

Personalized potassium and phosphorus intake recommendations can be reasoned for end-stage renal failure patients by simulating with hierarchical Bayesian multivariate model

Supplementary Materials

JARI TURKIA^{1,2} URSULA SCHWAB^{3,4} VILLE HAUTAMÄKI^{1,5}

¹ School of Computing, University of Eastern Finland, 80101 Joensuu, Finland

² CGI Suomi, Joensuu, Finland

³ School of Medicine, Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland

⁴ Department of Medicine, Endocrinology and Clinical Nutrition, Kuopio University Hospital, Kuopio, Finland

⁵ Department of Electrical and Computer Engineering, National University of Singapore, Singapore

This notebook reproduces in detail the analysis of personal diet recommendations described in the main article. The notebook starts visualizing the collected raw data, prepares it for analysis and estimates personal reaction models with these data. The personal reaction models are combined with the estimation of the current personal diets for constructing personal graphical models. These personal models generate the levels of blood concentrations when a diet is given, they are used in simulating recommended personal diets for reaching predefined normal concentrations. Finally, these personal diet recommendations are compared for showing the divergence among the studied patients.

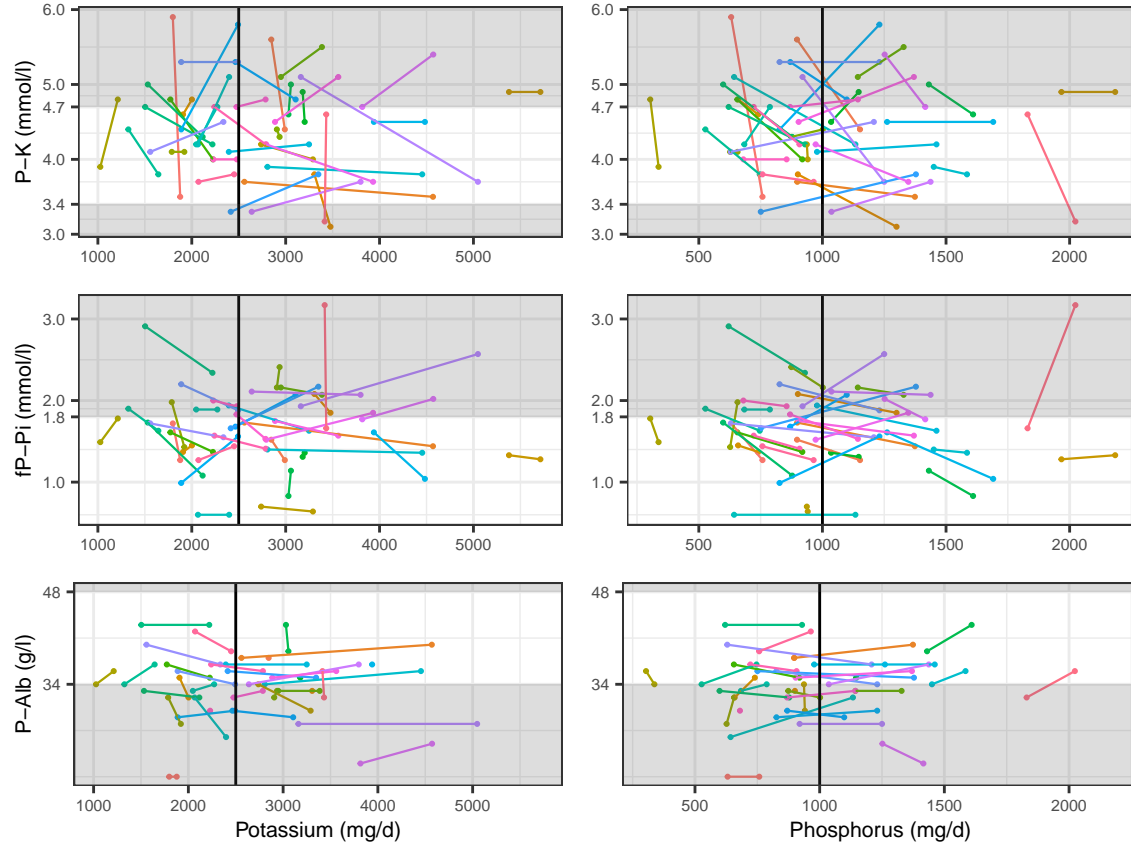
The notebook execution generates all the figures and tables that are included in the article, and produces also the referenced supplementary figures. The article is accompanied with a PDF rendition of the notebook that shows all the supplementary figures and important parts of the program code so that the analysis can be followed in detail. The executable RMarkdown notebook with data can be found in a public Github repository of the corresponding author.

Dialysis patient data

The analyzed dataset consists of food records and laboratory measurements from end-stage renal patients in dialysis. Following nutrients are possible considered as predictors of concentrations. Note that we use energy-% of fats and protein as unit in our analysis. This is referred as Table 1 in the main article.

and also following personal details and medication are considered as predictors. This is referenced as Table 2 in the article.

Let us explore then how the intake of dietary potassium and phosphorus corresponds in data to plasma concentrations of potassium, phosphate and albumin



Supplementary Figure S 1: Figure shows the progress between two observations of plasma potassium (P-K), fasting plasma phosphate (fP-Pi) and plasma albumin (P-Alb) concentrations of the studied patients. White regions in the panels show the recommended concentration levels, P-K 3.4 - 4.7 mmol/l, fP-Pi < 1.8 mmol/l and P-Alb 34 - 48 g/l. Vertical black lines denote the commonly recommended maximum intakes of these nutrients. The goal is to find personal intake levels that keep the concentrations in recommended levels, if possible. The figure is plotted with ggplot2 package for R language (v 3.3.5, <https://ggplot2.tidyverse.org>).

Aim of this analysis is to find such personal levels of potassium and phosphorous intakes that keep all these concentrations in their normal levels marked with white regions, if possible.

Development of nutrition reaction model

In this work we construct personal generative models for concentrations that allow conditioning personal diet recommendations. Essential part of these models is the personal reactions to nutrients and other predictors. Simultaneous reactions on all considered concentrations are modeled as multivariate model that has all the concentrations are response variables.

For comparison, we estimate multivariate systems with and without cross-model covariance. With cross-model covariance estimated, the model corresponds to seemingly unrelated model system, and without the model is Bayesian network with separated local distributions. This simpler model is estimated first with only potassium and phosphorous concentrations as responses.

```
initial_graph <- mebn.fully_connected_bipartite_graph(datadesc_fat_epros)
```

```
pk_fppi_targets <- datadesc_fat_epros[datadesc_fat_epros$Name %in% c('pk','fppi'),]

dialdiet_gamma <- mebn.bipartite_model(reaction_graph = initial_graph,
                                     inputdata = dialysis,
                                     predictor_columns = assumedpredictors_fat_epros,
                                     assumed_targets = pk_fppi_targets,
                                     group_column = "potilas",
                                     local_estimation = mebn.sampling,
                                     local_model_cache = "models/BLMM_gamma_separate",
                                     stan_model_file = "mebn/v2/BLMM_gamma.stan",
                                     normalize_values = TRUE)

# Write the generated graph in a GraphML file
write.graph(dialdiet_gamma, "graphs/dialysis_gamma_separate.graphml", "graphml")
```

In Bayesian network both responses were estimated separately. Next, we estimate a multivariate model where both distribution are estimated during single sampling. It does not factorize into separate distributions, but allows using more data.

```
dialdiet_gamma_mv2_epros <- mebn.bipartite_multivariate(reaction_graph = initial_graph,
                                                       inputdata = dialysis,
                                                       predictor_columns = assumedpredictors_fat_epros,
                                                       assumed_targets = pk_fppi_targets,
                                                       group_column = "potilas",
                                                       local_estimation = mebn.multivariate_sampling,
                                                       local_model_cache =
                                                         "models/BLMM_gamma_qr_multivariate2/fat_epros",
                                                       stan_model_file = "mebn/v2/BLMM_gamma_qr_mv.stan",
                                                       normalize_values = TRUE)

write.graph(dialdiet_gamma_mv2_epros,
            "graphs/dialysis_gamma_multivariate2_epros.graphml", "graphml")
```

Next we like to add plasma albumin concentration as a third constraint in the model, but unfortunately 8 of 37 patients have missing albumin measurements. From such a small dataset we don't want to remove any patients and so we predict the missing albumin levels and impute them to dataset.

For prediction, estimate the model without missing values in P-Alb. The rows with missing values are held out from the density estimation, but patients are kept in the model for estimating their parameters.

```
pk_fppi_palb_targets <-
  datadesc_fat_epros[datadesc_fat_epros$Name %in% c('pk','fppi','palb'),]

# 0/1-index for palb = NA
holdout_index <- as.vector(as.numeric(is.na(dialysis$palb)))

# Stan does not support NA in data (in Y), so let's change NA to magic number
if (anyNA(dialysis$palb)) dialysis[is.na(dialysis$palb),]$palb <- -1

initial_graph <- mebn.fully_connected_bipartite_graph(datadesc_fat_epros)

dialdiet_gamma_mv3_missing_palb <- mebn.bipartite_multivariate(
  reaction_graph = initial_graph,
```

```

inputdata = dialysis,
targetdata = holdout_index,
predictor_columns = assumedpredictors_fat_epros,
assumed_targets = pk_fppi_palb_targets,
group_column = "potilas",
local_estimation = mebn.multivariate_sampling,
local_model_cache =
  "models/BLMM_gamma_qr_multivariate3/fat_epros_missing_palb",
stan_model_file = "mebn/v2/BLMM_gamma_qr_mv_cv.stan",
normalize_values = TRUE)

```

Personal data imputation models

Now we can create personal models for patients that have missing plasma albumin measurements. These models are then used for making personal predictions for replacing missing values.

```

# Extract personal generative models for patients who have missing P-Alb values

patients_with_missing_palb <- unique(as.vector(dialysis[is.na(dialysis$palb),]$potilas))

# - initial graph structure
initial_graph <- mebn.fully_connected_bipartite_graph(datadesc_fat_epros)

# - previously estimated graphical model with all the persons
local_distributions <- pk_fppi_palb_targets
local_distributions$modelcache <-
  "models/BLMM_gamma_qr_multivariate3/fat_epros_missing_palb"

# - get personal data, normalized and original

# - statistics for vertex levels are calculated from normalized data
predictors <- nrow(assumedpredictors_fat_epros)
normalized_input <- sapply(1:predictors, mebn.scale_gaussians,
  data = dialysis, datadesc = assumedpredictors_fat_epros)
normalized_input_df <- as.data.frame(normalized_input)

datadesc <- datadesc_fat_epros

```

Then we predict missing values with these data imputing models

```

for (i in 1:nrow(rows_with_missing_palb)) {

  datarow <- rows_with_missing_palb[i,]

  # get model for patient in this datarow

  personal_model_dir <- paste0("data_imputation_models/", datarow$potilas)
  print(paste0("Reading personal data imputation model ", personal_model_dir,
    "/personal_graph.graphml"))

  personal_graph <- read.graph(paste0(personal_model_dir, "/personal_graph.graphml"), "graphml")
}

```

```

# and use the data in this row to predict palb
evidence <- rows_with_missing_palb[i, assumedpredictors_fat_epros$Name]

posterior_prediction <- mebn.personal_prediction(reaction_graph = personal_graph,
  graph_dir = personal_model_dir,
  evidence = evidence,
  stan_model_file = "diet/posterior_prediction.stan")

# personal_predictions contains predictions multivariate predictions
# P-K and fP-Pi are known, but P-Alb is missing

posterior <- rstan::extract(posterior_prediction, par= "posterior[3]")

# use predicted posterior mean for missing P-Alb value
# - this is i:th NA value in dialysis
predicted_palb <- mean(posterior$posterior[3])

# rows in 'rows_with_missing_palb' and 'original_palb' are in same order
# so we can imput in the NA values at 'original_palb'

for (m in 1:imput_length)
{
  if (is.na(original_palb[m]))
  {
    original_palb[m] <- predicted_palb
    break;
  }
}
}

dialysis2 <- dialysis
dialysis2$palb <- original_palb
saveRDS(dialysis2, "data/DIALYSIS_imputed_palb.rds")

```

With this data imputation we can estimate a cross-covariance model with three responses

```

pk_fppi_palb_targets <- datadesc_fat_epros[datadesc_fat_epros$Name %in% c('pk','fppi','palb'),]

initial_graph <- mebn.fully_connected_bipartite_graph(datadesc_fat_epros)

dialysis_imputed <- readRDS("data/DIALYSIS_imputed_palb.rds")
no_holdout <- rep(0, nrow(dialysis_imputed))

dialdiet_gamma_mv3 <- mebn.bipartite_multivariate(reaction_graph = initial_graph,
  inputdata = dialysis_imputed,
  targetdata = no_holdout,
  predictor_columns = assumedpredictors_fat_epros,
  assumed_targets = pk_fppi_palb_targets,
  group_column = "potilas",
  local_estimation = mebn.multivariate_sampling,
  local_model_cache =
    "models/BLMM_gamma_qr_multivariate3/imputed_palb",

```

```

stan_model_file = "mebn/v2/BLMM_gamma_qr_mv_cv.stan",
normalize_values = TRUE)

write.graph(dialdiet_gamma_mv3,
            "graphs/dialysis_gamma_multivariate3_imputed.graphml", "graphml")

```

Finally, we consider also the effect of dialysis treatment type as new level of grouping in data. This allows us to estimate average effects of nutrition for each treatment type and then also personal effects within those treatments.

```

dialysis_imputed <- readRDS("data/DIALYSIS_imputed_palb.rds")

# add the dialysis treatment type as a grouping factor
dialysis_imputed$hoitoryhma <- as.factor(dialysis_imputed$hoitomuoto)

# and sort the data by treatment/patient/observation
dialysis_imputed <- dialysis_imputed[order(dialysis_imputed$hoitoryhma,
                                           dialysis_imputed$potilas, dialysis_imputed$havainto),]

dialdiet_gamma_mv3_two_level <- mebn.bipartite_two_level_multivariate(
  reaction_graph = initial_graph,
  inputdata = dialysis_imputed,
  targetdata = no_holdout,
  predictor_columns = assumedpredictors_fat_epros,
  assumed_targets = pk_fppi_palb_targets,
  group_column = "hoitoryhma",
  subject_column = "potilas",
  local_estimation = mebn.two_level_multivariate_sampling,
  local_model_cache =
    "models/BLMM_gamma_mv_cross/two_levels",
  stan_model_file =
    "mebn/v2/BLMM_gamma_two_level_grouping.stan",
  normalize_values = TRUE)

write.graph(dialdiet_gamma_mv3_two_level,
            "graphs/dialysis_gamma_two_level_grouping.graphml", "graphml")

```

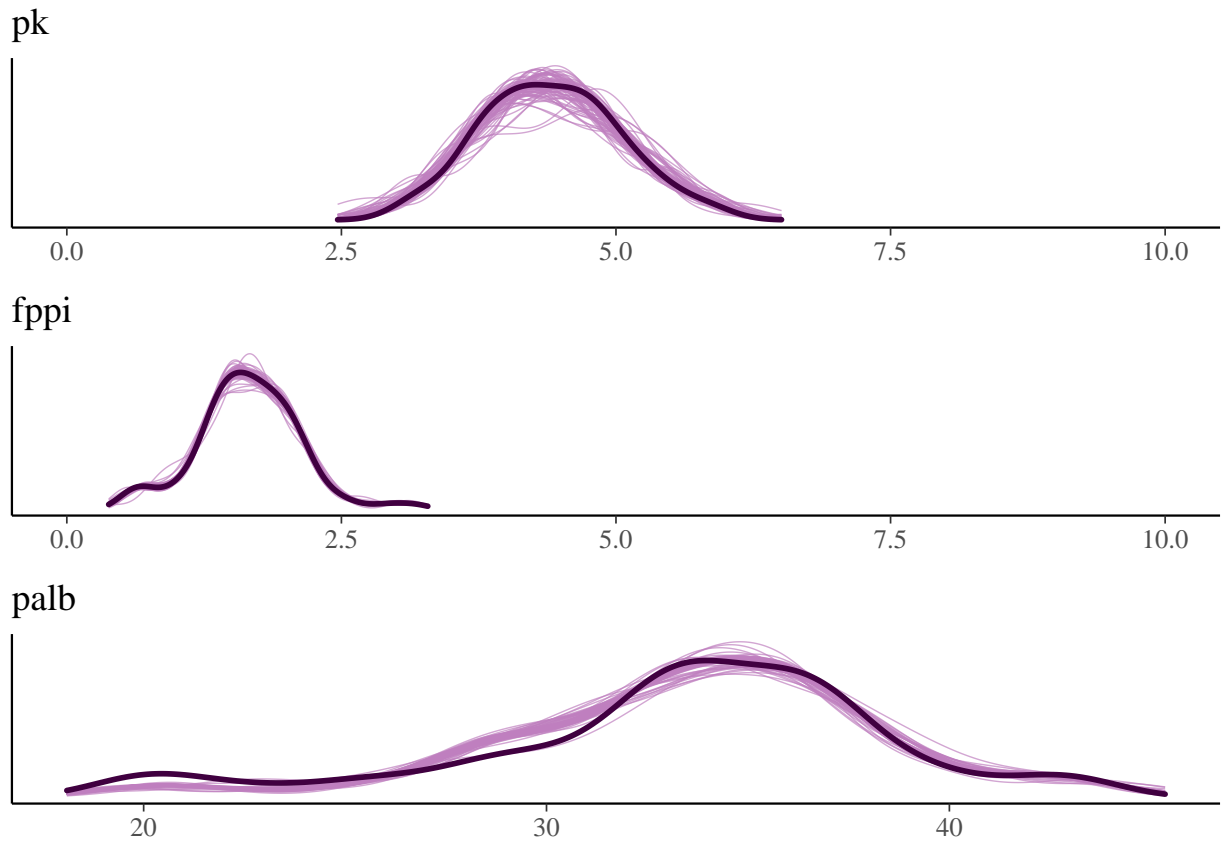
Model analysis

Here we evaluate the model's ability to repeat the measured observations with normalized root mean square error (NRMSE) and compare how adding the dialysis treatment as an explicit hierarchical layer in the model affects this error. We also asses the model's performance with visual posterior predictive check by comparing samples from the model with measured values. This would give away possible bias in the model.

Supplementary Table S 1: Personal graphical models with different reaction model candidates are evaluated with NRMSE for each modelled concentration and average model error.

Reaction model	NRMSE			
	P-K	fP-Pi	P-Alb	average error
mv3_cross_two_levels	0.004	0.007	0.002	0.004
mv3_cross_single_level	0.036	0.13	0.059	0.036

```
## [1] "pk"
## [1] "fppi"
## [1] "palb"
```

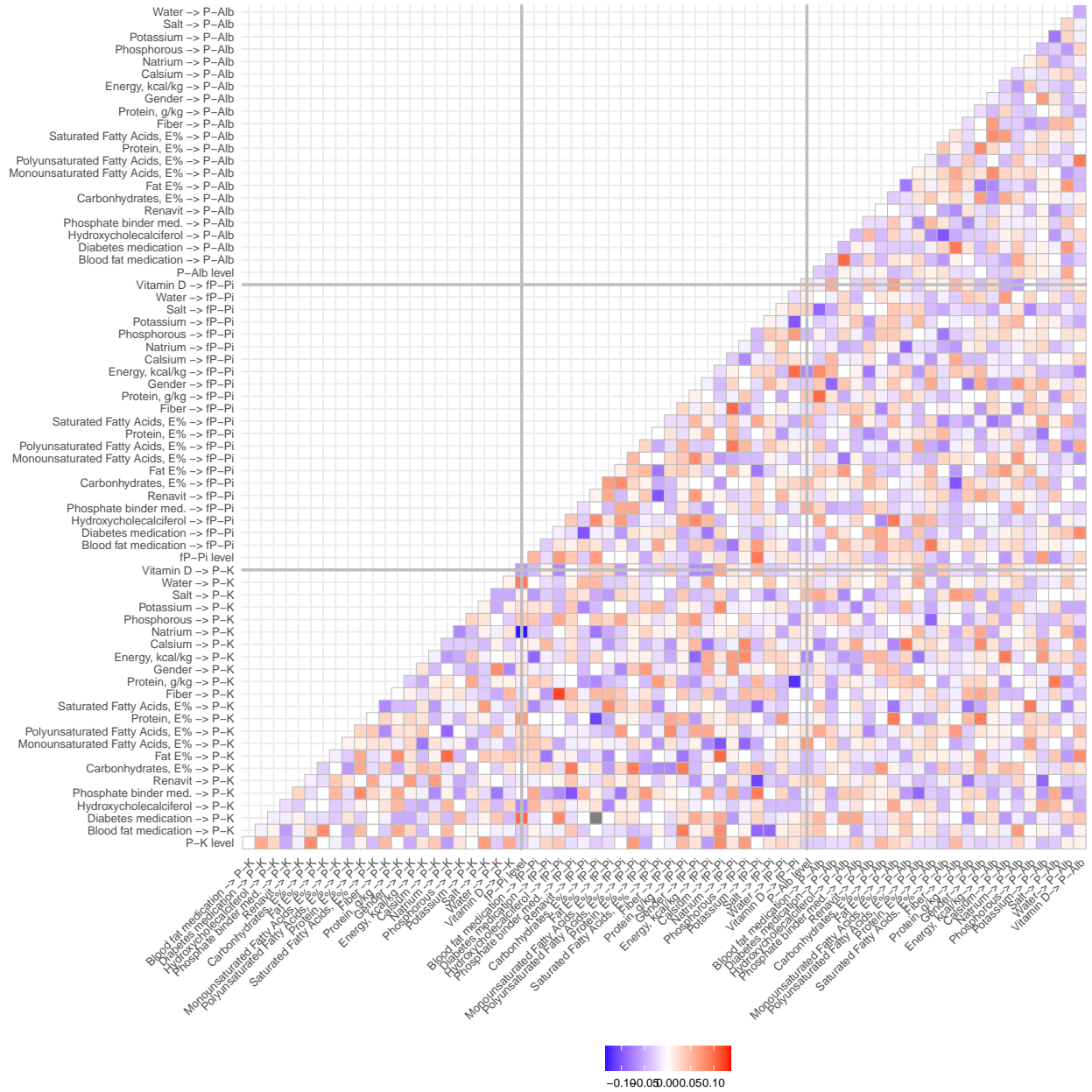


Supplementary Figure S 2: Posterior predictive check of the model where three concentrations and their parameters are stacked into one univariate model for estimating cross-model correlations.

Then we drill into the estimated correlation matrices of effects. The model estimates how much the effects of nutrients vary from general effects in dialysis treatment level and further how the effects vary personally within a treatment. These correlation plots show how the effects are correlated.

```
## Scale for 'fill' is already present. Adding another scale for 'fill', which
## will replace the existing scale.
```





Supplementary Figure S 4: Correlation plot of matrix C_b that includes the estimated within-model and cross-model correlations of personal effects

Supplementary Table S 2: Table shows 40 highest positive or negative correlations between treatment effects of potassium and phosphorous with other treatment effects. This structure of correlations is used in estimating the personal effects based on personal intake and matching concentrations.

Treatment-level effects of nutrients		
Effect 1	Effect 2	Correlation
Energy, kcal/kg -> P-K	Potassium -> P-K	0.083
Natrium -> P-K	Potassium -> fP-Pi	0.073
Hydroxycholecalciferol -> fP-Pi	Potassium-> P-Alb	0.070
Phosphorous -> P-K	Potassium -> fP-Pi	0.065
Calsium -> fP-Pi	Potassium -> P-K	0.063
Diabetes medication -> fP-Pi	Potassium-> P-Alb	0.060
Polyunsaturated Fatty Acids, E% -> fP-Pi	Potassium -> P-K	0.057
Water -> P-Alb	Potassium -> P-K	0.056
Diabetes medication -> P-K	Potassium -> fP-Pi	0.053
Protein, g/kg -> fP-Pi	Potassium -> P-K	0.046
Blood fat medication -> P-Alb	Potassium -> P-K	0.042
Potassium -> fP-Pi	Potassium -> P-K	-0.040
Carbonhydrates, E% -> P-Alb	Potassium -> fP-Pi	-0.045
Protein, E% -> P-K	Potassium-> P-Alb	-0.048
Natrium -> fP-Pi	Potassium-> P-Alb	-0.050
fP-Pi level	Potassium-> P-Alb	-0.052
Fat E% -> P-K	Potassium -> P-K	-0.056
Gender -> P-Alb	Potassium -> fP-Pi	-0.057
Phosphate binder med. -> P-Alb	Potassium -> fP-Pi	-0.064
Protein, g/kg -> P-K	Potassium -> P-K	-0.076
Protein, g/kg -> P-K	Potassium -> fP-Pi	-0.087
Fiber -> fP-Pi	Phosphorous-> P-Alb	0.093
Water -> P-K	Phosphorous-> P-Alb	0.067
Potassium -> fP-Pi	Phosphorous -> P-K	0.065
Carbonhydrates, E% -> P-K	Phosphorous -> P-K	0.058
Fat E% -> fP-Pi	Phosphorous -> P-K	0.056
Protein, E% -> P-Alb	Phosphorous -> P-K	0.051
Monounsaturated Fatty Acids, E% -> fP-Pi	Phosphorous-> P-Alb	0.048
Fat E% -> P-K	Phosphorous -> P-K	0.047
Saturated Fatty Acids, E% -> P-K	Phosphorous-> P-Alb	0.046
Monounsaturated Fatty Acids, E% -> P-K	Phosphorous -> fP-Pi	-0.048
Protein, E% -> fP-Pi	Phosphorous -> fP-Pi	-0.050
Blood fat medication -> P-K	Phosphorous -> fP-Pi	-0.051
Fat E% -> fP-Pi	Phosphorous -> fP-Pi	-0.053
Phosphate binder med. -> P-Alb	Phosphorous-> P-Alb	-0.054
Phosphate binder med. -> fP-Pi	Phosphorous -> fP-Pi	-0.056
Calsium -> P-Alb	Phosphorous-> P-Alb	-0.056
fP-Pi level	Phosphorous-> P-Alb	-0.062
Protein, E% -> P-K	Phosphorous -> P-K	-0.071
Phosphorous -> P-Alb	Phosphorous -> fP-Pi	-0.073
Renavit -> P-K	Phosphorous -> fP-Pi	-0.091

Supplementary Table S 3: Table shows 40 highest positive or negative correlations between personal effects of potassium and phosphorous with other personal effects. This structure of correlations is used in estimating the personal effects based on personal intake and matching concentrations.

Personal effects of nutrients		
Effect 1	Effect 2	Correlation
Phosphate binder med. -> P-K	Potassium -> fP-Pi	0.094
Calsium -> fP-Pi	Potassium -> P-K	0.078
fP-Pi level	Potassium-> P-Alb	0.071
Gender -> P-Alb	Potassium-> P-Alb	0.068
Calsium -> P-K	Potassium-> P-Alb	0.059
Saturated Fatty Acids, E% -> fP-Pi	Potassium -> fP-Pi	0.056
Saturated Fatty Acids, E% -> fP-Pi	Potassium-> P-Alb	0.055
Polyunsaturated Fatty Acids, E% -> P-Alb	Potassium -> fP-Pi	0.052
Gender -> fP-Pi	Potassium-> P-Alb	0.050
Diabetes medication -> fP-Pi	Potassium -> fP-Pi	-0.050
Monounsaturated Fatty Acids, E% -> P-K	Potassium -> fP-Pi	-0.053
Water -> P-Alb	Potassium -> P-K	-0.053
Blood fat medication -> P-Alb	Potassium -> P-K	-0.054
Protein, E% -> P-Alb	Potassium -> P-K	-0.055
Monounsaturated Fatty Acids, E% -> P-K	Potassium -> P-K	-0.060
Phosphate binder med. -> P-Alb	Potassium -> P-K	-0.067
Salt -> P-Alb	Potassium-> P-Alb	-0.077
Protein, E% -> fP-Pi	Potassium-> P-Alb	-0.079
Saturated Fatty Acids, E% -> P-K	Potassium -> fP-Pi	-0.089
Vitamin D -> fP-Pi	Potassium -> fP-Pi	-0.104
Saturated Fatty Acids, E% -> P-K	Phosphorous-> P-Alb	0.089
Calsium -> P-K	Phosphorous -> fP-Pi	0.077
Vitamin D -> fP-Pi	Phosphorous -> fP-Pi	0.071
Gender -> fP-Pi	Phosphorous -> P-K	0.066
Monounsaturated Fatty Acids, E% -> fP-Pi	Phosphorous -> P-K	0.056
Polyunsaturated Fatty Acids, E% -> fP-Pi	Phosphorous -> fP-Pi	0.046
Polyunsaturated Fatty Acids, E% -> P-K	Phosphorous-> P-Alb	0.045
Fat E% -> fP-Pi	Phosphorous-> P-Alb	0.045
Fiber -> fP-Pi	Phosphorous-> P-Alb	0.044
Protein, g/kg -> P-K	Phosphorous -> fP-Pi	-0.045
Diabetes medication -> P-K	Phosphorous-> P-Alb	-0.046
fP-Pi level	Phosphorous-> P-Alb	-0.047
Energy, kcal/kg -> P-K	Phosphorous -> P-K	-0.051
Renavit -> P-Alb	Phosphorous -> fP-Pi	-0.052
Protein, g/kg -> P-Alb	Phosphorous -> P-K	-0.054
Fiber -> P-Alb	Phosphorous-> P-Alb	-0.058
Water -> P-Alb	Phosphorous-> P-Alb	-0.063
Salt -> fP-Pi	Phosphorous-> P-Alb	-0.065
Calsium -> fP-Pi	Phosphorous -> fP-Pi	-0.074
Monounsaturated Fatty Acids, E% -> P-K	Phosphorous -> fP-Pi	-0.088

Overview of nutritional effects

Following tables include all the estimated nutrition effects in general, dialysis treatment and personal levels.

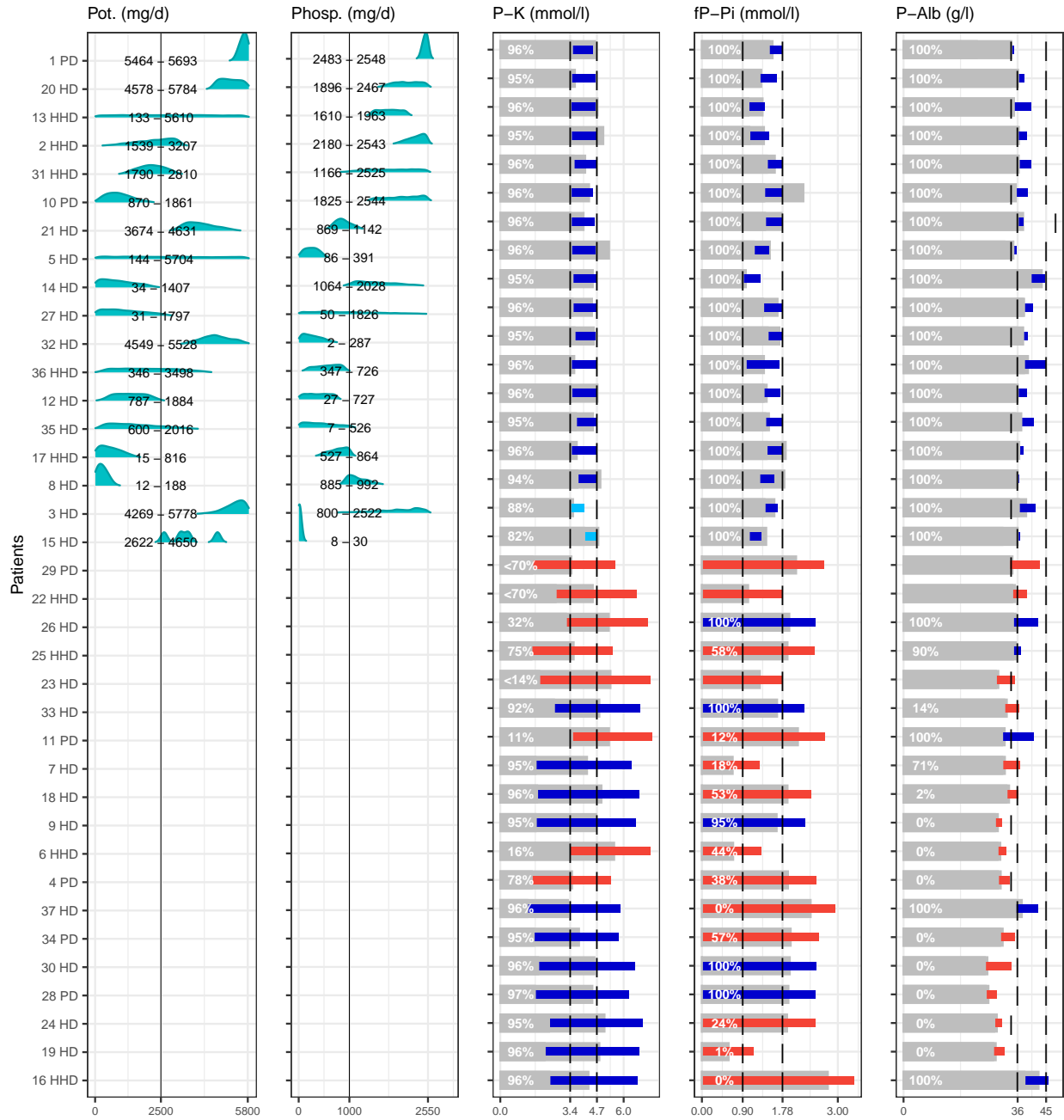
Supplementary Table S4: Nutrition effect magnitudes from nutrients and other modeled features ($j = 1, \dots, 22$) to blood concentrations ($i = 1, \dots, 3$) for analyzed patients ($p = 1, \dots, 37$) in all three additive levels of the model. General effects ($\hat{\beta}_{ij}$) are shown to vary between patients in home hemodialysis, hospital hemodialysis, and peritoneal dialysis. First column of each dialysis type (avg) shows typical effect of the treatment ($\hat{\beta}_{ij} + \hat{g}_{ijk}, k = 1, \dots, 3$) that can further vary personally. Minimum and maximum of these personal effects are shown within each treatment ($\hat{\beta}_{ij} + \hat{g}_{ijk} + \hat{b}_{ijp}$). The table is sorted in decreasing order of between-treatment variation ($\hat{\sigma}_g$) and all the estimates include their 90%-credible intervals.

Nutrient	Conc.	General effect	Home hemodialysis			Hospital hemodialysis			Peritoneal dialysis		
			avg	min	max	avg	min	max	avg	min	max
Water	P-Alb	[-0.94; 2.79]	-1.33	-2.09	-0.99	-0.43	-0.77	0.36	-1.53	-2.08	-0.97
Natrium	P-Alb	[-2.60; 7.58]	-0.92	-2.78	0.21	-0.27	-1.87	1.34	-6.70	-7.97	-5.36
Energy, kcal/kg	P-Alb	[3.46; 15.59]	2.63	1.07	3.59	3.42	1.76	4.16	3.49	2.91	4.13
Phosphorous	P-Alb	[0.24; 9.18]	0.83	-0.40	1.45	-0.87	-2.26	0.61	0.85	-0.06	1.79
Diabetes medication	P-Alb	[0.98; 2.55]	-2.22	-2.99	-1.75	0.99	0.01	1.73	0.99	-0.28	1.26
Renavit	P-Alb	[7.67; 10.56]	8.89	8.78	9.72	5.50	4.28	6.86	6.41	6.07	7.41
Hydroxycholecalciferol	P-Alb	[3.73; 4.17]	2.74	0.88	2.86	3.01	1.68	4.57	2.26	1.19	3.46
Potassium	P-Alb	[-0.33; -0.22]	-0.97	-2.20	0.45	0.22	-1.41	1.48	0.90	0.12	1.85
Phosphate binder med.	P-Alb	[-1.28; -2.86]	-0.19	-2.12	1.38	-1.18	-4.28	0.51	-0.40	-0.58	1.29
Carbonhydrates, E%	P-Alb	[-0.08; -1.17]	0.12	0.01	0.97	-0.42	-1.34	0.67	-0.39	-1.57	-0.38
Fiber	P-Alb	[0.67; 1.37]	0.74	0.62	0.96	0.89	0.63	1.25	0.54	0.49	0.66
Gender	P-Alb	[-1.11; 0.04]	-0.82	-2.29	-0.30	2.62	1.14	4.31	-1.74	-3.39	-0.90
Blood lipid medication	P-Alb	[-1.17; -0.48]	0.65	0.06	1.68	-1.66	-2.85	-0.36	1.96	1.50	2.29
Blood lipid medication	P-K	[-1.42; -1.74]	-0.22	-0.30	0.02	-0.41	-0.53	-0.25	-0.42	-0.58	-0.27
Diabetes medication	P-K	[-0.77; -0.09]	-1.04	-1.17	-0.62	-0.40	-0.75	-0.16	-1.64	-1.85	-1.39
Gender	P-K	[-0.37; -0.33]	0.35	-0.32	0.81	0.20	-0.35	0.60	0.97	0.79	1.34
Carbonhydrates, E%	P-Pi	[0.27; 0.21]	-0.07	-0.10	-0.05	0.42	0.38	0.45	0.12	0.10	0.16
Fat E%	P-K	[-0.68; -0.26]	-0.71	-0.85	-0.49	-0.67	-0.95	-0.47	-0.68	-0.96	-0.58
Water	P-K	[0.23; 0.23]	2.52	2.46	2.77	2.74	2.52	3.06	3.20	2.88	3.39
Renavit	P-K	[2.45; 6.63]	-4.12	-4.28	-4.03	-2.38	-2.23	-2.24	-2.46	-3.27	-2.35
Protein, g/kg	P-Alb	[-3.36; -1.96]	-6.42	-7.96	-4.16	-3.61	-6.61	-1.58	-2.80	-4.29	-1.43
Monounsaturated Fatty Acids, E%	P-Alb	[-0.21; -1.41]	-0.81	-1.56	0.30	0.65	-1.04	2.12	-0.32	-1.23	0.97
Calcium	P-Alb	[1.71; 2.37]	1.20	0.47	1.62	-0.01	-0.41	0.71	0.96	0.57	1.18
Fat E%	P-Alb	[3.41; 12.51]	1.82	1.02	2.89	1.77	1.02	3.21	2.29	2.10	3.09
Vitamin D	P-Alb	[1.02; 1.80]	1.38	0.97	2.03	1.26	0.99	1.66	1.19	0.89	1.40
Phosphorous	P-K	[0.18; 0.06]	-0.16	-0.37	0.08	0.24	0.02	0.60	-0.15	-0.51	0.09
Hydroxycholecalciferol	P-K	[-2.20; -0.70]	-1.44	-1.63	-1.23	-0.23	-0.56	0.27	-1.41	-1.79	-1.29
Polyunsaturated Fatty Acids, E%	P-Alb	[-2.95; -3.20]	-1.50	-1.87	-1.12	-3.06	-3.49	-2.55	-1.91	-2.16	-1.61
Salt	P-Alb	[7.19; -1.91]	1.87	1.48	2.14	1.30	0.76	1.99	3.87	3.68	4.37
Energy, kcal/kg	P-K	[-0.23; -1.01]	1.00	0.80	1.17	-0.53	-0.89	-0.35	-0.75	-0.96	-0.56
Natrium	P-K	[-1.94; -0.62]	-1.36	-1.67	-0.90	-0.57	-0.96	-0.23	-1.74	-2.18	-1.68
Saturated Fatty Acids, E%	P-Alb	[-3.58; -5.11]	-2.69	-2.91	-2.38	-2.15	-2.72	-1.74	-1.81	-1.88	-1.35
Hydroxycholecalciferol	P-Pi	[0.27; 0.27]	-0.16	-0.33	0.09	0.50	0.13	0.77	0.10	0.07	0.28

Supplementary Table S4: Nutrition effect magnitudes from nutrients and other modeled features ($j = 1, \dots, 22$) to blood concentrations ($i = 1, \dots, 3$) for analyzed patients ($p = 1, \dots, 37$) in all three additive levels of the model. General effects ($\hat{\beta}_{ij}$) are shown to vary between patients in home hemodialysis, hospital hemodialysis, and peritoneal dialysis. First column of each dialysis type (avg) shows typical effect of the treatment ($\hat{\beta}_{ij} + \hat{g}_{ijk}, k = 1, \dots, 3$) that can further vary personally. Minimum and maximum of these personal effects are shown within each treatment ($\hat{\beta}_{ij} + \hat{g}_{ijk} + \hat{b}_{ijp}$). The table is sorted in decreasing order of between-treatment variation ($\hat{\sigma}_g$) and all the estimates include their 90%-credible intervals (table continues).

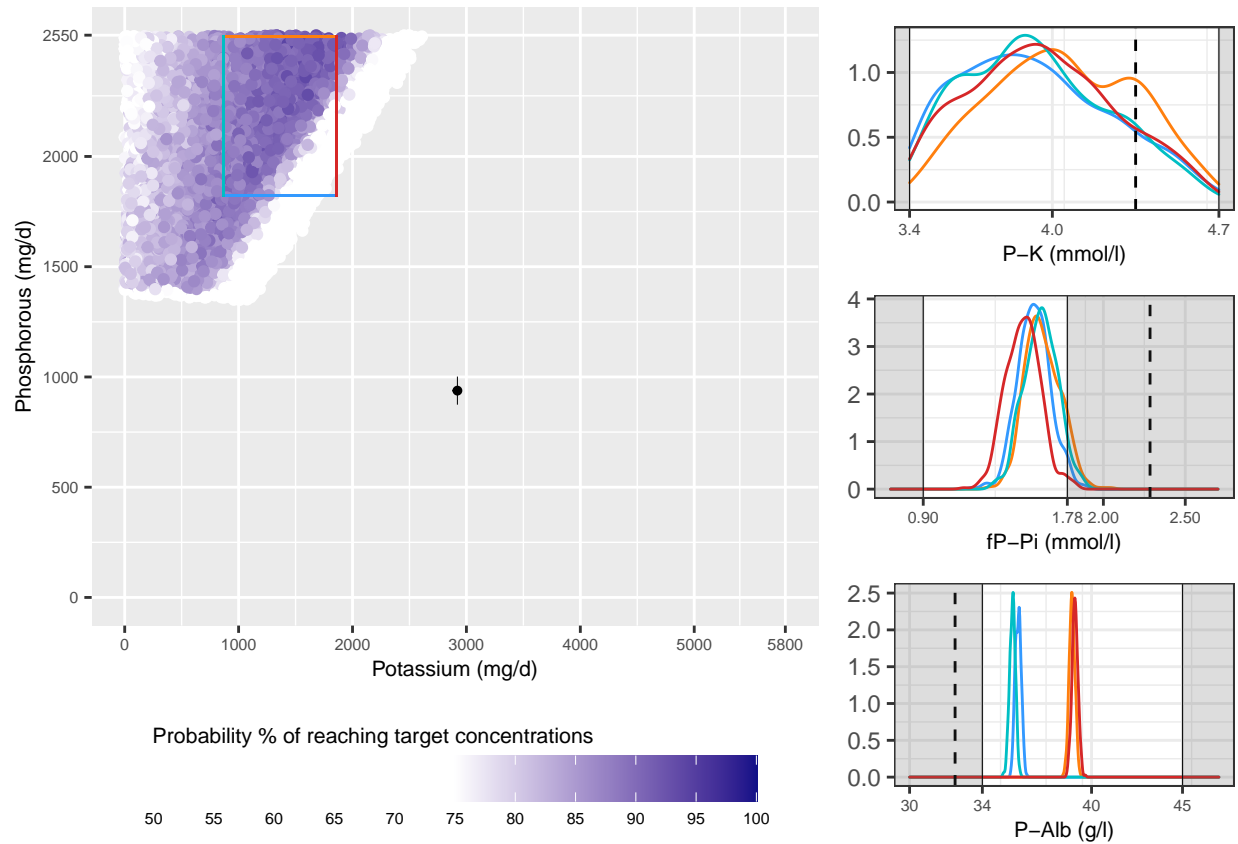
Nutrient	Conc.	General effect	Home hemodialysis			Hospital hemodialysis			Peritoneal dialysis		
			avg	min	max	avg	min	max	avg	min	max
Protein, E%	P-Alb	2.61 [2.41; 9.62]	1.43 [-4.90; 5.88]	1.05 [-5.71; 6.62]	2.68 [-4.73; 7.60]	1.85 [-4.02; 6.45]	0.95 [-5.27; 5.72]	2.76 [-3.46; 8.24]	2.57 [-5.36; 10.19]	1.79 [-6.12; 8.54]	2.88 [-4.90; 10.60]
Fiber	fP-Pi	0.49 [0.10; 2.28]	0.12 [-0.61; 0.82]	0.04 [-0.75; 0.61]	0.16 [-0.66; 0.78]	-0.15 [-0.69; 0.51]	-0.26 [-0.86; 0.49]	-0.09 [-0.60; 0.55]	-0.11 [-0.73; 0.99]	-0.16 [-0.80; 0.85]	-0.07 [-0.80; 0.99]
Polyunsaturated Fatty Acids, E%	P-K	-0.05 [0.00; 1.43]	-0.25 [-1.47; 0.73]	-0.35 [-1.50; 0.77]	-0.14 [-1.42; 1.10]	-0.09 [-0.93; 0.53]	-0.20 [-1.19; 0.57]	-0.01 [-0.97; 0.90]	0.02 [-0.97; 1.06]	-0.05 [-0.98; 0.83]	0.07 [-1.07; 1.09]
Monounsaturated Fatty Acids, E%	P-K	1.62 [1.27; 4.01]	1.26 [-1.07; 3.33]	1.06 [-1.22; 2.63]	1.55 [-0.94; 3.59]	0.67 [-0.81; 1.85]	0.28 [-1.62; 1.65]	0.92 [-0.92; 2.24]	0.38 [-1.28; 2.10]	-0.22 [-2.35; 1.53]	0.47 [-1.06; 2.53]
Carbohydrates, E%	P-K	2.12 [0.60; 10.33]	0.01 [-3.61; 3.31]	-0.50 [-3.96; 3.25]	0.33 [-3.62; 3.31]	-0.09 [-3.12; 3.70]	-0.40 [-3.32; 3.78]	0.24 [-2.99; 3.84]	-0.42 [-4.84; 3.11]	-0.80 [-5.05; 3.11]	-0.25 [-4.96; 3.09]
Phosphate binder med.	P-K	1.89 [1.25; 6.13]	1.01 [-2.11; 2.99]	-0.60 [-4.01; 3.17]	2.01 [-1.78; 5.02]	0.58 [-2.20; 2.63]	-0.34 [-4.75; 2.67]	2.14 [-2.67; 6.54]	0.85 [-1.18; 3.46]	-0.61 [-5.61; 4.33]	1.70 [-1.33; 4.36]
Blood lipid medication	fP-Pi	-0.49 [-0.10; 0.73]	-0.16 [-2.09; 1.28]	-0.26 [-2.12; 1.30]	-0.07 [-2.08; 1.55]	-0.23 [-1.13; 0.54]	-0.44 [-1.27; 0.51]	-0.09 [-1.22; 0.67]	0.18 [-1.65; 1.80]	0.11 [-1.74; 1.82]	0.22 [-1.67; 1.98]
Protein, E%	fP-Pi	-0.27 [-0.26; 1.07]	0.06 [-0.87; 0.70]	-0.07 [-0.96; 0.70]	0.15 [-0.86; 0.83]	0.16 [-0.43; 1.15]	0.08 [-0.59; 1.19]	0.33 [-0.37; 1.21]	0.11 [-0.75; 1.38]	0.02 [-1.01; 1.49]	0.19 [-0.67; 1.46]
Calsium	P-K	0.04 [0.18; 2.18]	-0.17 [-1.88; 2.04]	-0.48 [-2.60; 2.34]	0.24 [-1.00; 2.30]	0.50 [-0.69; 1.75]	-0.16 [-1.44; 1.22]	0.84 [-0.63; 2.88]	0.26 [-0.83; 2.27]	0.84 [-1.53; 1.82]	0.63 [-1.01; 2.61]
Phosphate binder med.	fP-Pi	-0.05 [-0.23; 1.67]	-0.18 [-1.40; 1.40]	-0.53 [-2.78; 1.76]	0.56 [-1.48; 1.86]	0.10 [-1.26; 1.40]	-0.35 [-1.78; 1.72]	0.58 [-1.56; 2.12]	-0.21 [-1.34; 1.04]	-0.36 [-1.53; 1.18]	0.04 [-1.88; 1.24]
Protein, g/kg	P-K	0.43 [-0.26; 4.73]	-0.93 [-5.97; 2.43]	-1.03 [-6.08; 2.43]	-0.85 [-5.87; 2.44]	-0.01 [-5.03; 2.51]	-0.18 [-5.04; 2.62]	0.14 [-4.87; 2.60]	0.42 [-2.78; 3.61]	0.29 [-2.77; 3.55]	0.54 [-2.82; 3.50]
Fat E%	fP-Pi	0.95 [0.68; 5.36]	0.36 [-2.04; 3.66]	0.12 [-2.17; 3.65]	0.67 [-2.21; 3.87]	0.55 [-1.09; 3.21]	0.33 [-1.34; 3.28]	0.79 [-1.12; 3.23]	0.06 [-2.57; 2.91]	-0.08 [-2.51; 3.07]	0.23 [-2.59; 3.16]
Monounsaturated Fatty Acids, E%	fP-Pi	-0.07 [0.19; 1.09]	-0.04 [-1.96; 1.01]	-0.15 [-2.07; 1.06]	-0.04 [-2.04; 1.05]	-0.14 [-1.25; 0.73]	-0.33 [-1.63; 0.76]	0.01 [-1.11; 0.97]	-0.08 [-1.04; 1.19]	-0.08 [-1.01; 1.28]	0.03 [-1.02; 1.46]
Saturated Fatty Acids, E%	fP-Pi	-1.13 [-0.33; 1.61]	-0.15 [-1.88; 1.22]	-0.20 [-1.95; 1.16]	-0.12 [-1.82; 1.30]	-0.14 [-1.02; 1.12]	-0.19 [-1.10; 1.09]	-0.08 [-1.00; 1.24]	-0.02 [-1.20; 1.72]	-0.03 [-1.21; 1.64]	0.03 [-1.14; 2.00]
Calsium	fP-Pi	-0.01 [-0.39; 2.45]	-0.18 [-0.94; 0.74]	-0.26 [-0.91; 0.99]	0.00 [-0.94; 0.88]	-0.20 [-0.64; 0.20]	-0.41 [-0.98; 0.18]	0.01 [-0.63; 0.50]	-0.01 [-0.98; 1.08]	-0.04 [-1.09; 1.13]	0.18 [-0.95; 1.32]
Phosphorous	fP-Pi	0.02 [0.03; 2.03]	0.00 [-1.12; 1.54]	-0.12 [-1.35; 1.40]	0.09 [-1.01; 1.56]	0.03 [-1.00; 0.78]	-0.05 [-1.15; 0.81]	0.13 [-0.88; 0.97]	-0.12 [-1.60; 1.44]	-0.16 [-1.49; 1.37]	-0.09 [-1.56; 1.47]
Diabetes medication	fP-Pi	-0.24 [-0.31; 1.53]	-0.45 [-2.01; 1.01]	-0.66 [-2.46; 1.09]	-0.14 [-1.85; 1.16]	0.09 [-0.73; 1.09]	-0.17 [-1.06; 1.14]	0.22 [-0.87; 1.09]	0.64 [-1.26; 2.88]	0.60 [-1.32; 2.86]	0.85 [-1.13; 3.00]
Renavit	fP-Pi	-3.72 [-1.64; 2.92]	-1.90 [-10.81; 3.65]	-2.01 [-11.83; 3.68]	-1.70 [-9.90; 3.83]	-0.54 [-2.69; 2.10]	-0.66 [-2.90; 2.11]	-0.43 [-2.12; 2.23]	-2.77 [-14.84; 3.19]	-2.88 [-15.22; 3.15]	-2.71 [-14.52; 3.19]
Potassium	fP-Pi	-0.05 [-0.22; 0.72]	0.13 [-0.65; 1.08]	0.01 [-0.81; 1.01]	0.25 [-0.66; 1.58]	-0.07 [-0.58; 0.48]	-0.18 [-0.81; 0.47]	0.15 [-0.45; 1.47]	0.17 [-0.46; 0.90]	0.15 [-0.63; 1.06]	0.27 [-0.39; 1.37]
Energy, kcal/kg	fP-Pi	0.20 [0.39; 2.00]	0.30 [-1.74; 1.79]	0.21 [-1.83; 1.99]	0.43 [-1.63; 2.09]	0.63 [-1.09; 1.71]	0.53 [-1.25; 1.60]	0.77 [-0.97; 1.88]	0.48 [-2.37; 2.65]	0.42 [-2.55; 2.62]	0.57 [-2.27; 2.65]
Protein, g/kg	fP-Pi	-0.69 [-1.19; 2.13]	-0.55 [-1.93; 1.48]	-0.61 [-1.89; 1.52]	-0.49 [-1.84; 1.58]	-0.60 [-1.74; 1.19]	-0.75 [-2.09; 1.13]	-0.46 [-1.68; 1.19]	-0.77 [-2.30; 1.62]	-0.88 [-2.51; 1.56]	-0.68 [-2.41; 1.70]
Vitamin D	P-K	-0.04 [-0.15; 0.89]	-0.06 [-1.10; 0.72]	-0.14 [-1.18; 0.49]	0.22 [-0.85; 1.15]	-0.31 [-0.82; 0.19]	-0.49 [-1.61; 0.19]	-0.10 [-0.67; 0.57]	-0.06 [-0.73; 0.60]	-0.16 [-1.02; 0.53]	0.12 [-0.75; 0.80]
Fiber	P-K	0.46 [0.54; 2.53]	0.31 [-0.77; 1.04]	0.25 [-0.92; 1.07]	0.37 [-0.70; 1.08]	0.17 [-0.72; 1.26]	0.01 [-1.36; 0.94]	0.29 [-0.52; 1.84]	0.59 [-1.38; 1.93]	0.66 [-1.70; 1.81]	0.66 [-1.55; 2.12]
Potassium	P-K	0.02 [-0.15; 1.95]	-0.03 [-1.40; 1.53]	-0.25 [-1.91; 1.01]	0.01 [-1.34; 1.30]	0.17 [-0.91; 0.83]	-0.17 [-1.11; 0.55]	0.40 [-1.05; 1.45]	0.00 [-1.09; 2.00]	-0.10 [-1.17; 1.81]	0.20 [-1.08; 1.67]
Saturated Fatty Acids, E%	P-K	0.44 [0.61; 2.10]	0.09 [-2.07; 1.52]	-0.09 [-2.67; 1.49]	0.20 [-1.99; 1.60]	0.27 [-1.88; 1.67]	0.16 [-2.14; 1.74]	0.39 [-1.71; 1.80]	0.61 [-1.16; 1.99]	0.54 [-1.32; 2.00]	0.64 [-1.20; 2.08]
Water	fP-Pi	-0.08 [0.19; 0.89]	0.16 [-0.49; 0.81]	0.04 [-0.61; 0.85]	0.24 [-0.57; 1.22]	0.16 [-0.15; 0.58]	-0.05 [-0.54; 0.66]	0.28 [-0.23; 0.99]	0.12 [-1.01; 0.88]	0.04 [-1.21; 0.84]	0.26 [-1.00; 1.17]
Gender	fP-Pi	-0.10 [0.08; 1.79]	0.10 [-1.41; 1.42]	-0.05 [-1.73; 1.38]	0.19 [-1.40; 1.43]	-0.30 [-1.13; 0.78]	-0.50 [-2.01; 0.64]	-0.19 [-1.13; 1.14]	-0.58 [-1.89; 0.93]	-0.63 [-2.16; 1.00]	-0.51 [-2.02; 1.35]
Polyunsaturated Fatty Acids, E%	fP-Pi	-0.19 [-0.21; 0.62]	-0.23 [-1.36; 0.89]	-0.27 [-1.47; 0.90]	-0.15 [-1.24; 1.25]	-0.19 [-0.59; 0.35]	-0.26 [-0.87; 0.35]	-0.10 [-0.63; 0.60]	-0.08 [-0.88; 0.92]	-0.10 [-0.93; 0.95]	-0.04 [-0.88; 0.95]
Protein, E%	P-K	0.45 [0.74; 2.36]	0.39 [-1.22; 1.84]	0.34 [-1.25; 1.74]	0.52 [-1.10; 2.38]	-0.24 [-1.24; 1.60]	-0.37 [-1.46; 1.35]	-0.14 [-1.17; 2.11]	-0.36 [-1.92; 2.03]	-0.46 [-1.78; 1.80]	-0.27 [-1.89; 2.14]
Natrium	fP-Pi	0.20 [0.58; 1.47]	0.13 [-1.71; 1.14]	0.08 [-1.82; 1.15]	0.26 [-1.64; 1.44]	0.39 [-0.52; 1.13]	0.30 [-0.66; 0.93]	0.50 [-0.48; 1.39]	0.22 [-1.50; 1.89]	0.15 [-1.63; 1.74]	0.27 [-1.53; 2.08]
Salt	P-K	0.26 [0.58; 2.59]	1.90 [-0.98; 8.85]	1.68 [-0.90; 8.76]	2.14 [-0.92; 9.03]	0.42 [-0.61; 1.28]	0.19 [-0.73; 1.37]	0.72 [-0.51; 1.59]	0.81 [-2.20; 4.45]	0.57 [-2.43; 4.29]	1.04 [-2.17; 4.50]
Vitamin D	fP-Pi	-0.13 [0.02; 0.36]	-0.10 [-0.69; 0.32]	-0.17 [-0.81; 0.30]	0.08 [-0.62; 0.73]	0.08 [-0.23; 0.38]	-0.09 [-0.57; 0.43]	0.29 [-0.18; 0.67]	0.12 [-0.38; 0.71]	-0.03 [-0.51; 0.77]	0.22 [-0.50; 0.86]
Salt	fP-Pi	-0.08 [-0.42; 1.70]	-0.16 [-1.11; 1.58]	-0.30 [-1.15; 1.53]	-0.05 [-1.15; 1.57]	-0.34 [-0.96; 0.47]	-0.48 [-1.27; 0.50]	-0.15 [-0.89; 0.51]	-0.26 [-1.68; 1.38]	-0.42 [-1.70; 1.47]	-0.17 [-1.59; 1.52]

Overview of personal recommendations



Supplementary Figure S 5: The figure shows in two left-most panels personal recommendations of potassium and phosphorous intake ($\hat{Q}^{min} - \hat{Q}^{max}$) from Algorithm (1) with predictive distributions of \hat{Q} in the background. Each row gives a numeric label of the patient and the type of patient's dialysis treatment (HD = hospital hemodialysis, HHD = home hemodialysis, PD = peritoneal dialysis). Personal recommendations are given for those patients whose resulting plasma concentration levels could be predicted in either over 90% or 80% probability. Three right-most panels show the estimated concentrations that match the recommended intake. In these panels, grey bars indicate the estimated concentration without the effect of potassium and phosphorous intake, μ_{q0} . Blue bars indicate the range of concentration that is resulted by modifying potassium and phosphorous intake. It is required that these simulated concentrations stay within the personal target ranges denoted with vertical black lines. The light blue bar indicates satisfying this requirement in $P^{max}_m > 80\%$ confidence and dark blue $P^{max}_m > 90\%$ confidence. The best exact probabilities P^{max}_m are shown with percentage figures. Red bars indicate that even the best concentration estimation has $P^{max}_m < 80\%$ confidence and personal recommendations are not given for these patients. For these patients, the red and blue bars show the whole reachable ranges. The figure is plotted with ggplot2 package for R language (v 3.3.5, <https://ggplot2.tidyverse.org>)

Personal recommendation for a patient



Supplementary Figure S 6: Figure shows detailed intake recommendation for patient 10 from the previous recommendation table. The intake plot on the left shows the posterior samples of diet configurations that result concentrations of plasma potassium (P-K), fasting plasma phosphate (fP-Pi) and plasma albumin (P-Alb) to stay within their recommended limits. These levels are marked with vertical solid lines in the concentration panels. The black point in the middle of intake plot represents the patient's current potassium and phosphorous intake. Current concentrations matching this intake are shown with dashed vertical lines. Reported recommendation is shown with a rectangle that contains 95% of diet proposals that result recommended concentrations over 90% accuracy. Colouring of the rectangle sides match the concentration estimates in the right hand panels. The figure is plotted with ggplot2 package for R language (v 3.3.5, <https://ggplot2.tidyverse.org>).