

# Archimedes Cardio-Metabolic Risk (CMR) Forecast Dataset Specifications

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The Cardio-Metabolic Risk (CMR) Dataset contains the results of 19 simulated controlled trials that compare current levels of care ("standard care") with 20 different interventions for managing obesity, blood pressure, cholesterol, hyperglycemia, cardiovascular disease risk, and smoking.

## Design

- Definition of "standard care"
  - In "Standard care" people are screened and managed according to national guidelines at levels of adherence seen in people currently diagnosed with the relevant conditions<sup>1</sup>. People are recommended for follow-up visits according to national guidelines and follow those recommendations at currently observed levels of adherence. People can seek care spontaneously for symptoms. Anyone newly diagnosed with a condition during the follow-up period, either through symptoms or a test performed at a visit, is treated according to national guidelines at levels of adherence seen in currently diagnosed people.
- Initial screening and treatment with "Standard Care"(Figure 1)
  - At the start of the trial, all subjects are screened to identify people already diagnosed with obesity, hypertension, dyslipidemia, or hyperglycemia, and to identify any people who have these conditions but who have not yet been diagnosed.
  - People with previously diagnosed conditions continue to receive care at current levels of adherence.
  - People with previously undiagnosed obesity, hypertension, dyslipidemia, or hyperglycemia are treated according to national guidelines at adherence levels that match those seen in previously diagnosed people (i.e., standard care for those conditions).
    - Guidelines for hypertension, dyslipidemia, and hyperglycemia all include recommendations of lifestyle modification for treating people with the respective conditions and "pre-conditions" (e.g., pre-diabetes). "Standard care" includes the recommended lifestyle modification<sup>2</sup>, at current levels of adherence.
    - Sources: JNC-7 guidelines for hypertension ATP-3, guidelines for dyslipidemia, Institute for Clinical Systems Improvement (ICSI) guidelines for weight control, and ADA guidelines for hyperglycemia.

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<sup>1</sup> Hypertension, dyslipidemia, obesity, hyperglycemia, nephropathy, neuropathy, retinopathy, diabetic ketoacidosis, hypoglycemia, aspirin use, treatment of diagnosed MI, angina and coronary artery disease, congestive heart failure, stroke, ventricular fibrillation, atrial fibrillation, colorectal cancer, lung cancer, breast cancer, hormone replacement therapy.

<sup>2</sup> Lifestyle modification is assumed to reduce weight by approximately 3% (Source: Tsai AG, Wadden TA. Annals of Internal Medicine.2005;142:56-66)

- Interventions (Figure 2)
  - The resulting population, with every case of obesity, hypertension, dyslipidemia, and hyperglycemia (as well as overweight, pre-hypertension and pre-diabetes) diagnosed and treated to current levels of adherence, along with everyone without a diagnosis of those conditions, is then used to simulate 19 different trials.
  - Each trial has a target population, and from one to three treatment arms. We use the term “Scenario” to describe a particular intervention for a particular target population. A simulated trial will typically include a control scenario in which the target population continues to receive only standard care, and an intervention scenario in which the target population receives a particular intervention in addition to standard care. Some trials include multiple intervention scenarios. The target populations and intervention scenarios for each trial are described below (see **Interventions**).
  - The trials include three main types of interventions
    - “Magic Pills”. Many of the trials use hypothetical treatments, created to achieve precisely the objective of a guideline or prevention recommendation. They are included to show what would happen if a recommended treatment goal were actually achieved. Magic pills include interventions for controlling BMI, SBP, LDL, FPG, HbA1c, and smoking to specified levels.
    - Achievement of 100% adherence to guidelines. These interventions deliver care as specified in current guidelines, including steps to add or switch drugs as indicated by a guideline to try to reach a goal. Trials with these types of treatments show the effects of improving performance on guidelines. Four of the trials – involving BP, LDL, glucose and weight treatments – are of this type (see Trials 4, 6, 10, and 15 below). Depending on the patient’s initial level of a physiological variable and response to treatments, the desired treatment goal will not necessarily be achieved in all patients.
    - Specific drugs. Three of the trials involve specific drugs (Metformin, aspirin, and a polypill of aspirin, a statin and a beta blocker). These trials are included to show the effects of adding these drugs to standard care for target populations that are not receiving the drugs under standard care (see Trials 16, 17, and 18 below). There is no titration to a goal.
  - Effects of treatments. The effects of all real drugs (other than magic pills) are based on clinical trials.
- Follow-up and measurement of outcomes
  - For each trial, the people are followed for 20 years and a range of physiological variables, utilization and health outcomes, and cost generating events are recorded for each individual (see **Outcomes**).
  - People not in the target population for a particular trial are excluded from follow-up in that trial.
  - Outcomes and events are recorded as they occur (e.g. patients seek care for symptoms or a test is performed when a patient has a visit for another reason) and at annual intervals. Results are reported in Tables at annual intervals.

- Visits are scheduled and visits for different indications are clustered appropriately to represent the scheduling and clustering of visits in reality.

## Participants

- 100,000 individuals age 30-85 representative of the US population
  - Source: National Health and Nutrition Examination Survey (NHANES) 1999 – 2006
- Different target populations indicated for treatment with each particular intervention (see [Interventions](#))

## Study settings

- US population and healthcare delivery systems
- Ambulatory, outpatient, and inpatient care practices based on national guidelines
  - For details see [Representation of Care Processes in CMR](#) below
- Adherence to guidelines calibrated to match actual levels of care in the US
  - Sources: NHANES, National Hospital Ambulatory Medical Care Survey (NHAMCS), National Ambulatory Medical Care Survey (NAMCS), National Hospital Discharge Survey (NHDS)
- Costs based on Medicare data sets
  - Sources: Medicare Inpatient LDS Dataset (DRGs), Medicare LDS Physician Dataset and Medicare Current Beneficiary Survey (MCBS) (CPTs), National averages from Centers for Medicare and Medicaid Services (APC), Medicare Part D Drug Dataset, and DrugStore.com (medications), additional published sources. (see [Sources for Cost Assumptions in CMR](#), below).
  - Costs are adjusted to 2010 values.
  - Assumptions can be modified in Archimedes Outcomes Analyzer (AOA)
- Quality of life assumptions based on Sullivan and Ghushchyan 2006, Coffey et al. 2002
  - Assumptions can be modified in Archimedes Outcomes Analyzer (AOA)

## Interventions

- Control: standard care
  - Trial 1: Guidelines standard care
    - Target population: Total population.
    - Scenario 1: Standard Care. Guidelines applied at current rates of adherence. No additional interventions. Guidelines are applied to new patients diagnosed with any condition at any time in follow-up period, with current rates of adherence.
- Weight management trials
  - Trial 2: BMIAbove30
    - Target population: People with BMI > 30 kg/m<sup>2</sup>.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus reduce BMI to 30 kg/m<sup>2</sup> and maintain at 30 kg/m<sup>2</sup>
  - Trial 3: BMIAbove25
    - Target population: People with BMI > 25 kg/m<sup>2</sup>.
    - Scenario 1: Standard care only

- Scenario 2: Standard care plus reduce BMI to 25 kg/m<sup>2</sup> and maintain at 25 kg/m<sup>2</sup>
    - Scenario 3: Standard care plus reduce BMI by 5% not to go below 25 kg/m<sup>2</sup>, maintain 5% reduction
  - Trial 4: Guidelines\_WeightManagementFullAdherence
    - Target population: Total population<sup>3</sup>.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus, if indicated for weight loss by guideline then take weight loss intervention<sup>4</sup> with 100% adherence. Apply guideline with 100% adherence to new patients diagnosed overweight or with obesity at any time in follow-up period.
- Blood pressure management
  - Trial 5: SBPAbove130
    - Target population: People with SBP > 130 mmHg.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus reduce SBP to 130 mmHg and maintain at 130 mmHg
  - Trial 6: Guidelines\_BPManagementFullAdherence
    - Target population: Total population<sup>3</sup>.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus, if indicated for treatment by BP guideline, then start lifestyle modifications and take medications (ACE-I / ARB, diuretic, beta blocker, CCB) as specified by guideline with 100% adherence. Apply guideline with 100% adherence to new patients diagnosed with pre-hypertension or hypertension at any time in follow-up period.
- Cholesterol management
  - Trial 7: LDLAbove100
    - Target population: People with LDL > 100 mg/dL.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus reduce LDL to 100 mg/dL and maintain at 100 mg/dL
  - Trial 8: LDLAbove130
    - Target population: People with LDL > 130 mg/dL.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus reduce LDL to 130 mg/dL and maintain at 130 mg/dL
  - Trial 9: LDLAbove160
    - Target population: People with LDL > 160 mg/dL.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus reduce LDL to 160 mg/dL and maintain at 160 mg/dL

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<sup>3</sup> The target populations for guidelines for hypertension, dyslipidemia, hyperglycemia, and obesity are the total population because the guidelines include testing for those conditions, and the entire population needs to be followed and tested as indicated by the guidelines

<sup>4</sup> Lifestyle and weight loss program assumed to reduce weight by approximately 3%. Source: Tsai AG, Wadden T A. Systematic Review: An Evaluation of Major Commercial Weight Loss Programs in the United States. Annals of Internal Medicine 2005;142(1): 56-66

- Trial 10: Guidelines\_CholesterolManagementFullAdherence
  - Target population: Total population<sup>3</sup>.
  - Scenario 1: Standard care only
  - Scenario 2: Standard care plus, if indicated for statins by current dyslipidemia guideline, then start lifestyle modifications and take statins (simvastatin, atorvastatin) as specified by guideline with 100% adherence. Apply guideline with 100% adherence to new patients if they are diagnosed with dyslipidemia at any time in follow-up period.
- Glucose management
  - Trial 11: FPGAbove126\_ReduceTo126
    - Target population: People with FPG > 126 mg/dL.
    - Scenario 1: Standard care only
    - Scenario 2: Reduce FPG to 126 mg/dL and maintain at 126 mg/dL
  - Trial 12: HbA1cAbove7\_ReduceTo7
    - Target population: People with HbA1c above 7%.
    - Scenario 1: Standard care only
    - Scenario 2: Reduce HbA1c to 7% and maintain at 7%
  - Trial 13: HbA1cAbove8\_ReduceTo8
    - Target population: People with HbA1c above 8%.
    - Scenario 1: Standard care only
    - Scenario 2: Reduce HbA1c to 8% and maintain at 8%
  - Trial 14: HbA1cAbove9\_ReduceTo9
    - Target population: People with HbA1c above 9%.
    - Scenario 1: Standard care only
    - Scenario 2: Reduce HbA1c to 9% and maintain at 9%
  - Trial 15: Guidelines\_GlycemicManagementFullAdherence
    - Target population: Total population<sup>3</sup>
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus, if indicated for treatment by current diabetes guidelines, start lifestyle modifications and take medications (metformin, glitazone, sulfonylurea, insulin) as specified by guidelines with 100% adherence. Apply guideline with 100% adherence to new patients if they are diagnosed with pre-diabetes or hyperglycemia at any time in follow-up period.
  - Trial 16: FPGBetween100And126
    - Target population: FPG of 100 mg/dL or above and less than 126 mg/dL.
    - Scenario 1: Standard care only
    - Scenario 2: Reduce FPG by 10%, not to go below 100 mg/dL, maintain 10% reduction
    - Scenario 3: Standard care plus take metformin 850 mg/day
- Aspirin and polypill
  - Trial 17: DMorCAD\_TreatWithPolypill
    - Target population: People diagnosed with diabetes or coronary artery disease (CAD).
    - Scenario 1: Standard care only

- Scenario 2: Standard care plus take fixed doses of generic aspirin, statin, and beta blocker. No titration to goal.
  - Trial 18: MIorIschemicStroke\_TreatWithASA
    - Target population: People who have had MI or stroke.
    - Scenario 1: Standard care only
    - Scenario 2: Standard care plus take aspirin 81 mg/day<sup>5</sup>
- Smoking Cessation
  - Trial 19: Smoker\_TreatWithSmokingCessation
    - Target population: Current smoker
    - Scenario 1: Standard care only
    - Scenario 2: Stop smoking and remain nonsmoker

## Outcomes

- Baseline data on total population and target populations for each intervention
- Diagnoses of MI, stroke, MACE (major cardiovascular events: fatal and nonfatal MI and stroke, cardiovascular death), revascularization, diabetes, diabetic proliferative retinopathy, bilateral blindness, ESRD, diabetic foot ulcer, diabetic foot amputation.
- Total deaths, CHD deaths, stroke deaths
- Life years
- Quality adjusted life years (QALYs), discounted QALYs
- Total medical costs, discounted total medical costs, cost per QALY, cost per averted event (e.g. death, stroke, MI)
- Biomarkers and risk factors: proportion smokers, BMI, weight, systolic blood pressure, diastolic blood pressure, LDL, HDL, total cholesterol, triglycerides, FPG, HbA1c, serum creatinine
- Utilization (years on medication): aspirin, antihypertensives, ACE-inhibitor, beta blocker, CCB, diuretics, dyslipidemia medications, oral DM agents, metformin, sulfonylurea, TZD, insulin, weight loss interventions, “Magic pills” that affect physiological variables (BMI, HbA1c, FPG, LDL, and SBP), and a polypill (aspirin, betablocker, statin)

## Time horizon

- 20 years
  - Any time window for viewing outcomes can be set in Archimedes Outcomes Analyzer (AOA)

## Statistical methods

- Cumulative values
- Kaplan-Meier
- Average values
- Other standard statistical methods. See Outcomes tab, for more information about statistical methods

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<sup>5</sup> Aspirin is not given to people who have had a hemorrhagic stroke, consistent with stroke guidelines

## Results

- Results are contained in the CMR Dataset which can be analyzed interactively using the Archimedes Outcomes Analyzer (AOA)
  - AOA enables users to create tables, bar charts, and time-line charts for any outcome with any intervention over any time period. Results of any set of interventions can be compared.
  - Results can be viewed from the perspective of the entire US population, the target population of any intervention, or the average individual in any target population
  - Results can be recalculated for any set of assumptions about performance levels, intervention costs, general background costs (costs other than the costs of interventions), quality of life weights, and discount rates.
  - Results can be displayed for sub-populations (see below)

## Subpopulation analyses

- Total population
- Target population of any intervention
- Average individual in any target population of any intervention
- Any of the above can be stratified by any of the following
  - Gender
    - Male
    - Female
  - Age
    - 30-49
    - 50-64
    - 65-85
  - Comorbidity
    - Has CAD (MI or angina)
    - Has DM (type I or type II)
    - Has neither CAD or DM

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Figure 1

# Initial Screening and Treatment with “Standard Care”

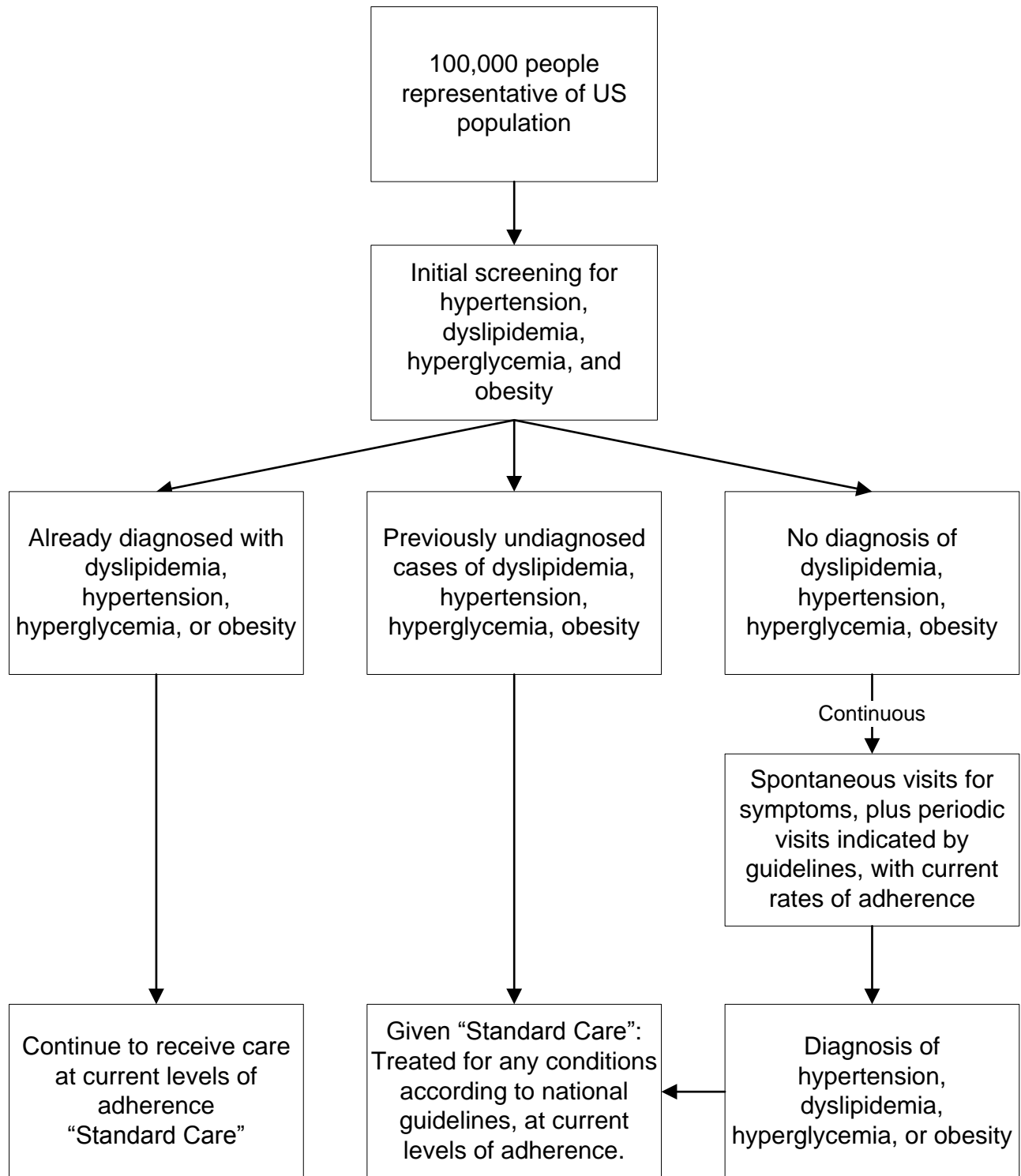
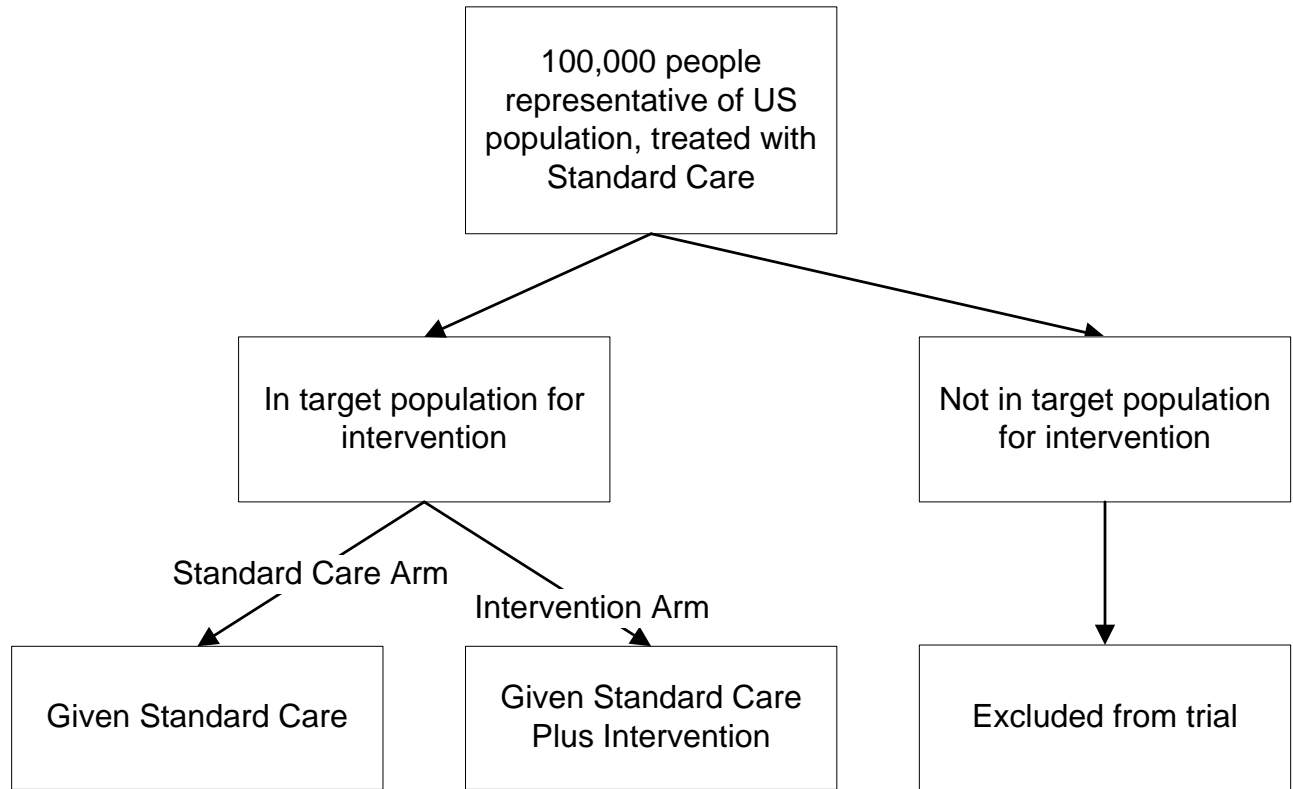


Figure 2

## Controlled Trial of Intervention



# Representation of Care Processes in CMR

Healthcare processes in the Archimedes Model are based on national guidelines. The table below describes the guidelines incorporated in the Model. These guidelines represent ideal care; in actual practice there are wide variations in care practices. In the Archimedes Model, physician and patient behaviors are adjusted to reflect the average care people receive in the US today. This “average” or “standard” care takes into account both physician performance and patient adherence to tests, treatments, and follow-up care.

Representation of patients' interactions with the healthcare system is quite detailed in the Archimedes Model. At any time during the follow-up period a patient can experience a symptom and decide to seek care. Depending on the type of symptom and their past behavior, the patient could seek acute care or consult a specialist or their primary care physician (PCP). When a patient presents for care, the PCPs can also screen the individual for any other conditions that are relevant given their demographics, risk factors, and screening history. Follow-up appointments are scheduled according to guidelines and grouped when possible to mimic what happens in reality.

The following are the guidelines in the Archimedes Model most pertinent to this analysis.

Name	Description
<b>Hypertension</b>	Care processes for hypertension are based on the JNC-7. Thresholds of 140/90 for systolic blood pressure/diastolic blood pressure are used to diagnose and treat hypertension, unless the subject has diabetes or CKD, in which case a threshold of 130/80 is used. For diagnosis and treatment of pre-hypertension, we use the JNC-7 treatment goal of 120/80. Both those diagnosed with hypertension and pre-hypertension are prescribed lifestyle changes. Anti-hypertension medications are prescribed as needed until patients achieve goals set by the guidelines. Anti-hypertension medications include diuretics, ACE-inhibitors, beta blockers and CCBs.
<b>Dyslipidemia</b>	Care processes for dyslipidemia are based on the NCEP ATP-III thresholds of 100 for LDL to diagnose and treat dyslipidemia for high risk (CHD or CHD equivalents) individuals, 130 for moderate risk (2+ risk factors) individuals, and 160 for low risk individuals. Patients diagnosed with dyslipidemia are treated to goal with lifestyle changes and statins.
<b>Obesity</b>	The Model includes the guidelines for prevention and management of obesity, recommended by the Institute for Clinical Systems Improvement (ICSI). Obesity Classes I-III are diagnosed based on BMI measurements of 30, 35, and 40 kg/m <sup>2</sup> respectively. Patients are diagnosed as overweight when BMI >= 25 kg/m <sup>2</sup> . Those diagnosed as overweight or obese are recommended lifestyle changes, which in the Archimedes Model causes a weight loss of 3%.
<b>Diabetes</b>	The care protocol for diabetes uses the FPG threshold of 126 recommended by ADA's standards of medical care in diabetes to diagnose diabetes. Patients are treated to an HbA1c of 7% as recommended by the guideline. An FPG between 100 and 125 is diagnosed as prediabetes. The guideline's recommendation for a diet for patients with prediabetes and metformin and diet for patients with diagnosed diabetes is included. Additional oral agents such as sulfonylureas and glitazones are recommended, ultimately advancing to insulin as necessary to achieve a goal of HbA1c less than or equal to 7%.

<b>Nephropathy</b>	The Model includes the guidelines recommended by ADA's standards of medical care in diabetes to diagnose and treat diabetic nephropathy. Chronic kidney disease (CKD) stages 1-5 are diagnosed based on glomerular filtration rate (GFR) calculations, where stage 3 is diagnosed when GFR is less than 60 and stage 5/ESRD when GFR is less than 15. Those with ESRD may be treated with dialysis and/or kidney transplant.
<b>Neuropathy and diabetic foot ulcer (DFU)</b>	The Model includes the guidelines described by the ADA's standards of medical care in diabetes, in which sensory neuropathy, ulcers and individuals requiring toe, ankle, knee and above-knee amputations are identified with foot exams (10g monofilament test, reflexes, visible factors, etc).
<b>Retinopathy</b>	The Model includes guidelines recommended by the preferred practice pattern document on diabetic retinopathy prepared by the American Academy of Ophthalmology Retina/Vitreous Panel. Several retinopathy levels ranging from non-proliferative diabetic retinopathy to bilateral blindness can be diagnosed based on eye exam results. Treatments are prescribed according to the guideline and include laser photocoagulation treatment, retinal attachment and vitrectomy.
<b>Diabetic ketoacidosis (DKA)</b>	The Model includes guidelines described in the ADA's document on hyperglycemic crises in diabetes. Patients presenting with DKA symptoms, plasma glucose above 250, and positive ketones are diagnosed with DKA while those with a negative ketones test are diagnosed with hyperglycemia. Both are treated with insulin to an FPG goal of 200 with follow-up management.
<b>Hypoglycemia</b>	The Model includes recommendations of the Endocrine Society Clinical Practice Guidelines' document on Evaluation and Management of Adult Hypoglycemic Disorders, where hypoglycemia is diagnosed when symptoms are present and glucose is less than 70 mg/dL. Treatment follows, with a goal to bring glucose to 90.
<b>Aspirin primary prevention</b>	The Model includes guidelines for the primary prevention of cardiovascular disease using Aspirin, as specified by the US Preventive Services Task Force (USPSTF). Eligibility for primary prevention is based on gender, age and the Coronary Heart Disease Framingham Risk Score (CHD-FRS). Those eligible are prescribed 81 mg/day of aspirin.
<b>MI, angina and CAD</b>	The Model includes ACC/AHA guidelines for diagnosing MI, unstable angina and stable angina based on evaluation of symptoms, cardiac enzymes, and EKG. Follow-up care for CAD patients includes immediate medical therapy, and possibly cardiac catheterization, CABG or PCI. Long-term care for CAD patients includes EKG, echocardiogram, x-ray, catheterizations and possible revascularization according to ACC/AHA guidelines for the treatment of chronic stable angina caused by coronary atherosclerosis.
<b>CHF</b>	The Model includes guidelines recommended by ACC/AHA, in which systolic or diastolic CHF is diagnosed based on symptoms and echocardiogram findings. Guidelines recommend treatment with beta blockers, ACE-inhibitor, diuretic or digoxin, depending on severity and other symptoms such as fluid retention.
<b>Stroke</b>	The Model includes guidelines recommended by the AHA/ASA, and bases the diagnosis of ischemic or hemorrhagic stroke for a patient with acute stroke symptoms on a CT scan of the brain. The Model includes the cost of follow-up care, but does not include specific follow-up protocols.
<b>Ventricular fibrillation</b>	The Model includes ventricular fibrillation and protocol for its diagnosis and treatment. Ventricular fibrillation is diagnosed based on symptoms. Treatment is calibrated to capture the likelihood of successful defibrillation depending on the patient's location. For example a patient has a higher chance of surviving if they are

	already receiving care in the CCU than if they are at home.
<b>Atrial fibrillation</b>	The Model includes the occurrence of chronic atrial fibrillation but does not include subsequent symptoms of atrial fibrillation. The Model includes guidelines recommended by the AHA/ASA, Recommendations for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack Guidelines, to treat patients with chronic atrial fibrillation. Recommended treatments include beta blockers, CCBs, warfarin and aspirin, depending on current medication.
<b>Colorectal cancer</b>	The Model includes guidelines recommended by the Joint Group of the American Cancer Society, US Multi-Society Task force on Colorectal Cancer and the American College of Radiology to diagnose colorectal cancer. Screening occurs as defined by the guideline, and diagnoses of colorectal adenoma, colorectal IBD dysplasia, colorectal polyposis, colorectal low-risk adenoma, colorectal advanced adenoma, high risk for colorectal cancer, or colorectal cancer stages 1-4 can be made. If indicated, a polypectomy is performed. The effect of colorectal cancer treatment is included in the colorectal cancer survival model, but individual treatments are not explicitly included.
<b>Lung cancer</b>	The model includes the development of symptoms for lung cancer as well as screening programs. The effect of lung cancer treatments is included in the lung cancer survival model, but individual treatments are not explicitly included.
<b>Breast cancer</b>	Screening mammograms begin at age 40 for women. Positive screening mammograms or symptoms trigger diagnostic tests, which diagnose breast cancer at stages 0-4. The effects of treatment are included in the breast cancer survival model, but individual treatments are not explicitly included.
<b>Hormone replacement</b>	Because hormone replacement therapy is an important factor affecting breast cancer, the Archimedes Model includes protocols to prescribe and stop hormone replacement therapy in women who have gone through menopause.

# Sources for Cost Assumptions in CMR

The following sources used to compute costs in the Model.

## Medicare Current Beneficiary Survey (MCBS)

This is a survey of a nationally representative sample of aged, disabled, and institutionalized Medicare beneficiaries. The MCBS Cost and Use files link Medicare claims to survey-reported events and provide complete expenditure and source of payment data on all health care services, including those not covered by Medicare.

## Medicare Part D Drug data

This is part of the MCBS data mentioned above and is the primary source for most of the medication costs in the Model.

## Medicare Limited Data Set (LDS)

This data set contains beneficiary level health information for 5% of the entire Medicare population. Because of the large sample size, it provides good data on cost and utilization across various disease spaces, even for less common types of procedures, hospitalizations, and other services.

## Literature

For diseases that are not represented fully in the Medicare data sets, or diseases that have not been explicitly modeled to the level of detail that would allow us to capture costs of utilization accurately, we have estimated costs from published literature. Literature sources are:

- Curry, S. J., Grothaus, L. C., McAfee, T. &Pabiniak, C. (1998). *Use and cost effectiveness of smoking-cessation services under four insurance plans in a health maintenance organization*. The New England journal of medicine 339(10): 673-679.
- Esposito, D., Bagchi, A. D., Verdier, J. M., Bencio, D. S. &Kim, M. S. (2009). *Medicaid Beneficiaries With Congestive Heart Failure: Association of Medication Adherence With Healthcare Use and Costs*. The American Journal of Managed Care 15(7): 437-445.
- Kutikova, L., Bowman, L., Chang, S., Long, S. R., Obasaju, C. &Crown, W. H. (2005). *The economic burden of lung cancer and the associated costs of treatment failure in the United States*. Lung Cancer 50(2): 143-154.
- Samsa, G. P., Bian, J., Lipscomb, J. &Matchar, D. B. (1999). *Epidemiology of recurrent cerebral infarction: a medicare claims-based comparison of first and recurrent strokes on 2-year survival and cost*. Stroke 30(2): 338-349.
- Tsai, A. G. & Wadden, T. A. (2005). *Systematic Review: An Evaluation of Major Commercial Weight Loss Programs in the United States*. Annals of Internal Medicine 142(1): 56-66.

- Wu, E. Q., Birnbaum, H. G., Mareva, M., Tuttle, E., Castor, A. R., Jackman, W. & Ruskin, J. (2005). *Economic burden and co-morbidities of atrial fibrillation in a privately insured population*. *Curr Med Res Opin* 21(10): 1693-1699.
- Zauber, A. G., Lansdorp-Vogelaar I., Wilschut J., Knudsen, A.B., van Ballegooijen M., Kuntz, K.M. (2007). *Cost-effectiveness of DNA stool testing to screen for colorectal cancer: Report to AHRQ and CMS from the Cancer Intervention and Surveillance Modeling Network (CISNET) for MISCAN and SimCRC Models*.
- Drugstore.com: For medications where no data is available in Medicare Part D drug data, we have estimated costs from Drugstore.com.