Project: **PATH-BP**

Title of paper: **Regular Acetaminophen Use and Blood Pressure in People With Hypertension: The PATH-BP Trial**

Reference: Circulation. 2022;145:416–422

Authors: IM MacIntyre, EJ Turtle, TE Farrah, C Graham, JW Dear and DJ Webb for the PATH-BP (Paracetamol in Hypertension–Blood Pressure) Investigators

URL: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.056015

Summary: Paracetamol, the most widely prescribed analgesic globally (including 1 in 10 of the Scottish population), is often used as first-line therapy for chronic pain due to its perceived safety and the assumption that, unlike non-steroidal anti-inflammatory drugs, it has little or no effect on blood pressure (BP). Although observational studies suggest that paracetamol may increase BP, clinical trials are lacking. Professor David Webb and colleagues in Edinburgh, with grant support from the British Heart Foundation, studied the effects of regular paracetamol dosing on BP in individuals with hypertension in a double-blind, placebo-controlled, crossover study.

110 individuals were randomized to receive paracetamol 1g four times daily or matched placebo for 2 weeks followed by a 2-week washout period before crossing over to the alternate treatment. 24-hour ambulatory BP was measured at the beginning and end of each treatment period and the primary outcome was a comparison of the change in mean daytime systolic BP from baseline to end of treatment between placebo and paracetamol arms.

103 patients completed the study. Regular paracetamol, compared to placebo, resulted in a significant increase in mean daytime systolic BP (133±11 to 137±10 mmHg vs. 134±10 to 133±10, $p<0.0001$) with a placebo-corrected increase of 4.7 mmHg (95% CI 2.9-6.6). Mean daytime diastolic BP showed a placebo-corrected increase of 1.6 mmHg (95% CI 0.5-2.7) and similar findings were seen for 24-hr ambulatory and clinic BP.

The study concluded that regular paracetamol intake of 4g daily increases systolic BP in individuals with hypertension by around 5 mmHg when compared to placebo, increasing cardiovascular risk and calling into question the safety of regular paracetamol use in this situation, most commonly for chronic pain, where its benefits are, at best, modest.

Project: **CREDENCE**

Title of paper: **Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy**

Reference: N Engl J Med 2019; 380:2295-2306

Authors: V Perkovic, MJ Jardine, B Neal, S Bompoint, HJL Heerspink, DM Charytan, R Edwards, R Agarwal, G Bakris, S Bull, CP Cannon, G Capuano et al. for the CREDENCE Trial Investigators

URL: https://www.nejm.org/doi/full/10.1056/nejmoa1811744

Summary: Type 2 diabetes mellitus (T2DM) is the leading cause of kidney failure worldwide, but

few effective long-term treatments are available. This study looked at the potential role of an oral SGL2 inhibitor, canagliflozin, in improving renal outcomes in patients with T2DM and albuminuric chronic kidney disease.

The relative risk of the primary outcome (a composite of end-stage kidney disease [dialysis, transplantation, or a sustained estimated GFR of <15 ml per minute per 1.73 m2], a doubling of the serum creatinine level, or death from renal or cardiovascular causes) was 30% lower in the canagliflozin group than in the placebo group, with event rates of 43.2 and 61.2 per 1000 patient-years, respectively (P=0.00001). The relative risk of the renal-specific composite of end-stage kidney disease, a doubling of the creatinine level, or death from renal causes was lower by 34% (P<0.001), and the relative risk of end-stage kidney disease was lower by 32% (P=0.002). The canagliflozin group also had a lower risk of cardiovascular death, myocardial infarction, or stroke.

In patients with T2DM and kidney disease, the risk of kidney failure and cardiovascular events was lower in the canagliflozin group than in the placebo group.

Project: **DAPA-LVH**

Title of paper: **A randomized controlled trial of dapagliflozin on left ventricular hypertrophy in people with type two diabetes: the DAPA-LVH trial**

Reference: Eur Heart J. 2020 Sep 21;41(36):3421-3432

Authors: AJM Brown, S Gandy, R McCrimmon, JG Houston, AD Struthers, CC Lang

URL: https://pubmed.ncbi.nlm.nih.gov/32578850/

Summary: DAPA-LVH was a single-centre, double-blind, placebo-controlled trial designed to evaluate the efficacy of dapagliflozin 10 mg once daily compared with placebo on left ventricular hypertrophy (LVH) in participants with T2DM and LVH. 66 participants with T2DM, LVH, and controlled blood pressure (BP) were randomised to receive dapagliflozin 10 mg once daily or placebo for 12 months. The primary endpoint was change in absolute left ventricular mass (LVM).

Dapagliflozin treatment significantly reduced LVM and LVH. The reduction in LVM was accompanied by reductions in systolic BP, body weight, visceral and subcutaneous adipose tissue, insulin resistance, and high-sensitivity C-reactive protein. The regression of LVM suggests dapagliflozin can initiate reverse remodelling and changes in left ventricular structure that may partly contribute to the cardio-protective effects of dapagliflozin.

Project: **VERTIS**

Title of paper: **Cardiovascular Outcomes with Ertugliflozin in Type 2 Diabetes**

Reference: N Engl J Med 2020; 383:1425-1435

Authors: CP Cannon, R Pratley, SD Jack, J Mancuso, S Huyck, U Masiukiewicz, B Charbonnel, R Frederich, S Gallo, F Cosentino, WJ Shih, I Gantz et al., for the VERTIS CV Investigators

URL: https://www.nejm.org/doi/full/10.1056/NEJMoa2004967

Summary: This multicentre, double-blind RCT sought to establish the cardiovascular effects of ertugliflozin, an inhibitor of sodium–glucose co-transporter 2. Over 8,000 patients with T2DM and atherosclerotic cardiovascular disease took part. Patients were randomly assigned to receive 5 mg or 15 mg of ertugliflozin or placebo once daily. With the data from the two ertugliflozin dose groups pooled for analysis ertugliflozin was shown to be noninferior to placebo with respect to the composite outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. Overall the trial did not find significant benefits for those taking ertuglilozin compared to those taking placebo.

Project: **4P Study**

Title of paper: **BNP for personalised primary prevention in diabetes**

Reference: European Heart Journal, Volume 41, Issue Supplement 2, November 2020, ehaa946.2942

Authors: VH Chong, JSS Singh, E Dow, RJ McCrimmon, CC Lang, AD Struthers

URL: https://academic.oup.com/eurheartj/article/41/Supplement_2/ehaa946.2942/6004878

Summary: A major problem in T2DM is the high incidence of silent cardiac abnormalities, namely myocardial ischaemia, left ventricular hypertrophy, left ventricular systolic dysfunction, left ventricular diastolic dysfunction, and left atrial enlargement. To improve primary prevention of cardiovascular disease in diabetes, we need to first identify the type of silent cardiac abnormality and treat accordingly. However cardiac phenotyping in all people with T2DM would be prohibitively expensive.

This study examines the prevalence of these cardiac abnormalities, and the accuracy of biomarkers in identifying them, in a cohort of 246 patients with well-controlled T2DM and blood pressure with no known cardiovascular symptom or disease. 57.3% had silent cardiac abnormalities. 36.6% had 1 abnormality, 17.9% had 2 and 2.8% had 3. The most prevalent was left ventricular enlargement; followed by left ventricular hypertrophy and left ventricular diastolic dysfunction.

Of the biomarkers measured, both N-terminal pro b-type natriuretic peptid (NT-proBNP) and high-sensitivity cardiac Troponin (hs-cTnI) performed best in detecting silent cardiac abnormalities with p-values of 0.02 and 0.0004. Increasing NT-proBNP and hs-cTnI levels correlated to increasing number of concomitant cardiac abnormalities. Our key new finding is that biomarkers identify those with multiple silent cardiac abnormalities.

BNP and hs-cTnI appear to identify those with multiple silent cardiac abnormalities which may make them useful screening tests so that cardiac investigations are focused on this high-risk subset, with a view to intensifying potential therapies on this subset to reduce the cardiotoxic effect of diabetes.

Project: **FAST trial**

Title of paper: **Long-term cardiovascular safety of febuxostat compared with allopurinol in patients with gout (FAST): a multicentre, prospective, randomised, open-label, non-inferiority trial**

Reference: The Lancet Vol 396; 10264, 28 Nov–4 Dec 2020: 1745-1757

Authors: IS Mackenzie, I Ford, G Nuki, J Hallas, CJ Hawkey, J Webster, SH Ralston, M Walters, M Robertson, R De Caterina, E Findlay, F Perez-Ruiz, JJV McMurray, TM MacDonald and the FAST Study Group

URL: https://www.sciencedirect.com/science/article/pii/S0140673620322340?via%3Dihub

Summary: The FAST trial was a prospective, randomised, open-label, blinded-endpoint, non-inferiority trial of febuxostat versus allopurinol in over 6000 patients with gout and one additional cardiovascular risk factor. The study was carried out in the UK, Denmark, and Sweden, following concerns about the cardiovascular safety of febuxostat.

The study found that febuxostat is non-inferior to allopurinol therapy with respect to the primary cardiovascular endpoint (a composite of hospitalisation for non-fatal myocardial infarction or biomarker-positive acute coronary syndrome; non-fatal stroke; or cardiovascular death). Long-term use of febuxostat is not associated with an increased risk of death or serious adverse events compared with allopurinol.

Project: **ETHOS – there are 4 publications from this study:**

Title of paper 1: **Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-very-Severe COPD**

Reference: N Engl J Med. 2020 Jul 2;383(1):35-48

Authors: KF Rabe, FJ Martinez, GT Ferguson, C Wang, D Singh, JA Wedzicha, R Trivedi, E St Rose, S Ballal, J McLaren, P Darken, M Aurivillius, C Reisner, P Dorinsky and the ETHOS Investigators

URL: https://pubmed.ncbi.nlm.nih.gov/32579807/

Summary: *This paper compared the effect of triple v's dual therapy on exacerbation rate.*

Triple fixed-dose regimens of an inhaled glucocorticoid, a long-acting muscarinic antagonist (LAMA), and a long-acting β2-agonist (LABA) for COPD have been studied at single dose levels of inhaled glucocorticoid, but not at two dose levels. ETHOS was a 52 week, phase 3 RCT to evaluate the efficacy and safety of triple therapy at two dose levels of inhaled glucocorticioid in patients with moderate to very severe COPD who had at least one exacerbation in the last year.

Over 8500 patients from 26 countries took part. They were assigned in a 1:1:1:1 ratio to receive twice-daily inhaled doses of triple therapy (inhaled glucocorticoid [320 µg or 160 µg of budesonide], a LAMA [18 µg of glycopyrrolate], and a LABA [9.6 µg of formoterol]) [BGF group] or one of two dual therapies (18 µg of glycopyrrolate plus 9.6 µg of formoterol [GF group] or 320 µg of budesonide plus 9.6 µg of formoterol [BF group]).

The annual rates of moderate or severe exacerbations were 1.08 in the 320-µg BGF group, 1.07 in the 160-µg BGF group, 1.42 in the GF group, and 1.24 in the BF group. The rate was significantly lower with 320-µg BGF therapy than with GF (24% lower: rate ratio, 0.76; 95% CI, 0.69 to 0.83; P<0.001) or BF (13% lower: rate ratio, 0.87; 95% CI, 0.79 to 0.95; P = 0.003). Similarly, the rate was significantly lower with 160-µg BGF therapy than with GF (25% lower: rate ratio, 0.75; 95% CI, 0.69 to 0.83; P<0.001) or BF (14% lower: rate ratio, 0.86; 95% CI, 0.79 to 0.95; P = 0.002). The incidence of any adverse events was similar across the treatment groups (range, 61.7 to 64.5%); the incidence of confirmed pneumonia ranged from 3.5 to 4.5% in the groups that included inhaled glucocorticoid use and was 2.3% in the GF group.

The study found that triple therapy BGF (at either the 160-µg or 320-µg dose of budesonide), resulted in a lower rate of moderate or severe COPD exacerbations than GF or BF.

Title of paper 2: **Reduced All-Cause Mortality in the ETHOS Trial of budesonide / Glycopyrrolate / Formoterol for Chronic Obstructive Pulmonary Disease. A Randomized, Double-Blind, Multicenter, Parallel-Group Study**

Reference: Am J Respir Crit Care Med. 2021 Mar 1;203(5):553-564

Authors: FJ Martinez, KF Rabe, GT Ferguson, JA Wedzicha, D Singh, C Wang, K Rossman, E St Rose, R Trivedi, S Ballal, P Darken, M Aurivillius, C Reisner, P Dorinsky

URL: https://pubmed.ncbi.nlm.nih.gov/33252985/

Summary: Please refer to previous ETHOS publication for explanation of abbreviations.

This paper reports on the effect of triple therapy compared with dual therapy on the risk of death.

Risk of death with BGF 320 was significantly lower than GF (hazard ratio, 0.51; 95% CI 0.33-0.80; unadjusted P = 0.0035). There were no significant differences in mortality when comparing BGF 320 with BF (hazard ratio, 0.72; 95% CI 0.44-1.16; P = 0.1721), nor when comparing BGF 160 against either dual comparator. Results were similar when the first 30, 60, or 90 days of treatment were excluded from the analysis. Deaths from cardiovascular causes occurred in 0.5%, 0.8%, 1.4%, and 0.5% of patients in the BGF 320, BGF 160, GF, and BF groups, respectively.

The study found that triple therapy with BGF 320 reduced the risk of death compared with GF, but was not shown to significantly reduce the risk of death compared with BF,

in patients with COPD. Triple therapy containing a lower dose of inhaled corticosteroid (budesonide 160-µg / glycopyrrolate / formoterol) was not shown to significantly reduce the risk of death compared with the dual therapy comparators.

Title of paper 3: **Benefits of budesonide / glycopyrrolate / formoterol fumarate (BGF) on symptoms and quality of life in patients with COPD in the ETHOS trial**

Reference: Respir Med. Aug-Sep 2021;185:106509

Authors: FJ Martinez, KF Rabe, GT Ferguson, JA Wedzicha, R Trivedi, M Jenkins, P Darken, M Aurivillius, P Dorinsky

URL: https://pubmed.ncbi.nlm.nih.gov/34171789/

Summary: Please see the first ETHOS publication for explanation of the abbreviations.

This paper reports findings on the long-term effects of triple therapy BGF vs GF and BF on symptoms and health-related quality of life (HRQoL) over 52 weeks.

BGF significantly reduced rescue medication use vs GF and BF (-0.53 puffs/day [$p < 0.0001$] and -0.35 puffs/day [$p = 0.0002$], respectively, with BGF 320 over 52 weeks). BGF 320-µg also significantly improved St George's Respiratory Questionnaire (SGRQ) total score over 24 and 52 weeks vs dual therapies, resulting in the greatest proportion of SGRQ responders vs dual therapies over 24 weeks (52.5% vs 42.5% [GFF] and 45.2% [BF]) and 52 weeks (47.0% vs 37.8% [GF] and 41.0% [BF]). Similar results were observed with BGF 160-µg. Benefits were also observed vs dual therapies in symptomatic endpoints including Transition Dyspnea Index focal score, EXAcerbations of Chronic pulmonary disease Tool total scores and Evaluating Respiratory Symptoms in COPD total scores over 24 and 52 weeks.

The study found that BGF triple therapy improved symptoms and HRQoL vs dual therapies over 24 and 52 weeks.

Title of paper 4: **Improvements in lung function with budesonide / glycopyrrolate / formoterol fumarate metered dose inhaler versus dual therapies in patients with COPD: a sub-study of the ETHOS trial**

Reference: Ther Adv Respir Dis. 2021 Jan-Dec; 15: 17534666211034329

Authors: KF Rabe, FJ Martinez, D Singh, R Trivedi, M Jenkins, P Darken, M Aurivillius, P Dorinsky

URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8392797/

Summary: Please see the first ETHOS publication for an explanation of the abbreviations.

This publication reports results from the ETHOS pulmonary function test (PFT) sub-study.

A subset of patients participated in the 4-hour PFT study; primary endpoints were change from baseline in morning pre-dose trough forced expiratory volume in one second (FEV1) versus GFF and FEV1 area under the curve from 0 to 4 hours (AUC0–4) versus BFF at week 24.

The PFT modified intent-to-treat population included 3088 patients (mean age 64.4 years; mean reversibility post-albuterol 16.7%; mean post-albuterol FEV1% predicted 42.8). BGF 320/18/9.6 µg and 160/18/9.6 µg significantly improved morning pre-dose trough FEV1 at week 24 versus GF ($p \leqslant 0.0035$ for both). Improvements in trough FEV1 were also observed at week 52 for BGF 320/18/9.6 µg and 160/18/9.6 µg versus GF ($p \leqslant 0.0005$ for both). For FEV1 AUC0-4 at week 24, BGF 320/18/9.6 µg and 160/18/9.6 µg showed significant improvements versus BF ($p < 0.0001$ for both). Improvements were maintained at week 52 ($p < 0.0001$).

The study found that BGF 320/18/9.6 µg and 160/18/9.6 µg significantly improved trough FEV1 versus GFF and FEV1 AUC0-4 versus BFF at week 24. The lung function benefits with both doses of BGF were maintained following 52 weeks of treatment.

Project: **INTREPID**

Title of paper: **INTREPID: single- versus multiple-inhaler triple therapy for COPD in usual clinical practice**

Reference: ERJ Open Research 2021 7: 00950-2020;

Authors: DMG Halpin, S Worsley, AS Ismaila, K-M Beeh, D Midwinter, JWH Kocks,E Irving, JM Marin, N Martin, M Tabberer, NG Snowise, C Compton

URL: https://openres.ersjournals.com/content/7/2/00950-2020

Summary: Real-world trial data comparing single- with multiple-inhaler triple therapy (MITT) in COPD patients are currently lacking. The effectiveness of once-daily single-inhaler of fluticasone furoate (FF), umeclidinium (UMEC) and vilanterol (VI) and MITT were compared in usual clinical care.

INTREPID was a multicentre, randomised, open-label, phase IV effectiveness study comparing FF/UMEC/VI 100/62.5/25 µg via the ELLIPTA inhaler with a clinician's choice of any approved non-ELLIPTA MITT in usual COPD clinical practice in over 3,000 patients in five European countries. The primary end-point was proportion of COPD Assessment Test [CAT] responders (≥2-unit decrease in CAT score from baseline) at week 24.

The proportion of CAT responders at week 24 was significantly greater with FF/UMEC/VI versus non-ELLIPTA MITT (OR 1.31, 95% CI 1.13–1.51; p<0.001) and mean change from baseline in FEV1 was significantly greater with FF/UMEC/VI (77 mL versus 28 mL; treatment difference 50 mL, 95% CI 26–73 mL; p<0.001). The percentage of patients with at least one critical error in inhalation technique was low in both groups (FF/UMEC/VI 6%; non-ELLIPTA MITT 3%). Safety profiles, including incidence of pneumonia serious adverse events, were similar between treatments.

The study found that in a usual clinical care setting, treatment with once-daily single-inhaler FF/UMEC/VI resulted in significantly more patients gaining health status improvement and greater lung function improvement versus non-ELLIPTA multiple-inhaler triple therapy.

Project: **PACT**

Title of paper: **Asthma prescribing according to Arg16Gly beta-2 genotype: a randomised trial in adolescents**

Reference: European Respiratory Journal Jan 2021, 2004107

Authors: T Ruffles, CJ Jones, C Palmer, S Turner, J Grigg, R Tavendale, F Hogarth, P Rauchhaus, K Pilvinyte, R Hannah, H Smith, R Littleford, B Lipworth, S Mukhopadhyay

URL: https://erj.ersjournals.com/content/early/2021/01/14/13993003.04107-2020.long

Summary: The A allele of rs1042713 (Arg16 amino acid) in the β2 adrenoreceptor is associated with poor response to long-acting β2-agonist (LABA) in young people with asthma. The study aim was to assess whether the prescribing of second line controller with LABA or a leukotriene receptor antagonist (LTRA) according to Arg16Gly genotype would result in improvements in pediatric asthma-related quality of life questionnaire (PAQLQ).

This was a pragmatic RCT carried out in Scotland and England. Participants were age 12–18 years with asthma who were taking inhaled corticosteroids. 241 participants were randomised (1:1) to receive personalised care (genotype directed prescribing) or standard guideline care. The primary outcome measure was change in PAQLQ.

Genotype directed prescribing resulted in an improvement in PAQLQ compared to standard care 0.16, (95%CI 0.00–0.31; p=0.049). The AA genotype was associated with a larger improvement in PAQLQ with personalised versus standard care 0.42, (95%CI 0.02–0.81; p=0.041).

This is the first RCT demonstrating that genotype driven asthma prescribing is associated with a significant improvement in a clinical outcome compared to standard

care. Adolescents with the AA homozygous genotype benefited most. The potential role of such β2-adrenoceptor genotype directed therapy in younger and more severe childhood asthma warrants further exploration.

Project: **ECLS**

Title of paper: **Earlier diagnosis of lung cancer in a randomised trial of an autoantibody blood test followed by imaging**

Reference: European Respiratory Journal 2021 57: 2000670;

Authors: FM Sullivan, FS Mair, W Anderson, P Armory, A Briggs et al., on behalf of the ECLS Team

URL: https://doi.org/10.1183/13993003.00670-2020

Summary: The EarlyCDT-Lung test is a high specificity blood-based autoantibody biomarker that could contribute to predicting lung cancer risk. Here we report on the results of a phase IV biomarker evaluation of whether using the EarlyCDT-Lung test and any subsequent CT scanning to identify those at high risk of lung cancer reduces the incidence of patients with stage III/IV/Unspecified lung cancer at diagnosis, compared with the standard clinical practice.

ECLS was an RCT of 12,208 participants at risk of developing lung cancer in Scotalnd. The intervention arm received the EarlyCDT-Lung test and, if test positive, low-dose CT scanning six-monthly for up to 2 years. EarlyCDT-Lung test negative and control arm participants received standard clinical care. Outcomes were assessed at 2 years post-randomisation using validated data on cancer occurrence, cancer staging, mortality and comorbidities.

At 2 years, 127 lung cancers were detected in the study population (1.0%). In the intervention arm, 33/56 (58.9%) lung cancers were diagnosed at stage III/IV compared to 52/71 (73.2%) in the control arm. The hazard ratio for stage III/IV presentation was 0.64 (95% confidence interval 0.41, 0.99). There were non-significant differences in lung cancer and all-cause mortality after 2 years.

The observation of a stage-shift towards earlier-stage lung cancer diagnosis merits further investigations to evaluate whether the EarlyCDT-Lung test adds anything to the emerging standard of LDCT.

Project: **MAMMOTH**

Title of paper: **Maintaining musculoskeletal health using a behavioural therapy approach: a population-based randomised controlled trial (the MAmMOTH Study**

Reference: Ann Rheum Dis 2021;80:903–911.

Authors: GJ Macfarlane, M Beasley, N Scott, H Chong, P McNamee, J McBeth, N Basu, PC Hannaford , GTJones , P Keeley, GJ Prescott, K Lovell

URL: https://ard.bmj.com/content/annrheumdis/80/7/903.full.pdf

Summary: Cognitive–behavioural therapy (CBT) has been shown to be effective in the management of chronic widespread pain (CWP); this study tests whether it can prevent onset among adults at high risk.

This was a population-based RCT, with recruitment through UK general practices. A mailed screening questionnaire identified adults at high risk of CWP. Participants received either usual care (UC) or a short course of telephone CBT (tCBT). The primary outcome was CWP onset at 12 months.

The study found that a short course of tCBT did not prevent onset of chronic widespread pain in adults at high risk (tCBT: 18.0%vs UC: 17.5%; OR 1.05; 95%CI 0.75 to 1.48), but improved quality of life and was cost-effective. A low-cost, short-duration intervention benefits persons at risk of chronic widespread pain.

Project: **RADAR**

Title of paper: **Safety and efficacy of losartan for the reduction of brain atrophy in clinically diagnosed Alzheimer's disease**

Reference: Lancet Neurol 2021; 20: 895–906

Authors: PG Kehoe, N Turner, B Howden, L Jarutyte, SL Clegg, IB Malone et al. on behalf of the RADAR investigators

URL: https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00263-5/fulltext

Summary: Drugs modifying angiotensin II signalling could reduce Alzheimer's disease pathology, thus decreasing the rate of disease progression. The study investigated whether the angiotensin II receptor antagonist losartan, compared with placebo, could reduce brain volume loss, as a measure of disease progression, in clinically diagnosed mild-to-moderate Alzheimer's disease.

This UK multicentre RCT enrolled patients aged 55 years or older, previously untreated with angiotensin II drugs and diagnosed with mild-to-moderate Alzheimer's disease. 197 patients completed the study. 12 months of treatment with losartan was well tolerated but was not effective in reducing the rate of brain atrophy. Further research is needed to assess the potential therapeutic benefit from earlier treatment in patients with milder cognitive impairment or from longer treatment periods.

Project: **SCALE-UP BP**

Title of paper: **Telemonitoring at scale for hypertension in primary care: An implementation study**

Reference: PLOS Medicine June 17, 2020

Authors: V Hammersley, R Parker, M Paterson, J Hanley, H Pinnock, P Padfield, A Stoddart, HG Park, A Sheikh, B McKinstry

URL: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003124

Summary: While evidence from RCTs shows that telemonitoring for hypertension is associated with improved blood pressure (BP) control, healthcare systems have been slow to implement it, partly because of inadequate integration with existing clinical practices and electronic records. The study explored the feasibility and impact of implementing an integrated telemonitoring system for hypertension into routine primary care.

Seventy-five primary care practices enrolled 3,200 patients with established hypertension. The main outcome measures were intervention uptake, change in BP, change in clinician appointment use, and participants' views on features that facilitated or impeded uptake of the intervention.

In an evaluation subgroup of 8 practices, mean systolic BP fell by 6.55 mm Hg (SD 15.17), and mean diastolic BP by 4.23 mm Hg (SD 8.68). Compared with the previous year, participating patients made 19% fewer face-to-face appointments, compared with 11% fewer in patients with hypertension who were not telemonitoring. Total consultation time for participants fell by 15.4 minutes (SD 68.4), compared with 5.5 minutes (SD 84.4) in non-telemonitored patients.

It was found that improvements in BP control similar to those found in RCTs of telemonitoring in hypertension can be achieved when implemented in routine practice and at scale and that this is accomplished with no increase in workload.

Project: **STRENGTH**

Title of paper: **Effect of High-Dose Omega-3 Fatty Acids vs Corn Oil on Major Adverse**

Cardiovascular Events in Patients at High Cardiovascular Risk

Reference: JAMA. 2020;324(22):2268-2280

Authors: SJ Nicholls; AM Lincoff; M Garcia et al

URL: https://pubmed.ncbi.nlm.nih.gov/33190147/

Summary: This RCT aimed to determine whether the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) reduce cardiovascular risk. It compared a carboxylic acid formulation of EPA and DHA (4g/d omega-3 CA) with corn oil in >13,000 statin-treated participants with high cardiovascular risk, hypertriglyceridemia, and low levels of high-density lipoprotein cholesterol (HDL-C). Participants were recruited from 22 countries.

The trial was stopped early as there was no significant difference in a composite outcome of major adverse cardiovascular events (hazard ratio 0.99). The study concluded that among statin-treated patients at high cardiovascular risk, the addition of omega-3 CA, compared with corn oil, to usual background therapies resulted in no significant difference in a composite outcome of major adverse cardiovascular events. These findings do not support use of this omega-3 fatty acid formulation to reduce major adverse cardiovascular events in high-risk patients.

Project: **USEFUL**

Title of paper: **Patterns of symptoms possibly indicative of cancer and associated help-seeking behaviour in a large sample of United Kingdom residents—The USEFUL study**

Reference: PLOS ONE January 24, 2020

Authors: PC Hannaford, AJ Thornton, P Murchie, KL Whitaker, R Adam, AM Elliott

URL: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0228033

Summary: Cancer awareness campaigns aim to increase awareness of the potential seriousness of signs and symptoms of cancer, and encourage their timely presentation to healthcare services. Enhanced understanding of the prevalence of symptoms possibly indicative of cancer in different population subgroups, and associated GP help-seeking behaviour, will help to target cancer awareness campaigns more effectively.

More than16,000 patients age 50+ from 21 GP practices in Scotland and England took part in this questionnaire-based study.

Over half of respondents (58.5%) had experienced at least one symptom possibly indicative of cancer in the last year. The prevalence of individual symptoms varied widely. Red flag symptoms were uncommon. Female gender, inability to work because of illness, smoking, a history of a specified medical diagnosis, low social support and lower household income were consistently associated with experiencing at least one symptom possibly indicative of cancer. The proportion of people who had contacted their GP about a symptom experienced in the last month varied between 8.1% (persistent cough) and 39.9% (unexplained weight loss) and in the last year between 32.8% (hoarseness) and 85.4% (lump in breast). Nearly half of respondents experiencing at least one red flag symptom in the last year did not contact their GP about it. Females, those aged 80+ years, those unable to work because of illness, ex-smokers and those previously diagnosed with a specified condition were more likely to report a symptom possibly indicative of cancer to their GP; and those on high household income less likely.

Symptoms possibly indicative of cancer were common, although they were not evenly distributed. Help- seeking responses to different symptoms also vary. The results suggest important opportunities to provide more nuanced messaging and targeting of symptom-based cancer awareness campaigns.

Project: **VESUVIUS**

Title of paper: **Cardiovascular Effects of Switching From Tobacco Cigarettes to Electronic Cigarettes**

Reference: Journal of the American College of Cardiology 2049 v74; issue 25 pp 3121-3123

Authors: J George, M Hussain, T Vadiveloo, S Ireland, P Hopkinson, AD Struthers, PT Donnan, F Khan, CC Lang

URL: https://www.sciencedirect.com/science/article/pii/S0735109719381938

Summary: E-cigarette (EC) use is increasing exponentially worldwide. This study sought to determine the early cardiovascular effects of switching from tobacco cigarettes (TC) to EC in chronic smokers.

114 chronic smokers completed the study. Within 1 month of switching from TC to EC, there was a significant improvement in endothelial function (linear trend β = 0.73%; 95% CI: 0.41 to 1.05; p < 0.0001; TC vs. EC combined: 1.49%; 95% CI: 0.93 to 2.04; p < 0.0001) and vascular stiffness (−0.529 m/s; 95% CI: −0.946 to −0.112; p = 0.014). Females benefited from switching more than males. Those who complied best with EC switch demonstrated the largest improvement. There was no difference in vascular effects between EC with and without nicotine within the study timeframe.

TC smokers, particularly females, demonstrate significant improvement in vascular health within 1 month of switching from TC to EC. Switching from TC to EC may be considered a harms reduction measure.

Project: **VITILIGO**

Title of paper: **Randomized controlled trial of topical corticosteroid and home-based narrowband ultraviolet B for active and limited vitiligo: results of the HI-Light Vitiligo Trial**

Reference: Volume184, Issue5, May 2021,BJD Vol 184 issue 5 2021 pp 828-839

Authors: KS Thomas, JM Batchelor, P Akram, JR Chalmers, RH Haines, GD Meakin, L Duley et al, on behalf of the UK Dermatology Clinical Trials Network's HI-Light Vitiligo Trial Team

URL: https://doi.org/10.1111/bjd.19592

Summary: Evidence for the effectiveness of vitiligo treatments is limited. This study aimed to determine the effectiveness of (i) handheld narrowband UVB (NB-UVB) and (ii) a combination of potent topical corticosteroid (TCS) and NB-UVB, compared with TCS alone, for localized vitiligo.

Primary outcome data were available for 370 (72%) participants. The study found that combination treatment with home-based handheld NB-UVB plus TCS is likely to be superior to TCS alone for treatment of localized vitiligo. Combination treatment was relatively safe and well tolerated