June 8, 2009

Definition of Highly Active Antiretroviral Therapy (HAART): While this term is quickly becoming anachronistic, we maintain use of this term for use of combination antiretroviral therapy to distinguish it from truly 'suboptimal' monotherapy or combinations.

Definition used subsequent to April 1, 2008 (visits 28+):

The following is a paragraph defining HAART for the "Methods Section" of WIHS publications (as of April 1, 2008) that are related to HAART.

> The definition of HAART was guided by the DHHS/Kaiser Panel [DHHS/Kaiser 2008] guidelines and is defined as: the reported use of three or more antiretroviral medications, one of which has to be a PI, an NNRTI, one of the NRTIs abacavir or tenofovir, an integrase inhibitor (e.g., raltegravir), or an entry inhibitor (e.g., Maraviroc or enfuvirtide).

WDMAC has implemented the new HAART definition in the VERTAIDSDRUG summary file (in the THRPY and THRPYV variables) across all visits, and a new version of VERTAIDSDRUG is now available for use in analyses (Comm Memo #542). The summary file HIVHIST also has been revised, to reflect the changes in HAART-related variables, such as first HAART use. Please discontinue using the VERTAIDSDRUG and HIVHIST files included with the V28 Data Freeze CD.

Summary statistics for the updated definition in comparison to the old definition of HAART, used for visits 21 through 27, are as follows:

(1) The updated definition encompasses the old definition of HAART — everyone who was previously identified as taking HAART is also identified as such using the new definition.

(2) As of visit 28, there are 1,452 visits amongst HIV+. Most of these are HAART (75%) or No Therapy (21%) visits. Of the remaining women, 29/41 (71%) individuals who were labeled COMBO using the old definition have changed to HAART. This is primarily due to the addition of women on integrase and entry inhibitors, drugs that were not included in the prior definition of HAART. The remaining 29% stay on COMBO therapy. There are also a few women (10) who were classified as monotherapy under the old definition — 5/10 have changed to HAART therapy (these are women reporting use of three PIs by themselves).

(3) Overall the entirety of WIHS, 41,533 person-visits have been completed. A little over 10% (4,725) were non-HAART COMBO visits using the old definition. Using the new definition, 10% (N=472) switch from COMBO to HAART; the remaining 90% remain as non-HAART COMBO. There is a smattering of additional changes (N<30).

(4) Similar results are seen for the "at-visit" therapy variables (e.g., for THRPYV, in addition to THRPY).

The revised WIHS HAART definition is concordant with what many other studies, including the European groups, have been doing for years. While the new HAART definition may contain some combinations that are more or less efficacious, investigators should note that report of antiretroviral use is not the same as ensuring the antiretroviral is behaving in an "effective" manner — resistance measures will remain largely unmeasured in WIHS as they are prohibitively expensive, but we have both adherence and, perhaps more importantly, viral load data that supplement the reported use of therapy. Several WIHS papers have used combinations of THRPYV = 3 and VLOAD $\leq$ 80 to define individuals on "effective HAART," and WDMAC recommends that WIHS investigators do this more frequently in the future.

When defining ARV usage, an investigator may still opt to use the “old” HAART definition which was in place between visits 21 and visit 27. The variable THRPYONE reflects this old coding — details are as follows.

Definition used October 1, 2004, through March 31, 2008 (visits 21 through 27):

The following is a paragraph defining HAART for the "Methods Section" of WIHS publications (as of October 1, 2004). The percentages are based on total HIV+ person-visits with available therapy data from July 1995 to September 2004. The first paragraph may be used for papers that are related to HAART.

> The definition of HAART was guided by the DHHS/Kaiser Panel [DHHS/Kaiser 2004] guidelines and defined as: (a) two or more NRTIs in combination with at least one PI or one NNRTI (88% of observations classified as HAART); (b) one NRTI in combination with at least one PI and at least one NNRTI (5%); (c) a regimen containing ritonavir and saquinavir in combination with one NRTI and no NNRTIs (1%); and (d) an abacavir or tenofovir containing regimen of three or more NRTIs in the absence of both PIs and NNRTIs (6%), except for the three-NRTI regimens consisting of: abacavir + tenofovir + lamivudine OR didanosine + tenofovir + lamivudine.

Combinations of zidovudine (AZT) and stavudine (d4T) with either a PI or NNRTI were not considered HAART.

The most frequent case of monotherapy was of one NRTI (92%). Of the other monotherapy cases, taking only PIs accounted for 6%; while taking only NNRTIs accounted for 2%.

All other ART regimens were classified as combination therapy. The three most frequent cases of combination therapy were: (a) only two NRTIs (67%); (b) three or more NRTIs without abacavir or tenofovir and in the absence of PIs and NNRTIs (11%); and (c) at least one PI and at least one NNRTI in the absence of NRTI (4%).

Reference:

DHHS/Henry J. Kaiser Family Foundation Panel on Clinical Practices for the Treatment of HIV infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. October 2008 revision. Available at: http://aidsinfo.nih.gov/ContentFiles/AboutHIVTreatmentGuidelines_FS_en.pdf.

Definitions:

HAART = highly active antiretroviral therapy
NNRTI = non-nucleoside reverse transcriptase inhibitor
NRTI = nucleoside or nucleotide reverse transcriptase inhibitor
PI = protease inhibitor