**PCRIF.PTML Models for Advancing Cystic Fibrosis Care**

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**Table S1:** Discrete variables partitions, partition names, variable names, number of levels, and examples.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Partition** | **Name** | **variables** | **n0 levels** | **Examples** |
| **s**I | Genetic and age group | s1 = Mutation 1 | 12 Mutations | [delta]I507, [delta]F508, Y1092X, etc. |
| s2 = Mutation 2 | 24 Mutations | R334W, [delta]I507, R1066C, G85E, etc. |
| s3 = Group name | 2 Age group | adults, children |
| s4 = Gender | 2 Gender | Masculine (M), Femenine(F) |
| s5 = Neonatal screening | 2 Options | NO= 0 , YES = 1 |
| **s**II | Disease conditions | s6 = Pansreatis Insufficiency. 2020 | 2 Options | NO= 0 , YES = 1 |
| s7 = Diabetes | 2 Options | NO= 0 without insulin, YES =1 with insulin |
| s8 = Hepatis Disease | 3 Options | NO = 0, without cirrhosis HTP= 2, Hepatic disease without cirrhosis=4 |
| s9 = Exaserbation | 4 Options | No (0), Mild (1), Moderate (2), Severe (3), High severity (4) |
| **s**III | Medical & Pharm general support | s10 = Hypertonic Saline Solutions (HSS) | 2 Options | NO= 0 , YES = 1 |
| s11= Deoxyribonuclease (Dnasa) | 2 Options | NO= 0 , YES = 1 |
| s12= Azitromisine | 2 Options | NO= 0 , YES = 1 |
| s13= Bronchodilator | 2 Options | NO= 0 , YES = 1 |
| s14 = corticoid-oral | 2 Options | NO= 0 , YES = 1 |
| s15 = corticoid-inh | 2 Options | NO= 0 , YES = 1 |
| s16 = Modulator | 5 Options | No= 0, Ivacaftor = 1, Lumacaftor-Ivacaftor =2, Etc. |
| s17 = O2 | 2 Options | NO= 0 , YES = 1 |
| s18 = Non-invasive ventilation (NIV) | 3 Options | NO= 0 , YES = 1 |
| s19 = Proton pump inhibitor (PPI) | 2 Options | NO= 0 , YES = 1 |
| **s**IV | Inhalate antibiotic (ATBinh) | s20= Inhalate antibiotic (ATBinh01) | 5 types | No= 0 , Colistin=1, Ceftazidime=4, Tobramycin=2,Etc. |
| s21 = Inhalate antibiotic (ATBinh02) | 3 types | No= 0 , Tobramycin=2, Ceftazidime=4 |
| s22 = Inhalate antibiotic (ATBinh03) | 3 types | No= 0, Aztreonam=3,Vancomycin=7,Ceftazidime=4 |
| **s**V | Oral antibiotic (ATBoral) | s23 = Oral antibiotic (ATBoral) | 6 Types of antibiotics | Amoxicillin-Clavulanic Acid=9, Trimethoprim=10, Etc. |
| s24 = Continuous antibiotic (ATBc) | 6 Types of antibiotics | Trimethoprim =10, Cefaclor =17, Cefuroxime=19 |
| s25 = Oral antibiotic (ATBoral01) | 10 Types of antibiotics | Amoxicillin=8, Trimethoprim=10, Ciprofloxacin=11, Etc. |
| s26 = Oral antibiotic (ATBoral02) | 9 Types of antibiotics | Trimethoprim=10, Ciprofloxacin=11, Etc. |
| s27 = Oral antibiotic (ATBoral03) | 6 Types of antibiotics | Minocycline=12, Levofloxacin=13,Etc. |
| s28 = Oral antibiotic (ATBoral04) | 5 Types of antibiotics | Levofloxacin=13, Fusidic Acid=16, Cefaclor =17 |
| **s**VI | Intravenous Antibiotic (ATBiv) | s29 = Intravenous Antibiotic (ATBiv01) | 5 Types of antibiotics | Ceftazidime=4, Meropenem =6, Etc. |
| s30 = Intravenous Antibiotic (ATBiv02) | 5 Types of antibiotics | Colistin=1, Ceftazidime =4, Etc. |
| s31 = Intravenous Antibiotic (ATBiv03) | 5 Types of antibiotics | Colistin=1, Imipenem=22 |
| s32 = Intravenous Antibiotic (ATBiv04) | 5 Types of antibiotics | Aztreonam=3 |
| **s**VII |  | s33 = Sample | 4 Types of samples | Sputum, Pharyngeal Smear |
|  | s34 = NBAA01 | 21 Types of bacteria | *Haemophilus parainfluenzae, Staphylococcus aureus, Streptococcus parasanguinis, etc.* |
| Metagenomics: Not abundant more than 5% | s35 = NBAA02 | 33 Types of bacteria | *Veillonella tobetsuensis, Stenotrophomonas maltophilia, Campylobacter concisus, etc.* |
|  | s36 = NBAA03 | 38 Types of bacteria | *Neisseria perflava, Streptococcus salivarius, Streptococcus sanguinis, etc.* |
|  |  | s37 = NBAA04 | 40 Types of bacteria | *Veillonella atypica, Streptococcus parasanguinis, Oribacterium asaccharolyticum, etc.* |
|  |  | s38 = NBAA05 | 40 Types of bacteria | *Megasphaera micronuciformis, Granulicatella adiacens, Streptococcus mitis, etc.* |
|  |  | s39 = NBAA06 | 45 Types of bacteria | *Veillonella parvula, Streptococcus mitis, Oribacterium sinus, etc.* |
|  |  | s40 = NBAA07 | 41 Types of bacteria | *Prevotella melaninogenica, Streptococcus pseudopneumoniae, etc.* |
|  |  | s41 = NBAA08 | 50 Types of bacteria | *Aggregatibacter aphrophilus, Streptococcus oralis, Streptococcus bereretti, etc.* |
| **s**vIII |  | s42 = NBAA09 | 48 Types of bacteria | *Streptococcus salivarius, Veillonella atypica, Veillonella infantium, etc.* |
| Metagenomics: Moderate Abundance (5%-1%) | s43 = NBAA10 | 45 Types of bacteria | *Prevotella pallens, Granulicatella elegans, Granulicatella adiacens, etc.* |
|  | s44 = NBAA11 | 50 Types of bacteria | *Campylobacter concisus, Staphylococcus aureus, Streptococcus infantis, etc.* |
|  | s45 = NBAA12 | 54 Types of bacteria | *Veillonella dispar, Oribacterium parvum, Megasphaera micronuciformis, etc.* |
|  |  | s46 = NBAA13 | 52 Types of bacteria | *Peptostreptococcus stomatis, Parvimonas micra, Granulicatella elegans, etc.* |
|  |  | s47 = NBAA14 | 56 Types of bacteria | *Haemophilus parainfluenzae, Haemophilus parahaemolyticus, etc.* |
|  |  | s48 = NBAA15 | 53 Types of bacteria | *Haemophilus haemolyticus, Gemella haemolysans, Gemella morbillorum, etc.* |
|  |  | s49 = NBAA16 | 57 Types of bacteria | *Aggregatibacter segnis, Streptococcus mutans, Shigella flexneri, etc.* |
|  |  | s50 = NBAA17 | 60 Types of bacteria | *Streptococcus parasanguinis, Prevotella histicola, Shigella sonnei, etc.* |
|  |  | s51 = NBAA18 | 58 Types of bacteria | *Alloprevotella tannerae, Neisseria macacae, Streptococcus oralis, etc.* |
|  |  | s52 = NBAA19 | 53 Types of bacteria | *Fusobacterium periodonticum, Fusobacterium periodonticum, etc.* |
| **s**IX | Metagenomics: Less Abundant (1%-0.5%) | s53 = NBAA20 | 61 Types of bacteria | *Campylobacter showae, Peptostreptococcus stomatis, etc.* |
|  |  | s54 = NBAA21 | 59 Types of bacteria | *Porphyromonas pasteri, Haemophilus parahaemolyticus, Scardovia odontolytica, etc.* |
|  |  | s55 = NBAA22 | 57 Types of bacteria | *Streptococcus oralis, Staphylococcus caprae, Staphylococcus aureus, etc.* |
|  |  | s56 = NBAA23 | 63 Types of bacteria | *Gemella sanguinis, Prevotella melaninogenica, Lachnoanaerobaculum gingivalis, etc.* |
|  |  | s57 = NBAA24 | 62 Types of bacteria | *Prevotella massilia timonensis, Staphylococcus simiae, Streptococcus infantis, etc.* |

**Table S2:** Continuous variables partitions, partition names, variable names, levels, examples, and units.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Partition** | **Name** | **variables** | **n0 levels** | **Examples** | **Units** |
| **c**I | Medical and Personal data | v1= Diagnosis Age (DA) | 27 Ages | 3,5; 41,9; 19; 6,5, etc. | (Yr) |
| v2=Age First Interview (AFI) | 48 Interview | 52,74; 7,22;48,9;25,73,etc. | (Yr) |
| v3=Initial Weight (Kg) | 38 Weights | 52,6; 49; 48,3;69;45,etc. | (Kg) |
| v4=Initial Eight (IE) | 40 Eight | 164;158,4;161;173,etc. | (m) |
| v5=Initial Body Mass Index (BMI) | 46 BMI | 19,56;19,53;18,63;23,05,etc. | (Kg/m) |
| v6= Sample-Inform Time lag (SITL) | 32 Times | 136;44;9;50,etc. | (dd) |
| **c**II | Treatment duration | v7=months with modulator (MWM) | 12-Month options | 3,5;11,5;9,etc. | (mth) |
| v8= Days oral antibiotic 1 (DATBO01) | 19 Days options | 240; 249; 184; 87,etc. | (dd) |
| v9= Days oral antibiotic 2 (DATBO02) | 24 Days options | 42; 84; 260; 28,etc. | (dd) |
| v10= Days intravenous antibiotic 2 (DATBiv) | 7 Days options | 15; 21; 41; 42,etc. |  |
|  |  | v11 =Inhalate antibiotic doses (ATBDinh01) | 5 Options | 2;1;300;75,etc. | (uu) |
|  |  | v12 =Inhalate antibiotic doses (ATBDinh02) | 4 Options | 1;75;300,etc. | (uu) |
|  |  | v13=Inhalate Antibiotic doses (ATBDinh03) | 4 Options | 1;75;500,etc. | (uu) |
|  |  | v14= Oral antibiotic doses (ATBDoralc01) | 6 Options | 100;40;1000,etc. | (uu) |
|  |  | v15= Oral antibiotic doses (ATBDoralc02) | 6 Options | 30;100;1680;500;1000,etc. | (uu) |
| cIII | Pharmacology drug cocktails | v16= Oral antibiotic doses (ATBDoral01) | 13 Options | 15;20;30;40,etc. | (uu) |
|  |  | v17= Oral antibiotic doses (ATBDoral02) | 11 Options | 10;15;20;40;600,etc. | (uu) |
| v18= Oral antibiotic doses (ATBDoral03) | 6 Options | 15;40;500;100,etc. | (uu) |
| v19= Oral antibiotic doses (ATBDoral04) | 5 Options | 15;500;600;1000,etc. | (uu) |
| v20= Intravenous Antibiotic doses (ATBDiv01) | 4 Options | 3,3;30;2000,etc. | (uu) |
| v21= Intravenus Antibiotic doses (ATBDiv02) | 7 Options | 2;30;500;2000;22500,etc. | (uu) |
| v22= Intravenus Antibiotic doses(ATBDiv03) | 4 Options | 1;2500;22500,etc. | (uu) |
| v23= Intravenus Antibiotic doses (ATDiv04) | 2 Options | 0.2 | (uu) |
| **c**IV | Pharmacology drug regime | v24=inhalate (inh01) | 3 Options | 0,12,8 | (uu) |
| v25=inhalate (inh02) | 3 Options | 0,12,8 | (uu) |
| v26=inhalate (inh03) | 3 Options | 0,12,8 | (uu) |
| v27=continuous (c01) | 3 Options | 0,12,8 | (uu) |
| v28=continuous (c02) | 3 Options | 0,12,8 | (uu) |
| v29=oral (oral01) | 4 Options | 0,8,12,24 | (uu) |
| v30=oral (oral02) | 4 Options | 0,8,12,24 | (uu) |
| v31=oral (oral03) | 4 Options | 0,8,12,24 | (uu) |
| v32=oral (oral04) | 3 Options | 0,8,24 | (uu) |
| v33=intravenous (iv01) | 3 Options | 0,8,24 | (uu) |
| v34=intravenous (iv02) | 3 Options | 0,8,12 | (uu) |
| v35=intravenous (iv03) | 3 Options | 0,8,6 | (uu) |
| v36=intravenous (iv04) | 2 Options | 0,8 | (uu) |
|  |  | v37 = Bacteria (ABBA 01) | 94 bacterial abundance | 28,00; 33,52; 21,72; 46,01; etc, | (%) |
| **c**V | Metagenomics: Most abundant | v38 = Bacteria (ABBA 02) | 95 bacterial abundance | 7,87; 19,14; 17,81; 10,70; etc, | (%) |
|  |  | v39 = Bacteria (ABBA 03) | 96 bacterial abundance | 6,30; 4,46; 13,76; etc, | (%) |
|  |  | v40 = Bacteria (ABBA 04) | 94 bacterial abundance | 4,94;3,01;6,70;4,06,etc. | (%) |
|  |  | v41 = Bacteria (ABBA 05) | 95 bacterial abundance | 4,55;2,20;4,34;2,65,etc. | (%) |
|  |  | v42 = Bacteria (ABBA 06) | 96 bacterial abundance | 4,28;2,01;4,12;2,06,etc. | (%) |
|  |  | v43 = Bacteria (ABBA 07) | 97 bacterial abundance | 3,66;1,99;3,96;1,80;2,32,etc. | (%) |
|  |  | v44= Bacteria (ABBA 08) | 98 bacterial abundance | 2,35;1,82;3,70;1,72;2,01 | (%) |
| **c**VI | Metagenomics: Moderate abundance | v45 = Bacteria (ABBA 09) | 99 bacterial abundance | 2,30;1,74;3,13;1,25;1,46,etc. | (%) |
|  |  | v46 = Bacteria (ABBA 10) | 100 bacterial abundance | 2,24;1,68;2,08;1,31;1,45,etc. | (%) |
|  |  | v47 = Bacteria (ABBA 11) | 101 bacterial abundance | 1,80;1,47;2,91;1,13,etc. | (%) |
|  |  | v48 = Bacteria (ABBA 12) | 102 bacterial abundance | 1,73; 1,34; 1,23; 1,07,etc | (%) |
|  |  | v49 = Bacteria (ABBA 13) | 103 bacterial abundance | 1,60;1,29;1,01;0,92;0,97,etc. | (%) |
|  |  | v50 = Bacteria (ABBA 14) | 104 bacterial abundance | 1,53;1,23;1,04;0,98;0,85,etc. | (%) |
|  |  | v51 = Bacteria (ABBA 15) | 105 bacterial abundance | 1,47;0,85;1,03;0,94;0,75,etc. | (%) |
|  |  | v52= Bacteria (ABBA 16) | 94 bacterial abundance | 1,19; 0,84; 1,00; 0,94; 0,70,etc. | (%) |
|  |  | v53 = Bacteria (ABBA 17) | 95 bacterial abundance | 1,09; 0,83; 0,71; 0,75; 0,67,etc. | (%) |
|  |  | v54 = Bacteria (ABBA 18) | 96 bacterial abundance | 0,92; 0,70; 0,49; 0,61; 1,21,etc. | (%) |
|  |  | v55 = Bacteria (ABBA 19) | 97 bacterial abundance | 0,78; 0,64; 0,48; 0,55; 0,59,etc. | (%) |
| **c**VII | Metagenomics: Less abundant | v56 = Bacteria (ABBA 20) | 98 bacterial abundance | 0,77; 0,64; 0,54; 0,29; 0,52,etc. | (%) |
|  |  | v57 = Bacteria (ABBA 21) | 99 bacterial abundance | 0,74; 0,62; 0,30; 0,49,etc. | (%) |
|  |  | v58 = Bacteria (ABBA 22) | 100 bacterial abundance | 0,74; 0,62; 0,34; 0,48,etc. | (%) |
|  |  | v59 = Bacteria (ABBA 23) | 101 bacterial abundance | 0,74; 0,61; 0,32; 0,44,etc. | (%) |
|  |  | v60 = Bacteria (ABBA 24) | 102 bacterial abundance | 0,71; 0,59; 0,31; 0,43; 0,46,etc. | (%) |

**Table S3**. IFPTML-DSS applications to Personalized Medicine and Biomedical Science.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Use | Va.  Set | Name | Input variables a | IFPTML-DSS Applications |
| **1** | **c**I | Medical and  Personal data | v1 = Diagnosis Age (DA) | **Personalization of Treatment dose**.  By predicting the outputs FEV1, and FVCc after changing personal input variables (**cI**) together with dose input variables (**cIII**) you can personalize treatment dose. |
| v3 = Initial Weight (IW), *etc*. |
| v5 = Body Mass Index (BMI), *etc*. |
| **2** | **c**II | Treatment duration | v7 = months with modulator (MWM) | **Personalization of Treatment Duration.**  By predicting output outcomes **s0**c (FEV1, FVC after changing time treatment (**cII**), pharmacology drug cocktails (**cIII**) and disease conditions (**sII**), you can personalize treatment duration. |
| v8 = Days oral antibiotic 1 (DATBO01),*etc.* |
| **3** | **s**I | Genetic and age group | s1 = Mutation 1  s5 = Neonatal screaming,  *etc.* | **Detection of Clinically Relevant Mutations.**  Scanning different input patient's mutations (s1 *vs*. treatment duration (**cII**) and the pharmacological drug regimen (**cIII**) could help to decide intervention and/or predicting clinical relevant mutations. |
| **4** | **s**II | Disease conditions | s6 = Pancreatitis Insufficiency.  s7= Diabetes*.*  s9 = Exaserbations, *etc.*  s9 = Exaserbations, *etc.* | **Co-morbidities effects study.**  You can study the effect of co-morbidities over patients-follow up and/or admission/interventio by predicting the outcomes (**s**0)c (Hospital days ATBiv days) after scanning different patient's concomitant diseases (**s**II) vs. Medical And Personal data (**cI**), Pharmacology drug cocktail (**cIII**), and/or drug regime (**cIV**), *etc*. |
| **5** | **c**III | Pharmacol. drug cocktails | v11 = Inhalate antibiotic doses (ATBDinh01), etc.  v14 = Oral antibiotic doses (ATBDoralc01), *etc*.  v20= Intravenous Antibiotic doses (ATBDiv01) | **Dose/duration vs. route personalization.** You can predict interventional outcomes **(s**0)c (FEV1, FVC, Hospital days, ATBiv days)c after changing input Medical personal data **(cI**), treatment duration (**cII**), plus drug cocktails and administration route (**cIII**) in order to personaliz drug dose/duration ratios vs. treatment route. |
| **6** | **Hospital Admission/Intervention decision making.**  Prediction of interventional outcomes **(s**0)c (Hospital days, ATBiv days) after changing these inputs (**c**III and **c**II )may help also to support admission/discharge and/or pharmacological intervention decisions. |
| v27 = continuous (c01) |
| v29 = oral (oral01), *etc.* |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **7** | **s**VIII | Meta genomicsb | s40 = Sample | **Correlation of clinical outcomes with any other variable for groups of patients**  We can predict the outcomes **(s**0)c for each patient, considering input, Genetic & age group **s**I, Medical Pharm general support (**s**IV), *etc,* an Treatment  Duration (**c**II), Metagenomics (**s**VIII),*etc* |
| s41 = NBBA01,etc. |

a There is no exhaustive list in this table, see full details list in file SI00 Supporting Information.docb Most abundant more than 5%. c The four outcomes **s**0 we can predict for each patient are of two types: (1) patient follow-up functional outcomes (FEV1, FVC) useful for patient follow-up and (2) patient follow-up and admission/intervention outcomes (Hospital days, ATBiv days) useful to decide patient admission/discharge decisions and or necessity of intravenous antibiotic administration.