
MEDICINE ABSTRACTS

Annals of Internal Medicine

D. J. Jones et al., **Conflicts of Interest Ethics: Silencing Expertise in the Development of International Clinical Practice Guidelines**, *Ann Intern Med* 156.11 (June 5, 2012): 809–816 • *Background*: It is unclear whether global experts with financial conflicts of interest (FCOIs) should be included in, be excluded from, or have a limited role in developing international clinical practice guidelines (CPGs). Optimal management of FCOIs to ensure independent, expert CPGs remains ethically contested. *Objective*: To manage FCOIs and examine whether an ethics framework with discussion recusal by experts with FCOIs affects deliberations and voting on a CPG. *Design*: Development of an ethics framework grounded on transparency and proportional management of COIs, including self-recusal, evaluation of the effect on COIs and CPG process by quantification of voting on recommendations, and qualitative assessment of experts' ethics dialogue. *Setting*: International consensus meeting to formulate a CPG in gastroenterology. *Participants*: 34 experts from 15 countries. *Measurements*: Counting the votes of experts with and without declared FCOIs and qualitative assessment of ethics discussions. *Results*: 62% of experts reported at least 1 FCOI. Eight out of 21 recommendations presented potential FCOIs. Experts with conflicts recused themselves from discussing 6 of the 8 recommendations, leaving a majority of nonconflicted discussants (median, 22; range, 19 to 26) for the 6 recommendations. Recusals did not affect voting outcomes but may have diluted the richness of the discussions. Ethics dialogue revealed accord on transparency but underscored challenges to proportional management of COIs beyond basic disclosure. Concerns about bias, COI definitions, expertise, and integrity express important international ethics questions.

Limitation: Small participant numbers and application of the framework to only 1 meeting of 1 CPG. *Conclusions*: An ethics framework may help to identify and manage COIs and catalyze both ethics dialogue and innovative COI standards that seek to balance impartiality and expertise for trusted CPGs. Optimal balancing remains contested. Recommendations include frameworks, interdisciplinary analysis, and international policy initiatives to better manage COIs in the CPG process.

Archives of Internal Medicine

B. Zhang et al., **Factors Important to Patients' Quality of Life at the End of Life**, *Arch Intern Med* 172.15 (August 13, 2012): 1133–1142 • *Background*: When curative treatments are no longer options for patients dying of cancer, the focus of care often turns from prolonging life to promoting quality of life (QOL). Few data exist on what predicts better QOL at the end of life (EOL) for advanced cancer patients. The purpose of this study was to determine the factors that most influence QOL at the EOL, thereby identifying promising targets for interventions to promote QOL at the EOL. *Methods*: Coping With Cancer is a US multisite, prospective, longitudinal cohort study of 396 advanced cancer patients and their informal caregivers who were enrolled from September 1, 2002, through February 28, 2008. Patients were followed up from enrollment to death a median of 4.1 months later. Patient QOL in the last week of life was a primary outcome of Coping With Cancer and the present report. *Results*: The following set of 9 factors, preceded by a sign indicating the direction of the effect and presented in rank order of importance, explained the most variance in patients' QOL at the EOL: 1 = (–) intensive care unit stays in the final week (explained 4.4% of the variance in QOL

at the EOL), 2 = (–) hospital deaths (2.7%), 3 = (–) patient worry at baseline (2.7%), 4 = (+) religious prayer or meditation at baseline (2.5%), 5 = site of cancer care (1.8%), 6 = (–) feeding-tube use in the final week (1.1%), 7 = (+) pastoral care within the hospital or clinic (1.0%), 8 = (–) chemotherapy in the final week (0.8%), and 9 = (+) patient-physician therapeutic alliance at baseline (0.7%). The vast majority of the variance in QOL at the EOL, however, remained unexplained. *Conclusion:* Advanced cancer patients who avoid hospitalizations and the intensive care unit, who are less worried, who pray or meditate, who are visited by a pastor in the hospital/clinic, and who feel a therapeutic alliance with their physicians have the highest QOL at the EOL.

Critical Care Medicine

J. L. Hart et al., Perceptions of Organ Donation after Circulatory Determination of Death among Critical Care Physicians and Nurses: A National Survey, Crit Care Med 40.9 (September 2012): 2595–2600 • *Objective:* We sought to identify factors related to critical care physicians' and nurses' willingness to help manage potential donors after circulatory determination of death, and to elicit opinions on the presence of role conflict in donors after circulatory determination of death and its impact on end-of-life care. *Design and Setting:* Randomized trial administered by Web or post of four donors after circulatory determination of death vignettes. Response rates were 31.0% and 44.3%, respectively. *Subjects:* Two thousand two hundred and six academic intensive care unit physicians and 988 intensive care unit nurses in the United States. *Measurements and Main Results:* Majorities of intensive care unit physicians (72.5%; 95% confidence interval 69.2–75.9) and nurses (74.3%; 95% confidence interval 70.2–78.5) believed they should help manage potential donors after circulatory determination of death. 14.7% (95% confidence interval 12.0–17.4) of physicians and 14.3% (95% confidence interval 11.0–17.6) of nurses believed that management of donors after circulatory determination of death would create

professional role conflicts. 33.8% (95% confidence interval 30.0–37.4) of physicians and 55.1% (95% confidence interval 50.3–59.7) of nurses believed that preserving opportunities for donors after circulatory determination of death could improve end-of-life care. More favorable views of donors after circulatory determination of death were provided by clinicians randomly assigned to vignettes depicting donors with previously denoted preferences for organ donation; similar effects were not introduced by vignettes in which surrogates actively initiated donation discussions. *Conclusions:* These findings suggest that critical care physicians and nurses are generally supportive of managing donors after circulatory determination of death, particularly when patients were registered organ donors. However, minorities of clinicians harbor concerns regarding conflicts of interest, and many are uncertain of the practice's impact on end-of-life care.

A. Majesko et al., Identifying Family Members Who May Struggle in the Role of Surrogate Decision Maker, Crit Care Med 40.8 (August 2012): 2281–2286 • Although acting as a surrogate decision maker can be highly distressing for some family members of intensive care unit patients, little is known about whether there are modifiable risk factors for the occurrence of such difficulties. *Objectives:* To identify: 1) factors associated with lower levels of confidence among family members to function as surrogates and 2) whether the quality of clinician–family communication is associated with the timing of decisions to forgo life support. *Methods:* We conducted a prospective study of 230 surrogate decision makers for incapacitated, mechanically ventilated patients at high risk of death in four intensive care units at University of California San Francisco Medical Center from 2006 to 2007. Surrogates completed a questionnaire addressing their perceived ability to act as a surrogate and the quality of their communication with physicians. We used clustered multivariate logistic regression to identify predictors of low levels of perceived ability to act as a

surrogate and a Cox proportional hazard model to determine whether quality of communication was associated with the timing of decisions to withdraw life support. *Results:* There was substantial variability in family members' confidence to act as surrogate decision makers, with 27% rating their perceived ability as 7 or lower on a 10-point scale. Independent predictors of lower role confidence were the lack of prior experience as a surrogate (odds ratio 2.2, 95% confidence interval [1.04–4.46], $p = 0.04$), no prior discussions with the patient about treatment preferences (odds ratio 3.7, 95% confidence interval [1.79–7.76], $p < 0.001$), and poor quality of communication with the ICU physician (odds ratio 1.2, 95% confidence interval [1.09–1.35] $p < 0.001$). Higher quality physician–family communication was associated with a significantly shorter duration of life-sustaining treatment among patients who died ($[\beta] = 0.11$, $p = 0.001$). *Conclusions:* Family members without prior experience as a surrogate and those who had not engaged in advanced discussions with the patient about treatment preferences were at higher risk to report less confidence in carrying out the surrogate role. Better-quality clinician–family communication was associated with both more confidence among family members to act as surrogates and a shorter duration of use of life support among patients who died.

Human Reproduction

L. Johannesson et al., Uterus Transplantation in a Non-human Primate: Long-Term Follow-Up after Autologous Transplantation, Hum Reprod 27.6 (June 2012): 1640–1648 • Background: Uterus transplantation (UTx) may provide the first available treatment for women affected by uterine infertility. The present study aimed to further develop a surgical technique for autologous UTx in a non-human primate species and to assess long-term function. *Methods:* Female baboons ($n=16$) underwent autologous transplantation of the uterus with the Fallopian tubes and ovaries, performed with a previously published surgical

technique ($n= 6$, Group 1) or using a modified technique ($n= 10$; Group 2). The uterine arteries were dissected to the proximal end of the anterior branch (Group 1) or the entire (Group 2) internal iliac artery, and the ovarian veins were dissected to the crossing over the ureter (Group 1) or further cranially to include greater lengths and patches of the cava/renal vein (Group 2). Back-table preparation created common venous and arterial ends with arterial anastomosis either end-to-side to the left external iliac artery (Group 1) or end-to-end to the left internal iliac artery (Group 2). *Results:* Overall short-time survival of the animals was 88% (66% in Group 1 and 100% in Group 2). Of all the operated animals, 75% (66% in Group 1 and 80% in Group 2) resumed ovarian cyclicity. Regular menstruation after UTx was demonstrated only in Group 2 (60%). Menstruating animals ($n= 6$) were each exposed to timed mating for ≥ 5 menstrual cycles, but pregnancy did not occur. Adhesions and tubal blockage were seen in post-mortem analysis. *Conclusions:* The modified UTx model of Group 2 is a safe procedure and shows resumed long-term uterine function in a majority of the animals, although pregnancy could not be demonstrated.

S. Leppälahti et al., Trends in Teenage Termination of Pregnancy and Its Risk Factors: A Population-Based Study in Finland, 1987–2009, Hum Reprod 27.9 (September 2012): 2829–2836 • Study Question: What are the current trends in teenage termination of pregnancy (TOP) and its risk factors? *Summary Answer:* The incidence of teenage TOP fluctuated substantially during the study period and the incidence of repeat TOP among adolescents increased markedly in the 2000s. *What Is Known Already:* Teenage pregnancy is associated with difficulties in psychological, sexual and overall health. The proportion of teenage pregnancies resulting in termination varies by country and time, but only few countries have reliable statistics on TOPs. *Study Design, Size, Duration:* This nationwide retrospective register study included all the TOPs ($n= 52\ 968$) and deliveries ($n= 58\ 882$) in Finland between

1987 and 2009 among girls <20 years of age at the beginning of pregnancy. *Participants/Materials, Setting, Methods:* The cohorts were divided into three subgroups; 13–15- (n= 6087), 16–17- (n= 18 826) and 18–19- (n= 28 055) year-olds. *Main Results and the Role of Chance:* After an initial steady decline, the incidence of teenage TOP increased by 44% between 1993 (8.0/1000) and 2003 (11.5/1000), and thereafter declined by 16% until 2009 (9.7/1000). The incidence was higher in older adolescents, but the trends were alike in all age groups. Early TOPs (performed at <56 days of gestation) more than tripled from 11 to 36% during the study period. However, the proportion of second-trimester TOPs remained steady at 7%. Young age [13–15 years: odds ratio (OR) 1.75 (95% confidence interval (CI) 1.57–1.94), 16–17 years: OR 1.13 (1.05–1.23), 18–19 years: OR 1 (reference category)] and non-use of contraception [(OR 11.16 (10.15–12.27))] were related to a higher risk of second-trimester TOP. The incidence of repeat TOP increased by 95% from 1.9/1000 to 3.7/1000 in 18–19-year-olds and by 120% from 0.5/1000 to 1.1/1000 in 16–17-year-olds between 1993 and 2009. Increasing age [13–15 years: OR 0.16 (95% CI 0.14–0.19), 16–17 years: OR 0.49 (0.45–0.52), 18–19 years 1 (Ref)], living in an urban area [rural: OR 0.62 (0.56–0.67), urban: OR 1 (Ref)] and having undergone a second-trimester TOP [OR 1.46 (1.31–1.63)] were risk factors for repeat TOP. The planned use of intrauterine contraception for post-abortion contraception increased from 2.6 to 6.2% and among girls with repeat TOP from 10 to 19%. *Limitations:* The retrospective nature of the study remains a limitation and the quality of the data is reliant on the accuracy of reporting. We were not able to link repeat TOPs of the same woman in our data set. However, the share of repeat abortions was moderate. *Wider Implications of the Findings:* The rate of teenage TOP seems to rapidly reflect changes in national sexual and reproductive health services and policy. The rising rate of repeat TOP is alarming and may represent a sign of marginalization among these girls. All efforts to maintain a low rate of teenage pregnancy are welcomed.

M. Mihara et al., Uterine Autotransplantation in Cynomolgus Macaques: The First Case of Pregnancy and Delivery, Hum Reprod 27.8 (2012): 2332–2340 · Background: For women with congenital uterine infertility, or for those who have undergone hysterectomy, uterine transplantation is one of the potential treatments to regain fertility. In this study, we utilized a primate model of uterine transplantation, and evaluated the patency of our microsurgical anastomoses, and the perfusion of the transplanted uterus. *Methods:* Two female cynomolgus monkeys underwent surgery. We anastomosed two arteries and one vein in Case 1 and two arteries and two veins in Case 2. The arteries used were the uterine arteries and the anastomosis was done to the external iliac artery. We used one of the ovarian veins in both animals, but resected the ovary from the Fallopian tube. Uterine arterial blood flow and uterine size were determined by intraoperative indocyanine green (ICG) angiography and ultrasonography. The biopsy of the uterine cervix was performed after surgery. *Results:* ICG angiography showed that the unilateral uterine artery perfused the bilateral uterine bodies and cervix. In Case 1, ICG angiography showed the occlusion of one of the anastomosed arteries during the operation and the uterus appeared atrophied 2 months after operation. In Case 2, the transplanted uterus survived and normal menstruation occurred. The animal achieved a natural pregnancy and was delivered by the Caesarean section due to early separation of the placenta. The newborn suffered fetal distress. *Conclusions:* These results show the anastomosis of at least the bilateral uterine arteries and the unilateral ovarian vein is required for uterus transplantation. This is the first report of a natural pregnancy in a primate following uterine autotransplantation.

Journal of General Internal Medicine

C. H. Braddock III et al., The Patient-Centered Medical Home: An Ethical Analysis of Principles and Practice, J Gen Intern Med 28.21 (January 2013):

141–146 • The patient-centered medical home (PCMH), with its focus on patient-centered care, holds promise as a way to reinvigorate the primary care of patients and as a necessary component of health care reform. While its tenets have been the subject of review, the ethical dimensions of the PCMH have not been fully explored. Consideration of the ethical foundations for the core principles of the PCMH can and should be part of the debate concerning its merits. The PCMH can align with the principles of medical ethics and potentially strengthen the patient-physician relationship and aspects of health care that patients value. Patient choice and these ethical considerations are central and at least as important as the economic and practical arguments in support of the PCMH, if not more so. Further, the ethical principles that support key concepts of the PCMH have implications for the design and implementation of the PCMH. This paper explores the PCMH in light of core principles of ethics and professionalism, with an emphasis both on how the concept of the PCMH may reinforce core ethical principles of medical practice and on further implications of these principles.

N. S. Wenger et al., Implementation of Physician Orders for Life Sustaining Treatment in Nursing Homes in California: Evaluation of a Novel Statewide Dissemination Mechanism, J Gen Intern Med 28.21 (January 2013): 51–57 • *Background:* Implementing Physician Orders for Life Sustaining Treatment (POLST) forms aims to improve communication of life-sustaining treatment preferences across care venues. California enabled this clinical tool in 2009, and a novel intervention of community coalitions was undertaken to advance POLST in localities around the state. Coalitions engaged facilities, including nursing homes (NHs), to foster POLST adoption. Eighteen months after introduction of POLST, we studied POLST implementation in California NHs. *Methods:* NHs randomly selected in coalition and non-coalition areas were mailed surveys about POLST preparation and use in 2010. Coalitions identified which NHs they worked with. *Results:* Of

546 NHs surveyed, 143 (52%) in coalition areas and 141 (52%) in non-coalition areas responded. In 82% of responding NHs, staff received POLST education and 59% of NHs reported having a formal policy on handling POLST. Two-thirds of NHs had admitted a resident with a POLST, and 15% of newly admitted residents over the past month had a POLST (range 0–100%). Eighty-one percent of NHs had completed a POLST with a resident. Fifty-four percent of residents were estimated to have a POLST (range 0–100%) (coalition area NHs 60% vs. non-coalition area NHs 48%, $p=0.02$). Within coalition areas, NHs that had worked with coalitions were more likely to have completed a POLST with a resident after admission than NHs that had not worked with coalitions. Few NHs (7%) reported difficulty following POLST orders, but 38% noted difficulty involving physicians in POLST completion. *Conclusion:* Less than 2 years after introduction, many California nursing homes report using POLST, although some NHs reported no experience. A novel community coalition intervention facilitated POLST implementation.

New England Journal of Medicine

J. Z. Julian et al., Redefining Physicians' Role in Assisted Dying, N Engl J Med 367.2 (July 12, 2012): 97–99 • Terminally ill patients spend their final months making serious decisions about medical care and the disposition of their assets after death. Increasingly, they are also choosing to make decisions about the manner and timing of their death, and many are completing advance directives to withhold life-sustaining treatment. A controversial facet of this trend toward a more self-directed dying process is the question of assisted dying—whether patients should have the option of acquiring a lethal dose of medication with the explicit intention of ending their own life.

B. Luke et al., Cumulative Birth Rates with Linked Assisted Reproductive Technology Cycles, N Engl J Med 366.26 (June 28, 2012): 2483–2491 • *Background:* Live-birth rates after treatment with assisted reproductive technology have traditionally been

reported on a per-cycle basis. For women receiving continued treatment, cumulative success rates are a more important measure. *Methods:* We linked data from cycles of assisted reproductive technology in the Society for Assisted Reproductive Technology Clinic Outcome Reporting System database for the period from 2004 through 2009 to individual women in order to estimate cumulative live-birth rates. Conservative estimates assumed that women who did not return for treatment would not have a live birth; optimal estimates assumed that these women would have live-birth rates similar to those for women continuing treatment. *Results:* The data were from 246,740 women, with 471,208 cycles and 140,859 live births. Live-birth rates declined with increasing maternal age and increasing cycle number with autologous, but not donor, oocytes. By the third cycle, the conservative and optimal estimates of live-birth rates with autologous oocytes had declined from 63.3% and 74.6%, respectively, for women younger than 31 years of age to 18.6% and 27.8% for those

41 or 42 years of age and to 6.6% and 11.3% for those 43 years of age or older. When donor oocytes were used, the rates were higher than 60% and 80%, respectively, for all ages. Rates were higher with blastocyst embryos (day of transfer, 5 or 6) than with cleavage embryos (day of transfer, 2 or 3). At the third cycle, the conservative and optimal estimates of cumulative live-birth rates were, respectively, 42.7% and 65.3% for transfer of cleavage embryos and 52.4% and 80.7% for transfer of blastocyst embryos when fresh autologous oocytes were used. *Conclusions:* Our results indicate that live-birth rates approaching natural fecundity can be achieved by means of assisted reproductive technology when there are favorable patient and embryo characteristics. Live-birth rates among older women are lower than those among younger women when autologous oocytes are used but are similar to the rates among young women when donor oocytes are used. (Funded by the National Institutes of Health and the Society for Assisted Reproductive Technology.)