

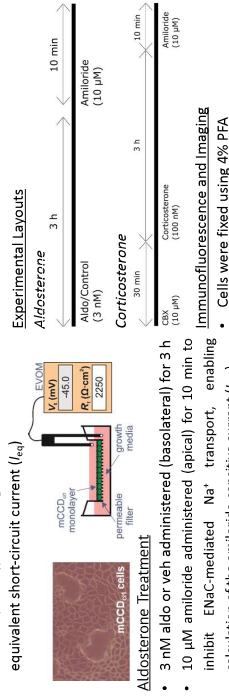
Introduction

- Sodium (Na^+) is an important determinant of effective circulating volume and therefore blood pressure. Na^+ excretion is required for blood pressure homeostasis and is regulated in the aldosterone-sensitive distal nephron (ASDN) of the kidney.
- In the ASDN, the amiloride-sensitive epithelial sodium channel (ENaC) enables transepithelial Na^+ transport and is regulated by corticosteroids such as aldosterone (aldo) and, under pathological conditions, corticosterone (cort).
- Corticosterone is normally metabolized by the 11β -HSD2 enzyme, which may be inhibited by carbenoxolone (CBX).
- Although lipophilic corticosteroids diffuse into renal cells, recent mass spectrometry data demonstrate that following exposure of a monolayer of polarized murine collecting duct (mCCD_{cl1}) cells to corticosteroids, these hormones become asymmetrically distributed, suggesting a novel renal active transport mechanism for corticosteroids^[1], supported by evidence of corticosteroid active transport in tissue such as adipose^[2] and brain^[3].
- Transcriptomic profiling of mCCD_{cl1} cells via RNA-sequencing revealed several key corticosteroid-regulated organic anion/cation (OAT/OCT) and ATP-binding cassette (ABC) transporters^[1], including ABCC1, ABCB1, and ABCB5.
- This work aims to determine whether a change in protein expression occurs for the ABCC1, ABCB1, and ABCB5 transporters following acute treatment with corticosteroids.**

Methods

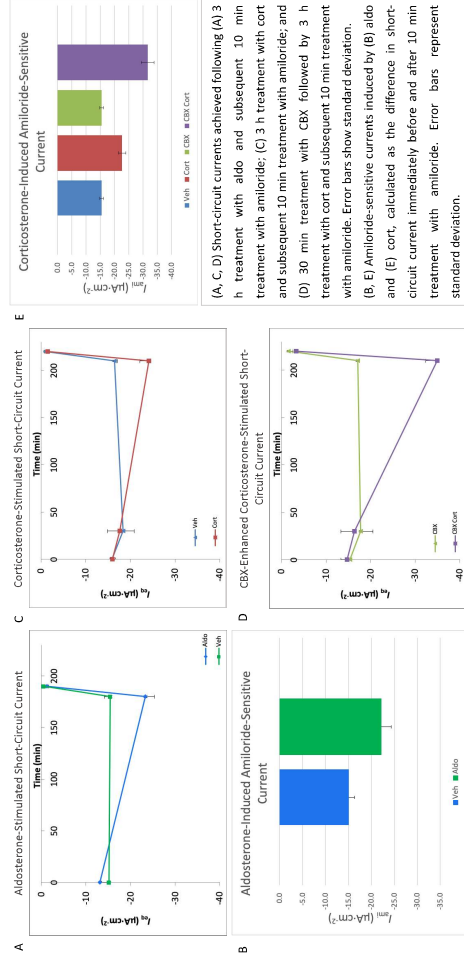
Cell Culture

- mCCD_{cl1} cells, a model of cortical collecting duct
- principal cells, were grown on permeable filter membranes over 9 – 11 days to allow formation of a polarized epithelium
- Corticosterone Treatment
 - 10 μM CBX or solvent vehicle (veh) administered (apical and basolateral) for 30 min
 - 100 nM cort or veh administered (basolateral) for 3 h
 - 10 μM amiloride administered as described for aldo
- Trans epithelial voltage (mV) and resistance (Ω) were measured using an epithelial Volt-Ohm-meter (EVOM), enabling calculation of the equivalent short-circuit current (I_{sc})



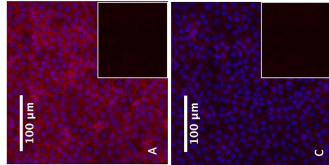
Results

1. Na^+ transport across mCCD_{cl1} cells is upregulated in response to corticosteroids.

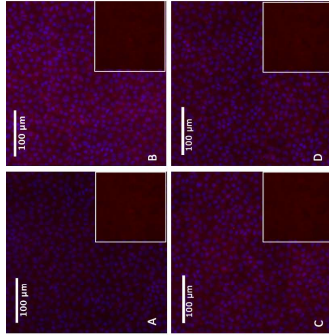


2. Detection of ABCC1, ABCB1, and ABCB5 in mCCD_{cl1} cells.

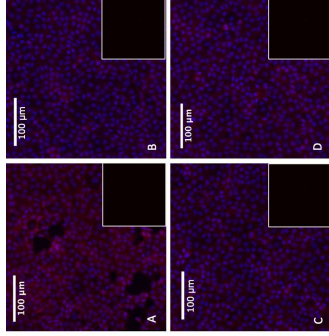
i. ABCC1



ii. ABCB1



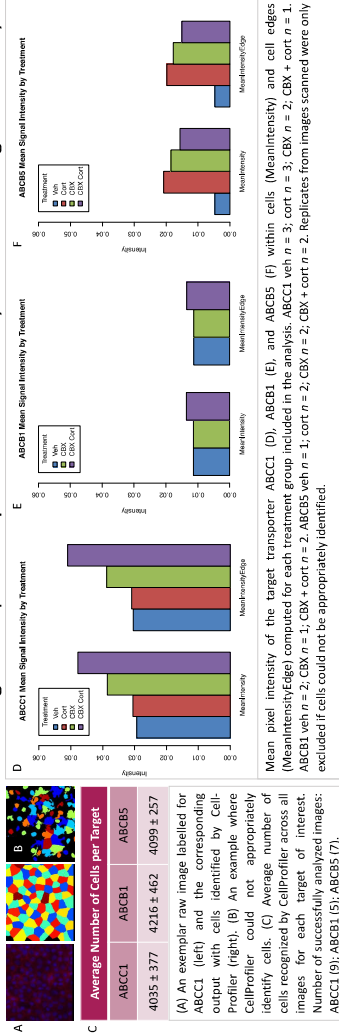
iii. ABCB5



Target transporter ABCC1 (i), ABCB1 (ii), and ABCB5 (iii) signal excited with 555 nm light (red) shown with a DAPI nuclear counterstain excited with 405 nm light (blue).

(A) Solvent vehicle control; (B) corticosterone treatment; (C) CBX treatment; (D) combined CBX-corticosterone treatment. Insets show no primary antibody (secondary only) controls.

3. Effect of corticosterone on target transporter expression indicated by fluorescence signal intensity.



Conclusions

- mCCD_{cl1} cells responded to acute treatment with aldosterone and corticosterone with an increase in short-circuit current.
- The proportion of this current attributable to Na^+ transport through ENaC was calculated as the amiloride-sensitive current, which demonstrated that both aldosterone and corticosterone cause an upregulation of ENaC-mediated Na^+ transport.
- Treatment with 100 nM corticosterone alone elicited only a small response compared to treatment with 100 nM corticosterone following administration of 10 μM CBX. As CBX is an inhibitor of 11β -HSD2 enzyme activity, this observation implies that 11β -HSD2 was present in the mCCD_{cl1} cells.
- A signal within the 555 channel was detected from each of the three target transporters, suggesting that ABCC1, ABCB1, and ABCB5 are each expressed within mCCD_{cl1} cells and therefore the ASDN in a murine model.
- ABCC1 and ABCB5 had negligible levels of non-specific background fluorescence signals detected from the secondary-antibody-only controls.
- By contrast, non-specific signal from the ABCB1 controls, although low, may suggest the need for further experiments to confirm presence of ABCB1.
- The mean signal intensity within cells and cell edges were almost identical across all three targets.
- Corticosterone-treated cells (with or without CBX) appeared to have higher signal intensity than those treated only with a solvent vehicle across targets.

References

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Acknowledgements

I sincerely thank Dr Morag K. Mansley for support and supervision of this project; Struan Loughlin for advice and useful discussions; and Dr In Hwa Um for generously providing guidance on imaging. This work was funded by the Society for Endocrinology as a Summer Studentship Grant.

Factors contained in Electronic Health Records that are associated with risk of lung cancer: A systematic review

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Introduction

- Lung cancer is one of the most common and aggressive forms of cancer with low survival rates and high mortality¹
- Early diagnosis has been found to improve chances of survival but it is a challenge as it relies on clinical presentation²
- Risk prediction models have been developed to help identify high-risk populations and risk factors associated with lung cancer such as smoking and age^{3,4}
- A unique opportunity to study lung cancer epidemiology and possibly construct new risk models for early lung cancer screening presents with the widespread use of Electronic Health Records (EHRs)^{5,6}

Objective

- This review will seek to examine data features present in EHRs that provide risk estimates. With the aim of the review to determine what data features contained in EHRs are associated with risk of lung cancer in current, ever, and former smoking populations.

Methodology

Systematic review methodology was developed according to PRISMA-P statement. The review was done via Covidence. Four different databases were searched, along with the reference lists of two EHR databases. There were no restrictions on publication period or country of publication. A total of 248 papers were obtained, after duplicates were removed 186 studies were screened. The study is registered with PROSPERO CRD42021246781.

Results

After abstract and full text screening, a total of 3 studies fit the inclusion criteria. These were cohort studies that had various lengths of follow up. After data extraction, the CASP tool was utilised to appraise methodology, validity of results, and bias of studies. Data does not allow for meaningful meta-analysis.

Table 1. Summary of descriptive data, follow up length, and measures of effect for risk factors for studies

	Adie et al. ⁷	Hubbard et al. ⁸	Schnatter et al. ⁹
Study methodology	Retrospective cohort study	Cohort study	Cohort study
Total number of participants	41,615	6,774	17,216
Length of follow up	Median: 2.9 y Mean: 4.4 y Range: 0.0028-19.9 y	2 y	29 y
Descriptive information	- Study looks at association between ADI and lung cancer by smoking status and demographic data - Mean age: 61.45y ±0.65 - Female (52.3%) - Male (47.7%) - Former smokers: 41.6% - Current smokers: 41.6% - Total population stratified into 4 groups according to Area Deprivation Index (ADI)	- Study looks at association between CFA and lung cancer by smoking status 890 participants with cryptogenic fibrosing alveolitis (CFA) 5,884 participants as control with no CFA - Mostly men participants	- Study looks at association between lung cancer, petroleum workers and, current and unknown smokers. - All male participants due to few female deaths - Average employment length of 8.9 y
Measure of effect for lung cancer risk	Lung cancer risk according to ADI, Adjusted IRR (95% CI) - Former smokers = reference - Current smokers = 1.44 (1.24-1.68) - Lowest ADI 1-50% = reference 51-75% ADI = 1.11 (0.92-1.33) 76%-90% ADI = 1.23 (1.02-1.47) - Highest ADI 91-100% = 1.70 (1.07-1.65) - Packs per day = 2.02 (1.67-2.45) - Smoking duration per 10 year increase = 1.22 (1.16-1.29) - Age per 10 year increase = 1.40 (1.26-1.54) - BMI per 5 kg/m² increase = 0.85 (0.61-0.89) - Female = reference - Male = 1.01 (0.89-1.14) - White = reference - Black = 1.02 (0.89-1.16) - Hispanic = 0.93 (0.97-0.77) - Other = 0.46 (0.30-0.70) - Commercial insurance = ref - Medicaid = 0.95 (0.78-1.17) - Medicare = 1.16 (0.97-1.40) - Self-paid = 1.13 (0.94-1.35) - Family history of lung cancer = 1.23 (1.00-1.52) - Diagnosis COPD = 1.97 (1.73-2.24) - Personal history of lung cancer = 1.43 (1.26-1.62)	Association between CFA and lung cancer by smoking status, RR (95% CI) - Non smokers = 14.83 (3.23-68.10) - Ex-smokers = 1.00 (0.06-16.99) - Pipe/cigar smoker = N/A - Current smokers = 7.36 (1.54-35.19) Control group RR (95% CI) for number of cigarettes smoked/day 1-10 = reference 11-20 = 1.98 (0.67-5.88) >21 = 5.40 (1.45-20.05)	Model 1 - RR (95% CI) - Current smokers = 11.0 (1.4-101) - Unknown smoking status = 11.2 (1.4-93.7) - Quebec province = 0.90 (0.2-4.10) Model 2 - RR (95% CI) - Current smokers = 6.2 (0.6-59.1) - Unknown smoking status = 4.6 (0.4-50.4) - Ever maintenance = 6.1 (1.0-39.2) Optimum discrete variable model - RR (95% CI) - Current smokers = 8.76 (1.21-63.4) - Unknown smoking status = 9.88 (1.36-71.5) - Quebec province = 2.21 (0.98-5.01) - Ever maintenance = 2.56 (1.00-6.56) - Age y = 2.5 (5.15-90.1)

Table 2. Summary of CASP appraisal for studies.

	Are the results of study valid?	What are the results?	Will the results help locally?
Adie et al. ⁷	✓	Participants residing in most disadvantaged areas had significantly increase incidence of lung cancer diagnoses compared to those in the least disadvantaged areas, even with adjustment for race and other factors. ✓ Results are believable	✓
Hubbard et al. ⁸	✓	Incidence of lung cancer markedly increased among patients with CFA even with adjustment for previous smoking history. CFA is independent from smoking as a factor for lung cancer incidence. ? More accurate assessment of heavy vs light smokers	✓ Results can be applied to local population ✗ Does not fit other available evidence ? Further implications of result
Schnatter et al. ⁹	✗ Exposure was not accurately measured to minimise bias ✗ Not taken account of confounding factors ✗ Not long enough follow up	Maintenance work may be associated with lung cancer incidence although exposure to single agents did not emerge as strong predictors of lung cancer incidence. Results may be affected by residual confounding due to smoking or other sociodemographic factors. ? Research is funded by Imperial Oil Limited and some co-authors work there. Others work/ed for ExxonMobil Biomedical Sciences Inc who partly owned by ExxonMobil Corporation	✓ Results can be applied to local population. ? Contradicting evidence due to authors having bias as they are hired staff of oil companies.

- The most robust study for lung cancer risk prediction in a smoker population is Adie et al. – could be reproducible.
- Hubbard et al. uses both smoking status and number of cigarettes smoked as risk factors for lung cancer risk predictions – this could be replicated in a different set of data to see if it can be a valid methodology of prediction.
- Schnatter et al. study is heavily biased due to authors' ties to oil industry. The models showed overdispersion and estimates had wide confidence intervals suggesting instability in results.

Conclusion

The 3 papers have radically different measures of effect for lung cancer risk in a smoking population for various risk factors/exposures.

Next steps

- Check papers that were excluded and included to check for potential new references or missed studies
- Use ROBINS-I to further assess risk of bias in included papers

References



'We are hear for you' – Experiences and challenges of conducting primary care consultations remotely during the COVID-19 pandemic

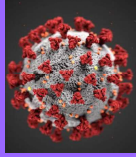


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SCHOOL OF
MEDICINE

Introduction

- On 11th March 2020 COVID-19 was declared a pandemic by the World Health Organisation¹
- Rapid changes occurred to healthcare delivery to reduce social contact.
- The proportion of remote (telephone and video) consultations increased from 31% in April 2019 to 90% by April 2020²
- Not all medical consultations involve only the patient and HCP (healthcare professional), consultations involving 3 people are known as triadic and can involve one healthcare professional, the patient and one additional person whose role is to support the patient.
- Triadic consultations occur for a number of reasons, for example to assist patients with pre-existing communication difficulties or in paediatric consultations.
- Remote and triadic consultations raise a variety of individual challenges, such as communication barriers and technological issues, therefore the combination of consultations being both remote and triadic may raise multiple challenges for primary care clinicians and their patients.



Aim

- To investigate the experiences and challenges of healthcare practitioners using telephone and online consultations in primary care, specifically triadic consultations.

Methods

Participants

- Eligible participants were clinical educators working at St Andrews School of Medicine, who hold a clinical role in primary care and have experience of conducting remote consultations during COVID-19.

Semi-structured Interviews

- Semi-structured (SS) interviews took place using Microsoft Teams and were audio recorded
- Interviews topics included:

- Overview of participant's experience with remote triadic consultations
- Challenges and benefits of such consultations
- Relevant training participants have undertaken or would value

Data Analysis

- Audio recordings from SS interviews were transcribed
- Thematic analysis of the transcription documents was conducted.³

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Results

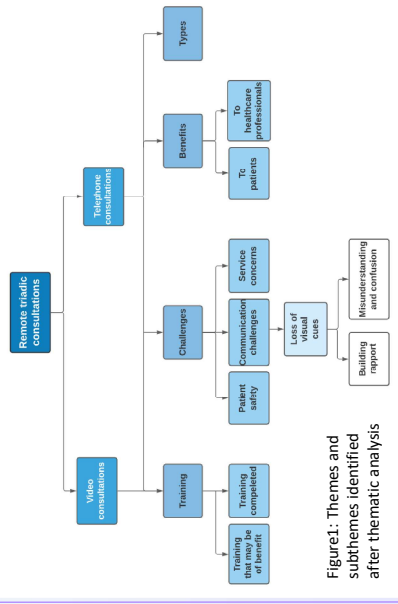


Figure1: Themes and subthemes identified after thematic analysis

Challenges

Communication challenges

Most communication challenges described related to loss of visual information and the resultant effects that participants experienced.

Loss of information

- Concerns about missing potential physical signs of illness, frailness abuse, missed opportunities to assess mental wellbeing.
- Building rapport – detrimental impacts on building relationships between HCPs and patients, particularly those who were meeting for the first time
- Consequent effects on patient care, as HCPs were used to some patients raising the most important issue towards the end of a consultation when trust had been built up.

'they're not seeing your facial expressions, they've not seen that you're trying to show empathy, or support or encouragement. So, I think patients, because patients can't see your facial reactions and your body expressions, things like giving lifestyle advice, telling people to stop smoking, telling people they need to eat differently, might not be received as well because they can't see the manner in which it's being delivered' Quote 1: Participant ID 3768

- Misunderstanding and confusion – exacerbated by not being able to see to the other person; more time spent checking, summarising and repeating information, in order to confirm patients understanding.

Patient safety

- Patient confidentiality difficult to ensure and patients unlikely to be aware that potentially sensitive questions may be asked. This includes triadic consults where patients state they consent to a relative being present. Coercion may be harder to identify in a triadic telephone consult.

- Difficult for HCPs who have never met the patient in person, to verify identity, prior to discussing sensitive and potentially valuable information during a telephone consult.

Service concerns

- Decreased face to face (f-2-f) interaction made working in general practice less enjoyable.
- Role of a GP conducting remote consultations was perceived to be different from f-2-f, clinical decisions were of a different nature to those participants had trained for.

'I think it's shifted from that history, examination, sort of investigations and management to; telephone call, do I need to bring them in to examine them, yes or no? And then, so that's been challenging because you're having to decide whether you want to examine a patient who 12 months ago you have examined without thinking about it, so that has been challenging' Quote 2: Participant ID 3768

Results

Results
Four participants took part in SS-interviews (50% female). Through a deductive thematic analysis, four main themes were identified, with sub themes.

Types

Types
Patient factors and demographics were raised as examples of common remote triadic consultations:

- These included parents with young children or adolescent children, elderly and frail couples and adults with another person who is concerned about the patient, such as a friend, neighbour or relative. Mental health concerns were identified as likely to be triadic.
- Patients and carers were generally located in the same place during the consultation, although there were examples of remote triadic consultations involving the patient and additional person situated in different locations to each other.

Benefits

Most participants identified some benefits to patients and HCPs from conducting remote triadic telephone consultations, although one participant did not feel the same way.

'Does anyone benefit. I can't see any particular benefit. It is adequate, but no real benefit to anyone'. Quote 3: Participant ID 5197

To patients

- Convenience, such as decreased impact on work or family life, as well as a decreased risk of being infected with COVID-19.
- Benefits related to triadic consultations in general, such as the involvement of a third person potentially aiding the patient's management, and the patient benefitting from support in situations where information is serious or complex.

To healthcare professionals

- Decreased risk of COVID-19 infection by HCPs, as well as some suggestions that remote triadic consultations can save time for the HCP, although this depended heavily on the original reason for the consultation.

'So I suppose it depends on what the consultations about, because there are definitely advantages for the patient if it's something simple that can be dealt with without the need for a face-to-face appointment' Quote 4: Participant ID 5197

- Advantages of triadic consultations included views that it is useful in a HCP's clinical decision making to gain the carer or additional person's view or concerns. For example, when the patient had a hearing or cognitive impairment, was experiencing significant mental distress or was acutely physically unwell.

Training

Training completed

- No participants had been trained in conducting remote consultations, although one participant had carried out some self-directed learning, reading resources related to remote consultations found on the RCGP website. None had training in triadic consultations. Training that may be of benefit

- A need for training in general IT skills was mentioned frequently, as well as specific teaching on using NearMe, a lack of which contributed to one participant not using the platform at all. Training in communication skills relevant to remote and triadic consultations was also suggested.

'Well if there are specific ways of starting and finishing a consultation for example "... communication specifically tailored for online, or for remote consultations or over the phone consultations.' Quote 5: Participant ID 2056

- Participants were keen to emphasise the benefits of continuity of care when consultations are remote, the importance of taking a thorough history, and several participants wished to highlight the time-consuming nature of remote consultations, especially those involving three people, and the need to build rapport in such situations.

Discussion

- Patient safety was a central issue, relevant to many of the themes outlined above. For example, the challenge of ensuring patient safety is maintained when consultations are remote and triadic, to the benefit to patient and HCP safety of remote consultations in the context of the COVID-19 pandemic due to the risk of infection.
- The awareness of HCPs to the variety of complex challenges experienced in remote triadic consultations and how these interplay to affect patient safety is an important aspect which would benefit from further study.
- Exploration of the remote and triadic consultation training currently being used globally and the effect of this on patient safety may be useful to consider.
- As the sample of participants was limited in number and geographic location, generalisation of findings may not be possible. However, the interview approach to data collection enabled a deep understanding of participant's experiences to be gained.

1. BACKGROUND

- Sputum culture is a simple non-invasive procedure useful in the management of respiratory infection.
- Results can inform antibiotic use through sensitivity testing and/or reviewing the persistence of specific organisms.
- The long processing culture times can negate these benefits.
- Culture results typically take 48 hours, with a further 24 hours before release of sensitivities.
- By this time, the patient may either deteriorated further or improved, both of which could render the results meaningless.
- In this context, its benefit to clinical practice is unclear.

2. AIMS & OBJECTIVES

- To assess the burden of sputum processing for all patients in 2019, and with an emphasis on pneumonia
- To review the indications for sputum culture and the respiratory and non-respiratory co-morbidities
- To identify the key pathogens associated with pneumonia and the percentage yields from sputum
- To assess the impact from sputum results on patient management, where possible
- To provide recommendations for future policy

3. METHODS

- All sputum sample records processed by Microbiology services were obtained for NHS Fife for the year, 2019
- Key clinical parameters were defined ahead of the study
- Electronic patient records were used to investigate these parameters; a subset of patients with confirmed pneumonia was created for further analyses.
- Samples associated with confirmed pneumonia from selected medical wards (W43, AU1, MHDU) were further studied.
- The project was carried out as part of service review and approved by NHS Fife Research and Development

4. RESULTS & DISCUSSION

Assessing the Burden of Sputum Processing

- Overall 4857 sputum samples were received, 889 (18%) of these were inpatients and 3968 (82%) outpatients. The number of in-patients on the 3 wards was 394 and of that 99 patients had confirmed pneumonia.

Assessing the Impact of Sputum Results

- The total number of positive sputum results was 1624 (33%) and 3233 negative (67%) this correlated almost exactly with the total number of positive and negative sputum results for all in patients with confirmed pneumonia on the 3 wards. The number of positive results for in-patients with pneumonia was 34 (34%) and the number of negative being 65 (66%). Included in both of these negative results were yeasts due to them rarely being a cause of serious infection.

Figure 1. Total number of positive cultures

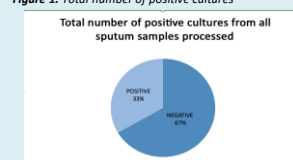
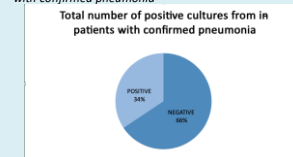
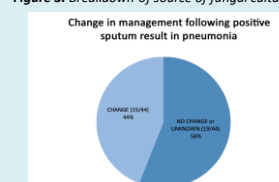


Figure 2. Total number of positive cultures from in-patients with confirmed pneumonia



- The graph below shows the how often treatment was changed as a result of positive culture. Of the 34 positive sputum results, treatment was unchanged/stopped/unclear in 19 (56%) cases and treatment was changed based on culture results in 15 (44%) of cases. Out of the total 99 patients with confirmed pneumonia, just 8% had their treatment changed based on the result of the sputum culture.

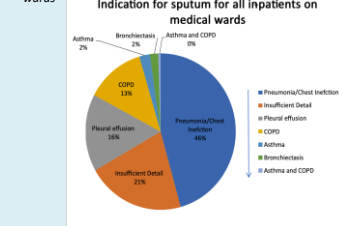
Figure 3. Breakdown of source of fungal cultures



Reviewing Reported Indications for Sputum Processing

- Within the 3 chosen wards the most common indication for testing was pneumonia/chest infection n=180 (46%), then Insufficient detail n=83 (21%), Pleural Effusion n=63 (16%), COPD n=50 (13%), Asthma n=9 (2%), Bronchiectasis n=7 (2%), Asthma and COPD n=2 (<1%).

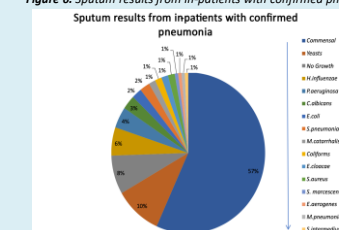
Figure 4. Indication for sputum for all in-patients on medical wards



Key Causative Pathogens

- Below shows the pathogens which constituted the 1624 positive sputum samples. *H. influenzae* was the most common pathogen. It made up 643 out of the 1624 positive samples (35%), *M. catarrhalis* was second n=247 (14%), then *P. aeruginosa* n=163 (9%), Yeasts n=159 (9%), *S. pneumoniae* n=156 (9%) and *S. aureus* n= 135 (7.4%).

Figure 6. Sputum results from in-patients with confirmed pneumonia

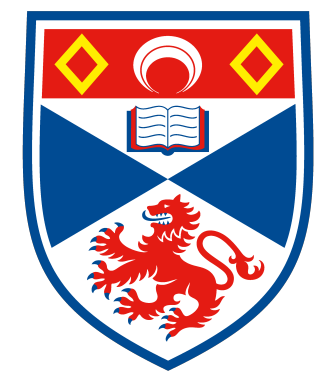


5. RECOMMENDATIONS

- When requesting a sputum sample it must have a clear and specific indication with potential causative organisms included if there is particular suspicion eg pseudomonas. This will include alteration of the request form to ensure all necessary tests take place when a sputum sample is processed
- It would be useful to also update guidelines to make clear that specific tests for specific indications/organisms exist as it highlights the importance of specificity
- Guidelines for the use of sputum in patients with pneumonia should be revised and other methods considered.
- CURB65 score must be stated on the indication if patients has pneumonia. If it is below 2 it is not currently within guidelines to request a sputum sample.

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Conflicts of Interest in Medicine: a summer project

Ronald MacDonald (ScotGEM '23)

Background & Rationale

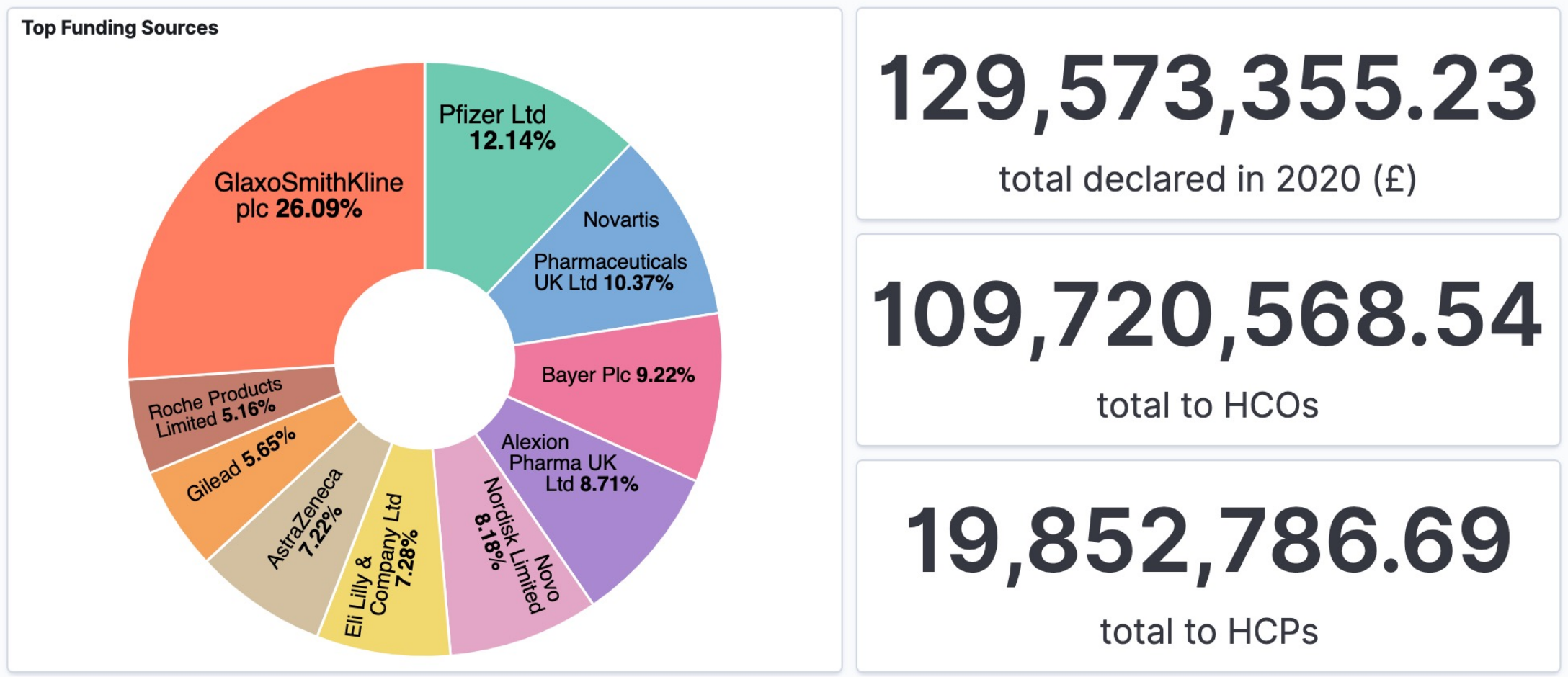
Pharmacological interventions and medical devices are big business. £20.9bn was spent last year on drugs alone¹ (list price, E&W, 2019/20). Spend on medical devices – an elusive figure – was likely higher still.

Those involved in deciding whether to use a particular intervention may include clinicians, senior non-clinical management, commissioning bodies, regulatory bodies, guideline authors, among others. At each step of the process, those involved are expected – morally, ethically, legally – to declare any conflicts of interest that may influence how decisions have been reached.

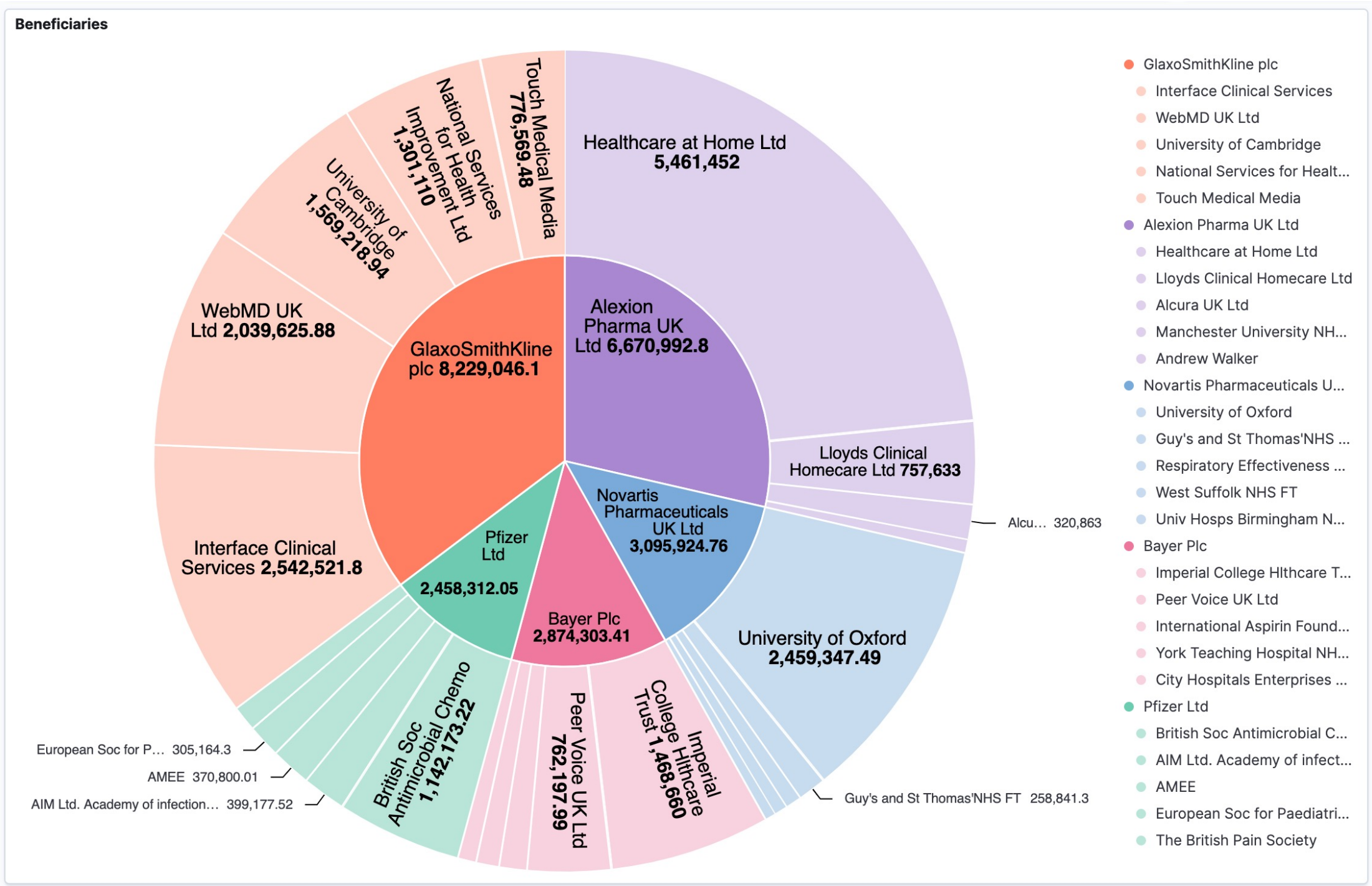
Unfortunately, clinicians are known to have surreptitiously received financial and other forms of recompense to publish favourable ‘research’ in order to support the use of a particular device, treatment or drug. In cases, the results have been disastrous and repercussions long-lasting².

Purpose

The purpose of the research I helped with over the summer was to understand how declarations regarding conflicts of interest are made by all that may be involved in choosing and using a particular drug or medical device.



Using data published by the Association of the British Pharmaceutical Industry³, the top chart shows amount of funding, in Pounds Sterling, declared as having been given to healthcare professionals (HCPs) and healthcare organisations (HCOs) in 2020. The bottom chart shows the top five beneficiaries (for the top five funding sources) based on this same dataset.



Role

My role over the summer was to support in any way that could help streamline data acquisition and analysis. This involved importing and cleaning up data, automating some of the more time-consuming tasks and prototyping and publishing research questionnaires.

Project work I undertook included organising and checking invitation letters to research participants, tracking responses, performing pilot searches for data re conflicts of interest and then collating such data in a standardised format.

Further support I was able to provide the project included creating and testing a research questionnaire that will be sent out to members of the public before the end of the year. This included participation in some focus groups that had been convened to test and refine said questionnaire, with a view to making it as robust, accessible and inclusive as possible.

References

1. NHS. Prescribing Costs in Hospitals and the Community 2018 - 2019 [Internet]. NHS Digital. 2020 [cited 2021 Sep 20]. p. 1–13. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/prescribing-costs-in-hospitals-and-the-community/2018-2019>
2. McCartney M. The pelvic mesh scandal makes it clear: doctors must declare any funding. The Guardian [Internet]. 2020 Jul 9; Available from: <https://www.theguardian.com/commentisfree/2020/jul/09/pelvic-mesh-scandal-doctors-public-register-healthcare-professionals-industry-patients>
3. Association of the British Pharmaceutical Industry. Disclosure UK database 2020. 2021.