SUPPLEMENTARY DATA

ONLINE_SUPPLEMENTAL_MATERIAL-AFAM_V3_CX01.DOCX

ONLINE SUPPLEMENTAL MATERIAL

Type 1 diabetes risk in African-ancestry participants and utility of an ancestry-specific genetic risk score

Suna Onengut-Gumuscu*[1,2], Wei-Min Chen*[1,2], Catherine C. Robertson[1], Jessica K. Bonnie[1], Emily Farber[1], Zhennan Zhu[1], Jorge R. Oksenberg[3], Steven R. Brant[4], S. Louis Bridges Jr[5], Jeffrey C. Edberg[5], Robert P. Kimberly[5], Peter K. Gregersen[6], Marian J. Rewers[7], Andrea K. Steck[7], Mary H. Black[8], Dana Dabelea[9], Catherine Pihoker[10], Mark A. Atkinson[11], Lynne E. Wagenknecht[12], Jasmin Divers[13], Ronny A. Bell[12], SEARCH for Diabetes in Youth[*], Type 1 Diabetes Genetics Consortium[*], Henry A. Erlich[14], Patrick Concannon[1]#, and Stephen S. Rich[1,2]#

* These authors contributed equally

# These authors contributed equally

[*] Authors listed in Supplementary Information (Supplementary Note)

SUPPLEMENTARY DATA

INDEX:

SUPPLEMENTARY TABLES:

SUPPLEMENTARY FIGURE:

Complete list of the members of the Type 1 Diabetes Genetics Consortium and SEARCH for Diabetes in Youth Study

SUPPLEMENTARY DATA

SUPPLEMENTARY TABLES:

Supplementary Table 1. Sample summary

	Total	**Case**			**Control**	
Cohort*	**Number of participants (n)**	**n**	**Male n (%)**	**Age at diagnosis†**	**n**	**Male n (%)**
BDC	101	59	24 (40.7)	10 (2-22) ‡	42	17 (40.5)
CLEAR	368	-	-	-	368	105 (28.5)
GoKinD	41	41	17 (41.5)	13 (5-30)	-	-
NYCP	801	-	-	-	801	173 (21.6)
SEARCH	255	255	112 (43.9)	9 (0-19)	-	-
T1DGC	1262	666	290 (43.5)	9 (1-40) §	596	160 (26.9)
UAB	659	-	-	-	659	176 (26.7)
UCSF	462	-	-	-	462	160 (34.6)
Overall	3949	1021	449	9 (0-40)	2928	785

* Description of cohort abbreviations: BDC = Barbara Davis Center (18); CLEAR = Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis (19); GoKinD = Genetics of Kidneys in Diabetes (17); NYCP = New York Control Population (20); SEARCH = SEARCH for Diabetes in Youth study (16); T1DGC = Type 1 Diabetes Genetics Consortium (15); UAB = University of Alabama at Birmingham (21); UCSF = University of California, San Francisco (22).

† Age at diagnosis, data are presented as median age in years (range).

‡ Age at diagnosis is missing for 17 participants

§ Age at diagnosis is missing for 1 participant

SUPPLEMENTARY DATA

Supplementary Table 2. Association results of type 1 diabetes associated 99% credible SNPs in African-ancestry dataset (Uploaded as separate excel table,

https://virginia.box.com/s/fqqig93jwkuj946hs44u8hqjinivp389)

Supplementary Table 3. HLA imputation accuracy

HLA Locus	**2-digit accuracy**	**4-digit accuracy**
A	0.964	0.916
B	0.944	0.855
C	0.998	0.946
DPA1	0.996	0.959
DPB1	0.934	0.933
DQA1	0.991	0.99
DQB1	0.996	0.973
DRB1	0.945	0.882

(indicate that 2-digit = 1 field; 4-digit = 2 fields)

SUPPLEMENTARY DATA

Supplementary Table 4. Quartiles for the sum of dosages across alleles by HLA locus

Locus	**q2.5**	**q50**	**q97.5.**
A	2	2	2.39
B	1.89	2	2.17
C	2	2	2.18
DQA1	2	2	2
DQB1	2	2	2
DRB1	1.91	2	2.06
DPA1	2	2	2.01
DPB1	1.94	2	2.06
Combined	1.98	2	2.06

Supplementary Table 5. Associations of type 1 diabetes in African-ancestry populations with classical HLA alleles (Uploaded as separate excel table, https://virginia.box.com/s/9nmreysywe8pfrhlfr5v533xjfzzph08)

SUPPLEMENTARY DATA

Supplementary Table 6. Fifteen HLA class II haplotypes are independently associated with T1D in African Americans

DRB1	**DQA1**	**DQB1**	**OR**	**P**
03:01	05:01	02:01	3.74	4.7×10^{-49}
09:01	03:01	02:01	5.75	2.5×10^{-34}
04:05	03:01	03:02	7.66	9.6×10^{-32}
04:01	03:01	03:02	6.66	4.1×10^{-26}
07:01	03:01	02:01	4.69	6.4×10^{-15}
04:04	03:01	03:02	3.73	4.5×10^{-09}
15:03	01:02	06:02	0.21	5.6×10^{-15}
03:02	04:01	04:02	0.2	6.5×10^{-10}
15:01	01:02	06:02	0.08	1.5×10^{-06}
11:01	01:02	06:02	0.14	6.0×10^{-07}
11:01	05:01	03:01	0.25	3.1×10^{-08}
08:04	04:01	03:01	0.35	1.0×10^{-04}
10:01	01:01	05:01	0.34	8.3×10^{-04}
13:01	01:03	06:03	0.48	9.9×10^{-04}
14:01	01:01	05:03	0.17	4.8×10^{-03}

Odds ratios (OR) and *P*-values generated by multivariable logistic regression of T1D risk, including 2 principal components, sex, and all 15 alleles as independent variables. Significance evaluated at a $P<1.5 \times 10^{-3}$ threshold (Bonferroni correction at family-wise error rate of 0.05 given ≤33 haplotypes tested at each round of conditional analysis).

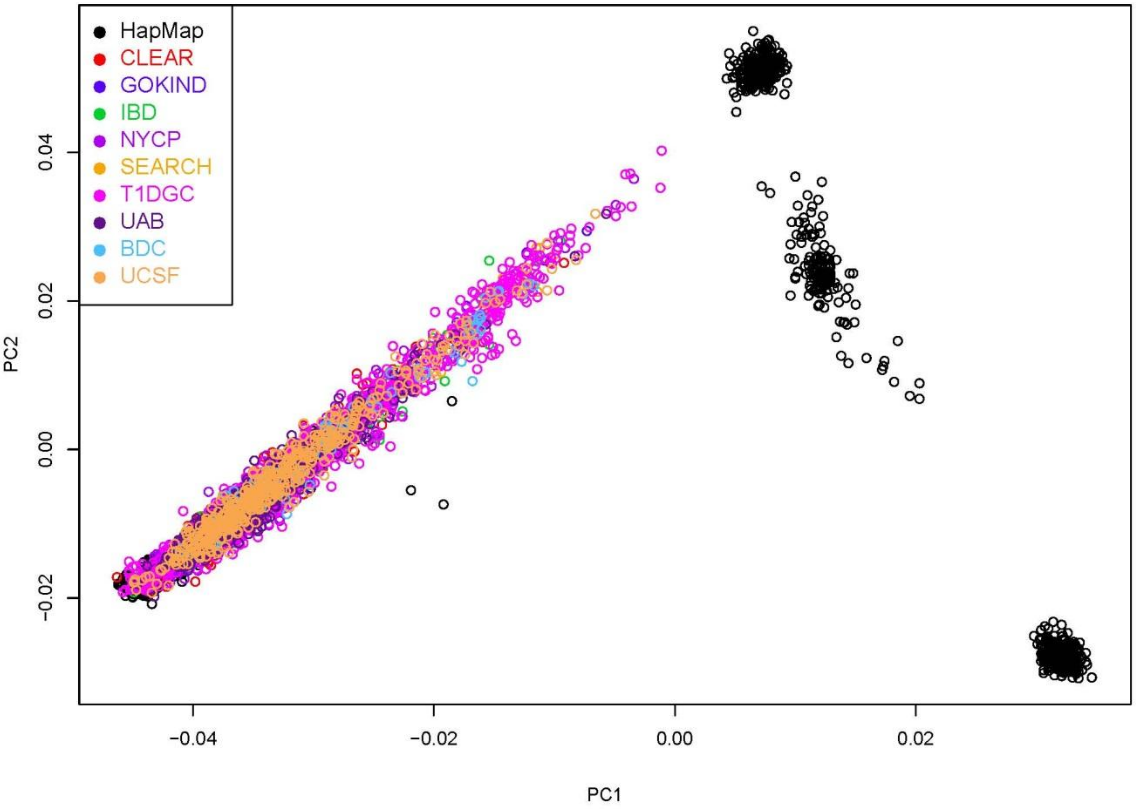
Supplementary Table 7 – Type 1 diabetes-associated SNPs included in the African-ancestry genetic risk score (GRS) with weights; the "effect allele" is the risk increasing allele on the positive strand

SNP	**Chr**	**Position (bp)**	**Effect Allele**	**Effect Allele Frequency**	**Odds Ratio (OR)**	**Weight**
rs34303755	6	32450613	C	0.216	2.94	1.079
rs34850435	6	32583299	T	0.345	2.31	0.839
rs9271594	6	32591213	G	0.095	6.06	1.801
rs2187668	6	32605884	T	0.076	3.93	1.367
rs9273363	6	32626272	A	0.131	5.48	1.702
rs689	11	2182224	T	0.265	1.50	0.403
rs2290400	17	38066240	C	0.459	1.34	0.295

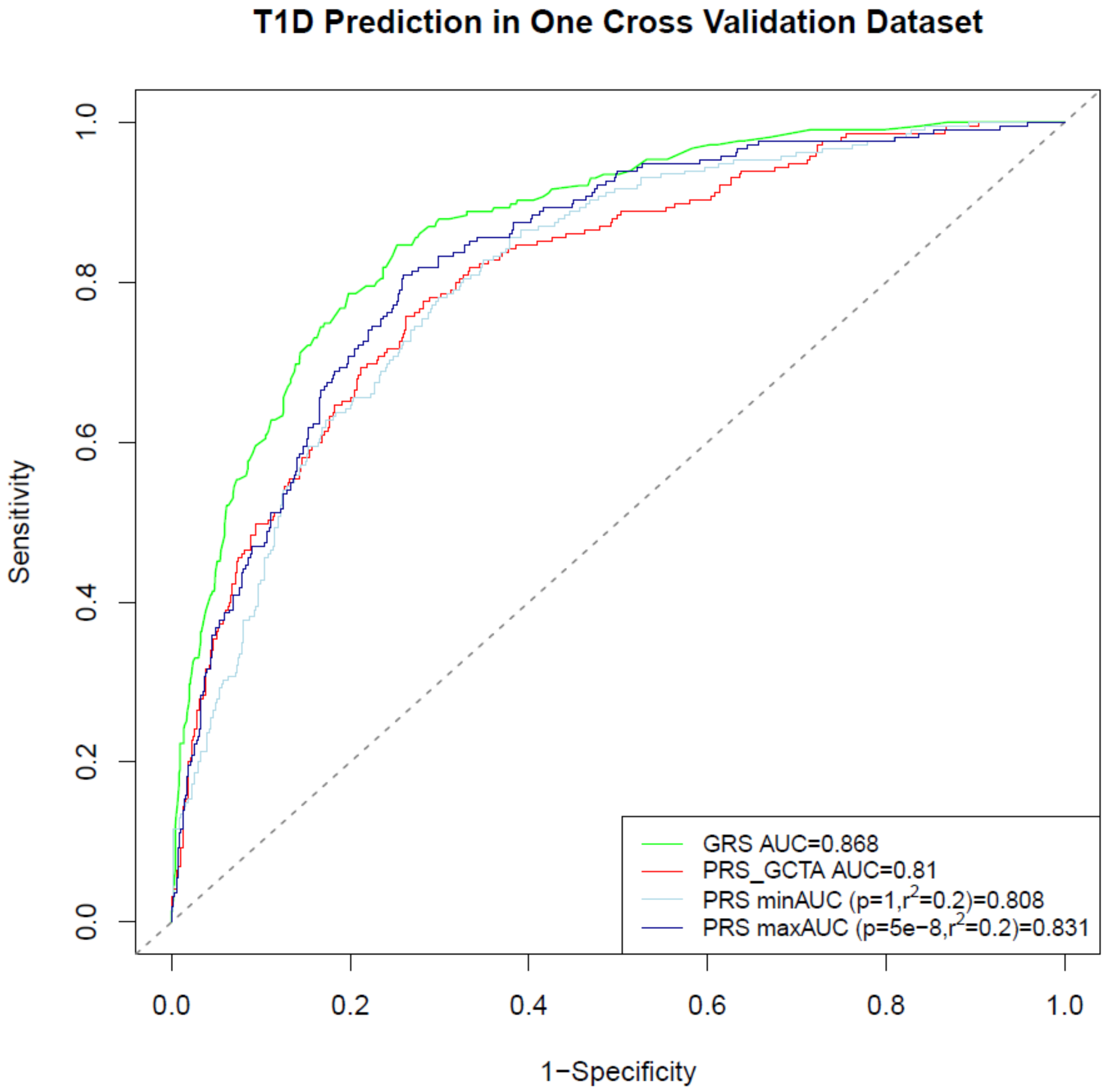
SUPPLEMENTARY DATA

SUPPLEMENTARY FIGURE:

Supplementary Figure 1. Principal component analysis (PCA) in African-ancestry type 1 diabetes cases and controls projected on HapMap 3 coordinates.



Supplementary Figure 2. Performance of different type 1 diabetes prediction models



SUPPLEMENTARY DATA

Members of the Type 1 Diabetes Genetics Consortium (T1DGC):

Asia-Pacific Network: Karen Alcantara, Tracey Baskerville, Nines Bautista, Eesh Bhatia, Francois Bonnici, Thomas Brodnicki, Pik To Cheung, Peter Colman, Andrew Cotterill, Jenny Couper, Kim Donaghue, Denise Li-Meng Goh, Len Harrison, Hiroshi Ikegami, Tim Jones, Khalid Abdul Kadir, Nor Azmi Kamaruddin, Uma Kanga, Alok Kanungo, Gurvinder Kaur, Tania Kelly, Yann-Jinn Lee, Margaret Lloyd, Kah Yin Loke, Amanda Loth, Narinder Mehra, Tony Merriman, Grant Morahan, Namid Munkhtuvshin, Araceli Panelo, Fraser Pirie, Niru Ratnam, C. B. Sanjeevi, Sandeep Sreedharan, Brian Tait, Allison Thomas, Jinny Willis, Sang Yanmei.

European Network: Francisco J. Ampudia-Blasco, Jesus Argente, Magdalena Avbelj, Gulja Babadjanova, Klaus Badenhoop, Lubomir Barak, Christos Bartsocas, Tadej Battelino, Emilia Belda, Polly Bingley, Bernhard O. Boehm, Ezio Bonifacio, Fatima Bosch, Eulalia Brugues, Raffaella Buzzetti, Joyce Carlson, Luis Castano, Anna Casu, Ondrej Cinek, Alberto de Leiva, Virginia Ruiz Esquide, Ana Fagulha, Marta Hernandez Garcia, Per-Henrik Groop, Cristian Guja, Alona Hamou, Erifili Hatziagelaki, Dan Headon, Simon Heath, Kaire Heilman, Robert Hermann, Nora Hosszufalusi, Lorenzo Iughetti, Cecile Julier, Ida Kinalska, Ingrid Kockum, Kalinka Koprivarova, Adam Kretowski, Dora Krikovszky, Nebojsa Lalic, Nicole Lambracht, Merce Lara, Mark Lathrop, Katharina Laubner, Ake Lernmark, Claire Levy-Marchal, Johnny Ludvigsson, Mara Marga, Antonio Martinez, Didac Mauricio, Nina Meier, Jorn Nerup, Antanas Norkus, Anna Okruszko, Carla Paganin, Xavier Palomer, Teresa Pedro, Moshe Phillip, Valdis Pirags, Flemming Pociot, Galina Popova, Paolo Pozzilli, Jean-Francois Prud’Homme, Bart O. Roep, Ute Christine Rogner, Silke Rosinger, Ana Maria Varela Sande, Ilhan Satman, Edith Schober, Jochen Seufert, Jan Skrha, Gyula Soltesz, Giatgen Spinas, Juraj Stanik, Tanya Szendeffy, Erik Thorsby, Vallo Tillmann, Dag Undlien, Vaidotas Urbanavicius, Luciana Valente, Bart Van der Auwera, Andriani Vazeou-Gerasimidi, Dzilda Velickiene, Ana Wagner, Markus Walter, Alistair Williams, Lotte Albret Wissing, Miroslav Wurzburger, Anette-G Ziegler.

North American Network: Alan Aldrich, Marilyn Alford, Linda Amstutz, Mark Anderson, Beenu Aneja, Bonita Baker, Janice Bartos, Holly Baugh, Dorothy Becker, Christophe Benoist, Noureddine Berka, Kathleen Breen, Sonya Bridgeman, Patricia Cleary, Debbie Conboy, Patrick Concannon, Roberta Cook, Robert Couch, Lori Covell, Mark Daly, Jayne Danska, Larry Dolan, David Donaldson, Alessandro Doria, Janice Dorman, Angela Dove, Lee Ducat, George Eisenbarth, Henry Erlich, Pamela Fain, Rosanna Fiallo-Scharer, Lois Finney, Kenneth Gabbay, Gladys Gaillard-McBride, Terri Gammer, Daniel Geraghty, Soumitra Ghosh, Steven Gitelman, Nat Goodman, Gregory Goodwin, Jinko Graham, Carla Greenbaum, David Greenberg, William Hagopian, Mary Halvorson, John Hansen, Stephanie Higgins, Joel Hirschhorn, Kim Holmquist, Leroy Hood, Michelle Hull, Anhaita Jamula, Judith Johansen, Kevin Kaiserman, Fouad Kandeel, Francine Kaufman, Liz Langeland, Jean Lawrence, Nancy Lewis, Victoria Magnuson, Jennifer Marks, Andrea Martin, Della Matheson, Beth Mayer-Davis, Marli McCulloh-Olson, Richard McIndoe, Brad McNeney, Eric Mickelson, Priscilla Moonsamy, Antoinette Moran, Patricia Mueller, Mary Murray, Gerald Nepom, David Ng, Janelle Noble, Jill Norris, Tihamer Orban, David Owerbach, Andrew Paterson, Helen Patrie, Diana B. Petitti, Catherine Pihoker, Constantin Polychronakos, Donna Prokopczak, Alberto Pugliese, Beeca Pyle, Philip Raskin, Natasha Razack, Marian Rewers, Karen Riley, Henry Rodriquez, John Rogus, Ami Romanowski, Jerry Rotter, Monique Roy, Penny Satterwhite, Desmond Schatz, Gary Schoch, Mara Semel, Jin-Xiong She, Terry Smith, Janice Sowinski, Richard Spielman, Debbie Standiford, Caroline Suh, Christine Tam, Kent Taylor, Chrystal Thomas, Joan Thomas, Jay Tischfield, Ellen Toth, Deborah Truell, Diane Wherrett, Michelle Whiting, Theodora Wilson, Darrell Wilson, Lue Ping Zhao.

United Kingdom Network: Francesco Cucca, David Dunger, Graham Alec Hitman, Simon Howell, Sarah Nutland, Helen Rance, Luc Smink, John Todd, Jaakko Tuomilehto, Neil Walker, Barry Widmer, Heather Withers.

Latin America: Arturo Alvarado, Cresio Alves, Pablo Aschner, Elena Carrasco, Martha de Sereday, Laerico Franco, Teresa Frazer, Gustavo Frechtel, Clara Gorodezky, Jorge Jiminez, Ana Maria Jorge, Roberto Lanes, Ingrid Libman, Leonardo Mancillas, Carmen Mazza, Miguel Pasquel, Francisco Perez, Francisco Gomez Perez, Carmen Pisciottano, Ivelise Ramos, Olga Ramos, Maria Isabel Rojas, Antonio Selman-Geara, Gladys Veray.

Coordinating Center: Don Babcock, Stephanie Beck, Mark Brown, Cralen Davis, Mark Espeland, Mark Hall, Teresa Harnish, Laura Hemrick, Joan Hilner, Letitia Howard, Ethan M. Lange, Carl Langefeld, Josyf Mychaleckyj, June Pierce, David Reboussin, Stephen Rich, Scott Rushing, Michele Sale, Elizabeth Sides, Michael Steffes, Augy Thiel, Lynne Wagenknecht, Dustin Williams, Jianzhao Xu.

Members of the SEARCH for Diabetes in Youth Study:

The writing group for this manuscript wishes to acknowledge the contributions of the following individuals to the SEARCH for Diabetes in Youth Study:

California: Jean M. Lawrence, ScD, MPH, MSSA; Corinna Koebnick, PhD, MSc; Kristi Reynolds, PhD, MPH; Xia Li, MS; Eva Lustigova, MPH; and Kim Holmquist, BS, Certificate in Public Health for the Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena California, and David J. Pettitt, MD, Santa Barbara, California

Colorado: Dana Dabelea, MD, PhD, Richard F. Hamman, MD, DrPH, Lisa Testaverde, MS, Anna Bellatorre, PhD, for the Department of Epidemiology, Colorado School of Public Health, University of Colorado Denver, Georgeanna J. Klingensmith, MD, Marian J. Rewers, MD, PhD, David Maahs, MD and Paul Wadwa, MD for the Barbara Davis Center for Childhood Diabetes, Stephen Daniels, MD, PhD, Greta Wilkening, PsyD, Michael G. Kahn, MD, PhD, Department of Pediatrics and Children's Hospital, Clifford A. Bloch, MD, for the Pediatric Endocrine Associates, Jeffrey Powell, MD, MPH, for the Navajo Area Indian Health Promotion Program, Kathy Love-Osborne, MD, for the Denver Health and Hospital Authority, and Diana C. Hu, MD for the Pediatrics Department, Tuba City Regional Health Care Center, Tuba City, AZ.

Ohio: Lawrence M. Dolan, MD and Debra A. Standiford, MSN, CNP for the Cincinnati Children's Hospital Medical Center

Carolinas: Elizabeth J. Mayer-Davis, PhD, Amy Mottl, MD, MPH, Joan Thomas MS, RD for the University of North Carolina, Chapel Hill, Christine Turley, Angela D. Liese, PhD, MPH, Malaka Jackson, MD, Lisa Knight, MD for the University of South Carolina, Deborah Bowlby, MD for the Medical University of South Carolina, James Amrhein, MD, Bryce Nelson, MD for Greenville Health System, and Eau Claire Cooperative Health Center

Washington: Catherine Pihoker, MD, Irl Hirsch, MD, Lenna L. Liu, MD, MPH, Maryam Afkarian, MD, Grace Kim, MD, Craig Taplin, MD, Faisal Malik, MD, MSHS, Angel Nip, MD, Joyce Yi-Frazier, PhD, Lina Merjaneh, MD, Davene Wright, PhD, and Alissa Roberts, MD for the University of Washington, Beth Loots, MPH, MSW, Natalie Beauregard, BA, Sue Kearns, RN, Mary Klingsheim, RN, Michael Pascual, BA and Cordelia Franklin, BS for Seattle Children's Hospital, and Carla Greenbaum, MD for Benaroya Research Institute

Centers for Disease Control and Prevention: Giuseppina Imperatore, MD, PhD, Sharon H. Saydah, PhD

National Institute of Diabetes and Digestive and Kidney Diseases, NIH: Barbara Linder, MD, PhD

Central Laboratory: Santica M. Marcovina, PhD, ScD, Vinod P. Gaur, PhD, Greg Strylewicz, PhD, Alan Chait, MD and Jessica Harting for the University of Washington Northwest Lipid Research Laboratories

Coordinating Center: Ralph D'Agostino, Jr., PhD, Lynne E. Wagenknecht, DrPH, Jasmin Divers, PhD, Beth Reboussin, PhD, Elizabeth T. Jensen, PhD, Leora Henkin, MPH, MEd, Maureen T. Goldstein, BA, Carrie Williams, MA, CCRP, Scott Isom, MS, Jeanette Stafford, MS, Cynthia Suerken, MS, June Pierce, AB for Wake Forest School of Medicine