**Acta Paediatrica**

J. Koper et al., Dutch Neonatologists Have Adopted a More Interventionist Approach to Neonatal Care, *Acta Paediatr* 104.9 (September 2015): 888–893 • **Aim:** This study investigated whether continuous improvements to neonatal care and the legalisation of newborn euthanasia in 2005 had changed end-of-life decisions by Dutch neonatologists. **Methods:** We carried out a retrospective study of foetuses and neonates of more than 22 weeks’ gestation that died in the delivery room or in the neonatal intensive care unit (NICU) of a tertiary referral hospital in the Netherlands, comparing end-of-life decisions and mortality in 2001–2003 and 2008–2010, before and after euthanasia legislation was introduced. **Results:** In 2008–2010, there were more deaths in the delivery room due to termination of pregnancy than in 2001–2003 (17% versus 29%, p = 0.031), and fewer infants received comfort medication (12% versus 20%, p = 0.078). The main mode of death in the NICU was the withdrawal of life-sustaining therapy. The number of days that infants lived increased significantly between 2001–2003 (11.5 days) and 2008–2010 (18.4 days, p < 0.006). Most infants received comfort medication, and neuromuscular blocking agents were administered incidentally. **Conclusion:** Terminations increased after changes in healthcare regulations. Modes of death in the NICU remained similar over 10 years. The increased duration of NICU treatment before dying suggests a more interventionist approach to treatment in 2008–2010.

**American Journal of Public Health**

V.M. Oddo and J. Mabli, Association of Participation in the Supplemental Nutrition Assistance Program and Psychological Distress, *Am J Public Health* 105.6 (June 2015): 30–35 • **Objectives:** We assessed whether households’ participation in the Supplemental Nutrition Assistance Program (SNAP) was associated with improvements in well-being, as indicated by lower rates of psychological distress. **Methods:** We used longitudinal data for 3146 households in 30 states, collected between October 2011 and September 2012 for the SNAP Food Security survey, the largest longitudinal national survey of SNAP participants to date. Analyses compared households within days of program entry to the same households approximately 6 months later. We measured psychological distress in the past 30 days on a 6-item Kessler screening scale and used multivariable regression to estimate associations between SNAP participation and psychological distress. **Results:** A smaller percentage of household heads exhibited psychological distress after 6 months of participation in SNAP than at baseline (15.3% vs 23.2%; difference = -7.9%). In adjusted models, SNAP participation was associated with a decrease in psychological distress (adjusted relative risk = 0.72; 95% confidence interval = 0.66, 0.78). **Conclusions:** Continuing support for federal nutrition programs, such as SNAP, may reduce the public health burden of mental illness, thus improving well-being among vulnerable populations.

**Circulation Research**

E. C. Perin et al., A Phase II Dose-Escalation Study of Allogeneic Mesenchymal Precursor Cells in Patients with Ischemic or Nonischemic Heart Failure, *Circ Res* 117.6 (August 28, 2015): 576–584 • **Rationale:** Allogeneic mesenchymal precursor cells (MPCs) have been effective in large animal models of ischemic and nonischemic heart failure (HF). **Objective:** To evaluate the feasibility and safety of 3 doses (25, 75, or 150 million cells) of immunoselected
allogeneic MPCs in chronic HF patients in a phase 2 trial. Methods and Results: We sequentially allocated 60 patients to a dosing cohort (20 per dose group) and randomized them to transendocardial MPC injections (n=15) or mock procedures (n=5). The primary objective was safety, including antibody testing. Secondary efficacy endpoints included major adverse cardiac events (MACE; cardiac death, myocardial infarction, or revascularization), left ventricular imaging, and other clinical-event surrogates. Safety and MACE were evaluated for up to 3 years. MPC injections were feasible and safe. Adverse events were similar across groups. No clinically symptomatic immune responses were noted. MACE was seen in 15 patients: 10 of 45 (22%) MPC-treated and 5 of 15 (33%) control patients. We found no differences between MPC-treated and control patients in survival probability, MACE-free probability, and all-cause mortality. We conducted a post hoc analysis of HF-related MACE (HF hospitalization, successfully resuscitated cardiac death, or cardiac death) and events were significantly reduced in the 150 million MPC group (0/15) versus control (5/15; 33%), 25 million MPC group (3/15; 20%), and 75 million MPC group (6/15; 40%); the 150 million MPC group differed significantly from all groups according to Kaplan-Meier statistics >3 years (P=0.025 for 150 million MPC group versus control). Conclusions: Transendocardial injections of allogeneic MPCs were feasible and safe in chronic HF patients. High-dose allogeneic MPCs may provide benefits in this population.

**Diabetes and Metabolic Syndrome**

A. Tavakolian Arjmand, M. Nouri, and S. Tavakolian Arjmand, *Surprisingly Low Infertility Rate in Married Type 2 Diabetic Women: A Rather Curious Paradox to the Current Opinion of Insulin Resistance as the Joint Pathogenesis of Poly Cystic Ovary Syndrome and Type 2 Diabetes Mellitus*, Diabetes Metab Syndr 9.4 (August 22, 2015): 201–204 • Background: Sharing the same pathophysiologic principle which is insulin resistance, type 2 diabetes mellitus (T2DM) and poly cystic ovary syndrome (PCOS) are usually considered closely related and easily interchangeable medical entities. Numerous attempts have been made to document this illusory perspective. Objective: Based on a delicate pathophysiologic notion, we believe that fully developed T2DM is infrequently observed with fully featured PCOS. Materials and Methods: In an observational descriptive study 257 married T2DM women were consecutively included and meticulously investigated for fertility history and, albeit, clinical and biochemical features of PCOS. Results: Of 257 married diabetic women only six (2.3%) had no children. In one case a male problem (azoospermia) and in the second case, late marriage (aged 45 at wedding ceremony) was the cause of infertility. Thus, only four (1.6%) might have been labeled as true female factor infertility. Astounding to report was the average pregnancies for each participant which was 5.1±2.5, ranging from zero to fifteen. Conclusion: we would suggest that, despite the well-established fact of insulin resistance as the common pathophysiologic process for T2DM and PCOS, they are definitely separate medical entities. As a matter of fact T2DM and PCOS are the two opposite aspects of the insulin resistance coin.

**European Heart Journal**

S. Hamshere et al., *Randomized Trial of Combination Cytokine and Adult Autologous Bone Marrow Progenitor Cell Administration in Patients with Non-Ischaemic Dilated Cardiomyopathy: The REGENERATE-DCM Clinical Trial*, Eur Heart J 36.44 (November 21, 2015): 3061–3069 • Aims: The REGENERATE-DCM trial is the first phase II randomized, placebo-controlled trial aiming to assess if granulocyte colony-stimulating factor (G-CSF) administration with or without adjunctive intracoronary (IC) delivery of autologous bone marrow-derived cells (BMcs) improves global left ventricular (LV) function in patients with dilated cardiomyopathy (DCM) and significant cardiac dysfunction. Methods and Results: Sixty patients with DCM and left ventricular dysfunction were enrolled. Patients were randomly assigned to one of four dosage groups: 75 million (n=15), 150 million (n=15), 250 million (n=15), or placebo (n=15). The primary objective was safety, including antibody testing. Secondary efficacy endpoints included major adverse cardiac events (MACE; cardiac death, myocardial infarction, or revascularization), left ventricular imaging, and other clinical-event surrogates. Safety and MACE were evaluated for up to 3 years. MPC injections were feasible and safe. Adverse events were similar across groups. No clinically symptomatic immune responses were noted. MACE was seen in 15 patients: 10 of 45 (22%) MPC-treated and 5 of 15 (33%) control patients. We found no differences between MPC-treated and control patients in survival probability, MACE-free probability, and all-cause mortality. We conducted a post hoc analysis of HF-related MACE (HF hospitalization, successfully resuscitated cardiac death, or cardiac death) and events were significantly reduced in the 150 million MPC group (0/15) versus control (5/15; 33%), 25 million MPC group (3/15; 20%), and 75 million MPC group (6/15; 40%); the 150 million MPC group differed significantly from all groups according to Kaplan-Meier statistics >3 years (P=0.025 for 150 million MPC group versus control). Conclusions: Transendocardial injections of allogeneic MPCs were feasible and safe in chronic HF patients. High-dose allogeneic MPCs may provide benefits in this population.
ejection fraction (LVEF) at referral of ≤45%, New York Heart Association (NYHA) classification ≥2 and no secondary cause for the cardiomyopathy were randomized equally into four groups: peripheral placebo (saline), peripheral G-CSF, peripheral G-CSF and IC serum, and peripheral G-CSF and IC BMC. All patients, except the peripheral placebo group, received 5 days of G-CSF. In the IC groups, this was followed by bone marrow harvest and IC infusion of cells or serum on Day 6. The primary endpoint was LVEF change from baseline to 3 months, determined by advanced cardiac imaging. At 3 months, peripheral G-CSF combined with IC BMC therapy was associated with a 5.37% point increase in LVEF (38.30% ± 12.97 from 32.93% ± 16.46 P = 0.0138), which was maintained to 1 year. This was associated with a decrease in NYHA classification, reduced NT-pro BNP, and improved exercise capacity and quality of life. No significant change in LVEF was seen in the remaining treatment groups. **Conclusion:** This is the first randomized, placebo-controlled trial with a novel combination of G-CSF and IC cell therapy that demonstrates an improvement in cardiac function, symptoms, and biochemical parameters in patients with DCM.

**Human Reproduction**

*J. D. Habbema et al., Realizing a Desired Family Size: When Should Couples Start?, Hum Reprod 30.9 (September 2015): 2215–2221, doi: 10.1093/humrep/dev148* • *Study Question:* Until what age can couples wait to start a family without compromising their chances of realizing the desired number of children? **Summary Answer:** The latest female age at which a couple should start trying to become pregnant strongly depends on the importance attached to achieving a desired family size and on whether or not IVF is an acceptable option in case no natural pregnancy occurs. **What Is Known Already:** It is well established that the treatment-independent and treatment-dependent chances of pregnancy decline with female age. However, research on the effect of age has focused on the chance of a first pregnancy and not on realizing more than one child. **Study, Design, Size, Duration:** An established computer simulation model of fertility, updated with recent IVF success rates, was used to simulate a cohort of 10,000 couples in order to assess the chances of realizing a one-, two- or three-child family, for different female ages at which the couple starts trying to conceive. **Participants/ Materials, Settings, Methods:** The model uses treatment-independent pregnancy chances and pregnancy chances after IVF/ICSI. In order to focus the discussion, we single out three levels of importance that couples could attach to realizing a desired family size: (i) Very important (equated with aiming for at least a 90% success chance). (ii) Important but not at all costs (equated with a 75% success chance) (iii) Good to have children, but a life without children is also fine (equated with a 50% success chance). **Main Results and the Role of Chance:** In order to have a chance of at least 90% to realize a one-child family, couples should start trying to conceive when the female partner is 35 years of age or younger, in case IVF is an acceptable option. For two children, the latest starting age is 31 years, and for three children 28 years. Without IVF, couples should start no later than age 32 years for a one-child family, at 27 years for a two-child family, and at 23 years for three children. When couples accept 75% or lower chances of family completion, they can start 4–11 years later. The results appeared to be robust for plausible changes in model assumptions. **Limitations, Reasons for Caution:** Our conclusions would have been more persuasive if derived directly from large-scale prospective studies. An evidence-based simulation study (as we did) is the next best option. We recommend that the simulations should be updated every 5–10 years with new evidence because, owing to improvements in IVF technology, the assumptions on IVF success chances in particular run the risk of becoming outdated. **Wider Implications of the Findings:** Information on the chance of family completion at different starting ages is important for prospective parents in planning their family, for preconception counselling, for inclusion in educational courses in human biology, and for increasing public awareness on human reproductive possibilities and limitations.
JAMA

E. Leshem et al., Acute Gastroenteritis Hospitalizations among US Children following Implementation of the Rotavirus Vaccine, JAMA 313.22 (June 9, 2015): 2282–2284, doi: 10.1001/jama.2015.5571 • Routine rotavirus vaccination of US children was implemented in 2006, with 2 or 3 doses recommended before the age of 8 months. Previous studies have demonstrated the association of rotavirus vaccine introduction with reductions in health care use during the early postintroduction period or with limited insurance databases. Because laboratory testing and coding for rotavirus are not routinely performed for patients with diarrhea, we examined both all-cause acute gastroenteritis and rotavirus-coded hospitalizations among children younger than 5 years from 2000 through 2012.

JAMA Intern Med

M. R. Larochelle et al., Rates of Opioid Dispensing and Overdose after Introduction of Abuse-Deterrent Extended-Release Oxycodeone and Withdrawal of Propoxyphene, JAMA Intern Med 175.6 (June 2015): 978–987 • Importance: In the second half of 2010, abuse-deterrent extended-release oxycodeone hydrochloride (OxyContin; Purdue Pharma) was introduced and propoxyphene was withdrawn from the US market. The effect of these pharmaceutical market changes on opioid dispensing and overdose rates is unknown. Objective: To evaluate the association between 2 temporally proximate changes in the opioid market and opioid dispensing and overdose rates. Design, Setting, and Participants: Claims from a large national US health insurer were analyzed, using an interrupted time series study design. Participants included an open cohort of 31.3 million commercially insured members aged 18 to 64 years between January 1, 2003, and December 31, 2012, with median follow-up of 20 months (last follow-up, December 31, 2012). Exposures: Introduction of abuse-deterrent OxyContin (resistant to crushing or dissolving) on August 9, 2010, and market withdrawal of propoxyphene on November 19, 2010. Main Outcomes and Measures: Standardized opioid dispensing rates and prescription opioid and heroin overdose rates were the primary outcomes. We used segmented regression to analyze changes in outcomes from 30 quarters before to 8 quarters after the 2 interventions. Results: Two years after the opioid market changes, total opioid dispensing decreased by 19% from the expected rate (absolute change, -32.2 mg morphine-equivalent dose per member per quarter [95% CI, -38.1 to -26.3]). By opioid subtype, the absolute change in dispensing by milligrams of morphine-equivalent dose per member per quarter at 2 years was -11.3 (95% CI, -12.4 to -10.1) for extended-release oxycodeone, 3.26 (95% CI, 1.40 to 5.12) for other long-acting opioids, -8.19 (95% CI, -9.30 to -7.08) for propoxyphene, and -16.2 (95% CI, -18.8 to -13.5) for other immediate-release opioids. Two years after the market changes, the estimated overdose rate attributed to prescription opioids decreased by 20% (absolute change, -1.10 per 100,000 members per quarter [95% CI, -1.47 to -0.74]), but heroin overdose increased by 23% (absolute change, 0.26 per 100,000 members per quarter [95% CI, -0.01 to 0.53]). Conclusions and Relevance: Opioid dispensing and prescription opioid overdoses decreased substantially after 2 major changes in the pharmaceutical market in late 2010. Pharmaceutical market interventions may have value in combatting the prescription opioid overdose epidemic, but heroin overdose rates continue to increase. Complementary strategies to identify and treat opioid abuse and addiction are urgently needed.

JAMA Oncology

M. L. Neuhouser et al., Overweight, Obesity, and Postmenopausal Invasive Breast Cancer Risk: A Secondary Analysis of the Women’s Health Initiative Randomized Clinical Trials, JAMA Oncol 1.5 (August 1, 2015): 611–621, doi: 10.1001/jamaoncol.2015.1546 • Importance: More than two-thirds of US women are overweight or obese, placing them at increased risk for postmenopausal breast cancer. Objective: To investigate in this secondary analysis the associations of overweight and obesity with risk of postmenopausal invasive breast cancer after extended follow-up in the Women’s Health
Initiative (WHI) clinical trials. **Design, Setting, and Participants:** The WHI clinical trial protocol incorporated measured height and weight, baseline and annual or biennial mammography, and adjudicated breast cancer end points in 67,142 postmenopausal women ages 50 to 79 years at 40 US clinical centers. The women were enrolled from 1993 to 1998 with a median of 13 years of follow-up through 2010; 3,388 invasive breast cancers were observed. **Main Outcomes and Measures:** Height and weight were measured at baseline, and weight was measured annually thereafter. Data were collected on demographic characteristics, personal and family medical history, and personal habits (smoking, physical activity). Women underwent annual or biennial mammograms. Breast cancers were verified by medical records reviewed by physician adjudicators. **Results:** Women who were overweight and obese had an increased invasive breast cancer risk vs women of normal weight. Risk was greatest for obesity grade 2 plus 3 (body mass index [BMI], calculated as weight in kilograms divided by height in meters squared, >35.0) (hazard ratio [HR] for invasive breast cancer, 1.58; 95% CI, 1.40–1.79). A BMI of 35.0 or higher was strongly associated with risk for estrogen receptor-positive and progesterone receptor-positive breast cancers (HR, 1.86; 95% CI, 1.60–2.17) but was not associated with estrogen receptor-negative cancers. Obesity grade 2 plus 3 was also associated with advanced disease, including larger tumor size (HR, 2.12; 95% CI, 1.67–2.69; P=0.02), positive lymph nodes (HR, 1.89; 95% CI, 1.46–2.45; P=0.06), regional and/or distant stage (HR, 1.94; 95% CI, 1.52–2.47; P=0.05), and deaths after breast cancer (HR, 2.11; 95% CI, 1.57–2.84; P<0.001). Women with a baseline BMI of less than 25.0 who gained more than 5% of body weight over the follow-up period had an increased breast cancer risk (HR, 1.36; 95% CI, 1.1–1.65), but among women already overweight or obese we found no association of weight change (gain or loss) with breast cancer during follow-up. There was no effect modification of the BMI-breast cancer relationship by postmenopausal hormone therapy, and the direction of association across BMI categories was similar for never, past, and current hormone therapy use. **Conclusions and Relevance:** Obesity is associated with increased invasive breast cancer risk in postmenopausal women. These clinically meaningful findings should motivate programs for obesity prevention.

**Lancet**

A. Hasegawa et al., *Health Effects of Radiation and Other Health Problems in the Aftermath of Nuclear Accidents, with an Emphasis on Fukushima*, Lancet 386.9992 (August 1, 2015): 479–488 • 437 nuclear power plants are in operation at present around the world to meet increasing energy demands. Unfortunately, five major nuclear accidents have occurred in the past—i.e., at Kyshtym (Russia [then USSR], 1957), Windscale Piles (UK, 1957), Three Mile Island (USA, 1979), Chernobyl (Ukraine [then USSR], 1986), and Fukushima (Japan, 2011). The effects of these accidents on individuals and societies are diverse and enduring. Accumulated evidence about radiation health effects on atomic bomb survivors and other radiation-exposed people has formed the basis for national and international regulations about radiation protection. However, past experiences suggest that common issues were not necessarily physical health problems directly attributable to radiation exposure, but rather psychological and social effects. Additionally, evacuation and long-term displacement created severe health-care problems for the most vulnerable people, such as hospital inpatients and elderly people.

**Leukemia**

A. G. Dinmohamed, *Improved Survival in Adult Patients with Acute Lymphoblastic Leukemia in the Netherlands: A Population-Based Study on Treatment, Trial Participation and Survival*, Leukemia 30.2 (February 2016): 310–317, doi: 10.1038/leu.2015.230 • This nationwide population-based study assessed trends in treatment, trial participation and survival among 1833 adult patients diagnosed with acute lymphoblastic leukemia (ALL) in the Netherlands between 1989 and 2012 reported
The nATionAl cATholic bioeThics QuArTerly • WINTER 2015

766

to the Netherlands Cancer Registry. Patients were categorized into four periods and five age groups (18–24, 25–39, 40–59, 60–69 and ≥70 years). The application of allogeneic stem cell transplantation (alloSCT), particularly reduced-intensity conditioning (RIC) alloSCT, increased over time up to age 70 years. The inclusion rate in the trials was 67, 66, 55, 58 and 0% for the five age groups. Survival improved over time for patients below 70 years. Five-year relative survival in the period 2007–2012 was 75, 57, 37, 22 and 5% for the five age groups. In that same period, 5-year overall survival among patients aged 18–39 years was 68% for the chemotherapy-alone group and 66% for the alloSCT group. For patients aged 40–69 years, the corresponding estimates were 24 and 41%. Pronounced survival improvement observed among patients aged 18–39 years might mainly be explained by implementation of pediatric-based regimens since 2005, whereas among patients aged 40–69 years, increased application of RIC-alloSCT has contributed significantly to the observed improvement. Outcome of patients aged ≥70 remains unsatisfactory, indicating a need for specific trials for the elderly.

**Neurocritical Care**


- **Background**: It is common for patients who die from subarachnoid hemorrhage to have a focus on comfort measures at the end of life. The potential role of ethnicity in end-of-life decisions after brain injury has not been extensively studied. **Methods**: Patients with subarachnoid hemorrhage were prospectively followed in an observational database. Demographic information including ethnicity was collected from medical records and self-reported by patients or their family. Significant in-hospital events including do-not-resuscitate orders, comfort measures only orders (CMO; care withheld or withdrawn), and mortality were recorded prospectively. **Results**: 1255 patients were included in our analysis: 650 (52%) were White, 387 (31%) Hispanic, and 218 (17%) Black. Mortality was similar between the groups. CMO was more commonly observed in Whites (14%) compared to either Blacks (10%) or Hispanics (9%) (p = 0.04). In a multivariate analysis controlling for age and Hunt-Hess grade, Hispanics were less likely to have CMO than Whites (OR, 0.6; 95% CI, 0.4–0.9; p = 0.02). Of the 229 patients who died, 77% of Whites had CMO compared to 54% of Blacks and 49% of Hispanics (p < 0.01). In a multivariate analysis, Blacks (OR, 0.3; 95% CI, 0.2–0.7; p < 0.01) and Hispanics (OR, 0.3; 95% CI, 0.2–0.6; p < 0.01) were less likely to die with CMO orders than Whites. **Conclusion**: After subarachnoid hemorrhage, Blacks and Hispanics are less likely to die with CMO orders than Whites. Further research to confirm and investigate the causes of these ethnic differences should be performed.

**Oncologist**


- **Background**: The assessment of ovarian reserve in premenopausal women requiring anticancer gonadotoxic therapy can help clinicians address some challenging issues, including the probability of future pregnancies after the end of treatment. Anti-Müllerian hormone (AMH) and age can reliably estimate ovarian reserve. A limited number of studies have evaluated AMH and age as predictors of residual ovarian reserve following cytotoxic chemotherapy in breast cancer patients. **Materials and Methods**: To conduct a meta-analysis of published data on this topic, we searched the medical literature using the key MeSH terms “amenorrhea/chemically induced,” “ovarian reserve,” “anti-Mullerian hormone/blood,” and “breast neoplasms/drug therapy.” Preferred Reporting Items for Systematic Reviews and Meta-Analyses statements guided the search strategy. U. K. National Health Service guidelines were used in abstracting data and assessing data quality and validity. Area under the receiver operating characteristic curve (ROC/AUC) analysis was used to evaluate the predictive utility of baseline AMH
and age model. Results: The meta-analysis of data pooled from the selected studies showed that both age and serum AMH are reliable predictors of post-treatment ovarian activity in breast cancer patients. Importantly, ROC/AUC analysis indicated AMH was a more reliable predictor of post-treatment ovarian activity in patients aged younger than 40 years (0.753; 95% confidence interval [CI]: 0.602–0.904) compared with those older than 40 years (0.678; 95% CI: 0.491–0.866). We generated a nomogram describing the correlations among age, pretreatment AMH serum levels, and ovarian activity at 1 year from the end of chemotherapy. Conclusion: After the ongoing validation process, the proposed nomogram may help clinicians discern premenopausal women requiring cytotoxic chemotherapy who should be considered high priority for fertility preservation counseling and procedures. Implications for Practice: In general, a nomogram helps clinicians better visualize a specific risk for a single patient. In premenopausal women affected by early breast cancer who need adjuvant cytotoxic regimens, the proposed nomogram-based on the assessment of pretreatment age and anti-Müllerian hormone serum levels-can assess the personal probability of maintaining ovarian activity at 1 year from the end of chemotherapy. The ongoing validation process is also evaluating other key factors contributing to post-treatment ovarian activity (i.e., type of cytotoxic regimen) and will confirm the nomogram’s reliability and clinical utility.

Urology

J. Romero-Otero et al., Semen Quality Assessment in Fertile Men in Madrid during the Last 3 Decades, Urology 85.6 (June 2015): 1333–1338, doi: 10.1016/j.urology.2015.02.001 • Objective: To evaluate semen quality of men with proven fertility in Spain over the last 3 decades. Methods: We conduct a retrospective analysis of ejaculate samples of 992 men between 1985 and 2009. All patients had proven fertility as demonstrated by fathering at least 2 children and a semen analysis performed before they underwent vasectomy. A standardized procedure was used for the semen analysis. Semen volume, total sperm count, sperm concentration, motility, and percentage of morphologically normal spermatozoa were assessed. Mean values were calculated by examining microscopic fields of 100 spermatozoa. Results: Statistically significant differences were found in all semen parameters analyzed. For the periods 1985–1990, 1990–2000, and 2000–2009, the mean (standard deviation [SD]) sperm concentration was 27.7 (22.97), 20.73 (14.79), and 20.18 (20.79) × 10(6) (P < 0.0001). The mean (SD) progressive motility for each period was 53.19 (20.35), 47.22 (15.84), and 40.57 (15.15; P < 0.0001). The mean (SD) normal-shaped spermatozoa for each period was 67.69 (10.24), 58.87 (14.67), and 51.02 (15.76; P < 0.0001). Multivariate analysis using a logistic regression model showed that age had no significant effect in the variation of semen parameters at the cut-points analyzed, except for normal forms at percentile 25 (P = 0.001). Multivariate analysis revealed a trend for decline of semen in sperm concentration, progressive and nonprogressive motility, and the percentage of morphologically normal spermatozoa (P = 0.001–0.002). Conclusion: Over the last 3 decades, a decline in semen quality was found in all the parameters analyzed in Spanish men with proven fertility.