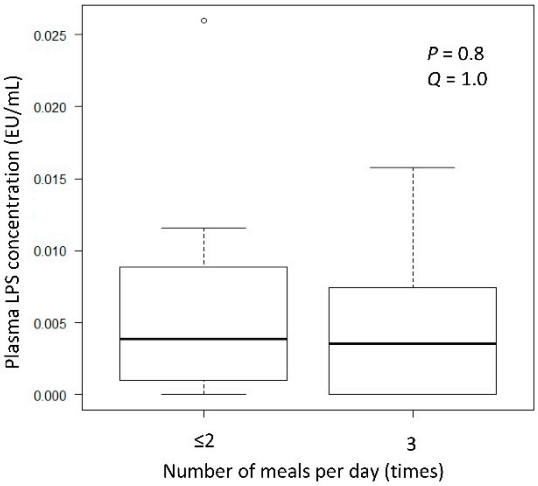

Figure S1. Association between plasma LPS concentrations and number of meals per day. In Study 1, plasma LPS concentrations were compared between groups who ate two or fewer meals a day and those who ate three meals a day. The horizontal line in the middle of the boxplots indicates the median, the lines below and above the boxes indicate the 25th and 75th percentile values, the error bars indicate the minimum and maximum values, and the circle indicate the outliers. Two or fewer meals a day ($n = 8$), three meals a day ($n = 28$). The P and Q values obtained from the Mann-Whitney U test are shown in the graph.

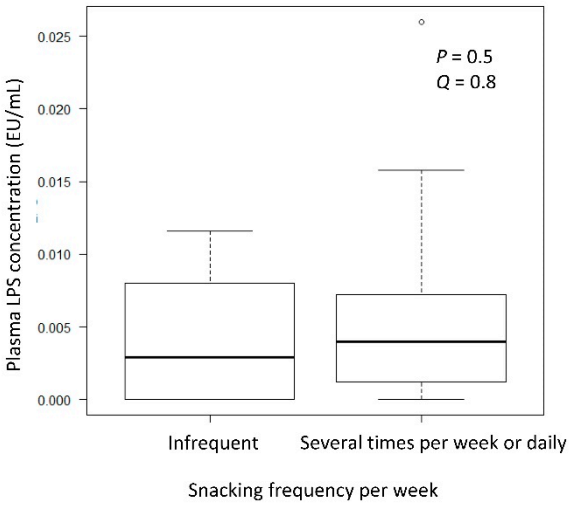

Figure S2. Association between plasma LPS concentrations and snacking frequency. In Study 1, the plasma LPS concentration was compared between two groups: one with an infrequent snacking per week, and the other with several times a week or daily intake of snacks. The horizontal line in the middle of the boxplots indicates the median, the lines below and above the boxes indicate the 25th and 75th percentile values, the error bars indicate the minimum and maximum values, and the circle indicate the outliers. Infrequent snacking per week (n = 14), several times a week or daily intake of snacks (n = 22). The P and Q values obtained from the Mann-Whitney U test are shown in the graph.

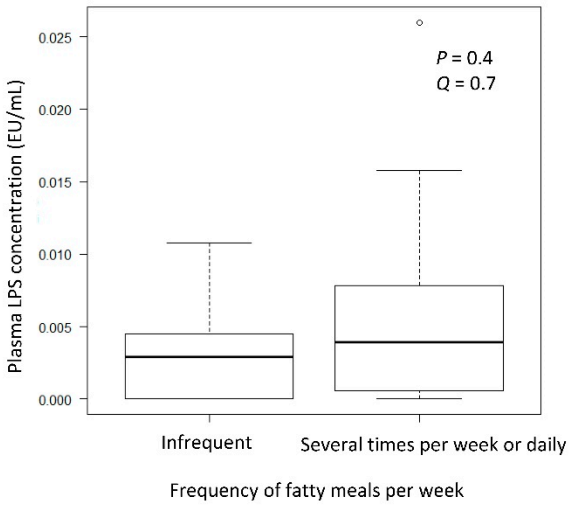

Figure S3. Association between plasma LPS concentrations and frequency of fatty meals. In Study 1, the plasma LPS concentration was compared between two groups: one with an infrequent consumption of fatty meals per week, and the other with several times a week or daily intake of fatty meals. The horizontal line in the middle of the boxplots indicates the median, the lines below and above the boxes indicate the 25th and 75th percentile values, the error bars indicate the minimum and maximum values, and the circle indicate the outliers. Infrequent consumption of fatty meals per week (n = 9), several times a week or daily intake of fatty meals (n = 27). The P and Q values obtained from the Mann-Whitney U test are shown in the graph.

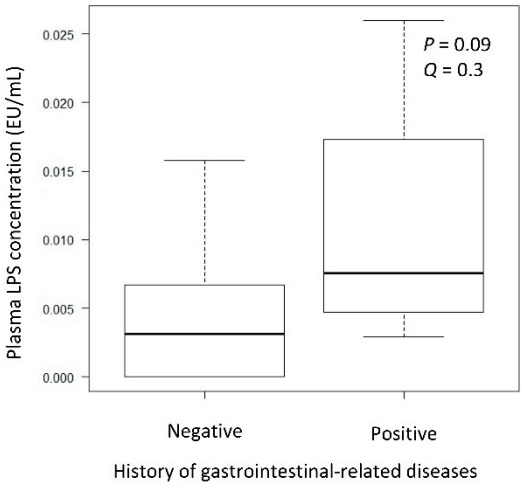

Figure S4. Association between plasma LPS concentrations and the presence or absence of a history of gastrointestinal-related diseases. In Study 1, the plasma LPS concentration was compared based on the presence or absence of a history of gastrointestinal-related diseases. The horizontal line in the middle of the boxplots indicates the median, the lines below and above the boxes indicate the 25th and 75th percentile values, the error bars indicate the minimum and maximum values, and the circle indicate the outliers. Negative (n = 32), and positive history of gastrointestinal-related diseases (n = 4). The P and Q values obtained from the Mann-Whitney U test are shown in the graph.

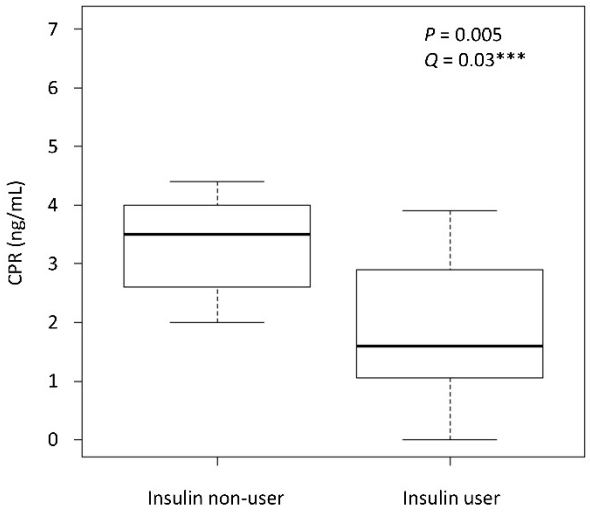

Figure S5. Comparison of C-peptide immunoreactivity (CPR) values between insulin users and non-users. In Study 2, CPR values were compared between insulin users and non-users. The horizontal line in the middle of the boxplots indicates the median, the lines below and above the boxes indicate the 25th and 75th percentile values, the error bars indicate the minimum and maximum values, and the circle indicate the outliers. Insulin users (n = 28), insulin non-users (n = 8). The Mann-Whitney U test. The P and Q values obtained from the Mann-Whitney U test are shown in the graph. ***$Q < 0.05$.

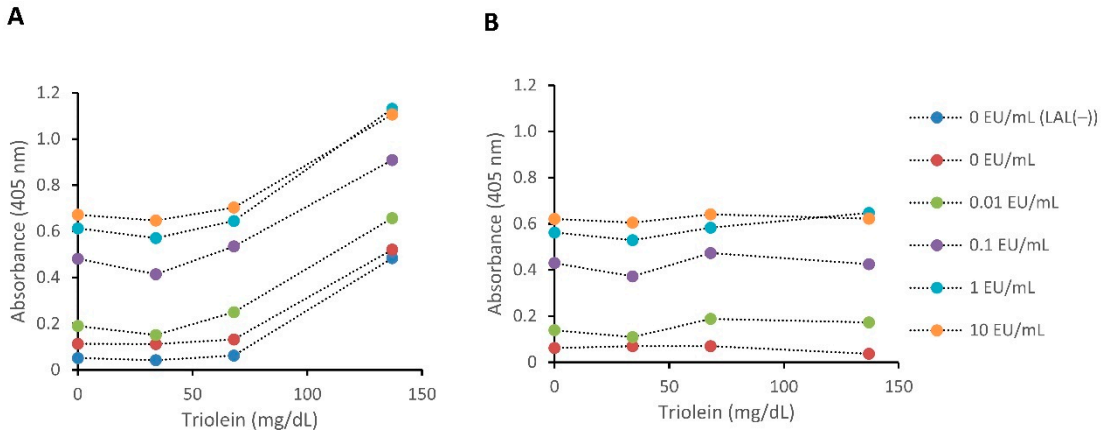

Figure S6. Effect of triglycerides on lipopolysaccharide (LPS) measurement. The plasma was collected from whole horse blood (Kohjin Bio Co., Ltd.). Triolein (FUJIFILM Wako Pure Chemicals Corporation, Osaka, Japan) diluted in dimethyl sulfoxide (DMSO; Fujifilm Wako Pure Chemicals Corporation) or DMSO alone was added to plasma. A mixture of plasma sample with LPS-free distilled water was also prepared to assess the effect of DMSO on the LAL reaction. These plasma samples were diluted with LPS-free distilled water and heated at 70°C for 10 min. Then, these plasma samples, LPS-free distilled water containing LPS, and LAL reagent were mixed in a 96-well plate. The concentrations of triolein in the plasma samples used for the LAL reaction were 0, 34, 68, and 137 mg/dL, and the LPS concentrations were 0, 0.01, 0.1, 1, and 10 EU/mL. To correct for the color of the plasma samples, samples with LPS-free distilled water instead of the LAL reagent were also prepared. The plate was incubated, and the Abs was measured using a microplate reader. As shown in (A), the measured Abs increased in an LPS- and triolein concentration-dependent manner (n = 1). However, the control sample without the LAL reaction (LAL (–)) also showed a triolein concentration-dependent increase in Abs. Therefore, the Abs of the corresponding control samples was subtracted from the Abs of each sample (B, n = 1). Subsequently, an LPS concentration-dependent increase in Abs was still observed; however, a triolein concentration-dependent increase in Abs was not observed. The Abs of the LPS samples (0–10 EU/mL) with DMSO (i.e., Triolein 0 mg/dL) was 1.1 ± 0.2 times higher than that of the samples with LPS-free distilled water. This indicated that DMSO had no effect on the LAL reaction. These results indicated that our method for measuring LPS concentration is not interfered by triglycerides.

Table S1. *P* values from the Shapiro–Wilk test

Characteristic	Study 1	Study 2	
		At admission	At discharge
Age	0.001*	0.366	NA
BMI	0.017*	0.001*	0.001*
LPS	0.000*	0.000*	0.000*
CPR	NA	0.036*	NA
HbA1c	NA	0.075	NA
Stage of diabetic nephropathy	NA	0.000*	NA
20/(CPR × FPG)	NA	0.000*	NA
FPG	NA	0.006*	0.075
GA	NA	0.011*	0.030*
TG	NA	0.000*	0.000*
TC	NA	0.496	0.102
HDL-C	NA	0.003*	0.139
LDL-C	NA	0.991	0.432
AST	NA	0.000*	0.000*
ALT	NA	0.000*	0.000*
γ-GTP	NA	0.000*	0.000*
SBP	NA	0.041*	0.835
hs-CRP	NA	0.000*	0.000*

*$P < 0.05$. CPR, C-peptide; FPG, fasting plasma glucose; GA, glycoalbumin; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transferase; SBP, systolic blood pressure; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein HbA1c, haemoglobin A1c; LPS, lipopolysaccharide. NA: not applied

Table S2. Multiple regression analysis between physiological and biochemical test values and the plasma lipopolysaccharide (LPS) concentration of patients at admission (type 1 diabetes excluded)

Characteristic	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6			Model 7		
	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*
CPR	41	<0.01	<0.05***	42	<0.01	<0.05***	41	<0.01	<0.05***	40	<0.01	<0.05***	-	-	-	-	-	-	-	-	-
HbA1c	35	0.14	0.36	35	0.15	0.36	35	0.15	0.36	37	0.06	0.21	-	-	-	-	-	-	-	-	-
Diabetic nephropathy	20	<0.01	<0.05***	21	<0.01	<0.05***	21	<0.01	<0.05***	21	<0.01	<0.05***	14	0.16	0.37	20	<0.05	<0.1**	-	-	-
20/(CPR × FPG)	-24	<0.05	<0.2*	-25	<0.05	<0.2*	-24	<0.05	<0.2*	-24	<0.05	<0.2*	-12	0.52	0.78	-	-	-	-23	0.09	0.30
FPG	791	<0.05	<0.2*	791	<0.05	<0.2*	787	<0.05	<0.2*	816	<0.05	<0.2*	-	-	-	-	-	-	-	-	-
GA	7.8	0.92	1.00	7	0.93	1.00	7	0.93	1.00	17	0.78	0.97	-	-	-	-	-	-	-	-	-
TG	2914	<0.01	<0.05***	2914	<0.01	<0.05***	2938	<0.01	<0.05***	2911	<0.01	<0.05***	-	-	-	2784	<0.01	<0.05***	2640	<0.01	<0.05***
TC	202	0.51	0.78	203	0.51	0.78	236	0.34	0.59	197	0.52	0.78	-	-	-	-	-	-	-	-	-
LDL-C	-133	0.59	0.83	-131	0.59	0.84	-110	0.61	0.85	-140	0.57	0.82	-	-	-	-	-	-	-	-	-
HDL-C	-161	0.09	0.30	-161	0.10	0.30	-157	0.10	0.30	-159	0.10	0.30	-	-	-	-	-	-	-	-	-
AST	-209	0.17	0.37	-206	0.15	0.36	-208	0.17	0.37	-211	0.16	0.37	-	-	-	-	-	-	-	-	-
ALT	-359	0.35	0.59	-351	0.30	0.54	-359	0.36	0.60	-368	0.34	0.59	-	-	-	-	-	-	-	-	-
γ-GTP	-504	0.23	0.45	-502	0.23	0.46	-516	0.22	0.44	-500	0.24	0.46	-	-	-	-	-	-	-	-	-
SBP	8.4	0.97	1.00	7	0.97	1.00	19	0.92	1.00	10	0.96	1.00	-	-	-	-	-	-	-	-	-
BMI	12	0.87	0.97	13	0.84	0.97	12	0.87	0.97	-	-	-	-	-	-	-	-	-	-	-	-
hs-CRP	-0.4	0.83	0.97	0	0.83	0.97	0	0.86	0.97	-1	0.69	0.90	-	-	-	-	-	-	-	-	-

CPR, C-peptide; FPG, fasting plasma glucose; GA, glycoalbumin; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transferase; SBP, systolic blood pressure; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; HbA1c, haemoglobin A1c. *$Q < 0.2$, **$Q < 0.1$, or ***$Q < 0.05$. Multiple regression analysis was performed. Model 1: unadjusted, Model 2: adjusted for age, Model 3: adjusted for sex, Model 4: adjusted for BMI, Model 5: adjusted for TG, Model

6: adjusted for 20/(CPR × FPG), Model 7: adjusted for stage of diabetic nephropathy. Model 5, 6 and 7 were only adopted for the multiple regression analysis for Diabetic nephropathy, 20/(CPR × FPG), and TG.

Table S3. Multiple regression analysis between physiological and biochemical test values and the plasma lipopolysaccharide (LPS) concentration of patients at discharge (type 1 diabetes excluded)

Characteristic	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6		
	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*
FPG	65	0.76	0.97	98	0.61	0.85	64	0.76	0.97	49	0.80	0.97	-	-	-	-	-	-
GA	2	0.97	1.00	10	0.86	0.97	2	0.97	1.00	-5	0.90	0.99	-	-	-	-	-	-
TG	2513	<0.01	<0.05***	2514	<0.01	<0.05***	2511	<0.01	<0.05***	2519	<0.01	<0.05***	-	-	-	2325	<0.01	<0.05***
TC	-276	0.37	0.61	-273	0.38	0.62	-278	0.34	0.59	-269	0.38	0.62	-	-	-	-	-	-
LDL-C	-413	0.14	0.36	-425	0.14	0.36	-414	0.13	0.36	-400	0.15	0.36	-	-	-	-	-	-
HDL-C	-184	<0.05	<0.1**	-177	<0.05	<0.1**	-184	<0.05	<0.1**	-189	<0.01	<0.05***	-39	0.76	0.97	-	-	-
AST	-399	0.17	0.37	-403	0.17	0.37	-398	0.17	0.37	-410	0.15	0.36	-	-	-	-	-	-
ALT	-583	0.18	0.38	-616	0.15	0.36	-581	0.18	0.38	-592	0.44	0.69	-	-	-	-	-	-
γ-GTP	-418	0.27	0.51	-418	0.28	0.52	-417	0.27	0.51	-425	0.27	0.51	-	-	-	-	-	-
SBP	25	0.82	0.97	29	0.80	0.97	25	0.83	0.97	27	0.81	0.97	-	-	-	-	-	-
BMI	-11	0.87	0.97	-23	0.71	0.93	-11	0.87	0.97	-	-	-	-	-	-	-	-	-
hs-CRP	0	0.68	0.90	-1	0.63	0.87	0	0.68	0.90	0	0.69	0.91	-	-	-	-	-	-

FPG, fasting plasma glucose; GA, glycoalbumin; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transferase; SBP, systolic blood pressure; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein. *$Q < 0.2$, **$Q < 0.1$, or ***$Q < 0.05$. Multiple regression analysis was performed. Model 1: unadjusted, Model 2: adjusted for age, Model 3: adjusted for sex, Model 4: adjusted for BMI, Model 5: adjusted for TG, Model 6: adjusted for HDL-C. Model 5 and Model 6 were only adopted for the multiple regression analysis for TG and HDL-C.

Table S4. Multiple regression analysis between changes in physiological and biochemical test values and changes in plasma lipopolysaccharide (LPS) concentrations (type 1 diabetes excluded)

Characteristic	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6		
	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*	β	*P*	*Q*
FPG	-79	0.89	0.98	55	0.93	1.00	-	-	-	-	-	-	-	-	-	-	-	-
GA	-25	0.58	0.83	1	0.97	1.00	-	-	-	-	-	-	-	-	-	-	-	-
TG	2041	<0.01	<0.05***	2076	<0.01	<0.05***	2060	<0.01	<0.05***	1929	<0.01	<0.05***	2027	<0.01	<0.05***	-	-	-
TC	-123	0.75	0.97	-48	0.90	0.99	-	-	-	-	-	-	-	-	-	-	-	-
LDL-C	-190	0.58	0.83	-107	0.76	0.97	-	-	-	-	-	-	-	-	-	-	-	-
HDL-C	-208	<0.05	<0.2*	-225	<0.05	<0.1**	-198	<0.05	<0.2*	-	-	-	-201	<0.05	<0.2*	-166	0.16	0.36
AST	26	0.94	1.00	13	0.97	1.00	-	-	-	-	-	-	-	-	-	-	-	-
ALT	116	0.81	0.97	93	0.85	0.97	-	-	-	-	-	-	-	-	-	-	-	-
γ-GTP	138	0.40	0.65	147	0.39	0.63	-	-	-	-	-	-	-	-	-	-	-	-
SBP	235	0.29	0.52	262	0.25	0.47	-	-	-	-	-	-	-	-	-	-	-	-
BMI	11	0.30	0.54	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
hs-CRP	1	0.48	0.74	2	0.47	0.74	-	-	-	-	-	-	-	-	-	-	-	-

FPG, fasting plasma glucose; GA, glycoalbumin; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transferase; SBP, systolic blood pressure; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein. *$Q < 0.2$, **$Q < 0.1$, or ***$Q < 0.05$. Multiple regression analysis was performed. Model 1: unadjusted, Model 2: adjusted for change in BMI, Model 3: adjusted for change in TC, Model 4: adjusted for change in HDL-C, Model 5: adjusted for change in LDL-C, Model 6: adjusted for change in TG. Model 3-6 were only adopted for the multiple regression analysis for TG and HDL-C.