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Research – clinical and translational posters

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Royal College of Physicians

Conundrum of D-dimer and Cerebral Venous Sinus Thrombosis (CVST)

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Aim

To assess the role of D-Dimer in diagnosis of Cerebral Venous sinus Thrombosis(CVST).

Methods

We retrospectively looked at our cohort of patients in Leicester Royal Infirmary Hospital who underwent computed tomography (CT) venogram for the diagnosis of acute non-traumatic presentation of venous sinus thrombosis from 1st November 2021 to 30th November 2022. Positive D-dimer cut-off value was ≥0.50.

Results

A total of 371 patients (Male n= 111, 30%, Female n=260, 70%).
341(92%) patients were negative for SVT. 30 (8%)patients had VST. 35 patients had D-dimers checked (9.5%). 16 patients had negative D-dimer and all those patients had no VST on the scan.

Conclusion

We found that central venous thrombosis was not present in patients with negative D-Dimer.

The Negative Predictive Value (NPV) holds 100% in our cohort of patient.
There is conflicting medical literature (1)(2) when it comes to the negative predictive value of D-dimers in excluding Cerebral venous sinus thrombosis (CVST).

We argue that D-Dimer can be useful tool in assessing patients seen at front door, with suspected CVST and could in future, after further research and evidence, facilitate formulation of simple clinical pathways for diagnosis of Central venous thrombosis. It could then help in rapid turn around and flow of such patients.

Due to small sample size, unavailability of -D-Dimer results in majority of the studied patients, definite conclusion cannot be drawn .We therefore propose to conduct further research and prospective studies to perform D-dimers for suspected CVST patients and then correlate the results with CT venogram reports to support (or negate) our findings. We aim to undertake one at our hospital.

Investigation results	Confirmed VST but no D-dimers done	Negative D-dimers and no VST (CT venogram done)	Negative D-dimers but VST present	Positive D-dimers but no VST (CT venogram done)	Positive D-dimers and confirmed VST (CT venogram done)	CT venogram normal and no D-dimer done	Total number of patient in study
No. of Patients	28	16	0	17	2	308	371

References

1. Alons IME, Jellema K, Wermer MJH, Algra A. D-dimer for the exclusion of cerebral venous thrombosis: A meta-analysis of low-risk patients with isolated headache. BMC Neurol [Internet]. 2015;15(1):1–7.
2. Crassard I, Soria C, Tzourio C, Woimant F, Drouet L, Ducros A, et al. A negative D-dimer assay does not rule out cerebral venous thrombosis: A series of seventy-three patients. Stroke. 2005;36(8):1716–9.

Pulmonary Manifestations, Treatments And Outcomes Of IgG4-Related Disease – A Systematic Literature Review

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[1]Liverpool University NHS Foundation Trust, [2] British Medical Association Library, BMA House, [3] Queen Elizabeth Hospital London

Background

- IgG4–related disease (IgG4-RD) is a multisystem fibroinflammatory condition.[1]
- Pulmonary manifestations may be the sole feature or can be present in association with other organs.
- This systematic literature review aims to summarise the pulmonary manifestations of IgG4-RD and their treatment and outcomes.

Methods

- Research question: "What are the pulmonary manifestations in patients with IgG4-RD?"
- Original articles in English were included
- Exclusion criteria: case reports, case series of less than five, opinion articles and reviews.

Methods

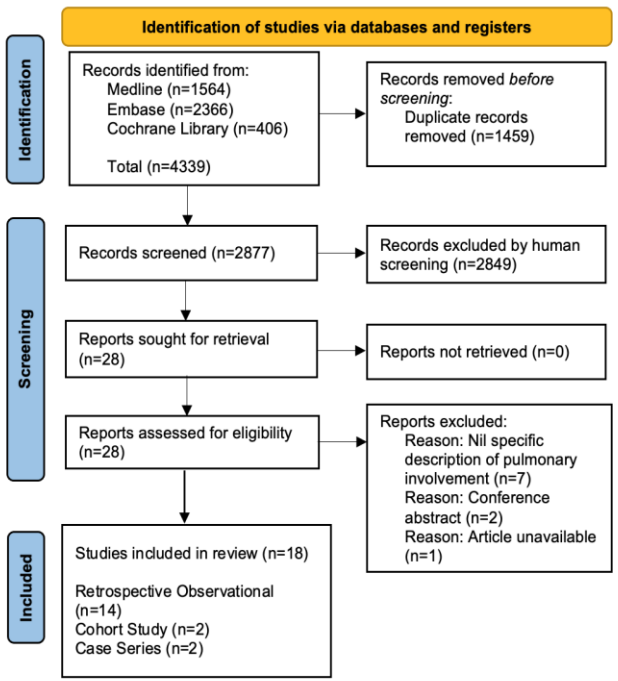
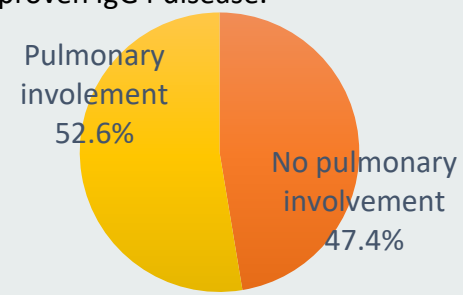


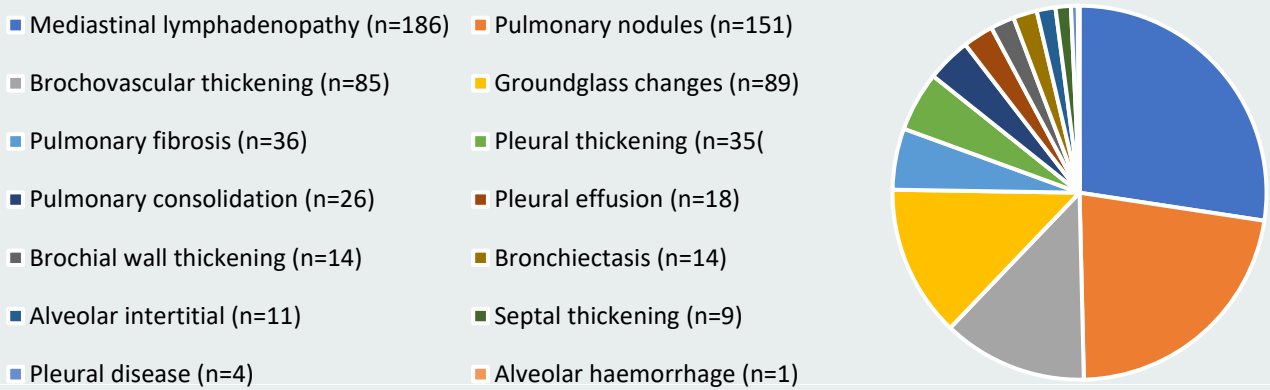
Figure 1: Flow diagram of stages of systematic literature review. Cochrane Library encompasses library of systematic reviews; systematic review protocols; controlled clinical trials.

Results

- 18 articles were included
- Study demographics: Asia (85.2%), Europe (14%) and North America (0.8%).
- A pooled total of 724 patients were included
- 68.6% male, mean age 59.4 years (SD 5.8 at disease onset).
- Of the total, 381 patients had pulmonary involvement of tissue proven IgG4 disease.



Results



- Where reported, 226 patients received treatment singular or combination therapy:
  - Glucocorticoids (n=211)
  - Other immunosuppression was used in 93 patients (44.1%): cyclophosphamide (n=31), azathioprine (n=18), mycophenolate mofetil (n=6), rituximab (n=6), methotrexate (n=5) and unspecified immunotherapy in 50 cases.
  - Surgical resection of the pulmonary nodule (n=20)
  - one patient had a liver transplant.
- Clinical outcomes reported in 263 patients: 196 patients - remission, 20 -relapse after initial remission, 35 - stable disease, four - progression and eight - death

Conclusion

- First SLR summarising pulmonary manifestations, treatments, and outcomes in patients with IgG4-RD
- Pulmonary involvement remains relatively common
- Important to consider as a differential diagnosis in patients presenting with pulmonary involvement to the acute unselected medical take
- Glucocorticoid remain the mainstay of treatment
- Future larger trials are needed to optimise the management

Reference: 1 Abraham M., Khosroshahi A., "Diagnostic and Treatment Workup for IgG4-related disease.," Expert Rev Clin Immunol, vol. 13, no. 9, pp. 867-75, 2017.

Clinical Characteristics, Disease Trajectories & Management of Vacuoles, E1 Enzyme, X-linked, Autoinflammatory, Somatic (VEXAS) Syndrome: A Systematic Review and Meta-analysis

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Liverpool University NHS Foundation Trust[1],British Medical Association Library[2], Queen Elizabeth Hospital, London[3], Southport & Ormskirk Hospital NHS Trust[4]

Introduction

- VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a newly identified disorder characterised by somatic mutation of the ubiquitin-like modifier activating enzyme 1 (UBA1) gene.[1]
- It is a severe adult-onset auto-inflammatory condition with haematological features (**Fig 1**).[2]
- **Aim**: summarise the multi-organ involvement, genotypes & management of VEXAS.

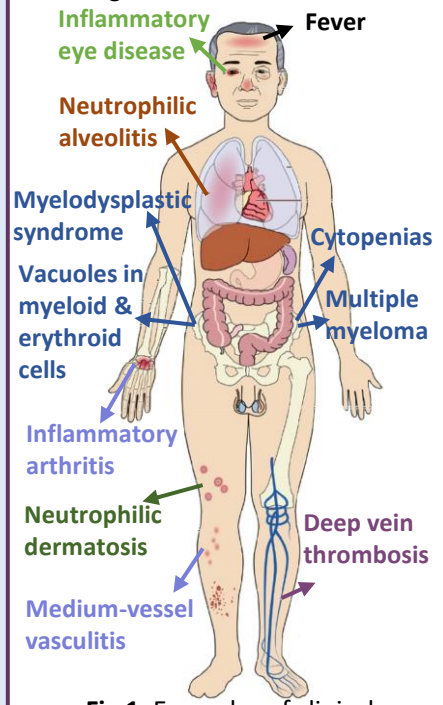

Fig 1. Examples of clinical manifestations of VEXAS. Figure adapted from Grayson et al.[2]

Methods

- Inclusion criteria: articles published until March 2023 discussing adults with VEXAS.
- Exclusion criteria: editorials, reviews, non-English articles, conference abstracts.
- Medline, Embase and Cochrane databases were searched.
- 2 researchers independently screened and extracted data from included articles.
- Data recorded: demographics, organ involvement, investigation results, genotype, treatment.
- Meta-analysis conducted for serological test values.

Results

1) Overview

- 139 articles retrieved → **64 included** (45 case reports; 17 case series; 2 cohort studies).
- Study cohorts were from: Europe (n=25); North America (n=18); Asia (n=16); Australasia (n=4); South America (n=1).
- **273 VEXAS patients included**, 96% male. Mean age at diagnosis: 67 years (SD 6.8).

2) Prior diagnoses

- **118 patients** were diagnosed with at least 1 autoimmune or haematological condition prior to VEXAS, with 16 being diagnosed with more than 1 (Fig 2).

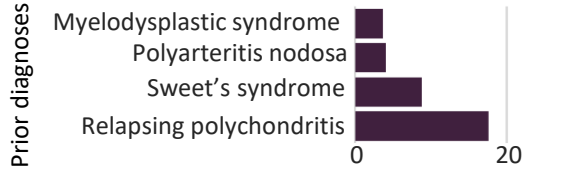

Fig 2: % of VEXAS patients with prior diagnoses

3) Organ involvement, clinical features & serology

- **Most frequently involved organ systems**: pulmonary, haematological, dermatological & musculoskeletal (Fig. 3).
- Additional **common systemic features**: fever (n=195; 71%) & weight loss (n=69; 25%).
- **Pooled estimates of serological results**: ESR 101.3 mm/hr (SE 4.8; n=246); CRP 144.2 mg/L (SE 14.1; n=258); Hb 91.0 g/L (SE 3.2; n=265); MCV 107.3 fL (SE 2.3; n=265).

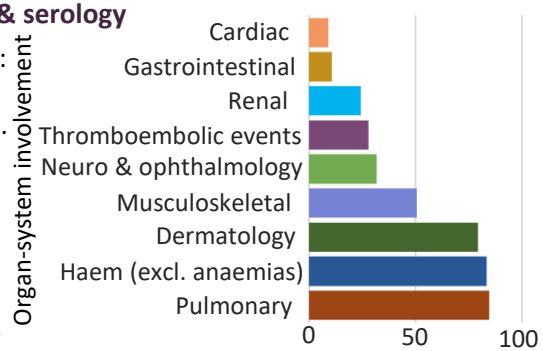

Fig 3: % of VEXAS patients with organ-system involvement

4) Genetic mutations

- **Fig 4.** shows most commonly identified genetic mutations of VEXAS.

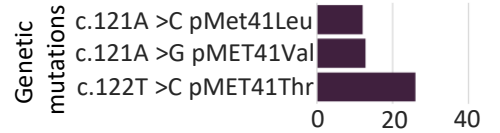

Fig 4: % of VEXAS patients with genetic mutation

5) Treatment & Prognosis

- **Fig 5.** shows treatments given for VEXAS. The most common treatments administered were glucocorticoids (49%), methotrexate (20%) and IL-6 inhibitions (17%).
- 1 patient had a splenectomy and 6 had bone marrow transplants.
- 44 (16%) patients died due to VEXAS complications.

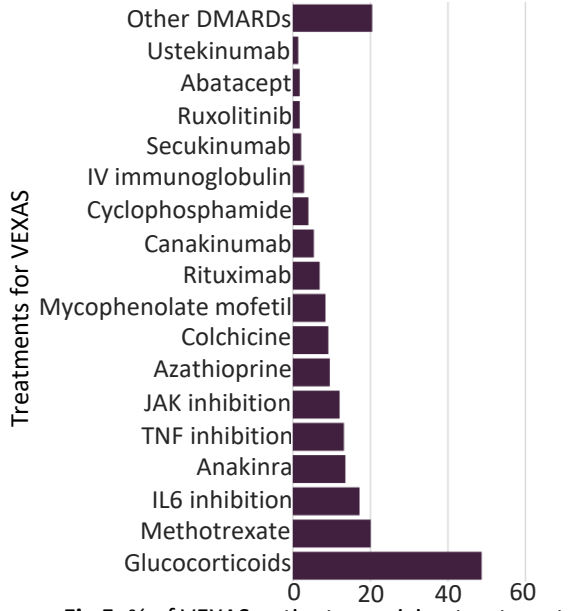

Fig 5: % of VEXAS patients receiving treatment

Conclusion

We summarised clinical manifestations, genetics and treatment of cases reported to date, in a large-pooled cohort of patients. VEXAS diagnosis remains a clinical challenge and further studies are needed to better understand genotype-phenotype correlations and optimize treatment.

References

1. Beck DB et al. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. *NEJM.* 2020 Dec;383(27):2628–38. 2. Grayson PC et al. VEXAS syndrome. *Blood*. 2021 Jul;137(26):3591–4

Manifestations, Management And Outcomes Of Interstitial Lung Disease Associated With Anti-synthetase Syndrome: A Systematic Literature Review

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Introduction

Anti-synthetase syndrome (ASS) is a chronic autoimmune inflammatory condition, characterised by myositis, interstitial lung disease (ILD), arthritis, Raynaud's phenomenon and mechanic's hands (1).

Aim

This systematic review (SR) aims to summarise the manifestations, management and outcomes of ILD associated with ASS (ASS-ILD).

Methods

- Inclusion criteria: articles discussing management and outcomes of ASS-ILD; English-language articles.
- Exclusion criteria: case reports, case series <10, reviews, conference abstracts.
- Databases: Medline, Embase, Cochrane.
- Data extracted: demographics, treatment, antibody serology, physiological and radiological findings at baseline and one-year.

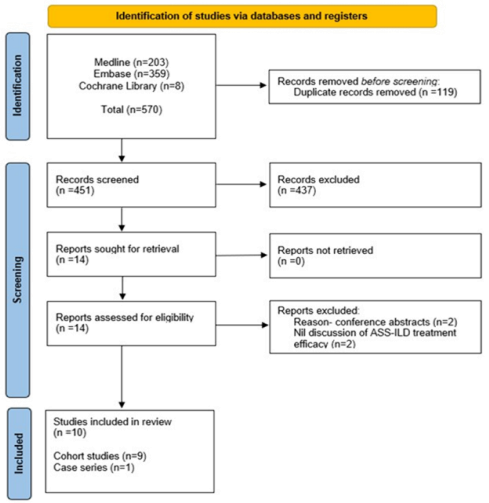


Figure 1: Flowchart of article selection

Results

- **10 studies comprising 514 patients included** (Fig 1)**.** 67.8% female, mean age 52.4 (SD 4.6) yrs at ILD induction therapy.
- Countries of study cohorts: Europe (n=5); North America (n=3); China (n=2).
- Distribution of **myositis-associated antibodies** are given in Fig 2. 143 patients (27.8%) also tested positive for anti-Ro52.
- **Baseline HRCT findings** (where available) are presented in Fig 3. NSIP subtype was reported in 12 patients (6 fibrotic, 6 cellular).
- **Pulmonary hypertension**: discussed in 2 cohorts, with 6 patients having a confirmed diagnosis.

Figure 2: Myositis-associated antibodies

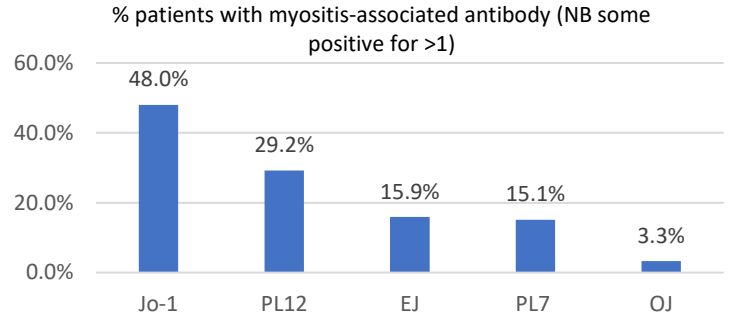
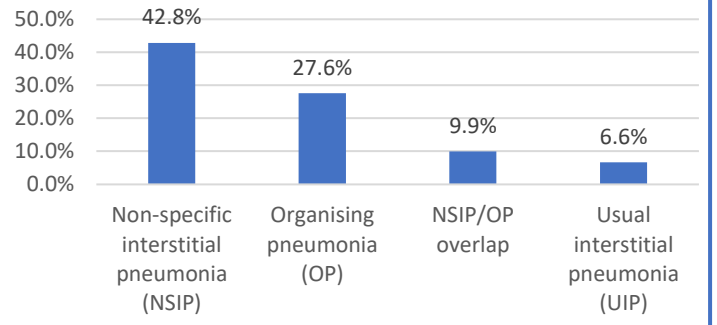


Figure 3: High resolution CT (HRCT) patterns



- **Induction therapy** (with glucocorticoids [GC]): cyclophosphamide (CYC) (n=136; 26.5%); rituximab (RTX) (n=88; 17.1%); calcineurin inhibitors (n=84; 16.3%); other disease modifying anti-rheumatic drugs (n=183; 35.6%); intravenous immunoglobulin (IVIG; n=17; 3.3%); GC only (n=20; 3.9%)
- Paired t-test: **significant overall improvement in FVC (p=0.007) and DLco (p=0.002) in pooled cohort (p<0.05).**
- Direct comparisons of treatment not possible due to heterogeneity between studies. Specific treatments:
  - Patients treated with RTX: mean 12.2% improvement in FVC; 2.9% increase in DLco at one year.
  - Patients treated with CYC: mean 17% improvement in FVC; 6.3% increase in DLco at one year.
- **5.4% (n=28) died post-treatment** due to: infection (n=8) including *Pneumocystis jirovecii* [n=2, both post-rituximab]; malignancy (n=3); multiorgan failure (n=2). 15 patients had no reported cause of death.

Conclusion

No significant difference was found between effectiveness of treatments with regards to physiological respiratory function. More robust trials required to reduce morbidity and mortality resulting from ASS-ILD.

1. Korsten P et al. Antisynthetase Syndrome-Associated Interstitial Lung Disease: Monitoring of Immunosuppressive Treatment Effects by Chest Computed Tomography. Front Med. 2021 Jan 25

Glasgow Prognostic Score In Lung Cancer Patients Over 70 Years

Lydia Gabriel, Xiaorong Wu, Charlotte Milner-Watts, Jaishree Bohslee, Michael Davidson, Anna Minchom, Mary O'Brien
Lung Unit, Royal Marsden Hospital, Sutton

Background

The Glasgow prognostic score (GPS) is an established inflammatory prognostic index in cancer patients.

It is calculated using serum C- Reactive Protein (CRP) level and serum albumin[1]. Elevated CRP and low albumin give a score associated with worse prognosis in lung cancer patients[2].

Overall Survival (OS) is worse with high GPS[1]. It is also associated with a poor response to treatment with chemotherapy in advanced disease[1].

CRP (mg/L)	Albumin (mg/dl)	GPS
≤10	≥35	0
≤10	<35	1
>10	≥35	1
>10	<35	2

Table 1: Glasgow prognostic score calculation

Aim

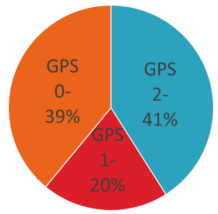
Our aim was to determine if there is a correlation between GPS, age and outcome amongst advanced lung cancer patients over 70 years.

REFERENCES
1. 1. Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ. Evaluation of Cumulative Prognostic Scores Based on the Systemic Inflammatory Response in Patients with Inoperable Non-small-cell Lung Cancer. *Br J Cancer* (2003) 89:1028–30. 10.1038/sj.bjc.6601242
2. Zhang CL, Fan K, Gao MQ, Pang B. Prognostic Value of Glasgow Prognostic Score in Non-small Cell Lung Cancer: A Systematic Review and Meta-Analysis. Pathol Oncol Res. 2022 Feb 15;28:1610109. doi: 10.3389/pore.2022.1610109. PMID: 35241974; PMCID: PMC8885527.

Methods

- Observational study, retrospective and prospective
- Adult patients > 70 years referred for advanced lung cancer or mesothelioma treatment at the Royal Marsden Hospital in Sutton between 1st March 2015-31st July 2016.
- Patient characteristics and clinical outcomes collected including relative dose intensity, treatment changes, toxicity, complications and OS.
- The GPS was calculated from blood results within a two month window of lung cancer diagnosis.

Results



Sample size 201 patients.
Median age 77 years: 36.3% of patients aged over 80 years.

116 patients were male (57.7%) and 85 female (42.3%).
NSCLC-adenocarcinoma was the most common histology (47.3%) then squamous cell carcinoma (23.4%), mesothelioma (12.9%), and SCLC (10.4%).
Most patients were smokers (21.9% current smokers and 74.3% ex-smokers, 3.8% not known).

Only 71% (144) patients had the Glasgow Prognostic Score (GPS) calculated- no CRP available within timeframe.
Most patients had GPS 2 41% (n=59), GPS 1 20% (n=29), GPS 0 39% (n=56).

GPS Score	0	1-2
Number/ %	56/39%	86/61%
Average age (years)	78	78
Male : female ratio	26:30	54:34
Performance status (mode)	0	1
Overall survival (months)	21.5	15.4
Average cycles chemotherapy	3	2

Conclusions

This is similar to previous data demonstrating that higher GPS confers a worse prognosis[2] . Higher GPS also may be linked to poorer performance status, reflecting systemic inflammation that impacts symptoms and activity level.

It is a simple test and may help clinicians determine the suitability of patients >70 years for systemic anti-cancer treatment and should be prospectively validated and compared to current tools for assessing older adults with cancer.

Investigating The Perceptions Of Older Adults On Deprescribing: A Systematic Review And Meta-Analysis.

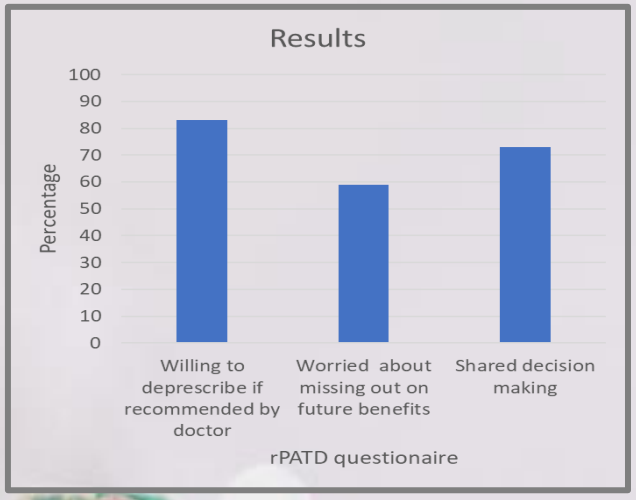
Opeyemi, Kafi [1], Oluwadara Makinde[2] , Ayomikun Odekunle[3]
1.George Eliot Hospital NHS Trust ; 2.Longford Chemist ;3.East Lancashire Hospitals NHS Trust .

Introduction

- Deprescribing is a set of interventions to identify inappropriate or unnecessary medications and discontinue them to improve patient outcomes[1].
- This systematic review aimed to provide an overview of older people's perspectives on deprescribing.

Method

- We conducted a systematic search using the EBSCOhost platform and Google Scholar from 2013 to July 2023.
- Studies were included if they concerned older people (≥65 years), with polypharmacy, and their perspectives on deprescribing.
- The Mixed Methods Assessment Tool was used to assess the quality of the studies.
- A meta-analysis of proportions (random-effects model) was conducted using MedCalc software.
- The primary outcomes encompassed the following proportions of patients according to the Revised Patients Attitude towards Deprescribing (rPATD) questionnaire:
  1. Those open to deprescribing following a physician's suggestion;
  2. Those worried about missing out on future benefits post-deprescribing;
  3. Those desiring active involvement in the decision-making process.
- The secondary outcome involved the identification of common themes in elderly patient perceptions



Results

- We included 23 studies (n=5,813 patients).
- There were 13 quantitative, 8 qualitative and 2 mixed studies . rPATD was the most common quantitative tool used.
- 83% (95% CI 72%-91%) were willing to deprescribe if recommended by their doctor although,
- 59 % (95% CI 44%-73%) were worried about missing out on future benefits if medications were deprescribed.
- Furthermore, 75% (95%CI 63%-86%) preferred a shared decision-making process about their medicines.
- In addition, four main themes were identified as factors influencing patients' perspectives: Shared decision-making, Appropriateness of cessation, Trust in clinicians, and Quality of life.

Conclusion

- These findings collectively shed light on the complex interplay of factors influencing older adults' attitudes toward deprescribing.
- Most patients are open to deprescribing if their concerns are duly addressed.
- There is a need for deprescribing interventions to be more patient-oriented.

Reference

1. Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, et al. Reducing Inappropriate Polypharmacy. JAMA Internal Medicine. 2015 May 1;175(5):827.

Corresponding author: opeyemi.kafi@geh.nhs.uk

Background image: https://www.nps.org.au/assets/Deprescribing-GettyImages-1067397640.jpg

Improving Clinical Research Participation, Engagement and Delivery: A Trainee Experience

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[1]Department of Renal Medicine, East and North Hertfordshire NHS Trust, UK, [2] School of Life and Medical Sciences, University of Hertfordshire, UK

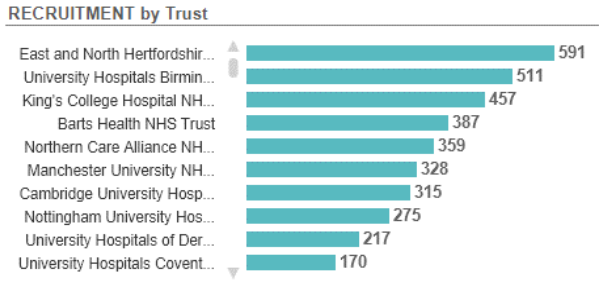
IMPROVING ENGAGEMENT

- Personal active involvement in clinical research since 2020
- Variety of investigator roles across nine studies (both commercial and non-commercial)
- NIHR Associate PI scheme for 2 studies:
  - TURING
  - H4RT
- Collaborations with:
  - Local R&D
  - Local University
  - Patients
  - Lay Representatives
  - CRN

INCREASING PARTICIPATION

- Proactive study recruitment enabled our Trust to become the lead National recruiter for NIHR Nephrology Portfolio studies in 2022-23 and lead European recruiter for the ALIGN study
- Chief Investigator for 3 studies with over 540 NIHR Portfolio recruits
- Successful funding from NIHR 'Widening Access to Research' scheme enabled recruitment of underrepresented groups into research studies
  - Important for renal studies where highest risk of adverse outcomes is amongst ethnic minority groups
  - Helped train and integrate multilingual researchers into study team

Figure 1 National Renal Specialty Data Recruitment 2022



SUSTAINING DELIVERY

- Collaboration with industry (Associates of Cape Cod, Inc) crucial to success of research examining beta-D-glucan in kidney disease
- Working closely with Research Nurses has helped develop 'Research Champions' amongst our satellite dialysis sites
  - Will help ensure recruitment can be maintained long term and integrated into clinical service

Royal College
of Physicians