OP32 ASSOCIATION BETWEEN OPTIMAL GUIDELINE-INDICATED CARE AND SURVIVAL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND LONG-TERM CONDITIONS: A POPULATION BASED COHORT STUDY

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Background Acute myocardial infarction (AMI) remains the largest cause of hospitalisation and death in Europe. Long term conditions (LTC) are common in people with AMI and patients with LTCs also experience lower survival. The effect of LTCs on treatment receipt has not been investigated.

Methods Myocardial Ischaemia National Audit Project (MINAP) data for 6 93 388 patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) were used to investigate associations between LTCs (including diabetes, chronic heart failure, chronic renal failure, COPD, peripheral vascular disease, and cerebrovascular disease) and treatment receipt. Poisson and binomial models were fitted to determine the association between LTCs and receipt of care, with treatment receipt as a count and a binary optimal care vs. sub-optimal care variable (receipt of all eligible care components vs. missing one or more) as the outcome and individual as well as cumulative LTCs as exposures. Model adjustments were informed by directed acyclic graphs. Flexible parametric survival models were fitted to investigate the interaction of LTCs and optimal care, and the impact on survival.

Results Receipt of optimal care was 11.3% (n=78,376), with patients receiving on average 67% of all care opportunities (Mean 0.67, SD 0.23; Median 0.7, IQR 0.5–0.86). In those with a LTC (n=257,929), 11% (n=28,357) received optimal care. Patients with ≥one LTC received 2.7% fewer treatments compared with no LTC (IRR 0.97, 95% CI 0.97–0.98); larger differences of 7.3% and 6.1% were evident, respectively, in patients with chronic heart failure (0.93, 0.92–0.93) and chronic renal failure (0.94, 0.93–0.94). The odds of receiving suboptimal care were not significantly different in patients with ≥one LTC than those with no LTC (OR 1.01, 95% CI 0.89,1.13), however the odds of receiving optimal care was significantly lower in chronic heart failure (0.53, 0.46–0.61) and chronic renal failure (0.52, 0.44–0.62) compared to patients without these conditions. There were 2 04 667 deaths over a mean follow-up time of 2.25 years. The hazard of death in optimally treated patients with ≥one LTC was double that of those without LTCs (HR 2.18, 95% CI 2.09–2.27) and 2.5-fold in sub-optimally treated patients with ≥one LTC compared with no LTCs (2.60, 2.52–2.69).

Conclusion Patients with LTCs received fewer treatments and were less likely to receive optimal care than those without. Treatment receipt was lowest in chronic heart failure and chronic renal failure. The worst survival was observed in patients with ≥one LTC receiving sub-optimal care.

Screening

OP33 SYMPTOMATIC VS PRE-SYMPTOMATIC TREATMENT OF TYROSINEMIA TYPE 1 WITH NITISINONE: A SYSTEMATIC REVIEW

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Background Tyrosinemia type 1 is a rare autosomal recessive disorder of amino acid metabolism, affecting approximately 1 in 1 00 000 people. Without treatment, death is common in childhood. Treatment with nitisinone is associated with reductions in mortality and morbidity; some studies suggest better outcomes when treatment is initiated before the symptoms of the disorder present. An apparent benefit of earlier versus later treatment has been used to support the implementation of newborn screening for Tyrosinemia type 1, but these studies have not been synthesised or quality appraised. We conducted a systematic review to examine if individuals treated following screen detection of the disorder had better outcomes than those treated following symptomatic detection.

Methods Standard systematic review methods were used. Embase, Medline, Pre-Medline, and Web of Science were searched. Participants were individuals with Tyrosinemia type 1. We compared people who received nitisinone following screen detection of the disorder (early treatment) with those who received nitisinone after symptomatic presentation (late treatment). Any reported outcomes were considered. Two reviewers independently screened and assessed records, and conducted quality appraisal (using the Quality Assessment Tool for Quantitative Studies). Data extraction was carried out by one reviewer, and checked by another. A narrative synthesis of results was carried out. Post-hoc comparisons were conducted to address confounding factors and applicability concerns.

Results The titles/abstracts of 470 unique records were examined, and 50 full texts assessed. Seven articles were included in the review. Study sample sizes ranged from 17 to 148. Methodological quality of the studies was moderate to weak. There was evidence of associations between early treatment with nitisinone and lower rates of death, liver disease and transplantations, and renal dysfunction. However, posthoc analyses suggested an association between earlier treatment and lower rates of liver transplantation but not mortality (analysis 1) or no differences in outcomes for those treated earlier versus later (analyses 2 and 3).

Discussion Evidence from observational studies suggests that treatment with nitisinone initiated during the pre-symptomatic period may be beneficial to people with Tyrosinemia type 1. However, this is subject to bias and applicability concern; the apparent benefits of early treatment may not be present when these issues are addressed. There are several challenges inherent in rare diseases research, including small and

heterogeneous populations, lack of appropriate comparator treatments, and limited knowledge about the disease. Our review suggests that alternative research methods or tolerance of lower levels of evidence may be required.

OP34 UNIVERSAL ANTENATAL CULTURE-BASED SCREENING FOR MATERNAL GROUP B *STREPTOCOCCUS* (GBS) CARRIAGE TO PREVENT EARLY-ONSET GBS DISEASE: A SYSTEMATIC REVIEW FOR THE UK NATIONAL SCREENING COMMITTEE (NSC)

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Background GBS is the leading cause of morbidity and mortality from neonatal sepsis in the UK and patient groups are keen for screening to be implemented. Intrapartum antibiotic prophylaxis (IAP) is offered to women identified with GBS carriage or GBS risk factors to prevent mother to baby transmission and early-onset GBS disease (EOGBS,<7 days). This review on universal GBS screening for pregnant women was undertaken to assist NSC policy decision-making. Review questions were on: epidemiology of GBS, diagnostic accuracy of tests, effectiveness of IAP treatment, and effectiveness of universal GBS screening.

Methods Medline, Embase, and Cochrane databases were searched. Grey literature included Public Health England, British Paediatric Surveillance Unit, Audits and Confidential Enquiries, and reference lists of included papers. Participants were pregnant women≥35 weeks or neonates<7 days. The intervention was selective culture from recto-vaginal swabs at 35–37 weeks followed by IAP treatment for those who were culture positive. Reviewers independently screened records, extracted data, and assessed methodological quality using appropriate tools for each question, including QUADAS-2, Cochrane RoB, and RoBANS tools. Data were synthesised narratively.

Results 73 studies were included from 6287 references. EOGBS in the UK affects 0.57 per 1000 live births with a case fatality of 5.2%. Twenty-two percent of EOGBS cases and 63% of deaths are in preterm births (many would be ineligible for screening). The natural history of GBS is not known. We estimate that universal GBS screening would be offered to approximately 7 18 126 pregnant term women annually.Approximately 63 347 (57.7%) women who test positive in labour and 3282 (8%) who test negative in labour would transmit GBS to their neonates, and approximately 350 (0.5%) neonates would develop EOGBS. We estimate the positive predictive value of selective culture to detect EOGBS to be around 0.2% (350/150,806). More than 1 50 450 (>99%) women would be false positive and unnecessarily treated. Harms from IAP are unclear but will include antibiotic resistance and other possible health problems. There were no randomised controlled trials of the effectiveness of GBS screening and observational studies gave inconsistent results for EOGBS mortality and morbidity.

Conclusion EOGBS is an important health condition. However, tests are not accurate predictors of maternal GBS transmission, or of EOGBS. Evidence on the harms and benefits of GBS screening is limited. Universal screening is therefore not recommended.

OP35 PRAGMATIC INTEGRATED TRIALS IN SCREENING: A BREAST SCREENING EXAMPLE INVOLVING 1.2 MILLION WOMEN

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Background Pragmatic integrated trials use routine data and systems to automate participant selection, randomisation, outcome measurements and/or other elements to deliver large trials at low cost. Here we present an example of a large pragmatic integrated trial in breast cancer screening, and discuss the situations in which these trials are appropriate and acceptable.

Methods The intervention was a simple change to the mammography test for breast screening. Interpreting whether screening mammogram show cancer is a difficult repetitive task that can result in missed cancers and false-positive recalls, and some studies have indicated that missed cancers may increase with time on task (the vigilance decrement). In the UK two readers independently evaluate each batch of mammograms to search for signs of cancer. The intervention was to change the order in which batches of mammograms were presented for interpretation, to reduce the effects of the vigilance decrement.

This was evaluated using a multicentre, double-blind, cluster randomised clinical trial at 46 breast screening centres in England for 1 year. Three hundred sixty readers participated. The primary outcome was cancer detection rate; secondary outcomes were rates of recall and disagreements between readers.

Results 1 194 147 women who had screening mammograms were randomised (596 642 in the intervention group; 597 505 in the control group), and 10 484 cases (0.88%) of breast cancer were detected. There was no significant difference in cancer detection rate with 5272 cancers (0.88%) detected in the intervention group vs 5212 cancers (0.87%) detected in the control group (difference, 0.01% points; 95% CI, −0.02% to 0.04% points). There was also no difference in recall rate, with 24 681 [4.14%] in intervention and 24 894 [4.17%] in the control group (difference, −0.03% points; 95% CI, −0.10% to 0.04% points). Patterns of cancer detection and recall with time since a break indicated that performance did not decline with time on task as predicted by the vigilance decrement theory. In fact, positive predictive value increased with time on task.

Discussion This pragmatic integrated trial in over 1 million women cost less than £300 k, and demonstrates that in certain circumstances this study design is appropriate. Considerations when planning a pragmatic integrated trial include whether consent is required at the individual or institutional level, whether the relevant outcomes are available in routine data, and the cost of the intervention.