Medicine Abstracts

BMJ Open

E. Koch et al., **Abortion Legislation, Maternal Healthcare, Fertility, Female Literacy, Sanitation, Violence against Women and Maternal Deaths: A Natural Experiment in 32 Mexican States**, *BMJ Open* 5.2 (February 23, 2015): e006013 • *Objective:* To test whether there is an association between abortion legislation and maternal mortality outcomes after controlling for other factors thought to influence maternal health. *Design:* Population-based natural experiment. *Setting and Data Sources:* Official maternal mortality data from 32 federal states of Mexico between 2002 and 2011. *Main Outcomes:* Maternal mortality ratio (MMR), MMR with any abortive outcome (MMRAO) and induced abortion mortality ratio (iAMR). *Independent Variables:* Abortion legislation grouped as less (n=18) or more permissive (n=14); constitutional amendment protecting the unborn (n=17); skilled attendance at birth; all-abortion hospitalisation ratio; low birth weight rate; contraceptive use; total fertility rates (TFR); clean water; sanitation; female literacy rate and intimate-partner violence. *Main Results*: Over the 10-year period, states with less permissive abortion legislation exhibited lower MMR (38.3 vs 49.6; $p<0.001$), MMRAO (2.7 vs 3.7; $p<0.001$) and iAMR (0.9 vs 1.7; $p<0.001$) than more permissive states. Multivariate regression models estimating effect sizes (β-coefficients) for mortality outcomes showed independent associations (p values between 0.001 and 0.055) with female literacy (β=-0.061 to -1.100), skilled attendance at birth (β=-0.032 to -0.427), low birth weight (β=0.149 to 2.166), all-abortion hospitalisation ratio (β=-0.566 to -0.962), clean water (β=-0.048 to -0.730), sanitation (β=-0.052 to -0.758) and intimate-partner violence (β=0.085 to 0.755). TFR showed an inverse association with MMR (β=-14.329) and MMRAO (β=-1.750) and a direct association with iAMR (β=1.383). Altogether, these factors accounted for (R(2)) 51–88% of the variance among states in overall mortality rates. No statistically independent effect was observed for abortion legislation, constitutional amendment or other covariates. *Conclusions:* Although less permissive states exhibited consistently lower maternal mortality rates, this finding was not explained by abortion legislation itself. Rather, these differences were explained by other independent factors, which appeared to have a more favourable distribution in these states.

Cochrane Database of Systematic Reviews

M. G. Showell, **Antioxidants for Male Subfertility**, *Cochrane Database Syst Rev* 1 (January 19, 2011): CD007411 • *Background:* Between 30% to 80% of male subfertility cases are considered to be due to the damaging effects of oxidative stress on sperm and 1 man in 20 will be affected by subfertility. Antioxidants are widely available and inexpensive when compared to other fertility treatments and many men are already using these to improve their fertility. It is thought that oral supplementation with antioxidants may improve sperm quality by reducing oxidative stress. Pentoxifylline, a drug that acts like an antioxidant, was also included in this review. *Objectives:* This Cochrane review aimed to evaluate the effectiveness and safety of oral supplementation with antioxidants for subfertile male partners in couples seeking fertility assistance. *Search Methods:* We searched the Cochrane Menstrual Disorders and Subfertility Group Specialised Register, CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO and AMED databases (from inception until January 2014); trial registers; sources of

unpublished literature and reference lists. An updated search was run in August 2014 when potentially eligible studies were placed in "Studies awaiting assessment." *Selection Criteria:* We included randomised controlled trials (RCTs) comparing any type or dose of antioxidant supplement (single or combined) taken by the subfertile male partner of a couple seeking fertility assistance with a placebo, no treatment or another antioxidant. *Data Collection and Analysis:* Two review authors independently selected eligible studies, extracted the data and assessed the risk of bias of the included studies. The primary review outcome was live birth; secondary outcomes included clinical pregnancy rates, adverse events, sperm DNA fragmentation, sperm motility and concentration. Data were combined, where appropriate, to calculate pooled odds ratios (ORs) or mean differences (MD) and 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the I(2) statistic. We assessed the overall quality of the evidence for the main outcomes using GRADE methods. *Main Results*: This updated review included 48 RCTs that compared single and combined antioxidants with placebo, no treatment or another antioxidant in a population of 4179 subfertile men. The duration of the trials ranged from 3 to 26 weeks with follow up ranging from 3 weeks to 2 years. The men were aged from 20 to 52 years. Most of the men enrolled in these trials had low total sperm motility and sperm concentration. One study enrolled men after varicocelectomy, one enrolled men with a varicocoele, and one recruited men with chronic prostatitis. Three trials enrolled men who, as a couple, were undergoing in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) and one trial enrolled men who were part of a couple undergoing intrauterine insemination (IUI). Funding sources were stated by 15 trials. Four of these trials stated that funding was from a commercial source and the remaining 11 obtained funding through non-commercial avenues or university grants. Thirty-three trials did not report any funding sources. A limitation of this review was that in a sense we had included two different groups of trials, those that reported on the use of antioxidants and the effect on live birth and clinical pregnancy, and a second group that reported on sperm parameters as their primary outcome and had no intention of reporting the primary outcomes of this review. We included 25 trials reporting on sperm parameters and only three of these reported on live birth or clinical pregnancy. Other limitations included poor reporting of study methods, imprecision, the small number of trials providing usable data, the small sample size of many of the included studies and the lack of adverse events reporting. The evidence was graded as "very low" to "low." The data were current to 31 January 2014. Live birth: antioxidants may have increased live birth rates (OR 4.21, 95% CI 2.08 to 8.51, P< 0.0001, 4 RCTs, 277 men, I(2) = 0%, low quality evidence). This suggests that if the chance of a live birth following placebo or no treatment is assumed to be 5%, the chance following the use of antioxidants is estimated to be between 10% and 31%. However, this result was based on only 44 live births from a total of 277 couples in four small studies. Clinical pregnancy rate: antioxidants may have increased clinical pregnancy rates (OR 3.43, 95% CI 1.92 to 6.11, P < 0.0001, 7 RCTs, 522 men, I(2) = 0%, low quality evidence). This suggests that if the chance of clinical pregnancy following placebo or no treatment is assumed to be 6%, the chance following the use of antioxidants is estimated at between 11% and 28%. However, there were only seven small studies in this analysis and the quality of the evidence was rated as low. Miscarriage: only three trials reported on this outcome and the event rate was very low. There was insufficient evidence to show whether there was a difference in miscarriage rates between the antioxidant and placebo or no treatment groups (OR 1.74, 95% CI 0.40 to 7.60, P = 0.46, 3 RCTs, 247 men, I(2) = 0%, very low quality evidence). The findings suggest that in a population of subfertile men with an expected miscarriage rate of 2%, use of an antioxidant would result in the risk of a miscarriage lying between 1% and 13%. Gastrointestinal upsets: there was insufficient

evidence to show whether there was a difference in gastrointestinal upsets when antioxidants were compared to placebo or no treatment as the event rate was very low (OR 1.60, 95% CI 0.47 to 5.50, P = 0.46, 6 RCTs, 429 men, I(2) = 0%).We were unable to draw any conclusions from the antioxidant versus antioxidant comparison as not enough trials compared the same interventions. *Authors' Conclusions:* There is low quality evidence from only four small randomised controlled trials suggesting that antioxidant supplementation in subfertile males may improve live birth rates for couples attending fertility clinics. Low quality evidence suggests that clinical pregnancy rates may increase. There is no evidence of increased risk of miscarriage but this is uncertain as the evidence is of very low quality. Data were lacking on other adverse effects. Further large well-designed randomised placebo-controlled trials are needed to clarify these results.

European Journal of Contraception and Reproductive Health Care

E. Berglund Scherwitzl, A. Lindén Hirschberg, and R. Scherwitzl, **Identification and Prediction of the Fertile Window Using NaturalCycles**, *Eur J Contracept Reprod Health Care*, e-pub January 16, 2015 • *Objectives:* The aim of the study was to evaluate the ability of a novel web and mobile application to identify a woman's ovulation day and fertile window, in order to use it as a method of natural birth control. *Methods:* A retrospective study was performed on 1501 cycles of 317 women aged 18 to 39 years. Women entered their basal body temperatures, ovulation test results and date of menstruation into the application. *Results:* The mean delay from the first positive ovulation test to the temperature-based estimation of the ovulation day was 1.9 days; the length of the luteal phase varied on average by 1.25 days per user. Only 0.05% of non-fertile days were falsely attributed and found within the fertile window. *Conclusions:* The method is effective at identifying a user's ovulation day and fertile window and can therefore be used as a natural method of birth control.

International Journal of Cancer

M. M. Reigstad et al., **Risk of Breast Cancer following Fertility Treatment—A Registry Based Cohort Study of Parous Women in Norway**, *Int J Cancer* 136.5 (March 1, 2015): 1140–1148 • Despite increasing numbers of women availing themselves of assisted reproductive technology (ART), effects on cancer risk remain unresolved. Given hormonal exposures, breast cancer risk is of particular concern. The aim of this study is to investigate breast cancer risk amongst women giving birth following ART as compared to that amongst women who gave birth without ART. Data on all women who gave birth in Norway with or without ART, between 1984 and 2010 were obtained from the Medical Birth Registry of Norway (MBRN). 808,834 women eligible for study were linked to the Cancer Registry of Norway. Cox proportional models computed hazard ratios (HR) and 95% confidence intervals (CI) of breast cancer between the two groups, adjusting for age, parity, age at first birth, calendar period and region of residence. In total, 8,037 women were diagnosed with breast cancer during the study period, 138 ART women and 7,899 unexposed. Total follow-up time was 12,401,121 person-years (median 16.0); median age at entry was 32.5 years (range 18.6–49.9) for ART women and 26.3 (range 10.5–54.6) for unexposed. Women exposed to ART had an elevated risk of breast cancer (adjusted HR 1.20, 95% CI 1.01–1.42). Subgroup analyses gave an HR of 1.30 (95% CI 1.07–1.57) for women treated with IVF and 1.35 (95 % CI 1.07–1.71) for women with follow-up >10 years, compared with controls. Our findings of increased risk in the study population warrant continued monitoring of women treated with ART as this population advances into more typical cancer age ranges.

JAMA

D. E. Arterburn et al., **Association between Bariatric Surgery and Long-Term Survival**, *JAMA* 313.1 (January 6, 2015): 62–70 • *Importance:* Accumulating evidence suggests that bariatric surgery improves

survival among patients with severe obesity, but research among veterans has shown no evidence of benefit. *Objective:* To examine long-term survival in a large multisite cohort of patients who underwent bariatric surgery compared with matched control patients. *Design, Setting, and Participants:* In a retrospective cohort study, we identified 2500 patients (74% men) who underwent bariatric surgery in Veterans Affairs (VA) bariatric centers from 2000–2011 and matched them to 7462 control patients using sequential stratification and an algorithm that included age, sex, geographic region, body mass index, diabetes, and Diagnostic Cost Group. Survival was compared across patients who underwent bariatric surgery and matched controls using Kaplan-Meier estimators and stratified, adjusted Cox regression analyses. *Exposure:* Bariatric procedures, which included 74% gastric bypass, 15% sleeve gastrectomy, 10% adjustable gastric banding, and 1% other. *Main Outcomes and Measures:* All-cause mortality through December 2013. *Results:* Surgical patients (n=2500) had a mean age of 52 years and a mean BMI of 47. Matched control patients (n=7462) had a mean age of 53 years and a mean BMI of 46. At the end of the 14-year study period, there were a total of 263 deaths in the surgical group (mean follow-up, 6.9 years) and 1277 deaths in the matched control group (mean follow-up, 6.6 years). Kaplan-Meier estimated mortality rates were 2.4% at 1 year, 6.4% at 5 years, and 13.8% at 10 years for surgical patients; for matched control patients, 1.7% at 1 year, 10.4% at 5 years, and 23.9% at 10 years. Adjusted analysis showed no significant association between bariatric surgery and all-cause mortality in the first year of follow-up (adjusted hazard ratio [HR], 1.28 [95% CI, 0.98–1.68]), but significantly lower mortality after 1 to 5 years (HR, 0.45 [95% CI, 0.36–0.56]) and 5 to 14 years (HR, 0.47 [95% CI, 0.39–0.58]). The midterm (>1–5 years) and long-term (>5 years) relationships between surgery and survival were not significantly different across subgroups defined by diabetes diagnosis, sex, and period of surgery. *Conclusions and Relevance:* Among obese patients receiving care in the VA health system, those who underwent bariatric surgery compared with matched control patients who did not have surgery had lower all-cause mortality at 5 years and up to 10 years following the procedure. These results provide further evidence for the beneficial relationship between surgery and survival that has been demonstrated in younger, predominantly female populations.

R. K. Burt et al., **Association of Nonmyeloablative Hematopoietic Stem Cell Transplantation with Neurological Disability in Patients with Relapsing-Remitting Multiple Sclerosis**, *JAMA* 313.3 (January 20, 2015): 275–284 • *Importance:* No current therapy for relapsing-remitting multiple sclerosis (MS) results in significant reversal of disability. *Objective:* To determine the association of nonmyeloablative hematopoietic stem cell transplantation with neurological disability and other clinical outcomes in patients with MS. *Design, Setting, and Participants:* Case series of patients with relapsing-remitting MS (n = 123) or secondary-progressive MS (n = 28) (mean age, 36 years; range, 18–60 years; 85 women) treated at a single US institution between 2003 and 2014 and followed up for 5 years. Final follow-up was completed in June 2014. *Interventions:* Treatment with cyclophosphamide and alemtuzumab (22 patients) or cyclophosphamide and thymoglobulin (129 patients) followed by infusion of unmanipulated peripheral blood stem cells. *Main Outcomes and Measures:* Primary end point was reversal or progression of disability measured by change in the Expanded Disability Status Scale (EDSS) score of 1.0 or greater (score range, 0–10). Secondary outcomes included changes in the Neurologic Rating Scale (NRS) score of 10 or greater (score range, 0–100), Multiple Sclerosis Functional Composite (MSFC) score, quality-of-life Short Form 36 questionnaire scores, and T2 lesion volume on brain magnetic resonance imaging scan. *Results:* Outcome analysis was available for 145 patients with a median follow-up of 2 years and a mean of 2.5 years. Scores from the EDSS improved significantly from a pretransplant median of 4.0 to 3.0

(interquartile range [IQR], 1.5 to 4.0; n = 82) at 2 years and to 2.5 (IQR, 1.9 to 4.5; n = 36) at 4 years (P < 0.001 at each assessment). There was significant improvement in disability (decrease in EDSS score of 1.0) in 41 patients (50%; 95% CI, 39% to 61%) at 2 years and in 23 patients (64%; 95% CI, 46% to 79%) at 4 years. Four-year relapse-free survival was 80% and progression-free survival was 87%. The NRS scores improved significantly from a pretransplant median of 74 to 88.0 (IQR, 77.3 to 93.0; n = 78) at 2 years and to 87.5 (IQR, 75.0 to 93.8; n = 34) at 4 years (P < 0.001 at each assessment). The median MSFC scores were 0.38 (IQR, −0.01 to 0.64) at 2 years (P < 0.001) and 0.45 (0.04 to 0.60) at 4 years (P = 0.02). Total quality-of-life scores improved from a mean of 46 (95% CI, 43 to 49) pretransplant to 64 (95% CI, 61 to 68) at a median follow-up of 2 years post-transplant (n = 132) (P < 0.001). There was a decrease in T2 lesion volume from a pretransplant median of 8.57 cm3 (IQR, 2.78 to 22.08 cm3) to 5.74 cm3 (IQR, 1.88 to 14.45 cm3) (P < 0.001) at the last posttransplant assessment (mean follow-up, 27 months; n = 128). *Conclusions and Relevance:* Among patients with relapsing-remitting MS, nonmyeloablative hematopoietic stem cell transplantation was associated with improvement in neurological disability and other clinical outcomes. These preliminary findings from this uncontrolled study require confirmation in randomized trials.

J. Iqbal et al., **Differences in Breast Cancer Stage at Diagnosis and Cancer-Specific Survival by Race and Ethnicity in the United States**, *JAMA* 313.2 (January 13, 2015): 165–173 • *Importance:* Women with early-stage breast cancers are expected to have excellent survival rates. It is important to identify factors that predict diagnosis of early-stage breast cancers. *Objective:* To determine the proportion of breast cancers that were identified at an early stage (stage I) in different racial/ethnic groups and whether ethnic differences may be better explained by early detection or by intrinsic biological differences in tumor aggressiveness. *Design, Setting, and Participants:* Observational study of women diagnosed with invasive breast cancer from 2004 to 2011 who were identified in the Surveillance, Epidemiology, and End Results (SEER) 18 registries database (N=452,215). For each of 8 racial/ethnic groups, biological aggressiveness (triple-negative cancers, lymph node metastases, and distant metastases) of small-sized tumors of 2.0 cm or less was estimated. The odds ratio (OR) for being diagnosed at stage I compared with a later stage and the hazard ratio (HR) for death from stage I breast cancer by racial/ethnic group were determined. The date of final follow-up was December 31, 2011. *Main Outcomes and Measures:* Breast cancer stage at diagnosis and 7-year breast cancer-specific survival, adjusted for age at diagnosis, income, and estrogen receptor status. *Results:* Of 373,563 women with invasive breast cancer, 268,675 (71.9%) were non-Hispanic white; 34,928 (9.4%), Hispanic white; 38,751 (10.4%), black; 25,211 (6.7%), Asian; and 5998 (1.6%), other ethnicities. Mean follow-up time was 40.6 months (median, 38 months). Compared with non-Hispanic white women diagnosed with stage I breast cancer (50.8%), Japanese women (56.1%) were more likely to be diagnosed (OR, 1.23 [95% CI, 1.15–1.31], P<0.001) and black women (37.0%) were less likely to be diagnosed (OR, 0.65 [95% CI, 0.64–0.67], P<0.001). Actuarial risk of death from stage I breast cancer at 7 years was higher among black women (6.2%) than non-Hispanic white women (3.0%) (HR, 1.57 [95% CI, 1.40–1.75]; P<0.001), and lower among South Asian women (1.7%) (HR, 0.48 [95% CI, 0.20–1.15]; P=0.10). Black women were more likely to die of breast cancer with small-sized tumors (9.0%) than non-Hispanic white women (4.6%) (HR, 1.96 [95% CI, 1.82–2.12]; P<0.001); the difference remained after adjustment for income and estrogen receptor status (HR, 1.56 [95% CI, 1.45–1.69]; P<0.001). *Conclusions and Relevance:* Among US women diagnosed with invasive breast cancer, the likelihood of diagnosis at an early stage, and survival after stage I diagnosis, varied by race and ethnicity. Much of the difference could be statistically accounted for by intrinsic biological differences such as lymph node metastasis, distant

metastasis, and triple-negative behavior of tumors.

J. F. Kawwass et al., **Safety of Assisted Reproductive Technology in the United States, 2000–2011**, *JAMA* 313.1 (January 6, 2015): 88–90 • Use of assisted reproductive technology (ART) continues to increase in the United States and globally. In an effort to improve patient safety, stimulation protocols have become less aggressive, oocyte retrieval has transitioned from laparoscopic to transvaginal, and pregnancy rates have improved. However, limited data exist regarding the incidence of maternal complications. We explored incidence and trends in reported patient and donor complications in fresh ART cycles using the US Centers for Disease Control and Prevention National ART Surveillance System (NASS).

N. M. Scheller et al., **Quadrivalent HPV Vaccination and Risk of Multiple Sclerosis and Other Demyelinating Diseases of the Central Nervous System**, *JAMA* 313.1 (January 6, 2015): 54–61 • *Importance:* Case reports have suggested a link between human papillomavirus (HPV) vaccination and development of multiple sclerosis and other demyelinating diseases. *Objective:* To investigate if quadrivalent HPV (qHPV) vaccination is associated with an increased risk of multiple sclerosis and other demyelinating diseases. *Design, Setting, and Participants:* Using nationwide registers we identified a cohort of all females aged 10 years to 44 years in Denmark and Sweden, followed up from 2006 to 2013, information on qHPV vaccination, and data on incident diagnoses of multiple sclerosis and other demyelinating diseases. The primary analysis used a cohort design including vaccinated and unvaccinated study participants. A secondary analysis used a self-controlled case-series design including only cases. Both analyses used a 2-year risk period following vaccination. *Exposures:* Information on qHPV vaccination was obtained through the national vaccination and prescription registers. *Main Outcomes and Measures:* The primary outcomes were multiple sclerosis and a composite end point of other demyelinating diseases. Incidence rate ratios were estimated using Poisson regression, comparing rates of events in the 2-year risk periods following vaccination and in unvaccinated time periods. *Results:* The study included 3,983,824 females, among whom 789,082 received a total of 1,927,581 qHPV vaccine doses. During follow-up, 4322 multiple sclerosis cases and 3300 cases of other demyelinating diseases were identified, of which 73 and 90, respectively, occurred within the risk period. In the cohort analysis, there was no increased risk of multiple sclerosis (crude incidence rates, 6.12 events/100,000 person-years [95% CI, 4.86–7.69] and 21.54 events/100,000 person-years [95% CI, 20.90–22.20] for the vaccinated and unvaccinated periods; adjusted rate ratio, 0.90 [95% CI, 0.70–1.15]) or other demyelinating diseases (crude incidence rates, 7.54 events/100,000 person-years [95% CI, 6.13–9.27] and 16.14 events/100,000 person-years [95% CI, 15.58–16.71]; adjusted rate ratio, 1.00 [95% CI, 0.80–1.26]) associated with qHPV vaccination. Similarly, no increased risk was found using the self-controlled case-series design (multiple sclerosis: incidence ratio, 1.05 [95% CI, 0.79–1.38]; other demyelinating diseases: incidence ratio, 1.14 [95% CI, 0.88–1.47]). *Conclusions and Relevance:* In this study with nationwide coverage of 2 Scandinavian countries, qHPV vaccination was not associated with the development of multiple sclerosis or other demyelinating diseases. These findings do not support concerns about a causal relationship between qHPV vaccination and demyelinating diseases.

Journal of Medical Ethics

P. Louhiala et al., **Finnish Physicians' Attitudes towards Active Euthanasia Have Become More Positive over the Last 10 Years**, *J Med Ethics* 41.4 (April 2015): 353–355 • *Introduction:* Most physicians are against active euthanasia. Very little is known about the possible changes in the attitudes of physicians. *Methods:* A questionnaire was sent to a random sample of 1003 Finnish physicians of working age. A similar questionnaire had been sent to a random sample of Finnish physicians also in 1993 and 2003. The questionnaire consisted of statements

about euthanasia, for which the participants were asked to express their agreement or disagreement on a 5-point Likert scale. *Results:* In general, Finnish physicians' attitudes towards active euthanasia have become considerably more positive. In 2003, 61% of the respondents were against the legalisation of euthanasia and 29% supported it. In 2013, both groups were of equal size (46%). The willingness to perform active euthanasia has not, however, increased significantly, even in a legalised setting. *Conclusions:* The attitudes of Finnish physicians towards active euthanasia became considerably more positive between 2003 and 2013. There was no significant change, however, in the willingness to practice euthanasia if it became legal.

Journal of Surgical Research

A. C. Kwok et al., **Invasive Procedures in the Elderly after Stage IV Cancer Diagnosis**, *J Surg Res* 193.2 (February 2015): 754–763 • *Background:* Invasive procedures are resource intense and may be associated with substantial morbidity. These harms must be carefully balanced with the benefits gained in life expectancy and quality of life. Prior research has demonstrated an increasing aggressiveness of care in cancer patients at the end-of-life. To better characterize surgical care in this setting, we sought to examine trends in the use of invasive procedures in patients diagnosed with metastatic cancer on presentation. *Materials and Methods:* Using Surveillance Epidemiology and End Results-Medicare data, we identified invasive procedure claims from 1994–2009 for patients diagnosed with incident stage IV breast, colorectal, lung, and prostate cancer patients in 1995–2006. We grouped procedures into surgically relevant categories, using an adaptation of the Clinical Classifications Software, and measured utilization and relative changes over time. *Results:* Of stage IV patients diagnosed in 2002–2006, 96% underwent a procedure during the course of their cancer care including 63% after the diagnostic period, and 25% in the last month of life. Between 1996 and 2006, minimal change was observed in utilization during the diagnostic period (+1.5%). However, there were significant increases during continuing care (+20.7%) and the last month of life (+21.5%). Procedures consistent with primary tumor resection decreased, whereas those with probable palliative intent and those unrelated to cancer increased. *Conclusions:* Nearly all patients who present with metastatic cancer undergo invasive procedures. Although overall utilization is increasing, the specific procedure types indicate that it may be appropriate, enhancing the quality of life in this vulnerable population.

Lancet

M. Brännström et al., **Livebirth after Uterus Transplantation**, *Lancet* 385.9968 (February 14, 2015): 607–616 • *Background:* Uterus transplantation is the first available treatment for absolute uterine infertility, which is caused by absence of the uterus or the presence of a non-functional uterus. Eleven human uterus transplantation attempts have been done worldwide but no livebirth has yet been reported. *Methods:* In 2013, a 35-year-old woman with congenital absence of the uterus (Rokitansky syndrome) underwent transplantation of the uterus in Sahlgrenska University Hospital, Gothenburg, Sweden. The uterus was donated from a living, 61-year-old, two-parous woman. In-vitro fertilisation treatment of the recipient and her partner had been done before transplantation, from which 11 embryos were cryopreserved. *Findings:* The recipient and the donor had essentially uneventful postoperative recoveries. The recipient's first menstruation occurred 43 days after transplantation and she continued to menstruate at regular intervals of between 26 and 36 days (median 32 days). 1 year after transplantation, the recipient underwent her first single embryo transfer, which resulted in pregnancy. She was then given triple immunosuppression (tacrolimus, azathioprine, and corticosteroids), which was continued throughout pregnancy. She had three episodes of mild rejection, one of which occurred during pregnancy. These episodes were all reversed by corticosteroid treatment. Fetal growth parameters and blood flows of the uterine arteries and umbilical cord were normal throughout pregnancy. The patient

was admitted with pre-eclampsia at 31 full weeks and 5 days, and 16 h later a caesarean section was done because of abnormal cardiotocography. A male baby with a normal birthweight for gestational age (1775 g) and with APGAR scores 9, 9, 10 was born. *Interpretation:* We describe the first livebirth after uterus transplantation. This report is a proof-of-concept for uterus transplantation as a treatment for uterine factor infertility. Furthermore, the results show the feasibility of live uterus donation, even from a postmenopausal donor.

New England Journal of Medicine

E. Muller et al., **HIV-Positive-to-HIV-Positive Kidney Transplantation—Results at 3 to 5 Years**, *N Engl J Med* 372.7 (February 12, 2015): 613–620 • *Background:* The outcome of kidney transplantation in human immunodeficiency virus (HIV)-positive patients who receive organs from HIV-negative donors has been reported to be similar to the outcome in HIV-negative recipients. We report the outcomes at 3 to 5 years in HIV-positive patients who received kidneys from HIV-positive deceased donors. *Methods:* We conducted a prospective, nonrandomized study of kidney transplantation in HIV-infected patients who had a CD4 T-cell count of 200 per cubic millimeter or higher and an undetectable plasma HIV RNA level. All the patients were receiving antiretroviral therapy (ART). The patients received kidneys from deceased donors who tested positive for HIV with the use of fourth-generation enzyme-linked immunosorbent assay at the time of referral. All the donors either had received no ART previously or had received only first-line ART. *Results:* From September 2008 through February 2014, a total of 27 HIV-positive patients underwent kidney transplantation. Survivors were followed for a median of 2.4 years. The rate of survival among the patients was 84% at 1 year, 84% at 3 years, and 74% at 5 years. The corresponding rates of graft survival were 93%, 84%, and 84%. (If a patient died with a functioning graft, the calculation was performed as if the graft had survived.) Rejection rates were 8% at 1 year and 22% at 3 years. HIV infection remained well controlled, with undetectable virus in blood after the transplantation. *Conclusions:* Kidney transplantation from an HIV-positive donor appears to be an additional treatment option for HIV-infected patients requiring renal-replacement therapy.

Pediatric Blood and Cancer

S. Jacobs et al., **Adolescent End of Life Preferences and Congruence with Their Parents' Preferences: Results of a Survey of Adolescents with Cancer**, *Pediatr Blood Cancer* 62.4 (April 2015): 710–714 • *Background:* Little is known about how well family members accurately represent adolescents when making EOL decisions on their behalf. This study reports on surveys given to adolescents with cancer and their parents as part of a larger study facilitating advanced care discussions, as well as the results of a survey for health care providers. *Procedure:* Trained facilitators administered surveys orally to adolescents and families in the intervention arm of the FAmily CEntered Advance Care Planning (ACP) for Teens with Cancer (FACE-TC) study. In addition, a post-hoc survey was sent to oncology providers. *Results:* Seventeen adolescent/family dyads completed this survey. Seventy five percent of adolescents believed it was appropriate to discuss EOL decisions early and only 12% were not comfortable discussing death. Most preferred to be at home if dying. There were substantial areas of congruence between adolescents and their surrogates, but lower agreement on the importance of dying a natural death, dying at home and "wanting to know if I were dying." Among providers, 83% felt their patients' participation in the study was helpful to the patients and 78% felt it was helpful to them as providers. *Conclusions:* Adolescents with cancer were comfortable discussing EOL, and the majority preferred to talk about EOL issues before they are facing EOL. There were substantive areas of agreement between adolescents and their surrogates, but important facets of adolescents' EOL wishes were not known by their families, reinforcing the importance of eliciting individual preferences and engaging dyads so parents can understand their children's wishes.

Social Science and Medicine

A. Danyliv and C. O'Neill, **Attitudes towards Legalising Physician Provided Euthanasia in Britain: The Role of Religion over Time**, *Soc Sci Med* 128 (March 2015): 52–56

• Hastening the death of another whether through assisted suicide or euthanasia is the subject of intense debate in the UK and elsewhere. In this paper we use a nationally representative survey of public attitudes—the British Social Attitudes survey—to examine changes in attitudes to the legalisation of physician provided euthanasia (PPE) over almost 30 years (1983–2012) and the role of religious beliefs and religiosity in attitudes over time. Compatible questions about attitudes to euthanasia were available in the six years of 1983, 1984, 1989, 1994, 2005, and 2012. We study the trends in the support for legalisation through these time points and the relationship between attitudes, religious denomination and religiosity, controlling for a series of covariates. In total, 8099 individuals provided answers to the question about PPE in the six years of the study. The support for legalisation rose from around 76.95% in 1983 to 83.86% in 2012. This coincided with an increase in secularisation exhibited in the survey: the percentage of people with no religious affiliation increasing from 31% to 45.4% and those who do not attend a religious institution (e.g. church) increasing from 55.7% to 65.03%. The multivariate analysis demonstrates that religious affiliation and religiosity as measured by religious institution attendance frequency are the main contributors to attitudes towards euthanasia, and that the main increase in support happened among the group with least religious affiliation. Other socio-demographic characteristics do not seem to alter these attitudes systematically across the years. Our study demonstrates an increase in the support of euthanasia legalisation in Britain in the last 30 years coincided with increased secularisation. It does not follow, however, that trends in public support are immutable nor that a change in the law would improve on the current pragmatic approach toward hastening death by a physician adopted in England and Wales in terms of the balance between compassion and safeguards against abuse offered.