Supplemental Material

Data S1.

Supplemental Methods

Elastic Net Model after partial least squares discriminant analysis.

For proteins with VIP>1, a logistic regression model with elastic net penalty[24] on each bootstrap dataset was further considered. The elastic net penalty shrinks some protein coefficients to zero in the logistic regression model so that proteins with zero coefficients can be deemed unimportant in discriminating cases and controls, and hence may be deleted. To select the elastic net regularization parameter, cross-validation using the *cv.glmnet* function in the R package *glmnet*[44] was used, and the elastic net parameter was set to $\alpha = 0.5$. PLSDA was carried out with the R package *DiscriMiner*.

Internal Validation via Bootstrap

In the absence of external validation data, we internally validated our findings using bootstrap. We repeated each step of the model development, from candidate protein biomarker selection to protein score development. We obtained 200 bootstrap samples and we kept the proportions of cases and controls similar to the proportions in the original data. For each bootstrap dataset, a two-component PLSDA model was fit, and proteins with VIP>1 were kept. This step selected 31 proteins (compared to 29 proteins in the original [discovery] analysis). There were 27 overlapping proteins meeting this criterion in both the discovery and validation PLSDA models. As in the original analysis, logistic regression models with elastic net were fit on each bootstrap validation data for proteins with VIP>1, and proteins with frequency of nonzero coefficients in the top 25th percentile were used to develop protein scores. We identified the same 8 proteins (FAM3B, ITGA11, IL6, HGF, CCL25, GT, PLA2G7, and SCGB3A2) that were found in the discovery analysis. We obtained 200 log-odds ratios for each protein using the bootstrap validation data, and a weighted mean (over 200 log-odds ratios) was ascertained. In the discovery analysis, the protein score and models were developed using the full dataset, but in order not to use the full dataset in

the validation step, we obtained a different set of bootstrap dataset (200 bootstrap datasets), and we developed protein scores for each bootstrap dataset. Then for each bootstrap data, we fit the two models: baseline, and baseline and protein score to obtain odds ratios and AUCs and their corresponding variances. A fixed-effect meta-analysis using inverse-variance method was used to obtain weighted averages and confidence intervals. The protein score from the validation analysis was statistically significant with an odds ratio of 2.78 (CI: 2.67-2.90) compared to an odds ratio of 2.17 (CI: 1.58 - 2.99) from the discovery set. The validation AUCs for the baseline and baseline plus protein score models were respectively 0.74 (CI: 0.73-0.75) and 0.79(CI: 0.78-0.80) (Table S12), representing an improvement in AUC above the baseline model of 6.8% compared to 5.8% in the discovery analyses.

Data S2. Appendix: Study Group Authors

FIRST Study Group:

Rodger D MacArthur, Richard M Novak, Grace Peng, Li Chen, Ying Xiang, Katherine Huppler Hullsiek, Michael J Kozal, Mary van den Berg-Wolf, Christopher Henely, Barry Schmetter, Marjorie Dehlinger, for the CPCRA 058 Study Team and the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA)

Contributors: RDM, RMN, GP, LC, MBW, BS, and MD designed the study and wrote the study protocol. RDM, RMN, GP, LC, YX, MJK, MBW, CH, and BS implemented the study. GP, LC, YX, and KHH did the statistical analyses. RDM, RMN, MJK, and MBW were responsible for patient accrual. All authors assisted with interpretation of results and manuscript preparation.

Trial participants:
Southern New Jersey AIDS Clinical Trials, Camden NJ, USA (K Casey, D Condoluci, D McIntyre); Wayne State University, Detroit MI, USA (L R Crane, P Chandrasekar, M Farrough); Houston AIDS Research Team, Houston TX, USA (R C Arduino, M Rodriguez-Barradas, F Visnegarwala); Richmond AIDS Consortium, Richmond, VA, USA (E Fisher, C Clark, M Pittman); North Jersey Community Research Initiative, Newark, NJ, USA (G Perez, R Roland, N Regevik); AIDS Research Alliance, Chicago, IL, USA (J P Uy, R Luskin-Hawk, M Giles); Harlem AIDS Treatment Group, New York, NY, USA (W El-Sadr, F Siegal, R Contreras); Henry Ford Hospital, Detroit, MI, USA (N P Markowitz, I Brar, L H Makohon); Denver Community Program for Clinical Research on AIDS, Denver, CO, USA (D Cohn, F Moran, R Fernandez); Louisiana Community AIDS Research Program, New Orleans, LA, USA (D Mushatt, M O Stuart, D L Dandridge); Research and Education Group, Portland OR, USA (J Sampson, D Antoniskis, J Leggett); Wide-Reaching AIDS Program, Washington DC, USA (M Turner, C Jones, D Thomas); Community Consortium of San Francisco, San Francisco CA, USA (R C Scott, P Pell); Bronx AIDS Research Consortium, Bronx, NY, USA (E E Telzak, R B Cindrich, J Shuter); Temple University, Philadelphia, PA, USA (E M Tedaldi, K Lattanzi, S Frederick); New England Program for AIDS Clinical Trials, New Haven, CT, USA (J Jensen, L Daly, L Andrews); Partners in Research New Mexico, Albuquerque, NM, USA (S B Williams, C S Nicholson, K Hammer); AIDS Research Consortium of Atlanta, Atlanta, GA, USA (B Sweeton, L Miller, M Thompson).

ESPRIT and SILCAT Study groups:

Writing Group: Members of the writing group for the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)– Evaluation of Subcutaneous Proleukin in a Randomized International Trial (ESPRIT) Study Group and the Subcutaneous Recombinant, Human Interleukin-2 in HIV-Infected Patients with Low CD4+ Counts under Active Antiretroviral Therapy (SILCAAT) Scientific Committee (D. Abrams, M.D. [cochair], Y. Lévy, M.D. [cochair], M.H. Losso, M.D. [cochair], A. Babiker, Ph.D., G.

Collins, M.S., D.A. Cooper, M.D., J. Darbyshire, M.B., Ch.B., S. Emery, Ph.D., L. Fox, M.D., F. Gordin, M.D., H.C. Lane, M.D., J.D. Lundgren, M.D., R. Mitsuyasu, M.D., J.D. Neaton, Ph.D., A. Phillips, Ph.D., J.P. Routy, M.D., G. Tambussi, M.D., and D. Wentworth, M.P.H.

Coordinating Centers: Copenhagen: B Aagaard, E Aragon, J Arnaiz, L Borup, B Clotet, U Dragsted, A Fau, D Gey, J Grarup, U Hengge, P Herrero, P Jansson, B Jensen, K Jensen, H Juncher, P Lopez, J Lundgren, C Matthews, D Mollerup, M Pearson, A Phillips, S Reilev, K Tillmann, S Varea. London: B Angus, A Babiker, B Cordwell, J Darbyshire, W Dodds, S Fleck, J Horton, F Hudson, Y Moraes, F Pacciarini, A Palfreeman, N Paton, N Smith, F van Hooff.

Minneapolis: J Bebchuk, G Collins, E Denning, A DuChene, L Fosdick, M Harrison, K Herman-Lamin, E Krum, G Larson, J Neaton, R Nelson, K Quan, S Quan, T Schultz, G Thompson, D Wentworth, N Wyman. Sydney: C Carey, F Chan, D Cooper, B Cordwell, D Courtney-Rodgers, F Drummond, S Emery, M Harrod, S Jacoby, L Kearney, M Law, E Lin, S Pett, R Robson, N Seneviratne, M Stewart, E Watts.

Washington: E Finley, F Gordin, A Sánchez, B Standridge, M Vjecha.

Endpoint Review Committee: W Belloso, R Davey, D Duprez, J Gatell, J Hoy, A Lifson, C Pederson, G Perez, R Price, R Prineas, F Rhame, J Sampson, J Worley.

Data and Safety Monitoring Board: J Modlin, V Beral, R Chaisson, T Fleming, C Hill, K Kim, B Murray, B Pick, M Seligmann, I Weller.

National Institute of Allergy and Infectious Disease: K Cahill, L Fox, M Luzar, A Martinez, L McNay, J Pierson, J Tierney, S Vogel.

International Drug Distribution (CTS Inc., Durham, North Carolina): V Costas, J Eckstrand.

Specimen Repository (SAIC Frederick, Inc.): S Brown.

Clinical Sites for ESPRIT and/or SILCAAT: Argentina: L Abusamra, E Angel, S Aquilia, W Belloso, J Benetucci, V Bittar, E Bogdanowicz, P Cahn, A Casiro, J Contarelli, J Corral, L Daciuk, D David, W Dobrzanski, A Duran, J Ebenrstejin, I Ferrari, D Fridman, V Galache, G Guaragna, S Ivalo, A Krolewiecki, I Lanusse, H Laplume, M Lasala, R Lattes, J Lazovski, G Lopardo, M Losso, L Lourtau, S Lupo, A Maranzana, C Marson, L Massera, G Moscatello, S Olivia, I Otegui, L Palacios, A Parlante, H Salomon, M Sanchez, C Somenzini, C Suarez, M Tocci, J Toibaro, C Zala. **Australia:** S Agrawal, P Ambrose, C Anderson, J Anderson, D Baker, K Beileiter, K Blavius, M Bloch, M Boyle, D Bradford, P Britton, P Brown, T Busic, A Cain, L Carrall, S Carson, I Chenoweth, J Chuah, F Clark, J Clemons, K Clezy, D Cooper, P Cortissos, N Cunningham, M Curry, L Daly, C D'Arcy-Evans, R Del Rosario, S Dinning, P Dobson, W Donohue, N Doong, C Downs, E Edwards, S Edwards, C Egan, W Ferguson, R Finlayson, C Forsdyke, L Foy, T Franic, A Frater, M French, D Gleeson, J Gold, P Habel, K Haig, S Hardy, R Holland, J Hoy, J Hudson, R Hutchison, N Hyland, R James, C Johnston, M Kelly, M King, K Kunkel, H Lau, J Leamy, D Lester, J Leung, A Lohmeyer, K Lowe, K MacRae, C Magness, O Martinez, H Maruszak, N Medland, S Miller, J Murray, P Negus, R Newman, M Ngieng, C Nowlan, J Oddy, N

Orford, D Orth, J Patching, M Plummer, S Price, R Primrose, I Prone, H Ree, C Remington, R Richardson, S Robinson, G Rogers, J Roney, N Roth, D Russell, S Ryan, J Sarangapany, T Schmidt, K Schneider, C Shields, C Silberberg, D Shaw, J Skett, D Smith, T Meng Soo, D Sowden, A Street, B Kiem Tee, Jl Thomson, S Topaz, R Vale, C Villella, A Walker, A Watson, N Wendt, L Williams, D Youds. **Austria:** A Aichelburg, P Cichon, B Gemeinhart, A Rieger, B Schmied, V Touzeau-Romer, N Vetter. **Belgium:** R Colebunders, N Clumeck, A DeRoo, K Kabeya, E O'Doherty, S de Wit. **Brazil:** C De Salles Amorim, C Basso, S Flint, E Kallas, G Levi, D Lewi, L Pereira Jr, M da Silva, T Souza, A Toscano. **Canada (CTN):** J Angel, M Arsenault, M Bast, B Beckthold, P Bouchard, I Chabot, R Clarke, J Cohen, P Coté, M Ellis, C Gagne, J Gill, M Houde, B Johnston, N Jubinville, C Kato, N Lamoureux, G Larson, J LatendrePaquette, A Lindemulder, A McNeil, N McFarland, J Montaner, C Morrisseau, R O'Neill, G Page, A Piche, B Pongracz, H Preziosi, L Puri, A Rachlis, E Ralph, I Raymond, D Rouleau, JP Routy, R Sandre,T Seddon, S Shafran, C Sikora, F Smaill, D Stromberg, S Trottier, S Walmsley, K Weiss, K Williams, D Zarowny. **Denmark:** B Baadegaard, Å Bengaard Andersen, K Boedker, P Collins, J Gerstoft, L Jensen, H Moller, P Lehm Andersen, I Loftheim, L Mathiesen, H Nielsen, N Obel, C Pedersen, D Petersen, L Pors Jensen, F Trunk Black. **France (ANRS):** JP Aboulker, A Aouba, M Bensalem, H Berthe, C Blanc, M Bloch, D Bornarel, O Bouchaud, F Boue, E Bouvet, C Brancon, S Breaud, D Brosseau, A Brunet, C Capitant, C Ceppi, C Chakvetadze, C Cheneau, JM Chennebault, P De Truchis, AM Delavalle, JF Delfraissy, P Dellamonica, AM Delavalle, C Dumont, N Edeb, G Fabre, S Ferrando, A Foltzer, V Foubert, JA Gastaut, J Gerbe, PM Girard, C Goujard, B Hoen, P Honore, H Hue,T Hynh, C Jung, S Kahi, C Katlama, JM Lang, V Le Baut, B Lefebvre, N Leturque, Y Lévy, J Loison, G Maddi, A Maignan, C Majerholc, C de Boever, JL Meynard, C Michelet, C Michon, M Mole, E Netzer, G Pialoux, I Poizot-Martin, F Raffi, M Ratajczak, I Ravaux, J Reynes, D Salmon-Ceron, M Sebire, A Simon, L Tegna, D TisneDessus, C Tramoni, JP Viard, M Vidal, C Viet-Peaucelle, L Weiss, A Zeng, D Zucman. **Germany:** A Adam, K Arasteh, G Behrens, F Bergmann, M Bickel, D Bittner, J Bogner, N Brockmeyer, N Darrelmann, M Deja, M Doerler, S Esser, G Faetkenheuer, S Fenske, S Gajetzki, D Gey, F Goebel, D Gorriahn, E Harrer, T Harrer, H Hartl, M Hartmann, S Heesch, W Jakob, H Jäger, H Klinker, G Kremer, C Ludwig, K Mantzsch, S Mauss, A Meurer, A Niedermeier, N Pittack, A Plettenberg, A Potthoff, M Probst, M Rittweger, J Rockstroh, B Ross, J Rotty, E Rund, T Ruzicka, Rt Schmidt, G Schmutz, E Schnaitmann, D Schuster, T Sehr, B Spaeth, S Staszewski, HJ Stellbrink, C Stephan, T Stockey, A Stoehr, K Tillmann, A Trein, T Vaeth, M Vogel, J Wasmuth, C Wengenroth, R Winzer, E Wolf. **Ireland:** F Mulcahy, Dl Reidy. **Israel:** Y Cohen, G Drora, I Eliezer, O Godo, E Kedem, E Magen, M Mamorsky, S Pollack, Z Sthoeger, H Vered, I Yust. **Italy:** F Aiuti, M Bechi, A Bergamasco, D Bertelli, R Bruno, L Butini, M Cagliuso, G Carosi, S Casari, V Chrysoula, G Cologni, V Conti, A Costantini, A Corpolongo, G D'Offizi, F Gaiottino, M Di Pietro, R Esposito, G Filice, M Francesco, E Gianelli, C Graziella, L Magenta, F Martellotta, R Maserati, F Mazzotta, G Murdaca, G Nardini, S Nozza, F Puppo, M Pogliaghi, D Ripamonti, C Ronchetti, S Rusconi, V Rusconi, P Sacchi, N Silvia, F Suter, G Tambussi, A Uglietti, M Vechi, B Vergani, F Vichi, P Vitiello. **Japan:** A Iwamoto, Y Kikuchi, N Miyazaki, M Mori, T Nakamura, T Odawara, S Oka, T Shirasaka, M Tabata, M Takano, C Ueta, D Watanabe, Y Yamamoto. **Morocco:** I Erradey, H Himmich, K Marhoum El Filali. **The Netherlands:** W Blok, R van Boxtel, K Brinkman H Doevelaar, A van Eeden, M Grijsen, M Groot, J Juttmann, M Kuipers, S Ligthart, P van der Meulen, J Lange, N Langebeek, S Ligthart, P Reiss, C Richter, M Schoemaker, L Schrijnders-Gudde, E Septer-Bijleveld, H Sprenger, J Vermeulen, R ten Kate, B van de Ven. **Norway:** J Bruun, D Kvale, A Maeland. **Poland:** E Bakowska, M Beniowski, A Boron-Kaczmarska, J Gasiorowski, A Horban, M Inglot, B Knysz, E Mularska, M Parczewski, M Pynka, W

Rymer, A Szymczak. **Portugal:** M Aldir, F Antunes, C Baptista, J da Conceicao Vera, M Doroana, K Mansinho, C Raquel A dos Santos, E Valadas, I Vaz Pinto. **Singapore:** E Chia, E Foo, F Karim, PL Lim, A Panchalingam, N Paton, A Quek. **Spain:** R AlcázarCaballero, E Aragon, J Arnaiz, J Arribas, J Arrizabalaga, X de Barron, F Blanco, E Bouza, I Bravo, S Calvo, L Carbonero, I Carpena, M Castro, B Clotet, L Cortes, M del Toro, P Domingo, M Elias, J Espinosa, V Estrada, E Fernandez-Cruz, P Fernández, H Freud, M Fuster, A Garcia, G Garcia, R Garrido, J Gatell, P Gijón, J Gonzalez-García, I Gil, A González, J González-Lahoz, P López Grosso, M Gutierrez, E Guzmán, J Iribarren, M Jiménez, A Jou, J Juega, J Lopez, P Lopez, F Lozano, L Martín-Carbonero, R Mata, G Mateo, A Menasalvas, C Mirelles, J de Miguel Prieto, M Montes, A Moreno, J Moreno, V Moreno, R Muñoz, A Ocampo, E Ortega, L Ortiz, B Padilla, A Parras, A Paster, J Pedreira, J Peña, R Perea, B Portas, J Puig, F Pulido, M Rebollar, J de Rivera, V Roca, F Rodríguez- Arrondo, R Rubio, J Santos, J Sanz, G Sebastian, M Segovia, V Soriano, L Tamargo, S Varea, P Viciana, M von Wichmann. **Sweden:** G Bratt, A Hollander, P Olov Pehrson, I Petz, E Sandstrom, A Sönnerborg. **Switzerland:** E Bernasconi, V Gurtner. **Thailand:** U Ampunpong, C Auchieng, C Bowonwatanuwong, P Chanchai, P Chetchotisakd, T Chuenyan, C Duncombe, M Horsakulthai, P Kantipong, K Laohajinda, P Phanuphak, V Pongsurachet, S Pradapmook, K Ruxruntham, S Seekaew, A Sonjai, S Suwanagool, W Techasathit, S Ubolyam, J Wankoon. **United Kingdom:** I Alexander, D Dockrell, P Easterbrook, B Edwards, E Evans, M Fisher, R Fox, B Gazzard, G Gilleran, J Hand, L Heald, C Higgs, S Jebakumar, I Jendrulek, M Johnson, S Johnson, F Karim, G Kinghorn, K Kuldanek, C Leen, R Maw, S McKernan, L McLean, S Morris, M Murphy, S O'Farrell, E Ong, B Peters, C Stroud, M Wansbrough-Jones, J Weber, D White, I Williams, M Wiselka, T Yee. **United States:** S Adams, D Allegra, L Andrews, B Aneja, G Anstead, R Arduino, R Artz, J Bailowitz, S Banks, J Baxter, J Baum, D Benator, D Black, D Boh, T Bonam, M Brito, J Brockelman, S Brown, V Bruzzese, A Burnside Jr., V Cafaro, K Casey, L Cason, G Childress, Cl Clark, D Clifford, M Climo, D Cohn, P Couey, H Cuervo, R Davey Jr, S Deeks, M Dennis, M Diaz-Linares, D Dickerson, M Diez, J Di Puppo, P Dodson, D Dupre, R Elion, K Elliott, W El-Sadr, M Estes, J Fabre, M Farrough, J Flamm, S Follansbee, C Foster, C Frank, J Franz, G Frechette, G Freidland, J Frische, L Fuentes, C Funk, C Geisler, K Genther, M Giles, M Goetz, M Gonzalez, C Graeber, F Graziano, D Grice, B Hahn, C Hamilton, S Hassler, A Henson, S Hopper, M John, L Johnson, M Johnson, R Johnson, R Jones, J Kahn, M Kelly, N Klimas, M Kolber, S Koletar, A Labriola, R Larsen, F Lasseter, M Lederman, T Ling, T Lusch, R MacArthur, C Machado, L Makohon, J Mandelke, S Mannheimer, N Markowitz, M Martínez, N Martinez, M Mass, H Masur, D McGregor, D McIntyre, J McKee, D McMullen, M Mettinger, S Middleton, J Mieras, D Mildvan, P Miller, T Miller, V Mitchell, R Mitsuyasu, A Moanna, C Mogridge, F Moran, R Murphy, D Mushatt, R Nahass, D Nixon, S O'Brien, J Ojeda, P Okhuysen, M Olson, J Osterberger, W Owen, Sr. S Pablovich, S Patel, G Perez, G Pierone Jr., R Poblete, A Potter, E Preston, C Rappoport, N Regevik, M Reyelt, F. Rhame, L Riney, M Rodriguez-Barradas, M Rodriguez, Milagros Rodriguez, J Rodriguez, R Roland, C Rosmarin-DeStefano, W Rossen, J Rouff, M Saag, J Sampson, S Santiago, J Sarria, S Wirtz, U Schmidt, C Scott, A Sheridan, A Shin, S Shrader, G Simon, D Slowinski, K Smith, J Spotkov, C Sprague, D States, C Suh, J Sullivan, K Summers, B Sweeton, V Tan, T Tanner, E Tedaldi, Z Temesgen, D Thomas, M Thompson, C Tobin, N Toro, W Towner, K Upton, J Uy, S Valenti, C van der Horst, J Vita, J Voell, J Walker, T Walton, K Wason, V Watson, A Wellons, J Weise, M White, T Whitman, B Williams, N Williams, J Windham, M Witt, K Workowski, G Wortmann, T Wright, C Zelasky, B Zwickl.

SMART Study Group:

Writing Group: W.M. El-Sadr [cochair], Harlem Hospital Center and Columbia University, New York; J.D. Lundgren [cochair], Hvidovre University Hospital, Denmark; J.D. Neaton [cochair], University of Minnesota, Minneapolis; F. Gordin, Washington Veterans Affairs Medical Center, Washington, DC; D. Abrams, University of California, San Francisco; R.C. Arduino, University of Texas Medical School, Houston; A. Babiker, Medical Research Council, London; W. Burman, Denver Public Health Department; N. Clumeck, Centre Hospitalier Universitaire SaintPierre, Brussels; C.J. Cohen, Community Research Initiative of New England, Boston; D. Cohn, Denver Public Health Department; D. Cooper, National Centre in HIV Epidemiology and Clinical Research, Sydney; J. Darbyshire, Medical Research Council, London; S. Emery, National Centre in HIV Epidemiology and Clinical Research, Sydney; G. Fätkenheuer, University Hospital, Cologne; B. Gazzard, Medical Research Council, London; B. Grund, University of Minnesota, Minneapolis; J. Hoy, National Centre in HIV Epidemiology and Clinical Research, Melbourne; K. Klingman, National Institute of Allergy and Infectious Diseases, Bethesda, MD; M. Losso, Hospital General de Agudos J.M. Ramos Mejia, Buenos Aires; N. Marko witz, Henry Ford Hospital, Detroit; J. Neu haus, University of Minnesota, Minneapolis; A. Phillips, Royal Free Hospital School of Medicine, London; and C. Rappoport, University of California, San Francisco

SMART study group are as follows:
Community Programs for Clinical Research on AIDS Chair's Office and Operations Center — F. Gordin (group leader), E. Finley, D. Dietz, C. Chesson, M. Vjecha, B. Standridge, B. Schmetter, L. Grue, M. Willoughby, A. Demers;

Regional Coordinating Centers — Copenhagen — J.D. Lundgren, A. Phillips, U.B. Dragsted, K.B. Jensen, A. Fau, L. Borup, M. Pearson, P.O. Jansson, B.G. Jensen, T.L. Benfield; London — J.H. Darbyshire, A.G. Babiker, A.J. Palfreeman, S.L. Fleck, Y. Collaco-Moraes, B. Cordwell, W. Dodds, F. van Hooff, L. Wyzydrag; Sydney — D.A. Cooper, S. Emery, F.M. Drummond, S.A. Connor, C.S. Satchell, S. Gunn, S. Oka, M.A. Delfino, K. Merlin, C. McGinley;

Statistical and Data Management Center — Minneapolis — J.D. Neaton, G. Bartsch, A. DuChene, M. George, B. Grund, M. Harrison, C. Hogan (deceased), E. Krum, G. Larson, C. Miller, R. Nelson, J. Neuhaus, M.P. Roediger, T. Schultz, L. Thackeray;

Electrocardiography Reading Center — R. Prineas, C. Campbell;

End Point Review Committee — G. Perez (cochair), A. Lifson (cochair), D. Duprez, J. Hoy, C. Lahart, D. Perlman, R. Price, R. Prineas, F. Rhame, J. Sampson, J. Worley;

NIAID Data and Safety Monitoring Board — M. Rein (chair), R. Der Simonian (executive secretary), B.A. Brody, E.S. Daar, N.N. Dubler, T.R. Fleming, D.J. Freeman, J.P. Kahn, K.M. Kim, G. Medoff, J.F. Modlin, R. Moellering, Jr., B.E. Murray, B. Pick, M.L. Robb, D.O. Scharfstein, J. Sugarman, A. Tsiatis, C. Tuazon, L. Zoloth; NIAID — K. Klingman, S. Lehrman;

SMART Clinical Site Investigators (numbers of enrolled patients are in parentheses)— Argentina (147) — J. Lazovski, W.H. Belloso, M.H. Losso, J.A. Benetucci, S. Aquilia, V. Bittar, E.P. Bogdanowicz, P.E. Cahn, A.D. Casiró, I. Cassetti, J.M. Contarelli, J.A. Corral, A. Crinejo, L. Daciuk, D.O. David, G. Guaragna, M.T. Ishida, A. Krolewiecki, H.E. Laplume, M.B. Lasala, L. Lourtau, S.H. Lupo, A. Maranzana, F. Masciottra, M. Michaan, L. Ruggieri, E. Salazar, M. Sánchez, C. Somenzini; **Australia** (170) — J.F. Hoy, G.D. Rogers, A.M. Allworth, J.S.C. Anderson, J. Armishaw, K. Barnes, A. Carr, A. Chiam, J.C.P. Chuah, M.C. Curry, R.L. Dever, W.A. Donohue, N.C. Doong, D.E. Dwyer, J. Dyer, B. Eu, V.W. Ferguson, M.A.H. French, R.J. Garsia, J. Gold, J.H. Hudson, S. Jeganathan, P. Konecny, J. Leung, C.L. McCormack, M. McMurchie, N. Medland, R.J. Moore, M.B. Moussa, D. Orth, M. Piper, T. Read, J.J. Roney, N. Roth, D.R. Shaw, J. Silvers, D.J. Smith, A.C. Street, R.J. Vale, N.A. Wendt, H. Wood, D.W. Youds, J. Zillman; **Austria** (16) — A. Rieger, V. Tozeau, A. Aichelburg, N. Vetter; **Belgium** (95) — N. Clumeck, S. Dewit, A. de Roo, K. Kabeya, P. Leonard, L. Lynen, M. Moutschen, E. O'Doherty; **Brazil** (292) — L.C. Pereira, Jr., T.N.L. Souza, M. Schechter, R. Zajdenverg, M.M.T.B. Almeida, F. Araujo, F. Bahia, C. Brites, M.M. Caseiro, J. Casseb, A. Etzel, G.G. Falco, E.C.J. Filho, S.R. Flint, C.R. Gonzales, J.V.R. Madruga, L.N. Passos, T. Reuter, L.C. Sidi, A.L.C. Toscano; **Canada** (102) — D. Zarowny, E. Cherban, J. Cohen, B. Conway, C. Dufour, M. Ellis, A. Foster, D. Haase, H. Haldane, M. Houde, C. Kato, M. Klein, B. Lessard, A. Martel, C. Martel, N. McFarland, E. Paradis, A. Piche, R. Sandre, W. Schlech, S. Schmidt, F. Smaill, B. Thompson, S. Trottier, S. Vezina, S. Walmsley; **Chile** (49) — M.J. Wolff Reyes, R. Northland; Denmark (19) — L. Ostergaard, C. Pedersen, H. Nielsen, L. Hergens, I.R. Loftheim, K.B. Jensen; **Estonia** (5) — M. Raukas, K. Zilmer; **Finland** (21) — J. Justinen, M. Ristola; **France** (272) — P.M. Girard, R. Landman, S. Abel, S. Abgrall, K. Amat, L. Auperin, R. Barruet, A. Benalycherif, N. Benammar, M. Bensalem, M. Bentata, J.M. Besnier, M. Blanc, O. Bouchaud, A. Cabié, P. Chavannet, J.M. Chennebault, S. Dargere, X. de la Tribonniere, T. Debord, N. Decaux, J. Delgado, M. Dupon, J. Durant, V. Frixon-Marin, C. Genet, L. Gérard, J. Gilquin, B. Hoen, V. Jeantils, H. Kouadio, P. Leclercq, J.-D. Lelièvre, Y. Levy, C.P. Michon, P. Nau, J. Pacanowski, C. Piketty, I. Poizot-Martin, I. Raymond, D. Salmon, J.L. Schmit, M.A. Serini, A. Simon, S. Tassi, F. Touam, R. Verdon, P. Weinbreck, L. Weiss, Y. Yazdanpanah, P. Yeni; **Germany** (215) — G. Fätkenheuer, S. Staszewski, F. Bergmann, S. Bitsch, J.R. Bogner, N. Brockmeyer, S. Esser, F.D. Goebel, M. Hartmann, H. Klinker, C. Lehmann, T. Lennemann, A. Plettenberg, A. Potthof, J. Rockstroh, B. Ross, A. Stoehr, J.C. Wasmuth, K. Wiedemeyer, R. Winzer; **Greece** (95) — A. Hatzakis, G. Touloumi, A. Antoniadou, G.L. Daikos, A. Dimitrakaki, P. Gargalianos-Kakolyris, M. Giannaris, A. Karafoulidou, A. Katsambas, O. Katsarou, A.N. Kontos, T. Kordossis, M.K. Lazanas, P. Panagopoulos, G. Panos, V. Paparizos, V. Papastamopoulos, G. Petrikkos, H. Sambatakou, A. Skoutelis, N. Tsogas, G. Xylomenos; **Ireland** (2) — C.J. Bergin, B. Mooka; **Israel** (13) — S. Pollack, M.G. Mamorksy, N. Agmon-Levin, R. Karplus, E. Kedem, S. Maayan, E. Shahar, Z. Sthoeger, D. Turner, I. Yust; **Italy** (88) — G. Tambussi, V. Rusconi, C. Abeli, M. Bechi, A. Biglino, S. Bonora, L. Butini, G. Carosi, S. Casari, A. Corpolongo, M. De Gioanni, G. Di Perri, M. Di Pietro, G. D'Offizi, R. Esposito, F. Mazzotta, M. Montroni, G. Nardini, S. Nozza, T. Quirino, E. Raise; **Japan** (15) — M. Honda, M. Ishisaka; **Lithuania** (4) — S. Caplinskas, V. Uzdaviniene; **Luxembourg** (3) — J.C. Schmit, T. Staub; **Morocco** (42) — H. Himmich, K. Marhoum El Filali; **New Zealand** (7) — G.D. Mills, T. Blackmore, J.A. Masters, J. Morgan, A. Pithie; **Norway** (17) — J. Brunn, V. Ormasssen; **Peru** (57) — A. La Rosa, O. Guerra, M. Espichan, L. Gutierrez, F. Mendo, R. Salazar; **Poland** (54) — B. Knytz, A. Horban, E. Bakowska, M. Beniowski, J. Gasiorowski, J. Kwiatkowski; **Portugal** (73) — F. Antunes, R.S. Castro, M. Doroana, A. Horta, K. Mansinho, A.C. Miranda, I.V. Pinto, E. Valadas, J. Vera; **Russia** (17) — A. Rakhmanova, E. Vinogradova, A. Yakovlev, N. Zakharova; **South Africa** (26) — R.

Wood, C. Orrel; **Spain** (100) — J. Gatell, J.A. Arnaiz, R. Carrillo, B. Clotet, D. Dalmau, A. González, Q. Jordano, A. Jou, H. Knobel, M. Larrousse, R. Mata, J.S. Moreno, E. Oretaga, J.N. Pena, F. Pulido, R. Rubio, J. Sanz, P. Viciana; **Switzerland** (91) — B. Hirschel, R. Spycher, M. Battegay, E. Bernasconi, S. Bottone, M. Cavassini, A. Christen, C. Franc, H.J. Furrer, A. Gayet-Ageron, D. Genné, S. Hochstrasser, L. Magenta, C. Moens, N. Müller, R. Nüesch; **Thailand** (159) — P. Phanuphak, K. Ruxrungtham, W. Pumpradit, P. Chetchotisakd, S. Dangthongdee, S. Kiertiburanakul, V. Klinbuayaem, P. Mootsikapun, S. Nonenoy, B. Piyavong, W. Prasithsirikul, P. Raksakulkarn; **United Kingdom** (214) — B.G. Gazzard, J.G. Ainsworth, J. Anderson, B.J. Angus, T.J. Barber, M.G. Brook, C.D. Care, D.R. Chadwick, M. Chikohora, D.R. Churchill, D. Cornforth, D.H. Dockrell, P.J. Easterbrook, P.A. Fox, R. Fox, P.A. Gomez, M.M. Gompels, G.M. Harris, S. Herman, A.G.A. Jackson, S.P.R. Jebakumar, M.A. Johnson, G.R. Kinghorn, K.A. Kuldanek, N. Larbalestier, C. Leen, M. Lumsden, T. Maher, J. Mantell, R. Maw, S. McKernan, L. McLean, S. Morris, L. Muromba, C.M. Orkin, A.J. Palfreeman, B.S. Peters, T.E.A. Peto, S.D. Portsmouth, S. Rajamanoharan, A. Ronan, A. Schwenk, M.A. Slinn, C.J. Stroud, R.C. Thomas, M.H. Wansbrough-Jones, H.J. Whiles, D.J. White, E. Williams, I.G. Williams, M. Youle; **United States** (2989) — D.I. Abrams, E.A. Acosta, S. Adams, A. Adamski, L. Andrews, D. Antoniskis, D.R. Aragon, R. Arduino, R. Artz, J. Bailowitz, B.J. Barnett, C. Baroni, M. Barron, J.D. Baxter, D. Beers, M. Beilke, D. Bemenderfer, A. Bernard, C.L. Besch, M.T. Bessesen, J.T. Bethel, S. Blue, J.D. Blum, S. Boarden, R.K. Bolan, J.B. Borgman, I. Brar, B.K. Braxton, U.F. Bredeek, R. Brennan, D.E. Britt, J. Brockelman, S. Brown, V. Bruzzese, D. Bulgin-Coleman, D.E. Bullock, V. Cafaro, B. Campbell, S. Caras, J. Carroll, K.K. Casey, F. Chiang, G. Childress, R.B. Cindrich, C. Clark, M. Climo, C. Cohen, J. Coley, D.V. Condoluci, R. Contreras, J. Corser, J. Cozzolino, L.R. Crane, L. Daley, D. Dandridge, V. D'Antuono, J.G. Darcourt Rizo Patron, J.A. DeHovitz, E. DeJesus, J. DesJardin, M. Diaz-Linares, C. Dietrich, P. Dodson, E. Dolce, K. Elliott, D. Erickson, M. Estes, L.L. Faber, J. Falbo, M.J. Farrough, C.F. Farthing, P. Ferrell-Gonzalez, H. Flynn, C. Frank, M. Frank, K.F. Freeman, N. French, G. Friedland, N. Fujita, L. Gahagan, K. Genther, I. Gilson, M.B. Goetz, E. Goodwin, F. Graziano, C.K. Guity, P. Gulick, E.R. Gunderson, C.M. Hale, K. Hannah, H. Henderson, K. Hennessey, W.K. Henry, D.T. Higgins, S.L. Hodder, H.W. Horowitz, M. Howe-Pittman, J. Hubbard, R. Hudson, H. Hunter, C. Hutelmyer, M.T. Insignares, L. Jackson, L. Jenny, M. John, D.L. Johnson, G. Johnson, J. Johnson, L. Johnson, J. Kaatz, J. Kaczmarski, S. Kagan, C. Kantor, T. Kempner, K. Kieckhaus, N. Kimmel, B.M. Klaus, N. Klimas, J.R. Koeppe, J. Koirala, J. Kopka, J.R. Kostman, M.J. Kozal, A. Kumar, A. Labriola, H. Lampiris, C. Lamprecht, K.M. Lattanzi, J. Lee, J. Leggett, C. Long, A. Loquere, K. Loveless, C.J. Lucasti, R. Luskin-Hawk, M. MacVeigh, L.H. Makohon, S. Mannheimer, N.P. Markowitz, C. Marks, N. Martinez, C. Martorell, E. McFeaters, B. McGee, D.M. McIntyre, J. McKee, E. McManus, L.G. Melecio, D. Melton, S. Mercado, E. Merrifield, J.A. Mieras, M. Mogyoros, F.M. Moran, K. Murphy, D. Mushatt, S. Mutic, I. Nadeem, J.P. Nadler, R. Nahass, D. Nixon, S. O'Brien, A. Ognjan, M. O'Hearn, K. O'Keefe, P.C. Okhuysen, E. Oldfield, D. Olson, R. Orenstein, R. Ortiz, J. Osterberger, W. Owen, F. Parpart, V. Pastore-Lange, S. Paul, A. Pavlatos, D.D. Pearce, R. Pelz, G. Perez, S. Peterson, G. Pierone, Jr., D. Pitrak, S.L. Powers, H.C. Pujet, J.W. Raaum, J. Ravishankar, J. Reeder, N. Regevik, N.A. Reilly, C. Reyelt, J. Riddell IV, D. Rimland, M.L. Robinson, A.E. Rodriguez, M.C. Rodriguez-Barradas, V. Rodriguez Derouen, R. Roland, C. Rosmarin, W.L. Rossen, J.R. Rouff, J.H. Sampson, M. Sands, C. Savini, S. Schrader, M.M. Schulte, C. Scott, R. Scott, H. Seedhom, M. Sension, A. Sheble-Hall, A. Sheridan, J. Shuter, L.N. Slater, R. Slotten, D. Slowinski, M. Smith, S. Snap, D.M. States, M. Stewart, G. Stringer, J. Sullivan, K.K. Summers, K. Swanson, I.B. Sweeton, S. Szabo, E.M. Tedaldi, E.E. Telzak, Z. Temesgen, D. Thomas, M.A. Thompson, S. Thompson, C. Ting Hong Bong, C. Tobin, J. Uy, A. Vaccaro, L.M. Vasco, I. Vecino, G.K.

Verlinghieri, F. Visnegarwala, B.H. Wade, V. Watson, S.E. Weis, J.A. Weise, S. Weissman, A.M. Wilkin, L. Williams, J.H. Witter, L. Wojtusic, T.J. Wright, V. Yeh, B. Young, C. Zeana, J. Zeh; **Uruguay** (3) — E. Savio, M. Vacarezza.

START Study Group:

Writing Group: Jens D. Lundgren, M.D. Abdel G. Babiker, Ph.D. [cochair], Fred Gordin, M.D. [cochair], Sean Emery, Ph.D., Birgit Grund, Ph.D., Shweta Sharma, M.S., Anchalee Avihingsanon, M.D., David A. Cooper, M.D., Gerd Fätkenheuer, M.D., Josep M. Llibre, M.D., Jean-Michel Molina, M.D., Paula Munderi, M.D., Mauro Schechter, M.D., Robin Wood, M.D., Karin L. Klingman, M.D., Simon Collins, H. Clifford Lane, M.D., Andrew N. Phillips, Ph.D., and James D. Neaton, Ph.D. [INSIGHT PI])

In addition to writing group, the following committee members contributed to the conduct of the START trial:
Community Advisory Board: C. Rappoport (INSIGHT community liaison), P.D. Aagaard, S. Collins, G.M. Corbelli,N. Geffen, C. Kittitrakul, T. Maynard, M. Meulbroek, D. Munroe, M.S. Nsubuga, D. Peavey, S. Schwarze, M. Valdez.

Substudy Chairs: J.V. Baker, D. Duprez (arterial elasticity); A. Carr, J. Hoy (bone mineral density); M. Dolan, A.Telenti (genomics); C. Grady (informed consent); G. Matthews, J. Rockstroh (liver fibrosis progression); W.H.Belloso, J.M. Kagan (monitoring); E. Wright, B. Brew, R.W. Price, K. Robertson, L. Cysique (neurology); K.M.Kunisaki, J.E. Connett, D.E. Niewoehner (pulmonary). Endpoint Review Committee: A. Lifson (chair), W.H.Belloso, R.T. Davey Jr., D. Duprez, J.M. Gatell, J. Hoy, C. Pedersen, R.W. Price, R. Prineas, J. Worley.

Central Drug Repository and Drug Distribution: K. Brekke, S. Meger, B. Baugh, J. Eckstrand, C. Gallagher, J. Myers, J. Rooney, J. Van Wyk.

Network Laboratory Group: J. Baxter, C. Carey, A. DuChene, E.B. Finley, M. George, J. Grarup, M. Hoover, R. Pedersen, C. Russell, B. Standridge.

Specimen Repositories: E. Flowers, M. Hoover, K. Smith (Advanced BioMedical Laboratories, LLC, Cinnaminson, NJ, United States); M. McGrath, S. Silver (AIDS and Cancer Specimen Resource, University of California, San Francisco, San Francisco, CA, United States).
Wake Forest ECG Reading Center, Winston-Salem, NC, United States: E.Z. Soliman, M. Barr, C. Campbell, S. Hensley, J. Hu, L. Keasler, Y. Li, T. Taylor, Z.M. Zhang.

Division of AIDS, National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States: B. Alston-Smith, E. DeCarlo, K. Klingman, M. Proschan.

Data and Safety Monitoring Board: S. Bangdiwala (chair), R. Chaisson, A.R. Fleischman, C. Hill, J. Hilton, O.H.M. Leite, V.I. Mathan, B. Pick, C. Seas, P. Suwangool, G. Thimothe, F. Venter, I. Weller, P. Yeni.

Minnesota Coordinating Center, University of Minnesota, Minneapolis, MN, United States: J.D. Neaton, K. Brekke, G. Collins, E.T. Denning, A. DuChene, N.W. Engen, M. George, B. Grund, M. Harrison, K.H. Hullsiek, L.H. Klemme, E. Krum, G. Larson, S. Meger, R. Nelson, J. Neuhaus Nordwall, K. Quan, S.F. Quan, T. Schultz, S. Sharma, G. Thompson.

International Coordinating Centers: Copenhagen HIV Programme, Rigshospitalet, University of Copenhagen, Denmark: J.D. Lundgren, B. Aagaard, A.H.D. Borges, M. Eid, J. Grarup, P. Jansson, Z. Joensen, B. Nielsen, M. Pearson, R. Pedersen, A.N. Phillips; The Kirby Institute, University of New South Wales, Sydney, Australia: S. Emery, N. Berthon-Jones, C. Carey, L. Cassar, M. Clewett, D. Courtney-Rodgers, P. Findlay, S. Hough, S. Jacoby, J. Levitt, S.L. Pett, R. Robson, V. Shahamat, A. Shambrook; Medical Research Council Clinical Trials Unit at UCL, London, United Kingdom: A.G. Babiker, B. Angus, A. Arenas-Pinto, R. Bennett, N. Braimah, E. Dennis, N. Doyle, M. Gabriel, F. Hudson, B. Jackson, A. Palfreeman, N. Paton, C. Purvis, C. Russell; Veterans Affairs Medical Center, Washington, DC, United States: F. Gordin, D. Conwell, H. Elvis, E.B. Finley, V. Kan, L. Lynch, J. Royal, A. Sánchez, B. Standridge, D. Thomas, M. Turner, M.J. Vjecha.

The following investigators participated in the START study, listed by country (country lead, numbers of participants enrolled) and clinical site:
Argentina (M.H. Losso, n=216): CAICI (Instituto Centralizado de Assistencia e Investigación Clínica Integral), Rosario Santa Fe: S. Lupo, L. Marconi, D. Aguila; FUNCEI, Buenos Aires: G. Lopardo, E. Bissio, D. Fridman; Fundación IDEAA, Buenos Aires: H. Mingrone, E. Loiza, V. Mingrone; Hospital General de Agudos JM Ramos Mejia, Buenos Aires: M. Losso, J.M. Bruguera, P. Burgoa; Hospital Interzonal General de Agudos Dr. Diego Paroissien, Buenos Aires: E. Warley, S. Tavella; Hospital Italiano de Buenos Aires, Buenos Aires: W. Belloso, M. Sanchez; Hospital Nacional Profesor Alejandro Posadas, Buenos Aires: H. Laplumé, L. Daciuk; Hospital Rawson, Cordoba: D. David, A. Crinejo; Argentinean SCC, Fundación IBIS, Buenos Aires: G. Rodriguez-Loria, L. Doldan, A. Moricz, I. Otegui, I. Lanusse. **Australia** (J. Hoy, n=109): Burwood Road General Practice, Burwood, VIC: N. Doong, S. Hewitt; Centre Clinic, St Kilda, VIC: B.K. Tee; East Sydney Doctors, Darlinghurst, NSW: D. Baker, E. Odgers; Holdsworth House Medical Practice, Darlinghurst, NSW: S. Agrawal, M. Bloch; Melbourne Sexual Health Centre, Carlton, VIC: T.R.H. Read, S.J. Kent; Prahran Market Clinic, Prahran, VIC: H. Lau, N. Roth; Royal Adelaide Hospital, Adelaide, SA: L. Daly, D. Shaw; Royal Perth Hospital, Perth, WA: M. French, J. Robinson; Sexual Health & HIV Service - Clinic 2, Brisbane, QLD: M. Kelly, D. Rowling; St Vincent's Hospital, Fitzroy, VIC: D.A. Cooper, A. J. Kelleher; Taylor Square Private Clinic, Surry Hills, NSW: C. Pell, S. Dinning; The Alfred Hospital, Melbourne, VIC: J. Hoy, J. Costa; Westmead Hospital, Westmead, NSW: D.E. Dwyer, P. King. **Austria** (A. Rieger, n=7): Otto-Wagner-Spital SMZ /Baumgartner Hoehe, Vienna: N. Vetter; B. Schmied; University Vienna General Hospital, Vienna: A. Rieger, V.R. Touzeau.**Belgium** (S. de Witt, n=102): Centre Hospitalier Universitaire St. Pierre (C.H.U. St. Pierre), Brussels: S. de Witt, N. Clumeck, K. Kabeya; Institute of Tropical Medicine, Antwerp: E. Cleve, E. Florence, L. van Petersen; Universitair Ziekenhuis Gasthuisberg, Leuven: H. Ceunen, E.H. van Wijngaerden; Universitaire Ziekenhuizen Gent, Gent: T. James, L. Vandekerckhove. **Brazil** (L.C. Pereira Jr., M. Schechter, n=619): Ambulatório de Imunodeficiências (LIM-56), Sao Paulo, SP: J. Casseb, E. Constantinov, M.A. Monteiro; Center for ID at UFES, Vitoria, ES: L.N. Passos, T. Reuter; Centro de Referência e Treinamento DST/AIDS, Sao Paulo, SP: S.T. Leme, J.V.R. Madruga, R.S. Nogueira;

Hospital Escola Sao Francisco de Assis, Rio de Janeiro, RJ: M. Barbosa Souza, C. Beppu Yoshida, M. Dias Costa; Instituto de Infectologia Emilio Ribas, Sao Paulo, SP: R. Castro, R.Cruz, S. Ito, T.N. Lobato Souza; Instituto FIOCRUZ, Rio de Janeiro, RJ: B. Grinsztejn, V.G. Veloso, S. Wagner Cardoso; SEI Serviços Especializados em Infectología LTDA, Salvador, Bahia: F. Bahia, C. Brites, J. Correia. **Chile** (M.J. Wolff, n=76): Fundación Arriarán, Santiago: M. Wolff, R. Northland, C. Cortés. **Czech Republic** (D. Sedlacek, n=13): Faculty Hospital Na Bulovce, Prague: D. Jilich; University Hospital Plzen, Plzen: D. Sedlacek. **Denmark** (J. Gerstoft, n=33): Hvidovre University Hospital, Hvidovre: P. Collins, L. Mathiesen; Odense University Hospital, Odense: L. Hergens, C. Pedersen; Rigshospitalet, Copenhagen: J. Gerstoft, L.P. Jensen; Århus Universitetshospital, Skejby, Århus: I.R. Lofthiem, L. Østergaard. **Estonia** (K. Zilmer, n=8): West Tallinn Central Hospital Infectious Diseases, Tallinn: K. Zilmer. **Finland** (M. Ristola, n=23): Helsinki University Central Hospital, Helsinki: M. Ristola, O. Debnam. **France** (B. Hoen, n=111): CHU Côte de Nacre – Caen, Caen: R. Verdon, S. Dargere; CHU de Besançon -Hôpital Jean-Minjoz, Besancon: B. Hoen, C. Chirouze; Groupe Hospitalier Pitié-Salpêtrière, Paris: C. Katlama, M-A. Valantin; Hôpital Antoine Béclère, Clamart: F. Boue, I. Kansau; Hôpital de Bicêtre, Le Kremlin-Bicetre: C. Goujard, C. Chakvetadze; Hôpital Européen Georges Pompidou, Paris: L. Weiss, M Karmochkine; Hôpital Foch, Suresnes: D. Zucman, C. Majerholc; Hôpital Gustava Dron, Tourcoing: O.Robineau, R. Biekre; Hôpital Henri Mondor, Creteil: Y. Levy, J.D. Lelievre; Hôpital Hôtel Dieu, Paris: J.P. Viard, J Ghosn; Hôpital Saint-Antoine, Paris: J. Pacanowski, B. Lefebvre; Hôpital Saint-Louis, Paris: J.-M. Molina, L. Niedbalski, M. Previlon; French SCC, ANRS-Inserm SC10, Paris: J.P. Aboulker, C. Capitant, B. Lebas, N. Leturque, L. Meyer, E. Netzer. **Germany** (G. Fätkenheuer, n=312): EPIMED, Berlin: K. Arastéh, T. Meier; Gemeinschaftspraxis Jessen-Jessen-Stein, Berlin: C. Zedlack, H. Jessen; ICH Study Center, Hamburg: S. Heesch, C. Hoffmann; Ifi - Studien und Projekte GmbH, Hamburg: A. Plettenberg, A. Stoehr; Johann Wolfgang Goethe - University Hospital, Frankfurt: G. Sarrach, C. Stephan; Klinik I für Innere Medizin der Universität zu Köln, Cologne: G. Fätkenheuer, E. Thomas; Klinikum der Universität München, Munich: J.R. Bogner, I. Ott; Klinikum Dortmund GmbH, Dortmund: M. Hower, C. Bachmann; Medizinische Hochschule Hannover, Hannover: M. Stoll, R. Bieder; Medizinische Universitätsklinik - Bonn, Bonn: J. Rockstroh, B. Becker; Universitätsklinikum Düsseldorf, Düsseldorf: B. Jensen, C. Feind; Universitätsklinikum Erlangen, Erlangen: E. Harrer, T. Harrer; Universitätsklinikum Essen, Essen: S. Esser, H. Wiehler; Universitätsklinikum Heidelberg, Heidelberg: M. Hartmann, R. Röger; Universitätsklinikum Regensburg, Regensburg: B. Salzberger, E. Jäger; Universitätsklinikum Würzburg, Würzburg: H. Klinker, G. Mark; Universitätsklinikum, Hamburg-Eppendorf: J. van Lunzen, N. Zerche; German SSC, Johann Wolfgang Goethe - University Hospital, Frankfurt: V. Müller, K. Tillman. **Greece** (G. Touloumi, n=101): AHEPA University Hospital, Thessaloniki Central Macedonia: S. Metallidis, O. Tsachouridou; Attikon University General Hospital, Athens: A. Papadopoulos, K. Protopapas; Evangelismos General Hospital, Athens: A. Skoutelis, V. Papastamopoulos; Hippokration University General Hospital of Athens, Athens: H. Sambatakou, I. Mariolis; Korgialenio-Benakio Hellenic Red Cross, Athens: M. K. Lazanas, M. Chini; Syngros Hospital, Athens: S. Kourkounti, V. Paparizos; Greek SCC, National Kapodistrian University of Athens, Athens: G. Touloumi, V. Gioukari, O. Anagnostou. **India** (n=91): Institute of Infectious Diseases, Pune Maharashtra: A. Chitalikar, S. Pujari; YRGCARE Medical Centre VHS, Chennai CRS: F. Beulah, N. Kumarasamy, S. Poongulali. **Ireland** (P. Mallon, n=7): Mater Misericordiae University Hospital, Dublin: P. Mallon, P. McGettrick. **Israel** (E. Kedem, n=28): Rambam Medical Center, Haifa: E. Kedem, S. Pollack; Tel Aviv Sourasky Medical Center, Tel Aviv: D. Turner. **Italy** (G. Tambussi, n=33): Lazzaro Spallanzani IRCSS, Rome: A. Antinori, R. Libertone; Ospedale San Raffaele S.r.l., Milan: G. Tambussi, S. Nozza, M.R. Parisi. **Luxembourg** (T.

Staub, n=5): Centre Hospitalier de Luxembourg, Luxembourg: T. Staub, C. Lieunard. **Malaysia** (n=18): University Malaya Medical Centre, Kuala Lumpur: R.I.S.R. Azwa. **Mali** (S. Dao, n=41): SEREFO/ CESAC Mali, Bamako, Bamako: B. Baya, M. Cissé, D. Goita. **Mexico** (n=48): INCMNSZ (Instituto Nacional de Ciencias Médicas y Nutrición), Tlalpan D.F.: J. Sierra-Madero, M.E. Zghaib. **Morocco** (K.M. El Filali, n=44): University Hospital Centre Ibn Rochd, Casablanca: K.M. El Filali, I. Erradey, H.Himmich. **Nigeria** (n=50): Institute of Human Virology-Nigeria (IHVN), Garki, Abuja FCT: E. Ekong, N. Eriobu. **Norway** (V. Ormaasen, n=15): Oslo University Hospital, Ulleval, Oslo: V. Ormaasen, L. Skeie. **Peru** (A. La Rosa, n=215): Hospital Nacional Edgardo Rebagliati Martins, Lima, Lima: M. Espichan Gambirazzio, F. Mendo Urbina; Hospital Nacional Guillermo Almenara Irigoyen, Lima, Lima: R. Salazar Castro, J. Vega Bazalar; IMPACTA Salud y Educación, Lima, Lima: M.E. Guevara, R. Infante, J. Sanchez, M. Sanchez; IMPACTA San Miguel, Lima, Lima: R. Chinchay, J.R. Lama, M. Sanchez; Via Libre, Lima, Lima: E.C. Agurto, R. Ayarza, J.A. Hidalgo. **Poland** (A.J. Horban, n=68): EMC Instytut Medyczny SA, Wroclaw: B. Knysz, A. Szymczak; Uniwersytecki Szpital Kliniczny, Bialystok: R. Flisiak, A. Grzeszczuk; Wojewodzki Szpital Zakazny, Warsaw: A.J. Horban, E. Bakowska, A. Ignatowska. **Portugal** (L. Caldeira, n=67): Hospital Curry Cabral, Lisbon: F. Maltez, S. Lino; Hospital de Egas Moniz, Lisbon: K. Mansinho, T. Bapista; Hospital de Santa Maria, Lisbon: M. Doroana, A. Sequeira, L. Caldeira; Hospital Joaquim Urbano, Oporto: J. Mendez, R.S.E. Castro. **South Africa** (R. Wood, n=518): 1 Military Hospital, Pretoria Gauteng: S.A. Pitsi; Desmond Tutu HIV Centre - Cape Town, Cape Town, Western Province: R. Kaplan, N. Killa, C. Orrell, M. Rattley; Durban International Clinical Research Site, Durban, KwaZulu Natal: U.G. Lalloo, R. Mngqibisa, S. Pillay; Durban International Clinical Research Site WWH, Durban, KwaZulu Natal: J. Govender, M. John; University of Witwatersrand, Johannesburg, Gauteng: S. Badal-Faesen, N. Mwelase, M. Rassool. **Spain** (J.R. Arribas, n=234): Complejo Hospitalario Xeral Cies, Vigo Pontevedra: A.O. Hermida, F. Warncke; Hospital Clínic de Barcelona, Barcelona: J.M. Gatell, A. Gonzalez; Hospital Clínico San Carlos, Madrid: V. Estrada, M. Rodrigo; Hospital de la Santa Creu i Sant Pau, Barcelona: P. Domingo, M. Gutierrez; Hospital del Mar, Barcelona: H.J. Knobel, A. Gonzalez; Hospital La Paz, Madrid: J.R. Arribas, M. Montes Ramirez; Hospital La Princesa, Internal Medicine and Infectious Disease Service CRS, Madrid: I. de los Santo Gil, J. Sanz Sanz; Hospital Universitari Germans Trias i Pujol, Badalona: B. Clotet, J.M. Llibre, P. Cobarsi; Hospital Universitari Mutua Terrassa, Terrassa Barcelona: D. Dalmau, C. Badia; Hospital Universitario Doce de Octubre, Madrid: R. Rubio, M.M. del Amo; Hospital Universitario Príncipe de Asturias, Alcala de Henares Madrid: J. Sanz Moreno; Hospital Universitario y Politécnico La Fe, Valencia: J. López Aldeguer, S. Cuellar; Spanish SSC, Acoiba, Madrid: P. López, B. Portas, P. Herrero. **Sweden** (M. Gisslén, n=2): Sahlgrenska University Hospital, Sweden: M. Gisslén, L. Johansson; Skåne University Hospital, Malmö: C. Håkangård, K. Törqvist. **Switzerland** (H. Furrer, n=31): Bern University Hospital, Bern: H. Furrer, A. Rauch; Unite VIH/SIDA Genèva, Genèva: A.L. Calmy, B. Hirschel (retd), T Lecompte; University Hospital Basel, Basel: M. Stoeckle; University Hospital Zurich, Zürich: N. Muller, M. Rizo-Oberholzer; Swiss SCC, Bern University Hospital, Bern: H. Furrer, C. Bruelisauer, A. Christen, M. Lacalamita. **Thailand** (K. Ruxrungtham, n=248): Bamrasnaradura Infections Diseases Institute, Nonthaburi: W. Prasithsirikul, S. Thongyen; Chiangrai Prachanukroh Hospital, Chiang Rai: P. Kantipong, S. Khusuwan; Chonburi Regional Hospital, Chonburi: C. Bowonwatanuwong, U. Ampunpong; Chulalongkorn University Hospital, Bangkok: K. Ruxrungtham, A. Avihingsanon, W. Thiansanguankul; Khon Kaen University, Srinagarind Hospital, Khon Kaen: P. Chetchotisakd, P. Motsikapun, S. Anunnatsari; Ramathibodi Hospital, Bangkok: S. Kiertiburanakul, N. Sanmeema; Research Institute for Health Sciences (RIHES), Chiang Mai: K. Supparatpinyo, P. Sugandhavesa; Sanpatong Hospital, Chiang

Mai: V. Klinbuayaem, Y. Siriwarothai; Siriraj Hospital, Bangkok Noi: W. Ratanasuwan, T Anekthananon; Thai SCC, The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), Bangkok: W. Harnnapachewin, T. Jupimai, P. Rerksirikul. **Uganda** (P. Mugyenyi, n=349): Joint Clinical Research Center (JCRC), Kampala: P. Mugyenyi, C. Kityo, H. Mugerwa; MRC/UVRI Research Unit on AIDS, Entebbe: P. Munderi, B. Kikaire, J. Lutaakome; MRC/UVRI Research Unit on AIDS, Masaka – satellite site: Z. Anywaine. **United Kingdom** (M.A. Johnson, n=339): Barts Health NHS Trust, London: C. Orkin, J. Hand; Belfast Health and Social Care Trust (RVH), Belfast Northern Ireland: C. Emerson, S. McKernan; Birmingham Heartlands Hospital, Birmingham West Midlands: D. White, C. Stretton; Brighton and Sussex University Hospitals NHS Trust, Brighton East Sussex: M. Fisher, A. Clarke, A. Bexley; Chelsea and Westminster Hospital, London: B. Gazzard, C. Higgs, A. Jackson; Coventry and Warwickshire NHS partnership Trust, Coventry West Midlands: S. Das, A. Sahota; Gloucestershire Royal Hospital, Gloucester: A. de Burgh-Thomas, I. Karunaratne; Guy's and St.Thomas' NHS Foundation Trust, London: J. Fox, J.M. Tiraboschi; Imperial College Healthcare NHS Trust, London: A. Winston, B. Mora-Peris; Leicester Royal Infirmary, Leicester Leicestershire: M.J. Wiselka, L. Mashonganyika; Lewisham and Greenwich NHS Trust, London: S. Kegg, T. Moussaoui; North Manchester General Hospital, Manchester: E. Wilkins, Y. Clowes; Queen Elizabeth Hospital Birmingham, Birmingham West Midlands: J. Ross, J. Harding; Royal Berkshire Hospital, Reading Berkshire: F. Chen, S. Lynch; Royal Bournemouth Hospital, Bournemouth Dorset: E. Herieka, J. Ablorde; Royal Free London NHS Foundation Trust, London: M.A. Johnson, M. Tyrer, M. Youle; Sheffield Teaching Hospital NHS Foundation Trust, Sheffield South Yorkshire: D. Dockrell, C. Bowman; Southmead Hospital, Bristol: M. Gompels, L. Jennings; St. George's Healthcare NHS Trust, London: P. Hay, O. Okolo; The James Cook University Hospital, Middlesbrough Cleveland: D.R. Chadwick, P. Lambert; University College London Medical School, London: I. Williams, A. Ashraf. **United States** (K. Henry, n=507): Adult Clinical Research Center, Newark, NJ: M. Paez-Quinde, S. Swaminathan; Boston University Medical Center, Boston, MA: I. Bica, M. Sullivan; Bronx-Lebanon Hospital Center, Bronx, NY: R.B. Cindrich, L.M. Vasco; Community Research Initiative of New England, Boston, MA: J. Green, H.B. Olivet; Cooper University Hospital, Camden, NJ: J. Baxter, Y. Smith; Cornell CRS, New York, NY: V. Hughes, T. Wilkin; Denver Public Health, Denver, CO: E.M. Gardner, J. Scott; Duke University, Durham, NC: J. Granholm, N. Thielman; Florida Department of Health in Orange/Sunshine Care Center, Orlando, FL: W.M. Carter, N.D. Desai; George Washington University Medical Center, Washington, DC: D.M. Parenti, G.L. Simon; Georgetown University Medical Center, Washington, DC: P. Kumar, M. Menna; Hennepin County Medical Center, Minneapolis, MN: J. Baker, R. Givot; Henry Ford Hospital, Detroit, MI: L.H. Makohon, N.P. Markowitz; Hillsborough County Health Department, Tampa, FL: M. Chow, C. Somboonwit; Infectious Disease Associates of Northwest Florida, Pensacola, FL: A.B. Brown, B.H. Wade; Lurie Children's Hospital, Chicago, IL: J. Jensen, A. Talsky; Maternal, Child and Adolescent Center for ID/Virology USC, Alhambra, CA: A. Kovacs, L. Spencer; Mayo Clinic, Rochester, MN: S. Rizza, Z. Temesgen; Medical College of Wisconsin, Milwaukee, WI: M. Frank, S. Parker; Montefiore Medical Center, Bronx, NY: C. Rosario, J. Shuter; Mt Sinai Hospital, Chicago, IL: K. Rohit, R. Yogev; National Military Medical Center, Bethesda, MD: I. Barahona, A. Ganesan; Naval Medical Center Portsmouth NMCP, Portsmouth, VA: S. Banks, T. Lalani; Naval Medical Center San Diego NMCSD, San Diego,CA: M.F. Bavaro, S. Echols; NICE, Southfield, MI: M. Farrough, R.D. MacArthur; NIH, Bethesda, MD: R.T.Davey Jr., R. McConnell; Ohio State University, Columbus, OH: H. Harber, S.L. Koletar; Orlando Immunology Center, Orlando, FL: E. DeJesus, A.F. Garcia; Regional Center for Infectious Disease, Greensboro, NC: K. Epperson, C.N. Van Dam; San Antonio Military Health System,

JBSA Fort Sam Houston, TX: J.F. Okulicz, T.J. Sjoberg; San Juan Hospital, San Juan, PR: M. Acevedo, L. Angeli; St. Jude Children's Research Hospital, Memphis, TN: P.M. Flynn, N. Patel; Temple University, Philadelphia, PA: C. Geisler, E. Tedaldi; Texas Children's Hospital- Baylor College of Medicine, Houston, TX: C. McMullen-Jackson, W.T. Shearer; The Research & Education Group, Portland, OR: M.D. Murphy, S.M. Sweek; Tulane University Health Sciences Center, New Orleans, LA: D. Mushatt, C. Scott; UCLA CARE 4 Families, Los Angeles, CA: M. Carter, J. Deville; UCSD Mother-Child-Adolescent HIV Program, San Diego, CA: S.A. Spector, L. Stangl; University of Florida, Department of Pediatrics, Jacksonville, FL: M.H. Rathore, K. Thoma; University of Florida, Jacksonville, FL: M. Sands, N. Wilson; University of Illinois at Chicago, Chicago, IL: R.M. Novak, T. Pearson; University of Miami, Miami, FL: M.A. Kolber, T. Tanner; University of North Carolina, Chapel Hill, NC: M. Chicurel-Bayard, E. Hoffman; University of North Texas Health Science Center, Fort Worth, TX: I. Vecino, S.E. Weis; University of Puerto Rico, San Juan, PR: I. Boneta, J. Santana; University of Texas Southwestern Medical Center, Dallas, TX: M.K. Jain, M. Santos; Veterans Affairs Greater LA Healthcare System, Los Angeles, CA: M.B. Goetz, W.L. Rossen; Virginia Commonwealth University, Richmond, VA: D. Nixon, V. Watson; Wake County Human Services, Raleigh, NC: D. Currin, C. Kronk; Wake Forest University Health Sciences, Winston-Salem, NC: L. Mosley, A. Wilkin; Washington DC Veterans Administration, Washington, DC: A.M. Labriola, D.W. Thomas; Yale University School of Medicine, New Haven, CT: D. Chodkowski, G. Friedland.

Table S1: Cause of CVD case status:

Cause of CVD	N
MI	26
Coronary Revascularization	64
Stroke	24
CVD Death or Unwitnessed Death and cause unknown	17
CVD Total	131

Table S2: Average variable importance in projection (VIP) for all 107 proteins. Some proteins were represented in more than one panel.

Protein	Average VIP	Protein	Average VIP	Protein	Average VIP	Protein	Average VIP	Protein	Average VIP
GT	2.24	PLA2G7	1.12	CCL19	0.94	CST5	0.84	PCSK9	0.79
ITGA11	1.43	EPHB4	1.11	KIM1	0.93	CCL3	0.83	COL18A1	0.79
ICAM1	1.39	CDCP1	1.11	IL10RB	0.93	LAMP3	0.83	REG3A	0.79
BTN3A2	1.30	TNFR1	1.06	TRAILR2	0.92	PGF	0.82	CPA1	0.79
SCGB3A2	1.28	IL6	1.06	MCP1	0.92	HNMT	0.82	PRSS2	0.78
TNFR2	1.28	UPAR	1.05	PRSS8	0.91	GAL4	0.82	KRT19	0.77
TNFRSF10A	1.28	CST3	1.04	CKAP4	0.90	IL8	0.82	ADM	0.77
CD83	1.28	CCL25	1.02	CDH1	0.89	TFF3	0.82	CCL11	0.77
GAS6	1.23	TCN2	1.01	CCL18	0.89	IL6	0.82	CCL20	0.76
EFEMP1	1.22	CHI3L1	1.00	SPON2	0.89	CCL14	0.810	MCP3	0.76
HOSCAR	1.20	UPA	1.00	MCP1	0.88	MMP10	0.81	CCL11	0.76
LILRB4	1.18	IL18R1	0.99	NTPROBNP	0.88	CXCL16	0.81	ST2	0.76
FAM3B	1.17	CX3CL1	0.97	LIFR	0.87	TNFSF13B	0.81	CPB1	0.75
GDF15	1.17	CTSZ	0.97	IL2RA	0.86	CTSL1	0.81	AREG	0.75

HGF	1.16	IL6	0.97	GAL9	0.85	PON3	0.81	SPON1	0.74
TNFRSF9	1.16	NCR1	0.96	IL17C	0.85	MMP7	0.80	AMBP	0.74
GRN	1.16	VEGFA	0.95	IGLC2	0.84	CLEC6A	0.80	TIMD4	0.74
TIMP1	1.15	IGFBP7	0.95	FLT3L	0.84	FGF21	0.80	BNP	0.73
IL18BP	1.13	LTBR	0.94	FGF23	0.84	ACE2	0.80	SIT1	0.72
CSF1	1.12	OPG	0.94	OPG	0.84	CLEC7A	0.79	RARRES2	0.72
								QPCT	0.71
								FGF21	0.71
								CLEC4D	0.68
								CHIT1	0.68
								CLEC4C	0.66
								ITM2A	0.66
								DPP10	0.63

Table S3: Summary statistics for the number of times elastic net model had non-zero coefficients across the 200 bootstrap sets.

Protein	Counts	Proportions
HGF	199	0.995
IL6	193	0.965
FAM3B	187	0.935
SCGB3A2	187	0.935
GT	186	0.930
CCL25	180	0.900
ITGA11	179	0.895
PLA2G7	167	0.835
GDF15	159	0.795
ICAM1	146	0.730
TNFR1	140	0.700
GRN	138	0.690
EFEMP1	128	0.640
UPAR	127	0.635
CDCP1	123	0.615
CST3	123	0.615
LILRB4	119	0.595
CSF1	119	0.595
BTN3A2	116	0.580
TCN2	116	0.580
TIMP1	115	0.575
CD83	114	0.570
GAS6	114	0.570
IL18BP	113	0.565
TNFRSF9	112	0.560
HOSCAR	112	0.560
TNFRSF10A	111	0.555
TNFR2	109	0.545
EPHB4	109	0.545

Table S4: Conditional logistic regression model of CVD on standardized protein score. (This was used to generate forest plot in Figure 1. Here, n=375 as there were 15 samples with missing values.) OR for similar model with viral load categorized as: viral load (>=500 copies/ML) vs viral load (< 500 copies/ML) was 1.31 (CI: 0.60-2.84).

Variable	Odds Ratio	Std Error	Pr(>|z|)	LCI	UCI
CD4	1.00	0.00	0.95	1.00	1.00
RNA	1.00	0.00	0.85	1.00	1.00
Females vs Males	0.53	0.47	0.18	0.21	1.33
Age	1.20	0.05	<0.01	1.08	1.33
BMI	1.01	0.03	0.63	0.96	1.07
Diabetes	0.72	0.56	0.56	0.24	2.16
Black Race	1.19	0.40	0.67	0.54	2.59
Lipid-lowering medication	0.96	0.38	0.92	0.45	2.04
BP-lowering medication	1.46	0.39	0.33	0.68	3.15
CVD	3.22	0.71	0.10	0.81	12.90
Protein Score	2.17	0.16	<0.01	1.58	2.99

Table S5: Odds ratios and AUC from categorizing protein score

Protein Score	**Case individuals (n)**	**Control individuals (n)**	**Odds ratio (95% CI)**	**AUC**
Median				0.74
Below	38	157	1.00	
Above	93	102	3.15 (1.83- 5.41)	
Top 25% vs bottom 75%				0.69
1 (Top)	55	43	2.91 (1.65,5.12)	
2	76	216	1.00	
Above 0 vs below 0 protein score				0.75
Below	39	159	1.00	
Above	92	100	3.20 (1.86 to 5.49)	

Table S6: Incremental contribution of proteins and protein score to CVD risk when added to the baseline model. The baseline model includes the coagulation biomarker D-dimer. Here, n=364.

Model	AUC	LCI	UCI	Change in AUC from Baseline	NRI among cases	NRI among controls	Overall NRI
Baseline*	0.69	0.60	0.78	-	-	-	-
+ FAM3B	0.73	0.65	0.81	0.04	0.15(-0.03,0.32)	0.02(-0.10,0.15)	0.17(-0.04,0.39)
+ ITGA11	0.70	0.61	0.79	0.01	0.08(-0.09,0.26)	-0.01(-0.13,0.12)	0.07(-0.14,0.29)
+ IL6	0.70	0.61	0.78	0.01	0.15(-0.03,0.32)	0.12(-0.01,0.24)	0.26(0.05,0.48)
+ HGF	0.73	0.64	0.81	0.04	0.23(0.06,0.40)	0.11(-0.02,0.23)	0.34(0.12,0.55)
+ CCL25	0.69	0.60	0.78	0.00	0.02(-0.16,0.19)	0.15(0.02,0.27)	0.17(-0.05,0.38)
+ GT	0.73	0.65	0.82	0.05	0.28(0.11,0.45)	0.15(0.02,0.27)	0.43(0.22,0.64)
+ PLA2G7	0.72	0.64	0.80	0.03	0.16(-0.01,0.34)	0.12(0.00,0.25)	0.29(0.07,0.50)
+SCGB3A2	0.71	0.63	0.80	0.03	0.10(-0.08,0.27)	0.12(-0.01,0.24)	0.21(0.00,0.43)
+ Protein score from all 8 proteins	0.73	0.65	0.82	0.05	0.36 (0.20, 0.53)	0.24 (0.12,0.36)	0.60 (0.40,0.81)

Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, prior history of CVD, lipid lowering medication, blood pressure lowering medication and D-dimer (log2 transformed).

The proteins FAM3B, IL6, HGF, GT, and PLA2G7 were each statistically significant (p-value<0.05) when added to the baseline model.

Protein score was statistically significant ($p < 0.00001$) when added to the baseline model. Odds ratio for protein score: 2.09 (CI: 1.52, 2.88)

Of note, D-dimer was statistically significant (p-value =0.03) in the baseline model but not in the baseline + protein score model (p-value>0.05).

Integrated Discriminant Index when protein score was added to the baseline* model was 0.08 (0.05, 0.10).

Table S7: Incremental contribution of proteins and protein score to CVD risk when added to the baseline model. The baseline model includes the inflammatory biomarker hsCRP. Here, n=364.

Model	AUC	LCI	UCI	Change in AUC from Baseline	NRI among cases	NRI among controls	Overall NRI
Baseline*	0.73	0.65	0.81	-	-	-	-
+ FAM3B	0.72	0.63	0.80	-0.01	0.26(0.09,0.43)	0.02(-0.10,0.15)	0.29(0.07,0.50)
+ ITGA11	0.73	0.64	0.81	0.00	0.08(-0.09,0.26)	0.01(-0.12,0.13)	0.09(-0.13,0.31)
+ IL6	0.70	0.62	0.79	-0.03	0.03(-0.14,0.21)	0.13(0.01,0.26)	0.17(-0.05,0.38)
+ HGF	0.72	0.64	0.80	-0.01	0.21(0.04,0.39)	0.12(-0.01,0.24)	0.33(0.11,0.54)
+ CCL25	0.73	0.64	0.81	-0.01	0.05(-0.13,0.23)	0.12(0.00,0.25)	0.17(-0.04,0.39)
+ GT	0.73	0.65	0.81	0.00	0.30(0.13,0.46)	0.16(0.03,0.28)	0.45(0.24,0.66)
+ PLA2G7	0.72	0.63	0.80	-0.01	0.16(-0.01,0.34)	0.14(0.02,0.27)	0.30(0.09,0.52)
+SCGB3A2	0.72	0.62	0.79	-0.02	0.13(-0.04,0.31)	0.12(0.00,0.25)	0.26(0.04,0.47)
+ Protein score from all 8 proteins	0.75	0.66	0.83	0.02	0.37 (0.20, 0.53)	0.19 (0.07,0.31)	0.56 (0.35,0.76)

Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, prior history of CVD, lipid lowering medication, blood pressure lowering medication and hsCRP (log2 transformed).

The proteins FAM3B, IL6, HGF, GT, and PLA2G7 were each statistically significant (p-value<0.05) when added to the baseline model. SCGB3A2 was marginally significant (p-value=0.051).

Protein score was statistically significant ($p < 0.00001$) when added to the baseline model. Odds ratio for protein score: 2.14 (CI: 1.54, 2.97).

Of note, hsCRP was not statistically significant in both baseline and baseline + protein score models (p-value>0.05).

Integrated Discriminant Index when protein score was added to the baseline* model was 0.08 (0.05, 0.10).

Table S8: Incremental contribution of protein factors to CVD risk when added to baseline model. Analyses restricted to PLWH on ART at baseline, n=269

Model	AUC	LCI	UCI	Change in AUC from Baseline	NRI among cases	NRI among controls	Overall NRI
Baseline*	0.70	0.60	0.80	-	-	-	-
+ FAM3B	0.69	0.59	0.79	-0.01	0.09 (-.12,.29)	0.01 (-.14,.15)	0.09 (-.16,.34)
+ ITGA11	0.69	0.59	0.79	-0.01	0.13 (-0.07,0.33)	-0.01 (-0.15,0.14)	0.12 (-0.13,0.38)
+ IL6	0.69	0.59	0.79	-0.01	0.35 (0.16,0.54)	0.18 (0.03,0.32)	0.523 (0.28,0.76)
+ HGF	0.69	0.59	0.79	-0.01	0.09 (-0.12,0.29)	0.09 (-0.06,0.23)	0.17 (-0.08,0.42)
+ CCL25	0.70	0.60	0.80	0.01	-0.02 (-0.23,0.18)	0.11 (-0.04,0.25)	0.09 (-0.17,0.34)
+ GT	0.71	0.61	0.81	0.01	0.30 (-0.11,0.50)	0.10 (-0.05,0.24)	0.40 (0.16,0.64)
+ PLA2G7	0.69	0.59	0.79	-0.01	0.17 (-0.03,0.38)	0.13 (-0.02,0.28)	0.30 (0.06,0.55)
+SCGB3A2	0.71	0.61	0.81	0.01	0.15 (-0.05,0.35)	0.11 (-0.04,0.25)	0.26 (0.01,0.51)
+ Protein score from all 8 proteins	0.74	0.64	0.83	0.04	0.28 (-0.09, 0.48)	0.16 (-0.02, 0.31)	0.45 (-0.20, 0.69)

Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, prior history of CVD, lipid lowering medication, and blood pressure lowering medication.

The proteins IL6, HGF, and GT were each statistically significant (p-value<0.05) when added to the baseline model. PLA2G7 was marginally significant (p-value =0.06).

Protein score was statistically significant ($p < 0.01$) when added to the baseline model. Odds ratio for protein score: 1.93 (CI: 1.35-2.77); Integrated Discriminant Index: 0.06 (0.04-0.09)

Table S9: Incremental contribution of protein factors to CVD risk when added to baseline model. Analyses restricted to individuals with no prior history of CVD (n=356)

Model	AUC	LCI	UCI	Change in AUC from Baseline	NRI among cases	NRI among controls	Overall NRI
Baseline*	0.66	0.56	0.75	-	-	-	-
+ FAM3B	0.67	0.58	0.76	0.01	0.24 (0.06, 0.42)	0.04 (-0.08, 0.16)	0.28 (0.06,0.50)
+ ITGA11	0.65	0.56	0.75	-0.01	0.05 (-0.13,0.24)	0.00 (-0.12,0.12)	0.05 (-0.17, 0.28)
+ IL6	0.67	0.58	0.77	0.01	0.33 (0.15, 0.50)	0.17 (0.05, 0.29)	0.50 (0.28, 0.71)
+ HGF	0.67	0.58	0.77	0.01	0.22 (0.04, 0.40)	0.11 (-0.01, 0.24)	0.33 (0.11, 0.55)
+ CCL25	0.67	0.57	0.76	0.01	0.11 (-0.08, 0.30)	0.12 (-0.00, 0.25)	0.23 (0.01, 0.45)
+ GT	0.68	0.59	0.77	0.02	0.24 (0.06,0.42)	0.08 (-0.04, 0.21)	0.32 (0.10, 0.54)
+ PLA2G7	0.70	0.61	0.79	0.04	0.22 (0.04, 0.40)	0.11 (-0.02, 0.23)	0.32 (0.10, 0.54)
+SCGB3A2	0.68	0.59	0.78	0.03	0.18 (-0.00, 0.37)	0.18 (0.06, 0.30)	0.36 (0.14, 0.58)
+ Protein score from all 8 proteins	0.70	0.61	0.79	0.04	0.46 (0.29, 0.62)	0.26 (0.14,0.38)	0.72 (0.51, 0.92)

Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, lipid lowering medication, and blood pressure lowering medication.

The proteins FAM3B, IL6, HGF, CCL25, GT, PLA2G7 and SCGB3A2 were each statistically significant (p-value<0.05) when added to the baseline model.

Protein score was statistically significant ($p < 0.00001$) when added to the baseline model. Odds ratio for protein score: 2.16 (CI: 1.57-2.96)

Integrated Discriminant Index when protein score was added to baseline model: 0.010 (0.07-0.12)

Table S10: Conditional logistic regression model of CVD on standardized protein score restricted to patients with smoking status reported at baseline. The sample size is 149 (50 CVD cases and 99 CVD controls). Here, we adjust for smoking status at baseline.

Variable	Odds Ratio	Std Error	Pr(>|z|)	LCI	UCI
CD4	1.00	0.00	0.62	1.00	1.00
RNA	1.00	0.00	0.56	1.00	1.00
Females vs Males	0.26	0.78	0.09	0.06	1.21
Age	1.25	0.11	0.04	1.01	1.53
BMI	1.06	0.06	0.34	0.95	1.18
Diabetes	0.63	0.93	0.62	0.10	3.90
Black Race	1.93	0.61	0.28	0.58	6.43
Lipid-lowering medication	1.42	0.71	0.63	0.35	5.71
BP-lowering medication	1.02	0.55	0.97	0.35	2.98
CVD	2.55	0.96	0.33	0.39	16.62
Smoking status (Yes vs No)	2.11	0.62	0.23	0.63	7.10
Protein Score	2.85	0.35	<0.01	1.45	5.63

Table S11: Incremental contribution of protein factors to CVD risk when added to baseline model that includes smoking status. The sample size is 149 (50 CVD cases and 99 CVD controls).

Model	AUC	LCI	UCI	Change in AUC from Baseline	NRI among cases	NRI among controls	Overall NRI
Baseline* (includes smoking status)	0.79	0.68	0.91	-	-	-	-
+ FAM3B	0.84	0.73	0.94	0.04	0.48(0.24,0.72)	0.07(-0.12,0.27)	0.55(0.24,0.86)
+ ITGA11	0.77	0.65	0.90	-0.02	0.24(-0.03,0.51)	0.05(-0.14,0.25)	0.29(-0.04,0.62)
+ IL6	0.77	0.65	0.90	-0.02	0.12(-0.16,0.40)	0.09(-0.10,0.29)	0.21(-0.13,0.55)
+ HGF	0.76	0.64	0.89	-0.03	0.28(0.01,0.55)	0.15(-0.04,0.34)	0.43(0.10,0.76)
+ CCL25	0.81	0.70	0.93	0.02	0.12(-0.16,0.40)	0.13(-0.06,0.32)	0.25(-0.08,0.59)
+ GT	0.81	0.70	0.93	0.02	0.08(-0.20,0.36)	0.11(-0.08,0.30)	0.19(-0.15,0.53)
+ PLA2G7	0.82	0.71	0.94	0.03	0.20(-0.07,0.47)	0.09(-0.10,0.29)	0.29(-0.04,0.62)
+SCGB3A2	0.77	0.65	0.89	-0.02	-0.12(-0.40,0.16)	0.13(-0.06,0.32)	0.01(-0.32,0.35)
+ Protein score from all 8 proteins	0.81	0.69	0.94	0.02	0.44(0.19, 0.69)	0.19(0.00,0.38)	0.63 (0.32, 0.95)

Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, prior history of CVD, lipid lowering medication, blood pressure lowering medication, and smoking status.

No individual protein was statistically significant (p-value> 0.05) when added to the baseline model that included smoking status.

Protein score was statistically significant (p =0.0025) when added to the baseline model that included smoking status. Odds ratio for protein score: 2.56(CI: 1.39 – 4.70)

Integrated Discriminant Index when protein score was added to baseline model: 0.10 (0.05-0.14)

Table S12: Odds ratios and AUCs for discovery and validation sets.

Model	Discovery	Internal Validation
Baseline	0.69 (95% CI:0.60-0.78)	0.74 (95% CI: 0.73-0.74)
Baseline + Protein Score	0.73 (95% CI:0.65-0.81)	0.79 (95% CI: 0.78- 0.80)

Odds ratios for protein score in validation set is 2.78 (CI: 2.67, 2.90) and discovery set is 2.17 (CI: 1.58-2.99)
Baseline* is a model with the following variables: CD4, RNA, sex, age, BMI, diabetes status at baseline, prior history of CVD, lipid lowering medication, and blood pressure lowering medication,

Figure S1: Schematic representation of statistical approach

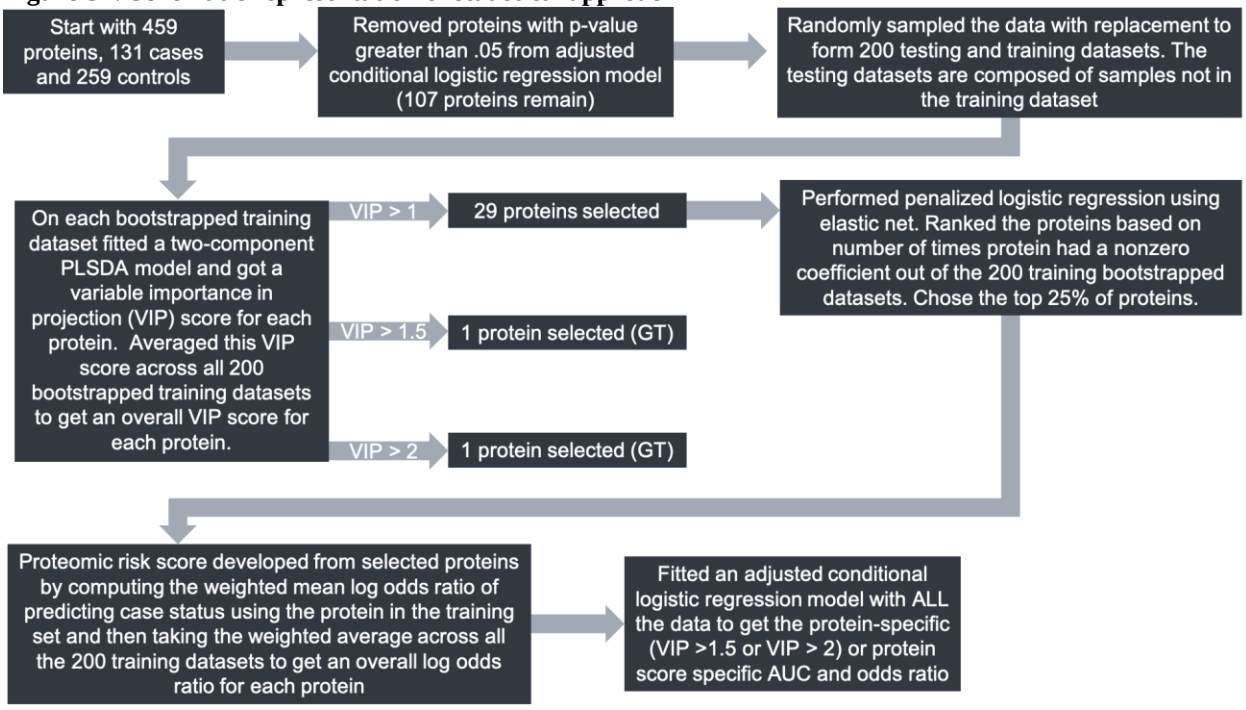
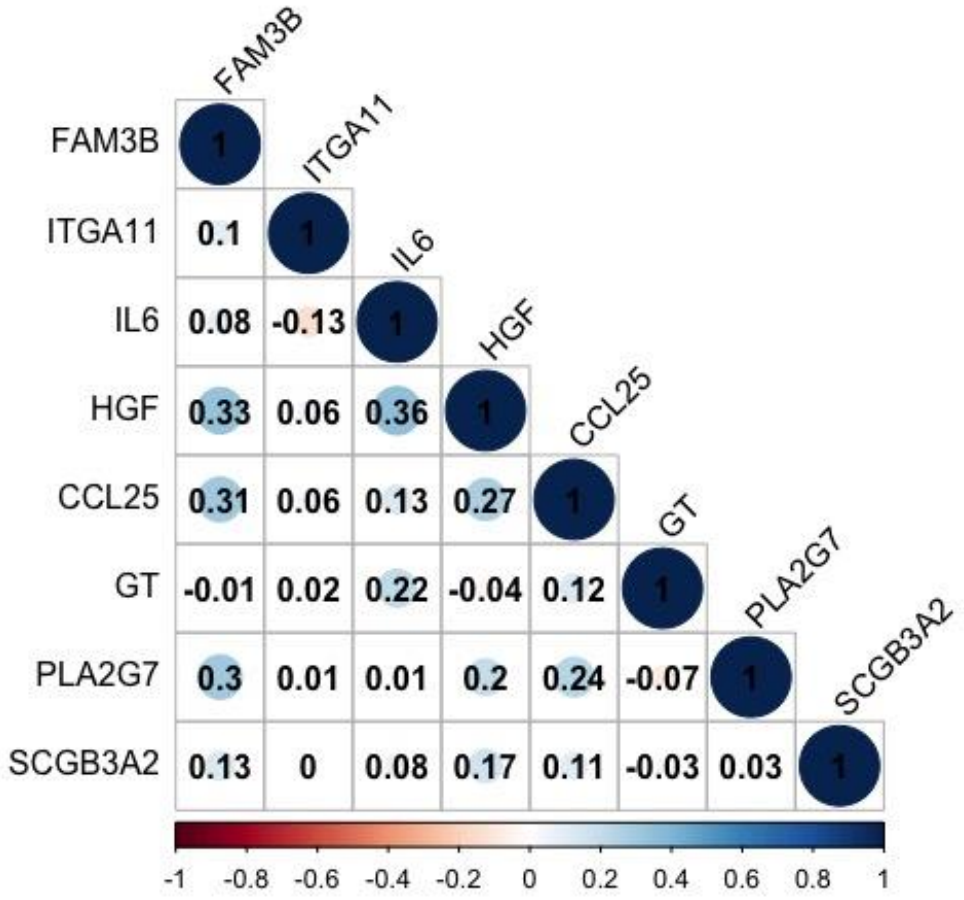


Figure S2: Correlation between pairs of proteins used in the protein score.



C. Description of Proteins Used in the Protein Score

Inflammation Panel:

Hepatocyte Growth Factor (HGF):
The protein HGF and its receptor c-MET are involved in tissue repair and respond to tissue injury. HGF has been proposed as a potential clinical biomarker for CVD[45] HGF has already been shown to be associated with stroke, CHD, atherosclerosis, and the progression of atherosclerosis in an ethnically diverse, general population.[31,32]

C-C motif chemokine 25 (CCL25):
CCL-25 is involved in T-cell development. T-cells are involved in the development and progression of CVDs, including atherosclerosis.[36]

Immune Response Panel:

Protein FAM3B (FAM3B):
Vascular smooth muscle cells (VSMCs) play an important role in the development of CVDs. [35] FAM3B is secreted with insulin and regulates glucose homeostasis. As such, dysregulation of FAM3B is associated with diabetes, which is a risk factor known to be associated with CVD. [35]

Integrin α11 (ITGA11):
Integrins have two functions: 1) extracellular matrix cell attachment and 2) signal transduction from the extracellular matrix.[37] In mouse models, overexpression of integrin α11 induces cardiac fibrosis and left ventricular hypertrophy.[38]

Interleukin-6 (IL6):
IL6 has been extensively studied in both healthy and HIV positive populations. IL6 is a marker of inflammation and coagulation. Increased levels of plasma IL6 has been shown to associated with increased risk of CVD, atherosclerosis, and mortality in an HIV positive population even when treated with ART[17,29,30]

Cardiovascular 2 Panel:

Gastrotropin (GT):
Gastrotropin, also known as the ileal fatty acid binding protein, (FABP6) is a member of the fatty acid-binding protein (FABPs) family, which regulates general metabolic function via FABPs central role in fatty acid transport, metabolism, and storage. FABPs have been associated with a number of diseases including cardiovascular disease and are thought to serve an integral role in metabolic function.[39] FABP6 is more specifically known to be involved in bile acid metabolism. There has been shown to be a protective association between FABP6 Thr79Met polymorphism and incident type 2 diabetes.[40]

Cardiovascular 3 Panel

Platelet-activating factor acetylhydrolase (PLA2G7):

PLA2G7 is found in both high-density lipoprotein (HDL) and low-density lipoprotein (LDL). In population studies it has been shown that overexpression of PLA2G7 is associated with increased coronary heart disease (CHD). [33, 34] It is thought that with individuals with low LDL cholesterol levels it can help predict CHD risk. [33,34]

Cardiometabolic Panel

Secretoglobin Family 3A Member (SCGB3A2):

A case-control study in a Korean population on SNPs in the SCGB3A2 gene potentially contributes to susceptibility to asthma. [41] The SCGB3A2 gene is also known as the uterus globulin associated protein 1 (UGRP1) found that UGRP1 may be able to predict graves' disease patients who develop hypothyroidism.[42]

D. **Sensitivity and Subgroup Analyses**

When we added the inflammatory biomarkers D-dimer and hsCRP individually (as $\log_2$-transformed measures) to the baseline model and we considered the protein score + baseline model, the protein score was again statistically significant ($p < 0.0001$) [Tables S6-S7]. Further, the AUCs and NRIs estimates from the baseline + protein score model were again higher than those from the baseline + individual proteins models. With the exception of the protein SCGB3A2, the proteins FAM3B, IL-6, HGF, GT, and PLA2G7 were each statistically significant (p-value<0.05) when added to the baseline model.

Considering the 269 participants with complete data (92 cases and 177 controls) who were on ART at baseline, we observed that a one standard deviation increase in the protein score was associated with an odds ratio for CVD of 1.93 (CI: 1.35 - 2.78) [Table S8] compared to 2.17 (CI: 1.58 - 2.99) [Figure 1] in the combined data (i.e. data on those with ART and no ART at baseline). Unlike in the combined data where IL6 was likely driving the effect of the protein score, in this subpopulation, no individual protein had an AUC that was comparable to the protein score (Table S8). Further, the AUC for the baseline model was 0.70 (CI: 0.60- 0.80), and the AUC for the baseline + protein score model was 0.74(CI: 0.64 - 0.83). There was a 16.7% increase in prediction when the analysis was restricted to those on ART at baseline, compared to a 17.4% increase in prediction for the full population. The NRI for the protein score + baseline model was 0.45 (CI: 0.20 - 0.69) in this subgroup as compared to 0.66 (CI: 0.46 - 0.86) in the combined data. Table S8 gives the NRI and IDI estimate for the protein score + baseline model restricted to individuals on ART at baseline as well as the incremental contributions of each protein.

When we restricted our analyses to individuals with no history of CVD (n=356, 110 cases and 246 controls), the protein score was again statistically significant (Table S9). A one standard deviation increase in the protein score was associated with an odds ratio for CVD of 2.16 (CI: 1.57-2.96) compared to 2.17 (CI: 1.58 - 2.99) in the combined data. The AUC for the baseline model was 0.66 (CI: 0.56-0.75). The AUC when PLA2G7 was added to the baseline model was the same as the AUC when the protein score was added to the baseline model (0.70) but the protein score + baseline model had a higher NRI (0.72 vs 0.32); the NRI for the full population was 0.66 (CI: 0.46 - 0.86).

We considered a sensitivity analysis that included individuals with smoking status. Here, the sample size was 149 with 50 CVD cases and 99 CVD controls. When we added smoking status to the baseline model, the protein score from the protein score + baseline model was statistically significant (p-value =0.0024) [Table S10]. On the other hand, no individual protein achieved statistical significance when each was added to the baseline model that included smoking status as a covariate. A one standard deviation increase in the protein score was associated with an odds ratio for CVD of 2.85 (CI: 1.45- 5.63). The AUC for the baseline model was 0.79 (CI: 0.68- 0.91), and the AUC for the baseline + protein score model was 0.81 (CI: 0.69 - 0.94). This corresponded to a 6.8% increase in prediction compared to a 17.4% increase for the full population. Further, FAM3B, CCL25, GT, and PLA2G7 had AUC values that were similar or slightly higher than the AUC from the protein score + baseline model (Table S11). However, the NRI for these individual proteins were lower than the NRI from the baseline + protein score model.