Medical Xpress

Biostatistics research could improve resource use in AIDS treatment in poor nations

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In wealthy countries, antiretroviral therapy (ART) has transformed AIDS into an often-manageable chronic condition, as patients can receive both the therapeutics and the constant monitoring that ensures the therapies remain effective. Developing nations, however, frequently need to balance expansion of treatment access versus the economic resources to sustain the routine blood testing that ART requires. At a time when global funding commitments for AIDS therapy programs are being cut, there is a great need to find new strategies to maximize available resources.

Now, researchers at The Wistar Institute and the University of Massachusetts Amherst, with global collaborators, introduce a new "prediction-based classification" (PBC) system that could potentially reduce the burden of monitoring patients on ART experienced by medical laboratories in developing nations. Their findings, published today in the journal *PLoS Medicine,* introduce a mathematical system that can predict which patients on antiretroviral therapy may not experience a rise in CD4 T cells (a type of white blood cell), thereby triaging tests only to those who may need it.

Their study, a retrospective analysis that applies the new approach based on measuring total white blood cell count measures only, potentially could eliminate nearly 54 percent of CD4 tests. As a result, the proposed algorithm could allow doctors in resource-deprived regions to forgo costly routine CD4 counts, investing the savings into expanding their CD4 count test capacity, and increase the number of people who can

receive life-saving ART all within the same laboratory infrastructure.

Currently, World Health Organization standards recommend that patients go on antiretroviral therapy when their CD4 T counts drop below a threshold of 350 cells per microliter of blood, and patients on ART require routine CD4 count testing to see if they begin developing resistance to their current drug regimen.

"A CD4 count is the standard marker for immune recovery after ART treatment as a reliable indicator of patient health, but it is also a capacity and resource-intensive process," said Luis J. Montaner, senior author of the study, Wistar professor, and director of the Institute's HIV-1 Immunopathogenesis Laboratory. "Our algorithm could be used as a triage tool to direct available laboratory CD4 testing capacity to high-priority individuals, that is, those likely to experience a dangerously low CD4 count."

"We think that, with additional testing and refinement, prediction-based classification could increase the overall capacity of existing laboratory infrastructure in poorer countries," Montaner said. "Our data raises the possibility that we could save money in order to save more lives."

"By using these new statistical tools, we can decide how to allocate resources to the patients who need them the most," added Andrea S. Foulkes, Associate Professor of Biostatistics at the University of Massachusetts Amherst School of Public Health and Health Sciences. "In other words, we identify which patients are most likely to benefit from secondary testing."

According to Montaner, their prediction-based classification system uses commonly measured indicators (such as white blood cell counts and relative percentages of white blood cell types) to reliably determine how a given patient will progress over time.

To test their algorithm, the researchers studied repeated CD4 count measurements from over 1,000 HIV-infected people from seven sites around the world (including North/South America, Europe, Africa, and Asia). Starting with the CD4 count taken as patients begin treatment but only using less costly tests for white blood cell counts afterwards, the tool correctly classified about 92 percent of the CD4 cell counts that were below 200 cells per microliter in the first year of ART. With this threshold, the researchers estimate a potential savings in CD4 testing capacity of 54 percent. With a CD4 count threshold of 350 cells per microliter, the potential savings in testing capacity was about 34 percent. The results over a three-year follow-up were similar.

Prediction based classification is intended to help prioritize patients who may need routine CD4 count tests, but not as a replacement for CD4 testing, Montaner says.

The researchers say that additional studies are now needed to demonstrate the feasibility, clinical effectiveness, and cost-effectiveness of the PBC approach. "Before it can be put into practice, we need to find out whether the tool can be used over extended periods of time, and to see whether the accuracy of its predictions can be improved by, for example, adding in periodic CD4 testing," Montaner said.

More information: Azzoni L, Foulkes AS, Liu Y, Li X, Johnson M, et al. (2012) Prioritizing CD4 Count Monitoring in Response to ART in Resource-Constrained Settings: A Retrospective Application of Prediction-Based Classification. PLoS Med 9(4): e1001207.doi:10.1371/journal.pmed.1001207 . www.plosmedicine.org/article/info %3Adoi%2F10.1371%2Fjournal.pmed.1001207