research highlights

Findings Shed Light on Sex Differences in Diabetes, Suggest Potential for Earlier Diagnosis and Treatment

DIABETES RESEARCHERS have long observed sex differences in how the disease develops and in its manifestations, particularly with regard to vascular complications. Women bear much of the diabetes risk burden. For example, studies have shown that overweight is a more powerful risk factor for diabetes in women than in men. In addition, type 2 diabetes is a more powerful risk factor for heart disease mortality in women than in men: It increases the risk of heart disease mortality by approximately 250 percent in women, vs. approximately 100 percent in men. But little has been known about the biological reasons for these differences.

Now, a series of 2007 papers published in major peer-reviewed journals by the research group of Dr. Simin Liu, professor in the UCLA School of Public Health, and David Geffen School of Medicine, has shed new light on the biology of the disease, linking three major physiological systems (metabolism, immunity, and reproduction) that contribute to the sex differences in diabetes development. Liu and collaborators assessed these physiological functions across multiple ethnic populations (whites, African Americans, Latinos, and Asians) and identified three sets of biological markers that enabled them to forecast the development of diabetes in apparently healthy women.

The findings suggest the potential for strategies that could lead to a much earlier diagnosis of the disease, which would potentially facilitate interventions at an earlier stage in the disease course, when they might be more likely to succeed. The biological markers identified by Liu's group could also lead to new prevention and treatment approaches.

Publishing in the journals *Diabetes, Archives of Internal Medicine and Diabetologia*, Liu and colleagues identified a set of biochemical markers (inflammation and endothelial dysfunction) in women that were highly and significantly predictive of diabetes years ahead of actual disease development. In addition, they reported that these biochemical markers appear to be interacting with sex steroids in determining an individual's risk of developing diabetes, independent from the traditional risk factors.

The findings, which culminate an eight-year research effort of Liu's research program, contribute to an improved understanding of the genetic and biochemical roles of sex steroids in the inflammation that occurs not only in the development of type 2 diabetes, but also in heart disease and certain cancers.

"These findings provide some new biological insight in explaining an age-old observation of sex differences in the etiology of diabetes and its vascular complications," Liu says. "Ultimately, this should allow us to build predictive and diagnostic models for diabetes that will work far better than our conventional practice of testing for blood glucose levels. In addition, the molecules we have identified as biological markers can serve as important targets for improved prevention and treatment of this disease."

The findings could lead to predictive and diagnostic models for diabetes that work far better than the current practice of testing for blood glucose levels.

PG-13 Films Not Safe for Kids?

PG-13 FILMS have lots of "happy violence" – as defined by the late communications theorist George Gerbner, that which is "cool, swift and painless" – without considering the consequences of violent acts, such as injury, death and the shattered lives of the people involved, according to a study by researchers at the school's Southern California Injury Prevention Research Center.

Homicide is the second leading cause of death among 15- to 24-year-olds in the United States. Media depictions of violence help teach such acts to children, leading to three effects – increased aggression, fear for their own safety, and a desensitization to the pain and suffering of others, according to the study team, which was led by Theresa Webb, a researcher in the Department of Epidemiology and at the center. The study was published in the journal *Pediatrics*.

Distribution of Violent Actions Among PG-13 Films, by Genre

Genre	Number (%) of Films with Violence	Number (%) of Violent Actions	Average Number of Acts Per Film*	Minimum Number of Acts Per Film	Maximum Number of Acts Per Film
Action (n = 13)	13 (16.9)	1,178 (52.3)	91	6	263
Comedy (n = 37)	31 (40.3)	747 (33.2)	20	0	137
Drama and Romance (n = 18)	14 (18.2)	75 (3.3)	4	0	28
Horror, Sci-Fi, Thiller (n = 9)	9 (11.7)	251 (11.2)	28	2	98
Total (n = 77)	67 (87.0)	2,251 (100)	29	0	263

* Includes all films in genre, both with and without violence

In a sample of 77 PG-13 rated films, Webb and her colleagues recorded a total of 2,251 violent actions, with almost half resulting in death. Although a small subset of this content contained violence that was associated with negative effects such as pain and suffering, only one film – *Pay It Forward*, in which the young hero is stabbed to death – contained violent acts that would demonstrate to youthful viewers how horrific violence can be.

"Violence permeated nearly 90 percent of the films in this study," Webb says. "And while the explanations and causes of youth violence are very complex, the evidence is clear that media depictions of violence contribute to the teaching of violence. This is especially true in our society, where the average young person's engagement with visual media in all its forms can run to as many as eight hours a day."

The researchers sampled all of the PG-13 rated films from among the 100 top-grossing movies of 1999 and 2000, as established by the *Hollywood Reporter*. To obtain their results, they coded each act of violence and the context in which it was presented based on features known to put violence in a good or bad light. Such features include the motivation for violence, the presence of weapons, the consequences of violence and the degree of realism.

The findings follow up on a 2005 study the researchers conducted that looked at movie violence in all ratings categories established by the Motion Picture Association of America (MPAA). In that study, they found that parents using the ratings system to gauge movie content receive little meaningful guidance related to violent content.

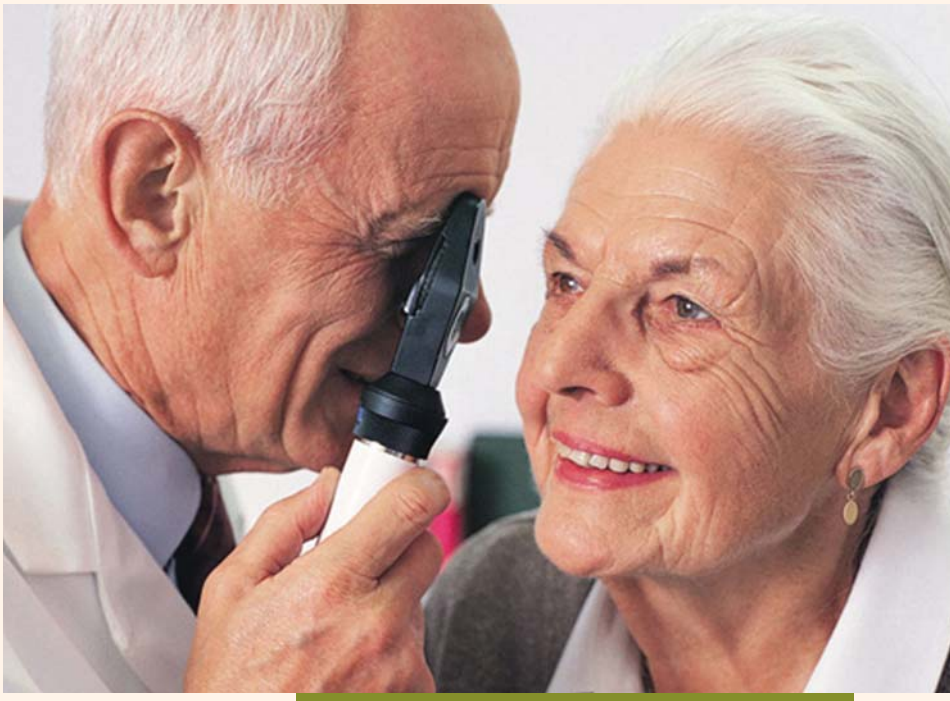
This time around, the researchers selected the PG-13 category because it has become a repository for action films. "These films are often the largest budgeted ones made by the Hollywood film industry and have also been found to be equally, if not more, violent than R-rated films," Webb notes.

Maintaining Strong Bones May Protect Older Women Against Age-Related Maculopathy

GREATER BONE MINERAL DENSITY reduces the risk of age-related maculopathy in elderly women, according to the findings of a research team led by Dr. Anne L. Coleman, professor of epidemiology in the UCLA School of Public Health and professor of ophthalmology at UCLA's Jules Stein Eye Institute.

Age-related maculopathy (ARM), a leading cause of severe visual impairment among older adults in developed countries, affects the central vision of approximately 9 million people in the United States. "Because we have such a poor understanding of the pathogenesis of ARM and limited available treatment options, identifying prevention strategies is crucial to addressing the burden of this disease," Coleman says.

In a study published in the *Journal of the American Geriatric Society*, Coleman reported that greater bone mineral density (BMD) decreased by at least 34% the likelihood of ARM in 1,042 white women aged 75 and older who were enrolled in the multi-center cohort Study of Osteoporotic Fractures. "To our knowledge, ours is the first study to investigate the association between BMD and ARM, and further research is needed to confirm these results," says Coleman. "But our findings suggest that maintaining healthy bones, which we already know to be beneficial in preventing osteoporosis, falls and injuries, and cognitive decline, is also beneficial in fighting AMD." She notes that current prevention strategies for AMD are limited: Intake of antioxidants and zinc has been found to slow the progression of the disease.



Given the limited treatment options, identifying new prevention strategies is crucial to addressing the burden of age-related maculopathy, a leading cause of visual impairment among older adults.

The way in which BMD might affect AMD is unknown. One hypothesis is that a higher estrogen level over the course of a woman's lifetime is what is protective of ARM. "Women with greater exposure to estrogen during their lifetimes tend to have stronger bones," Coleman says. "Past research has suggested that longer reproductive life, also a marker for higher lifetime estrogen levels, decreases the likelihood of having AMD." Coleman adds that fruit and vegetable consumption, which has been found to be associated with BMD, is another factor that might have contributed to the findings.

Identifying risk factors associated with AMD is all the more important given the significant financial costs of the disease. In a separate study using data from a random sample of 1995-1999 Medicare beneficiaries, Coleman's group estimated that the annual cost of treatment of some forms of AMD was $569 million, though the costs might be much greater given that the Medicare database allowed for the inclusion of only reimbursed eye-related professional fees. Non-reimbursed costs that increase the burden from AMD and were unaccounted for in the study include low-vision aids, pharmacy costs, nursing care costs, and indirect care costs in the form of lost productivity.

Proximity to High Traffic Density, Air Pollution Linked to Poorly Controlled Asthma

DESPITE MAJOR ADVANCES in the development of anti-inflammatory medications in the last two decades, many U.S. residents have poorly controlled asthma. In California in 2000, nearly 25 percent of adults diagnosed as having asthma experienced symptoms every day or week, 7 percent reported at least one emergency department visit for asthma, and 2 percent reported they were hospitalized for the condition, according to findings from the 2001 California Health Interview Survey, based in the school's Center for Health Policy Research. Poorly controlled asthma is difficult to treat and contributes disproportionately to the overall costs associated with the condition, but little is understood about the reasons behind it.

Adults with asthma living in the highest-density traffic areas are twice as likely to have severe asthma as those living in the lowest-density areas.

A team of researchers from the UCLA School of Public Health and California Department of Public Health has identified a major factor: traffic and air pollution levels near one's home. Publishing in the *Annals of Allergy, Asthma and Immunology*, Dr. Ying-Ying Meng and colleagues reported that adults with asthma living in the highest-density traffic areas are twice as likely to have severe asthma as those living in the lowest traffic density areas, even after adjusting for age, sex, race, and poverty, with the strongest association found among the elderly. Ozone exposures are associated with poorly controlled asthma among elderly adults and men, whereas particulate matter less than 10 μm appears to affect primarily women, even at levels below the U.S. Environmental Protection Agency air quality standard. The varying effects by population group indicate differences in susceptibility to specific pollutants, the researchers noted.

Most previous studies on the subject have focused on the effects of short-term (one- to five-day) pollutant exposures on hospitalizations and emergency care, especially among children; this has left unanswered questions about the potential role air pollution plays in asthma exacerbation among adults and whether certain subpopulations such as elderly adults and women respond to pollutant exposures differently, notes Meng, a senior research scientist at the Center for Health Policy Research. Using 2001 California Health Interview Survey data, Meng and colleagues examined whether exposure to air pollution, measured via traffic density and ambient air-monitoring data near residences, increases the prevalence of poorly controlled asthma among various subpopulations of adults with asthma living in Los Angeles and San Diego counties.

"Our study provides much-needed information on the possible association of long-term exposure – a year or more – to outdoor air pollution and asthma severity in an ethnically diverse adult population," Meng says. "The findings suggest that more consideration should be given to residential proximity to heavy traffic and outdoor pollutant levels for those adults with poorly controlled asthma."

Quality of Life Benefits Shown for Patients in Public Assistance Program for Prostate Cancer

MEN WHO WERE DENIED ACCESS to California's public assistance program for prostate cancer during the state's 2005 fiscal woes experienced significantly more symptom-related distress and less perceived self-efficacy than enrollees in the program, even when comparing individuals with the same disease burden. These are among the findings of a study headed by Drs. Jennifer Anger, assistant professor of urology in UCLA's David Geffen School of Medicine, and Dr. Mark S. Litwin, professor of urology in UCLA's David Geffen School of Medicine and of health services in the UCLA School of Public Health. The findings underscore the importance of the IMPACT program, which has since been made a permanent part of the California Department of Public Health, and which has been headed by Litwin since it was established in 2001.

IMPACT (Improving Access, Counseling and Treatment for Californians with Prostate Cancer) is designed to reduce barriers to accessing health care and needed psychosocial services among uninsured men with prostate cancer. The program gives access to providers throughout California – in the individual's own community where possible. Besides the direct patient care, IMPACT provides case and symptom management, culturally and linguistically appropriate patient-education materials, and extensive social-service resources. The program was designed not only to remove health-system access barriers faced by uninsured men with prostate cancer, but also to diminish health-outcome barriers associated with minority status, low socioeconomic status, low levels of education and health literacy, language, and cultural differences.

Average Baseline Health-Related Quality of Life Scores for Prostate Cancer Patience Enrolling in IMPACT Program vs. Patients Told They Were Being Waitlisted

	Enrolled Patients	Waitlisted Patients	Difference in Negative Outcome for Waitlisted
SDS (Symptom Distress Scale)*	21	24	14%
PEPPI (Perceived Efficacy in Patient-Physician Interactions)**	8.1	10.6	31%

* SDS measures the degree of distress perceived by patients for 10 specific cancer symptoms. Responses are scored from 1 to 5 and added together, with higher scores indicating more symptom-related distress.

**PEPPI measures patients' perceived sense of effectiveness in interacting with physicians and obtaining needed health care. Responses to each of five items are scored from 1 to 5 and added together, with a higher score reflecting lower self-efficacy.

In February 2005, in the midst of a state fiscal crisis, IMPACT enrollment was closed; men needing program services were put on a waiting list in the hope that enrollment would reopen in the future. "Suspension of enrollment in IMPACT afforded a unique opportunity to assess the health-related quality of life of a population of men rarely studied," says Anger. "Health-related quality of life is an important component of treatment decision-making for men with prostate cancer, and researchers have just recently begun to look at how it is affected by access to care."

Waitlisted men were interviewed every three months until enrollment was reopened and their health-related quality of life was compared with a group of enrolled men matched by disease stage, age and race. In addition to showing significantly more symptom distress and less self-efficacy than the enrolled men, the waitlisted men were significantly less likely to have access to a doctor or other medical treatments and services. Results of the study were published in *Public Health Reports*.

"The negative impact on health-related quality of life in men with prostate cancer denied access to IMPACT supports the position that ongoing and continuous financial support is crucial for this program," says Litwin. IMPACT, which has provided prostate cancer treatment to more than 1,000 men, was made permanent with passage by the California Legislature of a bill signed into law by Gov. Schwarzenegger in the fall of 2005 placing the program in the state's newly formed Department of Public Health. In April 2006, UCLA was awarded the IMPACT administration contract in a new three-year, $9.7 million agreement.