

APPENDIX I: LIST OF EQUATIONS FOR THE BASE RUN

Blood

$$\text{HDLC}(t) = \text{HDLC}(t - dt) + (\text{Cholesterol_Uptake_by_HDL} - \text{HDLC_Transport_to_Liver} - \text{CETP_Regulated_C_Transfer}) * dt$$

$$\text{INIT HDLC} = 31.555$$

INFLOWS:

$$\text{Cholesterol_Uptake_by_HDL} \quad (\text{IN SECTOR: Extrahepatic Tissue})$$

OUTFLOWS:

$$\text{HDLC_Transport_to_Liver} \quad (\text{IN SECTOR: Liver})$$

$$\text{CETP_Regulated_C_Transfer} = \text{HDLC} * \text{CETP_Activity_Rate}$$

$$\text{IDL}(t) = \text{IDL}(t - dt) + (\text{VLDL_Turnover} - \text{IDL_Turnover} - \text{Extrahepatic_Uptake_of_IDL} - \text{Hepatic_Uptake_of_IDL}) * dt$$

$$\text{INIT IDL} = 18.575$$

INFLOWS:

$$\text{VLDL_Turnover} = \text{VLDLC} * \text{VLDL_Turnover_Rate}$$

OUTFLOWS:

$$\text{IDL_Turnover} = \text{IDL} * \text{IDL_Turnover_Rate}$$

$$\text{Extrahepatic_Uptake_of_IDL} = \text{IDL} * \text{Effect_of_ET_Receptor_Activity_on_IDL_Uptake}$$

$$\text{Hepatic_Uptake_of_IDL} = \text{IDL} * \text{Effect_of_HP_Receptor_Activity_on_IDL_Uptake}$$

$$\text{LDLC}(t) = \text{LDLC}(t - dt) + (\text{IDL_Turnover} -$$

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Dependent_Activity} - \text{Hepatic_Uptake_of_LDL} - \text{Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity}) * dt$$

$$\text{INIT LDLC} = 111.45$$

INFLOWS:

$$\text{IDL_Turnover} = \text{IDL} * \text{IDL_Turnover_Rate}$$

OUTFLOWS:

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Dependent_Activity} =$$

$$\text{LDLC} * \text{Effect_of_ET_Receptor_Activity_on_LDL_Uptake}$$

$$\text{Hepatic_Uptake_of_LDL} = \text{LDLC} * \text{Effect_of_HP_Receptor_Activity_on_LDL_Uptake}$$

$$+ \text{LDLC} * \text{Receptor_Indep_HP_Uptake_Rate}$$

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity} =$$

$$\text{LDLC} * \text{Receptor_Indep_ET_Uptake_Rate}$$

$$\text{VLDLC}(t) = \text{VLDLC}(t - dt) + (\text{VLDLC_Secretion} + \text{CETP_Regulated_C_Transfer} -$$

$$\text{VLDL_Turnover}) * dt$$

$$\text{INIT VLDLC} = 25.0$$

INFLOWS:

$$\text{VLDLC_Secretion} =$$

$$\text{Base_VLDLC_Secretion} * \text{Effect_of_Hepatic_Chol_Pool_on_VLDLC_Secretion}$$

$$- 9.18 + \text{Effect_of_Saturated_Fats_on_VLDLC_Secretion} * \text{Absorbed_Saturated_Fats}$$

$$+ 12.97 + \text{Effect_of_Polyunsaturated_Fats_on_VLDLC_Secretion} * \text{Absorbed_Polyunsaturated_Fat}$$

s

$$+ \text{Effect_of_Body_Weight_on_VLDLC_Secretion}$$

$$\text{CETP_Regulated_C_Transfer} = \text{HDLC} * \text{CETP_Activity_Rate}$$

OUTFLOWS:

$VLDL_Turnover = VLDLC * VLDL_Turnover_Rate$
 $CETP_Activity_Rate = 0.25$
 $Effect_of_ET_Receptor_Activity_on_IDL_Uptake = ET_Receptor_Activity / 60 * 5 * 0.3$
 $Effect_of_ET_Receptor_Activity_on_LDL_Uptake = ET_Receptor_Activity / 60 * 0.3 * 0.3$
 $Effect_of_HP_Receptor_Activity_on_IDL_Uptake = (HP_Receptor_Activity / 60) * 5 * 0.7$
 $Effect_of_HP_Receptor_Activity_on_LDL_Uptake = HP_Receptor_Activity / 60 * 0.3 * 0.7$
 $HDL_Removal_Time = 4$
 $IDL_Turnover_Rate = 2.4$
 $Normal_HDL_Efficiency = 15.78$
 $Receptor_Indep_ET_Uptake_Rate = 0.1 * 0.3$
 $Receptor_Indep_HP_Uptake_Rate = 0.1 * 0.7$
 $Total_Chol_to_HDL_ratio = total_cholesterol / HDLC$
 $total_cholesterol = HDLC + IDLC + LDLC + VLDLC$
 $VLDL_Turnover_Rate = 5.5$

Body Weight

$Basal_Metabolism(t) = Basal_Metabolism(t - dt) + (BM_Change) * dt$
 $INIT\ Basal_Metabolism = 1800$
 INFLOWS:
 $BM_Change = (Base_Basal_Metabolism * Effect_of_Body_Weight_on_basal_metabolism - Basal_Metabolism) / BM_Change_Rate + Metabolic_Adjustment_Effect$
 $Body_Weight(t) = Body_Weight(t - dt) + (Weight_Change) * dt$
 $INIT\ Body_Weight = 74$
 INFLOWS:
 $Weight_Change = (Energy_Surplus_or_Shortage / Adjustment_Time_for_Weight_Change) / energy_kg_convertor$
 $Adjustment_Time_for_Weight_Change = 1$
 $Base_Basal_Metabolism = 1800$
 $Base_Body_Weight = 74$
 $BM_Change_Rate = 0.5$
 $Effect_of_Body_Weight_on_VLDLC_Secretion = (Body_Weight - Base_Body_Weight) * 1.95$
 $Effect_of_Body_Weight_on_HDL_Efficiency = (Base_Body_Weight - Body_Weight) * 0.351$
 $energy_kg_convertor = 7716$
 $Energy_Surplus_or_Shortage = (Total_Available_Dietary_Energy - Total_Energy_Need) * Effect_of_Fat_Conversion_to_Energy_balance$
 $Metabolic_Adjustment_Effect = (IF(Energy_Surplus_or_Shortage <= 0) THEN (Energy_Surplus_or_Shortage * Metabolic_Adjustment_Rate) ELSE (0))$
 $Metabolic_Adjustment_Rate = 0.1$
 $Total_Available_Dietary_Energy = ((Absorbed_Polyunsaturated_Fats + Absorbed_Saturated_Fats + Absorbed_Monounsaturated_Fats) * energy_per_gr_fat + Absorbed_Carbohydrates * energy_per_gr_carbonydrate +$

Absorbed_Proteins*energy_per__gr_protein)*(1-Thermic_Effect_per_cent_of_Foods)
 Total__Energy__Need = Basal_Metabolism+Exercise_and_Normal_Activities
 Effect_of_Body_Weight_on_basal_metabolism = GRAPH(Body_Weight/Base__Body_Weight)
 (0.6, 0.563), (0.7, 0.628), (0.8, 0.73), (0.9, 0.897), (1, 1.00), (1.10, 1.05), (1.20, 1.11), (1.30,
 1.16), (1.40, 1.21), (1.50, 1.29), (1.60, 1.40), (1.70, 1.53), (1.80, 1.70)
 Effect_of_Fat_Conversion_to_Energy_balance =
 GRAPH(Total_Available_Dietary_Energy/Total__Energy__Need)
 (0.9, 1.00), (0.925, 1.00), (0.95, 1.01), (0.975, 1.02), (1.00, 1.04), (1.02, 1.08), (1.05, 1.11), (1.07,
 1.16), (1.10, 1.20), (1.12, 1.22), (1.15, 1.24), (1.17, 1.25), (1.20, 1.25)

Diet and Exercise

Base_Level_of_High_Fibers = 10
 Carbohydrate_Intake = 281.25
 +step(281.25,5)*0
 Cholesterol_Intake = 510
 Exercise_and_Normal_Activities = 150
 High_Fibers = 10
 Monounsaturated_Fat_Intake = 50
 +step(50,5)*0
 Polyunsaturated_Fat_Intake = 25
 +step(25,5)*0
 Protein_Intake = 84.375
 Saturated_Fat_intake = 12.5
 +step(12.5,5)/2*0
 Effect_of_Exercise_on_HDLC_Efficiency = GRAPH(Exercise_and_Normal_Activities)
 (100, 0.00), (175, 0.8), (250, 2.10), (325, 3.78), (400, 4.83), (475, 5.31), (550, 5.52), (625, 5.64),
 (700, 5.67)

Digestive System

Bile_Chol(t) = Bile_Chol (t - dt) + (Bile_Secretion - Bile_Loss_in_Feces) * dt
 INIT Bile_Chol = 3000
 INFLOWS:
 Bile_Secretion(IN SECTOR: Liver)
 OUTFLOWS:
 Bile_Loss_in_Feces = Base_Bile__Loss_Rate*Effect_of_High_Fibers_on_Bile_Loss
 Absorbed_Carbohydrates = Carbohydrate_Intake*Normal_Carbohydrate_Absorption_Rate
 Absorbed_Cholesterol =
 Cholesterol_Intake*Normal_Cholesterol_Absorbtion_Ratio*Effect_of_Bile_on__Cholesterol_A
 bsorbtion__per_cent
 Absorbed_Monounsaturated_Fats = Fat_Absorption__per_cent*Monounsaturated_Fat_Intake
 Absorbed_Polyunsaturated_Fats = Fat_Absorption__per_cent*Polyunsaturated_Fat_Intake
 Absorbed_Proteins = Normal_Protein_Absorption_Rate*Protein_Intake
 Absorbed__Saturated_Fats = Fat_Absorption__per_cent*Saturated_Fat_intake
 Base_Bile__Loss_Rate = 500

$\text{Effect_of_Bile_on_Cholesterol_Absorbtion_per_cent} = \text{Bile_Chol} / \text{Normal_Bile}$
 $\text{Effect_of_Polyunsaturated_Fats_on_VLDLC_Secretion} = -1.16 * 9 / 22.5 / 0.95$
 $-0.23 / 4$
 $\text{Effect_of_Saturated_Fats_on_VLDLC_Secretion} = 2.1 * 9 / 22.5 / 0.95$
 $-0.442 / 4$
 $\text{energy_per_gr_fat} = 9$
 $\text{energy_per_gr_carbonydrate} = 4$
 $\text{energy_per_gr_protein} = 4$
 $\text{Normal_Bile} = 3000$
 $\text{Normal_Carbohydrate_Absorption_Rate} = 0.99$
 $\text{Normal_Cholesterol_Absorbtion_Ratio} = 0.55$
 $\text{Normal_Protein_Absorption_Rate} = 0.90$
 $\text{Thermic_Effect_per_cent_of_Foods} = 0.1$
 $\text{Effect_of_High_Fibers_on_Bile_Loss} = \text{GRAPH}(\text{High_Fibers} / \text{Base_Level_of_High_Fibers})$
 $(0.5, 0.939), (0.6, 0.941), (0.7, 0.946), (0.8, 0.955), (0.9, 0.975), (1, 1.00), (1.10, 1.03), (1.20,$
 $1.06), (1.30, 1.09), (1.40, 1.10), (1.50, 1.10)$
 $\text{Fat_Absorption_per_cent} = \text{GRAPH}(\text{Bile_Chol} / \text{Normal_Bile})$
 $(0.00, 0.00), (0.1, 0.175), (0.2, 0.465), (0.3, 0.73), (0.4, 0.84), (0.5, 0.9), (0.6, 0.93), (0.7, 0.937),$
 $(0.8, 0.943), (0.9, 0.947), (1, 0.95), (1.10, 0.951), (1.20, 0.951)$

Extrahepatic Tissue

$\text{ET_Receptor_Activity}(t) = \text{ET_Receptor_Activity}(t - dt) + (\text{Receptor_Adaptation_in_ET}) * dt$
 $\text{INIT ET_Receptor_Activity} = 60$

INFLOWS:

$\text{Receptor_Adaptation_in_ET} =$

$\text{Receptor_Surplus_or_Need_in_ET} / \text{ET_Receptor_Adjustment_Time}$

$\text{Intracellular_Cholesterol}(t) = \text{Intracellular_Cholesterol}(t - dt) + (\text{C_from_Blood} +$
 $\text{Metabolic_Chol_Effect} - \text{Cholesterol_Uptake_by_HDL} - \text{IC_Cellular_Usage}) * dt$

$\text{INIT Intracellular_Cholesterol} = 1450$

INFLOWS:

$\text{C_from_Blood} =$

$\text{Extrahepatic_Uptake_of_IDL} + \text{Extrahepatic_Uptake_of_LDL_by_Receptor_Dependent_Activ}$
 $\text{ity} + \text{Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity}$

$\text{Metabolic_Chol_Effect} = (\text{Normal_Chol_Level_in_Extrahepatic_Tissues} -$
 $\text{Intracellular_Cholesterol}) / \text{Metabolic_Chol_Effect_Adjustment_Time}$

OUTFLOWS:

$\text{Cholesterol_Uptake_by_HDL} = \text{Normal_HDL_Efficiency} +$

$(\text{Effect_of_Body_Weight_on_HDLC_Efficiency}) * \text{Normal_HDLC_Uptake_Rate} +$
 $(-0.5633 + \text{Effect_of_Exercise_on_HDLC_Efficiency}) * \text{Normal_HDLC_Uptake_Rate} +$

$(-5.25 + \text{Effect_of_Saturated_Fats_on_HDLC_Efficiency}) * \text{Absorbed_Saturated_Fats}$
 $-5.50 + \text{Effect_of_Polyunsaturated_Fats_on_HDLC_Efficiency} * \text{Absorbed_Polyunsaturated_Fats}$

-

$+ \text{Effect_of_Monounsaturated_Fats_on_HDLC_Efficiency} * \text{Absorbed_Monounsaturated_Fats}) *$

$\text{Normal_HDLC_Uptake_Rate}$

IC_Cellular_Usage =
 Intracellular_Cholesterol/Normal_Chol_Level_in_Extrahepatic_Tissues*Base_IC__Cellular_Usage
 Base_IC__Cellular_Usage = 25.463635
 Effect_of_Monounsaturated_Fats_on_HDLC_Efficiency = 0.1/0.95
 Effect_of_Polyunsaturated_Fats_on_HDLC_Efficiency = 0.22/0.95
 Effect_of_Saturated_Fats_on_HDLC_Efficiency = 0.42/0.95
 ET_Receptor_Adjustment_Time = 2.5
 Metabolic_Chol_Effect_Adjustment_Time = 2
 Normal_Chol_Level_in_Extrahepatic_Tissues = 1450
 Normal_HDLC_Uptake_Rate = 1/2
 Receptor_Surplus_or_Need_in_ET = (Receptor_Goal_in_Extrahepatic_Tissues-
 ET_Receptor_Activity)
 Receptor_Goal_in_Extrahepatic_Tissues =
 GRAPH(Intracellular_Cholesterol/Normal_Chol_Level_in_Extrahepatic_Tissues)
 (0.8, 75.0), (0.85, 75.0), (0.9, 71.3), (0.95, 67.0), (1.00, 60.0), (1.05, 50.0), (1.10, 42.5), (1.15,
 31.0), (1.20, 16.6), (1.25, 15.0), (1.30, 15.0)

Liver

Hepatic_Chol(t) = Hepatic_Chol(t - dt) + (Uptake__from_Blood + Hepatic_Synthesis_Control +
 Chol_from__Diet - Bile_Secretion - VLDLC_Secretion) * dt
 INIT Hepatic_Chol = 1700
 INFLOWS:
 Uptake__from_Blood =
 Hepatic_Uptake_of_IDL+Hepatic_Uptake_of_LDL+HDLC_Transport__to_Liver
 Hepatic_Synthesis_Control = (Normal_Chol__Level_in_Liver-
 Hepatic_Chol)/Hepatic_Synthesis_Control_Rate
 +245
 Chol_from__Diet = Absorbed_Cholesterol
 OUTFLOWS:
 Bile_Secretion = Normal_Bile_Secretion*Effect_of_Hepatic__Chol_on_Bile__Secretion
 +Bile_Discrepancy/Bile__Adjustment__Time
 VLDLC_Secretion (IN SECTOR: Blood)
 HP_Receptor_Activity(t) = HP_Receptor_Activity(t - dt) + (HP_Receptor_Adaptation) * dt
 INIT HP_Receptor_Activity = 60
 INFLOWS:
 HP_Receptor_Adaptation =
 Receptor_Surplus_or_Need_in_Liver/HP_Receptor_Adaptation_Time
 HDLC_Transport__to_Liver = HDLC/HDL_Removal_Time
 OUTFLOW FROM: HDLC (IN SECTOR: Blood)
 Base_VLDLC_Secretion = 137.5-7.884
 Bile_Discrepancy = Normal_Bile- Bile_Chol
 Bile__Adjustment__Time = 0.5
 Hepatic_Synthesis_Control_Rate = 0.5
 HP_Receptor_Adaptation_Time = 2.5

Normal_Bile_Secretion = 500

Normal_Chol_Level_in_Liver = 1700

Receptor_Surplus_or_Need_in_Liver = HP_Receptor_Goal-HP_Receptor_Activity

Effect_of_Hepatic_Chol_Pool_on_VLDLC_Secretion =

GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)

(0.75, 0.9), (0.8, 0.9), (0.85, 0.907), (0.9, 0.92), (0.95, 0.953), (1.00, 1.00), (1.05, 1.05), (1.10, 1.10), (1.15, 1.13), (1.20, 1.15), (1.25, 1.15)

Effect_of_Hepatic_Chol_on_Bile_Secretion =

GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)

(0.00, 0.00), (0.1, 0.127), (0.2, 0.237), (0.3, 0.457), (0.4, 0.82), (0.5, 0.919), (0.6, 0.957), (0.7, 0.979), (0.8, 0.989), (0.9, 0.995), (1, 1.00), (1.10, 1.00), (1.20, 1.00)

HP_Receptor_Goal = GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)

(0.8, 75.0), (0.85, 75.0), (0.9, 71.3), (0.95, 67.0), (1.00, 60.0), (1.05, 50.0), (1.10, 42.5), (1.15, 31.0), (1.20, 16.6), (1.25, 15.0), (1.30, 15.0)

APPENDIX II: LIST OF EQUATIONS FOR THE FAMILIAL HYPERCHOLESTEROLEMIC CASE

Blood

$$\text{HDLC}(t) = \text{HDLC}(t - dt) + (\text{Cholesterol_Uptake_by_HDL} - \text{HDLC_Transport_to_Liver} - \text{CETP_Regulated_C_Transfer}) * dt$$

$$\text{INIT HDLC} = 31.555$$

INFLOWS:

$$\text{Cholesterol_Uptake_by_HDL} \quad (\text{IN SECTOR: Extrahepatic Tissue})$$

OUTFLOWS:

$$\text{HDLC_Transport_to_Liver} \quad (\text{IN SECTOR: Liver})$$

$$\text{CETP_Regulated_C_Transfer} = \text{HDLC} * \text{CETP_Activity_Rate}$$

$$\text{IDL}(t) = \text{IDL}(t - dt) + (\text{VLDL_Turnover} - \text{IDL_Turnover} - \text{Extrahepatic_Uptake_of_IDL} - \text{Hepatic_Uptake_of_IDL}) * dt$$

$$\text{INIT IDL} = 18.575$$

INFLOWS:

$$\text{VLDL_Turnover} = \text{VLDLC} * \text{VLDL_Turnover_Rate}$$

OUTFLOWS:

$$\text{IDL_Turnover} = \text{IDL} * \text{IDL_Turnover_Rate}$$

$$\text{Extrahepatic_Uptake_of_IDL} = \text{IDL} * \text{Effect_of_ET_Receptor_Activity_on_IDL_Uptake}$$

$$\text{Hepatic_Uptake_of_IDL} = \text{IDL} * \text{Effect_of_HP_Receptor_Activity_on_IDL_Uptake}$$

$$\text{LDLC}(t) = \text{LDLC}(t - dt) + (\text{IDL_Turnover} -$$

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Dependent_Activity} - \text{Hepatic_Uptake_of_LDL} - \text{Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity}) * dt$$

$$\text{INIT LDLC} = 111.45$$

INFLOWS:

$$\text{IDL_Turnover} = \text{IDL} * \text{IDL_Turnover_Rate}$$

OUTFLOWS:

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Dependent_Activity} =$$

$$\text{LDLC} * \text{Effect_of_ET_Receptor_Activity_on_LDL_Uptake}$$

$$\text{Hepatic_Uptake_of_LDL} = \text{LDLC} * \text{Effect_of_HP_Receptor_Activity_on_LDL_Uptake}$$

$$+ \text{LDLC} * \text{Receptor_Indep_HP_Uptake_Rate}$$

$$\text{Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity} =$$

$$\text{LDLC} * \text{Receptor_Indep_ET_Uptake_Rate}$$

$$\text{VLDLC}(t) = \text{VLDLC}(t - dt) + (\text{VLDLC_Secretion} + \text{CETP_Regulated_C_Transfer} -$$

$$\text{VLDL_Turnover}) * dt$$

$$\text{INIT VLDLC} = 25.0$$

INFLOWS:

$$\text{VLDLC_Secretion} =$$

$$\text{Base_VLDLC_Secretion} * \text{Effect_of_Hepatic_Chol_Pool_on_VLDLC_Secretion}$$

$$- 9.18 + \text{Effect_of_Saturated_Fats_on_VLDLC_Secretion} * \text{Absorbed_Saturated_Fats}$$

$$+ 12.97 + \text{Effect_of_Polyunsaturated_Fats_on_VLDLC_Secretion} * \text{Absorbed_Polyunsaturated_Fat}$$

s

$$+ \text{Effect_of_Body_Weight_on_VLDLC_Secretion}$$

CETP_Regulated_C_Transfer = HDLC*CETP_Activity_Rate

OUTFLOWS:

VLDL_Turnover = VLDLC*VLDL_Turnover_Rate

CETP_Activity_Rate = 0.25

Effect_of_ET_Receptor_Activity_on_IDL_Uptake = ET_Receptor_Activity/60*5*0.3

Effect_of_ET_Receptor_Activity_on_LDL_Uptake = ET_Receptor_Activity/60*0.3*0.3

Effect_of_HP_Receptor_Activity_on_IDL_Uptake = (HP_Receptor_Activity/60)*5*0.7

Effect_of_HP_Receptor_Activity_on_LDL_Uptake = HP_Receptor_Activity/60*0.3*0.7

HDL_Removal_Time = 4

IDL_Turnover_Rate = 2.4

Normal_HDL_Efficiency = 15.78

Receptor_Indep_ET_Uptake_Rate = 0.1*0.3

Receptor_Indep_HP_Uptake_Rate = 0.1*0.7

Total_Chol_to_HDLC_ratio = total_cholesterol/HDLC

total_cholesterol = HDLC+IDLC+LDLC+VLDLC

VLDL_Turnover_Rate = 5.5

Body Weight

Basal_Metabolism(t) = Basal_Metabolism(t - dt) + (BM_Change) * dt

INIT Basal_Metabolism = 1800

INFLOWS:

BM_Change = (Base_Basal_Metabolism*Effect_of_Body_Weight_on_basal_metabolism-
Basal_Metabolism)/BM_Change_Rate

+Metabolic_Adjustment_Effect

Body_Weight(t) = Body_Weight(t - dt) + (Weight_Change) * dt

INIT Body_Weight = 74

INFLOWS:

Weight_Change =

(Energy_Surplus_or_Shortage/Adjustment_Time_for_Weight_Change)/energy_kg_convertor

Adjustment_Time_for_Weight_Change = 1

Base_Basal_Metabolism = 1800

Base__Body_Weight = 74

BM_Change_Rate = 0.5

Effect_of_Body_Weight_on_VLDLC_Secretion = (Body_Weight-Base__Body_Weight)*1.95

Effect_of_Body_Weight_on__HDLC_Efficiency = (Base__Body_Weight-
Body_Weight)*0.351

energy_kg_convertor = 7716

Energy_Surplus_or_Shortage = (Total_Available_Dietary_Energy-
Total__Energy__Need)*Effect_of_Fat_Conversion_to_Energy_balance

Metabolic_Adjustment_Effect = (IF(Energy_Surplus_or_Shortage<=0) THEN

(Energy_Surplus_or_Shortage*Metabolic__Adjustment_Rate)

ELSE (0))

Metabolic__Adjustment_Rate = 0.1

Total_Available_Dietary_Energy =
 ((Absorbed_Polyunsaturated_Fats+Absorbed__Saturated_Fats+Absorbed_Monounsaturated_Fat
 s)*energy_per_gr_fat+
 Absorbed_Carbohydrates*energy_per_gr_carbonydrate+
 Absorbed_Proteins*energy_per_gr_protein)*(1-Thermic_Effect_per_cent_of_Foods)
 Total__Energy__Need = Basal_Metabolism+Exercise_and_Normal_Activities
 Effect_of_Body_Weight_on_basal_metabolism = GRAPH(Body_Weight/Base__Body_Weight)
 (0.6, 0.563), (0.7, 0.628), (0.8, 0.73), (0.9, 0.897), (1, 1.00), (1.10, 1.05), (1.20, 1.11), (1.30,
 1.16), (1.40, 1.21), (1.50, 1.29), (1.60, 1.40), (1.70, 1.53), (1.80, 1.70)
 Effect_of_Fat_Conversion_to_Energy_balance =
 GRAPH(Total_Available_Dietary_Energy/Total__Energy__Need)
 (0.9, 1.00), (0.925, 1.00), (0.95, 1.01), (0.975, 1.02), (1.00, 1.04), (1.02, 1.08), (1.05, 1.11), (1.07,
 1.16), (1.10, 1.20), (1.12, 1.22), (1.15, 1.24), (1.17, 1.25), (1.20, 1.25)

Diet and Exercise

Base_Level_of_High_Fibers = 10
 Carbohydrate_Intake = 281.25
 +step(281.25,5)*0
 Cholesterol_Intake = 510
 Exercise_and_Normal_Activities = 150
 High_Fibers = 10
 Monounsaturated_Fat_Intake = 50
 +step(50,5)*0
 Polyunsaturated_Fat_Intake = 25
 +step(25,5)*0
 Protein_Intake = 84.375
 Saturated_Fat_intake = 12.5
 +step(12.5,5)/2*0
 Effect_of_Exercise_on_HDLC_Efficiency = GRAPH(Exercise_and_Normal_Activities)
 (100, 0.00), (175, 0.8), (250, 2.10), (325, 3.78), (400, 4.83), (475, 5.31), (550, 5.52), (625, 5.64),
 (700, 5.67)

Digestive System

Bile_Chol (t) = Bile_Chol (t - dt) + (Bile_Secretion - Bile_Loss_in_Feces) * dt
 INIT Bile_Chol = 3000
 INFLOWS:
 Bile_Secretion(IN SECTOR: Liver)
 OUTFLOWS:
 Bile_Loss_in_Feces = Base_Bile__Loss_Rate*Effect_of_High_Fibers_on_Bile_Loss
 Absorbed_Carbohydrates = Carbohydrate_Intake*Normal_Carbohydrate_Absorption_Rate
 Absorbed_Cholesterol =
 Cholesterol_Intake*Normal_Cholesterol_Absorbtion_Ratio*Effect_of_Bile_on__Cholesterol_A
 bsorbtion_per_cent
 Absorbed_Monounsaturated_Fats = Fat_Absorption__per_cent*Monounsaturated_Fat_Intake

Absorbed_Polyunsaturated_Fats = Fat_Absorption__per_cent*Polyunsaturated_Fat_Intake
 Absorbed_Proteins = Normal_Protein_Absorption_Rate*Protein_Intake
 Absorbed__Saturated_Fats = Fat_Absorption__per_cent*Saturated_Fat_intake
 Base_Bile__Loss_Rate = 500
 Effect_of_Bile_on__Cholesterol_Absorbtion__per_cent = Bile_Chol/Normal_Bile
 Effect_of_Polyunsaturated_Fats_on_VLDLC_Secretion = -1.16*9/22.5/0.95
 -0.23/4
 Effect_of_Saturated_Fats_on_VLDLC_Secretion = 2.1*9/22.5/0.95
 -0.442/4
 energy_per_gr_fat = 9
 energy_per_gr__carbonyhydrate = 4
 energy_per__gr_protein = 4
 Normal_Bile = 3000
 Normal_Carbohydrate_Absorption_Rate = 0.99
 Normal_Cholesterol_Absorbtion_Ratio = 0.55
 Normal_Protein_Absorption_Rate = 0.90
 Thermic_Effect_per_cent_of_Foods = 0.1
 Effect_of_High_Fibers_on_Bile_Loss = GRAPH(High_Fibers/Base_Level_of_High_Fibers)
 (0.5, 0.939), (0.6, 0.941), (0.7, 0.946), (0.8, 0.955), (0.9, 0.975), (1, 1.00), (1.10, 1.03), (1.20,
 1.06), (1.30, 1.09), (1.40, 1.10), (1.50, 1.10)
 Fat_Absorption__per_cent = GRAPH(Bile_Chol/Normal_Bile)
 (0.00, 0.00), (0.1, 0.175), (0.2, 0.465), (0.3, 0.73), (0.4, 0.84), (0.5, 0.9), (0.6, 0.93), (0.7, 0.937),
 (0.8, 0.943), (0.9, 0.947), (1, 0.95), (1.10, 0.951), (1.20, 0.951)

Extrahepatic Tissue

ET_Receptor_Activity(t) = ET_Receptor_Activity(t - dt) + (Receptor_Adaptation_in_ET) * dt
 INIT ET_Receptor_Activity = 60

INFLOWS:

Receptor_Adaptation_in_ET =

Receptor_Surplus_or_Need_in_ET/ET_Receptor_Adjustment_Time

Intracellular_Cholesterol(t) = Intracellular_Cholesterol(t - dt) + (C_from_Blood +
 Metabolic_Chol_Effect - Cholesterol_Uptake_by_HDL - IC_Cellular_Usage) * dt

INIT Intracellular_Cholesterol = 1450

INFLOWS:

C_from_Blood =

Extrahepatic_Uptake__of_IDL+Extrahepatic__Uptake_of_LDL_by_Receptor_Dependent_Activ
 ity+Extrahepatic_Uptake_of_LDL_by_Receptor_Independent_Activity

Metabolic_Chol_Effect = (Normal_Chol_Level_in_Extrahepatic_Tissues-
 Intracellular_Cholesterol)/Metabolic_Chol_Effect_Adjustment_Time

OUTFLOWS:

Cholesterol_Uptake_by_HDL = Normal_HDL_Efficiency+

(Effect_of_Body__Weight_on__HDLC_Efficiency)*Normal_HDLC_Uptake_Rate+
 (-0.5633+Effect_of_Exercise_on_HDLC_Efficiency)*Normal_HDLC_Uptake_Rate+

(-5.25+Effect_of_Saturated_Fats_on_HDLC_Efficiency*Absorbed__Saturated_Fats

-5.50+Effect_of_Polyunsaturated_Fats_on_HDLC_Efficiency*Absorbed_Polyunsaturated_Fats

-

$5 + \text{Effect_of_Monounsaturated_Fats_on_HDLC_Efficiency} * \text{Absorbed_Monounsaturated_Fats} * \text{Normal_HDLC_Uptake_Rate}$

$\text{IC_Cellular_Usage} =$

$\text{Intracellular_Cholesterol} / \text{Normal_Chol_Level_in_Extrahepatic_Tissues} * \text{Base_IC_Cellular_Usage}$

$\text{Base_IC_Cellular_Usage} = 25.463635$

$\text{Effect_of_Monounsaturated_Fats_on_HDLC_Efficiency} = 0.1 / 0.95$

$\text{Effect_of_Polyunsaturated_Fats_on_HDLC_Efficiency} = 0.22 / 0.95$

$\text{Effect_of_Saturated_Fats_on_HDLC_Efficiency} = 0.42 / 0.95$

$\text{ET_Receptor_Adjustment_Time} = 2.5$

$\text{Metabolic_Chol_Effect_Adjustment_Time} = 2$

$\text{Normal_Chol_Level_in_Extrahepatic_Tissues} = 1450$

$\text{Normal_HDLC_Uptake_Rate} = 1/2$

$\text{Receptor_Surplus_or_Need_in_ET} = (\text{Receptor_Goal_in_Extrahepatic_Tissues} - \text{ET_Receptor_Activity})$

$\text{Receptor_Goal_in_Extrahepatic_Tissues} =$

$\text{GRAPH}(\text{Intracellular_Cholesterol} / \text{Normal_Chol_Level_in_Extrahepatic_Tissues})$

$(0.8, 75.0), (0.85, 75.0), (0.9, 71.3), (0.95, 67.0), (1.00, 60.0), (1.05, 50.0), (1.10, 42.5), (1.15, 31.0), (1.20, 16.6), (1.25, 15.0), (1.30, 15.0)$

Liver

$\text{Hepatic_Chol}(t) = \text{Hepatic_Chol}(t - dt) + (\text{Uptake_from_Blood} + \text{Hepatic_Synthesis_Control} + \text{Chol_from_Diet} - \text{Bile_Secretion} - \text{VLDLC_Secretion}) * dt$

$\text{INIT Hepatic_Chol} = 1700$

INFLOWS:

$\text{Uptake_from_Blood} =$

$\text{Hepatic_Uptake_of_IDL} + \text{Hepatic_Uptake_of_LDL} + \text{HDLC_Transport_to_Liver}$

$\text{Hepatic_Synthesis_Control} = (\text{Normal_Chol_Level_in_Liver} -$

$\text{Hepatic_Chol}) / \text{Hepatic_Synthesis_Control_Rate}$

$+245$

$\text{Chol_from_Diet} = \text{Absorbed_Cholesterol}$

OUTFLOWS:

$\text{Bile_Secretion} = \text{Normal_Bile_Secretion} * \text{Effect_of_Hepatic_Chol_on_Bile_Secretion}$

$+ \text{Bile_Goal} / \text{Bile_Adjustment_Time}$

VLDLC_Secretion (IN SECTOR: Blood)

$\text{HP_Receptor_Activity}(t) = \text{HP_Receptor_Activity}(t - dt) + (\text{HP_Receptor_Adaptation}) * dt$

$\text{INIT HP_Receptor_Activity} = 60$

INFLOWS:

$\text{HP_Receptor_Adaptation} =$

$\text{Receptor_Surplus_or_Need_in_Liver} / \text{HP_Receptor_Adaptation_Time}$

$\text{HDLC_Transport_to_Liver} = \text{HDLC} / \text{HDL_Removal_Time}$

OUTFLOW FROM: HDLC (IN SECTOR: Blood)

$\text{Base_VLDLC_Secretion} = 137.5 - 7.884$

$\text{Bile_Goal} = \text{Normal_Bile} - \text{Bile_Chol}$

Bile_Adjustment_Time = 0.5
Hepatic_Synthesis_Control_Rate = 0.5
HP_Receptor_Adaptation_Time = 2.5
Normal_Bile_Secretion = 500
Normal_Chol_Level_in_Liver = 1700
Receptor_Surplus_or_Need_in_Liver = HP_Receptor_Goal-HP_Receptor_Activity
Effect_of_Hepatic_Chol_Pool_on_VLDLC_Secretion =
GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)
(0.75, 0.9), (0.8, 0.9), (0.85, 0.907), (0.9, 0.92), (0.95, 0.953), (1.00, 1.00), (1.05, 1.05), (1.10,
1.10), (1.15, 1.13), (1.20, 1.15), (1.25, 1.15)
Effect_of_Hepatic_Chol_on_Bile_Secretion =
GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)
(0.00, 0.00), (0.1, 0.127), (0.2, 0.237), (0.3, 0.457), (0.4, 0.82), (0.5, 0.919), (0.6, 0.957), (0.7,
0.979), (0.8, 0.989), (0.9, 0.995), (1, 1.00), (1.10, 1.00), (1.20, 1.00)
HP_Receptor_Goal = GRAPH(Hepatic_Chol/Normal_Chol_Level_in_Liver)
(0.8, 75.0), (0.85, 75.0), (0.9, 71.3), (0.95, 67.0), (1.00, 60.0), (1.05, 50.0), (1.10, 42.5), (1.15,
31.0), (1.20, 16.6), (1.25, 15.0), (1.30, 15.0)