Programme

6.00 Buffet & Poster viewing
6.40 Welcome

6.45 **Keynote presentation: Medicinal aspects of murder**
Professor Dyfrig Hughes, Bangor University
Professor Robin Ferner, University of Birmingham

7.00 Exploring what influences persistence with medicines: A multinational discrete choice experiment of 2549 patients
Dr Emily Holmes, Bangor University

7.30 Glucose limitation restructures the cellular DNA damage response
Dr Thomas Caspari, Bangor University

8.15 Cost effectiveness of *HLA-B*58:01 genotyping prior to prescription of allopurinol
Dr Catrin Plumpton, Bangor University

8.40 Preregistration pharmacist recruitment in Wales
Joanne Kember, WCPPE

9.00 Close and depart

Directions
Bod Erw is located on exit junction 27 of the A55. For Satnav or Google maps, use postcode LL17 0LA.
### Rhaglen

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<th>Time</th>
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<td>Dr Emily Holmes, Prifysgol Bangor</td>
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<td>Dr Thomas Caspari, Prifysgol Bangor</td>
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<td>Glucose limitation restructures the cellular DNA damage response</td>
<td>Dr Catrin Plumpton, Prifysgol Bangor</td>
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<td>Cost effectiveness of <em>HLA-B</em>(^{<em>58:01</em>} ) genotyping prior to prescription of allopurinol</td>
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### Cyfarwyddiadau

Mae Bod Erw ar gyffordd 27 yr A55. Defnyddiwch y codpost LL17 0LA ar gyfer Satnav neu mapiau Google.
Professor Robin Ferner is Director of the West Midlands Centre for Adverse Drug Reactions, a largely retired Consultant Physician and Clinical Pharmacologist in Birmingham, and Honorary Professor at the University of Birmingham, where he has helped to teach how to use medicines safely and rationally for over 20 years. He is Secretary of the British Pharmacological Society–Royal College of Physicians Joint Specialist Committee on Clinical Pharmacology and of the Birmingham Medico-legal Society. He now works part-time.

He is the author of Forensic Pharmacology (Oxford University Press, 1996 reprinted 2001), and a number of papers with colleagues on 'medical manslaughter.'

He has been an expert in several criminal cases, including R -v- Beverley Allitt, R -v- Graham Norris, and R -v- Victorino Chua, all nurses convicted of murder.
CYFLWYNIADAU LLAFAR / ORAL PRESENTATIONS
Title
Exploring what influences persistence with medicines: A multinational discrete choice experiment of 2549 patients

Authors
Emily Holmes, Val Morrison, Dyfrig Hughes on behalf of the ABC project team. CHEME, Bangor University

Introduction
Persistence with medication may be an outcome of a decision patients consciously make about whether continued taking of their medications will increase their utility. Patients’ utility can be examined using stated preference discrete choice experiments (DCE).

Methods
We designed a DCE based on four medication attributes (treatment benefit, mild yet common adverse drug reactions (ADRs), rare but potentially life threatening ADRs and dosing frequency). Respondents were presented with nine binary choices and asked: Which medicine would you be most likely to continue taking? The survey was translated, piloted and approved for eleven European countries. Target sample was 100 ≤ n ≤ 323 patients prescribed anti-hypertensives per country, recruited by posters in community pharmacies or general practices. Results were analysed in STATA using a random effects logit model. Results: 2549 patients from nine countries completed the DCE. All attributes significantly influenced patients’ stated preference to persist with medications (P < 0.05). Patients were willing to trade treatment benefit to reduce the risk of a severe ADR, to reduce the risk of mild ADR, and to reduce to once daily dosing. Psychosocial and sociocognitive characteristics significantly influenced preferences (p<0.05).

Discussion
Patients’ intention to persist with treatment was associated with their willingness to trade potential benefits, harms and dosing frequency. Psychosocial and sociocognitive factors influenced the extent of trading. The utility model may have value in assessing patients’ likelihood of persisting with medicines and to tailor treatment to maximize persistence.
Title
Glucose limitation restructures the cellular DNA damage response

Author
Thomas Caspari, School of Medical Sciences, Bangor University

Introduction
Glucose concentrations are up to 10-times lower in tumours compared to the surrounding tissue. Whether this affects the vital DNA damage response pathways, which drive cancer cells into programmed cell death, is as yet unknown.

Methods
Using fission yeast as a model, we provide evidence that a 10-fold reduction in glucose activates the main DNA damage sensors ATR and ATM kinase.

Results
Within the first 4 hours of starvation, ATR kinase transiently arrests cell division which coincides with the modification of the chromatin and the activation of a third kinase. Prolonged starvation (5-24h) triggers the ATR- and ATM-dependent degradation of some DNA damage response proteins while others increase in abundance. We also show that ATR kinase regulates the up-regulation of Glucose Transporter 4, but has no impact on the induction of Glucose Transporter 5.

Conclusion
In summary, our results strongly imply that low glucose concentrations may help cancer cells to survive because of these changes to the DNA damage response kinases. They may also shed light on the enigmatic observation that some Ataxia telangiectasia patients, who have mutations in ATM kinase, suffer from diabetes type 2.
Title
Cost effectiveness of HLA-B*58:01 genotyping prior to prescription of allopurinol

Authors
Catrin Plumpton, Munir Pirmohamed, Dyfrig Hughes, CHEME, Bangor University, Department of Molecular and Clinical Pharmacology, University of Liverpool

Introduction
Gout is a common inflammatory disease affecting 1-2% of the population. Standard treatment for the long term management of gout includes urate lowering agents, with allopurinol being the most commonly prescribed in the UK. Allopurinol can cause severe cutaneous adverse drug reactions which is associated with the presence of the HLA-B*58:01 allele. We estimate the cost-effectiveness of HLA-B*58:01 genotyping prior to prescription of allopurinol in the UK healthcare setting.

Methods
A short-term, decision analytic model was developed to estimate the outcomes and costs associated with a policy of routine testing (with febuxostat prescribed for patients who test positive) versus the current standard of care, which is allopurinol prescribed without testing. A Markov model was used to estimate total costs and quality-adjusted life-years (QALYs) over a lifetime to account for differences in drug effectiveness and the long-term consequences of adverse drug reactions.

Results
Testing reduced the expected rate of cutaneous adverse drug reactions from 0.8 to 0.38 per 10,000 patients. The incremental cost-effectiveness ratio for pharmacogenetic testing versus standard care was £46,561 per QALY gained. The probability of testing being cost-effective at a threshold of £30,000 per QALY was 0.21. The ICER is sensitive to the cost of both the pharmacogenetic test and febuxostat, and the prevalence of HLA-B*58:01

Conclusion
Routine testing for HLA-B*58:01 in order to reduce the incidence of cutaneous adverse drug reactions in patients being prescribed allopurinol is not a cost-effective use of health care resources.
Title
Pre-registration pharmacist recruitment in Wales

Author
Joanne Kember, Welsh Centre for Professional Pharmacy Education

Introduction
There is a need for preregistration recruitment to be strengthened to ensure equity in standards and processes across the system, and optimise governance arrangements. The national web based platform recruitment for hospital posts uses Pharmalife for which the service level agreement expires in 2017.

Aims
To investigate the pre-registration pharmacist recruitment process in Wales. To determine how it could be strengthened to ensure equity in standards and optimise governance. Make recommendations for any changes or modifications needed to the recruitment process in Wales.

Methods
A 5 phase qualitative methodology: Investigation of recruitment processes across the UK and compilation of process maps; Exploration of the use of Oriel for recruitment; Observation of interview and assessment process for managed sector candidates in September 2015; Semi-structured interviews conducted using a piloted questionnaire, with candidates and recruitment pharmacists; investigation of the planning and delivery of the assessment day for the integrated posts in North Wales.

Results
The evaluation highlighted the lack of standardised mechanisms and quality assurance the recruitment process. The functionality of the Oriel system which has been piloted with other specialities has the flexibility to adapt to the needs of pharmacy. The values based recruitment (VBR) model used in North Wales was formulated from evidence based techniques and has robust quality assurance.

Discussion
The evaluation demonstrated the need to strengthen and ensure equity in standards and processes across the system using more robust and highly standardised values based assessment, with an all Wales assessment centre model. This should be supported by a web platform which provides centralised all Wales recruitment using a nationally agreed and standardised person specification.
CYFLWYNIADAU POSTERI /
POSTER PRESENTATIONS
Title
Antipsychotic use for inpatients with BPSD in dementia – How are we doing?

Authors
Elizabeth Bond, Dr Seema Gupta, BCUHB

Introduction
Behavioural and psychological symptoms of dementia (BPSD), is an umbrella term for a cluster of non-cognitive symptoms, including agitation, aggression, persistent hallucinations and mood disorder. NICE CG42 recommends that antipsychotics are only used for patients with dementia where BPSD are not responding to personalised care and cause extreme distress, or pose a risk of harm to self / others. A BPSD Toolkit was developed as a checklist to aid compliance with NICE CG42 in 2012.

Aim
This study was an audit of inpatients admitted to OPMH wards to assess whether NICE guidance (CG42) was being followed whether antipsychotic choice was in line with NICE and BPSD Toolkit recommendations.

Methods
The audit proforma was developed using NICE CG42 standards and completed for inpatients prescribed antipsychotic on OPMH Dementia wards across 3 Hospital sites (50 beds). Data was collected across 3 sites on 12 September 2015 and analysed by the audit department.

Results
Out of the 50 inpatients with dementia, 19 (38%) were receiving antipsychotics and therefore eligible for audit. 11 (58%) patients were prescribed the antipsychotic olanzapine, risperidone or quetiapine as recommended. Of the 19 patients prescribed an antipsychotic 84% had documented evidence of non-drug interventions tried prior to antipsychotic. Only 12 (63%) patients had documented evidence that the decision to prescribe had been discussed with the carer. The reason for prescribing the antipsychotic (target symptoms) was documented for 16 (84%) patients. All patients had been reviewed in the last 3 months, but the assessment of the benefit of antipsychotic was only documented in 67% cases.

Discussion
This audit highlights that standards of documentation fell short of the NICE recommendations. For patients prescribed an antipsychotic by the specialist, clear documentation is essential to enable ongoing monitoring and review whether by the specialist team or the GP. Where symptoms are stable or improved, the antipsychotic should be reviewed and gradually reduced. The results of this audit have been presented to clinicians across the Health Board and a guideline produced to guide staff on the initiation and review of antipsychotics. The use of antipsychotics in patients with dementia has since been re-audited as part of a national audit (POMH-UK) and results are expected in the autumn.
Title
Patients’ preferences for anti-epileptic drugs (AEDs)

Authors
Emily Holmes, Anthony Marson, Dyfrig Hughes, CHEME, Bangor University; University of Liverpool

Introduction
Relatively little is known about what patients consider important outcomes of AED treatment, and how these influence their preferences.

Methods
Web-based discrete choice experiments (DCEs) to elicit preferences of adults with epilepsy, recruited via Epilepsy Action. Important outcomes were identified using patient interviews, a focus group with prescribers, and clinical trial data. There were two versions of the DCE with four attributes in common: remission, fewer seizures, depression, memory problems. The fifth attribute was aggression, or risk of foetal abnormality (in subgroup of women with potential to become pregnant). Data was analysed in STATA using a random effects logit model.

Results
56 patients and 8 prescribers participated in the qualitative phase, 414 patients completed the DCE. All attributes were significant and in the expected direction (p<0.05). Patients were willing to reduce the chance of remission by 4.02 percentage points (95% CI 3.20, 5.11) for a 1 percentage point reduction in aggression, 3.34 percentage points (95% CI 2.53, 4.35) for a 1 percentage point reduction in poor memory, and 3.34 percentage points (95% CI 2.56, 4.19) for a 1 percentage point reduction in depression. Women with the potential to become pregnant (n=105) were willing to reduce the chance of remission by 4.96 percentage points (95% CI 4.13, 6.30) for a 1 percentage point reduction in the risk of foetal abnormality.

Discussion
Exploring what patients consider important for measuring AED effectiveness will ensure clinical services are focus on patient-defined needs and that future research is designed to assess appropriate patient-defined outcomes.
Title
Societal preferences for funding orphan Drugs in the UK

Authors
Siobhan Bourke, Catrin Plumpton, Dyfrig Hughes, Bangor University

Background
This study aims to identify features of Orphan Drugs (OD) that may influence reimbursement decisions, and design a survey of the general population to evaluate their preferences for OD funding.

Methods
Features that the National Health Service (NHS) should consider important in making recommendations for funding OD were identified using a mixed method approach including; a quantitative ranking of attributes, qualitative surveys and focus groups of key stakeholder groups. An online survey was designed and administered to patients and carers who were recruited from patient support groups, clinicians with a special interest in rare diseases via Orphanet, and UK policy makers from membership of health technology assessment organisations.

Results
A total of 114 participants were recruited into the study, consisting of 70 patients/carers, 27 policy makers and 17 healthcare professionals. The study identified the six characteristics that the NHS should consider in making funding decisions: ability to improve everyday life, treatment effectiveness, the level of clinical evidence, availability of other treatments, the severity of disease and cost-effectiveness. Individual group analysis found slight differences in the ranking of importance of these features between groups. Overall, however, there was little disagreement of which attributes were most important. In the qualitative analysis, patients and carer-givers discussed the difficulties in receiving timely diagnosis, access to treatment and loss of confidence in the NHS.

Discussion
OD are expensive and may not provide value for money by standard measures of cost-effectiveness. Their general availability by the NHS suggests that special criteria apply for their reimbursement. Our study is the first comprehensive attempt to gather public preferences for the funding of orphan drugs, in order to estimate the societal value and to test whether there is support for the prioritisation of OD funding.
Title
Switching to subcutaneous trastuzumab (Herceptin) administration; Drug Cost, Time and Wastage Benefits

Authors
Rob Challoner, North Wales Cancer Treatment Centre, BCUHB

Background
Trastuzumab (Herceptin) is a monoclonal antibody frequently used in the treatment of HER2 receptor positive metastatic breast cancer. Trastuzumab is a high cost drug with a short expiry; therefore IV doses are only made up aseptically in cytotoxic clean rooms within pharmacy on confirmation that the patient has arrived on the day ward and is fit to receive treatment. IV trastuzumab is dosed on a mg/kg basis and then rounded to the nearest 21mg. Trastuzumab is only available in 150mg vials meaning some doses result in significant amounts of unused drug which is discarded.

In July 2014 administration was switched from IV to subcutaneous (SC) for all breast cancer patients receiving trastuzumab at the North Wales Cancer Treatment Centre in accordance with NICE evidence summary advice 2013. (1) Patients receive a flat dose of 600mg of trastuzumab the licensed SC dose. (2) Administration of trastuzumab SC takes significantly less time; 5 minutes rather than 90minutes. In addition preparation of a subcutaneous dose can be carried out on the day unit rather than in a pharmacy.

Objectives
To establish the effect of switching to SC administration of trastuzumab on

- Pharmacy time to prepare doses
- Chemotherapy day unit time to administer doses
- Average drug cost
- Drug wastage – unused part vials
- Cost of pharmacy consumables
- The time patients wait on the day unit to receive doses

Methods
Electronic and paper pharmacy records were analysed to establish all IV trastuzumab doses administered to patients at the North Wales Cancer Treatment Centre between 01JAN14 and 31MAR14 and all SC doses between 01JAN16 and 31MAR16. Use of pharmacy capacity planning figures to quantify pharmacy time and chemotherapy day unit booking slots to establish changes to day unit time.

Results
126 IV doses and 201 SC doses were analysed. Baseline data for IV dosing between JAN-MAR14 was used to calculate the costs as if a switch not taken place and all SC dosing between JAN-MAR16 had instead been administered IV. Comparison of both groups allowed savings to be calculated per individual patient dose and extrapolated to show annual savings.
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<td>IV</td>
<td>SC</td>
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<td>Pharmacy time</td>
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<td>5mins</td>
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<tr>
<td>Chemotherapy day ward time</td>
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<td>Average drug cost</td>
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<td>Drug wastage – unused part vials</td>
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<td>Cost of pharmacy consumables</td>
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<td>Waiting time from pharmacy to unit</td>
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**Discussion/Conclusions**

Switching to SC trastuzumab administration has provided significant saving in pharmacy time, chemotherapy day unit time, drug cost and patient time. It is important to note the patent for IV trastuzumab has expired but SC trastuzumab has a separate patent protecting the manufacturer from competition. Currently there are no IV bioequivalent products available but they are anticipated to be available in the future although it is unclear when. Monoclonal antibodies are expensive to produce and it is expected the most efficient manufacturers will be able to market bioequivalent products at around two thirds of the current price. In this case the economic benefits of SC administration would be less apparent Time and capacity benefits remain unchanged. Furthermore the population of patients receiving trastuzumab is continually expanding due to treatment being lifelong therefore time and capacity considerations will only become more pressing.

**Declarations**

Author; no interests to declare

**Acknowledgements**

Pharmacy staff at North Wales Cancer Treatment Centre. Tracy Parry-Jones Lead Oncology Pharmacist BCUHB

**References**

Title
Do CRP analysers reduce antibiotics? Experience of piloting a C-reactive protein point of care test analyser to support antibiotic prescribing decisions in a General Practice.

Authors
Alison Hughes, Sharman Harris, Lois Gwyn, Claire Clarke, BCUHB

Introduction
The National Institute of Clinical Excellence (NICE) issued guidance on Pneumonia in Adults. It recommends Point of Care C-Reactive Protein (CRP) analysers where clinical assessment is inconclusive. If the CRP is less than 20mg/L – no antibiotics should be offered; 20-100mg/L delayed prescriptions should be considered; over 100mg/L offer an antibiotic.

Methods
A pilot study was undertaken in a general practice surgery to determine whether CRP point of care testing had an impact on the prescribing of antibiotics. CRP is a marker of infection and inflammation. It is high in bacterial infections but very low or nil in viral infections. The pilot describes the experience of introducing the analyser into clinical practice. The pilot was undertaken over a 3 month period. The evaluation included a patient focus group and user questionnaire.

Results
CRP point of care tests were carried out in 94 patients. These were 71 taken for acute respiratory tract infections and 23 other indications. From the 71 respiratory patients, 53 (74.6%) did not receive an antibiotic. Comparing the same period the previous year - antibiotic items decreased by 22%. Patient and user feedback was positive.

Conclusion
There is limited experience of CRP Point of Care analysers in GP practices and this report discusses the practical experience and learning for further rollout.
Title
Topical delivery of gabapentin (GabaGel™) for neuropathic pain: A ‘proof of concept’ study

Authors
Sarah Hiom, Cardiff and Vale University Health Board

Introduction
Some patients cannot tolerate oral gabapentin for neuropathic pain. Topical gabapentin, manufactured as a pharmaceutical ‘special’, has been used as a treatment alternative in chronic pain clinics [1]. These preparations meet immediate clinical need but are limited in that they lack robust evidence to support safety, efficacy and quality. We performed a local retrospective observational study to assess the effectiveness and tolerability of 6% w/w gabapentin gel, manufactured by a local NHS pharmacy manufacturing unit, for the treatment of a variety of peripheral and localized neuropathic pain conditions. The wider collaborative research group also explored mechanisms of action using human tissue and animal studies and quality aspects of formulation development. We present here a “proof of concept” study to investigate safety and efficacy of topical gabapentin for a variety of peripheral neuropathic pain conditions.

Methods
We present a single centre, retrospective, observational series of case studies (n=23) where pain (BPI NRS 1-10), Quality of Life (QOL) and sleep scores pre/post treatment were assessed. Data was collected monthly from notes of patients being treated with gabapentin gel after the relevant ethics and governance approvals were obtained. A clinically significant reduction in pain score = 2. The case mix included Post Herpetic Neuralgia (PHN), Diabetic Peripheral Neuropathy (PDPN), Chronic Post Surgical Pain (CPSP), Complex Regional Pain Syndrome (CRPS) and vulvodynia. Patient treatment regimens followed local neuropathic pain guidelines [2]. Patients were only treated with topical gabapentin if proven refractory or suffering intolerable side effects to standard regimens.

Results
Data analysis demonstrates statistically and clinically significant reduction in pain scores after one-month treatment (n=20) with remaining patients (n=3) reporting unaltered pain scores. Mean pain, sleep and QOL scores at baseline and 1 month after treatment changed from 8.2 (SD 1.5) to 5.6 (SD 1.6), 5.8 to 7.1 and 4.2 to 5.5 respectively with Wilcoxon signed rank test indicating strong tendency for the pain score to decrease after 1 month (p<0.001). Individual patients reported between 30-80% pain relief. All patients with vulvodynia (4/4), PDPN (1/1) and 2/3 patients with PHN responded positively to topical gabapentin. Patients with pain reduction at one month showed similar improvements at 6 months. Individual analysis of each case indicated the gel was effective for burning pain, autonomic hyperactivity and post surgical neuropathic pain and was ineffective for dysaesthesias. However this study is limited by small sample size and absence of specific neuropathic pain measures.

Discussion
Our study suggests that topical delivery of gabapentin can elicit a therapeutic response. A reduction in any experienced central side effects and a lower delivery dose were observed when compared to oral delivery. Topical gabapentin resulted in rapid improvement of symptoms (<1month) when compared to the gradual titration required with oral administration (< 8 weeks), with the associated patient and institution benefits. Results support anecdotal evidence that topical gabapentin is safe and efficacious for use in refractory focal peripheral neuropathic pain. Further randomised controlled trials will be required to validate these results.

References
2. CG173 Neuropathic pain - pharmacological management: NICE guideline 20 November 2013
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