4. SCREENING BASELINE VISIT

4.1 INTRODUCTION

Consistent with the philosophy and design of a large study, screening activities performed during the Baseline Visits have been kept streamlined. Screening activities may be performed in whatever sequence best fits the needs of the site consistent with the safety of the proband/relative and the goals of the study.

The purpose of the Baseline Visit is to:

a) Establish rapport with the proband/relative and promote further interest in the Study.

b) Fully inform the proband/relative of the goals and requirements of the study.

c) Obtain informed consent for the study.

d) Screen for exclusion criteria.

e) Confirm eligibility and willingness to participate.

a) Collect baseline measurements and blood and urine specimens for eligibility. Collect genetics specimens.

4.1 PREPARATION

Before the Baseline Visit, the study coordinator will carry out the following preparatory activities:

1) Phone the participant and complete the appropriate section of the Checklist for Proband/Relatives (Form 200GK).

2) Ask the participant to bring in their medication for hypertension, kidney disease, diabetes, and elevated lipids.

4.2 RECEPTION

Greet participants by name, welcome and thank them for attending Visit. For example:

"Hello, Mr./Ms. (individual's name). My name is _____. Thank you for coming down to hear more about the GoKinD trial. Were you able to find us okay?"

4.3 REVIEW PURPOSE OF STUDY AND STUDY REQUIREMENTS

Escort participants to a quiet, pleasant and private seating area to read the GoKinD brochure and review the purpose of the study and study requirements. If the patient is eligible, give a copy of the GoKinD brochure to the participant and indicate that it is for the participant to take home and share with his/her family.

The general information to be discussed with participants who appear eligible is summarized in the following sample script:

> "GoKinD is a research program arranged by the Juvenile Diabetes Research Foundation to study the genetic basis of diabetic nephropathy and to collect a repository of DNA and clinical information from a large number of patients with type 1 diabetes. About 4,300 men and women in the United States and Canada will be joining the study.
>
> At today's visit, we'll find out if you are able to join GoKinD and if you want to do so. Today I'll measure your blood pressure, collect blood and urine samples, and record some of your past and current medical background. This is good medical practice to evaluate your current health status."

4.4 INFORMED CONSENT

Informed consent must be obtained at the beginning of the Screening Baseline Visit. However, failure to provide informed consent is one of the exclusion criteria for the study. The Baseline Visit can be considered over as soon as the participant refuses to sign the informed consent form.

Answer any questions the participant may have, review the consent form with him/her and obtain his/her signature. Points to emphasize in obtaining informed consent are that:

1) Participation is completely voluntary.

2) Participants may discontinue participating at any time.

3) Information provided for the study is confidential except as stated in the consent form. All data collected will be used only as summary reports and the participant's data will be kept totally confidential.

4) Although the results of standard medical tests will be given to the participant, study results from his/her DNA will not.

Sign the consent form as a witness. Be sure to get the investigator's signature before filing each consent form. Give a copy to the participant. Guidelines for obtaining informed consent are given in Chapter 3 of the GoKinD Manual of Operations.

4.5 REVIEW OF EXCLUSION CRITERIA

Review all exclusions after clarifying any issues or unknowns with the patient. See Chapter 2 of the GoKinD manual for eligibility and exclusion criteria.

4.6 BASELINE VISIT

1) Complete the Medical History and Physical Examination Form (Form 210GK) to the extent possible, assessing medical history and family history of diabetic nephropathy.

2) Complete the Current Medication Form (Form 211GK). Table 4.1 contains the names of commonly used drugs for various conditions.

At the Baseline Visit, all activities should be carried out in a friendly, professional manner in an effort to provide accurate information in response to spoken and, possibly, unspoken questions; establish rapport with the participant; and provide enthusiasm about the study.

4.7 PHYSICAL MEASURES

4.8.1 Blood Pressure

For prospective participants eligible for the study, systolic and diastolic blood pressure need to be obtained. These should be obtained in a sitting position.

Sitting Blood Pressure: The participant should be seated comfortably in a quiet room for five minutes. The arm muscles should be relaxed and the forearm supported. The arm should be at the heart level when the measurement is done.

Measurement: A mercury sphygmomanometer should be used and a cuff size selected according to the circumference of the arm (AC): ordinary cuff up to AC of 33 cm, large cuff for AC of 33 -41 cm, and thigh cuff for AC above 41 cm. The cuff is then applied evenly and firmly to the exposed upper arm. If possible, the right arm should be selected and the same side used in the future. The cuff should be inflated to about 30 mm Hg above expected systolic blood pressure. The cuff is then slowly deflated, about 2-3 mm Hg per beat, during which time the Korotkoff sounds are listened to through a stethoscope placed over the brachial artery. The pressure at which the sounds are first heard is the systolic pressure. The diastolic pressure is defined as the pressure at which the sounds disappear. The systolic and diastolic blood pressures should be measured at least twice over a period of at least five minutes and the second value is to be recorded on the GoKinD Medical History and Physical Examination Form (Form 210GK).

Blood pressure should be recorded to the nearest 2 mm Hg. In the absence of digit preference, readings ending in 0, 2, 4, 6, and 8 will be equally expected.

A repeat blood pressure should be taken 5 minutes after the first reading.

4.8.2 Hypertension

Hypertension is defined as systolic blood pressure (SBP) of 140 mm HG or greater, diastolic blood pressure (DBP) of 90 mm HG or greater or taking antihypertensive medication.[1] Table 4.2 provides a classification of blood pressure for adults (aged 18 years and older). These criteria are for individuals who are not taking antihypertensive medication and who have no acute illness. This classification is based on the average of two or more blood pressure readings taken in accordance with the following recommendations at each of two or more visits after an initial screening visit. When the SBP and DBP fall into different categories, the higher category should be selected to classify the individual's blood pressure.

4.8.3 Guidelines for Measuring Weight, Stature, and Circumference

All measurements should be taken to the nearest unit as allowed on the Medical History and Physical Examination Form (Form 210GK). After each measurement is taken, its value is recorded in the appropriate space. If a recorder is present, the recorder should repeat the value that was called aloud by the examiner.

All measurements will be done twice. If the two measures differ by more than the recommended amount, two additional measures are taken and recorded. **NOTE:** A set of measurements is taken and then repeated. Do not take the same measure twice in a row.

Recommended limits for difference between measures are:

Weight:	Within 200 grams, or 0.2 kg
Stature:	Within 1.0 cm
Waist Circumference:	Within 0.5 cm

4.8.3.1 Weight

To minimize variability in the weight measurement, patients should be requested to wear lightweight clothing and to remove shoes before the weight is taken. Other steps to consider to reduce variability are: 1) Ask the patient to empty his/her bladder before weight is taken; 2) encourage the patient to eat relatively the same volume of food at meals that precede an appointment.

Ask the patient to stand in the center of the scale and not touch or support themselves on anything. The patient should stand so that his/her weight is equally distributed on both feet. Two measures will be taken. The patient should step off the scale between measurements and the scale should be reset to zero. Repeated measurements should agree within 200 grams. If they do not, two more measures should be taken and recorded. Check the scale at "0" to be sure it balances each morning. The scale should be left with the weights at zero when not in use.

4.8.3.2 Stature

Ask the patient to stand with his/her back against the stadiometer, with the heels together, and both heels touching or a minimal distance from the wall (no greater than the depth of the stadiometer). The back (scapula) and buttocks should also be in contact with the board.

Occasionally it will be impossible to position the patient's heels, buttocks, scapula, and the back of the head in one vertical plane against the board and still have him/her stand naturally and comfortably. His/her back may be arched due to the large size of the buttocks. If this occurs, move the patient forward and have only the buttocks and heels in contact with the board.

Be sure that in this position the patient maintains erect posture, that is, no slouching. Heels should be together and the medial borders of the feet at an angle of about 45 degrees, with the weight equally distributed and the head in the "Frankfort Horizontal Plane". This requires the subject to look straight ahead. A line running from the opening of the ear to the corner of the eye should be parallel to the floor. The movable headboard is brought down firmly on top of the head. It may be necessary, upon occasion, to remove or alter the hairdress of some of the patients. This may be necessary for the headboard to maintain a right angle and to make contact with the top of the scalp.

Have the patient inhale deeply, again not altering position by, for example, raising the heels off the floor. Stature is measured just before the patient exhales. The measurement is recorded to the nearest millimeter and agreement between measurements must be within 1.0 cm.

4.8.3.3 Circumference Measurements

Measurement of waist circumferences will require two individuals. The measurements will be recorded on the Medical History and Physical Examination Form (Form 210GK). Two different waist references are to be used to provide maximum comparability to data published by other trials. Whenever possible, all requested data should be provided, even for extremely obese individuals.

Insulin can cause both atrophy and hypertrophy of fat. Lipoatrophy is reported to be the more common of the two and is usually seen in children and young women. The areas affected show circumscribed depressions from the deep dermal and subcutaneous loss of fat. Insulin hypertrophy is less common and clinically resembles lipomas. It may be important for the analysis of the waist-to-hip ratio to know the extent of the prevalence of these two conditions. The assessment of the presence of lipohypertrophy or lipoatrophy affecting these measurements will be made most appropriately by a nurse or physician that has some experience with these conditions.

4.8.3.3.1 Natural Waist

The patient wears little clothing so that the tape may be correctly positioned. The measurements should not be made over clothing. If clothing must be worn, subjects should undress to light underwear and wear only a cloth or paper smock during the measurements. The subject stands erect with the abdomen relaxed, the arms at the sides and the feet together. The measurer faces the subject and places an inelastic tape around the subject, in a horizontal plane, at the level of the natural waist, which is the narrowest part of the torso, as seen from the rear. An assistant is needed to help position the tape in a horizontal plane. In some obese subjects, it may be difficult to identify a waist narrowing. In such cases, the smallest horizontal circumference should be measured in the area between the ribs and iliac crest. The measurement should be taken at the end of a normal expiration, without the tape compressing

the skin. It is recorded to the nearest 0.5 cm. If the patient is measured with a gown, it should be pulled tight so that landmarks are obvious.

4.8.3.3.2 Iliac Crest Waist

The patient is in a standing position. The patient is asked to hold up his/her gown. The examiner stands behind the patient and palpates the hip area for the right iliac crest. The examiner marks a horizontal line at the high point of the iliac crest and then crosses the line to indicate the midaxillary line of the body. The pants and underclothing of the patient must be lowered slightly for the examiner to palpate directly on the hip area for the iliac crest. The examiner then stands on the patient's right side and places the measuring tape around the trunk in a horizontal plane at the level marked on the right side of the trunk. The recorder walks around the patient to make sure that the tape is parallel to the floor and that the tape is snug, but does not compress the skin. The measurement is made at minimal respiration to the nearest 0.5 cm. If the patients are measured with a gown, it should be pulled tight so that landmarks are obvious.

4.8 BASELINE BLOOD, URINE, AND DNA SAMPLES

Blood, urine, and DNA samples drawn for central assay will be collected and shipped to the Central Biochemistry Laboratory. See Chapter 8 for details.

4.9 SCREENING FOR PERSISTENT PROTEINURIA

Investigators are provided with 10-mL plastic vials for urine sampling. A first sample will be obtained from each patient, and shipped to the CBL. If albumin/mg of urine creatinine is at least 300 μg in the absence of leukocyturia or hematuria (detected by Multistix text strips), the investigator will be asked to obtain and send a second urine sample from the patient. If albumin/mg of urine creatinine is at least 300 μg in the second sample, and the other selection criteria are as required by the protocol, the patient is declared eligible. If the second sample is less than 300 μg, a third sample can be sent to the CBL.

When using historical data for the first urine screen only, the following tests may also be used timed urine greater than 208 μg/min (300 mg/24 hr), overnight collection greater than 200 μg/min, or total urinary protein greater than 500 mg/24 hr. **The actual value of the historical ACR measurement should be maintained in the GoKinD patient file at the clinic.**

4.10 SCREENING FOR PERSISTENT NORMOALBUMINURIA

Persistent normoalbuminuria is defined as at least 2 out of 3 ACR measurements (at least 1 month apart) in random urine specimens being less than 20 μg of albumin/mg of creatinine. If 3 ACR measurements are needed, the highest must also be less than 40 μg of albumin/mg of creatinine.

Use of historical information for the initial urine screen is allowed if the last ACR in the past 12 months is less than 40 μg of albumin/mg of creatinine. If historical information is used, it is considered as the first urine screen. If the value of the historical screen is 20 ≤ ACR1 < 40, then ACR2 and ACR3 must be less than 20 μg of albumin/mg of creatinine. When using historical data for the first urine screen only, the following tests may also be used timed urine less than 30 μg/min (< 40 mg/24 hr), overnight collection less than 30 μg/min, total urinary protein less than 230 mg/24 hr, or dipstick negative-trace. **The actual value of the historical ACR measurement should be maintained in the GoKinD patient file at the clinic.**

4.11 INFORMATION FEEDBACK

All results of the centrally assayed assessments will be returned to the GoKinD clinic. It is the responsibility of the GoKinD clinic to forward the information to the proband/relative and his/her physician. More detailed follow-up, to include implications and recommended follow-up for abnormal test values will be provided to them and his/her physician. No information about the results of DNA genotyping will be released to them, their physician, or to the GoKinD clinic. The procedures and formats for returning the information to the clinic will be uniformly followed (see Figures 4.1, 4.2, 4.3, and 4.4).

References

1. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Archives of Internal Medicine 157: 2413-2446, 1997.

TABLE 4.1
LIST OF MEDICATIONS

ACE Inhibitors	Psych-(cont.)	Hormone	Anti-Hypertensive(cont.)	Anti-Hypertensive(cont.)
Accupril (Quinapril)	Pamelor	Cycrin	Cardizem	Nadolol
Aceon (Perindopril)	Paxil	Demulen	Cardizem CD	Nicardipine
Altace (Ramipril)	Prozac	Estrace	Cardura	Nifedipin
Capoten (Captopril)	Resroril	Estraderm	Carteolol	Nisoldipine
Capozide (Captopril+HCT)	Risperdal	Estrogen	Carvedilol	Normadyne
Lexxel (Elanapril+Felodipine)	Ritaliln	Premarin	Catapres	Norvasc
Lotensin (Benazepril)	Serzone	Prempro	Chlorthalidone	Penbutolol
Lotensin HCT (Benazepril+HCT)	Trazadone	Progesteron	Clonidine	Pindolol
Lotrel (Amlodipine+Benazepril)	Valium	Provera	Corgard	Plendil
Mavik (Trandolapril)	Xanax	Triphazal	Dilacor	Polythiazide
Monopril (Fosinopril)	Zoloft		Diltiazem	Prazosin
Prinivil (Lisinopril)		**Lipid Lowering**	Diltiazem SR	Procardia
Prinizide (Lisinopril+HCT)	Gastric	Gemfribrozil	Diovan	Procardia XL
Tarka (Trandolapril+Verapimil)	Alu-Cap	Lescol	Diuril	Propranolol
Uniretic (Moexipril+HCT)	Axid	Lipitor	Doxazosin	Propranolol HCL
Univasc (Moexipril)	Bethanechol chloride	Lopid	Dyazide	Spironolactone
Vaseretic (Elanapril)	Docusate	Mevacor	Dynacirc	Tenoretic
Vasotec (Elanapril)	Duphalac	Niacin(Vitamin B3)	Enalaprilat	Tenormin
Zestoretic (Lisinopril+HCT)	Lo-Trel	Pravastatin	Esmolol	Terazosin
Zestril (Lisinopril)	Pepcid	Provachol	Ethacrinate	Tiazac
	Prevacid	Zocor	Felodidine	Timolol
Diuretics	Prilosec		Guanabenz	Toprol
Bumex	Propulsid	**Thyroid**	Guanadrel	Torsemide
Demadex	Reglan	L thyroxine	Guanethidine	Tranchlormathiazide
Furosemide	Zantac	Levothroid	HCTZ	Verapamil
Lasix		Levoxine	Hytrin	Verelan
Triamterene	Heart	Levoxyl	Indapamide	Visken
Triamterene HCTZ	Adalat	Synthroid	Inderal	Zaroxolyn
	Digoxin		Isordil	Ziac
Psych	Imdur	**Anti-Hypertensive**	Isradipine	
Ambien	Minitran	Acetabutolol	Labetalol	**Angiotensin II Receptor Blockers**
Amitriptyline	Nitro-Dur	Aldactone	Lanoxin	Actacand (Candesartan Cilexetil)
Antivert	Nitroglycerin	Aldomet	Lopressor	Avapro (Irbesartan)
Ativan	Nitrostat	Amiloride	Methylchlorthiazide	Avalide (Irbesartan)
Buspar	Norpace	Amlodipine	Methildopa	Cozaar (Losartan Potassium)
Dexedrine	Persantine	Atenolol	Metolazone	Diovan (Valsartan)
Doxepin	Quinidex	Bendoflumethiazide	Metoprolol	Diovan HCT (Valsartan)
Haldol	Quinidine gluconate	Betaxolol	Mibefradil	Hyzaar (Losartan Potassium)
Imipramine		Bisprolol	Midamor	Micardis (Telmisartan)
Lithium		Bretylium	Minipress	
MS Contin		Calan	Minoxidil	

TABLE 4.2

CLASSIFICATION OF BLOOD PRESSURE FOR ADULTS AGED 18 YEARS AND OLDER[1]

Category	Blood Pressure (mm Hg)		
	Systolic		Diastolic
Optimal	<120	and	<80
Normal	<130	and	<85
High-normal	130-139	or	85-89
Hypertension			
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	≥180	or	N≥110

References

1. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Archives of Internal Medicine 157: 2413-2446, 1997.

FIGURE 4.1

Dr. Robert Doe
Acme Medical Assoc.
1 Main St.
Boston, MA 00000

Sept. 28, 2000

Dear Dr. Doe,

On 9/18/00, a patient of yours, John Doe (DOB 11/26/25), participated in the ***Juvenile Diabetes Research Foundation GoKind Study***, a collaborative effort to investigate the factors involved in diabetic renal complications. As requested, we are forwarding the results obtained from an examination carried out by a patient recruiter from the Joslin Diabetes Center. All samples were processed by our Central Biochemistry Laboratory at the University of Minnesota and validated at our Data Coordinating Center at the George Washington University Biostatistics Center.

If you have any questions regarding these results, please feel free to contact me at (617) 264-2739, or via e-mail at andrea.segal@Joslin.harvard.edu.

Sincerely,

Andrea Segal
Project Manager, Joslin Diabetes Center

FIGURE 4.2

Date: 10/22/01
Clinic: 135: GWU CLINIC
CBL Site: 135: GWU CLINIC
Initials: GDM
Barcode: G7500
Specimen Date: 10/06/01
Screen Number: S2

Study ID#: 1350500503

Central Biochemistry Laboratory: University of Minnesota
Patient Recruitment Center: GWU

Urinary Albumin = 1300 mg/L
Urinary Albumin2 = 510 mg/L
Urinary Albumin3 = mg/L

Urinary Creatinine = 42 mg/dL
Urinary Creatinine2 = 16 mg/dL
Urinary Creatinine3 = mg/dL

Albumin/Creatinine Ratio = 3095.2 ug/mg
Albumin/Creatinine Ratio2 = 3187.5 ug/mg
Albumin/Creatinine Ratio3 = ug/mg

Total Cholesterol = 195 mg/dL

HDL = 50 mg/dL

Glycohemoglobin A1C = 9.5%

Serum Creatinine = 4.7 mg/dL

Serum Cystatin = 2.86

FIGURE 4.3

Family ID #: 1350500503 Date of Today: 04 /02 /2002
Date of Birth: 04 /03 /1955 Initials: GDM
Age at Screening: 46 Year
(must be between 18-54)

Diagnosed Before 31: YES
Insulin Taken Within 1 Year of Diagnosis: YES
PATIENT HAS TYPE 1 DIABETES: YES
Duration of Type 1 Diabetes: 26 YEAR

Presence of Diabetic Nephropathy:
- Duration of T1D >=10 Years: YES
- ESRD:
  - Kidney Transplant: NO
  - Kidney/Pancreas Transplant: NA
  - Dialysis: NO
- Persistent Proteinuria:
  - Historic ACR Positive without an ACR value:

	ACR RATIO VALUE
USCR1:	3095.2 ug/mg
USCR2:	3187.5 ug/mg
USCR3:	_____._ ug/mg

** 2 out of 3 values must be positive or greater than 300 ug albumin/mg urine creatinine

PATIENT IS ELIGIBLE AS A CASE: YES

Absence of Diabetic Nephropathy:
- Duration of T1D >= 15 years:
- Treated with ACE inhibitor:
- Using antihypertensives:
- Persistent Normoalbuminuria:
  - Historic ACR Positive without an ACR value:

	ACR RATIO VALUE
USCR1:	_____._ ug/mg
USCR2:	_____._ ug/mg
USCR3:	_____._ ug/mg

** 2 out of 3 values must be less than 20 ug albumin/mg urine creatinine and if a third is needed the highest value must also be less than 40 ug albumin/mg urine creatinine.

PATIENT IS ELIGIBLE AS A CONTROL: NO

PATIENT IS ELIGIBLE AS A MICROALBIMINURIC: NO

FIGURE 4.4

GoKinD Guidelines for Interpreting Laboratory Data

Albumin/Creatinine Ratio (ACR)
If ACR <20 ug/mg, this result is in the normal range.

If ACR elevated (20-300 ug/mg), this is considered out of the normal range. This result must be re-checked and confirmed by your doctor. Please contact your physician to discuss this result.

If ACR >300 ug/mg, this result is proteinuric. This result must be re-checked and confirmed by your doctor. Please contact your physician to discuss this result.

Hemoglobin A1c (HbA1c)
Normal range is 5.0 ± 1.0 ($\bar{X} \pm 2$ St. Dev.)[1]

A value under 6.0% is considered normal.

If a parent is not diabetic with an abnormal A1c level (>6.0%), it is important for you to follow-up this elevated result with your physician.

Serum Creatinine (mg/dL)
If serum creatinine <1.5 mg/dL, the level is within normal range for men.
If serum creatinine <1.3 mg/dL, the level is within the normal range for women.

If serum creatinine $\geq$1.5 mg/dL, the result is out of the normal range for men. Please follow-up this result with your doctor.

If serum creatinine $\geq$1.3 mg/dL, the result is out of the normal range for women. Please follow-up this result with your doctor.

Serum Cystatin
Serum cystatin is considered experimental data, and we do not yet have a way to interpret the value. It is not necessary to release this value to the study participants or their physicians.

Total Cholesterol and HDL Cholesterol (mg/dL)
If total cholesterol <200 and HDL cholesterol >40, total cholesterol and HDL cholesterol levels are within normal ranges.

If total cholesterol >200, your cholesterol level is considered out of the normal range. Please follow-up your cholesterol level with your doctor.

If HDL cholesterol <40, your HDL level is below the normal range. Please follow-up your cholesterol with your doctor.

[1]The DCCT Research Group. Feasibility of Centralized Measurements of Glycated Hemoglobin in the Diabetes Control and Complications Trial: A Multicenter Study. Clinical Chemistry 1987; 33:2267-71.