## HEART OF THE MATTER

# Diabetes and CVD: To Be, Or Not to Be, Aggressive?

Because cardiovascular deaths account for 65%-70% of deaths in patients with diabetes, the disease has been labeled by various guideline committees as a coronary heart disease risk equivalent. Although there has been some debate regarding this, the recent data from a meta-analysis of 102 prospective studies with 8.49 million person-years of follow-up – showing that diabetes confers a twofold excess risk for CHD, major strokes, and deaths attributable to other vascular diseases – leaves little room for discussion in this regard (Lancet 2010;375:2215-22).

PRAKASH DEEDWANIA, M.D.

The vast majority of national and international guidelines have recommended aggressive management strategies to reduce blood glucose, blood pressure, and lipids in patients with diabetes in the hope of reducing CV events, despite the paucity of data from well-designed, prospective, randomized, controlled trials (RCTs). However, during the past decade, several well-designed RCTs have examined and compared the role of intensive versus usual management strategies in reducing the risk of macrovascular and microvascular events in DM .These studies include the Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease (ADVANCE), and the Veterans Affairs Diabetes Trial (VADT).

Results from all of these well-designed RCTs have been somewhat perplexing, and contrary to the prevailing concepts. First of all, the results from the intensive glucose control arm from all three trials showed that the intensive glucose control strategy was not only associated with lack of benefit in primary end point, but indeed was harmful in a certain subset of patients due to the risks associated with resultant hypoglycemia. The results of the ACCORD study are particularly important because there was increased mortality in the ACCORD intensive glycemic control arm, which persisted even 1.5 years after the therapy for intensive control of glucose was stopped. The risk of hypoglycemia is further emphasized by the recent presentation from the ADVANCE group in showing that severe symptomatic hypoglycemia was associated with nearly threefold increased risks of macrovascular events, cardiovascular mortality, and all-cause mortality (N. Engl. J. Med. 2010;363:1410-8).

The lack of benefit of an intensive glucose control strategy should not be entirely surprising, because the prevailing wisdom was based on epidemiologic data showing higher risk of CV events with higher levels of glucose. However, it is important to realize that such an association might be due to other risks and/or risk factors. For now, based on the totality of the data it seems appropriate to be not too aggressive in controlling blood glucose and to stick with the current target of $HbA_{1C}$ below 7% for most patients with diabetes.

The lack of benefits reported from the ACCORD and ADVANCE blood pressure arms of the studies also deserves mention. In ACCORD, intensive antihypertensive therapy was targeted to a systolic pressure of less than 120 mm Hg and standard therapy treated to a systolic pressure target of less than 140 mm Hg. After 1 year, the mean systolic BP was 119 mm Hg in the intensive therapy group and 134 mm Hg in the standard-therapy group. At 1 year there was no difference in the primary composite outcome (nonfatal MI, nonfatal stroke, or death from cardiovascular causes).

It should perhaps not come as a surprise that there was no improvement in the primary composite outcome, since control of BP to less than 130 mm Hg systolic has not been shown to improve coronary events in most studies. On the other hand, there has been a close correlation between systolic BP and risk of stroke rate down to a lower value of 115 mm Hg, and in the ACCORD BP study also it was shown that decreasing systolic BP to a mean value of 119 mm Hg was associated with a 41% decrease in all stroke and also a significant reduction in nonfatal strokes.

Results from the ADVANCE study are also instructive in the management of hypertension in the diabetic patient. Compared with patients assigned placebo, those who received active therapy had a mean reduction in systolic BP of 5.6 mm Hg (mean 135 mm Hg in the active group vs. 140 mg Hg with placebo) and diastolic blood pressure of 2.2 mm Hg (mean 75 mm Hg and 77 mm Hg, respectively). The relative risk of death from cardiovascular disease was reduced by 18%, and death from any cause was reduced by 14%, both significant differences. This benefit was attributed mostly to reduction in microvascular events. Thus, unlike the aggressive glucose arms of the studies it appears that the BP control strategy does work and reduces the macrovascular end points directly related to BP.

Based on these results, it is fair to conclude that the evidence supports a comprehensive risk-reduction strategy addressing most risk factors in diabetes. However, such a strategy should include consideration of possible hazards of aggressive therapy. As always, the benefit:risk ratio should be carefully evaluated for each individual patient. We should remember the old maxim and Hippocratic oath, that above all we should do no harm. ■

DR. DEEDWANIA *is chief of cardiology at Veterans Affairs Central California Health Care System, Fresno. He reported no relevant financial disclosures.*

Cardiology News

**President, IMNG** Alan J. Imhoff

**Editor in Chief** Mary Jo M. Dales

**Executive Editors** Denise Fulton, Kathy Scarbeck

**Managing Editor** Catherine Hackett

**Senior Editors** Christina Chase, Kathryn DeMott, Jeff Evans, Lori Buckner Farmer, Keith Haglund, Gina L. Henderson, Sally Koch Kubetin, Teresa Lassman, Mark S. Lesney, Jane Salodof MacNeil, Renée Matthews, Catherine Cooper Nellist, Amy Pfeiffer, Terry Rudd, Leanne Sullivan, Elizabeth Wood

**Editorial Production Manager** Carol Nicotera-Ward

**Associate Editors** Felicia Rosenblatt Black, Therese Borden, Lorinda Bullock, Jay C. Cherniak, Richard Franki, Virginia Ingram-Wells, Jane Locastro, January Payne,

**Reporters** *Chicago:* Patrice Wendling; *Denver:* Bruce Jancin; *Germany*: Jennie Smith; *Miami:* Damian McNamara; *Mid-Atlantic:* Michele G. Sullivan; *New England:* Diana Mahoney; *New York:* Mary Ellen Schneider; *Philadelphia:* Mitchel L. Zoler; *San Diego:* Doug Brunk; *San Francisco:* Sherry Boschert, Robert Finn; *Washington:* Alicia Ault, Elizabeth Mechcatie, Naseem S. Miller, Heidi Splete, Miriam E. Tucker, Kerri Wachter

**Multimedia Producer** Nick Piegari

**Contributing Writers** Christine Kilgore, Mary Ann Moon

**Project Manager** Susan D. Hite

**Assignments Manager** Megan Evans

**Executive Director, Operations** Jim Chicca

**Director, Production/Manufacturing** Yvonne Evans

**Production Manager** Judi Sheffer

**Production Specialists** Maria Aquino, Anthony Draper, Rebecca Slebodnik

**Creative Director** Louise A. Koenig

**Design Supervisor** Elizabeth Byrne Lobdell

**Senior Designers** Sarah L.G. Breeden, Yenling Liu

**Designer** Lisa M. Marfori

**Photo Editor** Catherine Harrell

**Senior Electronic Production Engineer** Jon Li

**Sales Director, IMNG**
Mark E. Altier, 973-290-8220, m.altier@elsevier.com

**National Account Manager**
Courtney Leonard, 973-290-8223, c.leonard@elsevier.com

**Advertising Offices** 60 Columbia Rd., Bldg. B, 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250

**Classified Sales Manager, IMNG**
Robert Zwick 973-290-8226, fax 973-290-8250, r.zwick@elsevier.com

**Classified Sales Representative**
Andrea LaMonica 800-381-0569, fax 914-381-0573, a.lamonica@elsevier.com

**Editorial Offices** 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 877-524-9335, cardiologynews@elsevier.com

**Address Changes** Fax change of address (with old mailing label) to 973-290-8245 or e-mail change to subs@elsevier.com

**Reprints** Call 240-221-2419

**Director of Information Technology** Doug Sullivan

**Senior Systems Administrators** Lee J. Unger, Kreg M. Williams

**Systems Administrator/Application Support** Peter Ayinde

**Sr. Program Manager, Customized Programs** Malika Wicks

**Circulation Analyst** Barbara Cavallaro, 973-290-8253, b.cavallaro@elsevier.com

**Program/Marketing Manager** Jennifer Eckert

**Business Controller** Dennis Quirk

**Adv. Services Manager** Joan Friedman

**Credit Supervisor** Patricia H. Ramsey

**Manager, Administration/Conventions** Lynne Kalish

**Receptionist** Linda Wilson

**Accounts Payable Coordinator** Daniela Silva

CARDIOLOGY NEWS is an independent newspaper that provides the practicing specialist with timely and relevant news and commentary about clinical developments in the field and about the impact of health care policy on the specialty and the physician's practice.

The ideas and opinions expressed in CARDIOLOGY NEWS do not necessarily reflect those of the Publisher. Elsevier Inc. will not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to the products, drugs, or services mentioned herein.

POSTMASTER Send changes of address (with old mailing label) to CARDIOLOGY NEWS Circulation, 60 Columbia Rd., Bldg. B, 2nd flr., Morristown, NJ 07960.

CARDIOLOGY NEWS (ISSN 1544-8800) *is published monthly by Elsevier Inc., 60 Columbia Rd., Bldg. B, 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250. Subscription price is $109.00 per year.*

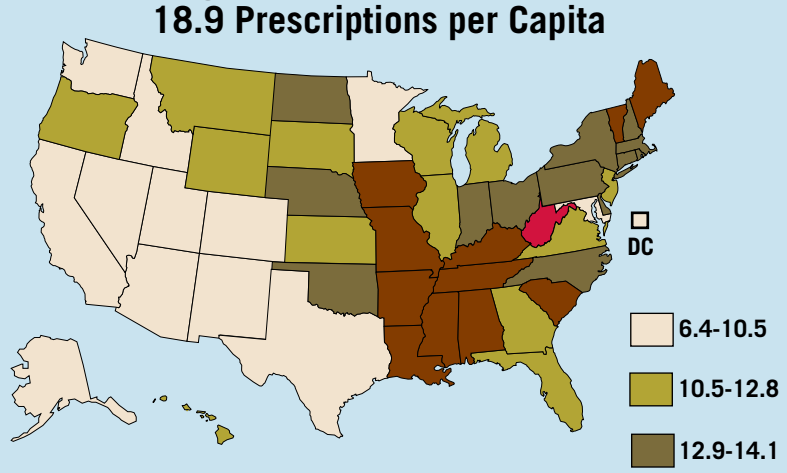


ELSEVIER INTERNATIONAL MEDICAL NEWS GROUP

BPA WORLDWIDE

## VITAL SIGNS

### West Virginia Led the U.S. in 2009 With 18.9 Prescriptions per Capita




Note: Based on data from Vector One: National by SDI Health.
Data include prescriptions filled at pharmacies only.
Source: Kaiser Family Foundation

ELSEVIER GLOBAL MEDICAL NEWS