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Survey of Midlife in Japan (MIDJA): Biomarker Project, 2009-2010

Clinic Visit Documentation

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Survey of Midlife in Japan (MIDJA): Biomarker Project, 2009-2010

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DOCUMENTATION
for

MIDJA 1
CLINIC VISIT
DATA COLLECTION
PROTOCOLS

University of Wisconsin ♦ Institute on Aging
July 2018

INTRODUCTION

This document provides an overview of the data collection protocols implemented at the Clinic Visit for the MIDJA 1 Biomarker Protocol. It describes the protocols for assessment of vital signs and morphometrics, collecting and processing tissue samples, and also provides information about the construction and usage of related administrative and constructed variables. In addition, it contains descriptions of the biomarker assay methods including details about assay ranges, reference ranges, and inter-, and intra- assay covariation.

Data users are also encouraged to review the MIDJA 1 Biomarker DataFile Notes.doc. This document provides information about naming conventions, administrative and filter variables, and the order in which variables appear in the data file. It also includes information about how we handled missing values and other issues that arose over the course of the study.

This document will be periodically revised and updated as more information is gathered, and researchers continue to work with the MIDJA 1 Biomarker data. If there are suggestions or comments, please contact Gayle Love (glove@wisc.edu) or Barry Radler (bradler@wisc.edu).

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SECTION A

OVERVIEW OF DATA FILE AND COLLECTION PROTOCOLS

OVERVIEW OF DATA AND COLLECTION PROTOCOLS

The MIDJA Biomarker clinic visit includes collection of:

- Vital signs and morphometrics:
  - blood pressure
  - height, weight, waist and hip
- Blood samples for biomarker assay
- Medication data

As described in "MIDJA Biomarker Data File Notes", the naming convention organizes variables according to the data type or method used for data collection. The variable names for the Clinic Visit data, unless otherwise noted below, begin with the unique 3 character set "J2C".

The remainder of this section provides some administrative details as well as an overview of the following sections.

Vital Signs & Morphometrics

A copy of the form completed during the clinic visit appears in Section B. This section also includes detailed instructions for obtaining vital signs and morphometrics according to the same protocols for collecting the corresponding data in the MIDUS Biomarker study.

Blood Assays

The blood samples allow for assessment of multiple indicators within the following major systems as follows:

- *Cardiovascular:* Cholesterol Panel (Total, HDL), Glycosylated Hemoglobin (HA1c)
- *Neuroendocrine:* DHEA, DHEA-S, Creatinine
- *Inflammatory:* CRP(C-Reactive Protein), IL6 (InterLeukin 6), sIL6r (soluble IL-6 receptor), Fibrinogen

Blood samples were collected and processed into fresh and frozen aliquots using standardized protocols. Details about these protocols appear in Section C. The aliquots were then sent to Syowa Medical Service Co. LTD, in Tokyo, Japan (SMS) for further processing and some assays as follows:

- Fresh aliquots are assayed by SMS for:
  - Glycosylated hemoglobin (HA1c) – this MIDUS biomarker requires whole blood that is fresh or has been refrigerated for just a few days thus it is conducted in Japan.
  - Life Style Assessments – these are routine tests performed as a part of clinic visits in Japan and include: tests of cholesterol, HDL and LDL cholesterol, tryglycerides, liver function (GPT, gamma GPT, GOT), kidney function (BUN, uric acid), blood glucose, and anemia (e.g. red cell count, hematocrit).
- Frozen aliquots were packaged and shipped to the MIDUS BioCore lab at the University of Wisconsin. Samples were shipped to the U.S. so they could be assayed at the same labs that were used for MIDUS biomarker assays.

Details about the methods used to assay the tissue samples appear in Section D. This section includes details about assay method and sensitivity for inclusion in manuscripts, as well as information about any changes in assay method and subsequent corrections to the data. Assays corresponding to MIDUS measures are listed first followed by the Lifestyle assays done at the Syowa Laboratory in Tokyo. A table summarizing assay ranges, reference ranges, and

intra- and inter-assay co-variation appears at the end of this section.
Please also note the following:

- Variable names for assays performed in the U.S begin with the unique 3 character set "J2B".
- Although saliva samples are collected at home details about the saliva cortisol assay and sensitivity are also include in Section D.
- Variable names for the saliva data begin with the unique 3 character set "J2S".

Medication Data

Participants are instructed to bring medications or information about medications to the clinic visit. At the end of the visit staff record medication names, dosage, route of administration, frequency, how long the participant has been taking the medication and why they think they are taking it. A copy of the form used to collect this information and additional details about data collection and processing are included in Section E along with details about the structure of the data and basic processing.

MIDJA medication data are also processed (i.e. reasons for taking medications are coded, therapeutic and pharmacologic class codes are added) according to a standardized set of procedures developed with the MIDUS Biomarker Medication data. ***These protocols are described in a separate document that applies to data from both studies. (See Documentation for MIDUS and MIDJA Medication Data).***

SECTION B

CLINIC VISIT FORM AND INSTRUCTIONS

CLINIC VISIT RECORD FORM

#ID_____ DATE_____

NAME_____

◆**Record of Last Meal**：
When did you have a meal last time?

DATE:_____ TIME:_____

◆**Record of Body Measurement**：

HEIGHT（cm）	WEIGHT（kg）

WAIST（cm）	ABDOMINAL GIRTH（cm）	HIP（cm）

BLOOD PRESSURE 1 (high/low)	BLOOD PRESSURE 2 (high/low)	BLOOD PRESSURE 3 (high/low)

◆**Blood Sample**：

①Took blood → □Yes □No
（Reason： ）

②Date and time of taking blood→ Date:_____, Time:_____

Data Collection Protocols: Vital Signs and Morphometrics

The following provides a general overview of the steps completed by project staff to obtain the indicated measurements. More detailed instructions are provided at item B, below as appropriate.

A. **General Instructions**:

1. *Hip and Waist*: measured using a Gulik II Tape measure according to the detailed according to the instructions below
2. *Weight and Height*:
    a. For weight measurement, participants should take off their shoes and empty their pockets.
    b. They do not have to take off any other clothing.
3. *Blood Pressure*:
    a. Have respondent sit quietly for 5 minutes
    b. Measure blood pressure 3 times allowing a maximum of 30 seconds between each measurement.

B. **Detailed Instructions**: Hip & Waist Measurement

Project staff use a Gulik II Tape Measure to obtain hip and measurements. These measurements are recorded to 1 decimal place. The following standard is used for 'rounding':

If less than 0.05 (centimeters) round down
If greater than or equal to 0.05 (centimeters) round up

Measurements should be made directly on skin or over a single layer of clothing.
If, for some reason, these measurements have to be done over loose clothing, make sure to smooth the clothing as flat as possible DO NOT BUNCH the material.

Have participant stand erect with feet placed shoulder width apart and toes pointing forward.

1. Waist Circumference is measured directly on skin or over a single layer of clothing if the garment is a camisole or undershirt. DO NOT measure over a loose fitting blouse or shirt):
    a. Place tape around narrowest point between ribs and the iliac crest (tips of the large bones of the pelvis).
    b. Be sure the tape goes around evenly (parallel to the floor).
    c. Record measurement to the nearest millimeter (1 decimal place).

2. Hip Circumferences is measured over a single layer of clothing, typically subject's underwear:
    a. 1st circumference (Iliac Crest):
        - Ask subject to point to their hipbone.
        - Place the tape measure at the iliac crest and wrap around the body.
        - Make sure the measure is parallel to the floor.
        - Record measurement to the nearest millimeter (1 decimal place).

    b. 2nd circumference (Maximum Extension):
        - Place the tape measure at the maximum diameter of the buttocks and wrap it around the body.
        - Stand to the side of the participant to see that the tape is placed at the point of maximum buttock extension.
        - Record measurement to the nearest millimeter (1 decimal place).

SECTION C

BLOOD COLLECTION AND PROCESSING PROTOCOLS

Blood Collection Protocol

Blood samples are collected in the order described below. Collect blood samples and process as follows:

a. Preparation for blood draw
   i. Use non-dominant arm if possible.
   ii. Make reasonable number of attempts to get needed samples (e.g., 3 or so tries is generally sufficient – if unable to obtain samples, indicate this on Clinic Visit form, above)
   iii. Subject should avoid strenuous activity before blood draw.

b. Fill tubes in the following order and then process as indicated:
   i. Three 8.5-ml SST (Serum Separator Tube) tubes, gently invert tube 3-5 times after draw.
   ii. Two 1.8ml citrated tubes.
   iii. One 2.0-ml FNa tube (whole blood for HA1c), gently invert tube 3-5 times after draw and cool at 4 degree.
   iv. One 2.0-ml EDTA2K tube (for blood counts for lifestyle assessment), gently invert tube 3-5 times after draw and cool at 4 degrees.

c. Complete the Clinic Visit Record Form
   i. Record the time that the participate last ate, using 24-hour clock
   ii. Record date and time blood draw began using 24-hour clock.
   iii. Indicate if the blood draw was completed or not.
   If no blood was drawn record the reason it was not collected.
   iv. Record any problems encountered or other information regarding aspects of the collection that are not standard (per protocol).

Blood Sample Processing Protocol

Blood samples were processed by study staff on the University of Tokyo (UT) campus at the time of the clinic visit and then sent to Syowa Medical services for HbAlc testing, lifestyle assessments, and storage until shipment to the Biocore lab in Madison WI, USA, as indicated below.

1. FNa tube containing fresh blood is cooled at 4°C and tested for HA1c at Syowa.
2. EDTA2K tube containing fresh blood is cooled at 4°C and sent to Syowa for blood counts.
3. Two 1.8 ml Citrate tubes:
   a. Centrifuge as soon as possible to separate plasma
      i. Use refrigerated centrifuge (4°C).
      ii. Centrifuge samples for 15 minutes.
      iii. Set speed at 2000-3000 rpm.
      iv. On form, record time centrifuge begun.
   b. From two citrate tube, aliquot all plasma into two tubes, with 1.0ml plasma in each tube, apply blue label.
   c. On form, indicate amount of plasma aliquoted into vial.
   d. Store in a MIDJA freezer in designated freezer (-60 to -80 degrees) for delivery to Syowa for shipment to the US.
   e. Record the time the specimens were stored in freezer on the form.
4. Three 8.5-ml SST tubes (Serum Separator Tube).
   a. Let stand for 15-30 minutes after draw (maximum of 2 hours allowed between draw and centrifuging).
   b. Centrifuge to separate sera at UT.
      i. Use refrigerated centrifuge (4°C)
      ii. Centrifuge samples for 10 minutes.
      iii. Set speed at 2000-3000 rpm.

iv. Record the time centrifugation was begun on the form.

c. From three SST tubes, aliquot sera into two 10 ml vials (4 ml sera in each tube) for shipment to UW.
d. Aliquot the remaining 2 or more ml of sera into a 10ml vial for Syowa.
e. On form, indicate number of aliquots filled of each type.
f. If none were filled or fewer than number specified were filled, please indicate why.
g. Store two red capped tubes in MIDJA storage box in designated freezer (-60 to -80 degrees) for delivery to Syowa for shipment to the US. The remaining tube is kept at 4 degree and sent to Syowa for measurement of biochemical indicators at Syowa.
h. Record the time specimens were stored in freezer on the form.

SECTION D

BLOOD ASSAY DOCUMENTATION

Blood Assay Descriptions
Assay Sensitivity Summary Table

MIDJA 1 BIOMARKER ASSAY DESCRIPTIONS

Overview

The following provides information about laboratory assays of tissue samples collected as part of the MIDJA Biomarker Protocol, including details about assay method and sensitivity for inclusion in manuscripts. If the assay method changed during the data collection period, information about the change and any corrections to the data are also provided. Assays are listed first by tissue source (blood, saliva), and then by physiological system assessed (cardiovascular, inflammatory etc). Each section begins with a brief overview of sample collection and processing. Information about the assays was provided by the lab performing the assay or was developed by Dr. Chris Coe's lab (i.e. MIDUS Biocore lab). The MIDJA protocol included a set of blood assessments (assays and cell counts), performed at Showa Medical Science, that were reported back to Japanese patients as part of a standard physical exam. A few of these assessments replicate MIDUS blood assays. Where appropriate, information about assays done in both locations is included below. A summary table listing all the assays along with the specimen type, assay type and sensitivity appears in Appendix A at the end of this document.

Information about corresponding assays in the MIDUS II Project 4 (Biomarker) protocol can be found in the "BloodUrineSaliva.pdf" documentation file in the public archive at ICPSR
http://www.icpsr.umich.edu/icpsrweb/NACDA/studies/29282/documentation

I. Blood Assays

A. Sample Collection:
Blood samples were collected from each participant at the clinic visit, which could occur at any time during the day. Participants were encouraged not to eat at least one hour before the visit. The last time they ate was recorded prior to the blood draw. To ensure consistency, all samples were collected and processed using standardized procedures. Frozen samples were stored in a -60° C to -80° C freezer until shipped on dry ice to the MIDUS Biocore Lab. Samples were subsequently stored in a -65° C freezer until assayed.

- *Whole blood* samples (sodium fluoride-anticoagulated) as well as freshly-separated *sera,* were refrigerated and delivered to the Showa Lab in Tokyo Japan within 24 hours of collection for
  - Complete blood count (CBC) and HA1c determination
  - Serum chemistry: Cholesterol (Total, HDL, LDL) Triglycerides, Glutamic oxaloacetic transaminase (GOT), Glutamic pyruvic transaminase (GPT), γ-Glutamyl transpeptidase (GGTP), Blood urea nitrogen (BUN), Uric acid (UA).

- *Frozen serum and plasma* samples were shipped to the MIDUS Biocore Lab monthly for the following biomarker assays:
  - Cardiovascular markers – Cholesterol, HDL Cholesterol
  - Hormone markers - DHEA and DHEA-S
  - Inflammation markers - IL-6, s-IL6-r, C-Reactive protein, Fibrinogen
  - Serum Creatinine

B1. Assay Details - Cardiovascular Markers

Glycosylated Hemoglobin (HA1c):

HA1c assays were performed at the Showa lab in Tokyo Japan. Glycosylated hemoglobin (HA1c) was measured using antibodies attached to latex particles, which specifically bind HA1c. Remaining free antibodies are agglutinated with a synthetic polymer. The change in turbidity is inversely related to the quantity of bound glycopeptides and is measured turbidometrically. Hemoglobin concentration in blood is determined by adding sodium lauryl sulfate (SLS) to anticoagulated blood to lyse the cells, thus releasing their hemoglobin into the plasma so that it can be measured colorimetrically. Percent HA1c is determined by dividing the concentration of HA1c by the total hemoglobin concentration

Comparability with MIDUS values:
The original MIDJA HA1c value can be used in analyses of MIDJA-only data, or for comparison to HA1c values from other Japanese studies. For comparison with U.S. data (MIDUS), however, two issues must be addressed: 1) MIDJA values were less than the MIDUS (by 0.4 - 0.8% percentage points) and, 2) the U.S. HA1c assay at Meriter labs changed twice over over the course of MIDUS data collection and once since then.

To address the first issue, a small experiment was conducted to determine if the lower MIDJA values reflected differences in laboratory assay methods, or physiological variation. EDTA-anticoagulated blood was drawn from 10 individuals in Tokyo (4 in April 2010 and 6 in September 2010). Each sample was divided into two aliquots, one of which was assayed immediately for HA1c at the Showa lab, and one of which was sent to Madison and assayed within 1-2 days at Meriter Labs. From the two sets of data obtained on these ten samples a scatterplot (Figure 1, Appendix B) was made and a linear regression line generated: y = 0.6026x + 2.6129, where x is the value obtained in Tokyo and y is the value obtained in Madison. The coefficient of determination for this regression line is 0.6668.

To address the second issue, equations were obtained from the in-house comparisons at Meriter Labs to adjust their reported values to account for shifts occurring on May 22, 2006; February 29, 2007; and April 17, 2010[26, 27, 28].

- These three equations were combined to obtain the equation below to convert the 2010 Meriter-reported values (D) to bring them in line with the values in the MIDUS II data file (A):

  A = 1.3849 * D -2.1438

  where D represents the values reported by Meriter after April 17, 2010 and A represents the values reported by Meriter before May 22, 2006

- These MIDUS-adjusted values were plotted against the Tokyo values, and a second scatterplot was obtained. From this plot, a second equation was obtained, which was used to convert the Tokyo values (J) to pre-5/22/06 Meriter values:

  A = 0.8346*J + 1.4748

These equations have a coefficient of determination of 0.6668. The comparison data and graphs are shown in Appendix B.

The data file includes the original value (J2CHBA1C) obtained from the Showa lab and the final MIDUS adjusted value (HA1c, MIDUS-adjusted).

Cholesterol & HDL Cholesterol:
*Biocore Assays:*The Cholesterol and HDL Cholesterol assays were performed at Meriter Labs (GML) (Madison, WI) using a Cobas Integra® analyzer (Roche Diagnostics, Indianapolis, IN).

Cholesterol: The instrument uses the enzyme cholesterol esterase to cleave cholesterol esters into free cholesterol and fatty acids. Cholesterol oxidase then catalyzes the oxidation of cholesterol to cholest-4-en-3-one and hydrogen peroxide. In the presence of peroxidase, this hydrogen peroxide effects the coupling of phenol and 4-aminoantipyrine to form a red quinone-imine dye. The color intensity of the dye is directly proportional to the cholesterol concentration. It is determined by measuring the increase in absorbance at 512 nm.[1]

HDL-cholesterol: Serum is first mixed with synthetic polyanions, which adsorb to the surfaces of the other lipoproteins (LDL, VLDL, and chylomicrons); they are thereby transformed into detergent-resistant forms, whereas HDL is not. After solubilizing the HDL with detergent, it is measured as described above for total cholesterol.[2]

Showa Medical Science Assays: Cholesterol (Total, HDL, LDL) and Triglyceride assays were performed in Tokyo for Life Style Assessment reports that were sent to study participants. These values can be used in analysis of MIDJA-only data or for comparison to values from other Japanese studies.

> *Total serum cholesterol:* This procedure employs the enzyme cholesterol esterase (CE) to cleave cholesterol esters into free cholesterol and fatty acids. Cholesterol oxidase (COD) then catalyzes the oxidation of cholesterol to cholest-4-en-3-one and hydrogen peroxide. In the presence of peroxidase (POD), the hydrogen peroxide effects the oxidation of a dye, causing a color change which can be measured colorimetrically.
>
> *HDL- and LDL- cholesterol:* Each of these is isolated from the other lipoproteins, and then measured as described above for total cholesterol.
>
> *Triglycerides:* Triglycerides are hydrolyzed to glycerol and fatty acids. Free glycerol is then phosphorylated to glycerol-3-phosphate, which in turn is oxidized by glycerol phosphate oxidase (GPO) to dihydroxyacetone phosphate and hydrogen peroxide. In the presence of the enzyme peroxidase (POD) , the hydrogen peroxide oxidizes a dye, causing a color change which can be measured colorimetrically.

Comparability with MIDUS values-
Lipid profiles were run on sera from all 382 MIDJA participants in Tokyo (Showa lab). Frozen sera from these same participants were sent to Madison, where assays of HDL and total cholesterol were performed at Meriter Labs. These dual measurements were used to generate the scatter plots and linear regression lines shown in Appendix B (Figures 2-4) below. Across all three charts x values were obtained in Tokyo, while y values represent values obtained in the US as described below. Total Cholesterol values are plotted in the Figure 2.

The final 2 charts each include two sets of scatter plots. This was necessary due to a re-standardization of the HDL assay at Meriter in 2007[3,4] while the MIDUS data collection was ongoing. The MIDUS HDL values obtained after this re-standardization were adjusted to be consistent with the values obtained before this occurred.

Adjusted value = 1.1423(new value) - 0.9028[4]

For more information see the MIDUS BloodUrineSaliva.pdf in the public archive at: http://www.icpsr.umich.edu/icpsrweb/NACDA/studies/29282/documentation). To facilitate comparison with the MIDUS data, this correction was also applied to the MIDJA values. The mathematical adjustment to the HDL values also made it necessary to generate a second set of values for the Ratio of Total/HDL Cholesterol. Thus, the figures for HDL Cholesterol (Figure 3) and the Ratio of Total/HDL Cholesterol (Figure 4) include scatter plots comparing the Tokyo values to the original US values reported by Meriter (US-MIDJA), as well as the values that were adjusted to bring them in line with the MIDUS data (US-MIDUS).

Thus the data file includes the following measures of Total and HDL Cholesterol and the Ratio of Total /HDL Cholesterol:

	Variable names		
Measure	Meriter Lab Value	MIDUS Adjusted Value	Showa Lab Value
Total Cholesterol	J2BCHOL	Not applicable	J2CTCHOL
HDL Cholesterol	J2BHDL	J2BHDLA	J2CHDL
Ratio Total/HDL Cholesterol	J2BRTHDL	J2BRTHDA	J2CRTHDL

Although the values are very similar, investigators are encouraged to use the Meriter Lab values for comparisons using U.S. samples and the MIDUS Adjusted values for comparison to the MIDUS sample.

B2. Assay Details – Hormone Markers

DHEA and DHEA-S assays are performed at the Associated Regional & University Pathologists (ARUP) laboratory (Salt Lake City, UT).

DHEA:

A radioimmunoassay was performed using kit #DSL8900 from Diagnostic Systems Laboratories (Webster, TX). The procedure follows the basic principle of radioimmunoassay where there is competition between a radioactive and a non-radioactive antigen for a fixed number of antibody binding sites. The amount of [I-125]-labeled DHEA bound to the antibody is inversely proportional to the concentration of the unlabeled DHEA present. The separation of free and bound antigen is easily and rapidly achieved using a double antibody system.[5]

On May 18, 2009, ARUP began using LC-MS/MS (Liquid Chromatography tandem Mass Spectrometry) to assay DHEA.[6] Data collection began in January 2009; thus the initial 100 samples were assayed under the old method and the remainder under the new method. To maintain consistency with MIDUS data which were assayed under the earlier method, DHEA values were adjusted, as follows, to bring the new values in line with the existing data:

Adjusted value = 1.6145(new value) + 0.4668[7]

DHEA-Sulfate:

This assay was performed with a Roche Modular Analytics E170 analyzer, using an Elecsys® kit (Roche Diagnostics, Indianapolis, IN).

By incubating the serum with a DHEA-S specific biotinylated antibody, an immunocomplex is formed, the amount of which is dependent upon the DHEA-S concentration in the specimen. After addition of strepavidin-coated microparticles and a DHEA-S derivative labeled with a ruthenium complex, the still-vacant sites of the biotinylated antibodies become occupied, with formation of an antibody-hapten complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin.

The reaction mixture is aspirated into a measuring cell where the microparticles are magnetically captured onto the surface of an electrode. Unbound substances are removed. Application of a voltage to the electrode then induces chemiluminescent emission, which is measured by a photomultiplier.[8]

B3. Assay Details – Inflammation Markers

IL-6 and Il-6sr were assayed in the MIDUS Biocore Laboratory (University of Wisconsin, Madison, WI). The fibrinogen and CRP assays are performed at the Laboratory for Clinical Biochemistry Research (University of Vermont, Burlington, VT).

IL6:

IL6 was measured using the Quantikine® High-sensitivity ELISA kit #HS600B (R & D Systems, Minneapolis, MN). This is a sandwich ELISA using a microplate precoated with a monoclonal antibody specific for IL6. Standards and samples are pipetted into the wells, and any IL6 present is bound by the immobilized antibody. After washing away the unbound substances, an alkaline phosphatase-labeled detection antibody specific for IL6 is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate (NADPH) is added, which is converted to NADH. After an incubation period, an amplifier solution containing two additional enzymes whose actions are coupled to the cycling of NADH and NAD+ (diaphorase and alcohol dehydrogenase) and their respective substrates (iodonitrotetrazolium-violet and ethanol) are added. The diaphorase converts the iodonitrotetrazolium-violet to formazan, a red-colored product. The reaction is stopped at a predetermined endpoint with sulfuric acid, and the absorbance, which is proportional to the concentration of IL6 in the sample, is read at 490 nm using a Dynex MRXe plate reader (Magellan Biosciences, Chantilly, VA).[9]

Soluble Receptors for IL6 (IL6-sr):

Concentration of IL6-sr was measured using the Quantikine® ELISA kit #DR600 (R & D Systems, Minneapolis, MN). This is a sandwich ELISA using a microplate precoated with a monoclonal antibody specific for IL6-sr. Standards and samples are pipetted into the wells, and any IL6-sr is bound by the immobilized antibody. After washing away the unbound substances, a horseradish peroxidase-labeled detection antibody specific for IL6-sr is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate (tetramethylbenzidine) is added to the wells, and a blue-colored product develops. This reaction is stopped at a predetermined endpoint using sulfuric acid, which changes the color to yellow. Absorbance is read at 450 nm using a Dynex MRXe plate reader (Magellan Biosciences, Chantilly, VA), and is proportional to the concentration of IL6-sr in the samples.[10]

Fibrinogen:

Fibrinogen antigen was measured using the BNII nephelometer (N Antiserum to Human Fibrinogen; Dade Behring Inc., Deerfield, IL). The amount of fibrinogen present in the sample is quantitatively determined by immunochemical reaction. Complexes formed between antigen and antibody molecules scatter light passing through the sample. The intensity of the scattered light is proportional to the concentration of the antigen (fibrinogen) in the sample.[11]

C-reactive protein (CRP):

CRP was measured using the BNII nephelometer from Dade Behring utilizing a particle enhanced immunonepholometric assay. Polystyrene particles are coated with monoclonal antibodies to CRP, which, in the presence of antigen (CRP) agglutinate to cause an increase in the intensity of scattered light. The increase in scattered light is proportional to the amount of CRP in the sample.[11]

UPDATE - Samples falling below the assay range for CRP by this method were re-assayed by immunoelectrochemiluminescence using a high-sensitivity assay kit (Meso Scale Diagnostics #K151STG)[30].

B4. Assay Details – Serum Creatinine

Creatinine was measured using a Cobas Integra® analyzer (Roche Diagnostics, Indianapolis, IN).

Serum Creatinine:

This assay employs the enzymes creatininase, creatinase, and sarcosine oxidase which react with creatinine and produce hydrogen peroxide as one of the end products. This reacts with aminophenazone and HT1B to form a quinine imine chromogen as an end product. The absorbance of this colored end product is measured at 552 nm and is directly proportional to the creatinine concentration in the serum.[12]

B5. Assay Details – Japanese Life Style Assessments

In Japan clinic visits routinely include collection of blood samples for assessment of life-style related diseases. Serum samples, refrigerated never frozen, were sent to Showa Medical Sciences for these assessments and a report of these results were sent to study participants. These results are also included in the MIDJA Biomarker data file and can be used with other MIDJA data and for comparison to other Japanese samples. In addition to the HA1c, Cholesterol, and Triglyceride assays described above, the following measurements of liver and kidney function were obtained along with a complete blood count::

Liver Function: Glutamic oxaloacetic transaminase (GOT) , Glutamic pyruvic transaminase (GPT), γ-Glutamyl transpeptidase (GGTP)

Kidney Function: Blood Urea Nitrogen (BUN), Uric Acid (UA)

Liver Function Assays:

Glutamic oxaloacetic transaminase (GOT): In this assay, aspartate and α-ketoglutarate are mixed with serum, and the GOT in the serum catalyzes the conversion of these substrates to glutamate and

oxaloacetate. The oxaloacetate is then converted to malic acid by the enzyme malate dehydrogenase; this reaction consumes NADH, whose disappearance can be monitored by measuring UV absorbance at 340 nm.

Glutamic pyruvic transaminase (GPT): Alanine and α-ketoglutarate are mixed with serum, and the GPT in the serum catalyzes the conversion of these substrates to glutamate and pyruvate. The pyruvate is then converted to lactate by the enzyme lactate dehydrogenase; this reaction consumes NADH, whose disappearance can be monitored by measuring UV absorbance at 340 nm.

γ-Glutamyl transpeptidase (GGTP): A donor substrate, (γ-L-Glutamyl)-3-carboxy-4-nitroanilide, and an acceptor substrate are mixed with serum; the GGTP in the serum catalyzes the formation of 5-amino-2-nitrobenzoic acid, whose appearance can be monitored by measuring light absorbance at 410 nm.

Kidney Function Assays:

Blood urea nitrogen: This is a coupled enzymatic assay employing urease to convert urea to ammonium carbonate, and glutamate dehydrogenase (GLDH) and α-ketoglutarate to convert the ammonium ion to glutamic acid. The latter reaction consumes NADH, whose disappearance can be monitored by UV absorbance at 340 nm.

Uric acid: The enzyme uricase converts uric acid to allantoin, carbon dioxide, and hydrogen peroxide. The hydrogen peroxide product is reduced to water by the enzyme peroxidase (POD), and this reaction is coupled to an indicator reaction which can be monitored photometrically.

Complete Blood Count (CBC):

Hematocrit, Hemoglobin, Red blood cells, Mean cell volume, Mean cell hemoglobin, Mean cell hemoglobin concentration, White blood cells, Platelets: These measurements were automated.

II. Saliva Assays

A. Sample Collection:

Saliva samples were collected by participants in their homes over a 3 day period following the clinic visit. Three samples (morning, midday, evening) were collected each day. Samples are then frozen and shipped to the MIDUS Biocore lab for storage and subsequent cortisol assay.

B1. Assay Details – Saliva Cortisol

Salivary Cortisol:

Saliva samples were assayed at Dr. Clemens Kirschbaum's laboratory at the Technical University of Dresden, Germany. The samples for this assay were collected on cotton swabs in salivettes (Sarstedt Cat. #51.1534) and frozen. At the time of assay, they were thawed and centrifuged at 3000 rpm for 5 min, resulting in a particulate-free, clear fluid of low viscosity. Concentrations of free cortisol (the only type found in saliva) were determined using an immunoluminescence assay (kit #RE62011 manufactured by IBL International, Hamburg, Germany). Briefly, this assay uses a detection antibody conjugated to an agent capable of oxidizing luminol to 3-aminophthalic acid; this reaction emits light, which can be quantified, and which is proportional to the concentration of cortisol in the sample.[13, 14]

APPENDIX A: MIDJA ASSAY SENSITIVITY SUMMARY TABLE

A. MIDJA Bioassays from blood samples.

Assay	Assay Type	Performed at:	Assay Range	Variability	Reference Range
Hb(blood)	SLS-Hb method	Showa	0-25 g/dL	inter-assay CV: 1.0%	Male:13.5-17.6 Female::11.3-15.2
HA1c(blood)	Latex agglutination assay	Showa	3.0-13.0%	inter-assay CV: 10%	4.3-5.8 %
Total Cholesterol(serum)	Enzymatic colorimetric	Meriter	0-800 mg/dL[1]	inter-assay CV: 2.6%[15] intra-assay CV: 0.5-0.8%[1]	<200 mg/dL[16]
Total Cholesterol(serum)	Enzymatic colorimetric(CE-COD-POD)	Showa	2-700 Mg/dL	inter-assay CV: 3.0%	120-219 mg/dL
HDL-cholesterol (serum)	Enzymatic colorimetric	Meriter	0-155 mg/dL[2]	inter-assay CV: 6.5%[15] intra-assay CV: 1.1-1.4%[2]	≥40 mg/dL[16]
HDL-cholesterol(serum)	Enzymatic colorimetric	Showa	2-150 mg/dL	inter-assay CV: 5.0%	Male 40-70 mg/dL Female 40-75 mg/dL
LDL-cholesterol(serum)	Enzymatic colorimetric	Showa	1-450 mg/dL	inter-assay CV:5.0%	70-139 mg/dL
Triglycerides(serum)	Enzyme assay(Gpo-POD/free glycerol elimination technique)	Showa	2-600 mg/dL	inter-assay CV: 3.0%	35-149 mg/dL
DHEA-sulfate (serum)	Immunoelectro-chemiluminescent	Associated Regional & University Pathologists (ARUP)	min <1 µg/dL[17]	inter-assay CV: 2.9%[15] intra-assay CV: 0.8-3.8%[18]	Age Male Female[19] 30-39 120-520 45-270 40-49 95-530 32-240 50-59 70-310 26-200 60-69 42-290 13-130 ≥ 70 28-275 10-90
DHEA (serum)	LC-MS/MS (Liquid Chromatography tandem Mass Spectrometry)	ARUP	0.05-9 ng/mL[20]	inter-assay CV: <7.4%[20] intra-assay CV: <7.4%[20]	18-40 yr: 1.33-7.78[19] ≥ 41 yr: 0.63-4.70
Creatinine (serum)	Enzymatic colorimetric	Meriter	0-30.5 mg/dL[12]	inter-assay CV: 0.00%[15]	0.5-1.2 mg/dL[16]
IL-6 (serum)	ELISA	Univ. of Wisconsin (Coe Lab)	0.156-10 pg/mL[9]	inter-assay CV: 12.3%[21] intra-assay CV: 3.2%[22]	0.45-9.96 pg/mL[9]
IL6-sr (serum)	ELISA	University of Wisconsin (Coe Lab)	31.2-2000 pg/mL[10]	inter-assay CV: 6.8-7.3%[21] intra-assay CV: 1.4%[22]	14000-46000 pg/mL[10]
Fibrinogen (citrated plasma)	Immunonephelometric	Univ. of Vermont (Tracy Lab)	60-1200 mg/dL[23]	inter-assay CV: 2.6%[11] intra-assay CV: 2.7%[11]	180-350 mg/dL[11]
CRP (citrated plasma)	Immunonephelometric	Univ. of Vermont (Tracy Lab)	0.175-1100 ug/mL[11]	inter-assay CV: 2.1 – 5.7%[11] intra-assay CV: 2.3 – 4.4%[11]	≤3 ug/mL[11]
CRP (serum)	Immunoelectro-chemiluminescent	Univ. of Vermont (Tracy Lab)	0.014-216 ug/mL[29] min 10^{-6} ug/mL[30]	inter-assay CV: 4.72-5.16 %[29] intra-assay CV: 2.2-4.1 [30]	<3 ug/mL [11]
Glutamic Oxaloacetic	UV(JSCC*)	Showa	0-1500 U/L	inter-assay CV: 5.0%	10-40 IU/L

Assay	Assay Type	Performed at:	Assay Range	Variability	Reference Range
Transaminase (GOT)					
Glutamic Pyruvic Transaminase (GPT)	UV(JSCC*)	Showa	0-1500 U/L	inter-assay CV: 5.0%	5-45 IU/L
γ- Glutamyl Transpeptidase (GGTP)	5-amino-2-nitrobenzoic acid (JSCC*)	Showa	0-2000 U/L	inter-assay CV: 5.0%	Male 0-70 IU/L Female 0-35 IU/L
Blood Urea Nitrogen (BUN)	Urease/GLDH method (ammonia elimination)	Showa	2.25-200 mg/dL	inter-assay CV: 3.0%	8-23 mg/dL
Uric Acid	Enzyme Assay （Uricase/POD）	Showa	0.05-80 mg/dL	inter-assay CV: 5.0%	Male 3.4-7.0 mg/dL Female 2.4-7.0 mg/dL

* Japan Society of Clinical Chemistry (JSCC) recommended method

B. MIDJA saliva samples.

Assay	Assay Type	Performed at:	Assay Range	Variability	Reference Range
Cortisol (saliva)	Immunochemiluminescent	Dresden Lab Service, Dresden, Germany (Kirschbaum Lab)	min 0.43 n*M*[24]	inter-assay CV: 15%[25] intra-assay CV: 3%[25]	3-25 n*M*[24]

APPENDIX B: REGRESSION PLOTS

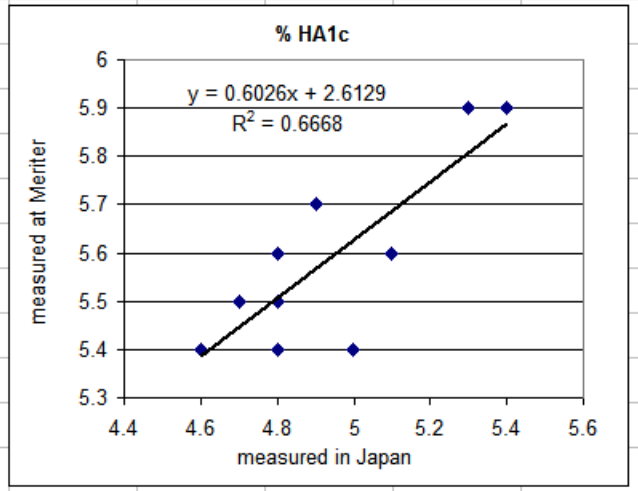
GLYCOSYLATED HEMOGLOBIN

Comparison of HA1c values obtained in Tokyo and at Meriter Labs

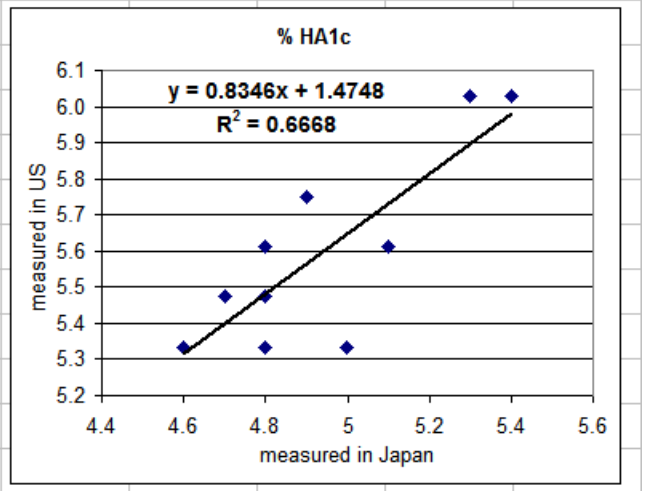
April-September, 2010

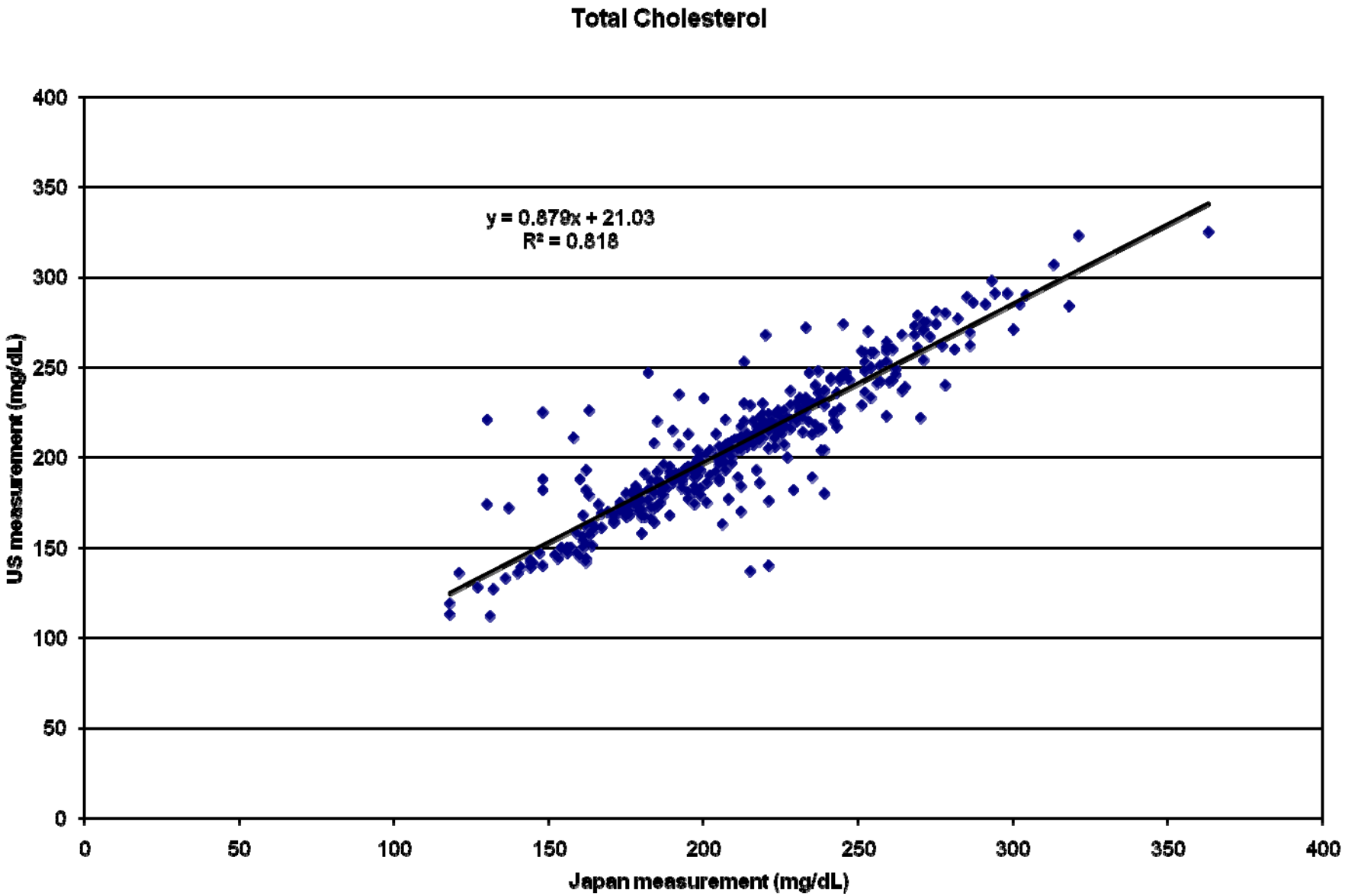
Japan	Meriter reported % US	Adjustment to MIDUS US
5.1	5.6	5.6
4.7	5.5	5.5
5.4	5.9	6.0
4.8	5.4	5.3
4.9	5.7	5.8
5.3	5.9	6.0
4.8	5.5	5.5
5.0	5.4	5.3
4.8	5.6	5.6
4.6	5.4	5.3

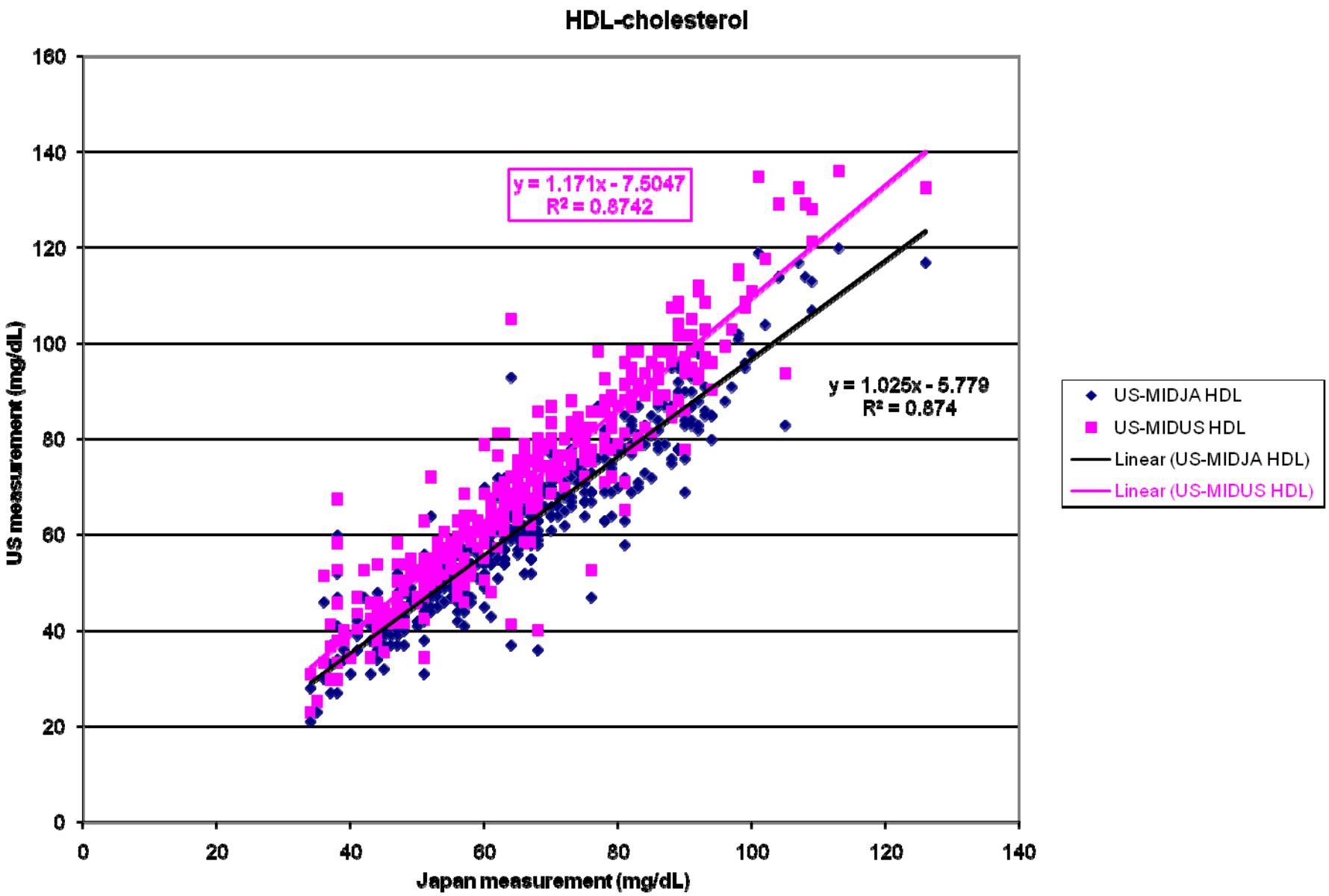
Adjusted to Meriter reported values (D):

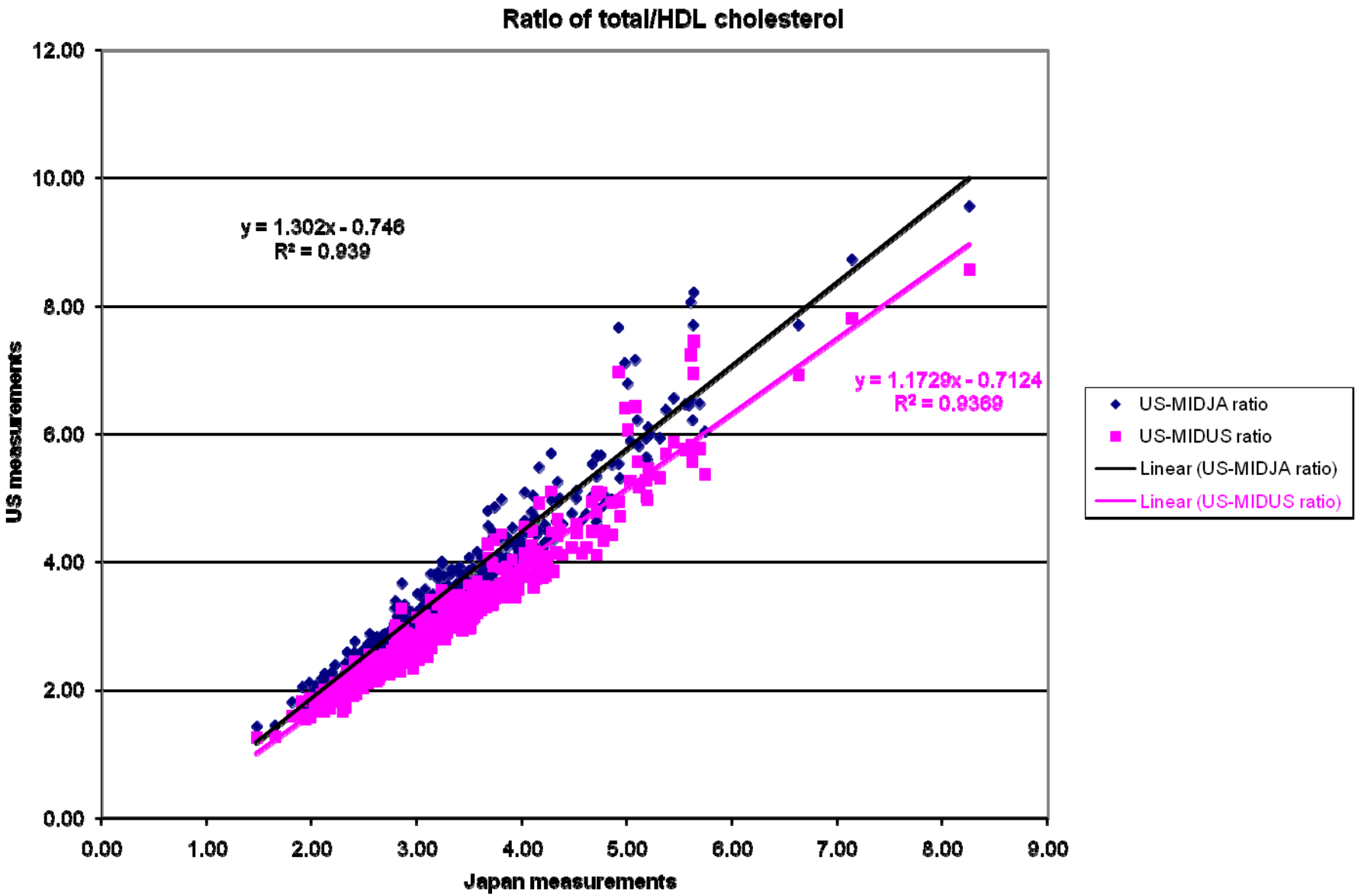


With corrected adjustment: equation includes Tokyo-to-Meriter and Meriter-to-MIDUS adjustment




Total Cholesterol
y = 0.879x + 21.03
R² = 0.818
US measurement (mg/dL)
Japan measurement (mg/dL)
0
50
100
150
200
250
300
350
400


HDL-cholesterol
US measurement (mg/dL)
Japan measurement (mg/dL)
0
20
40
60
80
100
120
140
160
y = 1.171x - 7.5047
R² = 0.8742
y = 1.025x - 5.779
R² = 0.874
US-MIDJA HDL
US-MIDUS HDL
Linear (US-MIDJA HDL)
Linear (US-MIDUS HDL)


Ratio of total/HDL cholesterol
12.00
10.00
8.00
6.00
4.00
2.00
0.00
US measurements
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
Japan measurements
y = 1.302x - 0.746
R² = 0.939
y = 1.1729x - 0.7124
R² = 0.9369
US-MIDJA ratio
US-MIDUS ratio
Linear (US-MIDJA ratio)
Linear (US-MIDUS ratio)

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30. MSD product insert, “Vascular Injury Panel 2 (human) Kits: V-Plex, August 2014.

SECTION E

MEDICATION DATA

Medication Data Collection and Processing Protocol

Data File Structure:

- **Administrative Variables**
- **Prescription and Quasi Medications**
- **Medication Allergies & Coding**
- **Therapeutic and Pharmacologic Classes**

Appendix A: Medication Chart

Appendix B: Generic Medication Names and DrugIDs

Appendix C: Reasons for Taking Medication – Codes and Category Names

Appendix D: Therapeutic and Pharmacologic Class Codes and Names

MEDICATION DATA COLLECTION AND PROCESSING PROTOCOLS

The MIDJA Biomarker data includes details about medications study participants are taking at the time of the clinic visit. Specifically information is recorded about the following:

- Prescription Medications
- Quasi Medications (i.e. non-prescription medications, equivalent to Over-The-Counter (OTC) and Alternative Medications in the U.S.)
- Medication Allergies

The Medication data appear at the end of the data file immediately following the Saliva data. A copy of the Medication Chart is included in Appendix A below. As described in "MIDJA Biomarker Data File Notes", the naming convention organizes variables according to the data type or method used for data collection. The variable names for the medication data begin with the unique 3 character set "J2M".

The remainder of this section provides general information about data collection as well as the structure and content of the medication data. The following also includes references to additional variables related to reasons for taking medications as well as therapeutic and pharmacologic class variables added to the data file following linkage to the Lexi-Data database. ***These variables are created using procedures that are applied to both MIDUS and MIDJA medication data, thus details are included in a unified document, 'Documentation for MIDUS and MIDJA Medications' that can be used for both studies***. Appendices B, C, and D below contain lists of medication names and corresponding drugIDs, and coding schemes related to reasons for taking medications along with lists of therapeutic and pharmacologic class codes and category names, respectively. Note, these lists are based on medication data collected in both MIDJA and MIDUS, thus some items listed may not appear in the MIDJA data.

Data Collection

In Japan, to help manage medications hospitals provide lists of medications individuals are taking and pharmacies also provide descriptions of medications. Thus, participants were asked to bring all their medications to the clinic or the list of medications provided by a hospital. We do this to ensure that we are able to record medication names and dosages accurately. Staff recorded detailed information (medication name, dosage, etc.) on the medication chart. If a participant did not bring medications or a list, staff asked participants about medication use and recorded their responses. The Medication Chart has three pages and includes sections to record information about:

- Prescription Medications: Medications prescribed by someone authorized/licensed in Japan, typically a physician.
- Quasi Medications: that include vitamins, minerals, non-prescription pain, antacids, anti-diarrheas, fiber, lubricating eye or nose preparations etc. as well as other supplements, herbs and homeopathics that the participant uses regularly and can be purchased "Over the Counter" (OTC) without a prescription.
- Medication Allergies: Any medication (prescription, OTC, alternative) that the participant reports being allergic to.

At the end of the visit project staff record the following information about medications on the medication chart:

- Medication name, dosage, and route of administration

- How often the medication is taken
- How long the participant has been taking a given medication
- Why they think they are taking the medication

NOTE: The order in which medications are recorded on the form is random and determined by the order in which the participant choses to report them. Thus there will be little direct correspondence between the medications or medication allergies reported in any given row of the form from wave to wave within a study or between MIDUS and MIDJA. The one exception is the first two rows in the Quasi section (OTC in MIDUS) which, as noted above, are reserved for reporting multi-vitamin and calcium supplement usage.

Data File Structure

The medication data are released in the traditional flat (wide) format as part of the larger MIDJA Biomarker aggregate data file to facilitate their use in standard between person analyses. Details about the variables in this file are included in the current document. The scope of the medication data however also lends itself to within person analysis of medication use, thus the medication data are also released in a standalone stacked (long) format. The stacked file only contains data about medications used, thus it does not include any information about study participants who do not take any medications. It also does not include any data about medication allergies. Details about the stacked file can be found in the Documentation for MIDUS and MIDJA Medications.

The aggregate (flat) file includes some administrative variables indicating whether or not the participant takes medication of the indicated type and, in some instances if yes, the number of medications. It also includes a standardized variable set characterizing each medication recorded along with information about medication allergies. The final section of the medication data is a set of variables indicating therapeutic and pharmacologic classification of the medications reported. The remainder of this section provides additional details about these variables.

Administrative Variables

There are 3 administrative variables at the beginning of the medication section:

- J2MTM – total number of medications
- J2MPMD – Yes/No, taking any prescription medications?
- J2MQMD – Yes/No, taking any quasi medications?

The first variable at the beginning of the Prescription and Quasi medication indicates the total number of medications of a given type that the participant takes (J2MPM, J2MQM, respectively). In addition, as noted above, the first two rows of the Quasi medication section are designated for Multivitamins and Calcium Supplements, thus it also includes the following 2 administrative variables:

- J2MQMV - Yes/No, taking a multivitamin?
- J2MQCS - Yes/No, taking a calcium supplement?

Prescription and Quasi Medications: Standardized Variable Sets

These variables appear in the following order for each medication reported. The "_" in the variable name is a place holder for the character indicating the medication type (P = Prescription, Q = Quasi) while the "#' at the end of the variable names is a place holder for the row number on the chart where information about a given medication is reported.

- Created variables from the Lexi-Data database (see Documentation of MIDUS and

MIDJA Medications for details, See Appendix B for a list of medication names and DrugIDs):
J2M_MID# - DrugID from the Lexi-Data database
J2M_GN# - Generic Drug Name associated with the DrugID

- Based on information from the medication chart:
  J2M_DD#, J2M_DU# – drug dosage (dosage, units)
  J2M_R# - route of administration (i.e. oral, inhaled, etc.)
  J2M_F#, J2M_FU# – how often the medication is taken (frequency, frequency units)
  J2M_T#, J2M_TU# – how long has the medication been taken (number, time units)

- Mutually exclusive code variables representing the reasons why the participant thinks s/he is taking the medication (See Documentation of MIDUS and MIDJA Medications for details about the coding process, See Appendix C below for a list of codes and category names):
  J2M_ICD9M -- 3 digit numeric codes representing major categories in the International Classification of Diseases, 9th Revision.
  J2M_MDC – 5 character alphanumeric variables representing a set of codes used to code reasons for taking a medication that could not be classified into an ICD-9 category

There are 13 sets of Prescription medication variables and 10 sets of Quasi medication variables in the MIDJA 1 Biomarker file. A few participants report more medications in a given category than the data file allows for (i.e. takes 13 Quasi medications). These additional medications are not included in the flat file as they would potentially add over a hundred variables (10 variables per medication) most of which would be designated as INAPP. These additional medications are however included in the stacked file. Cases with additional medications can be identified by looking at the frequency distribution for the number of Prescription (J2MPM) and Quasi (J2MQM) medications.

<u>Medication Allergies</u>
The final section of the Medication Chart is for reporting medication allergies. There are 2 administrative variables at the beginning of that section:

- J2ML – Yes/No does the respondent have Any Medication Allergies?
- J2MLM – number of allergies

There are 2 additional variables for each medication allergy reported (the # in the variable name indicates the row number in the chart):

- J2MLN# – text variable listing the medication name as reported by the participant
- J2MLRC# - Codes representing the allergic reaction to the medication (see below for details.

Note, the allergy variables are only included in the Flat file.

Coding Medication Allergy Reactions
Participant descriptions of allergic reactions to medications were recorded verbatim. The number of medication allergies reported was relatively small compared to the larger set of medication data thus they were coded using standard manual approaches. Medical definitions of common types of reactions and anaphylactic shock were used as a reference for making decisions about coding categories. Most of the categories correspond to specific individual

reactions reported (e.g. rash, nausea). If the participant reported multiple individual reactions that are part of the overall anaphylactic response then the code for anaphylaxis was assigned. Sometimes participants reported reactions that could not be identified as being either part of the anaphylactic response or a known reaction to a particular medication. In those instances the reaction was coded as 'Other'. The categories, codes, and key words are summarized below. Note, the same set of category codes is used for both MIDJA and MIDUS thus some categories (i.e. psychosis) may not appear in all files.

Code	Category Name	Keywords
1	ANAPHYLAXIS	Anaphylaxis, difficulty breathing, faint, wheezing, swelling & hives, sweating/shaking
2	RASH	Rash, Eczema
3	HIVES	Hives, eruptions, uticaria, blisters, welts
4	VOMITING	Vomiting, throwing up,
5	SWELLING	Swelling, swollen –hands, face, feet etc.
6	STOMACH UPSET	Upset stomach, feeling sick
7	ITCHING	Itching,
8	NAUSEA	Nausea
9	PSYCHOSIS	Psychosis, hallucinations, agitation, delirium, jitters
10	OTHER	Joints ache, no energy, headache, sweats, constipation

Therapeutic and Pharmacologic Classes

The final section of the data file contains a series of variables indicating whether or not the participant takes medications in commonly occurring categories of therapeutic (TC) and pharmacologic (PC) classes identified following linkage to the Lexi-Data database (see Appendix D for a list of these category names and class codes). The Lexi-Data linkage and creation of these variables along with corresponding count variables are described in the Documentation of MIDUS and MIDJA Medication.

The variable names for these dummies incorporate the first 5-6 characters of the corresponding TC and PC variables as well as the numeric code for the TC or PC class. The variable label incorporates both the TC or PC class code and the category name. If a count variable was also created, then an "N" is added as the final character to the dummy variable name. For example a common parent (top tier) therapeutic class is 115=Nutritional Products. The dummy and count variables for this TC class are named/labeled as follow:

Dummy variable: J2MTC_115 = 'Multum Therapeutic Class 115 - nutritional products: YES/NO?'

Count variable: J2MTC_115_N = 'Multum Therapeutic Class 115 – nutritional products: HOW MANY?'

APPENDIX A: MIDJA MEDICATION CHART

お医者様に処方された薬(prescribed medicine)

全部で何種類の薬を飲んでいらっしゃいますか?
(how many medicine all together) _____種類

薬の名前、1回の分量	飲み方	回数	期間?	どうして飲むことになりましたか?
Medication Name/Dosage	Route	Frequency	How long Taking?	Reason for taking?
1.				
2.				
3.				
4.				
5.				

お医者の処方によらない薬(医薬部外品など)

Without prescription,such as quasi-drug

全部で何種類の薬を飲んでいらっしゃいますか?
(how many medicine all together)_____種類

薬の名前、1回の分量	飲み方	回数	期間?	どうして飲むことになりましたか?
Medication Name/Dosage	Route	Frequency	How long Taking?	Reason for taking?
1. ビタミン剤　はい　いいえ vitamin yes no				
2. カルシウム　はい　いいえ Calcium Supplement yes no				
3.				
4.				
5.				

その他の薬や処方（ハーブや同毒療法など）

Other medicine or prescription（herbal, homeopathy）

全部で何種類の飲んでいらっしゃいますか? _____種類((how many medicine all together)

薬の名前、1回の分量	飲み方	回数	期間?	どうして飲むことになりましたか?
Medication Name/Dosage	Route	Frequency	How long Taking?	Reason for taking?
1.				
2.				
3.				
4.				
5.				

薬物アレルギー(alegy)

お薬でアレルギーがでたことがありますか? はい ・ いいえ(Have you had a allergy, yes no)

薬の名前	アレルギー反応
Medication Name	Reaction
1.	
2.	
3.	
4.	
5.	

APPENDIX B: GENERIC NAMES and DRUGIDs

The following lists the Lexi-Data DrugIDs and Generic Names in the MIDUS and MIDJA data files as of May 2017. The list is in order by DrugID and will be updated as needed with future data releases.

DRUG_ID	GENERIC_NAME
d00001	acyclovir
d00002	amiodarone
d00004	atenolol
d00006	captopril
d00011	ciprofloxacin
d00012	codeine
d00013	enalapril
d00015	ibuprofen
d00016	labetalol
d00018	nadolol
d00019	naproxen
d00021	ranitidine
d00022	warfarin
d00023	allopurinol
d00024	azaTHIOprine
d00025	chloramphenicol
d00027	haloperidol
d00028	ketoprofen
d00031	probenecid
d00032	propranolol
d00033	sulindac
d00034	zidovudine
d00037	doxycycline
d00039	indomethacin
d00043	clindamycin
d00044	cloNIDine
d00045	diltiazem
d00046	erythromycin
d00047	rifampin
d00048	verapamil
d00049	acetaminophen
d00050	methadone
d00051	NIFEdipine
d00056	cefuroxime
d00058	carBAMazepine
d00060	methotrexate
d00061	lithium
d00068	ethambutol
d00069	tobramycin
d00070	furosemide
d00071	fluconazole
d00078	didanosine
d00079	cycloSPORINE
d00083	valproic acid
d00084	prednisoLONE
d00086	amantadine
d00088	amoxicillin
d00089	amoxicillin-clavulanate
d00091	azithromycin
d00096	cephalexin
d00097	clarithromycin
d00101	isoniazid
d00102	itraconazole
d00106	methenamine
d00108	metroNIDAZOLE
d00110	minocycline
d00112	nitrofurantoin
d00117	pyrazinamide
d00124	sulfamethoxazole-trimethoprim
d00132	hydrALAZINE
d00134	metoprolol
d00135	minoxidil
d00137	pindolol
d00138	prazosin
d00140	cimetidine
d00141	famotidine
d00142	theophylline
d00143	phenytoin
d00144	nortriptyline
d00145	desipramine
d00146	amitriptyline
d00148	diazepam
d00149	LORazepam
d00150	colchicine
d00151	bacampicillin
d00164	adenosine
d00168	ALPRAZolam
d00169	aMILoride
d00170	aspirin
d00175	benztropine
d00176	betaxolol
d00179	bumetanide
d00181	buPROPion
d00182	busPIRone
d00191	chlorpheniramine
d00192	chlorthalidone
d00193	cholestyramine
d00197	clonazePAM
d00198	clorazepate
d00207	dextromethorphan
d00210	digoxin
d00212	diphenhydrAMINE
d00213	dipyridamole
d00217	doxepin
d00223	epoetin alfa
d00227	ethosuximide
d00231	felodipine
d00233	fentaNYL
d00234	flecainide

d00236 FLUoxetine
d00237 fluPHENAZine
d00241 folic acid
d00242 fosinopril
d00245 gemfibrozil
d00246 glipiZIDE
d00248 glyBURIDE
d00253 hydrochlorothiazide
d00254 hydrocortisone
d00255 HYDROmorphone
d00259 imipramine
d00260 indapamide
d00262 insulin
d00268 isosorbide dinitrate
d00269 isosorbide mononitrate
d00270 isradipine
d00273 ketorolac
d00275 leucovorin
d00278 levothyroxine
d00280 lovastatin
d00284 medroxyPROGESTERone
d00289 mercaptopurine
d00290 methimazole
d00293 methylPREDNISolone
d00298 metoclopramide
d00300 mexiletine
d00303 misoprostol
d00308 morphine
d00310 nabumetone
d00314 niacin
d00316 nicotine
d00321 nitroglycerin
d00322 nizatidine
d00325 omeprazole
d00328 oxybutynin
d00329 oxyCODONE
d00330 pancuronium
d00336 pentoxifylline
d00337 phenazopyridine
d00340 PHENobarbital
d00343 piroxicam
d00345 potassium chloride
d00346 povidone iodine topical
d00348 pravastatin
d00350 predniSONE
d00352 primidone
d00355 prochlorperazine
d00358 propafenone
d00363 pyridostigmine
d00365 quinapril
d00366 quiNINE
d00370 octreotide
d00371 sotalol
d00373 spironolactone
d00377 sucralfate
d00379 sulfaSALAzine
d00381 tamoxifen
d00384 temazepam
d00386 terazosin
d00395 traZODone
d00396 triamterene
d00397 triazolam
d00402 vitamin A
d00405 vitamin E
d00409 riboflavin
d00412 pyridoxine
d00413 cyanocobalamin
d00417 bioflavonoids
d00425 calcium carbonate
d00426 ascorbic acid
d00427 potassium phosphate-sodium phosphate
d00440 sodium bicarbonate
d00484 selenium
d00488 lysine
d00491 levOCARNitine
d00496 inositol
d00497 omega-3 polyunsaturated fatty acids
d00514 ticlopidine
d00529 tranexamic acid
d00534 estrone
d00537 estradiol
d00541 conjugated estrogens
d00542 esterified estrogens
d00543 estropipate
d00550 progesterone
d00555 norethindrone
d00557 levonorgestrel
d00558 testosterone
d00563 finasteride
d00572 chorionic gonadotropin (HCG)
d00578 arginine
d00583 desmopressin
d00595 glucose
d00598 calcitonin
d00608 fludrocortisone
d00609 cortisone
d00620 triamcinolone
d00628 betamethasone
d00646 trichlormethiazide
d00651 urea topical
d00653 isosorbide
d00655 thyroid desiccated
d00658 liothyronine
d00683 lidocaine topical
d00688 bepridil
d00689 amLODIPine
d00699 EPINEPHrine
d00701 mephentermine
d00704 phenylephrine
d00709 bisoprolol

d00726	doxazosin
d00728	ramipril
d00730	benazepril
d00732	lisinopril
d00743	sodium polystyrene sulfonate
d00746	simvastatin
d00749	albuterol
d00750	metaproterenol
d00755	pirbuterol
d00760	beclomethasone
d00761	flunisolide
d00762	acetylcysteine
d00769	pseudoephedrine
d00771	naphazoline ophthalmic
d00772	oxymetazoline nasal
d00773	tetrahydrozoline ophthalmic
d00787	promethazine
d00797	guaiFENesin
d00801	caffeine
d00806	phentermine
d00810	diethylpropion
d00813	benzocaine topical
d00814	methotrimeprazine
d00817	hydroxychloroquine
d00838	butorphanol
d00842	salsalate
d00848	diclofenac
d00851	etodolac
d00855	perphenazine
d00859	meclizine
d00861	dimenhyDRINATE
d00867	ondansetron
d00874	amoxapine
d00876	clomiPRAMINE
d00877	maprotiline
d00880	sertraline
d00900	methylphenidate
d00901	pemoline
d00907	hydrOXYzine
d00910	zolpidem
d00915	estazolam
d00960	carisoprodol
d00961	chlorphenesin
d00963	cyclobenzaprine
d00964	metaxalone
d00965	methocarbamol
d00966	orphenadrine
d00967	baclofen
d00970	trihexyphenidyl
d00972	biperiden
d00985	hyoscyamine
d00986	scopolamine
d00991	clidinium
d00992	glycopyrrolate
d00999	dicyclomine
d01002	pancrelipase
d01003	pancreatin
d01005	ursodiol
d01008	magnesium citrate
d01010	cascara sagrada
d01013	senna
d01015	bisacodyl
d01017	polycarbophil
d01018	psyllium
d01021	docusate
d01025	loperamide
d01026	bismuth subsalicylate
d01027	simethicone
d01031	mesalamine
d01032	olsalazine
d01133	immune globulin intravenous
d01185	apraclonidine ophthalmic
d01187	levobunolol ophthalmic
d01200	tropicamide ophthalmic
d01231	chlorhexidine topical
d01233	nystatin
d01244	tretinoin topical
d01256	etretinate
d01267	mupirocin topical
d01272	ciclopirox topical
d01274	tolnaftate topical
d01288	clobetasol topical
d01290	desonide topical
d01291	desoximetasone topical
d01293	fluocinolone topical
d01294	fluocinonide topical
d01296	fluticasone
d01300	mometasone topical
d01319	hydroquinone topical
d01321	capsaicin topical
d01322	aluminum chloride hexahydrate topical
d01325	arnica topical
d01333	benzalkonium chloride topical
d01353	leuprolide
d01373	hydroxyurea
d01376	PACLitaxel
d01385	beta-carotene
d01386	yohimbine
d01387	alprostadil
d01406	naltrexone
d01407	flumazenil
d01423	potassium citrate
d03050	loratadine
d03051	interferon beta-1b
d03052	hydrochlorothiazide-triamterene
d03061	butalbital
d03064	choline bitartrate
d03075	HYDROcodone
d03092	protease
d03126	calcitriol
d03128	ergocalciferol

d03129 cholecalciferol
d03130 thiamine
d03131 pantothenate
d03135 phytonadione
d03137 calcium-vitamin D
d03140 multivitamin
d03141 multivitamin with iron
d03145 multivitamin with minerals
d03148 multivitamin, prenatal
d03154 doxylamine
d03157 PARoxetine
d03159 choline
d03160 SUMAtriptan
d03180 risperiDONE
d03181 venlafaxine
d03182 gabapentin
d03183 fluvastatin
d03189 torsemide
d03191 terbinafine topical
d03195 miconazole topical
d03197 betamethasone topical
d03200 erythromycin topical
d03201 acyclovir topical
d03202 ketoconazole topical
d03204 fluorouracil topical
d03205 hydrocortisone topical
d03206 triamcinolone topical
d03208 metroNIDAZOLE topical
d03210 selenium sulfide topical
d03221 prednisoLONE ophthalmic
d03226 saliva substitutes
d03227 fluorometholone ophthalmic
d03229 levocabastine ophthalmic
d03238 ethinyl estradiol-norethindrone
d03241 ethinyl estradiol-norgestrel
d03242 ethinyl estradiol-levonorgestrel
d03245 esterified estrogens-methylTESTOSTERone
d03247 hydrochlorothiazide-spironolactone
d03258 atenolol-chlorthalidone
d03261 hydrochlorothiazide-propranolol
d03265 benazepril-hydrochlorothiazide
d03266 hydrochlorothiazide-lisinopril
d03289 acetaminophen-pseudoephedrine
d03292 ibuprofen-pseudoephedrine
d03296 acetaminophen-chlorpheniramine
d03298 chlorpheniramine-pseudoephedrine
d03300 chlorpheniramine-phenylephrine
d03311 brompheniramine-phenylephrine
d03313 chlorpheniramine/phenylephrine/pyrilamine
d03331 APAP/chlorpheniramine/phenylephrine
d03342 APAP/dextromethorphan/pseudoephedrine
d03349 acetaminophen/dextromethorphan/doxylamine/PSE
d03357 codeine-promethazine
d03359 chlorpheniramine-dextromethorphan
d03360 dextromethorphan-promethazine
d03379 guaiFENesin-pseudoephedrine
d03381 guaiFENesin-phenylephrine
d03389 estradiol-testosterone
d03393 codeine-guaifenesin
d03400 dextromethorphan-guaifenesin
d03409 dextromethorphan/guaiFENesin/pseudoephedrine
d03423 acetaminophen-codeine
d03425 APAP/butalbital/caffeine/codeine
d03428 acetaminophen-HYDROcodone
d03431 acetaminophen-oxyCODONE
d03432 aspirin-oxycodone
d03434 acetaminophen-propoxyphene
d03439 APAP/ASA/caffeine
d03443 APAP/Al hydroxide/ASA/caffeine/Mg hydroxide
d03445 acetaminophen-diphenhydrAMINE
d03449 aspirin-caffeine
d03455 APAP/butalbital/caffeine
d03456 acetaminophen-butalbital
d03459 APAP/dichloralphenazone/isometheptene
d03473 carbidopa-levodopa
d03478 Al hydroxide/Mg hydroxide/simethicone
d03485 atropine/hyoscyamine/PB/scopolamine
d03492 chlordiazePOXIDE-clidinium
d03495 belladonna/ergotamine/PHENobarbital
d03496 docusate-senna
d03506 atropine-diphenoxylate
d03517 benzoic acid/methenamine/sodium salicylate
d03524 bacitracin/neomycin/polymyxin B topical
d03536 dexamethasone-tobramycin ophthalmic
d03543 hydrocortisone/neomycin/polymyxin B otic
d03561 betamethasone-clotrimazole topical
d03562 nystatin-triamcinolone topical
d03566 captopril-hydrochlorothiazide
d03591 alginic acid/Al hydroxide/Mg carbonate

d03596 alginic acid/Al hydroxide/Mg trisilicate
d03640 budesonide nasal
d03644 lactobacillus acidophilus
d03650 candida albicans extract
d03655 lidocaine-prilocaine topical
d03663 lecithin
d03664 phenol topical
d03665 menthol topical
d03668 methyl salicylate topical
d03674 pectin
d03680 ASA/citric acid/Na bicarb
d03686 undecylenic acid topical
d03689 calcium acetate
d03740 enalapril-hydrochlorothiazide
d03744 bisoprolol-hydrochlorothiazide
d03751 dexbrompheniramine-pseudoephedrine
d03752 tacrolimus
d03756 bacitracin topical
d03759 salmeterol
d03760 diphenhydrAMINE topical
d03768 ocular lubricant
d03770 emollients, topical
d03781 ethinyl estradiol-norgestimate
d03782 desogestrel-ethinyl estradiol
d03788 calcipotriene topical
d03789 potassium gluconate
d03796 magnesium chloride
d03797 magnesium oxide
d03802 calcium lactate
d03803 calcium phosphate, tribasic
d03804 fluvoxaMINE
d03805 dorzolamide ophthalmic
d03807 metFORMIN
d03808 nefazodone
d03809 lamoTRIgine
d03818 loratadine-pseudoephedrine
d03819 conjugated estrogens-medroxyPROGESTERone
d03821 losartan
d03822 ferrous gluconate
d03823 iron polysaccharide
d03824 ferrous sulfate
d03825 nisoldipine
d03826 traMADol
d03827 cetirizine
d03828 lansoprazole
d03829 amLODIPine-benazepril
d03830 hydrochlorothiazide-losartan
d03833 divalproex sodium
d03835 moexipril
d03838 valACYclovir
d03839 mycophenolate mofetil
d03846 acarbose
d03847 carvedilol
d03848 azelaic acid topical
d03849 alendronate
d03850 bicalutamide
d03858 lamiVUDine
d03864 glimepiride
d03866 calcium citrate
d03873 anastrozole
d03879 cannabis (Schedule I substance)
d03884 trolamine salicylate topical
d03897 lactase
d03898 sodium chloride, hypertonic, ophthalmic
d03908 APAP/chlorpheniramine /dextromethorphan/PPA
d03922 acetaminophen-caffeine
d03923 acetaminophen-phenylephrine
d03957 calcium/ferrous fumarate /vitamin D
d03968 dexamethasone ophthalmic
d03984 ritonavir
d03990 carbamide peroxide otic
d04008 trandolapril
d04011 interferon beta-1a
d04012 terbinafine
d04015 adapalene topical
d04017 latanoprost ophthalmic
d04025 mirtazapine
d04029 nevirapine
d04031 pilocarpine
d04032 sulfacetamide sodium-sulfur topical
d04034 remifentanil
d04035 amphetamine-dextroamphetamine
d04037 timolol ophthalmic
d04039 carteolol ophthalmic
d04040 fexofenadine
d04047 midodrine
d04048 brimonidine ophthalmic
d04050 OLANZapine
d04052 pentosan polysulfate sodium
d04055 zinc chloride
d04056 zinc gluconate
d04057 zinc sulfate
d04058 melatonin
d04063 butenafine topical
d04066 albuterol-ipratropium
d04068 azelastine nasal
d04099 donepezil
d04101 ivermectin
d04102 tiZANidine
d04105 atorvastatin
d04106 fosfomycin
d04109 levofloxacin
d04111 glatiramer
d04113 valsartan

d04115 topiramate
d04117 olopatadine ophthalmic
d04120 caffeine-ergotamine
d04121 tamsulosin
d04125 imiquimod topical
d04141 hydrochlorothiazide-moexipril
d04142 chromium picolinate
d04145 pramipexole
d04156 letrozole
d04157 loperamide-simethicone
d04168 acetaminophen /diphenhydramine /pseudoephedrine
d04181 cysteine
d04186 phenylephrine nasal
d04195 chlorophyllin
d04197 hydrocortisone/neomycin /polymyxin B topical
d04210 estradiol topical
d04213 progesterone topical
d04215 rOPINIRole
d04219 lamivudine-zidovudine
d04220 QUEtiapine
d04222 irbesartan
d04223 mometasone nasal
d04233 triamcinolone nasal
d04235 ipratropium nasal
d04241 potassium chloride-sodium chloride
d04242 sodium chloride nasal
d04245 hydrochlorothiazide-irbesartan
d04248 methylcellulose
d04253 ZOLMitriptan
d04258 clopidogrel
d04261 raloxifene
d04266 eprosartan
d04267 repaglinide
d04268 dihydroergotamine nasal
d04270 fexofenadine-pseudoephedrine
d04271 diclofenac-misoprostol
d04273 testosterone topical
d04275 beclomethasone nasal
d04276 budesonide
d04279 flunisolide nasal
d04283 fluticasone nasal
d04284 fluticasone topical
d04285 naratriptan
d04286 fenofibrate
d04289 montelukast
d04290 calcium carbonate-magnesium hydroxide
d04292 loteprednol ophthalmic
d04293 hydrochlorothiazide-valsartan
d04294 tolterodine
d04298 phenylephrine topical
d04299 sildenafil
d04300 risedronate
d04303 dorzolamide-timolol ophthalmic
d04322 candesartan
d04328 rizatriptan
d04329 sodium hyaluronate
d04332 citalopram
d04341 estradiol-norethindrone topical
d04342 inFLIXimab
d04349 leflunomide
d04357 trastuzumab
d04362 copper gluconate
d04363 sevelamer
d04364 telmisartan
d04365 etanercept
d04369 insulin regular
d04370 insulin isophane
d04373 insulin lispro
d04374 insulin isophane-insulin regular
d04375 estradiol-norethindrone
d04376 abacavir
d04378 modafinil
d04380 celecoxib
d04382 cilostazol
d04395 clotrimazole topical
d04396 conjugated estrogens topical
d04399 nystatin topical
d04407 echinacea
d04408 St. John's wort
d04411 garlic
d04412 ginseng
d04413 ginkgo
d04414 ginger
d04415 saw palmetto
d04416 valerian
d04417 creatine
d04418 glucosamine
d04419 chondroitin
d04420 chondroitin-glucosamine
d04421 evening primrose
d04424 licorice
d04425 dehydroepiandrosterone
d04426 red yeast rice
d04427 levalbuterol
d04429 orlistat
d04432 carbonyl iron
d04434 rosiglitazone
d04440 perindopril
d04442 pioglitazone
d04448 RABEprazole
d04452 zaleplon
d04459 dofetilide
d04461 exemestane
d04460 entacapone
d04463 grape seed oil
d04465 gotu kola

d04466 milk thistle
d04467 cat's claw
d04469 bee pollen
d04470 cranberry
d04472 black cohosh
d04476 bilberry
d04477 slippery elm
d04478 wild yam
d04480 eyebright
d04481 royal jelly
d04484 shark cartilage
d04486 rose hips
d04487 peppermint
d04488 lavender
d04490 green tea
d04491 flax
d04499 levETIRAcetam
d04503 nedocromil ophthalmic
d04509 hydrochlorothiazide-quinapril
d04510 insulin lispro-insulin lispro protamine
d04513 OXcarbazepine
d04514 pantoprazole
d04521 nettles
d04522 papaya
d04523 ubiquinone
d04527 zonisamide
d04532 meloxicam
d04538 insulin glargine
d04541 azelastine ophthalmic
d04572 formoterol
d04611 fluticasone-salmeterol
d04695 colesevelam
d04697 insulin aspart
d04702 docosanol topical
d04703 glyBURIDE-metFORMIN
d04708 zoledronic acid
d04711 candesartan-hydrochlorothiazide
d04722 diclofenac topical
d04723 calcium carbonate/famotidine/Mg hydroxide
d04737 hydrochlorothiazide-telmisartan
d04740 tacrolimus topical
d04743 nateglinide
d04747 ziprasidone
d04749 esomeprazole
d04753 travoprost ophthalmic
d04754 bimatoprost ophthalmic
d04760 drospirenone-ethinyl estradiol
d04764 cetirizine-pseudoephedrine
d04765 hydrocortisone-lidocaine topical
d04766 acetaminophen-traMADol
d04773 ethinyl estradiol-etonogestrel
d04774 tenofovir
d04776 frovatriptan
d04778 valdecoxib
d04784 pimecrolimus topical
d04785 desloratadine
d04787 lovastatin-niacin
d04788 dutasteride
d04795 budesonide-formoterol
d04797 alfuzosin
d04798 tegaserod
d04801 olmesartan
d04803 voriconazole
d04806 sodium oxybate
d04812 escitalopram
d04813 horse chestnut
d04815 eplerenone
d04819 buprenorphine-naloxone
d04820 metFORMIN-rosiglitazone
d04823 glipiZIDE-metFORMIN
d04824 ezetimibe
d04825 ARIPiprazole
d04827 atomoxetine
d04828 teriparatide
d04829 tiotropium
d04835 adalimumab
d04836 cycloSPORINE ophthalmic
d04839 insulin aspart-insulin aspart protamine
d04844 camphor-menthol topical
d04849 eletriptan
d04851 rosuvastatin
d04857 gatifloxacin ophthalmic
d04860 moxifloxacin ophthalmic
d04875 betaine
d04878 hydrochlorothiazide-olmesartan
d04881 omalizumab
d04882 atazanavir
d04893 vardenafil
d04896 tadalafil
d04898 epinastine ophthalmic
d04899 memantine
d04901 fosamprenavir
d04929 trospium
d04939 sodium picosulfate
d05027 estriol
d05044 betamethasone-calcipotriene topical
d05048 amLODIPine-atorvastatin
d05062 carbocysteine
d05218 cinacalcet
d05234 hyaluronan
d05265 nebivolol
d05283 brimonidine-timolol ophthalmic
d05348 ezetimibe-simvastatin
d05350 polyethylene glycol 3350
d05352 emtricitabine-tenofovir
d05355 DULoxetine
d05357 ibandronate

d05365	dexchlorpheniramine /HYDROcodone/phenylephrin
d05413	solifenacin
d05414	natalizumab
d05421	eszopiclone
d05422	darifenacin
d05436	insulin detemir
d05471	alpha-D-galactosidase
d05488	pramlintide
d05508	pregabalin
d05526	alendronate-cholecalciferol
d05529	exenatide
d05578	ramelteon
d05583	APAP/dextromethorphan /phenylephrine
d05635	metFORMIN-pioglitazone
d05637	lactobacillus rhamnosus GG
d05646	saccharomyces boulardii lyo
d05702	methylsulfonylmethane
d05703	chondroitin/glucosamine /methylsulfonylmethane
d05719	ranolazine
d05748	brewer's yeast
d05770	omeprazole-sodium bicarbonate
d05776	iodine
d05807	varenicline
d05819	diphenhydrAMINE-ibuprofen
d05825	darunavir
d05847	efavirenz/emtricitabine/tenofovir
d05851	levocetirizine
d05856	glimepiride-pioglitazone
d05896	sitaGLIPtin
d05899	ciclesonide nasal
d05964	aloe vera
d06032	fluocinolone otic
d06214	collagen
d06297	paliperidone
d06370	turmeric
d06392	wheat dextrin
d06507	cinnamon
d06649	calcium carbonate-magnesium chloride
d06652	strontium gluconate
d06655	alpha-lipoic acid
d06662	amLODIPine-valsartan
d06663	lisdexamfetamine
d06720	metFORMIN-sitaGLIPtin
d06833	acetaminophen-aspirin
d06842	armodafinil
d06848	lutein
d06852	maraviroc
d06867	biotin
d06905	amlodipine-olmesartan
d07048	raltegravir
d07076	etravirine
d07113	desvenlafaxine
d07130	naproxen-SUMAtriptan
d07132	olopatadine nasal
d07137	dabigatran
d07315	glutamine
d07347	bifidobacterium infantis
d07349	lacosamide
d07354	silodosin
d07356	rivaroxaban
d07373	d-xylitol
d07374	bimatoprost topical ophthalmic
d07395	dexlansoprazole
d07397	febuxostat
d07400	bifidobacterium-lactobacillus
d07409	prasugrel
d07466	liraglutide
d07482	bepotastine ophthalmic
d07498	amLODIPine-telmisartan
d07505	copper
d07637	pitavastatin
d07639	acetaminophen/CPM /dextromethorphan/GG
d07640	denosumab
d07645	onabotulinumtoxinA
d07659	caffeine-magnesium salicylate
d07660	formoterol-mometasone
d07668	amlodipine/hydrochlorothiazide /olmesartan
d07693	aspirin-calcium carbonate
d07705	lurasidone
d07709	metformin-saxagliptin
d07717	acyclovir-hydrocortisone topical
d07740	vilazodone
d07754	azilsartan
d07764	famotidine-ibuprofen
d07767	linagliptin
d07804	apixaban
d07831	tyrosine
d07876	mirabegron
d07885	aclidinium
d07891	icosapent
d07902	linaclotide
d07905	teriflunomide
d07921	capsaicin-menthol topical
d08070	ospemifene
d08079	dimethyl fumarate
d08080	canagliflozin
d08117	dolutegravir
d08187	umeclidinium
d08272	tavaborole topical
d08275	empagliflozin
d08349	diphenhydramine-naproxen
d08362	olodaterol-tiotropium
d99999	Unmatched, no generic name

APPENDIX C: REASON FOR TAKING MEDICATIONS –

CODES AND CATEGORY NAMES

This Appendix contains two lists of codes representing reasons why participants think they are taking medications reported on the Medication Chart (See Appendix A above). The list of modified ICD-9 (__ICD9M) codes and category names is presented first and then the list of MIDUS (__MDC) codes and category names. See Section E above and the MIDUS-MIDJA Biomarker Medication Documentation for details about the coding process. The lists begin on the next page.

Modified ICD-9 Codes and Labels

The ICD9M category labels are based on clinical descriptions of diseases etc., thus this table also contains a column listing key words/common phrases indicating the conditions/symptoms etc. included in a given category.

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
10	PRIMARY TUBERCULOUS INFECTION	Tuberculosis bacillus
41	BACT INF IN OTH DIS/NOS	Infectious disease
42	HUMAN IMMUNO VIRUS DIS	HIV
53	HERPES ZOSTER	Shingles
54	HERPES SIMPLEX	Cold sores, herpes
78	OTHER VIRAL DISEASE	Warts
79	VIRAL INFECTION	Anti-viral, viral infection
110	DERMATOPHYTOSIS	Athlete's foot, toe nail fungus, fungal infection, ringworm
112	CANDIDIASIS	Yeast infection
133	SCABIES	Scabies
135	SARCOIDOSIS	Sarcoidosis
150	MALIGNANT NEOPLASM OF ESOPHAGUS	Esophagus cancer
173	OTHER MALIGNANT NEOPLASM OF SKIN	Skin cancer
174	MALIG NEO FEMALE BREAST	Breast cancer
185	MALIGN NEOPL PROSTATE	Prostate cancer
188	MALIGN NEOPL BLADDER	Bladder cancer
209	NEUROENDOCRINE TUMORS	Neuroendocrine carcinoid cancer
211	BENIGN NEOPLASM OF OTHER PARTS OF DIGESTIVE SYSTEM	Colon polyp
212	BENIGN NEOPLASM OF RESPIRATORY AND INTRATHORACIC ORGANS	Thymoma
218	UTERINE LEIOMYOMA	Fibroids, myoma of uterus
239	UNSPECIFIED NEOPLASM	Cancer non-specific

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
240	GOITER	Goiters-thyroid med, keeps goiters away
242	TOXIC DIFFUSE GOITER	Grave's disease
244	ACQUIRED HYPOTHYROIDISM	Hypothyroidism, thyroiditis
246	OTH DISORDERS OF THYROID	Thyroid hormone, thyroid
250	DIABETES MELLITUS	Diabetes, high blood sugar
251	OTH PANCREATIC DISORDER	Hypoglycemia
255	ADRENAL GLAND DISORDERS	Adrenal gland disorder, adrenal gland dysfunction
256	OVARIAN DYSFUNCTION	Polycystic ovarian syndrome
257	TESTICULAR DYSFUNCTION	Low testosterone levels
259	OTH ENDOCRINE DISORDERS	Imbalance in endocrine system
266	B-COMPLEX DEFICIENCIES	Low B12
267	ASCORBIC ACID DEFICIENCY	Vitamin C deficiency
268	VITAMIN D DEFICIENCY	Rickets, low vitamin D, vitamin D deficiency
269	OTH NUTRITION DEFICIENCY	Iodine deficiency, calcium deficiency
272	PURE HYPERCHOLESTEROLEM	High cholesterol, hyperlipidemia, high neutral lipid,
274	GOUT	Gout
275	DIS MINERAL METABOLISM	Magnesium supplement, reduce phosphate, supplement iron
276	FLUID/ELECTROLYTE DIS	Low potassium, hypokalemia
279	DISORDER OF IMMUNE MECHANISM	Autoimmune disease
280	IRON DEFICIENCY ANEMIA	Iron deficiency
281	PERNICIOUS ANEMIA	Pernicious anemia
285	ANEMIA NEC/NOS	Anemia
287	PURPURA & OTH HEMOR COND	Low platelet count
295	SCHIZOPHRENIC DISORDERS	Schizophrenia
296	AFFECTIVE PSYCHOSES	Bipolar disorder, mood swings

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
297	DELUSIONAL DISORDERS	Hallucinations, paranoia, ease up on symptoms of delusion
298	OTH NONORGANIC PSYCHOSES	Psychosis
300	NEUROTIC DISORDERS	Tranquilizer, stay calm, anxiety, nervousness, stabilizer
302	SEXUAL DISORDERS	Impotence, erectile dysfunction
303	ALCOHOL DEPENDENCE	Preventing craving alcohol
304	DRUG DEPENDENCE	Heroin addiction maintenance
305	NONDEPENDENT DRUG ABUSE	Smoking cessation
308	ACUTE REACTION TO STRESS	Stress
309	ADJUSTMENT REACTION	PTSD
311	DEPRESSIVE DISORDER NEC	Depression, anti-depressant
314	HYPERKINETIC SYNDROME	ADD, ADHD
323	ENCEPHALITIS, MYELITIS, AND ENCEPHALOMYELITIS	Myelitis
331	CEREBRAL DEGENERATION	Alzheimer's
332	PARKINSON'S DISEASE	Parkinson's disease
333	EXTRAPYRAMIDAL DIS NEC	Restless leg syndrome, tick in eye, tremors, Huntington's disease
337	AUTONOMIC NERVE DISORDER	Treat disorder of peripheral nerve, neuropathy in heart
338	PAIN, NOT ELSEWHERE CLASSIFIED	Pain, pain in multiple locations,
340	MULTIPLE SCLEROSIS	MS, Multiple sclerosis, muscle fatigue
345	EPILEPSY	Epilepsy, seizure disorder, focal seizures
346	MIGRAINE	Migraine
347	CATAPLEXY AND NARCOLEPSY	Narcolepsy
349	CNS DISORDER NEC/NOS	Neurological problems
350	TRIGEMINAL NERVE DISORDERS	Trigeminal neuralgia

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
354	CARPAL TUNNEL SYNDROME	Carpal tunnel syndrome
356	HERED & IDIOPATH PERIPH NEUROPATHY	Improvement of peripheral nervous system
358	MYONEURAL DISORDERS	Myasthenia gravis
361	RETINAL DETACHMENTS AND DEFEATS	Retinal detachment
362	RETINAL DISORDERS NEC	Macular degeneration
365	GLAUCOMA	Glaucoma, pressure in eye, lower ocular pressure
366	CATARACT	Cataract
370	KERATITIS	Ulcer in eye
371	CORNEAL OPACITY/DISORDER	Corneal problem
372	DISORDERS OF CONJUNCTIVA	Prevent eye infection
373	INFLAMMATION OF EYELIDS	Sty, blepharitis
375	LACRIMAL SYSTEM DISORDER	Dry eyes, lacrimal gland disorder
379	EYE DISORDERS NEC	Inflammation of eye, itchy eyes
380	DISORDER OF EXTERNAL EAR	Ear infection
386	VERTIGINOUS SYNDROMES	Meniere's disease, inner ear
388	DISORDERS OF EAR NEC	Ringing ears, tinnitus, ear pain, dry ear
389	HEARING LOSS	Helps with hearing, hearing loss
401	ESSENTIAL HYPERTENSION	High blood pressure, hypertension, reduce/lower blood pressure, blood pressure, anti-hypertensive
410	ACUTE MYOCARDIAL INFARCT	Myocardial infarction, cardiac infarction
413	ANGINA PECTORIS	Angina pectoris, angina
414	OTH CHR ISCHEMIC HRT DIS	Arterial sclerosis
415	ACUTE PULMONARY HEART DISEASE	Heart pulmonary embolism
424	OTH ENDOCARDIAL DISEASE	Mitral stenosis, prolapsed mitral valve
427	CARDIAC DYSRHYTHMIAS	Irregular pulse, atrial fibrillation
428	HEART FAILURE	Heart failure

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
429	ILL-DEFINED HEART DIS	Cardiac disease, heart dilation, dysraphism of aortic valve
431	INTRACEREBRAL HEMORRHAGE	Intracerebral hemorrhage, brain hemorrhage
434	CEREBRAL ARTERY OCCLUS	Cerebral infarction sequelae, cerebral thrombosis, mini stroke
435	TRANSIENT CEREB ISCHEMIA	TIA
440	ATHEROSCLEROSIS	Atherosclerosis
441	AORTIC ANEURYSM AND DISSECTION	Aortic aneurysm
442	OTHER ANEURYSM	Aneurysm
443	RAYNAUD'S SYNDROME	Raynaud's syndrome
446	POLYARTERIT NODOSA ET AL	Wegener's disease
447	OTHER ARTERIAL DISEASE	Twisted carotid artery, vasculitis
451	THROMBOPHLEBITIS	Recurring phlebitis
453	OTH VENOUS THROMBOSIS	Anticoagulant, thrombosis, prevent thrombosis, prevent blood clot, thrombus
455	HEMORRHOIDS	Hemorrhoids
458	HYPOTENSION	Low blood pressure
460	ACUTE NASOPHARYNGITIS	Treat Cold, acute upper respiratory infection
461	ACUTE SINUSITIS	Acute sinus problems, post nasal drip, nasal inflammation, nasal mucus
470	DEVIATED NASAL SEPTUM	Deviated septum
471	NASAL POLYPS	Polyps in sinus
472	CHR PHARYNG/NASOPHARYNG	Rhinitis, chronic nasal congestion, reduce swelling of nasal passages
473	CHRONIC SINUSITIS	Chronic sinus
477	ALLERGIC RHINITIS	Hay fever, dust allergy, allergic rhinitis
478	OTH UPPR RESPIRATORY DIS	Drippy/clogged nose
486	PNEUMONIA, ORGANISM NOS	Pneumonia

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
487	INFLUENZA	Flu
490	BRONCHITIS NOS	Bronchitis
492	EMPHYSEMA	Emphysema
493	ASTHMA	Asthma, pulmonary emphysema, emphysema
496	CHR AIRWAY OBSTRUCT NEC	COPD
518	OTHER LUNG DISEASES	Repair damage to lung
519	OTHER DISEASES OF RESPIRATORY SYSTEM	Bronchial spasm prevention
523	GINGIVAL/PERIODONTAL DIS	Gum disease/problems
524	DENOFACIAL ANOMALIES	Temporomandibular joint disorders, TMJ
525	OTHER DENTAL DISORDER	Extracted teeth, treatment for a tooth, toothache
526	DISEASES OF THE JAWS	Root canal, root canal infection
527	SALIVARY GLAND DISEASES	Dry mouth
528	ORAL SOFT TISSUE DISEASE	Stomatitis, chapped lips, canker sores, dental abscess
529	TONGUE DISORDERS	Geographic tongue
530	DISEASES OF ESOPHAGUS	Acid reflux, GERD, gastritis, esophagus trouble, backward flow of gastric acid,
531	GASTRIC ULCER	Gastric ulcer
532	DUODENAL ULCER	Duodenal ulcer
533	PEPTIC ULCER, SITE NOS	Helicobacter pylori, gastric & duodenal ulcer, peptic ulcer
535	GASTRITIS AND DUODENITIS	Inflammation of stomach
536	STOMACH FUNCTION DISORD	Gastric hyperacidity, dyspepsia, neutralize/reduce gastric acid, stomach pain
553	OTHER ABDOMINAL HERNIA	Hernia, high hiatal hernia
555	REGIONAL ENTERITIS	Crohn's disease
556	IDIOPATHIC PROCTOCOLITIS	Colitis
558	OTH NONINF GASTROENTERIT	Diarrhea, gastroenteritis

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
562	DIVERTICULA OF INTESTINE	Diverticulitis
564	FUNCT DIGESTIVE DIS NEC	Constipation, bowel movement, colon cramps, irritable bowel
569	OTH INTESTINAL DISORDERS	Intestinal disorder, inflammation of intestines, proctitis
571	CHR LIVER DIS/CIRRHOSIS	Liver disease, primary biliary cirrhosis
574	CHOLELITHIASIS	Gall stone
575	OTHER DISORDERS OF GALLBLADDER	Gallbladder polyp
579	INTESTINAL MALABSORPTION	Celiac disease nutrition
583	NEPHRITIS NOS	Lupus in kidneys
585	CHRONIC RENAL FAILURE	Kidney disease
586	RENAL FAILURE NOS	Renal failure
590	KIDNEY INFECTION	Kidney infection, antibiotics for kidney
592	RENAL/URETERAL CALCULUS	Kidney stones
593	OTH RENAL & URETERAL DIS	Prevention/help with renal insufficiency
596	OTHER BLADDER DISORDERS	Bladder tone, neurogenic bladder
599	OTH URINARY TRACT DISOR	Urinary tract infection, UTI
600	HYPERPLASIA OF PROSTATE	Prostatic hypertrophy, prostatic hyperplasia
601	PROSTATIC INFLAMMATION	Prostatitis, enlarged prostate, help reduce swelling of prostate
607	DISORDER OF PENIS	Due to prostate cancer/vitality
608	MALE GENITAL DIS NEC	Transitions
611	OTHER BREAST DISORDERS	Breast pain
616	INFLAMMATORY DISEASE OF CERVIX, VAGINA, AND VULVA	Vaginitis
625	FEMALE GENITAL SYMPTOMS	Dysmenorrhea, premenstrual tension
626	DISORDER OF MENSTRUATION	Menstrual pain, irregular period

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
627	MENOPAUSAL DISORDERS	Menopausal disorder, balancing hormones, stabilizer for menopause, menopause
628	FEMALE INFERTILITY	Fertility, prepare uterus
682	CELLULITIS AND ABSCESS, UNSPEC	Cellulitis
686	OTHER LOCAL INFECTIONS OF SKIN AND SUBCUTANEOUS TISSUE	Skin palmoplantar pustulosis
690	ERYTHEMATOSQUAMOUS DERM	Dry scalp
691	ATOPIC DERMATITIS AND RELATED CONDITIONS	Atopic dermatitis
692	CONTACT DERMATITIS	Eczema, dermatitis, poison oak
695	ERYTHEMATOUS CONDITIONS	Rosacea, lupus
696	PSORIASIS/LIKE DISORDERS	Psoriasis
697	LICHEN	Lichen
698	PRURITUS & LIKE COND	Itch, itching
702	OTHER DERMATOSES	Actinic keratosis
704	HAIR & FOLLICLE DISEASE	Hair thinning
705	DISORDERS OF SWEAT GLANDS	Miliaria
706	SEBACEOUS GLAND DISEASE	Acne
707	CHRONIC ULCER OF SKIN	Sores in ears (hearing aid), sores under arms
708	URTICARIA	Hives, chronic urticaria
709	OTHER SKIN DISORDERS	Scar
714	RHEUMATOID & OTH INFLAMM POLYARTHROP	Rheumatoid arthritis, RA
715	OSTEOARTHROSIS ET AL	Osteoarthritis
716	ARTHROPATHIES NEC/NOS	Arthritis, arthritis pain
718	OTHER JOINT DERANGEMENT	Pain in hip
719	JOINT DISORDER NEC & NOS	Knee, shoulder, joint etc. pain or problem, athralgia,
721	SPONDYLOSIS AND ALLIED DISORDERS	Undifferentiated spondyloarthropathy
722	INTERVERTEBRAL DISC DIS	Degenerative spine condition

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
723	OTHER CERVICAL SPINE DIS	Cervical vertebra pain, pinched nerve, neck pain
724	BACK DISORDER NEC & NOS	Back pain, sciatica, lumbar canal stenosis, back spasms
726	PERIPH ENTHESOPATHIES	Torn rotator cuff, tendonitis of jaw
727	OTH DIS SYNOV/TEND/BURSA	Bursitis
728	DIS OF MUSCLE/LIG/FASCIA	Muscle spasm
729	OTHER SOFT TISSUE DIS	Sore muscles, leg pain/cramps, muscle constriction, rheumatism
730	OSTEOMYELITIS, PERIOSTITIS, AND OTHER INFECTIONS INVOLVING BONE	Osteomyelitis
731	OSTEITIS DEFORMANS	Paget's disease, brittle bone
733	OTH BONE & CARTILAGE DIS	Osteoporosis, osteopenia, pain in bone, low bone density
745	CARDIAC SEPTAL CLOS ANOM	Foramen ovale
753	CONGENITAL ANOMALIES OF URINARY SYSTEM	Polycystic kidney disease
780	GENERAL SYMPTOMS	Sleep aid, night sweats, vasovagal syncope, sensitive to cold, stiff, giddy, insomnia, vertigo, memory problems
781	NERV/MUSCULSKEL SYS SYMP	Tremor
782	SKIN/OTH INTEGUMENT SYMP	Rash, numbness of feet/finger/legs, reduce keloidosis, reduce skin inflammation, edema
783	NUTRIT/METAB/DEVEL SYMP	Anorexia, weight loss, appetite suppressant
784	SYMPTOMS INVOL HEAD/NECK	Headache, sore throat
785	CARDIOVASCULAR SYS SYMP	Heart murmur
786	RESP SYS/OTH CHEST SYMP	Difficulty breathing, loosen phlegm, short breath, whooping cough, chest tightness
787	GI SYSTEM SYMPTOMS	Gassy, heartburn, nausea
788	URINARY SYSTEM SYMPTOMS	Urination disorder, frequent urination, urination trouble/problem, bladder control
789	OTH ABDOMEN/PELVIS SYMP	Stomach spasm, stomach cramp, groin pain

ICD9M CODE	ICD9 CODE LABEL	Key Words/Common Responses
790	NONSPECIFIC FINDINGS ON EXAMINATION OF BLOOD	High uric acid, hyperuricemia
795	ABN HISTOLOG/IMMUNO FIND	Positive TB test
797	SENILITY WITHOUT MENTION OF PSYCHOSIS	Memory
805	FRACTURE OF VERTEBRAL COLUMN WITHOUT MENTION OF SPINAL CORD INJURY	Broken back bone
904	INJURY TO BLOOD VESSELS OF LOWER EXTREMITY AND UNSPECIFIED SITES	Blood vessel injury
918	SUPERFICIAL INJURY OF EYE AND ADNEXA	Eye injury
919	SUPERFICIAL INJ OTH SITE	Blisters
957	INJURY TO NERVE NEC/NOS	Nerve damage
965	POIS-ANALGESIC/ANTIPYRET	Counteract Naproxen
993	EFFECTS OF AIR PRESSURE	Altitude sickness
994	EFFECT EXTERNAL CAUS NEC	Motion sickness
995	CERTAIN ADVERSE EFF NEC	Inflammation, food allergy, allergy (non-specific)
9996	UNABLE TO CLASSIFY	
9997	DON'T KNOW	
9998	MISSING	
9999	INAPP	

MIDUS Codes and Labels

To assist users in understanding the type of responses in the MIDUS code categories this table also contains a column listing key words/common phrases used to assign a response to a given category. Note all the MIDUS codes are alphanumeric and begin with an "M" followed by a 4 digit numeric code. The exception is the codes for Unable to Classify, Don't Know, Missing, and INAPP which begin with a "Z" and the usual missing value codes.

MIDUS CODE	MIDUS CODE LABEL	Key words/Common Phrases
M1000	GENERAL HEALTH	Health, for health, maintain health
M1010	IMPROVE HEALTH	Improve health, strengthen the system, for healing, recovery from (cancer, surgery, etc.), getting better
M1020	ENERGY	Gives me a boost, when feel run down, increase energy, improve drive, when tired
M1030	GENERAL HEALTH, OTHERS	Beauty, aging, stay younger, detox, cleanse body
M1040	GENERAL HEALTH, PREVENTIVE	Preventive, prevention, prevent potential sickness
M2000	SUPPLEMENT	Supplement (just the word)
M2010	VITAMIN SUPPLEMENT	Lacking vitamins, to supply vitamins, get balance of vitamins
M2020	CALCIUM SUPPLEMENT	Calcium, need more calcium, don't drink milk
M2030	DIETARY SUPPLEMENT	Supplement diet, balance diet needs
M2040	ENSURE NUTRITIONAL INTAKES	Nutrient fortification, add nutrients, balance nutrition
M2050	POOR DIET	Diet, don't always eat well, dietary reasons
M2060	ANTIOXIDANT	Antioxidants, help with free radicals,
M2070	SUPPLEMENT, OTHERS	Iron pill, resupply iron, omega 3, fiber, probiotics
M3010	CARDIOVASCULAR HEALTH	Heart health, good for heart, cardiovascular health
M3011	CARDIOVASCULAR HEALTH, PREVENTIVE	Cardiac family history, prevent clots/stroke/heart attack/atherosclerosis
M3012	CARDIOVASCULAR HEALTH, BLOOD THINNER	Blood thinner
M3013	CARDIOVASCULAR HEALTH, OTHERS	Improve blood circulation, neutral fat,
M3020	MUSCULOSKELETAL HEALTH	Bone health, because of broken bones, health leg and hip

MIDUS CODE	MIDUS CODE LABEL	Key words/Common Phrases
M3021	BONE STRENGTH/DENSITY	Bone strength/density/loss/mass
M3022	JOINT HEALTH	Healthy joints, good for bones-joints, maintain bone and joint health
M3023	MUSCULOSKELETAL HEALTH, PREVENTIVE	Prevent bone loss, prevent osteoporosis
M3024	MUSCULOSKELETAL HEALTH, OTHERS	Repair muscles, get older legs weaken, bone/muscle
M3030	DIGESTIVE HEALTH	Digestion, break down food, help digest food, condition of my stomach
M3031	INTESTINAL/COLON HEALTH	Colon health, cleans out colon, regularity, to condition intestinal functions
M3032	STOMACH ACID	Stomach acid
M3040	PROSTATE HEALTH	Prostate health, prostate gland, prostate problem,
M3050	EYE HEALTH	Eye health, good for eyes, nutrients for eyes, tired eyes, eye problem, uveal tract
M3060	BRAIN HEALTH	Boost cognitive abilities, memory, good for your brain, brain health, brain function, avoid senile brain
M3070	IMMUNE HEALTH	Boost/support immune system, beneficial for immune system,
M3071	PREVENT COLDS	Prevent catching cold, improve sensitivity to colds
M3072	IMMUNOSUPRESSION	Immunosuppressant, immunosuppressant after kidney transplant
M3080	INTEGUMENT HEALTH	Hair/Skin/Nail health, dry skin/hair, for skin, to avoid tanning/sunburn, liver spot, rough hands
M3090	OTHER TARGETED HEALTH	Low frequency reasons that cannot be assigned elsewhere (e.g. Multiple organ/system support (i.e. eye & bone, prevent cancer and strokes), bladder protection, protect liver from alcohol, liver, chronic illness)
M4010	MD RECOMMEND	Doctor suggested/prescribed/recommended/ "told me to"
M4020	GOOD FOR YOU/ME	Good for me/you, everyone says it's a good idea, healthy thing to do, heard it's good for you, saw on TV etc.

MIDUS CODE	MIDUS CODE LABEL	Key words/Common Phrases
M4030	FAMILY/FRIEND RECOMMEND	Friend, family member, mother, etc. recommended it, spouse puts it out
M5000	WEIGHT LOSS	Lose weight, weight management, diet plan pills
M5100	STRESS	For stress, helps with stress
M5200	CONTRACEPTION	Birth Control, prevent pregnancy
M5300	COUNTER/PREVENT DRUG SIDE EFFECTS	Counter the affects of statin, prevent side effect of Lipitor, help with side effects of atorvastatin, etc.
Z9996	UNABLE TO CLASSIFY	
Z9997	DON'T KNOW	
Z9998	MISSING	
Z9999	INAPP	

APPENDIX D: THERAPEUTIC AND PHARMACOLOGIC CLASS CODES AND NAMES

This Appendix contains two lists 1) Therapeutic Class (TC) codes and category names, and 2) Pharmacologic Class (PC) codes and categories included in the MIDUS and MIDJA data files as of May 2017. These lists will be updated as needed at future releases. See Section A above and MIDUS-MIDJA Biomarker Medication Documentation for details.

Therapeutic Class Codes and Names

The Therapeutic Classification (TC) system has three tiers consisting of a set of nested (parent-child) categories that parallels the ways in which clinicians think about medications. The system is polyhierarchical and each therapeutic class has a unique code. See Section B above for details. The list below is organized in nested in numeric order. The top tier (Parent/Grandparent) class codes are in the leftmost column. All middle tier (Parent/Child) class codes are listed under their top tier parent code. Similarly, all bottom tier (Child/Grandchild) class codes are listed under their middle tier "Parent" codes. All category names are listed in the rightmost column. Color coding is used to help illustrate the relationships among the therapeutic classes.

Multum Therapeutic Classes

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
1			ANTI-INFECTIVES
	2		AMEBICIDES
	3		ANTHELMINTICS
	4		ANTIFUNGALS
		235	POLYENES
		236	AZOLE ANTIFUNGALS
		237	MISCELLANEOUS ANTIFUNGALS
	5		ANTIMALARIAL AGENTS
		238	ANTIMALARIAL QUINOLINES
		239	MISCELLANEOUS ANTIMALARIALS
	6		ANTITUBERCULOSIS AGENTS
		232	RIFAMYCIN DERIVATIVES
		234	MISCELLANEOUS ANTITUBERCULOSIS AGENTS
		457	HYDRAZIDE DERIVATIVES
	7		ANTIVIRAL AGENTS
		175	PROTEASE INHIBITORS
		176	NRTIS
		177	MISCELLANEOUS ANTIVIRALS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
		227	NNRTIS
		229	PURINE NUCLEOSIDES
		281	NEURAMINIDASE INHIBITORS
		327	ANTIVIRAL COMBINATIONS
		364	ANTIVIRAL CHEMOKINE RECEPTOR ANTAGONIST
		366	INTEGRASE STRAND TRANSFER INHIBITOR
		480	ANTIVIRAL BOOSTERS
	9		CEPHALOSPORINS
		159	FIRST GENERATION CEPHALOSPORINS
		160	SECOND GENERATION CEPHALOSPORINS
		161	THIRD GENERATION CEPHALOSPORINS
	11		MACROLIDE DERIVATIVES
		304	MACROLIDES
	12		MISCELLANEOUS ANTIBIOTICS
	13		PENICILLINS
		224	AMINOPENICILLINS
		225	PENICILLINS BETA LACTAMASE INHIBITORS
	14		QUINOLONES
	15		SULFONAMIDES
	16		TETRACYCLINES
	17		URINARY ANTI INFECTIVES
	18		AMINOGLYCOSIDES
	240		LINCOMYCIN DERIVATIVES
20			ANTINEOPLASTICS
	23		ANTIMETABOLITES
	24		ANTINEOPLASTIC HORMONES
	454		PROTEASOME INHIBITORS
28			BIOLOGICALS
	34		IN VIVO DIAGNOSTIC BIOLOGICALS
40			CARDIOVASCULAR AGENTS
	42		ANGIOTENSIN CONVERTING ENZYME INHIBITORS
	43		ANTIADRENERGIC AGENTS PERIPHERALLY ACTING
	44		ANTIADRENERGIC AGENTS CENTRALLY ACTING
	45		ANTIANGINAL AGENTS
	46		ANTIARRHYTHMIC AGENTS
		385	GROUP I ANTIARRHYTHMICS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
		386	GROUP II ANTIARRHYTHMICS
		387	GROUP III ANTIARRHYTHMICS
		388	GROUP IV ANTIARRHYTHMICS
		389	GROUP V ANTIARRHYTHMICS
	47		BETA ADRENERGIC BLOCKING AGENTS
		274	CARDIOSELECTIVE BETA BLOCKERS
		275	NON-CARDIOSELECTIVE BETA BLOCKERS
	48		CALCIUM CHANNEL BLOCKING AGENTS
	49		DIURETICS
		154	LOOP DIURETICS
		155	POTASSIUM-SPARING DIURETICS
		156	THIAZIDE AND THIAZIDE-LIKE DIURETICS
	50		INOTROPIC AGENTS
	51		MISCELLANEOUS CARDIOVASCULAR AGENTS
	52		PERIPHERAL VASODILATORS
	53		VASODILATORS
	54		VASOPRESSORS
	55		ANTIHYPERTENSIVE COMBINATIONS
		467	ACE INHIBITORS WITH THIAZIDES
		470	MISCELLANEOUS ANTIHYPERTENSIVE COMBINATIONS
		472	BETA BLOCKERS WITH THIAZIDES
		473	ANGIOTENSIN II INHIBITORS WITH THIAZIDES
		474	BETA BLOCKERS WITH CALCIUM CHANNEL BLOCKERS
		475	POTASSIUM SPARING DIURETICS WITH THIAZIDES
		476	ACE INHIBITORS WITH CALCIUM CHANNEL BLOCKING AGENTS
		479	ANGIOTENSIN II INHIBITORS WITH CALCIUM CHANNEL BLOCKERS
	56		ANGIOTENSIN II INHIBITORS
	303		AGENTS FOR PULMONARY HYPERTENSION
	340		ALDOSTERONE RECEPTOR ANTAGONISTS
	433		CATECHOLAMINE VASOPRESSORS
57			CENTRAL NERVOUS SYSTEM AGENTS
	58		ANALGESICS
		59	MISCELLANEOUS ANALGESICS
		60	NARCOTIC ANALGESICS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
		61	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS
		62	SALICYLATES
		63	ANALGESIC COMBINATIONS
		191	NARCOTIC ANALGESIC COMBINATIONS
		193	ANTIMIGRAINE AGENTS
		278	COX-2 INHIBITORS
	64		ANTICONVULSANTS
		199	HYDANTOIN ANTICONVULSANTS
		200	SUCCINIMIDE ANTICONVULSANTS
		201	BARBITURATE ANTICONVULSANTS
		203	BENZODIAZEPINE ANTICONVULSANTS
		204	MISCELLANEOUS ANTICONVULSANTS
		311	DIBENZAZEPINE ANTICONVULSANTS
		345	FATTY ACID DERIVATIVE ANTICONVULSANTS
		347	GAMMA-AMINOBUTYRIC ACID ANALOGS
		348	TRIAZINE ANTICONVULSANTS
		350	PYRROLIDINE ANTICONVULSANTS
		351	CARBONIC ANHYDRASE INHIBITOR ANTICONVULSANTS
	65		ANTIEMETIC ANTIVERTIGO AGENTS
		195	5HT3 RECEPTOR ANTAGONISTS
		196	PHENOTHIAZINE ANTIEMETICS
		197	ANTICHOLINERGIC ANTIEMETICS
		198	MISCELLANEOUS ANTIEMETICS
	66		ANTIPARKINSON AGENTS
		205	ANTICHOLINERGIC ANTIPARKINSON AGENTS
		276	DOPAMINERGIC ANTIPARKINSONISM AGENTS
	67		ANXIOLYTICS SEDATIVES AND HYPNOTICS
		68	BARBITURATES
		69	BENZODIAZEPINES
		70	MISCELLANEOUS ANXIOLYTICS, SEDATIVES AND HYPNOTICS
	71		CNS STIMULANTS
	73		MUSCLE RELAXANTS
		74	NEUROMUSCULAR BLOCKING AGENTS
		178	SKELETAL MUSCLE RELAXANTS
	80		MISCELLANEOUS CENTRAL NERVOUS SYSTEM AGENTS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
	313		CHOLINESTERASE INHIBITORS
	378		DRUGS USED IN ALCOHOL DEPENDENCE
81			COAGULATION MODIFIERS
	82		ANTICOAGULANTS
		262	COUMARINS AND INDANEDIONES
		283	THROMBIN INHIBITORS
		285	FACTOR XA INHIBITORS
	83		ANTIPLATELET AGENTS
		211	PLATELET AGGREGATION INHIBITORS
	85		MISCELLANEOUS COAGULATION MODIFIERS
87			GASTROINTESTINAL AGENTS
	88		ANTACIDS
	90		ANTIDIARRHEALS
	91		DIGESTIVE ENZYMES
	92		GALLSTONE SOLUBILIZING AGENTS
	93		GI STIMULANTS
	94		H2 ANTAGONISTS
	95		LAXATIVES
	96		MISCELLANEOUS GI AGENTS
	272		PROTON PUMP INHIBITORS
	277		5 AMINOSALICYLATES
	355		FUNCTIONAL BOWEL DISORDER AGENTS
		89	ANTICHOLINERGICS ANTISPASMODICS
		455	GUANYLATE CYCLASE C AGONISTS
97			HORMONES/HORMONE MODIFIERS
	98		ADRENAL CORTICAL STEROIDS
		301	GLUCOCORTICOIDS
		302	MINERALOCORTICOIDS
	101		SEX HORMONES
		102	CONTRACEPTIVES
		182	ANDROGENS AND ANABOLIC STEROIDS
		183	ESTROGENS
		184	GONADOTROPINS
		185	PROGESTINS
		186	SEX HORMONE COMBINATIONS
		279	GONADOTROPIN-RELEASING HORMONE AND ANALOGS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
	103		THYROID HORMONES
	288		5 ALPHA REDUCTASE INHIBITORS
	411		CALCITONIN
	416		SOMATOSTATIN AND SOMATOSTATIN ANALOGS
	417		SELECTIVE ESTROGEN RECEPTOR MODULATORS
	418		PARATHYROID HORMONE AND ANALOGS
	420		ANTIANDROGENS
	423		AROMATASE INHIBITORS
105			MISCELLANEOUS AGENTS
	106		ANTIDOTES
	107		CHELATING AGENTS
	108		CHOLINERGIC MUSCLE STIMULANTS
	109		LOCAL INJECTABLE ANESTHETICS
	110		MISCELLANEOUS UNCATEGORIZED AGENTS
	114		ILLICIT STREET DRUGS
	192		ANTIRHEUMATICS
	270		ANTIPSORIATICS
	284		VISCOSUPPLEMENTATION AGENTS
	320		SMOKING CESSATION AGENTS
113			GENITOURINARY TRACT AGENTS
	263		IMPOTENCE AGENTS
	264		URINARY ANTISPASMODICS
	265		URINARY PH MODIFIERS
	266		MISCELLANEOUS GENITOURINARY TRACT AGENTS
115			NUTRITIONAL PRODUCTS
	116		IRON PRODUCTS
	117		MINERALS AND ELECTROLYTES
	118		ORAL NUTRITIONAL SUPPLEMENTS
	119		VITAMINS
	120		VITAMIN AND MINERAL COMBINATIONS
	121		INTRAVENOUS NUTRITIONAL PRODUCTS
122			RESPIRATORY AGENTS
	123		ANTIHISTAMINES
	124		ANTITUSSIVES
	125		BRONCHODILATORS
		126	METHYLXANTHINES

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
		180	ADRENERGIC BRONCHODILATORS
		181	BRONCHODILATOR COMBINATIONS
		299	ANTICHOLINERGIC BRONCHODILATORS
	127		DECONGESTANTS
	128		EXPECTORANTS
	130		RESPIRATORY INHALANT PRODUCTS
		296	INHALED CORTICOSTEROIDS
		407	INHALED ANTI INFECTIVES
	132		UPPER RESPIRATORY COMBINATIONS
	243		LEUKOTRIENE MODIFIERS
133			TOPICAL AGENTS
	135		ANTISEPTIC AND GERMICIDES
	136		DERMATOLOGICAL AGENTS
		137	TOPICAL ANTI INFECTIVES
		138	TOPICAL STEROIDS
		139	TOPICAL ANESTHETICS
		140	MISCELLANEOUS TOPICAL AGENTS
		141	TOPICAL STEROIDS WITH ANTI INFECTIVES
		143	TOPICAL ACNE AGENTS
		248	TOPICAL EMOLLIENTS
		290	TOPICAL ANTIBIOTICS
		292	TOPICAL ANTIFUNGALS
		381	TOPICAL DEPIGMENTING AGENTS
		382	TOPICAL ANTIHISTAMINES
		448	TOPICAL NON-STEROIDAL ANTI-INFLAMMATORIES
		450	TOPICAL ANTINEOPLASTICS
		453	TOPICAL RUBEFACIENT
		461	TOPICAL ANTI ROSACEA AGENTS
	146		MOUTH AND THROAT PRODUCTS
	147		OPHTHALMIC PREPARATIONS
		163	OPHTHALMIC ANTI-INFECTIVES
		164	OPHTHALMIC GLAUCOMA AGENTS
		165	OPHTHALMIC STEROIDS
		166	OPHTHALMIC STEROIDS WITH ANTI INFECTIVES
		167	OPHTHALMIC ANTI INFLAMMATORY AGENTS
		168	OPHTHALMIC LUBRICANTS AND IRRIGATIONS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
		169	MISCELLANEOUS OPHTHALMIC AGENTS
		267	OPHTHALMIC ANTIHISTAMINES AND DECONGESTANTS
		286	MYDRIATICS
	148		OTIC PREPARATIONS
		393	CERUMENOLYTICS
	151		VAGINAL PREPARATIONS
		268	VAGINAL ANTI-INFECTIVES
		269	MISCELLANEOUS VAGINAL AGENTS
	247		NASAL PREPARATIONS
		244	NASAL LUBRICANTS AND IRRIGATIONS
		245	NASAL STEROIDS
		246	NASAL ANTIHISTAMINES AND DECONGESTANTS
153			PLASMA EXPANDERS
218			ALTERNATIVE MEDICINES
	219		NUTRACEUTICAL PRODUCTS
	220		HERBAL PRODUCTS
	363		PROBIOTICS
242			PSYCHOTHERAPEUTIC AGENTS
	249		ANTIDEPRESSANTS
		76	MISCELLANEOUS ANTIDEPRESSANTS
		208	SSRI ANTIDEPRESSANTS
		209	TRICYCLIC ANTIDEPRESSANTS
		306	PHENYLPIPERAZINE ANTIDEPRESSANTS
		307	TETRACYCLIC ANTIDEPRESSANTS
		308	SSNRI ANTIDEPRESSANTS
	251		ANTIPSYCHOTICS
		77	MISCELLANEOUS ANTIPSYCHOTIC AGENTS
		210	PHENOTHIAZINE ANTIPSYCHOTICS
		341	ATYPICAL ANTIPSYCHOTICS
254			IMMUNOLOGIC AGENTS
	33		IMMUNE GLOBULINS
	104		IMMUNOSUPPRESSIVE AGENTS
		441	CALCINEURIN INHIBITORS
		442	TNF ALPHA INHIBITORS
		444	SELECTIVE IMMUNOSUPPRESSANTS
		445	OTHER IMMUNOSUPPRESSANTS

Top Tier (Parent/ Grandparent)	Middle Tier (Parent/ Child)	Bottom Tier (Child/ GrandChild)	Therapeutic Class Names
	437		IMMUNOSTIMULANTS
		439	OTHER IMMUNOSTIMULANTS
331			RADIOLOGIC AGENTS
	332		RADIOLOGIC ADJUNCTS
		374	CARDIAC STRESSING AGENTS
358			METABOLIC AGENTS
	19		ANTIHYPERLIPIDEMIC AGENTS
		173	HMG-COA REDUCTASE INHIBITORS
		174	MISCELLANEOUS ANTIHYPERLIPIDEMIC AGENTS
		241	FIBRIC ACID DERIVATIVES
		252	BILE ACID SEQUESTRANTS
		316	CHOLESTEROL ABSORPTION INHIBITORS
		317	ANTIHYPERLIPIDEMIC COMBINATIONS
	99		ANTIDIABETIC AGENTS
		213	SULFONYLUREAS
		214	BIGUANIDES
		215	INSULIN
		216	ALPHA-GLUCOSIDASE INHIBITORS
		271	THIAZOLIDINEDIONES
		282	MEGLITINIDES
		314	ANTIDIABETIC COMBINATIONS
		371	DIPEPTIDYL PEPTIDASE 4 INHIBITORS
		373	GLP 1 RECEPTOR AGONISTS
		458	SGLT 2 INHIBITORS
	194		ANTIGOUT AGENTS
	289		ANTIHYPERURICEMIC AGENTS
	293		GLUCOSE ELEVATING AGENTS
	359		PERIPHERALLY ACTING ANTIOBESITY AGENTS
	409		BONE RESORPTION INHIBITORS
		217	BISPHOSPHONATES
		415	MISCELLANEOUS BONE RESORPTION INHIBITORS
365			MEDICAL GAS
462			ALLERGENICS
999			INAPP

Pharmacologic Class Codes and Names

The Pharmacologic Classification (PC) system is flat thus the classes are in numeric order by class code. This system does not include parent/child relationships, but drugs can be assigned to multiple pharmacologic categories. Within MIDUS/MIDJA medications can be assigned to up to 6 PC categories. See Section A above and MIDUS-MIDJA Biomarker Medication Documentation for more details.

Multum Pharmacologic Classes	
Codes	Class Names
901	ACNE PRODUCTS
902	ACETYLCHOLINESTERASE INHIBITOR
903	ACETYLCHOLINESTERASE INHIBITOR (CENTRAL)
909	ADRENERGIC AGONIST AGENT
915	ALKALINIZING AGENT
918	ALPHA 1 AGONIST
919	ALPHA 1 BLOCKER
928	ALPHA-/BETA- AGONIST
930	ALPHA 2 -ADRENERGIC AGONIST
931	ALPHA 2 AGONIST, OPHTHALMIC
935	AMINOQUINOLINE (ANTIMALARIAL)
938	5-AMINOSALICYLIC ACID DERIVATIVE
943	ANALGESIC COMBINATION (OPIOID)
946	ANALGESIC, OPIOID
947	ANALGESIC NONOPIOID
951	ANALGESIC, TOPICAL
952	ANALGESIC, URINARY
953	ANALGESIC, MISCELLANEOUS
954	ANDROGEN
955	ANESTHETIC/CORTICOSTEROID
956	ANESTHETIC, TOPICAL
957	ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITOR
958	ANGIOTENSIN II RECEPTOR BLOCKER
961	ANTACID
963	ANTHELMINTIC
971	ANTIANGINAL AGENT
973	ANTIANXIETY AGENT, MISCELLANEOUS
976	ANTIARRHYTHMIC AGENT, CLASS IB
977	ANTIARRHYTHMIC AGENT, CLASS IC
978	ANTIARRHYTHMIC AGENT, CLASS II

Codes	Class Names
979	ANTIARRHYTHMIC AGENT, CLASS III
980	ANTIARRHYTHMIC AGENT, CLASS IV
983	ANTIARRHYTHMIC AGENT, MISCELLANEOUS
989	ANTIBIOTIC, AMINOGLYCOSIDE
994	ANTIBIOTIC, CEPHALOSPORIN (FIRST GENERATION)
995	ANTIBIOTIC, CEPHALOSPORIN (SECOND GENERATION)
998	ANTIBIOTIC/CORTICOSTEROID, OPHTHALMIC
1000	ANTIBIOTIC CORTICOSTEROID TOPICAL
1002	ANTIBIOTIC, MACROLIDE
1004	ANTIBIOTIC, OPHTHALMIC
1005	ANTIBIOTIC, ORAL RINSE
1008	ANTIBIOTIC, PENICILLIN
1009	ANTIBIOTIC, FLUOROQUINOLONE
1011	ANTIBIOTIC, SULFONAMIDE DERIVATIVE
1013	ANTIBIOTIC, TETRACYCLINE DERIVATIVE
1014	ANTIBIOTIC, TOPICAL
1017	ANTIBIOTIC, MISCELLANEOUS
1019	ANTICHOLINERGIC AGENT
1022	ANTICOAGULANT
1026	ANTICONVULSANT, BARBITURATE
1027	ANTICONVULSANT BENZODIAZEPINE
1029	ANTICONVULSANT, HYDANTOIN
1031	ANTICONVULSANT, SUCCINIMIDE
1032	ANTICONVULSANT, MISCELLANEOUS
1044	ANTIDEPRESSANT, ALPHA-2 ANTAGONIST
1050	ANTIDEPRESSANT, SELECTIVE SEROTONIN REUPTAKE INHIBITOR
1051	ANTIDEPRESSANT, SEROTONIN/NOREPINEPHRINE REUPTAKE INHIBITOR
1052	ANTIDEPRESSANT, SEROTONIN REUPTAKE INHIBITOR/ANTAGONIST
1057	ANTIDEPRESSANT, TRICYCLIC (SECONDARY AMINE)
1058	ANTIDEPRESSANT, TRICYCLIC (TERTIARY AMINE)
1063	ANTIDIABETIC AGENT, BIGUANIDE
1065	ANTIDIABETIC AGENT, SULFONYLUREA
1066	ANTIDIABETIC AGENT, THIAZOLIDINEDIONE
1069	ANTIDIARRHEAL
1073	CORTICOSTEROID PARENTERAL
1074	ANTIDOTE
1095	ANTIDOTE, EXTRAVASATION

Codes	Class Names
1122	ANTIEMETIC
1125	ANTIFLATULENT
1126	ANTIFUNGAL AGENT, IMIDAZOLE DERIVATIVE
1130	ANTIFUNGAL AGENT, ORAL
1131	ANTIFUNGAL AGENT, ORAL NONABSORBED
1134	ANTIFUNGAL AGENT, TOPICAL
1135	ANTIFUNGAL AGENT, VAGINAL
1138	ANTIGOUT AGENT
1156	ANTIHYPERTENSIVE
1162	ANTI-INFLAMMATORY AGENT
1169	ANTILIPEMIC AGENT, BILE ACID SEQUESTRANT
1170	ANTILIPEMIC AGENT, FIBRIC ACID
1171	ANTILIPEMIC AGENT, HMG-COA REDUCTASE INHIBITOR
1172	ANTILIPEMIC AGENT, MISCELLANEOUS
1173	ANTIMALARIAL AGENT
1174	ANTIMANIC AGENT
1177	ANTIMIGRAINE AGENT
1189	ANTINEOPLASTIC AGENT, ANTIMETABOLITE
1195	ANTINEOPLASTIC AGENT, AROMATASE INHIBITOR
1216	ANTINEOPLASTIC AGENT, MISCELLANEOUS
1219	ANTI-PARKINSON'S AGENT, ANTICHOLINERGIC
1221	ANTI-PARKINSON'S AGENT, DOPAMINE AGONIST
1225	ANTIPLATELET AGENT
1253	ANTIRETROVIRAL, PROTEASE INHIBITOR (ANTI-HIV)
1254	ANTIRETROVIRAL, REVERSE TRANSCRIPTASE INHIBITOR, NON-NUCLEOSIDE (ANTI-HIV)
1255	ANTIRETROVIRAL, REVERSE TRANSCRIPTASE INHIBITOR, NUCLEOSIDE (ANTI-HIV)
1257	ANTIRETROVIRAL, REVERSE TRANSCRIPTASE INHIBITOR, NUCLEOTIDE (ANTI-HIV)
1259	ANTIRHEUMATIC, DISEASE MODIFYING
1260	ANTISEBORRHEIC AGENT TOPICAL
1263	ANTISPASMODIC AGENT, URINARY
1268	ANTITUSSIVE
1277	ANTIVIRAL AGENT
1280	ANTIVIRAL AGENT, ORAL
1282	ANTIVIRAL AGENT, TOPICAL
1284	ASTRINGENT

Codes	Class Names
1286	BARBITURATE
1289	BENZODIAZEPINE
1291	BETA-BLOCKER, BETA-1 SELECTIVE
1293	BETA-BLOCKER, NONSELECTIVE
1294	BETA-BLOCKER WITH ALPHA-BLOCKING ACTIVITY
1295	BETA BLOCKER WITH INTRINSIC SYMPATHOMIMETIC ACTIVITY
1299	BETA 2 AGONIST
1303	BIOLOGICAL, MISCELLANEOUS
1305	BISPHOSPHONATE DERIVATIVE
1308	BLOOD VISCOSITY REDUCER AGENT
1313	CALCIUM CHANNEL BLOCKER
1314	CALCIUM SALT
1318	CARDIAC GLYCOSIDE
1320	CARDIOVASCULAR AGENT, MISCELLANEOUS
1326	CENTRAL NERVOUS SYSTEM DEPRESSANT
1343	CONTRACEPTIVE
1363	CORTICOSTEROID, INHALANT (ORAL)
1364	CORTICOSTEROID, NASAL
1365	CORTICOSTEROID, OPHTHALMIC
1367	CORTICOSTEROID, RECTAL
1369	CORTICOSTEROID, SYSTEMIC
1370	CORTICOSTEROID, TOPICAL
1379	COUGH PREPARATION
1380	DECONGESTANT
1382	DECONGESTANT/ANALGESIC
1390	DIAGNOSTIC AGENT
1428	DIETARY SUPPLEMENT
1435	DIURETIC, LOOP
1438	DIURETIC, POTASSIUM SPARING
1439	DIURETIC, THIAZIDE
1440	DIURETIC, THIAZIDE-RELATED
1447	ELECTROLYTE SUPPLEMENT, ORAL
1448	ELECTROLYTE SUPPLEMENT, PARENTERAL
1449	ENZYME
1463	ESTROGEN AND PROGESTIN COMBINATION
1464	ESTROGEN DERIVATIVE
1472	EXPECTORANT

Codes	Class Names
1481	GALLSTONE DISSOLUTION AGENT
1486	GASTROINTESTINAL AGENT, PROKINETIC
1488	GASTROINTESTINAL AGENT, MISCELLANEOUS
1489	GENERAL ANESTHETIC
1497	GONADOTROPIN
1504	HEMOSTATIC AGENT
1507	HISTAMINE H 2 ANTAGONIST
1509	HOMOCYSTINURIA, TREATMENT AGENT
1510	HORMONE
1523	HYPNOTIC, MISCELLANEOUS
1528	IMMUNOSUPPRESSANT AGENT
1534	IRON SALT
1536	KERATOLYTIC AGENT
1537	LAXATIVE
1539	LAXATIVE, BULK-PRODUCING
1543	LAXATIVE, OSMOTIC
1544	LAXATIVE, SALINE
1545	LAXATIVE, STIMULANT
1551	LEUKOTRIENE RECEPTOR ANTAGONIST
1554	LIPASE INHIBITOR
1557	LOCAL ANESTHETIC
1576	MAGNESIUM SALT
1577	MAST CELL STABILIZER
1585	MONOCLONAL ANTIBODY
1589	OPIOID ANTAGONIST
1597	NEUROMUSCULAR BLOCKER AGENT, TOXIN
1599	NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID)
1600	NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID), COX-2 SELECTIVE
1602	NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID), ORAL
1603	NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID), PARENTERAL
1604	NUTRITIONAL SUPPLEMENT
1607	OPHTHALMIC AGENT, ANTIGLAUCOMA
1611	OPHTHALMIC AGENT, TOXIN
1612	OPHTHALMIC AGENT, VASOCONSTRICTOR
1614	OPHTHALMIC AGENT, MISCELLANEOUS
1620	OVULATION STIMULATOR
1627	PHENOTHIAZINE DERIVATIVE

Codes	Class Names
1629	PHOSPHATE BINDER
1644	PROGESTIN
1646	PROSTAGLANDIN
1647	PROSTAGLANDIN, OPHTHALMIC
1651	PROTON PUMP INHIBITOR
1661	RETINOIC ACID DERIVATIVE
1665	SALICYLATE
1670	SEDATIVE
1671	SELECTIVE ESTROGEN RECEPTOR MODULATOR (SERM)
1672	SELECTIVE 5-HT 3 RECEPTOR ANTAGONIST
1681	SKELETAL MUSCLE RELAXANT
1683	SKIN AND MUCOUS MEMBRANE AGENT
1687	SKIN AND MUCOUS MEMBRANE AGENT, MISCELLANEOUS
1688	SMOKING CESSATION AID
1691	SOMATOSTATIN ANALOG
1694	STOOL SOFTENER
1700	SYMPATHOMIMETIC
1710	THYROID PRODUCT
1712	TOPICAL SKIN PRODUCT
1713	TOPICAL SKIN PRODUCT, ACNE
1718	TRACE ELEMENT
1719	TRACE ELEMENT, PARENTERAL
1729	URICOSURIC AGENT
1742	VASODILATOR
1750	VITAMIN
1752	VITAMIN D ANALOG
1753	VITAMIN, FAT SOLUBLE
1756	VITAMIN, WATER SOLUBLE
1757	XANTHINE OXIDASE INHIBITOR
1762	SEROTONIN 5-HT 1B, 1D RECEPTOR AGONIST
1765	CENTRAL NERVOUS SYSTEM STIMULANT
1768	HISTAMINE H 1 ANTAGONIST
1779	5 ALPHA-REDUCTASE INHIBITOR
1781	ANTILIPEMIC AGENT, 2-AZETIDINONE
1808	MONOCLONAL ANTIBODY, ANTI-ASTHMATIC
1810	N-METHYL-D-ASPARTATE RECEPTOR ANTAGONIST
1811	PHOSPHODIESTERASE-5 ENZYME INHIBITOR

Codes	Class Names
1822	ANTINEOPLASTIC AGENT, ANTIMETABOLITE (ANTIFOLATE)
1824	SUBSTITUTED BENZIMIDAZOLE
1825	ANTISEPTIC, TOPICAL
1827	SECOND GENERATION (ATYPICAL) ANTIPSYCHOTIC
1828	FIRST GENERATION (TYPICAL) ANTIPSYCHOTIC
1830	AMINO ACID
1831	TUMOR NECROSIS FACTOR (TNF) BLOCKING AGENT
1833	MONOCLONAL ANTIBODY, SELECTIVE ADHESION-MOLECULE INHIBITOR
37021	PROBIOTIC
309141	ANTIBIOTIC, LINCOSAMIDE
369942	INSULIN, INTERMEDIATE-ACTING
369943	INSULIN, LONG-ACTING
370141	INSULIN, RAPID-ACTING
512625	PARTIAL NICOTINE AGONIST
515063	IMIDAZOLINE DERIVATIVE
580286	ANTIDIABETIC AGENT, DIPEPTIDYL PEPTIDASE IV (DPP-IV) INHIBITOR
944618	ANTIRETROVIRAL, CCR5 ANTAGONIST (ANTI-HIV)
996578	ANTIRETROVIRAL, INTEGRASE INHIBITOR (ANTI-HIV)
996698	ANTINEOPLASTIC AGENT, ANTIMETABOLITE (PYRIMIDINE ANALOG)
1035979	ANILIDOPIPERIDINE OPIOID
1154061	RESCUE AGENT (CHEMOTHERAPY)
1154062	CHEMOTHERAPY MODULATING AGENT
1160459	BETA 2 -ADRENERGIC AGONIST, LONG-ACTING
1160479	BETA 2 AGONIST, LONG-ACTING
1163619	NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID), TOPICAL
1177583	HISTAMINE H 1 ANTAGONIST, SECOND GENERATION
1177584	HISTAMINE H 1 ANTAGONIST, FIRST GENERATION
1191179	VASODILATOR, DIRECT-ACTING
1274399	IMMUNOMODULATOR, SYSTEMIC
1284841	HISTONE DEACETYLASE INHIBITOR
1797079	CALCIUM CHANNEL BLOCKER, NONDIHYDROPYRIDINE
1797080	CALCIUM CHANNEL BLOCKER, DIHYDROPYRIDINE
1801719	CALCINEURIN INHIBITOR
1826674	ANTIPLATELET AGENT, THIENOPYRIDINE
2148013	ANTIDIABETIC AGENT, GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONIST
2759759	ANTI-PARKINSON'S AGENT, DECARBOXYLASE INHIBITOR

Codes	Class Names
2759760	ANTI-PARKINSON'S AGENT, DOPAMINE PRECURSOR
2792400	ANTINEOPLASTIC AGENT, ANTIMETABOLITE (PURINE ANALOG)
2807279	TRANSIENT RECEPTOR POTENTIAL VANILLOID 1 (TRPV1) AGONIST
2952225	ALKYLAMINE DERIVATIVE
2952299	ETHANOLAMINE DERIVATIVE
2952340	PIPERAZINE DERIVATIVE
2952559	PIPERIDINE DERIVATIVE
2965759	FIBER SUPPLEMENT
2988377	ANALGESIC, OPIOID PARTIAL AGONIST
3015214	ANTIDEPRESSANT, SELECTIVE SEROTONIN REUPTAKE INHIBITOR/5-HT 1A RECEPTOR PARTIAL AGONIST
3451903	BONE-MODIFYING AGENT
3501084	GABA ANALOG
3509782	ALPHA-ADRENERGIC AGONIST
3819764	BETA 3 AGONIST
3861322	PHOSPHODIESTERASE ENZYME INHIBITOR, NONSELECTIVE
3964448	PYRIMIDINE SYNTHESIS INHIBITOR
3974202	ANTILIPEMIC AGENT, OMEGA-3 FATTY ACIDS
3988862	ANTICHOLINERGIC AGENT, LONG-ACTING
4230723	SODIUM-GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR
4230724	ANTIDIABETIC AGENT, SODIUM-GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR
4230742	FUMARIC ACID DERIVATIVE
4496663	CARBONIC ANHYDRASE INHIBITOR (OPHTHALMIC)
4649822	ANTIHEMORRHOIDAL AGENT
4857382	ANTIHEPADNAVIRAL, REVERSE TRANSCRIPTASE INHIBITOR, NUCLEOSIDE (ANTI-HBV)
5002622	ANTICOAGULANT, FACTOR XA INHIBITOR
5002623	ANTICOAGULANT, VITAMIN K ANTAGONIST
5002625	ANTICOAGULANT, DIRECT THROMBIN INHIBITOR
5251182	MEDICAL FOOD
5357662	ANTIDEPRESSANT, DOPAMINE/NOREPINEPHRINE-REUPTAKE INHIBITOR
5585170	MINERALOCORTICOID (ALDOSTERONE) RECEPTOR ANTAGONISTS
6004244	ANTIFUNGAL AGENT ORAL NONABSORBED PARTIALLY ABSORBED
6024732	DIRECT ORAL ANTICOAGULANT DOAC
6433523	GUANYLATE CYCLASE C GC C AGONIST
9999999	INAPP