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CONFERENCE ABSTRACTS

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Various

Action research on athletes' need for information to avoid inadvertent doping (work in progress)

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Background: Athletes test positive for prohibited substances (according to WADA prohibited list) occasionally. Athletes' use of pharmaceuticals is occasionally highlighted in media, often times due to an athlete accidentally testing positive for prohibited substances. The athletes have the responsibility but may have challenges getting reliable information to avoid inadvertent doping. When tested, the athletes deliver a self-declaration form (doping control form), stating amongst others what pharmaceuticals and supplements they have used the foregoing seven days. The forms can be a valuable information source on trends in use of pharmaceuticals and supplements. Action research consists of a repeated circle identifying a problem, collecting and analysing data and reflecting on the analysis leading to the next round of identifying a problem etc. Purpose: To find ways to help athletes in reliably shouldering the responsibility for a safe own use of pharmaceuticals and food supplements. To evaluate if Action Research is a useful approach towards this aim.

Method: Action Research, researchers from Anti-Doping Norway and the University of Oslo in cooperation with umbrella organizations for the different types of sport. 1st round: the doping control forms entered into a database, the pharmaceuticals arranged by the ATC classification and the food supplement by another classification. Patterns identified.

2nd round: athletes in sports with a pattern deviating from the average interviewed in focus groups to identify reasons for the deviations. Many groups mention support staff as reliable providers of information.

3rd round: support staff interviewed in individual interviews. Many of the informants mention pharmacies as a reliable place for information and a reliable place to buy food supplements.

4th round: Simulated patient in pharmacies. The quality of the information varies.

5th round: individual interviews with pharmacists. The pharmacists are willing to take on an extended role in informing athletes on safer routines as regards pharmaceuticals.

6th and 7th rounds planned: interviewing athletes and surveying to map further the potential pharmacies might have as a provider of information and services.

The rounds will continue until a plan for providing adequate services for the athletes has been developed.

Results: Among the identified trends in 1st round were ice-hockey players' unusual liberal use of hypnotics, handball and football players' relatively liberal use of painkillers and certain endurance sports athletes' relatively large use of anti-asthmatics. The groups of athletes that have already been interviewed in 2nd round are: ice-hockey players, handball players and young football players. These groups directed the focus to support staff, whereof physicians and physiotherapists are being interviewed in 3th round. In the 5th round, insufficient knowledge among community pharmacists was revealed. The 6th and 7th rounds have started but are not yet completed.

Conclusion: Action Research seems to be a useful approach towards the aim of developing a pharmacy service that can complement the information service provided by Anti-Doping Norway.

Change in childhood vaccine-preventable infection rates before and after COVID-19 pandemic and the attitude of parents toward childhood vaccination

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Introduction: The COVID-19 pandemic and the global lockdown have affected all healthcare systems, including a negative impact on regular immunization uptake worldwide, where millions of children have been reported to not receiving vaccines in 2021. Saudi Arabia's vaccination program has had a historically high coverage rate since its establishment in 1979. However, the impact of the COVID-19 pandemic on vaccine-preventable infections (VPIs) and parental attitudes toward childhood vaccination hasn't been sufficiently explored. Therefore, this study aimed to assess changes in the rates of childhood VPIs in Saudi Arabia before and after the COVID-19 pandemic and the potential change in parental attitudes toward childhood vaccination after the pandemic.

Methods: A mixed-methods design was used in this study. It involved the analysis of epidemiological data obtained from the Saudi Ministry of Health's registry of the rates of childhood VPIs before and after COVID-19 pandemic (from 2019 throughout 2023).It also involved a cross-sectional study (between February-July 2024) of parents of children between the ages of 0-9 years living in four major cities in Saudi Arabia. The survey was completed via in-person interviews with the target population.

Results: Vaccination coverage rates were high, exceeding 96%, for all significant childhood VPIs from 2019 to 2023. The incidence of VPIs remained generally low. However, a slight numerical increase in the incidence rate per 100,000 population of Rubella and Hepatitis B infections was observed from 0.12 and 19.9, respectively, in 2019 to 0.54 and 22.72, respectively, in 2023. Of the 385 parents surveyed, 57.2% were females mostly in the age group of 35-44 years (47.2%), and half (50%) had a bachelor's degree. Among the particpants, 86.4% reported fully vaccinating their children, and 64.9% got vaccine information from primary care providers. Most parents (83.8%) responded that there has been no change in their children's vaccine routine since COVID-19; though at least 3.8% reported that the fear of side effects is the main reason that may hinder them from vaccinating their children. While 85.2% reported being comfortable with childhood vaccines before the pandemic, only 51.1% agreed to vaccinate their children against any diseases in the future.

Conclusion: The vaccination program in Saudi Arabia proved to be resilient during the pandemic and maintained high vaccination coverage despite unprecedented global disruptions. After the pandemic, increases in some VPIs rates are indicators that vigilance should be maintained. The study stresses the need to continue addressing parental concerns about vaccine safety and reinforcing public health strategies to curtail disease resurgence. Future interventions are recommended to improve healthcare infrastructure, target more interventions, and mobilize public education campaigns to sustain and raise vaccination coverage.

Influence of GLP1 receptor agonists on cardiovascular disease: A review from ClinicalTrials.gov

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Introduction: Cardiovascular disease (CVD) stands as the predominant global cause of death, with the annual number of mortalities estimated to be 17.9 million. It encompasses a spectrum of blood vessel and heart disorders and related conditions, including rheumatic heart disease, cerebrovascular disease, and coronary heart disease. Alarmingly, strokes and heart attacks account for over 80% of CVD-related deaths. One-third of such fatalities are premature, occurring among individuals who are under 70 years old. Glucagon-like peptide-1 (GLP-1) receptor agonists (GLP-1 RAs) are small peptide hormones released by gastrointestinal L cells as a response to the uptake of nutrients. They bind to GLP-1 receptors and exhibit incretin effects. Both preclinical investigations and clinical observations have validated the efficacy of GLP-1 RAs in enhancing GLP-1 activity and safeguarding the heart against hypertension, hypertrophy, and fibrosis. Consequently, this study aims to identify and deliver a complete overview of how GLP-1 RAs perform in clinical trials.

Methods: On August 29th, 2024, a search of the ClinicalTrials.gov database was undertaken using the search terms "cardiovascular disease," "GLP-1 receptor agonist (GLP-1 RAs)," "exenatide," "dulaglutide," "albiglutide," "semaglutide (Ozempic)," and "liraglutide (Saxenda)." Suitable clinical trials were selected using defined inclusion and exclusion criteria. This included completed trials with results and interventional trials that assessed the effect of GLP-1 RAs on cardiovascular disease.

Results: A total of 108 clinical trials were identified, with only thirteen focusing on investigating the effects of GLP-1 receptor agonists. The collective findings from these trials demonstrated that GLP-1 receptor agonists provided consistent cardiovascular benefits across various diabetes duration categories.

Conclusion: GLP-1 receptor agonists consistently exhibit cardiovascular benefits, rendering them appealing therapeutic options for individuals who have type 2 diabetes and are at high risk of cardiovascular disease.

Canertinib induces apoptosis in KRAS mutant colorectal cancer cells via SGK1 downregulation and FBXO32 upregulation

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Introduction: Colorectal cancer (CRC) remains a leading cause of cancer-related morbidity and mortality worldwide, affecting millions of individuals each year. Among the various subtypes of CRC, KRAS-mutant CRC presents significant treatment challenges due to its propensity for developing drug resistance and evading immune responses. This aggressive cancer form is often resistant to conventional therapies, resulting in poorer patient outcomes. These factors highlight the urgent need for novel therapeutic strategies that can effectively target KRAS-mutant CRC, aiming to improve treatment efficacy and enhance survival rates for patients suffering from this formidable disease. Developing innovative approaches is essential to overcome these hurdles and provide patients with more effective treatment options.

Method: We investigate the effects of canertinib, an irreversible inhibitor of EGFR and HER2, on the proliferation of KRAS-mutant colorectal cancer cells. A range of experimental techniques were employed to assess the impact of canertinib on KRAS-mutant CRC cells. Proliferation assays were conducted to evaluate cell growth inhibition using CCK-8. siRNA interference was used to disrupt EGFR/HER2 to investigate whether the antitumour effects of canertinib change with the knockdown of these known targets. RNA sequencing was performed to analyse gene expression changes following treatment with canertinib. Flow cytometry was utilised to determine the effects of canertinib on cell cycle distribution and apoptosis rates. Additionally, western blot analysis was conducted to examine the expression levels of SGK1 and FBXO32, which are implicated in cell cycle regulation and apoptosis.

Results: Our findings indicate that canertinib significantly inhibits the proliferation of KRAS-mutant colorectal cancer cells, specifically in the SW837 and HCT15 cell lines. Notably, even when EGFR and HER2 were knocked down, the inhibitory effects of canertinib persisted, suggesting that its antitumour action is independent of the expression levels of these two known targets. RNA sequencing data revealed that the gene expression alterations induced by canertinib predominantly affect pathways related to the cell cycle and DNA replication, highlighting the potential mechanisms through which the drug exerts its effects. Flow cytometry results demonstrated that treatment with canertinib resulted in S phase cell cycle arrest, accompanied by a marked increase in early apoptosis rates that correlated with higher drug concentrations. Furthermore, western blot analysis confirmed that treatment with canertinib led to significant increases in SGK1 expression and downregulation of FBXO32, even at low concentrations. These molecular changes collectively contribute to the observed cell cycle arrest and apoptosis induction, providing insights into the mechanisms underpinning canertinib's effectiveness against KRAS-mutant colorectal cancer.

Conclusion: These findings suggest that canertinib represents a promising therapeutic option for patients with KRAS-mutant colorectal cancer by targeting specific cellular mechanisms that drive tumour growth and survival. Further exploration of the molecular pathways influenced by canertinib could enhance our understanding of its therapeutic potential and facilitate the development of more effective treatment strategies for this difficult-to-treat cancer subtype.

Exploring the synergistic potential of statins and doxorubicin in colon cancer treatment: effects on sw-620 cell proliferation and apoptosis

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Introduction: Colon cancer is prevalent in modern healthcare, commonly treated with anticancer drugs that inhibit cell proliferation, induce apoptosis, and prevent angiogenesis and metastasis. Doxorubicin is critical in colon cancer therapy due to its ability to intercalate DNA strands, disrupting cancer cell replication and inducing apoptosis. However, its long-term use is limited by the development of resistance and adverse side effects, prompting a search for alternative treatments. Statins, which are primarily prescribed to manage hypercholesterolaemia by inhibiting 3-HMG-CoA reductase and reducing cholesterol levels, have shown potential beyond their lipid-lowering effects. Research indicates that statins may reduce cell proliferation, promote

apoptosis, and block significant cancer-related signalling pathways across various cancer types. This study focuses on investigating the roles of two statins, simvastatin and atorvastatin, in affecting the proliferation rate of SW-620 colon cancer cells and their potential synergistic effect with the anticancer agent doxorubicin.

Method: The study examined the effects of simvastatin (25µM) and atorvastatin (10µM) on SW-620 colon cancer cells, both individually and in combination with doxorubicin (1µM). To assess apoptosis, the expression of the anti-apoptotic protein Bcl-2 and the pro-apoptotic protein Bax was quantified. The research employed techniques including cell culture, viability assays, RNA isolation, cDNA synthesis, and Real-Time PCR to evaluate these effects.

Results: Preliminary findings indicated that simvastatin and atorvastatin effectively inhibited SW-620 cell growth and increased the rates of cell death. Simvastatin resulted in a cell death rate of 4.723%, compared to 2.33% in the control group, whereas atorvastatin demonstrated a rate of 18.546%. Simvastatin and atorvastatin reduced the expression levels of the anti-apoptotic protein Bcl-2 and increased the expression levels of the pro-apoptotic protein Bax, indicating activation of apoptotic pathway. When combined with doxorubicin, the statins exhibited synergistic actions, with simvastatin and atorvastatin reaching cell death rates of 23.95% and 7.17%, respectively. These findings suggest that statins enhance the apoptotic activity of doxorubicin in SW-620 colon cancer cells.

Conclusion: The combined use of simvastatin and atorvastatin with doxorubicin demonstrates significant potential in enhancing the therapeutic efficacy against SW-620 colon cancer cells. By promoting greater levels of apoptosis, as evidenced by the modulation of Bcl-2 and Bax protein levels, these statins appear to amplify the apoptotic response initiated by doxorubicin. This suggests a promising role for statins as adjunctive agents in colon cancer treatment strategies, warranting further investigation to optimize therapeutic protocols and understand the underlying mechanisms more thoroughly.

Effects of ripe tomato saponin esculeoside A in mice colorectal cancer models

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Introduction: In many cancer, immune suppression occurs within the body, and regulatory T cells (Tregs) are believed to be involved in the anti-tumor immune response. In various types of cancer, Tregs have been reported as poor prognostic factors; however, there have been different reports regarding colorectal cancer. Therefore, more detailed studies are needed on the immune response of Tregs in colorectal cancer. In Tregs, the transcription factor Foxp3 is involved in differentiation induction, and the expression of CD25 is essential. This study aims to explore new possibilities for the prevention and treatment of colorectal cancer and to investigate the anti-cancer effects of Esculeoside A (EsA), which is a major component of ripe tomato fruits with a content approximately four times higher than that of lycopene. Furthermore, the relationship with regulatory T cells was also examined.

Method: In this study, two types of mouse colorectal cancer models were used to investigate the anti-cancer effects of EsA. First, in the subcutaneous colorectal cancer xenograft model, EsA (20 or 100 mg per kg body weight) was orally administered to Balb/c mice by gavage, and one week later, CT-26 mouse colorectal cancer cells were transplanted subcutaneously on the dorsal side of the mice. EsA treatment was continued for 4 weeks, and tumor size were measured. Next, in the AOM/DSS (azoxymethane, dextran sulfate sodium)-induced inflammatory colorectal cancer model, AOM (10 mg/kg) was administered intraperitoneally, followed by 7 days of free drinking of DSS one week later. EsA was orally administered for 14 weeks after AOM injection. After the treatment, mice were euthanized, and tumor size were measured. Furthermore, the effects of EsA on spleen-derived regulatory T cells were investigated.

Results:

1. Effects in the Subcutaneous Colorectal Cancer Xenograft Model

Compared to the control, no anti-cancer effect was observed with EsA treatment. The proportion of CD4+ T cells in the cancer-bearing mice was significantly decreased compared to the normal mice.

2. Effects in the AOM/DSS-Induced Inflammatory Colorectal Cancer Model

EsA treatment resulted in a significant decrease in both the number and size of colorectal cancer tumors compared to the control. Flow cytometry (FACS) analysis of immune cells derived from the mouse spleen revealed a trend toward an increase in the proportion of Foxp3+/CD25+ regulatory T cells compared to the control.

Conclusion: Ripe tomato saponin EsA is considered to suppress the development of inflammatory colorectal cancer. There was no direct effect on colorectal cancer proliferation; instead, it is believed that the suppression of colorectal cancer development was due to the regulation of immune responses and anti-inflammatory effects via the increased expression of regulatory T cells. Additionally, in the subcutaneous colorectal cancer xenograft mouse model, the proportion of CD4+ T cells was significantly reduced, suggesting that immune responses may differ between the two colorectal cancer models used in this study.

Health literacy and understanding of pharmacists' instructions among urban and rural patients: A survey-based study

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Introduction: Health literacy plays a fundamental role in ensuring patient's ability to understand and follow medication instructions provided by healthcare professionals. Pharmacists, as key providers of medication-related education, are particularly important in settings where access to other healthcare professionals may be limited, such as rural areas. Understanding how patients comprehend pharmacists' instructions and identifying potential gaps in communication can inform more effective health interventions and promote better medication adherence.

This study investigates differences in health literacy and pharmacist-patient communication preferences between urban and rural populations. By identifying disparities in understanding, it aims to provide insights into improving communication strategies tailored to diverse patient needs.

Method: A cross-sectional survey was conducted among pharmacy patients in the cities of Bjelovar and Karlovac, Croatia, from January to March 2025. Participants provided demographic information, including age, gender, education level, and area of residence (urban or rural). The survey assessed various aspects of health literacy, including: confidence in understanding pharmacists' instructions, frequency of reading medication leaflets, ease of understanding medical terminology, comfort level in seeking clarification from pharmacists, preferred methods of receiving medication-related information, the extent to which pharmacists provide guidance on over-the-counter (OTC) medications.

Descriptive and comparative statistical analyses were performed to explore variations between urban and rural participants.

Results: Urban respondents were more confident (77.5%) in understanding medication instructions than rural respondents (68.8%), though more rural participants (27.3%) reported partial confidence. Reading frequency of medication leaflets was similar, but 15.6% of rural respondents admitted to rarely or never reading them, compared to 21.0% of urban participants. While 44.9% of urban respondents found medical terminology easy to understand, this percentage was higher among rural respondents (53.2%). Comfort in asking pharmacists questions was slightly greater in urban areas (61.6% vs. 57.1%). Urban respondents preferred verbal information (50.0%), while rural participants leaned toward written (41.6%) or digital formats (2.6%). Pharmacists in rural areas were more likely to proactively provide OTC medication instructions (68.8% vs. 57.2%).

Conclusion: These findings highlight key differences in health literacy and communication preferences between urban and rural patients. While urban respondents exhibited greater confidence in understanding medication instructions and demonstrated a stronger preference for verbal counselling, rural patients relied more on written materials but were also less likely to read them. The results suggest that pharmacists should employ a range of communication strategies, such as simplifying verbal explanations for rural patients while integrating digital resources to better support urban populations.

By tailoring counselling approaches to address varying health literacy levels, pharmacists can play a critical role in enhancing patient comprehension, improving medication adherence, and ultimately contributing to better health outcomes across diverse communities. Further research is warranted to explore additional factors influencing health literacy and to develop targeted interventions aimed at reducing disparities in pharmacist-patient communication.

Shaping the future of cell therapies in Portugal: Defining a strategic agenda for improved access and policy development

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Background: Chimeric Antigen Receptor T-cell (CAR-T) therapy is an innovative therapeutic approach in the treatment of B-lineage lymphoid neoplasms, especially in cases where first-line therapeutic options are ineffective or lose their efficacy over time. The journey of the patient eligible to receive CAR-T cell therapy is complex, presenting some significant challenges to its accessibility.

Purpose: This study aims to reflect on and discuss the future of cell therapies in Portugal, with a particular focus on CAR-T cell therapy. It aims to promote the development of a strategic agenda with a potential impact on the definition of public policies that improve access to this technology and on scientific and clinical progress in CAR-T cell treatment.

Method: A targeted literature review was conducted, followed by a Think Tank approach resorting to design thinking techniques. The study was led by a research team at NOVA Information and Management School (NOVA University of Lisbon) and guided by a Steering Committee of four national experts. The Think Tank consisted of three

meetings involving 26 participants from the Portuguese healthcare sector, including health professionals, patients, caregivers, researchers, and policy and executive decision-makers. The first meeting focused on the evidence, diagnosis, and referral process for CAR-T therapy-eligible patients; the second examined financial models; and the third discussed the management and governance of the patient journey.

Results: Following the results of the three Think Tank sessions, five key axes of action were identified to improve access to cell therapies in Portugal. The first axe of action is to invest in the capacity building of healthcare professionals and services. The second is to establish a centralized financing program. The third is to create a national referral network for cell therapies and standardize treatment eligibility criteria. The fourth is to provide comprehensive socio-economic, logistical, and training support for patients, caregivers, and families. Lastly, the fifth axe of action is to strengthen the ability to generate and share real-world evidence in the field of cell therapies. Implementing the proposed recommendations is expected to enhance the patient's journey, which is crucial in the experience of a cancer patient whose first lines of treatment have already failed.

Conclusion: The findings and recommendations from this study aim to inform policy decisions and foster adoption of cell therapies for patients living in Portugal. Although the study focuses on a national case study, its methodology, which involves engaging all parties' perspectives in reflecting on the adoption of personalized therapies, may offer valuable insights for adaptation in other countries.

Antimicrobial susceptibility testing of Klebsiella pneumoniae recovered from urine samples

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Introduction: Antimicrobial resistance (AMR) is a growing global health challenge, with microorganisms becoming increasingly resistant to antibiotics. Klebsiella pneumoniae plays a significant role in this menace, demonstrating multidrug resistance and the ability to transfer resistant genes. This poses serious health risks, including poor therapeutic outcomes and death. Additionally, Extended Spectrum Beta-Lactamase (ESBL) production in Klebsiella pneumoniae enables hydrolysis of extended-spectrum antibiotics, further complicating treatment options. In Ghana, Klebsiella pneumoniae infections are prevalent, accounting for 74.1% of Klebsiella isolates in a study conducted at Komfo Anokye Teaching Hospital. Despite this, data on drug resistance and ESBL prevalence in Ghana remains limited. Furthermore, West Africa has been identified as having significant information gaps concerning multidrug resistant Gram-negative bacteria, including Klebsiella pneumoniae.

Objective: This study investigated the antimicrobial susceptibility patterns and prevalence of ESBL in Klebsiella pneumoniae cultured from the urine of patients in Ghana.

Method: The study was carried out at the Bacteriology Department of the Noguchi Memorial Institute of Medical Research, University of Ghana. A total of seventy (70) isolates from three hospitals were used for this study. Ten (10) from Eastern Regional Hospital, twelve (12) from University of Ghana Hospital and forty-eight (48) from 37-Military Hospital. These isolates were collected from processed clinical specimen from the urine of patients presenting with urinary symptoms. This study involved four main steps, a. Culturing and subculturing of isolates. b. Identification of isolates using Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI TOF MS). c. Antimicrobial Susceptibility Test using the Kirby-Bauer disc diffusion method to determine the antimicrobial susceptibility profile of Klebsiella pneumoniae and d. Phenotypic detection of ESBL. A confirmatory test using the combination disc test was done to identify Klebsiella pneumoniae isolates that were ESBL producers. Data analysis was done using WHONET 2022 and Microsoft Excel.

Results: Out of the 70 isolates, 55 were identified to be Klebsiella pneumoniae. The antimicrobial resistance profile of Klebsiella pneumoniae from this study was Ampicillin (98.2%), Trimethoprim/Sulfamethoxazole (65.5%), Cefotaxime (54.5%), Norfloxacin (23.6%), Cefuroxime (50.9%), Ceftazidime (45.4%), Tetracycline (47.3%), Gentamicin (38.2%), Amikacin (10.9%), Meropenem (5.5%), Ciprofloxacin (38.2%), Cefoxitin (38.2%) and Chloramphenicol (30.9%). Thirty-nine (39) of the 55 Klebsiella pneumoniae isolates identified (70.9%) were multi drug resistant (MDR), 15 of them (27.27%) were possibly extensively drug resistant (XDR) and 1 of them (1.8%) was possibly pan drug resistant (PDR). Forty-nine (49%) of the Klebsiella pneumoniae isolates were described as potential ESBL producers. Out of this figure, 74% were found to be ESBL positive.

Conclusion: This study reveals high antimicrobial resistance rates in Klebsiella pneumoniae, including MDR, XDR, and ESBL-producing strains, posing a serious threat to treatment efficacy in Ghana. Strengthened antibiotic surveillance, stricter enforcement of the National Action Plan on AMR, and nationwide research are needed to estimate the national burden, combat resistance and improve infection management strategies.

Is early life exposure of male infants to acetaminophen impeding testicular development and functions? A concern supported by animal and human studies

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The over-the-counter analgesic and antipyretic drug Acetaminophen (n-acetyl-p-aminophenol, APAP; paracetamol) is a non-specific cyclooxygenase (Cox) inhibitor highly used by pregnant women (Bandoli et al. Paediatr Perinat Epidemiol; 2020; 34:237-246; Hider-Mlynarz et al. Br J Clin Pharmacol (2018) 84: 1324–1334) and given to babies. While male fertility rates have declined over the last decades, maternal exposure to APAP and common NSAIDs was found to be associated with increased risk of reproductive syndromes in male infants, such as reduced anogenital distance and cryptorchidism (Wu et al.; Front. Pharmacol; 2023; 14:1094435). These findings in humans were corroborated by animal studies reporting adverse effects of APAP on various male reproductive outcomes, observed in the first and second generations (Bauer et al. Nat Rev Endocrinol; 2021; 17:757-766). Our goal was to investigate the mechanism(s) by which APAP alters male testicular function in early postnatal ages, using APAP doses/concentrations equivalent to those measured in babies. Because of the intricate interactions between key cell types in the developing testis, we examined the in vivo and in vitro effects of APAP in neonatal and juvenile rodent models, assessing the transcriptome, protein levels and morphology in testis and testicular cells, in comparison to vehicle control and selective Cox-1 and -2 inhibitors.

In vivo studies performed by oral administration of vehicle or APAP at 0.7 and 1.4 mg/day to postnatal day (PND) 1 to 7 rat pups, revealed histological alterations and changes in testicular transcriptome by single cell RNAseq and quantitative real time PCR analyses. These changes included increased Sertoli cell vacuolization and increased Notch3 protein levels in spermatogenic cells at PND8 and 90 shown by immunofluorescence, as well as germ cell sloughing and increased testosterone production at PND90 (Culty et al. unpublished data).

In vitro studies of the undifferentiated C18-4 mouse spermatogonia cell line showed that APAP and the Cox2 selective inhibitor NS398 decreased differentiation gene markers in a dose-dependent manner, while the expression of differentiation genes was increased in Cox1 knockdown cells. In addition, the Tgfb, Wnt, and Notch pathways were upregulated by APAP and selective Cox inhibitors. These data indicated differential roles of Cox 1 and 2 in spermatogonia (Tran-Guzman et al. Andrology; 2024; 12:899-917). APAP also dysregulated the expression of key genes in immature TM4 murine Sertoli cells, including changes in Sox9, Lif and cJun genes critical for Sertoli cell function (Corpuz-Hilsabeck; Cells; 2023; 12:1804; and unpublished data). These data showed that neonatal exposure to APAP and early postnatal testicular cell treatments with APAP alter the development and function of germ, Sertoli and Leydig cells in rodents.

Taken together with published epidemiological and animal studies, our results indicate that APAP targets several early postnatal testicular cell types, which may be at the source of some of its adverse effects, e.g. developmental reproductive defects, cryptorchidism, and infertility. Since APAP purchase does not require a prescription, pharmacists could advise parents to avoid giving infants multiple doses of APAP for prolonged periods, as APAP exposure might affect testicular function and future fertility of their baby boys.

Making medicines safer for pregnancy: How pharmacokinetic modelling is transforming drug safety through real-world case studies

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Pregnancy significantly alters drug metabolism, distribution, and elimination due to physiological changes such as increased blood volume, altered enzyme activity, and enhanced renal clearance. These changes can lead to subtherapeutic drug levels or excessive foetal exposure, posing risks to both mother and baby. Traditional clinical trials in pregnant populations are limited due to ethical concerns, making Physiologically Based Pharmacokinetic (PBPK) modelling an essential tool for predicting drug behaviour and optimising dosing strategies in pregnancy. This study presents four case studies demonstrating the application of PBPK modelling and virtual clinical trials to improve medication safety and efficacy in pregnancy.

The first case study focuses on venlafaxine, a commonly used antidepressant metabolised by CYP2D6. PBPK simulations indicate that maternal venlafaxine concentrations progressively decline from the second trimester onwards, with 70–98% of patients in the extensive (EM) and ultrarapid metaboliser (UM) groups falling below the therapeutic threshold by the third trimester. Simulations also confirmed placental transfer of venlafaxine, raising concerns about foetal exposure. Model-based dose optimisation suggested an increase from 75 mg to 225–375 mg daily, depending on the CYP2D6 phenotype, to maintain therapeutic efficacy while minimising foetal drug levels.

The second case study examines fluvoxamine, another CYP2D6-dependent antidepressant. Simulations demonstrated that maternal plasma levels drop significantly by the third trimester, leading to subtherapeutic exposure in 50–80% of EM and UM patients. In contrast, poor metabolisers (PM) exhibited prolonged drug exposure, leading to higher foetal plasma levels. Adjusted dosing strategies were developed based on gestational stage and

CYP2D6 phenotype, ensuring adequate maternal drug exposure while preventing excessive foetal accumulation. The study highlights how PBPK modelling can refine dose adjustments based on genetic background and gestational age.

The third case study investigates methadone, used in opioid substitution therapy. Due to pregnancy-induced changes in CYP2B6 and CYP2C19 activity, standard methadone doses result in significant declines in maternal plasma concentrations, with 75–94% of pregnant women falling below therapeutic levels at term. PBPK-guided dose adjustments, increasing from 90 mg to 180 mg by late pregnancy, successfully restored maternal methadone levels while preventing excessive foetal exposure, crucial for reducing the risk of neonatal withdrawal syndrome (NAS).

The fourth case study examines sertraline, a selective serotonin reuptake inhibitor (SSRI) metabolised by CYP2C19. PBPK modelling confirmed that EM and UM phenotypes required dose increases of 100–150 mg daily throughout pregnancy, while PM individuals required a lower but stable dose (50 mg in trimester 1, 100 mg in trimesters 2 and 3). The study underscores the importance of genotype-informed dosing in ensuring stable maternal drug levels while controlling foetal exposure.

These case studies highlight how PBPK modelling can provide evidence-based guidance for precision dosing in pregnancy, integrating physiological, metabolic, and genetic factors to optimise medication safety. As clinical trials in pregnant populations remain limited, PBPK modelling offers a robust, ethical, and cost-effective approach to improving maternal and foetal health outcomes. Future research should expand this approach to additional high-risk medications, further advancing personalised medicine in pregnancy care.

Integrating graph convolutional networks and computational chemistry for pharmaceutical multicomponent crystal prediction and classification

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Introduction: Multicomponent crystals (MCCs), including cocrystals, salts, hydrates, solvates and their inherently overlapping constituents (e.g., cocrystal hydrates, salt solvates), offer significant potential for optimising the physicochemical properties of active pharmaceutical ingredients (APIs), including solubility, stability, and bioavailability. A key challenge in early-stage MCC development is efficient coformer screening, predicting crystal forms, and understanding the underlying mechanisms of MCC formation. Recent advancements i in computational chemistry and deep learning (DL) approaches, have led to more effective strategies for coformer screening and predicting MCC formation. However, existing methods are mainly limited to cocrystals, despite the frequent occurrence of other crystal forms in experimental settings. To address these limitations, a graph convolutional network (GCN)-based DL model, MCC-GCN, was developed for predicting and classifying MCCs into four categories: cocrystal, salt, hydrate, and fail. In addition, computational chemistry techniques were integrated with the model to enhance interpretability and elucidate the mechanisms of MCC formation.

Method: A dataset of 34,618 samples, extracted from the Cambridge Structural Database, CSD was curated, comprising 15,875 salts, 11,118 cocrystals, 6,573 hydrates, and 1,052 negative experimental samples. Data augmentation via coformer pair swapping doubled the dataset size. Molecular structures were characterised, and the MCC-GCN model was trained and validated using 10-fold cross-validation. Transfer learning was applied using MCC cases of minoxidil, kopexil, and kopyrrol. Experimental MCC samples of two model APIs (kopexil and kopyrrol) and 32 coformers were prepared via slow solvent evaporation in ethanol and methanol, and characterised using X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FTIR), and single-crystal X-ray diffraction (SXRD). Molecular electrostatic potential (MEP) surfaces were calculated to predict interaction strengths and identify potential reaction sites.

Results: MCC-GCN achieved 80.12% balanced accuracy (BACC) on the 10-fold cross-validation set, outperforming seven benchmark models (SVM, RF, GCN, DNN). For kopexil and kopyrrol, the model achieved 50.0% accuracy, with transfer learning enabling adaptation to structurally similar APIs. Experimentally, two cocrystals, five salts, and 17 hydrates of kopexil, along with five cocrystals, nine salts, and eight hydrates of kopyrrol, were successfully synthesised and confirmed by XRPD, DSC, FTIR, and SXRD. MCC-GCN correctly predicted 50% of the experimental cases, demonstrating its practical utility. MEP surface analysis revealed that intermolecular interactions are the primary driving force for new crystal formation, while hydrogen bond donor/acceptor groups (strength and numerical differences) and polar surface area influence the formation of distinct crystal forms.

Conclusion: The MCC-GCN model was successfully developed, achieving 80.12% BACC on the 10-fold cross-validation set and 50.0% accuracy for experimental cases involving kopexil and kopyrrol, highlighting its practical potential. A total of seven cocrystals, 14 salts, and 25 hydrates were experimentally prepared and characterised. The study demonstrated that intermolecular interactions drive crystal formation, while hydrogen bond donor/acceptor groups

(strength and numerical differences) and polar surface area play critical roles in determining the specific crystal forms. These findings highlight the utility of MCC-GCN in accelerating MCC development and providing profound insights into crystal engineering.

Cancer treatment focusing on cytotoxicity induction by combined use of nadifloxacin and UVA irradiation

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Background: New quinolone antibiotics (NQLs) are well known to cause drug-induced photosensitivity. This is a phototoxic or photoallergic reaction caused by exposure to ultraviolet or visible light after taking the medicine. In this study, we aimed to develop a cancer treatment that does not suffer from drug resistance. To confirm the possibility of drug repositioning of NQL into an anticancer drug, we investigated the antitumor effects of the combination of nadifloxacin (NDFX) and UVA in vitro and in vivo.

Materials and Methods: First, in vitro study, we measured the generation of singlet oxygen by the combination of NDFX and UVA using the decrease in absorbance of N,N-dimethyl-4-nitrosoaniline. Then, we evaluated DNA fragmentation using human promyelocytic leukemia HL-60 cells. Furthermore, we compared the proliferation rate up to 48 hours after treatment using Sézary syndrome HUT78 cells. Finally, in an in vivo study, we investigated the effect of treatment on the proliferation of sarcoma 180 solid tumors. The above conditions of the experiment were compared under non treatment, NDFX alone, UVA alone, and NDFX and UVA treatment.

Results: Combining NDFX with UVA results in significant production of singlet oxygen. No singlet oxygen generation was observed in non-treatment, NDFX alone, and UVA alone treatment. UVA alone and NDFX alone induced the same level of cell proliferation compared to non-treated cells. On the other hand, combined treatment with NDFX and UVA inhibited cell proliferation by approximately 90%, which correlated with the effect on singlet oxygen production. In addition, in vivo studies showed that solid tumors increased in the non-treatment, NDFX alone, and UVA alone, whereas the combined treatment of NDFX and UVA tended to reduce the size of solid tumors.

Conclusion: The cell damage by NDFX was significantly enhanced by UVA irradiation, which may suggest reactive oxygen species plays a primary role in photodynamically induced cytotoxicity. In addition, combined treatment with NDFX and UVA inhibited the growth of solid tumors in vivo study. It suggests that combined treatment with NDFX and UVA could be used for cancer therapy.

Experiences of innovative alternative medicine therapy, ortho-cellular nutrition therapy (OCNT) in community pharmacy

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Introduction: In modern society, people experience significant stress due to ever-changing environments. As a result, the immunity system has become more important than ever. Individuals with weaken immunity system are more susceptible to various diseases, including chronic inflammation, hypertension, diabetes, hyperlipidemia and cancers. While patients typically seek medical treatment from doctors and receive pharmaceutical medications, community pharmacists have an opportunity to support disease management through health functional nutrients.

Purpose: Ortho-Cellular Nutrition Therapy (OCNT) is an innovative approach that utilizes bioactive nutrient formulations, enhanced with nano-technology, to support cellular repair and optimize antioxidant, detoxification, and sirutuin-autophagy system. The CellMed Journal is published annually to report the cases studies on OCNT applications, sharing valuable insights with community pharmacists for their clinical practice.

Methods: Between 2023 and 2024, CellMed reported 109 cases of patients with various chronic diseases who had previously been treated with conventional medications but showed poor disease control. This study reviews those cases by disease category and presents the clinical efficacy of OCNT through five selected cases (2 cases of dermatological disease, 1 case of hyperlipidemia, 1 case of osteoporosis, 1 case of menopausal disorder). The effectiveness of OCNT was evaluated based on clinical records, including blood test, imaging records (X-ray, MRI), and patients interviews conducted at community pharmacies before and after OCNT treatment.

Results: 109 cases cover a range of patients having gastrointestinal, cardiovascular, metabolic disease, cancer and dermatological disorders. The initial treatment period phase of OCN, which involved high- dose of flavonoids, carotenoids, vitamin C lasted approximately four months, corresponding to the lifespan of red blood cells. For autoimmune disease, treatment lasted 6-12 months, with long-term therapy recommended to prevent recurrence.

LDL level in a hyperlipidemia patient is significant decreased after one month of OCNT treatment, dropping from

208mg/dL to 129mg.dL and further reducing to 109mg/dL after four months. Osteoporosis patient showed a T-score improvement to greater than -2.5, indicating enhanced bone marrow density (BMD). Menopausal syndromes completely disappeared after six months OCNT treatment. Additionally, non-chemical natural topical lotions and creams were provided to dermatological patients alongside OCNT. For example, patients with hand eczema showed significant improvement, as measured by Eczema Area and Severity Index (EASI), following OCNT treatment.

Conclusion: OCNT represents a new paradigm using health-functional nutrients to support patients in community pharmacies. While OCNT cannot replace conventional treatments for all chronic diseases, it has been shown to significantly enhance patients' quality of life in many cases. Furthermore, OCNT expands the role of community pharmacists as essential partners in health management. Therefore, it is recommended as a complementary approach for managing chronic diseases in community pharmacy. To further evaluate and optimize OCNT, establishing standardized guidelines for case reports is strongly recommended.

Novel controlled release nano-microneedles system combined with photodynamic therapy for malignant melanoma treatment

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Introduction: Malignant melanoma (MM) is an aggressive and often fatal form of skin cancer. Conventional chemotherapy and targeted therapies face substantial limitations. Triptolide (TP), a bioactive diterpenoid isolated from Tripterygium wilfordii, exhibits potent anti-melanoma activity but suffers from poor aqueous solubility, dose-limiting toxicity, and unfavorable pharmacokinetics. To address these constraints, it is crucial to develop a dual strategy that identifies a synergistic adjuvant to mitigate TP-associated toxicity while engineering a drug delivery system for improved pharmacokinetic profiles, ensuring toxicological safety and tumor-targeting precision. Based on these, our study aims to develop a novel controlled release nano-microneedles system (TP-Ce6-GA@MNs) through co-loading TP and the photosensitizer chlorin-e6 (Ce6) into a self-assembled GA hydrogel matrix. TP and Ce6 offer synergistic antitumor effects, while GA enhances efficacy by mitigating TP-induced toxicity and improving targeted delivery. The system is engineered to achieve optimised therapeutic precision with reduced toxicity for effective MM treatment.

Methods:
1. A stable GA hydrogel was synthesized as a TP carrier, with systematic optimization of the TP-to-Ce6 mass ratio. The resulting TP-Ce6-GA@MNs system was engineered and characterized for morphology, mechanical strength, drug loading, dissolution, and transdermal properties.
2. Antitumor efficacy was assessed through in vitro cytotoxicity, invasion inhibition, and apoptosis induction assays on A375 melanoma cells. Ce6 targeting specificity was verified by confocal microscopy, while flow cytometric analysis quantified cellular uptake and reactive ROS generation. ELISA revealed GA-mediated modulation of pro-inflammatory cytokines (IL-6, TNF-α). In vivo biodistribution studies tracked drug accumulation in major organs, complemented by transdermal pharmacokinetic profiling of TP via microdialysis (cutaneous and circulatory).
3. Therapeutic efficacy was evaluated through assessment of tumor volume, weight dynamics, growth inhibition rate, and apoptotic cell quantification via TUNEL assay.GA's anti-inflammatory effect was assessed by skin cytokine levels, and biosafety was evaluated through body weight, hemolysis, H&E staining, and blood tests.

Results:
1. The TP-Ce6-GA@MNs exhibited well-defined morphology and excellent mechanical properties. The drug loading capacity was 15.62 ± 0.07 μg/mg, remaining stable at 15.51 ± 0.17 μg/mg after 15 days of storage. The MNs demonstrated effective dissolution both in vitro and vivo, with complete drug release occurring within 24 hours.
2. TP-Ce6-GA@MNs demonstrated superior antitumor activity in vitro. Confocal microscopy and flow cytometry revealed significant cellular uptake within 24 hours, accompanied by high ROS generation. And GA treatment significantly reduced IFN-α, IL-6, and IL-1β expression. Microdialysis studies revealed key pharmacokinetic parameters of TP within the TP-Ce6-GA@MNs system, showing significantly higher TP accumulation in tumor tissues compared to normal skin.
3. TP-Ce6-GA@MNs achieved the most pronounced antitumor effects, with a tumor volume of 90.81 mm^3, tumor weight of 0.01 g, and a 94.21% inhibition rate. The TUNEL assay showed the highest apoptosis rate. Organ H&E staining, along with blood and biochemical tests, revealed no significant abnormalities, indicating high safety and low toxicity.

Conclusion: This study successfully developed a novel controlled release nano-microneedles system for the treatment of MM. The proposed strategy offers a promising approach for localized tumor therapy and may be extendable to other skin cancer models, supporting its potential for clinical translation.

Efficacy of GLP-1 analogues in the treatment of obesity

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Background information: Obesity is a global pandemic and according to the World Health Organization it is defined as an accumulation of abnormal or excessive fat that can be harmful to health. This metabolic pathology leads to the alteration of other parameters such as HbA1c related to diabetes mellitus. There are different treatments for obesity and the main objective of this work is to evaluate the effectiveness of GLP-1 analogues in the treatment of obesity and Type 2 diabetes mellitus compared to other therapeutic alternatives.

Purpose: To quantify the weight loss experienced by overweight or obese patients treated with a GLP-1 analogue drug over different time periods compared to placebo or other treatments and to assess the effectiveness of GLP-1 analogue drugs by quantifying the reduction in HbA1c levels compared to other alternatives or placebo.

Methodology: A systematic review and a meta-analysis of randomized controlled trials addressing the effectiveness of weight loss in kg and the variation of HbA1c in people treated with GLP-1 analogues were conducted.

We combine estimates from the different studies selected to estimate the mean difference (MD) with 95% CI. Heterogeneity was explored with Chi2 y Tau2 statistics. To learn consistency, I2 was also used

The overall estimates in the pooled analysis were obtained with the Review Manager version 5.3, also by this means, a forest and a funnel plot were obtained, this latter for visual investigation of publication bias. The systematic review was undertaken according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist

Results: We finally selected 26 studies. A weight loss of 4.30 kg was recorded in the general population and 6.30 kg in obese people. In relation to the time, weight loss was 0.99 kg in studies with a duration of weeks and 6.53 kg in the studies with a duration of >24 weeks. The HbA1c value decreased 0.90% in the entire population studied and 0.97% in obese people. According to the time, the decrease in the HbA1c value was 0.91% in studies with a duration of weeks and 0.88% in the studies with a duration of > 24 weeks.

Conclusions: There is weight loss with treatment with GLP-1 analogues, especially in obese people, and the HbA1c value improves with a small weight loss. The adverse events observed are not serious and subside within a few weeks of treatment. In addition to pharmacological treatment, a lifelong commitment to diet and physical exercise is necessary for the patient. Constant innovation makes that pharmacological treatment has a high cost and there is a lack of supply.

Prototyping of biofunctionalized labor monitoring equipment using 5G communication

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This proposal focuses on developing prototypes utilizing 3D technology and 5G for data transmission in medical applications. In recent years, 3D technology has been widely adopted in the medical field. Childbirth requires continuous monitoring to ensure the health and safety of both the mother and the fetus. Early detection and timely intervention are crucial to preventing complications, as unexpected adverse events during labor can pose significant risks. Effective monitoring and intervention can substantially reduce complications and improve birth outcomes. Currently, childbirth monitoring relies primarily on in-person observation, which can be time-consuming, labor-intensive, and prone to human error. This research presents significant scientific and commercial potential by integrating advanced technology with expertise in Pharmacology and Toxicology, offering a safe and effective solution to enhance animal welfare. Building upon previously achieved results, this project ensures a structured and secure approach to achieving its objectives. The primary goal is to develop a birth monitoring device prototype utilizing 5G for real-time data transmission. The proposed methodology involves designing the device's framework using PEEK filament in a 3D printer and encasing it in medical-grade silicone, creating a cost-effective solution. The device is activated by fetal movement shortly before birth, triggering an alert in the clinical manager's application. To guarantee the safety of the materials used, cytotoxicity, toxicity, and allergenicity tests were conducted. The results confirmed the absence of harmful effects, with testing methods including the comet assay, HET-CAM, BCOP, and CAM-TBS. Additionally, the application's source code is being officially registered with Brazil's National Institute of Industrial Property (INPI). This proposal contributes to society by fostering accessible technological innovation, eliminating the need for imported components, and enabling its integration into the Brazilian Unified Health System (SUS). The project has reached Technology Readiness Level (TRL) 6, facilitating market adoption and technology transfer. Among the UN/SDGs, this project is linked to Goal 3 (Ensure healthy lives and promote well-being for all), Goal 9 (Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation), Goal 12 (Renewable consumption and production) and Goal 17 (Strengthen the means of

implementation and revitalize the global partnership for sustainable development).

Berberine Inhibits ISG15 and pyroptosis to attenuate diabetic kidney disease inflammation and fibrosis

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Background: Diabetic kidney disease (DKD) is a severe microvascular complication of diabetes, characterized by inflammation and tubular fibrosis. These pathological changes significantly contribute to the progression of renal dysfunction in diabetic patients. Berberine (BBR) has been widely recognized for its diverse pharmacological effects, including anti-inflammatory and anti-fibrotic properties. However, the detailed mechanisms underlying its protective effects against DKD remain unclear. Purpose: To investigate the protective effects of BBR on diabetic kidney disease, specifically focusing on its impact on inflammation and tubular fibrosis in both in vivo and in vitro models.

Methods: We used STZ/HFD-induced DKD mice and high glucose (HG)-treated renal tubular epithelial cells (TECs) as our experimental models. The protective effects of BBR were evaluated by assessing the levels of inflammation and tubular fibrosis in these models. Molecular mechanisms were explored using qPCR and Western blotting assays to examine the expression of ISG15 and pyroptosis-related proteins. Additionally, we overexpressed ISG15 in kidneys and TECs to determine its role in renal tubular cell injury and the protective effects of BBR.

Results: We found that BBR treatment significantly reduced inflammation and tubular fibrosis in STZ/HFD-induced DKD mice. Histological analysis revealed a marked decrease in inflammatory cell infiltration and collagen deposition in the renal tubules of BBR-treated mice compared to untreated controls. Also, BBR effectively reversed the HG-induced inflammation and fibrosis in TECs. Specifically, BBR treatment normalized the expression of pro-inflammatory cytokines and fibrotic markers that were upregulated by HG exposure. Mechanistically, qPCR and Western blotting assays demonstrated that BBR abolished the HG-induced upregulation of ISG15, a key regulator of cellular stress responses. Additionally, BBR modulated the expression of pyroptosis-related proteins, thereby inhibiting the programmed cell death pathway associated with inflammation and tissue damage. Furthermore, overexpression of ISG15 in kidneys and TECs exacerbated renal tubular cell injury and abolished the protective effects of BBR against DKD. These findings highlight the critical role of ISG15 and pyroptosis in mediating the beneficial effects of BBR in DKD.

Conclusion: Our findings indicate that BBR can attenuate inflammation and tubular fibrosis in DKD by inhibiting ISG15 and pyroptosis. These results provide a novel potential therapeutic strategy for the treatment of diabetic kidney disease, highlighting the importance of targeting ISG15 and pyroptosis pathways in DKD management.

Medicines shortages: A comprehensive assessment of the causes and impact with recommendations for collaborative action.

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Background: Medicines shortages are increasing worldwide, with a growing concern about the impact on patient care.

Multiple indicators have shown an increase in medicines shortages at a level of complexity and scale not previously seen. Intensive work already happens to ensure the UK continues to maintain access to medicines for most patients with the majority of prescription items in primary care being dispensed to patients without issue. However, even though only 3% of medicines reimbursed by the National Health Service (NHS) are reported to be in shortage, the impact is felt across the system.

Those most negatively impacted are patients, with patient charities increasingly highlighting the difficulties patients are experiencing in accessing medicines. The impact on healthcare professionals is also significant, adding to workloads and increasing pressure.

Purpose: With growing concern from pharmacists and patient groups around the impact of medicines shortages, the Royal Pharmaceutical Society (RPS) supported by charities, patient groups and supply chain representatives, began work on producing a comprehensive report with subsequent recommendations to address these issues.

Method: A variety of qualitative and quantitative research methods were used to gather data to inform the report.

A rapid scoping review of the international evidence base for medicines shortages was conducted. Engagement sessions, focus groups and one to one interviews were held to understand the impact of medicines shortages on healthcare teams, and the innovative methods used to help manage shortages in practice. A patient survey gathered the patient experience and provided qualitative and quantitative data.

An independent Great Britain-wide advisory group was formed to support the work. Members represented the medicines regulator, national medicines supply teams, manufacturers, wholesalers, pharmacy and healthcare teams

together with patient representation. The group provided independent expertise and advice to aid the development of the report and its recommendations.

Results: Quantitative data gathered indicated the scale of the issue. 90% of respondents had problems sourcing a particular medicine more than once over a 12-month period, with 50% of respondents having problems on more than four occasions. Patients reported having to take multiple steps themselves to try to source a medicine; 51% had to return to the prescriber, 41% had to visit multiple pharmacies in search of medicines and 24% of respondents tried to source medicines online.

The culmination of this work was a final report with a series of recommendations for future collaborative action across five themes.

Conclusion: Medicines Shortages: Solutions for Empty Shelves provides a comprehensive assessment of the causes of medicines shortages, impact on patients, pharmacy teams and wider healthcare professionals and outlines what more needs to be done to mitigate against and manage medicines shortages.

Recommendations include a call for the UK government to develop a UK-wide strategy for shortages, enact legislation to enable community pharmacists to make minor amendments to prescriptions, enable greater data sharing to support planning and predict demand, and to develop cross-sector emergency protocols for shortages of life-critical medicines.

Needs assessment for a local pharmaceutical stockpile in the municipality of Bergen, Norway

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Introduction/Background information: In the aftermath of the covid-19 pandemic, the topic of preparedness was highly discussed in Norway. The Norwegian Pharmaceutical Stockpile (NPS) in 2020, with the aim of providing the secondary healthcare system with necessary medicines in emergency situations. For the primary healthcare system, the responsibility for pharmaceutical stockpiling is divided between the pharmaceutical wholesalers, who are obliged to have a limited number of pharmaceutical products in stock, and the municipalities, who are responsible for providing medications for their own institutions, such as care homes. Although tasked with the responsibility of providing a stockpile for their institutions, few guidelines have been provided for the practicalities. The latter has spurred a collaboration between the local municipality of Bergen and the Centre for pharmacy at the University of Bergen on development of a needs assessment for a local pharmaceutical stockpile.

Method: Two master projects were designed, in collaboration with a representative from the Bergen municipality, and the NPS. The aim of the project was to describe the existing pharmaceutical stockpiles of primary care emergency rooms and care homes, respectively. In addition, the students investigated relevant personnel's knowledge and attitudes towards pharmaceutical stockpile planning. Both projects used similar qualitative methodology, including observation of pharmaceutical stockpiles and semi-structured interviews with relevant healthcare personnel.

Results: The observation of the pharmaceutical stockpile at the primary care emergency rooms showed that the various locations stocked a limited supply of medications. The stock was conveniently planned, and did not follow a particular guideline. The participants in the interviews displayed little knowledge of preparedness planning. In general, they did not view the primary care emergency rooms as actors in pharmaceutical stockpiling, rather they saw their role as transient and acting as a temporary place where patients could be triaged for other levels in the healthcare system.

Conclusion: The needs assessment for a local pharmaceutical stockpile in the Bergen municipality performed in these master projects demonstrated that further analysis and planning is needed. Furthermore, healthcare personnel's knowledge about local preparedness planning is limited. Master projects in pharmacy can be designed in collaboration with government actors to achieve relevant results for societal needs.

Academic detailing service as a form of educational outreach to enhance evidence-based drug therapy prescribing in primary care

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Introduction: Academic detailing transforms complex, evidence-based medical information into practical, actionable insights for healthcare providers. This interactive educational outreach, ideally conducted one-on-one, offers unbiased, evidence-based information about medications and therapeutic decisions. The primary goal of academic detailing is to enhance patient care by ensuring healthcare providers have access to the latest, most accurate information they can apply in their clinical practice. By identifying and addressing knowledge gaps, academic detailing bridges the gap between research and practice,

empowering healthcare providers to make informed, individualized decisions that benefit their patients.

Purpose: Canada is home to four main academic detailing services, including the RxFiles Academic Detailing Service based in Saskatchewan. The primary objective of RxFiles is to support primary care providers by enhancing their knowledge and confidence in drug therapy management through personalized educational outreach. This service aims to promote evidence-based practices and improve clinical decision-making, ultimately leading to better patient care.

Method: RxFiles employs a team of trained academic detailers, all of whom are pharmacists, to conduct one-on-one educational sessions with healthcare providers. Sessions are based on the latest clinical evidence and are tailored to address specific therapeutic topics. The detailers use various educational materials, including drug comparison charts, newsletters, and infographics, to facilitate knowledge translation. The impact of these sessions is evaluated through post-session surveys, feedback forms, and performance metrics.

Results: The RxFiles Academic Detailing Service conducts two unique academic detailing campaigns annually, each addressing topics pertinent to primary care providers. Recent campaigns (2023 to Spring 2024) focused on anxiety, menopause, and acute otitis media, reaching 991, 1154, and 872 healthcare providers, respectively. Survey data from these campaigns indicated significant improvements in healthcare providers' knowledge and confidence in managing these therapeutic areas.
•Anxiety Campaign: 28% response rate, 100% of respondents reported enhanced knowledge, 96% reported increased confidence in managing drug therapy, and 36-76% indicated the information would change their practice based on the three key messages addressing practice gaps.
•Menopause Campaign: 14% response rate, with 100% of respondents reporting enhanced knowledge and increased confidence in managing drug therapy. Additionally, 43-66% indicated the information would change their practice based on the four key messages addressing practice gaps.
•Acute Otitis Media Campaign: 21% response rate, 99% of respondents reported enhanced knowledge, 97% reported increased confidence in managing drug therapy, and 34-80% indicated the information would change their practice based on the three key messages addressing practice gaps.

Conclusion: The RxFiles Academic Detailing Service has effectively enhanced healthcare providers' knowledge and confidence in managing various therapeutic areas through targeted educational campaigns. The positive outcomes from the anxiety, menopause, and acute otitis media campaigns demonstrate the service's success in bridging the gap between research and clinical practice. These findings highlight the value of academic detailing in promoting evidence-based practices and optimal drug therapy in primary care. Future efforts will focus on expanding the service's reach, exploring new therapeutic areas, and continuously improving educational materials based on provider feedback, all aimed at supporting evidence-based medicine and improving patient outcomes.

The impact of academic detailing on primary care providers and menopause management

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Introduction: Menopause is a significant phase in a woman's life, often accompanied by various symptoms that can affect quality of life. Despite its prevalence, there is a gap in knowledge and confidence among healthcare providers in managing menopause effectively. Academic detailing offers a personalised educational approach to bridge this gap by providing evidence-based information and practical guidance. This study aims to evaluate the impact of academic detailing sessions on healthcare providers' knowledge and confidence in managing menopause.

Purpose: The primary objective of this study was to assess the effectiveness of academic detailing in enhancing healthcare providers' understanding and management of menopause within the primary care setting in Saskatchewan, Canada. It was hypothesized that academic detailing would significantly improve providers' knowledge, confidence, and clinical practices related to menopause management.

Method: This study employed a mixed-methods design, combining a quantitative survey and qualitative feedback. Academic detailing sessions were conducted with healthcare providers in Saskatoon, focusing on evidence-based drug therapy management of menopause. Participants completed a post-session survey to measure changes in knowledge and confidence. Additionally, qualitative feedback was collected to gain insights into the perceived value and impact of the sessions.

Results: The results indicated a significant improvement in healthcare providers' knowledge and confidence in managing menopause post-session. 1154 healthcare providers received an academic detailing session (605 physicians, 252 pharmacists, 175 nurses, 122 others). Of the 165 providers who responded to the survey, 100% of respondents indicated that the program content enhanced their knowledge and increased their confidence in managing drug therapy in this area. Among the four key messages designed to address practice gaps, 43-66% of respondents indicated they would modify their practice based on the information provided. Qualitative feedback highlighted the practical applicability of the information provided and the value of personalized educational interactions. Providers reported increased comfort in discussing menopause with patients and implementing evidence-based practices.

Conclusion: This study demonstrated that academic detailing significantly enhances healthcare providers' knowledge and confidence in managing menopause. The findings indicate that personalized educational sessions effectively bridge practice gaps, with 43-66% of respondents willing to modify their practice based on the information provided. This improvement suggests that academic detailing is a valuable tool in continuing medical education. However, the methods could be improved by incorporating a larger sample size. Additionally, a longitudinal follow-up could assess the long-term impact of academic detailing on clinical practice. Future research should explore the impact of academic detailing on patient outcomes to provide a more comprehensive understanding of its benefits.

A case report of drug-induced liver injury (DILI) in a cervical cancer patient treated with toripalimab combined with chemotherapy

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Introduction: Toripalimab, a PD-1 inhibitor, has been approved for the treatment of melanoma, urothelial cancer, nasopharyngeal cancer, esophageal squamous cell cancer, non-small cell lung cancer, renal cancer, small cell lung cancer, and triple negative breast cancer. It has not been approved to treat cervical cancer, and the case of DILI caused by it has been rarely reported. The aim of the study was to report a case of drug-induced liver injury (DILI) caused by the combination of toripalimab and chemotherapy, and explore the key points in providing pharmaceutical care. Methods: The roles of clinical pharmacists in the treatment of a case of cervical cancer were reported, including differentiation diagnosis of the cause of DILI, optimization of the treatment regimen, and providing comprehensive patient education. Results: a 42-year old cervical cancer patient underwent neoadjuvant therapy with paclitaxel+carboplatin for the first cycle and paclitaxel+carboplatin+toripalimab for the second cycle. After 13 days, the patient experienced G4 liver injury. Clinical pharmacists analyzed that there was a high possibility of immune checkpoint inhibitors -induced immune related hepatoxicity (ICIH) and suggested the doctor to add methylprednisolone (1mg/kg, qd, ivgtt) until the patient showed significant improvement, and then change to prednisone for another 8 weeks (gradually tapered off). The patient fully recovered 65 days after the occurrence of liver injury. Conclusion: For patients with highly suspected ICIH, sufficient corticosteroid should be given to the patient throughout the treatment course. Comprehensive patient education should be provided to patients, and adverse drug reactions during hormone therapy should be closely monitored to ensure safety and efficacy of the treatment.

Exploring community-based pharmaceutical care: Identifying new medical problems due to deviations in medication adherence behaviour

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Background: Diseases are not exclusive to the elderly. However, many community residents lack adequate medical knowledge, which often leads to poor medication adherence. These individuals may also be overly confident in their own judgment, preventing them from following doctors' instructions. As a result, new medical problems can arise—such as strokes—that not only waste medical resources but also negatively impact individuals' physical, mental, and spiritual well-being. Pharmaceutical care for the public covers many items, such as physical assessment, nutrition, social life, biochemical data ,Mobility ,medication status, and there are also people who use folk remedies and cause many medical problem. Objective: Discuss community-based pharmaceutical care with pharmacy students and understand how poor medication adherence habits can lead to drug safety issues, and repeat medication。 reduced therapeutic effects, and new medication problems arise. the emergence of new diseases. The care of the community pharmacy to the community is whole-person care.

Method: Mr. Cai is a 56-year-old man who smokes and chews betel nut. He has diabetes, hypertension, and hyperlipidemia. He would occasionally return his unused diabetes and lipid-lowering medications to the pharmacy for disposal. He admitted that he rarely takes these medications because a previous experience with a lipid-lowering drug caused severe muscle pain and made it difficult for him to walk. In addition, he held the misconception that chewing betel nut could lower his blood sugar, There was no control over the patient's diet, Throughout this process, multiple consultations and health education sessions were provided, and the pharmacist even assisted in communicating his situation to his doctor. When the patient returned to the pharmacy to collect medication for chronic diseases, he was found to have re-medication with the prescription from another hospital. Actively communicate and educate him,and assist in communicating with physicians and conducting diabetes health education。 hoping to help him have correct medication behaviors and improve his health.

Result: After suffering a stroke, As a result, the problem of repeating the medication occurred. Afraid of upsetting his doctor, Mr. Cai insisted on sticking to his old medication habits. Despite many attempts at communication and counseling, I wanted to help patients communicate with their

physicians to integrate medications and perform diabetes health education. However, due to the psychological disorder of the individual case, the expected results have not yet been achieved.However, efforts to help him are ongoing.

Discussion: The public's knowledge of proper medication use is directly related to health, and promoting medication safety is the responsibility of pharmacists. Improving patients' adherence to their medication regimens is a crucial task for community pharmacists. Only through continuous communication and education can we reduce medication-related health issues and associated healthcare costs.The pharmacist of the community pharmacy is the first stop for the people's medication and health consultation, and is a good neighbor, please be friends with the pharmacist.

Enhancing medication understanding in patient and efficiency in community pharmacy with thermal-printed dispensing labels and colour-coded envelopes: The T-label initiative

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Introduction: Effective dispensing labels are crucial for the safe and appropriate use of medicines. Studies have shown that non-compliance with labelling standards is a potential source of medication errors. A cross-sectional study conducted in Penang, Malaysia, found that compliance with labelling standards varied significantly, with some labels lacking essential details such as patient names and complete dosage instructions (Neoh et al., 2009). Additionally, the Malaysian Ministry of Health's Guide to Good Dispensing Practice emphasises that all dispensed medicines should be labelled according to legal requirements, preferably printed, or if handwritten, should be neat and legible with clear instructions on use. However, challenges such as language diversity, time constraints, and operational costs hinder the effectiveness of traditional labelling methods. To address these issues, we implemented the T-Label Initiative, featuring thermal-printed multilingual dispensing labels, vector-based illustrations, and colour-coded envelopes to enhance patient comprehension and operational efficiency.

Method: The T-Label initiative was developed to improve medication labelling by integrating thermal-printed dispensing labels, multilingual adaptability, vector-based dosage illustrations, increased efficiency, and colour-coded medicine envelopes. The labels are printed using existing receipt printers, eliminating the need for additional sticker label printers and reducing operational costs. To accommodate Malaysia's multilingual population, the labels can be generated in Bahasa Malaysia, English, or Mandarin, improving patient comprehension. The system also enhances workflow efficiency by reducing manual writing time and eliminating the need for separate auxiliary label stickers, as auxiliary label information is included in the Professional Advice section.

Vector-based illustrations visually depict dosage instructions, showing patients when and how to take their medications, helping to prevent confusion. Furthermore, colour-coded medicine envelopes were introduced to differentiate internal and external use, reducing the risk of medication errors, such as accidental oral consumption of vaginal tablets.

A customer preference poll was further conducted among 500 customers across 10 Alpro Pharmacy outlets in Negeri Sembilan and Kuala Lumpur. Participants were randomly selected as they walked in and were asked to compare the new T-label with traditional labels, indicating which they found easier to understand. The survey focused on readability, clarity, and overall preference. Additionally, pharmacists in the respective pharmacy outlets provided feedback on how the T-Label system impacted operational efficiency and workflow improvements.

Results: Among 500 respondents, 78% preferred the T-label system, citing better readability and understanding. Pharmacists reported that manual labelling took approximately one minute per label, with the potential for omitting important information such as the patient's name. In contrast, the T-label system reduced labelling time to less than 10 seconds per label, ensuring completeness and accuracy. Pharmacists also highlighted that integrating auxiliary label information directly into the T-Label eliminated the need for additional stickers, reducing errors and improving counselling efficiency.

Conclusion: The T-Label Initiative has significantly improved medication comprehension and operational efficiency in community pharmacy settings. The system enhances patient safety, reduces labelling errors, and optimises pharmacy workflow by integrating cost-effective thermal-printed labels, multilingual support, vector-based dosage illustrations, and colour-coded envelopes. Future research should evaluate long-term adherence benefits and explore digital integration to enhance accessibility and patient engagement.

The collaboration of pharmacists from seperate health institutions through PharmaCloud System: awareness, evaluation of the suspected ADR induced by Donezepril

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Background: The medical records are managed seperately by each health institutions in many countries. In Taiwan, PharmaCloud System, which is established by the goverment

agency of health, is a sustainable resourse providing healthcare professionals to access autherized patients' medical records from separate healthcare providers through the patients' National Health Insurance cards.

A 80y/o man experienced sudden diaphoresis and alterd consiousness shortly after taking post-breakfast medication. He was promptly admitted to the emergency room of a medical center (hospital A) in middle Taiwan. After emergency management and evaluations, the electrocardiogram revealed significant conduction block and atrial fibration.

This survey aims to share how the suspected ADR induced by Donezepril was identified and evaluated through the PharmaCloud System by pharmasists from seperate health institutions.

Method: This survey was counducted by counseling the patient's caregivers, compiling the patient's medical history and consulting the evidence-based database, UpToDate.

Results: This patient is taking the medications of parkinson's disease and demetia; he has hypertention history without regular medication control. On the day of the his emergency visit, his son metioned that the neurological doctor affiliated at a different hospital (hospital B) adjusted his medicine three days ago. The doctor of hospital A reviewed the patient's medication history through PharmaCloud Systems so that he could identify the suspected medicine, Donezepril immediatedly according his son's statements, and ADR reporting process was conducted by the pharmacist. As the pharmacist of hospital B, after receiving the inquiry from the patient's family; reviewing the medication records from EMR and PharmaCloud system, the home blood pressure log and the literature, it was found that Donezepril has been associated with the patient's cardiovascular situation such as conduction abnormalities, blood pressure changes and syncope.

Conclusion: Donezepril is usually used as the first-line treatment for dementia and this case is a real world data. This medicine has an impact on the cardiovascular system, so the recommanded dose should be individualized for the elders with risk factors, such as cardiovascular disease. Both the public and healthcare professionals should be more aware of it. Although the medicine is well tolerated, the increment or withdrawl should be more careful in this population. Regarding the inquiry from the patient's family, the patient education about the information of Donezepril and self-management of hypertension was performed; it was also suggested that the patent's family should discuss with the doctor about the treatment of dementia and cadiovascular disease. Though this case, it emphassises the pharmacists' roles in health care system via integrated care and share how PharmaCloud System enpowers pharmacists in optimising health care delivery.

Analysis of changes in Montreal cognitive assessment scores after pharmacist-led medication counseling in patients taking anti-dementia drugs

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Background: Dementia treatment relies on pharmacological therapy, but medication adherence and appropriate use remain challenging. Pharmacist-led medication counseling may enhance drug effectiveness and cognitive outcomes.

Aim: This study evaluates changes in Montreal Cognitive Assessment (MoCA) scores following pharmacist-led medication counseling in patients receiving anti-dementia drugs.

Methods: Patients who regularly visited community pharmacies to collect dementia medications and were capable of independent living were recruited. MoCA scores were assessed before and after a pharmacist-led intervention. Paired t-tests were used to analyze score changes.

Results: A total of 28 patients were included, with a mean age of 72.68 ± 6.24 years and a mean BMI of 18.09 ± 1.28 kg/m². Among them, 46.4% were male. The most common comorbidities were hypertension (71.4%), Parkinson's disease (60.7%), and diabetes mellitus (32.1%). Regarding co-medications, 67.9% used psychiatric drugs, 57.1% took sedatives, and 35.7% used traditional Chinese medicine. Additionally, 35.7% used assistive devices, and 35.7% took dietary supplements. After the intervention, the total MoCA score showed a slight increase from 25.57 to 26.00 ($p = 0.14$). A significant improvement was observed in attention (pre-test: 3.89, post-test: 4.21, difference = 0.32, $p = 0.05$). Other cognitive domains, including visuospatial skills, language, delayed recall, calculation and orientation, and abstract reasoning, showed minimal or no change ($p > 0.05$).

Conclusion: Pharmacist-led medication counseling may enhance cognitive attention but did not significantly impact overall MoCA scores or other cognitive domains. Further studies with larger sample sizes are needed to confirm these findings.

Comparative study on adverse drug reactions (ADRs) and adverse drug reaction (ADR) reporting amongst staff of two organizations in Lagos State, Nigeria

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Background: Adverse drug reactions (ADRs) are a significant public health concern, and their underreporting is a major challenge in Nigeria. Despite the critical role of HCPs in reporting ADRs, there is a dearth of information on the detection and reporting of ADRs amongst patients. Patient reporting of ADRs empowers individuals to take an active role in their healthcare and contributes to the overall safety of medications. The lack of comparative data on ADRs and reporting practices by different categories of patients hinders the development of effective strategies to improve patient safety and minimize harm. This study aimed to determine knowledge, attitudes and practices (KAP) of staff of the National Agency for Food and Drug Administration and Control (NAFDAC) and the Federal Institute of Industrial Research Oshodi (FIIRO) in Lagos State, Nigeria, to ADR and ADR reporting, and identify ways of improving ADR reporting among the populace.

Methods: A cross sectional, questionnaire-based study was carried out. Using the Kish formula, a sample size of 384 with 10% overage gave minimum sample size of 423. Collected data were analyzed using IBM SPSS Statistics Version 26.0. Quantitative data were analyzed descriptively as frequencies, percentages and means. For the KAP scoring, correct responses attracted a score of 1 while 'no' and 'I don't know' responses were awarded scores of 0. The Student t-test was used to test the difference between knowledge about ADR, and attitude and practice to ADR reporting in both organizations. At 95% confidence interval, a 2-tailed p-value of ≤0.05 was considered significant. Ethical approval was obtained from the Health Research and Ethics Committee of the Lagos University Teaching Hospital, Idiaraba, Lagos.

Results: A total of 424 questionnaires were administered, with 399 completely filled and returned, giving a response rate of 94%. Majority of respondents were in the age group 45-54 years (41.2%), male (57.9%), married (81.0%), and senior staff (80.7%). Most gave correct definitions for ADRs (63.3%)s. Major reasons for patients not reporting ADRs are that 'I don't know where/how to report' (48.1%) and 'I think ADRs are not too serious so not necessary to report' (17.8%). Only 38.1% had ever reported an ADR. Mean knowledge score about ADRs and ADR reporting for NAFDAC and FIIRO was 81.4% (rated as excellent) and 70.3% (rated as good) respectively while mean attitude and practice score was 72.2% (Good) and 81.4% (Excellent) respectively. These differences were statistically significant with p-value of 0.000. Respondents opined that awareness on the need for reporting (29.9%), sensitization and education (17.7%) and 'taking necessary action on the report given (11.0%) are ways of improving ADR reporting while 'Concern for my health' (86.5) and 'Prevention of similar ADRs in other patients' (65.4%) will motivate ADR reporting.

Conclusion: Though the study shows good to excellent KAP about ADRs and ADR reporting there is room for improvement in specific details such as not knowing where or how to report and what the ADR reporting tool looks like. The study recommends enlightenment campaigns about ADR and ADR reporting among the general public consistently.

Vitamin K2 as an immunomodulator: evidence from an animal model of rheumatoid arthritis

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Vitamin K2 (VK2), a fat-soluble molecule, has various health benefits, including the promotion of musculoskeletal and cardiovascular health, as well as possible protection against various forms of non-communicable diseases such as type 2 diabetes, rheumatoid arthritis (RA) and neurodegenerative diseases. In addition to natural sources of this vitamin (fermented foods, certain animal products and cheese), it is often taken through supplements designed to promote bone health. The mechanisms of action of VK2 are known in some areas such as blood clotting and bone health. The role of VK2 in inflammation and its potential immunomodulatory action has been hypothesised, but the underlying mechanisms remain elusive. In this study, the anti-inflammatory/immunomodulatory properties of VK2 were investigated in an animal model of RA - collagen-induced arthritis (CIA).

In this study, female Dark Agouti rats were immunised with bovine type II collagen (CII) in incomplete Freund's adjuvant for CIA induction. VK2 (MK-7) was administered orally (50 mg/kg/day), starting one day before the immunisation and

continued until the end of the experiment, i.e. until the peak of clinical severity of the disease. Arthritis severity was evaluated using clinical scoring system for macroscopic assessment of ankle joint inflammation and histopathological analysis of these joints. Lymphoid organ (LO) cells, including splenocytes and draining lymph node (dLN) cells were collected, subjected to fluorescent immunostaining and analysed by flow cytometry for phenotypic and functional characterisation. Cytokine levels in the culture supernatants of hind paw tissue and serum anti-CII IgG antibodies were measured using ELISA. Parameters of redox status were determined in spleen homogenates.

VK2 treatment led to a reduction in ankle joint inflammation, which correlated with an increase in anti – inflammatory (IL-10) and decrease in pro-inflammatory (TNF-α and IL-6) cytokines in the affected paws. Furthermore, VK2 administration resulted in a less inflammatory phenotype of CD11b+ cells (monocyte/macrophage cells), that is characterised by reduced expression of: pro-inflamatory cytokines (TNF-α, IL-1β), costimulatory molecule CD86, antigen-presenting MHCII molecule, and TLR4- receptor that can detect danger signal and trigger inflammation. In dLNs, increased frequency of regulatory T cells, and decreased frequency of pathogenic Th1/Th17 cells was found. Additionally, lower serum levels of anti-CII-specific antibodies were associated with a reduced frequency of B cells (CD45RA+ cells) in LOs in VK2-treated CIA rats. Regarding redox status, decreased levels of pro-oxidant antioxidant balance and ischemia-modified albumin (pro-oxidative parameters) were found in VK2-treated CIA rats. This study showed that preventive VK2 treatment exerts beneficial effects on the inflammatory process in the animal model of RA, and highlighted potential anti-inflammatory/immunoregulatory mechanisms underlying its effects.

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Adherence and persistence among patients with type 2 Diabetes initiating glucagon-like peptide-1 receptor agonists: A real-world study in China

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Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) play a crucial role in the management of type 2 diabetes mellitus (T2DM), providing both glycemic control and cardiovascular benefits. However, real-world evidence on adherence and persistence to GLP-1 RAs among Chinese patients remains limited. This study aims to assess the utilization patterns of GLP-1 RAs and identify factors influencing adherence and persistence in this population.

Method: A retrospective cohort study was conducted using electronic medical records from a healthcare security administration database in an economically advanced province in Eastern China, with a registered population of 8.526 million. Adult patients (≥18 years) with T2DM who initiated either daily or weekly GLP-1 RAs between January 2018 and October 2024 were included. Patients were required to have continuous enrollment for at least 12 months post-index, defined as the date of first GLP-1 RA purchase. Adherence was measured by the proportion of days covered (PDC), with good adherence defined as PDC ≥80%. Persistence was assessed based on the time to discontinuation, defined as a failure to refill the index medication within 60 days. Multivariable logistic regression was employed to evaluate factors associated with good adherence, while Cox proportional hazards regression was used to analyze predictors of discontinuation.

Results: A total of 28,943 patients were included (mean age: 55.45 ± 14.28 years; 59.8% male). Over a 12-month follow-up, the mean PDC was 0.41 ± 0.33, with only 19.3% of patients achieving good adherence. The discontinuation rate was 21.3%, and the mean duration of continuous medication use was 306.56 ± 115.54 days. Patients using weekly GLP-1 RAs were significantly more likely to achieve good adherence (OR 1.436, 95% CI 1.332–1.549, $p < 0.001$). Those with a history of stroke (OR 1.117, 95% CI 1.025–1.217, $p < 0.001$) or nephropathy (OR 1.126, 95% CI 1.013–1.249, $p < 0.001$) also exhibited better adherence, whereas patients with diabetic neuropathy had lower adherence rates (OR 0.884, 95% CI 0.792–0.986, $p < 0.001$). Regarding persistence, weekly GLP-1 RA users were less likely to discontinue treatment compared to daily users (HR 0.925, 95% CI 0.878–0.975, $p = 0.003$), while patients with dyslipidemia had a higher likelihood of discontinuation (HR 1.063, 95% CI 1.006–1.123, $p = 0.029$).

Conclusion: Adherence to GLP-1 RAs among Chinese patients with T2DM remains suboptimal. Targeted interventions, including enhanced medication education and management, are necessary to improve adherence and persistence, particularly for patients at high cardiovascular risk.

Characteristics, comorbidities, and prescription medication treatment in Chinese patients with osteoporosis: A cross-sectional study

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Introduction: Osteoporosis is a condition marked by low bone mass and compromised bone quality, resulting in increasing fracture risk. The China Osteoporosis Epidemiological Survey reported a prevalence of 19.2% among individuals aged ≥50

years (32.1% in women, 6.0% in men). China's diverse pharmacological options, including vitamin D analogs and traditional Chinese medicine (TCM), may contribute to a unique treatment landscape distinct from international patterns. This study investigates osteoporosis treatment trends in China using large-scale real-world data.

Methods: This retrospective, cross-sectional study analyzed electronic medical records from a provincial healthcare security administration database in Eastern China (January 2019–October 2024). Patients diagnosed with osteoporosis who received at least one osteoporosis prescription were included. Exclusion criteria included prior cancer or Paget's disease diagnoses and osteoporosis-specific prescriptions within 12 months before the index date (first post-diagnosis prescription). Prescription patterns and medication utilization rates were analyzed at patient and prescription levels.

Results: A total of 363,237 patients (mean age: 65.05 ± 18.4 years; 72.44% female) were included. Common comorbidities included hypertension (51.4%), diabetes (26.3%), ischemic stroke (20.9%), rheumatoid arthritis (8.6%), heart failure (5.2%), COPD (5.1%), and depression (4.0%). Monotherapy was predominant (>90%), with dual therapy (~7%) and combination regimens (<1%) remaining rare. From 2019 to 2024, vitamin D analog prescriptions declined (71.8% to 63.4%), while denosumab use increased (0% to 9.9%). Combination therapy (7.8%) primarily paired bisphosphonates with vitamin D analogs (54.48%). Women had higher denosumab use (25.8% vs. 9.9%, P<0.01) and lower vitamin D analog use (62.7% vs. 71.9%, P<0.01) than men. TCM utilization increased with age (P<0.01), peaking at 13.1% in patients aged >81 years.

Conclusion: Osteoporosis pharmacological management in China remains predominantly mono-therapeutic, with active vitamin D analogs maintaining prescription dominance. Significant differences exist in medication utilization by age and gender, highlighting the need for tailored therapeutic strategies.

Increasing polypharmacy and medication use among patients with Diabetes: 2015-2021

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Introduction: The global prevalence of diabetes has been increasing in recent years. Prescription medications are crucial for the diabetes management and account for a substantial portion of healthcare expenditures. Patients with diabetes in China face a high burden of comorbidities, which may necessitate greater use of non-glucose-lowering medications. In addition, variations in availability of new medications, update and adoption of clinical pharmaceutical guidelines, and evolving medication-related policies may result in different medication patterns in the Chinese patient population. However, there is a lack of population-based, especially longitudinal studies to reveal medication use patterns in patients with diabetes in China. To address this knowledge deficit, our study systematically evaluates polypharmacy prevalence and prescription medication utilization patterns among Chinese patients with diabetes during 2015-2021, aiming to elucidate the evolving therapeutic landscape in this high-risk population.

Method: We conducted a retrospective observational cohort study using the Yinzhou Regional Health Care Database (YRHCD). We analyzed the utilization of prescription medications in general and by ATC class, assessed polypharmacy (use of ≥5 medications), and examined the number of medications assigned to specific classes. Additionally, we used logistic regression to identify risk factors for polypharmacy among Chinese patients with diabetes.

Results: During 2015-2021, 99619 patients with diabetes were included. The mean age was 61.6 years (SD: 12.5), with 48.4% being female. The average number of medications used per month per patient increased from 2.8 in 2015 to 3.6 in 2021, and the prevalence of polypharmacy increased from 18.4% to 32.6% (p-for-trend<0.01). Glucose-lowering medications were the most commonly prescribed medications, with sulfonylureas and biguanides being the most used subcategories. However, the proportion of glucose-lowering medications decreased from 92.3% in 2015 to 77.0% in 2021 (p-for-trend<0.01). Cardiovascular medications were the second most commonly used medications, with approximately 60.0% using antihypertensive medications and 40.0% using antihyperlipidemic medications. Additionally, the prevalence

of antibacterial medications and oral Chinese patent medications use was high. Increasing trends of polypharmacy were also found across all population subgroups. Compared to patients with type 1 diabetes (T1D), those with type 2 diabetes (T2D) used a greater number of medications and had a higher prevalence of polypharmacy (39.5% in T2D vs. 28.4% in T1D). Patients with comorbidities had a higher number of medications (mean 5.0 vs. 3.3) and a higher prevalence of polypharmacy than those without (40.0% vs. 18.4%). Advanced age (OR:1.02,95% CI: 1.02-1.03), male gender (OR:1.08,95% CI: 1.04-1.11), being employed (OR:1.20,95% CI: 1.15-1.24), and comorbidities (e.g., hypertension: OR:2.87, 95% CI:2.75-2.99; nephropathy: OR:1.54, 95% CI:1.44-1.64) significantly increased the risk of polypharmacy.

Conclusion: Medication use and polypharmacy have increased among patients with diabetes in China. The growing medication burden in this population warrants attention to the appropriate use of medication.

Effectiveness of unfractionated heparin vs enoxaparin in ARDS and metabolic dysfunction: A comparative study

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Introduction: Acute Respiratory Distress Syndrome is a lung disorder defined by the acute onset of hypoxemia, the commonest being abdominal sepsis. There has been increasing attention on the anti-inflammatory and immunomodulatory effects of UFH, suggesting its potential use as a therapeutic drug for a specific subset of septic patients. Many biomarkers have been studied for diagnostic prognostication and ARDS pharmacotherapy. The current study aimed to assess the protective effects of UFH versus Enoxaparin in sepsis-induced ARDS and related metabolic sequelae.

Methods: Sepsis was initiated through cecal ligation and puncture (CLP). Wistar rats were divided to: sham, CLP, CLP+ unfractionated Heparin, and CLP+ Enoxaparin and CLP + distilled water groups. Levels of serum Lipoxin A4 (LXA4), lipoprotein lipase (LPL), leukotriene E4 (LTE4), leukotriene B4 (LTB4), interleukin-8 (IL-8), were quantified. Furthermore, mRNA expression of receptors for advanced glycation end products (RAGE) and angiopoietin-2 (ANG-2) were assessed. Histopathological study was conducted to assess any lung injuries.

Results: Septic rats demonstrated higher levels of leukotriene E4, leukotriene B4, and interleukin-8, while treatment with unfractionated Heparin attenuated these levels but enoxaparin effectiveness on LTB-4 and IL-8 was not as significant as heparin while its was equally effective on LTE-4. Moreover, mRNA levels of RAGE and ANG-2 were enhanced in CLP rats. These elevations were mitigated by treatment with unfractionated Heparin and reduced by enoxaparin to a lesser extent. Treatment with unfractionated Heparin increased the lipoxin A4 and lipoprotein lipase levels but enoxaparin had no effect on the LPL level. Lung protective effect of unfractionated Heparin was further confirmed by histopathological observations of lung tissue samples.

Conclusion: Our study demonstrates that UFH can modulate ARDS and metabolic dysfunction in hyperinflammatory conditions like sepsis. Comparing the pharmacological benefits of UFH with enoxaparin, it was concluded that the effect of UFH had descent superiority complemented by its anti-inflammatory and positive protective metabolic profiles beyond anticoagulation, representing improved prognostication in ARDS. Lung expression of RAGE and ANG-2 was also reduced in rats in the treatment UFH group. We concluded that unfractionated heparin (UFH) has the potential as an anti-inflammatory support during persistent systemic inflammation in sepsis. Acute Respiratory Distress Syndrome (ARDS) is usual in sepsis patients and relared with poor prognosis. Here, we found that the UFH treatment window successfully decreased the levels of serum biomarkers of lipid mediators (LTB4 and LTE4) and enhanced lung inflammation resolution supported by histological findings while improving pro-resolving mediators (lipoxinA4 and LPL levels in septic rats). The level of Interlukin-8 representing diffuse alveolar damage was also declined notably suggestive of further damaged alveolar protection. Thus, UFH can modulate ARDS by suppressing archidonic metabolites following acute systemic inflammatory response in sepsis. Our study has facilitated to identification of potential biological theragnostic and lipidomic for more precise treatment which could lead to improved therapeutic strategies for acute systemic inflammation and ARDS. Several biomarkers have been identified as diagnostic, prognostic, and theragnostic for ARDS. Additionally, this study considers the cost effectiveness of both drugs and suggests using UFH as a inexpensive but effective drug.

Penicillin allergy delabelling guidelines: A global comparison of scope and recommendations

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Introduction: Penicillin allergy labels (PALs) affect over 10% of patients, yet fewer than 1% of those undergoing formal evaluation are truly allergic. These inaccurate labels lead to suboptimal antibiotic prescribing, increased antimicrobial resistance, poorer health outcomes, and avoidable healthcare costs. Penicillin allergy delabelling (PADL) can safely remove incorrect PALs, and numerous penicillin allergy delabelling guidelines (PADLGs) exist to support this process. However, the scope and consistency of recommendations across PADLGs remain unclear.

Purpose: This systematic review aimed to compare the scope, intended use, and key clinical recommendations of internationally published PADLGs to assess alignment and variation.

Method: PADLGs were identified through systematic searches of MEDLINE, EMBASE, CINAHL, Google, and Google Scholar. Additional searches were conducted on the websites of professional allergy societies (n=95), as well as Australian and international guideline repositories (n=16). Where allergy societies' guidelines were not publicly available (e.g. membership-only access), societies were contacted via email to request access.

Guidelines were included if they targeted healthcare professionals and contained PADL-specific recommendations. Data were extracted on publication year, geographical origin, drug classes covered, intended users and patient populations, clinical settings, and specific recommendations regarding risk stratification, testing, delabelling steps, and post-testing procedures.

Results: Eighteen guidelines were identified, published between 2014 and 2024, representing 12 countries from four regions. Seven focused solely on penicillin, while others included broader drug classes. Eleven guidelines included non-allergist clinicians as intended users, typically restricted to low-risk patients. Thirteen specified paediatric populations, and three addressed special groups: perioperative patients, pregnant women, and the elderly. Recommended settings varied from general practice to specialised hospital centres.

Sixteen guidelines recommended history taking for patient risk stratification, yet only four provided structured questionnaires or tools. Direct delabelling without testing was endorsed in nine guidelines, but criteria for eligibility were inconsistent. Recommendations for skin prick and intradermal testing were widespread (14 and 12 guidelines, respectively), though often not aligned with risk categories. Graded oral challenges were recommended by 15 guidelines, with timing and patient selection varying greatly. Full dose oral challenge was recommended by nine guidelines, sometimes without skin testing for low-risk patients.

Post-testing strategies to ensure allergy label removal were inconsistently reported. While most guidelines recommended updating health records, only nine specified written documentation for patients, and very few addressed notifications of delabelled status beyond hospital or medical settings (e.g. to community pharmacists or dental providers). Patient education around the confirmed or delabelled allergy status was explicitly included in five of the eighteen guidelines.

Conclusion: PADLGs demonstrate substantial variation in their scope, target users, and clinical recommendations. Inconsistencies in risk stratification tools, delabelling pathways, and post-delabelling communication may contribute to confusion and variability in implementation. Clearer, standardised recommendations—particularly for non-allergist-led PADL—are needed to support safe, scalable approaches and reduce the global burden of inappropriate PALs.

Global quality of penicillin allergy delabelling guidelines: An AGREE II appraisal

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Introduction: Penicillin allergy delabelling (PADL) is recognised as an essential antimicrobial stewardship strategy and an important public health measure. An increasing number of clinical guidelines directed to PADL have emerged over the past 15 years. However, no previous review has systematically evaluated their quality using validated appraisal tools.

Purpose: This study aimed to assess the quality of internationally published penicillin allergy delabelling guidelines (PADLGs) using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument.

Method: PADLGs were identified through systematic searches of MEDLINE, EMBASE, CINAHL, Google, and Google Scholar. Additional searches were conducted on the websites of professional allergy societies (n=95), as well as Australian and international guideline repositories (n=16). Where allergy societies' guidelines were not publicly available (e.g. membership-only access), societies were contacted via email to request access. Guidelines were eligible for inclusion if they targeted health professionals and contained PADL-specific recommendations. Four trained reviewers independently appraised each guideline using the AGREE II instrument, which scores guidelines across six domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. A guideline was deemed high quality if it scored ≥50% in Domain 3 (rigour of development) and in at least two other domains.

Results: Eighteen PADLGs published between 2014 and 2024 were appraised. Two guidelines met the high quality threshold: those developed by the American Academy of Allergy, Asthma & Immunology and The Dutch Working Party on Antibiotic Policy, both published in 2022. Overall, the highest scoring domains were Domain 1 (scope and purpose) and Domain 4 (clarity of presentation), with 13 and 12 guidelines scoring ≥50% in Domains 1 and 4 respectively. The lowest performing domains were Domain 5 (applicability) and Domain 6 (editorial independence), where only one and three guidelines, respectively, exceeded the ≥50% threshold. Relative to Domain 6, most guidelines lacked transparency about funding sources and conflicts of interest. Domain 2 (stakeholder involvement) was also weak, with limited evidence of patient or carer input in development processes.

Domain 3 (rigour of development) – the core domain assessing methodology, evidence use, and recommendation formulation – had a median score of 23.5%, with only two guidelines surpassing 50%. Many guidelines lacked documentation of systematic evidence review or failed to describe how recommendations were formulated. Only one guideline explicitly used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework to assess the certainty of evidence and strength of recommendations. No guideline scored ≥50% across all six domains.

Conclusion: The overall quality of PADLGs is low, with only two meeting predefined criteria for high quality development. Critical gaps include limited methodological rigour, poor stakeholder involvement, and lack of guidance for real-world implementation. To support consistent, evidence-based PADL practices, there is an urgent need for standardised, transparent, and high quality guideline development, informed by robust methodologies and inclusive of diverse healthcare settings and user groups.

Adjuvant care: Case of ozone therapy

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Introduction: So-called "ozone therapy" continues to receive attention in the field of personalised medicine, with aspects even as an adjuvant therapy. However, in most cases there is an approximate knowledge of this treatment. In fact, it is characterised by numerous therapeutic applications, based on multiple modes of administration. Therefore, apart from clinical evaluations, it is of interest to offer a contribution of clarity to highlight the peculiarities of different modes of administration of oxygen/ozone gas mixtures and their derivatives. Moreover, even if ozone therapy can be considered a safe practice, it is important to have the pharmacist as a third-party reference figure for reporting the

patient cases who experienced any form of complications following ozone administrations.

Method: It should be noted that drug dosages habitually are expressed in mass units, mainly mg or g. On the other hand, the possibility of dealing with ozone in the gaseous state mixed with another gas (i.e. oxygen) or it is still in the gaseous state but solubilised in a liquid (water, buffer solutions) leads to having to clarify some aspects of the mode of expression of the concentrations units. On the other hand, in the case of ozonated derivatives from vegetable matrices such as oils, ozone does not solubilise or dissolve in oil, but it reacts chemically at the level of double bonds mainly turning into the stable 1,2,4-trioxolane moiety. These features are very important, because the therapeutic activity of these functional dermatological matrices depends upon both the overall ozonation process and the variety of oil in use.

Results: In contrast to medicines in common dosage forms, the use of therapeutic gases carries peculiarities. All the more so, these aspects are even more evident in the case of gaseous oxygen-ozone mixtures. In fact, having to deal with an extemporaneous preparation due to the high instability of ozone, the physician also takes upon himself or herself the role of producer of the drug and administering the gas mixture. In this regard, the availability of the pharmacist as a competent expert in the aspects of: i) gaseous source for obtaining medical ozone; ii) materials adopted for ozone generation as well as for its manipulation; iii) devices for the ozone production; iv) modality of varying the ozone concentration; v) control and measuring devices for medical ozone quantitative evaluation, also in terms of their precision and accuracy; vi) warranty period and the local maintenance service, also in terms of ozone generator validation plan; vii) proper handling of the gas mixture and devices for its in vivo and/or ex-vivo application; and viii) safety evaluation represents an important added value for the success of the therapy and the patient's well-being.

Conclusion: The purpose of this note is to stimulate an attitude of knowledge for a careful evaluation of all the parameters that come into play even before adopting the clinical potential of the correct use of oxygen-ozone gaseous mixtures, with the aim of creating an inter-professional system of therapeutic treatments centred on the needs of the patient.

Penicillin allergy delabelling: A rapid overview of reviews and future directions for a living evidence base

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Penicillin allergy is frequently documented but often not correct. Penicillin allergy delabelling (PADL) is an approach used to investigate penicillin allergy in individuals and to safely remove or verify the label, and is endorsed as an effective antimicrobial stewardship strategy by the World Health Organization. A robust, consolidated evidence base is needed to support clinical implementation and guideline development. This study presents the first rapid overview of systematic reviews examining PADL.

Purpose: To report global secondary evidence on the effectiveness, safety and processes of PADL, identify evidence gaps, and inform the development of a living overview as a foundation for future guideline development in Australia.

Method: A rapid overview of reviews was conducted using methods adapted from Cochrane guidance for both Overviews of Reviews and Rapid Reviews. Results are reported as described in the included studies, and no additional analysis was undertaken in the overview. Five databases were searched for reviews published between January 2014 and December 2023. Eligible publications included systematic, scoping, and rapid reviews focused on any aspect of PADL. Data were synthesised narratively across three domains: PADL process, effectiveness, and safety. Review quality was appraised using relevant items from the A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2) instrument.

Results: Of 1441 records identified through database searches, 24 reviews met inclusion criteria. AMSTAR 2 assessments rated overall confidence in the results of all reviews as low or critically low.

Across nine reviews of individuals with penicillin allergy labels who were selected for drug challenges, tolerance rates exceeded 90%. Two of these reviews also evaluated the proportion of all individuals with a penicillin allergy label who were delabelled following formal evaluation, reporting a maximum of 41%. One large review of penicillin challenge studies found severe reactions, including anaphylaxis, were rare (<0.2%), as were non-severe reactions (<4.5%).

Evidence across all reviews revealed PADL as a sophisticated, multi-faceted process involving allergy history assessment, risk stratification, testing via varied methods, and post-testing follow up. History, risk stratification and follow up were poorly addressed in reviews. Critical evidence gaps include: validated history tools and consensus definitions, inconsistent terminology, and poor reporting of system-level enablers such as consent, personnel, setting, and costs. Evidence for sustained label removal after a negative test was especially limited.

Conclusion: While reviews report high tolerance rates (>90%) among patients selected for penicillin allergy testing, only ~40% of individuals with a penicillin allergy label may ultimately be delabelled following structured assessment. Severe and non-severe reactions appear rare, supporting the safety of delabelling in appropriately selected patients. However, most reviews focus on low-risk populations undergoing drug challenges, and confidence in the findings is limited by the low quality of included reviews. Evidence remains sparse for critical components of the PADL pathway, including allergy history assessment, risk stratification, consent processes, terminology, system-level enablers, follow-up, and cost. We have initiated a living overview of reviews (DOI: 10.17605/OSF.IO/ACYEM) to identify and consolidate emerging evidence to support safe, scalable PADL and inform future guidelines and policy.

Is the only content of hyaluronic acid sufficient for evaluating commercial artificial tears?

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Introduction: Dry eye disease (DED) is a complex multifactorial condition with a global prevalence estimated to range from 5% to 50% impairing normal vision for which a healthy and adequately moistened ocular surface is required. Maintaining a healthy ocular surface requires sufficient tears, normal tear film arrangement, normal eye closure and regular blinking. Specifically, the composition of human tears is characterised by water, electrolytes, small molecules such as carbohydrates and lipids, and a variety of proteins, many of which have enzymatic action. Therefore, tear deficiency results in drying of the corneal epithelium, ulceration and perforation of the cornea, increased incidence of infectious diseases and, in extreme cases, severe visual impairment and blindness. Thus, proper diagnosis and treatment are essential. The purpose of this research is the evaluation of the drainage pattern of a viscous material in a medium simulating tear fluid. Such an appraisal allows obtaining standardised and reproducible information traceable to the adhesive properties and consistency of ophthalmic preparations, with primary applications applicable to DED.

Methods: Products formulated with hyaluronic acid (HA) at the same concentration but with different degrees of purity were compared. Phosphate buffer with mucin was used to simulate tear fluid. A torsional oscillation viscometer, which is based on the evaluation of the absolute value of complex viscosity in the absence of mechanical stress, was used to estimate the residence time of the ophthalmic gels. The probe system is made of titanium and it is a balanced structure in terms of mass of inertia and vibration. The sensor and actuator are driven by piezoelectric sources, and the upper portion torsionally oscillates in opposite angular momentum to the lower detector. The resonance frequency of the instrument is 1kHz and the detector oscillation amplitude is 1 µm in the absence of resistance. The angular acceleration of the detector is measured and reported as an absolute value of the complex viscosity of the sample.

Results: The results obtained from the various samples showed different drainage profiles over time of potential clinical interest in terms of initial consistency and dwell time. The technique adopted offers an easily accessible method for characterising ophthalmic gels in terms of consistency, adhesion and clearance, also proving to be a useful tool for estimating dwell times on the ocular surface. In addition, the evaluation of the drainage behaviour of different commercial formulations compared to HA-based ophthalmic gels as well as in swab simulating tear fluid highlights the feasibility of

combined administrations of commercial preparations of different consistency, including multiple administrations, predominantly aimed at overnight rest.

Conclusions: The technique adopted is able not only to reveal appreciable distinctions between ophthalmic gels in drainage profiles, but also as well as the possible combination of two gels throughout the day.

Butyrate inhibits the progression of idiopathic pulmonary fibrosis by upregulating YBX1

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Introduction: Idiopathic pulmonary fibrosis (IPF), a progressive and fatal interstitial lung disease, is characterised by aberrant epithelial-mesenchymal transition (EMT) and excessive extracellular matrix (ECM) deposition, leading to irreversible loss of pulmonary function. Despite advances in therapeutic strategies, the molecular mechanisms driving IPF progression remain incompletely understood. Y-box binding protein 1 (YBX1), a multifunctional DNA/RNA-binding protein, has been implicated in fibrosis regulation and EMT modulation. However, its specific role in IPF pathogenesis remains elusive. Emerging evidence suggests that the gut-lung axis plays a critical role in pulmonary disease. Dietary fibre is metabolised by the gut microbiota into short-chain fatty acids (SCFAs), which demonstrate anti-fibrotic properties through immunomodulatory and epigenetic mechanisms. This study investigates whether SCFAs ameliorate IPF by regulating YBX1 expression to suppress EMT, thereby offering new avenues for IPF treatment.

Method: To investigate IPF, an in vitro model was established using transforming growth factor-β1 (TGF-β1)-stimulated human alveolar epithelial cells (A549), while an in vivo model was developed using bleomycin in C57BL/6JGpt mice. YBX1 expression was assessed RT-qPCR, Western blotting, immunofluorescence and Immunohistochemistry. Levels of SCFAs in faeces were quantified by gas chromatography-mass spectrometry (GC-MS). To investigate the function of YBX1, plasmids were utilised for in vitro overexpression, while adeno-associated viral (AAV) vectors were administered in vivo. RNA sequencing and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis were employed to identify downstream pathways regulated by YBX1. To explore the relationship between YBX1 and butyrate, molecular docking, molecular dynamics simulations, and cellular thermal shift assay (CETSA) were performed to detect the binding and stability between YBX1 and butyrate. Protein stability and ubiquitination assays, including cycloheximide chase and MG132 treatment, were conducted to evaluate the interactions between butyrate and YBX1 in IPF models.

Results: The expression of YBX1 was significantly downregulated in IPF. Overexpression of YBX1 in vitro significantly inhibited EMT markers, as evidenced by upregulation of E-cadherin and downregulation of vimentin. In vivo, YBX1 overexpression was associated with attenuated fibrotic lesions and improved fibrosis and EMT indicators, suggesting its potential role in mitigating fibrotic progression. Mechanistically, RNA sequencing combined with KEGG pathway analysis revealed that YBX1 inhibited EMT progression through modulation of the CYP1A1/NF-κB signalling axis. Specifically, YBX1 overexpression upregulated CYP1A1 expression and inhibited NF-κB activation. The high-fibre (HF) diet elevated butyrate levels, and butyrate upregulated YBX1 expression by binding to it and inhibiting ubiquitination, thereby suppressing the EMT process and ameliorating IPF.

Conclusion: This study delineates a novel mechanism by which gut microbiota-derived butyrate upregulates YBX1 expression through reducing its ubiquitination, and YBX1 subsequently suppresses EMT process via the CYP1A1/NF-κB signalling pathway, thereby ameliorating IPF. These findings not only elucidate the molecular crosstalk between SCFAs and IPF but also highlight the central role of the gut-lung axis in IPF pathogenesis. These results provide scientific evidence for the development of dietary intervention strategies, such as HF diets or SCFAs supplementation, as adjunct therapies for IPF. Future studies should explore the translational potential of these findings in clinical trials, aiming to validate the efficacy of dietary interventions in IPF patients.

Construction of a lung cancer 3D culture model based on alginate/ gelatin micro-beads for drug evaluation

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Background: Lung cancer is one of the most common malignant tumors worldwide. Despite advances in lung cancer treatment, patients still face challenges related to drug resistance and recurrence. Current methods for evaluating anti-cancer drug activity are insufficient, as they rely on two-dimensional (2D) cell culture and animal models. Therefore, the development of an in vitro drug evaluation model capable of predicting individual sensitivity to anti-cancer drugs would greatly enhance the success rate of drug treatments for lung cancer patients. The purpose of this research is to utilise conditional reprogramming technology to cultivate patient-derived lung cancer cells and to construct

an in vitro 3D culture model using sodium alginate (SA) and gelatin. The aim is to study the biological characteristics of cells in the 3D culture model and to further investigate the sensitivity of anti-cancer drugs based on the alginate-gelatin 3D culture model. This approach provides new means and insights for personalized precision anti-cancer therapy and the development of new anti-cancer drugs.

Methods: Conditional reprogramming technology was used to generate conditionally reprogrammed lung adenocarcinoma cells (CRLCs). Alginate-gelatin hydrogel micro-beads were created to explore their potential use in the assessment of anti-cancer drugs. Cell proliferation was also examined using the MTS assay method. Live/dead staining was performed to estimate cell distribution and viability using calcein acetoxymethyl ester/propidium iodide (calcein-AM/PI) double staining. Protein expression was assessed by Western blot.

Results: The cells grown in the three-dimensional (3D) culture were in a state of continuous proliferation, and there was an obvious phenomenon of cell mass growth. The drug sensitivity assay results demonstrated that compared with the 2D-grown cells, the CRLCs grown in the alginate-gelatin hydrogel micro-beads exhibited more resistance to anti-cancer drugs. The results also showed that the 3D-cultured CRLCs showed greater protein expression levels of stem cell hallmarks, such as Nanog Homeobox (NANOG), SRY-Box Transcription Factor 2 (SOX-2), and aldehyde dehydrogenase 1 family member A1 (ALDH1A1), than the 2D-grown cells.

Conclusions: These findings suggest that the 3D hydrogel cell culture models more closely mimicked the in vivo biological and clinical behavior of cells, and demonstrated higher innate resistance to anti-cancer drugs than the 2D cell culture models, and thus could serve as valuable tools for diagnosis, drug screening, and personalized medicine.

Can AI use a smoker's personality to predict quit success?

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Background: Research suggests there are links between personality type and the likelihood of quitting smoking. However, there is only limited evidence for how best to support each personality type to increase their chances of quitting smoking. Limitations include how they react to nicotine withdrawal, their motivation and self-efficacy (self-belief that they can quit), how they interact with smoking cessation interventions and likelihood of relapse after quitting.

Objective: To investigate the hypothesis "personality type is a contributing factor to successfully quitting smoking or increasing chances of relapse".

Method: We used a vendor's proprietary AI tool along with personality typing to encourage positive healthcare behaviour change and determine how to customise behavioural support interventions for personality types to improve therapeutic outcomes.

We defined personality clusters (personas) of successful quitters and compared these against methods used to quit. 113 personality traits were mapped using the Big Five personality types (Extraversion, Agreeableness, Openness, Conscientiousness and Neuroticism), plus specific needs, values and drives such as curiosity, self-enhancement and orientation towards health.

Using responses to an online survey including questions about nicotine use, attitudes and behaviours, 300-word natural language samples were taken from successful quitters and dissonant smokers. Data from 1807 participants (748 quitters &1059 dissonant smokers) was sampled. The AI tool analysed these typed text samples to identify specific personality types of successful quitters, including vaping converts from smoking.

Results: Individuals with high nicotine dependence and enjoyment of smoking exhibit higher sociability and happiness. Less-dependent nicotine users and those who have never attempted to quit are more aggressive and less empathetic. Those who perceive smoking as harmful and are motivated by financial savings are more sociable, family-oriented, and food-focused, with higher happiness levels. Quitters who have attempted to quit more than eight times are more sociable and have higher happiness levels. Four distinct personality clusters were identified based on quit methods, with clusters for nicotine-containing methods (Nicotine Gum and E-Cigarettes with Nicotine) being closer together compared to non-nicotine methods (Willpower and E-Cig without Nicotine). Quitters using gum and patches were more likely to be adventurous, wanting to experience new things.

Conclusions: The effectiveness of quitting methods and the likelihood of success may be closely tied to the personality traits and motivations of the individuals. Understanding these traits could help tailor support and interventions to better meet the needs of quitters and dissonant smokers, ultimately improving their chances of successfully quitting smoking.

Additional research is needed to test this further.

An assessment of availability, price and affordability of selected essential medicines for stroke management at the primary health care level in Ghana

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Introduction: Stroke is the second leading cause of death in Ghana after malaria as of 2019, requiring prioritized services. This study assessed and used availability and affordability of interventions for stroke management as an indicator of the health system's ability to provide a stroke benefit package at the Primary Care level in Ghana.

Methods: This study analyses secondary data from a cross-sectional survey undertaken by the Ministry of Health of Ghana from September to December 2023, based on World Health Organization (WHO) and Health Action International (HAI) methodology implemented through the MedMon digital platform hosted by WHO. The dataset comprised 1,097 records and 186 variables from a nationally representative sample of 58 healthcare facilities across six regions. The study assessed availability, median unit prices, and affordability—measured as the minimum wage units to afford standard stroke treatments. A multiple linear regression model analyzed predictors of medicine prices.

Results: Within primary-level care, medicines for stroke prevention and rehabilitation were available in up to 75% of health centres and 91 percent of district hospitals. In contrast, medicines for stroke treatment were largely unavailable: not available at health centres (by policy) and available at 9% of district hospitals, reflecting challenges in early response to strokes. Significant predictors of medicine prices included: region (18.89 units more expensive [p = 0.000] in Bono-Ahafo cluster and 7.86 units more expensive [p = 0.01] in Greater Accra - compared to Ashanti region); town (8.83 units less in Accra-Lapaz compared to Kumasi [p = 0.03]); therapeutic category (Direct Factor Xa inhibitors [medicine category preventing clot formation] were 69.25 units more expensive compared to others in the list [p = 0.000]); and facility type (private pharmacies were 5.39 units more expensive than the district hospitals [p = 0.06]). The lowest-paid government worker needs 0.75 to 59 days' wages to afford medicines for standard stroke prevention and rehabilitation regimens and approximately 27 days' wages for stroke treatment regimens. This is particularly challenging for rehabilitation in patients living with stroke-related disabilities, complicated by the economic effect of strokes on household income.

Conclusions: The unavailability of medicines for stroke treatment at primary care levels in Ghana reflects a low system capacity for urgent and prolonged stroke services. An effective stroke care package should consider the current health system capacity for delivery. Stroke management appears to be largely unaffordable to the average earner in Ghana, warranting mitigating measures and policies to counter financial hardships in accessing healthcare.

A systematic review of clinical practice guidelines on how to deprescribe medications in older persons

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Introduction: Deprescribing is defined as "the process of withdrawal of an inappropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcomes". It is an essential part of good prescribing practice to reduce adverse drug reactions (ADRs), prevent overprescribing of medications and reduce harm in the older population. Given the number of deprescribing guidelines for older persons in published literature, a systematic review is needed to appraise the quality of existing guidelines and summarise their recommendations.

Purpose: To systematically retrieve, appraise and summarize evidence-based guidelines that described the deprescribing of medications in older persons.

Methods: This systematic review was registered with PROSPERO and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A literature search was performed across five databases and guideline repositories [MEDLINE, CINAHL, EMBASE, Clinical Practice Guideline (CPG) Infobase, and the Guidelines International Network (G-I-N) International Guideline Library] that described deprescribing medications in older persons. Only the latest guideline version was included (if more than one version was found). Excluded were guidelines not published in English or only described the tools used to identify potentially inappropriate medications (PIMs). Systematic reviews and primary studies that provided recommendations on how to deprescribe medications in older persons were also excluded. Two reviewers independently screened titles and abstracts and assessed the quality of the included guidelines using the AGREE II tool. Any discrepancies were resolved through discussion between the reviewers. If consensus could not be reached, a third reviewer was consulted to mediate disagreements.

Results: Seventeen out of 18 included guidelines were of medium to high quality. The domain that scored highest was “scope and purpose” (86.5%), followed by “clarity of presentation” (78.1%), “stakeholder involvement” (62.6%), “applicability” (46.6%), “rigour of development” (45.6%) and “editorial independence” (34.6%). Based on the five-step patient-centred deprescribing process outlined by Reeve et al. (2014), 11.1% of the guidelines recommended a comprehensive medication history, 83.3% recommended identifying PIMs, 77.8% recommended determining whether the medication could be ceased and prioritized, 88.8% recommended planning the withdrawal regimen and 50% recommended monitoring, support and documentation.

Conclusion: Majority of the included deprescribing guidelines for older persons were of medium to high quality. These guidelines clearly outlined their objectives and provided key recommendations on the deprescribing process. To enhance the quality of future guidelines, greater emphasis should be placed on methodological rigor, transparency in conflict-of-interest disclosure, implementation details, clinical applicability, and feasibility testing. Additionally, future guidelines should integrate all five steps of the patient-centred deprescribing process to ensure a comprehensive and structured approach to medication discontinuation.