

## **Major Kidney Clinical Research Studies and Projects Inventory\***

### **Diabetic Renal Disease Study (DRDS)**

#### **1. Administrative Data**

(a) Name of study/research project and acronym:

Diabetic Renal Disease Study (DRDS)

(b) Type of study/research project (randomized clinical trial, epidemiological study, database, etc.):

Epidemiological prospective cohort

(c) Funding status (currently funded, study/project completed):

Project completed

(d) Recruitment status (recruitment completed, currently recruiting):

Recruitment completed

(e) For studies/project currently recruiting: indicate total sample size/ number currently enrolled, anticipated period of recruitment:

*199 subjects:*

- 31 Group 0: Normal glucose tolerance
- 30 Group 1: Impaired glucose tolerance
- 30 Group 2: Type 2, non-insulin dependent diabetes < 3 years
- 59 Group 3: Type 2, non-insulin dependent diabetes  $\geq$  5 years with microalbuminuria
- 35 Group 4: Type 2, non-insulin dependent diabetes  $\geq$  5 years with macroalbuminuria
- 14 Group 5: Type 2, non-insulin dependent diabetes  $\geq$  8 years with normal urinary albumin excretion

(f) Data coordinating center principal investigator contact information (mailing address, phone, fax, e-mail address):

Gerald Beck, Ph.D.  
Department of Biostatistics and Epidemiology, Wb4  
Cleveland Clinic Foundation  
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Cleveland, OH 44195  
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*Chair, Steering Committee:*

William Mitch, M.D., formerly at:  
Emory University School of Medicine  
Renal Division  
1364 Clifton Road, N.E.  
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*Project Officer:*

Gladys Hirschman, M.D.  
National Institutes of Health  
Division of Kidney, Urologic, and Hematologic Diseases  
NIDDK  
6707 Democracy Boulevard, Room 630  
Bethesda, MD 20892  
*Phone:* 301-594-7717  
*Fax:* 301-480-3150  
*E-mail:* hirschmang@extra.niddk.nih.gov

(g) Number of recruiting sites, list of principal investigators at recruiting sites and contact information as in (f) above:

One recruitment site: Gila River (Pima) Indian Community, Phoenix, AZ

Robert Nelson, M.D., Ph.D.  
National Institutes of Health  
Building One  
1550 East Indian School Road  
Phoenix, AZ 85014  
*Phone:* 602-200-5205  
*Fax:* 602-200-5225

*E-mail:* rnelson@phx.niddk.nih.gov

(h) List of principal investigators at central laboratories/facilities (identify type of central facility) and contact information as in (f) and (g) above:

*Central facilities:*

Renal Function Laboratory  
Bryan D. Myers, M.D.  
Stanford University Medical Center  
Division of Nephrology, Room S-069  
300 Pasteur Drive  
Stanford, CA 94305  
*Phone:* 415-723-6248  
*Fax:* 415-723-7917

Retinal Photography Laboratory  
Ronald Klein, M.D., M.P.H.  
Department of Ophthalmology  
University of Wisconsin-Madison Medical School  
610 North Walnut  
Madison, WI 53705  
*Phone:* 608-263-7758

(i) Roster of Data and Safety Monitoring Board/Scientific Advisory Committee or other oversight committee(s):

i.

*Executive Advisory Board:*

Harry R. Jacobson, M.D., Vanderbilt University  
Andrew Levey, M.D., New England Medical Center  
Edmund J. Lewis, M.D., Rush Presbyterian-St. Luke's Medical Center  
Jeffrey Roseman, M.D., Ph.D., M.P.D., University of Alabama at Birmingham  
Michael Steffes, M.D., Ph.D., University of Minnesota

(j) Private-sector support (type of support, e.g., financial, donation of drugs/placebo, etc.)

No private sector support.

## **2. Study Design**

(a) Objective, (b) Study design, (c) Major inclusion criteria, (d) Major exclusion criteria, (e) Description of the intervention(s), (f) Baseline/eligibility visit schedule (number of visits, major

assessments), (g) Follow-up contact schedule (frequency, type of visit/phone, in-clinic, major assessments), (h) Primary outcome, secondary outcomes:

Design: See *Acta Diabetol* 1991; 28:143-150

Primary outcome: See *N Engl J Med* 1996; 335:1636-1642

(i) Brief summary of power estimates used to justify sample size/duration, including critical assumptions (i.e., effect-size estimates, estimated event rates or rate of change in outcome measure):

Design: See *Acta Diabetol* 1991; 28:143-150

Primary outcome: See *N Engl J Med* 1996; 335:1636-1642

### 3. Data and Biological Sample Resources

(a) Biological samples collected in ongoing studies/research projects (specify the type of sample, e.g., blood, urine, etc., the amount, and the point in the study when samples were collected, e.g., baseline visit #1, baseline visit #2, follow-up visit #1; specify months after randomization/study entry):

*Biological samples collected are as follows:*

- Serum and urine collected every 6 months.
- Kidney biopsy in 20 patients.
- Nuclear pellet of DNA collected at initial and final clearance study.

(b) Biological samples currently in storage from completed trials (grid showing sample collection time, type of sample, amount, and number of study participants the sample was collected from, in addition to physical location of where the samples are stored):

Serum, urine, and DNA pellet samples stored at -70°C at the Diabetes and Arthritis Epidemiology Section Laboratory, NIDDK, Phoenix, Arizona. See Table 1 below. Biopsies stored at Renal Function Laboratory, Stanford University.

<b>Table 1. DRDS Stored Serum and Urine Samples (Same number of samples for serum and urine)</b>										
<b>Study Group</b>	<b>Time (months)</b>									<b>Total</b>
	0	6	12	18	24	30	36	42	48	
0	31	0	0	0	0	0	1	0	28	60
1	29	0	6	0	21	0	25	0	29	110
2	30	0	9	0	17	0	22	0	24	102
3	50	5	48	43	51	48	45	31	47	368
4	34	3	17	26	27	26	28	21	31	213
5	20	0	0	0	16	0	0	0	0	36
<b>Total</b>	194	8	80	69	132	74	121	52	159	889
Group 0: Normal glucose tolerance Group 1: Impaired glucose tolerance Group 2: Type 2, non-insulin dependent diabetes < 3 years Group 3: Type 2, non-insulin dependent diabetes ≥ 5 years with microalbuminuria Group 4: Type 2, non-insulin dependent diabetes ≥ 5 years with macroalbuminuria Group 5: Type 2, non-insulin dependent diabetes ≥ 8 years with normal urinary albumin excretion										

(c) Brief summary of typical informed consent provisions (template informed consent form acceptable), including major variables in participant consents, if applicable (e.g., “use for other studies or not”, “allow genetic studies or not” and whether consent includes use of samples in other studies that are not part of the main study):

Informed consent. Confidentiality: When results of a study such as this are reported in medical journals or at meetings, the identification of those taking part is withheld. Medical records of Clinical Center patients are maintained according to current legal requirements, and are made available for review, as required by the Food and Drug Administration or other authorized users, only under the guidelines established by the Federal Privacy Act.

(d) Data collected (grid of data collection by time/clinic visit with specificity on the type of information collected, e.g., quality of life with SF-MOS 36, measurement of kidney function by GFR, serum creatinine measurement, etc.)

See design paper [*Acta Diabetol* 1991; 28:143-150]. Depending upon group and visit, data collection includes the following:

<b>Table 2. DRDS Data Collected</b>			
<b>Initial Full Clearance Visit</b>	<b>Full Renal Clearance Study</b>	<b>Laboratory Investigations and Hormones</b>	<b>Dietary Assessments (Initial Clearance Only)</b>
Medical Hx and physical exam	Dextran sieving coefficients	Hematology screen (CBC)	Dietary survey
Blood pressure and medications	GFR by iothalamate infusion	Blood chemistry and liver function tests (SMAC)	24-hour dietary recall
2-Hour urine for albumin, IgG, and creatinine	Renal plasma flow	Hormones	Quantitative food frequency
Pregnancy test for females		Hemoglobin A <sub>1</sub> C, serum IgG, albumin, creatinine	
OGTT		Plasma colloid oncotic pressure	
		Retinal photography	
		Nuclear pellet of DNA (Initial and Final clearance only)	
		Renal ultrasound	
		Leukocyte dipstick	

(e) Any provisions for distributing resources outside of the study? What is the sharing plan?

Stored specimens and data have been given to external investigators, see 4b.

Requests for data or samples are sent to the DCC for review and approval.

#### **4. Ancillary Studies**

(a) Process and contact person (name, address, phone, fax, and e-mail address) for application to perform ancillary studies:

Gerald Beck, Ph.D.  
 Department of Biostatistics and Epidemiology, Wb4  
 Cleveland Clinic Foundation  
 9500 Euclid Avenue  
 Cleveland, OH 44195

(b) List of ancillary studies approved, completed and ongoing (including source of funding and amount):

- Kevin Lemley, M.D., Ph.D., Fibrogen. Serum and urine provided to measure connective tissue growth factor (ASN 2001)
- Paul Beisswenger, M.D., Duke University. Serum from patients with kidney biopsies provided to study relationship of methyl glyoxal levels (oxidative stress) and loss of glomerular podocytes.
- Andrew Levey, M.D., New England Medical Center. Provided serum creatinine and GFR data to validate MDRD GFR prediction equation in the DRDS population.

**5. List of Publications and Presentations (full citations, also note manuscripts in progress)**

See Appendix A

## Appendix A. DRDS Publications

Myers BD, Nelson RG, Williams GW, Bennett PH, Hardy SA, Berg RL, Loon N, Knowler WC, Mitch WE. Glomerular function in Pima Indians with noninsulin-dependent diabetes mellitus of recent onset. *J Clin Invest* 1991; 88:524-530

Nelson RG, for the Diabetic Renal Disease Study Group. Renal function in non-insulin-dependent diabetes mellitus: purposes and design of the Diabetic Renal Disease Study. *Acta Diabetol* 1991; 28:143-150

Nelson RG, Knowler WC, Pettitt DJ, Bennett PH. Histoire naturelle de la néphropathie dans le diabète non insulino-dépendant: leçons tirées des Indiens Pima. In: *Actualités Néphrologiques* Jean Hamburger, Hôpital Necker Paris: Flammarion, 1994:143-154

Nelson RG, Knowler WC, Pettitt DJ, Bennett PH. The natural history of renal disease in non-insulin-dependent diabetes mellitus: lessons from the Pima Indians. *Adv Nephrol Necker Hosp* 1995; 24:145-156

Myers BD, Nelson RG, Tan M, Beck GJ, Bennett PH, Knowler WC, Blouch K, Mitch WE. Progression of overt nephropathy in non-insulin-dependent diabetes. *Kidney Int* 1995; 47:1781-1789

Nelson RG, Bennett PH, Beck GJ, Tan M, Knowler WC, Mitch WE, Hirschman GH, Myers BD, for the Diabetic Renal Disease Study Group. Development and progression of renal disease in Pima Indians with non-insulin-dependent diabetes mellitus. *N Engl J Med* 1996; 335:1636-1642

Pagtalunan ME, Miller PL, Jumping-Eagle S, Nelson RG, Myers BD, Rennke HG, Coplon NS, Sun L, Meyer TW. Podocyte loss and progressive glomerular injury in type II diabetes. *J Clin Invest* 1997; 99:342-348

Nelson RG, Meyer TW, Myers BD, Bennett PH. Clinical and pathological course of renal disease in NIDDM: the Pima Indian experience. *Semin Nephrol* 1997; 17:124-131

Nelson RG, Meyer TW, Myers BD, Bennett PH. Course of renal disease in Pima Indians with non-insulin-dependent diabetes mellitus. *Kidney Int* 1997; 63:S-45-S-48

Nelson RG, Tan M, Beck GJ, Bennett PH, Knowler WC, Mitch WE, Blouch K, Myers BD. Changing glomerular filtration with progression from impaired glucose tolerance to Type II diabetes mellitus. *Diabetologia* 1999; 42:90-93

Meyer TW, Bennett PH, Nelson RG. Podocyte number predicts long-term urinary albumin excretion in Pima Indians with Type II diabetes and microalbuminuria. *Diabetologia* 1999; 42:1341-1344

Lemley KV, Abdullah I, Myers BD, Meyer TW, Blouch K, Smith WE, Bennett PH, Nelson RG. Evolution of incipient nephropathy in type 2 diabetes mellitus. *Kidney Int* 2000; 58:1228-1237

Lemley KV, Blouch K, Abdullah I, Boothroyd D, Bennett PH, Meyer TW, Myers BD, Nelson RG. Glomerular permselectivity at the onset of nephropathy in type 2 diabetes mellitus. *J Am Soc Nephrol* 2000; 11:2095-2105

**Appendix A**