Entering psychiatry is not a waste of a medical education	0.873	1.000	0.127	-0.048	0.303	0.153
Psychiatrists don't often abuse their legal powers	0.892	1.000	0.108	-0.049	0.264	0.175

Table 2: All FY1 doctors before training placements started versus FY1 doctors with a psychiatric post during FY1 training

	Before	After	Difference	L	U	p-value
Within medicine, psychiatry has a high status	-0.686	-0.745	-0.058	-0.242	0.125	0.531
I may consider pursuing a career in psychiatry in the future	-0.539	-0.617	-0.078	-0.332	0.177	0.547
Psychiatry is attractive because it is intellectually comprehensive	-0.500	-0.468	0.032	-0.214	0.278	0.798
Most non-psychiatric medical staff are not critical of psychiatry	-0.431	0.106	0.538	0.248	0.827	0.000
Physicians do not have time to deal with patients emotional problems	-0.294	-0.383	-0.089	-0.401	0.224	0.575
Psychiatrists understand and communicate better than other physicians	-0.127	-0.085	0.042	-0.260	0.345	0.783
Psychiatrists don't overanalyse human behaviour	0.147	0.340	0.193	-0.123	0.510	0.229
Expressing an interest in psychiatry is not seen as odd	0.157	0.106	-0.050	-0.378	0.277	0.761
Hospitalised patients are not given too much medication	0.167	0.362	0.195	-0.044	0.434	0.109
Psychiatrists don't make less money on average than other physicians	0.255	0.404	0.149	-0.092	0.391	0.224
Psychiatry is a rapidly expanding frontier of medicine	0.363	0.064	-0.299	-0.569	-0.029	0.030
Psychiatric curriculum and training are not too easy	0.520	0.596	0.076	-0.128	0.281	0.464
Psychiatrists are not fuzzy thinkers	0.578	0.596	0.017	-0.233	0.268	0.892
Psychiatrists should have the legal power to treat patients against their will	0.608	0.532	-0.076	-0.323	0.171	0.545
A placement in psychiatry can change one's negative views of psychiatry	0.618	0.574	-0.043	-0.290	0.203	0.730
Psychiatry is scientific and precise	0.627	0.702	0.075	-0.155	0.304	0.521
There is a place for ECT in modern medicine	0.755	0.511	-0.244	-0.427	-0.061	0.009
Psychiatric consultations are often helpful	0.853	0.745	-0.108	-0.289	0.073	0.239
Entering psychiatry is not a waste of a medical education	0.873	0.808	-0.064	-0.218	0.090	0.412
Psychiatrists don't often abuse their legal powers	0.892	0.766	-0.126	-0.279	0.027	0.105

Table 3: FY1 doctors who had a psychiatric post versus those who did not have one

Sorted by the size of the difference between the two groups.						t-test	ranksum
	Psychiatry	No Psychiatry	Difference	L	U	p-value	p-value
Most non-psychiatric medical staff are not critical of psychiatry	0.106	-0.500	-0.606	-1.000	-0.144	0.011	0.011
Psychiatrists don't make less money on average than other physicians	0.404	0.045	-0.359	-0.694	-0.024	0.036	0.034
Expressing an interest in psychiatry is not seen as odd	0.106	-0.136	-0.243	-0.735	0.249	0.329	0.322
Psychiatrists don't overanalyse human behaviour	0.340	0.364	0.023	-0.421	0.467	0.917	0.907

Psychiatric curriculum and training are not too easy	0.596	0.682	0.086	-0.210	0.382	0.564	0.497
Psychiatry is scientific and precise	0.702	0.818	0.116	-0.187	0.419	0.447	0.777
Psychiatric consultations are often helpful	0.745	0.864	0.119	-0.173	0.411	0.419	0.388
Within medicine, psychiatry has a high status	-0.745	-0.591	0.154	-0.130	0.437	0.283	0.391
Entering psychiatry is not a waste of a medical education	0.808	1.000	0.191	-0.020	0.403	0.075	0.058
There is a place for ECT in modern medicine	0.511	0.727	0.217	-0.117	0.551	0.200	0.192
Psychiatrists are not fuzzy thinkers	0.596	0.818	0.222	-0.114	0.559	0.192	0.190
Hospitalised patients are not given too much medication	0.362	0.591	0.223	-0.139	0.597	0.218	0.192
Psychiatrists don't often abuse their legal powers	0.766	1.000	0.234	-0.005	0.473	0.055	0.040
A placement in psychiatry can change one's negative views of psychiatry	0.574	0.864	0.289	-0.045	0.623	0.088	0.064
Psychiatrists should have the legal power to treat patients against their will	0.532	0.955	0.423	0.097	0.748	0.012	0.011
Psychiatrists understand and communicate better than other physicians	-0.085	0.364	0.449	0.000	0.897	0.050	0.050
I may consider pursuing a career in psychiatry in the future	-0.617	-0.136	0.481	0.084	0.878	0.028	0.017
Physicians do not have time to deal with patients emotional problems	-0.383	0.273	0.656	0.195	1.000	0.006	0.007
Psychiatry is a rapidly expanding frontier of medicine	0.064	0.727	0.663	0.269	1.000	0.001	0.002
Psychiatry is attractive because it is intellectually comprehensive	-0.468	0.273	0.741	0.352	1.000	0.000	0.001

mental illness after the clerkship, but no significant improvement in students' interest in psychiatry was detected<sup>1</sup>. Goldacre et al (2013) also acknowledged mixed outcomes of early experience of working in psychiatry as it might discourage some doctors. While highlighting positive effect of the doctors' experience of the speciality, they also cited it as a negative factor that influenced some doctors who had previously considered psychiatry as a career<sup>3</sup>.

Our study has limitations because of having a small sample and being carried out in one small region of the country. It is also worth mentioning that the group exposed to psychiatry may not have had a psychiatry placement as it also included those who had had taster days or experience in A&E. The brevity of these latter exposures cannot give someone a real sense of the specialty. The nature of this and the overall experience needs to be differentiated and the exposure quantified in the future studies. Our study findings also need to be replicated with future cohorts and in other regions for confirmation because FY training programme in the U.K. is relatively recent and placements in psychiatry have evolved<sup>4</sup>over the last few years through closer collaboration between different stakeholders in the Foundation Training Programmes.

#### Competing Interests

None declared

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## Attitudes of patients and doctors towards the use of medical professional terms in Psychiatry

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#### Abstract

Medical professional terms have developed contextually over time for professional communication and patient management. As a part of changes in the National Health Service in the U.K., an interesting trend to change or alter the use of professional terminology without consultation with affected professionals or patients has been noted. This practice is being perceived as a threat to medial professional identity and could be a potential source of inter-professional tensions and poses a risk to patient autonomy and safety. We report findings of a survey among patients and doctors in a psychiatric service to ascertain their attitudes towards some old and new medical professional terms. We found a preference among these important stakeholders for the old medical professional terms and also learned that they have never been consulted about changes in medical professional terminology.

Keywords: medical, professional, terminology

#### Introduction:

Medical professional terminology is used to communicate with each other, allied professions and differentiates professionals from patients<sup>1</sup>. As a tradition, it has perhaps evolved into a language of its own with a vocabulary of terms used as expressions, designations or symbols such as 'Patient', 'Ward Round' and 'Registrar'. This 'language' is not restricted to use by doctors or nurses - it is used among other professionals working in healthcare, e.g. medical coders and medico-legal assistants.

The National Health Service (NHS) in the U.K. has seen many changes in the last few decades. From within these changes, an interesting trend to change or alter the use of professional terminology, often without consultation with directly affected professionals or patients, has emerged. With new or changed roles, multidisciplinary teams have been observed to alter titles, even borrowing specific terms ascribed to doctors such as "consultant," "practitioner" and "clinical lead"<sup>2,3</sup>. On the other hand, Modernising Medical Careers initiative<sup>4</sup> has also led to changes in doctors' titles reflecting their experience levels, which have been reported to be unclear to patients and fellow professionals<sup>5</sup>.

Medical professional terms can be traced back to Hippocratic writings and their development is a fascinating study for language scholars<sup>1</sup>. Psychiatric terminology is particularly interesting, as it has evolved through scientific convention while absorbing relevant legal, ethical and political trends along the way. Superficially, it may appear pedantic to quibble over

terminology, but the power of language and its significance in clinical encounters is vital for high quality clinical care<sup>2,6</sup>. Since medical professional terminology is an established vehicle for meaningful communication, undue changes in its use can create inaccurate images and misunderstandings, leading to risks for professional identity. There is also evidence to suggest that such wholesale changes have been misleading<sup>7</sup> and a source of interprofessional tension.

Understanding of a professional's qualifications and experience is crucial for patient autonomy and for them to be able to give informed consent. We carried out a survey among foremost stakeholders of medical professional terminology, patients and doctors, within a psychiatric service to ascertain their attitudes to the changes they have experienced in recent years.

#### Method:

We gave out a self-report questionnaire to all adult psychiatric patients seen at a psychiatric service in the South East (U.K.) in a typical week and to all working psychiatrists/doctors. The questionnaire was developed after a review of the relevant literature and refined following feedback from a pilot project. The questionnaire contained demographic details and questions regarding attitudes towards medical professional terms for patient and professional identity, processes and working environments. The questions were mostly a "single best of four options" style, with one question involving a "yes" or "no" answer.

The datacollected was analysed by using SPSS statistical package<sup>8</sup>. Descriptive statistics were used to summarize the characteristics of the study population. The two sub-samples (patients & doctors) were compared with each other regarding different variables by using a *t*-test, which highlighted the absolute and relative differences among those.

#### **Results:**

196 subjects were approached to participate. 187 subjects (patients = 92, doctors = 95) participated, which represents a response rate of 95%.

Male to female ratio was roughly equal in the sample but there were more females in the medical group (56%) as compared to the patient (46%) group. Among responders, those over 40 years of age were more prevalent in the patient group (60% vs. 39%) compared to the medical group.

As shown in the Table 1, patients' and doctors' attitudes overwhelmingly leaned towards a patient being called a "patient" (as opposed to "client", "service user" or "customer"); understanding "clinician" as a doctor (as compared to being a nurse, social worker or psychotherapist), and believing psychiatrist to be a "consultant" (preferred to nurse practitioner, psychologist or social worker).

Table1: Patients' & doctors' attitudes to medical professional terms = "patient", "clinician" and "consultant"

	Doctors (%)	Patients (%)
Client	16 (17)	13 (14)
Patient	68 (72)	65 (71)
Service user	10 (11)	11 (12)
Customer	1 (1)	3 (3)
Don't know	0	0
Total	95	92
	'	Chi2 1.378, p = 0.710
Which of these is a clinic	cian?	
	Doctors (%)	Patients (%)
Nurse	14 (15)	14 15)
Social worker	4 (4)	2 (2)
Doctor	56 (59)	70 (76)
Psychotherapist	7 (7)	6 (6)
Don't know	14 (15)	0 (0)
Total	95	92
	<b>'</b>	Chi2 16.3, p<0.05
Which of these is a const	ultant?	
	Doctors (%)	Patients (%)
Psychiatrist	71 (75)	68 (74)
Psychologist	3 (3)	6 (7)
Social worker	10 (11)	10 (11)
Nurse practitioner	3 (3)	8 (9)
Don't know	8 (8)	0 (0)
Total	95	92
		Chi2 11.3, p<0.05

Patients and doctors seemed to prefer (>70%) calling the person who provides the patient support in the community as "carecoordinator" or "key worker".

It is worth noting that "key worker" is the main person looking after the patient admitted to hospital and "care-coordinator" has the same role when they are back in the community. Similarly, the majority of the patients deemed the terms "Acute ward" and "PICU" (psychiatric intensive care unit) appropriate for a psychiatric ward.

There was strong evidence to suggest that both patients and doctors were confused as to what a 'medication review' was; as approximately 35% of them thought it was a "nursing handover" and the rest were divided whether it was a "pharmacist meeting" or an "assessment". See Table 2.

This is understandable because the patients are used to an "Out Patient Appointment/Review" where a psychiatrist reviews patients in a holistic manner, which includes prescribing and adjusting their medications. Similar confusion prevailed regarding what has replaced the term "ward round", as both groups were universally divided among choices offered as "MDM" (multidisciplinary meeting), "Assessment", "CPA" (Care Programme Approach) and "Review".

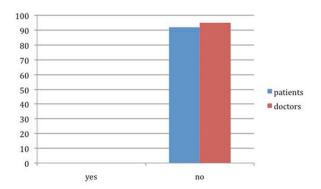
Table 2: Patients' & doctors' attitudes to what a "ward round" and "medication review" means?

	Doctors (%)	Patients (%)
Assessment	26 (27)	34 (37)
MDM	18 (19)	15 (16)
Review	34 (36)	29 (32)
CPA	16 (17)	14 (15)
Don't know	1 (1)	0 (0)
Total	95	92
		Chi2 2.82, p = 0.58
Which of these is a medi	cation review?	
	Doctors (%)	Patients (%)
OPD	19 (20)	11 (12)
Assessment	25 (26)	34 (37)
Pharmacist meeting	34 (36)	31 (34)
Nursing handover	14 (15)	12 (13)
Don't know	3 (3)	4 (4)
Total	95	92

Both patients and doctors were clear (84% vs. 69%) that they expected to see a doctor when they attended a "clinic". However, both groups were approximately equally divided between their preferences for what a psychiatry trainee should be called; "SHO" (37%) or "Psychiatric trainee" (36-40%). There was also a higher preference (approx. 50% vs. 30%) for the doctor a grade below consultant to be called a "Senior Registrar".

Patients and doctors were equivocal in their response that they have never been consulted about medical professional terminology.

Fig. 1 Has anyone consulted you about these terms?



#### Discussion:

In a survey of attitudes to the use of medical professional terms among patients and doctors in a psychiatric service, we have found a significant preference for the older and established medical terms as compared to the newer terms such as MDM, CT trainee, Specialty Trainee, etc.

While replicating findings of other studies<sup>3,7</sup>, we also found that no single term was chosen by 100% of participants in either group, showing confusion surrounding most psychiatric terms. This lack of consensus and confusion can be explained by the fact that no participant had ever been consulted about the changes or new nomenclature.

Limitations to this study should be taken into account before generalising the results. The patients' group is older than the doctors' group, which could skew the results due to age related bias in favour of familiarity and against change<sup>9</sup>. In a questionnaire about preference and understanding, participants may intuitively prefer the easiest to understand terms and ignore the subtle difference between other styles. Possibility of bias may have been introduced by some of those giving out questionnaires being doctors

Our sample was drawn only from a psychiatric service, which may restrict the implications of our findings to mental health.

Furthermore, involvement of other professionals and carers working in the psychiatric service would have been useful to expand the scope of this study.

Inconsistency regarding doctors' titles, unleashed by the Modernising Medical Careers (2008) initiative, has resulted in patients considering trainees as medical students<sup>5</sup>, not recognising 'Foundation Year 1 Trainees' as qualified doctors and being unable to rank doctors below consultant level<sup>3</sup>. Our findings have highlighted the uncertainty regarding qualifications and seniority of doctors – this can erode patients' confidence in their doctors' abilities, compromise therapeutic

relationship<sup>10</sup>, especially in psychiatry, and result in poor treatment compliance. Medical students may also find themselves mistaken for doctors, and feel daunted by future job progression where training structures and status are unclear.

Title changes introduced by local management or Department of Health (DoH), without consultation with stakeholders, have the potential to create inter-professional tensions and devalue the myriad skills offered by healthcare workers other than doctors. This could also be damaging to their morale and the confidence instilled in patients. It is interesting to note, however, that titles that do not give the impression of status and experience, such as "trainee", tend not to be adopted by nondoctor members of the multidisciplinary team3. On the other hand, in a profession steeped in tradition, there will be doctors who see other professionals' adoption of their respect-garnering and previously uncontested titles as a threat to the status of the medical profession<sup>6</sup>. Previous studies have shown that terminology has a significant effect on the confidence and selfview of doctors<sup>5</sup> and at a time where a multitude of issues has led to an efflux of U.K. junior doctors to other countries, and a vote for industrial action, re-examining a seemingly benign issue involving titles and terminology could have a positive impact.

Patients' attitudes to development of surgical skills by surgical nurses show that they would like to be informed if the person doing a procedure is not a doctor<sup>7</sup>.

The roles of a number of professionals involved in an individual's healthcare can be confusing and the possibility of mistaken identity could be considered misleading<sup>6</sup>, unethical, and even fraudulent. Introducing confusion by appropriating titles associated with doctors could be damaging to patients' trust, and is inappropriate in a health service increasingly driven towards patient choice. The challenge lies in how to keep the terminology consistent and used in the best-understood contexts.

Commissioners and managers may instead evaluate the implications of changing professional terms by making sure that all stakeholders are consulted beforehand. Perhaps the pressing source of inconsistency in staff job titles could also be rectified by a broader scale study to find national, multidisciplinary and patient preferences, and taking simple measures such as standardising staff name badges.

Our study has highlighted once again how the landscape of nomenclature in psychiatry/medicine is pitted with inconsistency. While language naturally evolves with time and it may be understandable to see increasing application of business models & terminology in the NHS<sup>9</sup>, medical professional terms have been determined contextually over the years with significant implications for patient management and safety. Therefore, it is important to question how changes in terminology affect patients, whether it occurs by gradual culture change or due to new initiatives. It would benefit patient care if

medical and psychiatric professional language could be standardised and protected from changes, which can lead to colleagues and patients being misled. DoH, Commissioners and Trust/Hospital management must recognise that changing terminology can have a significant impact and that serious discussion of such changes is important for reasons far beyond pedantry. For inter-professional communication a formalised consensus on titles would be beneficial for transparency, trust, patient safety and reducing staff stress levels.

#### **Competing Interests**

None declared

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