NORTH WALES MEDICINES RESEARCH SYMPOSIUM
Symposiwm Ymchwil Meddyginiaethau Gogledd Cymru

1st July 2015
Faenol Fawr Hotel, Bodelwyddan

Programme

6.00	Buffet & Poster viewing	
6.40	Welcome	Professor Dyfrig Hughes, Bangor University
6.45	Keynote presentation: “Medicines non-adherence: managing a complex problem”	Professor Andrew Farmer, University of Oxford
7.30	Magnetic nanoparticle-directed enzyme therapy	Dr Jenny Halliwell, Bangor University
7.50	Using medication-related acute kidney injury admissions to build a preventative cross-sector risk reduction response	Janet Thomas, Betsi Cadwaladr University Health Board
8.10	The role of nationally agreed Prescribing Indicators in promoting prudent prescribing: Experience in Wales (2002-14)	Professor Philip Routledge, Cardiff University
8.30	Economic evaluation of antibiotic central venous catheters in paediatric intensive care settings	Dr Colin Ridyard, Bangor University
9.00	Close and depart	

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SYMPOSIWM YMCHWIL MEDDYGINIAETHAU GOGLEDD CYMRU
North Wales Medicines Research Symposium

1af Gorffennaf 2015
Gwesty Faenol Fawr, Bodelwyddan

Rhaglen

6.00	Bwffe & Darllen posteri	
6.40	Croeso	Yr Athro Dyfrig Hughes, Prifysgol Bangor
6.45	Prif gyflwyniad: “Diffyg ymlyniad at feddyginiaeth: rheoli problem gymhleth”	Yr Athro Andrew Farmer, Prifysgol Rhydychain
7.30	Therapi ensymau a gyfeirir gan nanoronynnau magnetig	Dr Jenny Halliwell, Prifysgol Bangor
7.50	Defnyddio derbyniadau oherwydd anafiadau aciwt i'r arennau sy'n gysylltiedig â meddyginiaeth i ddatblygu ymateb traws-sector i leihau risgiau	Janet Thomas, Bwrdd Iechyd Prifysgol Betsi Cadwaladr
8.10	Swyddogaeth dangosyddion rhagnodi y cytunwyd arnynt yn genedlaethol i hyrwyddo rhagnodi doeth: Profiad yng Nghymru (2002-14)	Yr Athro Philip Routledge, Prifysgol Caerdydd
8.30	Gwerthusiad economaidd o gathetrau gwythiennol canolog gwrthfiotigau mewn lleoliadau gofal dwys pediatrig	Dr Colin Ridyard, Prifysgol Bangor
9.00	Diwedd ac ymadael	

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Professor / Yr Athro Andrew Farmer

Professor Andrew Farmer completed his vocational training at Thame Health Centre where he worked as a principal in the practice from 1985 to 2000. Between 2001 and 2006 he was a Senior Research Fellow in the Department of Primary Health Care holding an NHS R&D Senior Clinical Scientist Award. He was appointed University Lecturer in General Practice at Oxford University in 2007. He also works as a salaried general practitioner at South Oxford Health Centre and is a Senior Research Fellow in the Diabetes Trials Unit.

His work has focussed on research to improve the self-management of diabetes in general practice including the best use of blood glucose monitoring, supporting adherence to medication, and evaluating the use of telehealth to improve long-term outcomes. He was a Harkness Fellow of the Commonwealth Fund of New York in 1991, one of the first general practitioners to hold this award. He was appointed NIHR Senior Investigator in 2013 and currently has additional roles as Director of the Oxford Primary Care Trials Unit, Co-Director of the NIHR Comprehensive Local Research Network and was Deputy Chair of the NIHR Health Technology Assessment Programme Commissioning Board from 2007 to 2011.

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ORAL PRESENTATIONS

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Keynote presentation: Medicines non-adherence: managing a complex problem

Author
A Farmer

Department of Primary Health Care Sciences, University of Oxford

Failure to take medicines as planned is a major contributing factor to sub-optimal management of long-term medical conditions such as hypertension, heart disease and diabetes. Patients forego the benefits of proven treatment, medicines are wasted, and health care costs are increased with unnecessary admissions and higher costs of treatment. Up to 37% of diabetes patients have stopped their blood glucose lowering medication within a year of starting, and only 70 to 80% of drugs are taken as prescribed. Reasons for this are complex and vary widely in different circumstances

Clinical interventions to improve medication adherence to date are mostly complex and not very effective. Many studies testing their use have relied on self-report to judge their effectiveness and have not tried to understand how the interventions might support people with better medicines use. More systematic development processes aiming to simplify the interventions and objectively measure adherence can improve trial design so the findings of research can be more reliable.

There is a need to understand when and under what circumstances interventions to support people with medicines adherence are effective, whether they offer value for money, and how they can best be integrated into current health care practice. Large, simple trials with carefully measured outcomes need to be carried out in a wide range of clinical settings. In the meantime, however, there are lessons for routine practice in improving engagement with patients and better monitoring of medicines use.

Magnetic nanoparticle directed enzyme therapy

Authors
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Magnetic Nanoparticle Directed Enzyme Prodrug Therapy Cancer is one of the world's biggest killers responsible for 30% of deaths worldwide. Treatment has progressed rapidly over the past few years however there are still many problems associated such as side effects and lack of specificity between healthy and tumorous cells. Our patented method, magnetic nanoparticle directed enzyme prodrug therapy (MNDEPT), uses nitroreductases to convert minimally toxic prodrugs into their active, cytotoxic forms. These nitroreductases are tethered to gold coated iron oxide nanoparticles which can be directed to the tumour site by applying a magnetic field. This allows only the cancerous cells to be targeted by the activated prodrug as the nitroreductase only comes into contact with the prodrug at the tumour site. The nitroreductases are modified to include cysteine tags allowing them to form strong gold-sulfur bonds whilst retaining over 99% of the activity. We have screened a wide range of enzymes to determine their suitability for MNDEPT. Detection of Tuberculosis (Human and Bovine) Tuberculosis is a highly infectious disease caused by mycobacterium tuberculosis.

Traditional methods of diagnosis such as chest X rays and sputum smear microscopy are expensive and lengthy making them unsuitable for developing countries. We have developed a method of printing mycolic acids onto nitrocellulose membranes. These compounds are found on the cell walls of mycobacteria and are capable of binding to TB positive antibodies. Sera can then be added to the membrane and allowed to flow through past the mycolic acid allowing any positive antibodies to bind, a secondary antibody conjugated to gold nanoparticles is then added which bind to any TB antibodies on the surface giving a coloured spot as a sign of a positive result. As this test detects lipid antibodies it will also be able to detect TB in patients co-infected with HIV. This test is simple to run, takes only half an hour and importantly is under $5. It is thought that this approach could be used to detect other no n-tuberculosis mycobacterial infections such as Buruli Ulcers and Leprosy by using a range of mycolic acids. Detection of Botulinum Neurotoxins Botulinum neurotoxins are one of the most potent toxins known to man. With an LD50 of 1-5 ng/kg it would only take 50 g of the toxin to kill everyone on the planet. Whilst the dangers of the toxin are obvious, in small doses they can be used to treat a range of conditions from cervical dystonia to excessive sweating. Currently the toxin is detected through the mouse bioassay (MBA) which involves injecting live animals with a sample and observing them for signs and symptoms of the disease over a number of days. Due to the risks associated with the toxin it is imperative that alternative quick, accurate methods of detecting the toxin are developed that do not use animals. We have developed two patented methods of detecting the toxin both using the toxins natural substrate, the SNARE proteins, immobilised on a gold surface. Changes to the proteins are detected by a change in colour when they are bound to nanoparticles and via electrochemical impedance measurements when bound to electrodes.

Using medication-related acute kidney injury admissions to build a preventative cross-sector risk reduction response

Authors
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Introduction
Acute Kidney Injury (AKI) is predictable and deemed preventable in 20-30% of cases[1]; 60% being community acquired[2]. Renal auto-regulation prompts standard hospital practice of temporarily withholding nephrotoxic medication during AKI and 'at risk' periods. Medication-related admissions involve AKI with/without acute illness[3].Senior Admissions Pharmacists* developed a leaflet entitled 'dehydration and preventing side-effects of medicines'. Its public health safety potential needed maximising as National Institute for Health and Care Excellence AKI Clinical Guidance[4] recommendations encourage self-care.

Method
Between 1/1/2011 and 31/7/2013, Wrexham Maelor Hospital's pharmacists recorded AKI admissions involving medicines. The Patient Safety Pharmacist tracked the patient (study limitation) and conducted root cause analyses (RCA). Stakeholder collaboration created a cross-sector organisation-wide initiative with phased revised leaflet implementation and mandatory verbal counselling. Ethics approval was not required. This was a project to empower healthcare professionals and patients to adopt standard practice in primary care.

Results
RCA revealed patients (n=90) on acute or chronic 'aggravating medication', and/or with an acute clinical episode. AKI clinical impact was significant. The well received leaflet precipitated a positive culture change. Community Pharmacists welcomed new safety information to share with patients.

Discussion
AKI admission analyses correlated with some of NCEPOD's[1] AKI risk factors, guided the project, verified AKI awareness /leaflet need and drove change acceptance. RCA identified critical implementation points. Long term AKI risk-reduction impact (study limitation) requires continued research.

References

1. NCEPOD - AKI: Adding Insult to Injury Report (2009) http://www.ncepod.org.uk/2009aki.htm (accessed 27 May 2015).
2. Selby NM, Crowley L, Fluck RJ et al. Clinical Journal American Society of Nephrology 2012:7(4)533-40.
3. Thomas J. Facilitating avoidance of medication-related admissions. Poster session presented at Patient Safety Congress; 2011 May 16-18; Birmingham, UK. http://yhhiec.org.uk/wp-content/uploads/2012/05/PSC2011-Facilitating-Avoidance-of-medication-related-admissions-pdf.pdf (accessed 27 May 2015).
4. National Institute for Health and Care Excellence. Acute kidney injury Clinical Guideline 169, August 2013. http://www.nice.org.uk/guidance/CG169 (accessed 27 May 2015).

The role of nationally agreed prescribing indicators (NPIs) in promoting prudent prescribing; Experience in Wales (2002-2014)

Authors
P A Routledge, K Haines, J Hayes, K Jenkins, K Samuels

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Introduction
Prescribing should aim for optimal efficacy, safety and efficiency. Aims. We used national indicators (NPIs) to measure prescribing standards in primary care in Wales, for benchmarking purposes, to help target appropriate interventions and to measure any subsequent improvement (1).

Method
NPIs were agreed by national consensus using different measures of prescribing volumes (e.g. expressed per prescribing unit [PU] or defined daily dose [DDD]). They were endorsed by the All Wales Medicines Strategy Group and reviewed annually for continuing relevance, and were based on evidence-based clinical pharmacological principles.

Results
Twenty-eight different NPIs were used over the period of study, although more than half of these were subsequent refinements of the original NPIs. Almost all have moved in the desired direction towards previously agreed targets, although antibiotic prescribing volumes are still particularly resistant to change in Wales (see table).

Discussion
NPIs are an explicit mechanism for applying clinical pharmacological principles to prescribing. Further work using NPIs is needed to examine the relative roles of education, peer comparison/ competition and incentivisation in achieving prudent prescribing in primary care.

References

1. http://www.senedd.assembly.wales/documents/s10974/Action%20Point%20-%20Invest2save3%20English.pdf (accessed 30/01/2015)

Economic evaluation of antibiotic central venous catheters in a UK paediatric intensive care setting

Authors
C H Ridyard[1], C O Plumpton[1], R E Gilbert[2], D A Hughes[1] on behalf of the CATCH trial

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Introduction
Antibiotic-impregnated central venous catheters (CVCs) are effective in reducing bloodstream infections (BSIs) in patients admitted to intensive care units in England. There is, however, uncertainty, as to whether they represent good value for money in a paediatric intensive care unit (PICU) setting.

Method
This study is a trial-based, cost-effectiveness analysis to determine the incremental cost per BSI averted for antibiotic versus standard CVC in a PICU setting and is taken from a National Health Service (NHS) perspective. The costs of CVCs and of PICU, High Dependency Unit and ward stays (including readmissions), outpatient clinic visits and Accident and Emergency admissions were determined from data collected routinely and from the CATCH trial (NCT01029717).

Results
More BSIs occurred in children randomised to standard (18/502, 3.59%) CVCs than in the corresponding antibiotic (7/486, 1.44%) and heparin-impregnated (17/497, 3.42%) devices. There were no significant differences in lengths of stay between intervention groups. The incremental cost-effectiveness ratio of antibiotic versus standard CVCs was £54,057 per BSI averted but was sensitive to the time horizon of analysis. When costs were restricted to the index hospital stay, antibiotic CVCs dominated standard CVCs.

Interpretation
A policy of replacing standard CVCs with antibiotic CVCs in PICUs will be more beneficial in terms of fewer patients developing BSI but a level of uncertainty remains as to whether their use will dominate in terms of cost savings to the NHS.

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Development and optimisation of topical gabapentin formulations for the treatment of neuropathic pain conditions

Authors
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Introduction
Neuropathic pain (NP) is a complex, often chronic pain (Moore, 2014) arising from a "lesion or disease of the somatosensory system" (Jensen, 2011). Estimates for the prevalence of NP vary across Europe, but may be as high as 8% in the UK (Torrance, 2006). Conventional analgesics are usually not effective in treating NP (Toelle, 2013) and hence "unconventional" therapies, such as the antiepileptic gabapentin are often used (Moore, 2014). Oral gabapentin is licensed in the UK for the treatment of peripheral NP (EMC, 2009) but its efficacy is often limited by dose dependent toxicity (Hiom, 2014). Topical drug delivery is a safer, viable alternative to oral dosing where benefits can be derived from delivering lower doses of active ingredient directly to the site of action (Steen, 2000). A topical gabapentin product is manufactured as a pharmaceutical "special" at SMPU at the request of local and national chronic pain clinicians. Early proof of concept studies have demonstrated efficacy (Hiom, 2014), however the formulation affects the amount of drug delivered and hence requires optimisation.

Method
In this study a range of topical formulations containing gabapentin were developed. These included a variety of carbopol based hydrogel products and a proprietary oil-in-water (o/w) cream. The physico-chemical properties were assessed and carbopol gels were optimised to maintain gabapentin stability. The ability of formulations to release gabapentin was assessed using Franz diffusion cells and a nitrocellulose support membrane. Additionally, the potential for topical delivery from each formulation was assessed using heat separated human epidermal membranes as a barrier, whilst the stability of each was assessed following ICH guidelines. In all cases gabapentin concentration in samples was estimated by reversed-phase HPLC (Ciavarella, 2007).

Results
Carbopol gels containing 6% gabapentin and either 70% ethanol (A) or 5% dimethyl sulphoxide (B) or 10% gabapentin o/w cream (C) emerged as potential formulation candidates. The pH of all formulations ranged from 6.00 – 7.15, which is close to the optimal pH for gabapentin stability. All formulations were shown to release gabapentin, with the order of release kinetics being B > C ≥ A. Furthermore, all formulations delivered gabapentin across human skin. The corresponding permeability co-efficient values (cm/h) were B ($7.36 \pm 5.52 \times 10^{-4}$) > C ($4.13 \pm 1.54 \times 10^{-4}$) > A ($8.28 \pm 8.28 \times 10^{-5}$). The stability of formulations B and C stored at 25˚C was good, remaining at 96% stated content (sc) after 6 months and 98% sc after 12 months, respectively. The stability of formulation A was unpredictable, with large quantities of breakdown product formed; possibly due to evaporation of EtOH.

Conclusion
This study suggests that a hydrogel formulation containing 5% DMSO or an o/w cream may be suitable vehicles for the stable incorporation and delivery of gabapentin across human skin.

Health Technology Appraisal and Access To Medicines: Experience of the All Wales Medicines Strategy Group, 2002-2014

Authors
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Introduction
The All Wales Medicines Group (AWMSG) was established in 2002 to advise Welsh Government on the introduction of certain medicines into Wales. Aims. We decided to analyse the acceptance rate of all medicines submitted by manufacturers to AWMSG for health technology appraisal (HTA) in NHS Wales, as well as separately for a sub-group of those medicines indicated for the treatment of conditions with a prevalence in the European Union of ≤ 5 in 10,000 (sometimes called “orphan medicines”).

Method
HTA was conducted by AWMSG in its monthly meetings in public. “Recommended Medicines” were approved either according to the full licensed indication or for a restricted (“optimised”) indication.

Results
In the period September 1st 2002 to December 31st 2014, 184 (81%) of the 228 HTA’s resulted in the medicine being recommended, either in full or with restrictions (see Figure). In contrast only 20 (59%) of the 34 orphan medicines were recommended either in full or restricted (Fisher’s exact test, two-tailed p = 0.0072 c/w non-orphan medicines). In the case of ultra-orphan medicines (a sub-set of orphan medicines generally defined as being used to treat conditions with a prevalence of ≤ 1 in 50,000 in the EU), 8 (73%) of 11 medicines were recommended in full or with restrictions (Fisher’s exact test, two-tailed p = 0.2948, NS c/w other orphan medicines).

Discussion
Further work is required to develop timely, robust and transparent approaches to ensure that clinically effective medicines (including orphan and ultra-orphan medicines) can be made optimally available to patients within a finite health budget.

How useful are health psychology and behavioural economic theories at predicting adherence to medications in adult patients?

Authors
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Introduction
Suboptimal adherence to medications presents a significant challenge to safe, effective and cost-effective use of medicines. This PhD seeks to identify and test behavioural models that may further our understanding of adherence to medications in adult patients.

Method
A systematic review of 20-years of health psychology literature identified determinants of nonadherence that were tested in a multinational cross-sectional survey of self-reported non-adherence to antihypertensive medications across 11 countries. The survey also included a stated preference discrete choice experiment (DCE) of persistence with medications, and a time preference questionnaire to value of current and future medicines taking behaviour and its association with adherence to medication. Results were analysed using regression models in STATA.

Results
67 studies were included in the review: sociocognitive=35, self-regulation=21, social support=11. The survey (n=2595) found that low self-efficacy and a high number of perceived barriers are the main significant determinants of non-adherence, country explained 11% of the variance. The DCE (n=2549) found that medicines characteristics of benefit, harms and convenience have statistically significant effect on persistence with medication and clinical, demographic, and psychosocial influences may modify these preferences. The association between discount rates and adherence was significant in 2/8 countries.

Discussion and Conclusion
Behavioural theories are useful at predicting adherence to medications; however, no individual theory explained more than a limited amount of the variability in adherence. Consolidation of behavioural models may provide a strengthened theoretical basis for the development and assessment of adherence enhancing interventions that could promote sustainable behaviour change in clinical practice.

Research Programme for NHS Product Development - Topical Delivery of Gabapentin for Neuropathic Pain.

Authors
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Introduction

When there is an unmet clinical need, such as treatment for refractory peripheral neuropathic pain, holders of a Pharmaceutical Manufacturers Specials License can provide treatment in the form of "specials" to meet short term demand. These preparations are limited in that they lack evidence to support safety, efficacy and quality and have no IP protection. The basis of this research programme is therefore to explore the process by which special medicines can be developed through to licensed products within the NHS, specifically to determine safety, efficacy and pharmaceutical quality of topical gabapentin in view of this overarching process.

Method

License Application: Determine the minimum data set required to support a licensed application for topical gabapentin.
Pharmaceutical Quality: Develop and validate Gabapentin assay. Determine formulation, stability and shelf life.
Non Clinical: Develop Franz Cell technology and use to assess the in-vitro permeation of gabapentin across biological membranes. Test efficacy of topical gabapentin using animal models.
Clinical: Collected pain score data from neuropathic pain patients who are treated with topical gabapentin.

Results

Formulation and stability established as 12 months but on-going. Gabapentin permeated porcine skin (26 %) and human skin (0.3 %). Gabapentin efficacy demonstrated in animal model. Patients demonstrated reduced mean pain scores (8.0 to 5.3) after one month treatment ($p<0.001$). No side effects reported.

Conclusion

The development of "special" medicines within the NHS is being explored. Data demonstrates that topical gabapentin is safe and efficacious for neuropathic pain. Further controlled trials are required to validate these findings.

Self-attribution of facial appearance: predicting early treatment-response for depression

Author
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Introduction
Evaluation of treatment is dependent on its effectiveness and cost-effectiveness. Effectiveness is the extent to which a treatment achieves its intended effect in a clinical setting. Unfortunately, effectiveness of treatment for depression is being identified on a trial-and-error basis. This substantially prolongs the treatment-period, impacting on the quality-of-life of patients and societal costs.

Method
We report on a new measure of self-attribution based on individuals' perception of their own facial appearance and how that predicts treatment-response. Each participant's photograph was morphed towards an average neurotic face and an average emotionally stable face, creating morphs of gradual increments along a continuum of high to low neurotic appearance. These images were presented as a looped sequence in the self-attribution task and participants identified the images they perceived as their actual-self, ideal-self, positive-self (happy, emotionally stable, attractive), and negative self.

Results
In study-1, using nonclinical population, it was found that individuals with greater depression score identified more neurotic images as their actual-self. A separation index (SI) measured individual's distinction between their choice of actual and negative self. SI was found to decrease, indicating negative self-representation, with increasing depression. In study-2, self-attributions of depressed patients were assessed five times across 11-12 weeks. SI was found to gradually increase over the 11 weeks. Greater SI in the first week was a good predictor of reduced depression at week 11, implying a predictor of treatment-response as early as the first week.

Conclusion
An early predictor can reduce the lengthy period needed to identify an effective treatment for depression.

Societal views of funding for orphan drugs

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Orphan drugs are those which meet regulatory approval for the treatment of rare conditions. These drugs may be expensive to develop relative to the small numbers of patients who receive these treatments. As such, they tend to be high-cost and rarely meet conventional criteria for cost effectiveness. Unless there are special conditions for exceeding the cost-effectiveness threshold, many orphan drugs would not be routinely reimbursed on the NHS.

Policies have already been developed to incentivise pharmaceuticals companies to produce orphan drugs internationally, and many HTA organisations recommend orphan drugs for reimbursement despite their apparent cost-ineffectiveness. However, there remains controversy concerning whether or not orphan drugs should adhere to the rigor of traditional cost effectiveness standards, or whether there should be an alternate process for funding within national health care systems. An understanding of society's preferences for funding orphan drugs is therefore essential in determining any policy for funding orphan drugs within health care systems.

Previous studies of society's value of rare diseases have focused mainly on the characteristic of rarity. However, this is not the only characteristic of rare diseases that society may value. Rare diseases are usually serious and life threatening conditions, for which there are limited, or no alternative treatments available. While this is true also of some common diseases, it may be the case that society values the equity of access to treatment for rare diseases. However, the range of attributes relating to societies value of orphan drugs have yet to be fully explored.

The aim of present study is to identify the characteristics of importance to key stakeholder groups: Patients (and their informal carers), health care professionals responsible for managing patients with rare diseases, and policy makers. Once defined, these characteristics will be used in a Discrete Choice Experiment and Person Trade Off experiment of several thousand members of the UK general public to ascertain their preferences for NHS funding of orphan drugs.

Vancomycin in critical care patients – back to basics

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Introduction
Intravenous vancomycin is prescribed using the hospital wide protocol based on initial assessment of renal function in critical care patients. The aim of this protocol is to attain adequate therapeutic concentration of vancomycin. However, local experience in several critically ill patients demonstrates that this protocol leads to sub-therapeutic vancomycin levels measured at four dosing intervals after initiation. A change in vancomycin protocol is necessary addressing the need to achieve therapeutic levels within 24 to 48 hours of initiation.

Method
Based on literature evaluation, the recommendation is to administer vancomycin in critically ill patients as continuous intravenous infusion and adjust the rate to achieve vancomycin concentration within the therapeutic range.

A protocol was reproduced, agreed and implemented for use in critical care patients.

Results
Since January 2015, 10 critically ill patients have received intravenous vancomycin administered as continuous infusion. In 7 patients in whom the protocol was followed, therapeutic vancomycin level was achieved within 24hours in 4 patients and within 48hours in all patients. In the remaining three patients the protocol was not correctly followed due to incorrect reconstitution of vancomycin and administration. Other clinical monitoring parameters were also recorded to assess outcome of treatment.

Discussion
Introduction of continuous intravenous infusion of vancomycin in critically ill patients has demonstrably shown that therapeutic vancomycin concentrations where achieved in all patients within 48 hours where the guidance was followed. This is in contrast to our experience when using hospital wide vancomycin protocol used in the critically ill.

What factors influence smoking behaviour in young females?

Author
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Introduction
Tobacco smoking is the single biggest cause of cancer in the world. Although there is a lot of research on youth smoking, very few studies have looked at females in the 11-12 year age group – the age at which many studies suggest females start to smoke.

Methods
To estimate the prevalence of smoking in young females in North Wales, a two page bilingual survey was sent out to all 11-12 year old females in a total of 63 secondary schools, including special schools. In addition, five focus groups were conducted in areas with high levels of deprivation and high adult smoking prevalence. These focus groups were designed to explore in depth current knowledge, attitudes and behaviours to smoking.

Results
Our research found that there is an average smoking prevalence of 2% in 11-12 year old females in North Wales, although this more than doubled in deprived communities. All participants in the focus groups were aware of a family member that smokes. We found that if parents smoke, children are more likely to start. Another finding was that girls with low aspirations that did not take part in sport or after school activities were more likely to smoke or use e-cigarettes. Most participants knew where to purchase e-cigarettes and they were aware that they contain nicotine. Young females felt that smoking was generally unappealing, especially due to the more superficial consequences such as impact on their appearance.

Conclusion
Anti-smoking campaigns should target both parents and young people; campaigns also need to focus on raising aspirations and confidence in young women and stand alone anti-smoking messages are unlikely to work; young females respond best when they perceive themselves or a family member being harmed by smoking.

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Welsh cautionary and advisory labels for prescription medicines

Authors
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Introduction
The provision of Welsh language services within healthcare in Wales has been highly scrutinised. The Welsh Language Commissioner's inquiry found that a Welsh language or bilingual service is vital for the welfare of Welsh speaking patients. Specifically, a recommendation, later endorsed by the Chief Pharmaceutical Officer for Wales, was for bilingual labels on prescription medicines to be made available to patients.

The aim of the present study was to develop Welsh language versions of the 30 cautionary and advisory labels.

Method
Cautionary and advisory labels were identified from the most recent version of the BNF. A terminologist at the Language Technologies Unit, Bangor University provided initial translation which was published on Maes-T (http://maes-t.com), an interface for the creation and development of online terminology resources aimed to facilitate collaboration between terminologists and subject specialists. Feedback was provided by hospital and academic pharmacists, and a consensus meeting was held to agree a second draft. This was distributed to a small group of Welsh-speaking community pharmacists within BCUHB, to local members of Merched Y Wawr (a national women's organisation) and to the BCUHB service users Reader Panel. Comments were collated and discussed within the team, and with the involvement of a second terminologist, to arrive at the final version.

Results
All 30 cautionary and advisory labels were translated (see poster).

Discussion
Terminologists, pharmacists and members of the general public were in agreement with the wording of the majority of Welsh terms. However, some words posed specific challenges such as in relation to geography of use, as in *llaeth* or *llefrith* for milk (the latter being used in North Wales). The term *hydoddi* for dissolve is not used commonly, and stakeholders preferred *toddi* which means melt, but often used for dissolve. The colloquial term *dŵr* (meaning water) was preferred to *wrin* for urine.

The iterative approach to arrive at the final agreed list was inclusive of service users and subject specialists, and proved a robust approach to ensure generalisability across Wales. The final version will be published in the online and paper versions of the BNF.

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