Supplementary Materials

Supplemental Table 1. CONSORT Checklist

Table S1 | CONSORT checklist of information to include when reporting randomized crossover trials			
Section/topic	Item No	Description	Page No*
Title†	1a	Identification as a randomized crossover trial in the title	1
Abstract†	1b	Specify a crossover design and report all information outlined in table 2	1
Introduction:			
Background‡	2a	Scientific background and explanation of rationale	2-3
Objectives‡	2b	Specific objectives or hypotheses	3
Methods:			
Trial design†	3a	Rationale for a crossover design. Description of the design features including allocation ratio, especially the number and duration of periods, duration of washout period, and consideration of carry over effect	4, Figure 1
Change from protocol‡	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants‡	4a	Eligibility criteria for participants	5
Settings and location‡	4b	Settings and locations where the data were collected	5
Interventions†	5	The interventions with sufficient details to allow replication, including how and when they were actually administered	4-6
Outcomes‡	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	6-8
Changes to outcomes‡	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size†	7a	How sample size was determined, accounting for within participant variability	5
Interim analyses and stopping guidelines‡	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomization:			
Sequence generation‡	8a	Method used to generate the random allocation sequence	4-5
Sequence generation‡	8b	Type of randomization; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism‡	9	Mechanism used to implement the random allocation sequence§ (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation†	10	Who generated the random allocation sequence,§ who enrolled participants, and who assigned participants to the sequence of interventions	5
Blinding‡	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	4
Similarity of interventions‡	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods†	12a	Statistical methods used to compare groups for primary and secondary outcomes which are appropriate for crossover design (that is, based on within participant comparison)	9-10
Additional analyses‡	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)†	13a	The numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome, separately for each sequence and period	9 and Figure 2
Losses and exclusions†	13b	No of participants excluded at each stage, with reasons, separately for each sequence and period	9 and Figure 2
Recruitment‡	14a	Dates defining the periods of recruitment and follow-up	5
Trial end‡	14b	Why the trial ended or was stopped	N/A
Baseline data†	15	A table showing baseline demographic and clinical characteristics by sequence and period	Supplementary Table 4
Numbers analyzed†	16	Number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	10
Outcomes and estimation†	17a	For each primary and secondary outcome, results including estimated effect size and its precision (such as 95% confidence interval) should be based on within participant comparisons.¶ In addition, results for each intervention in each period are recommended	12-15 and Supplementary Table 4
Binary outcomes‡	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A

Ancillary analyses‡	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	N/A
Harms†	19	Describe all important harms or untended effects in a way that accounts for the design (for specific guidance, see CONSORT for harms[32])	N/A
Discussion:			
Limitations†	20	Trial limitations, addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses. Consider potential carry over effects	24
Generalizability‡	21	Generalizability (external validity, applicability) of the trial findings	24
Interpretation‡	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	20-24
Other information:			
Registration‡	23	Registration number and name of trial registry	1 and 4
Protocol‡	24	Where the full trial protocol can be accessed, if available	N/A
Funding‡	25	Sources of funding and other support (such as supply of drugs), role of funders	1

CONSORT=Consolidated Standards of Reporting Trials.
*Note: page numbers are optional depending on journal requirements. The page numbers shown here refer to the submitted manuscript.
†Modified original CONSORT item.
‡Unmodified CONSORT item.
§Random sequence here refers to a list of random orders, typically generated through a computer program. This should not be confused with the sequence of interventions in a randomized crossover trial, for example receiving intervention A before B for an individual trial participant.
¶A within participant comparison takes into account the correlation between measurements for each participant because they act as their own control, therefore measurements are not independent.

Supplemental Table 1. This study was conducted in compliance with the CONSORT checklist. Shown are the CONSORT checklist items and page numbers and/or figure/table numbers where the information can be found.

Supplemental Table 2. Nutrient Analysis Summary

	Comparator			**Chitin**		
	Baseline M (SD)	Final M (SD)	M_{diff}	Baseline M (SD)	Final M (SD)	M_{diff}
Kilocalories (kcal)	2078.46 (1091.61)	2773.98 (1676.70)	695.51	2181.88 (1219.97)	2236.30 (957.64)	54.42
Protein, Total (g)	88.72 (50.72)	96.17 (61.87)	7.45	87.80 (45.07)	84.59 (34.47)	-3.21
Protein (% kcal)	4.06 (1.09)	3.54 (0.64)	**-0.51**	3.86 (0.64)	3.83 (0.64)	**-0.03**
Carbohydrate, Total (g)	237.46 (130.45)	305.92 (186.56)	68.46	269.67 (194.83)	251.45 123.89	-18.22
Carbohydrate (% kcal)	11.30 (1.72)	10.99 (1.96)	**-0.31**	11.33 (1.77)	11.12 (1.52)	**-0.20**
Fat, Total (g)	78.66 (38.53)	124.31 (77.43)	45.64	93.97 (43.94)	95.32 (42.31)	1.35
Fat (% kcal)	4.12 (1.11)	4.51 (0.70)	**0.40**	4.26 (0.81)	4.37 (0.58)	**0.11**
Dietary Fiber, Total (g)	24.86 (13.25)	25.37 (11.72)	0.51	19.94 (8.23)	21.71 (11.45)	1.76
Dietary Fiber (% kcal)	1.39 (0.55)	0.91 (0.70)	**-0.47**	0.95 0.42	1.02 (0.39)	**0.07**
Alcohol (% kcal)	0.17 (0.33)	0.24 (0.30)	0.07	0.27 (0.54)	0.38 (0.47)	0.11

Supplemental Table 2. Shown are the intake of macronutrients and alcohol, calculated from 3-dayfood logs and returned at each study visit. Macronutrients are reported as totak intake in grams (g) and as percentage of total kilocalories (% kcal). Of note, all pre-post changes in macronutrients that are calculated as % kcal are under 1 percent; these values are bolded.

Supplemental Table 3. Micronutrient Composition of Cricket Chitin

	Concentration (mg/g)	Limit of Detection	Limit of Quantification
Al	1220	0.3	0.9
As	0.00438	2.00E-03	5.00E-03
B	0.232	0.05	0.1
Ba	4.11	3.00E-02	0.07
Be	2.27E-03	0.002	0.003
Ca	1670	2	4
Cd	0.0119	3.00E-03	0.008
Co	0.0167	2.00E-04	0.0007
Cr	0.629	0.003	0.009
Cu	40.1	0.02	0.05
Fe	63.6	0.3	0.8
K	19.3	0.6	2
Li	0.021	0.02	0.06
Mg	253	0.3	0.9
Mn	4.27	0.003	0.008
Mo	0.0211	0.0006	0.002
Na	66.2	0.9	3
Ni	0.394	0.003	0.0098
P	61.6	1	3
Pb	2.64	0.0008	0.002
S	<LOD	50	100
Se	<LOD	0.04	0.1
Sr	4.73	4.00E-03	0.01
V	0.138	2.00E-03	0.004
W	<LOD	2.00E-03	0.006
Zn	120	0.3	0.7

Supplemental Table 3. Shown is the micronutrient composition of cricket chitin, including micronutrient concentration, limit of detection, and limit of quantification values. These values represent the composition found in 22g of cricket chitin, which is the daily dose of the chitin intervention.

Supplemental Table 4. Overview of physiological measures throughout the study.

	Comparator			Chitin		
	Baseline	Final	Final - Baseline	Baseline	Final	Final - Baseline
Serum Inflammatory Biomarkers	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]
TNF-a	39.55 (24.23)	36.22 (20.79)	-3.326 [10.92 to 4.26]	21.36 (20.46)	19.04 (29.88)	-2.337 [10.86 to 6.18]
hsCRP	7669 (17.54)	7770 (22.48)	101.2 [-2667 to 2869]	8805 (28.36)	7726 (18.76)	-1079 [-4127 to 1970]
IL-10	249.83 (240.03)	249.3 (229.75)	-0.5000 [-72.17 to 71.17]	169.4 (181.34)	157.8 (200.61)	-11.58 [-89.21 to 66.04]
IL-6	12.62 (17.54)	13.24 (22.48)	0.6124 [-1.99 to 3.21]	14.79 (28.36)	11.04 (18.76)	-3.749 [-10.60 to 3.10]
serum lipocalin	17.12 (10.44)	15.40 (10.21)	-1.712 [-10.57 to 7.15]	16.02 (6.86)	15.75 (8.28)	-0.2670 [-7.49 to 6.97]
Fecal inflammatory biomarkers	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]
fecal calprotectin	86.87 (168.16)	29.17 (28.51)	-57.17 [-188.3 to 73.95]	42.61 (64.13)	37.17 (60.45)	-3.951 [-30.69 to 22.79]
fecal lipocalin	73.87 (27.12)	55.80 (22.11)	-18.07 [-76.57 to 40.44]	44.86 (41.40)	54.14 (43.98)	9.286 [-13.09 to 31.66]
sIGA	1.70 (1.14)	1.91 (1.48)	-0.3583 [-1.70 to 0.98]	3.04 (1.88)	2.52 (1.11)	-0.1232 [-1.34 to 1.09]
Lipid Panel	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]
TCH	184.6 (38.69)	186.47 (25.62)	1.571 [-16.03 to 19.17]	183.9 (35.39)	186.50 (31.05)	2.563 [-10.90 to 16.02]
HDL	62.71 (10.24)	66.43 (10.14)	3.714 [2.66 to 10.09]	61.50 (12.94)	63.88 (12.59)	2.375 [-3.32 to 8.07]
LDL	103.5 (27.67)	102.3 (19.01)	-1.224 [-13.71 to 11.26]	105.24 (27.17)	102.6 (27.83)	-2.633 [-14.44 to 9.18]
vLDL	20.69 (9.64)	20.07 (9.26)	-0.8736 [-4.81 to 3.06]	18.76 (7.21)	20.50 (5.70)	2.133 [-1.59 to 5.86]
Non-HDL	124.3 (34.26)	122.2 (21.67)	-2.155 [-14.85 to 10.54]	123.94 (32.17)	124.4 (28.19)	0.4868 [-11.50 to 12.47]
Triglycerides	104.1 (47.07)	95.79 (48.645)	-8.357 [-33.71 to 17.00]	90.50 (35.68)	103.13 (29.01)	12.63 [-9.86 to 35.11]
TC/HDL	3.01 (0.61)	2.87 (0.43)	0.1303 [-0.09 to 0.35]	3.07 (0.73)	3.07 (0.73)	0.08156 [-0.12 to 0.29]
Metabolic Panel	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]
Glucose	93.40 (5.67)	97.51 (6.99)	4.106 [0.48 to 7.73]	98.29 (6.46)	97.20 (4.59)	-1.093 [4.54 to 2.36]
BUN	12.02 (2.26)	11.48 (1.99)	-0.5387 [-2.24 to 1.16]	12.18 (2.35)	10.72 (2.73)	-1.455 [-3.09 to 0.18]
Creatinine	0.87 (0.26)	0.84 (0.20)	-0.02239 [-0.193 to 0.148]	0.94 (0.23)	0.79 (0.20)	-0.1483 [-0.31 to 0.02]
Na	141.19 (4.55)	139.90 (3.62)	-1.228 [-3.97 to 1.51]	141.00 (4.33)	140.56 (3.67)	-0.4126 [-3.03 to 2.21]
K	4.78 (0.39)	7.25 (10.45)	2.470 [-1.79 to 6.73]	4.63 (0.37)	4.57 (0.40)	-0.06100 [-4.19 to 4.07]
Cl	111.00 (4.07)	110.73 (2.12)	-0.2646 [-2.847 to 2.318]	110.65 (2.91)	111.19 (2.99)	0.5260 [-1.97 to 3.03]
Other	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]	M (SD)	M (SD)	M_{diff} [95% CI_{diff}]
BMI	25.09 (5.89)	24.95 (5.62)	-0.1320 [-0.48 to 0.22]	25.03 (5.83)	25.30 (5.74)	0.2752 [-0.10 to 0.65]

Supplemental Table 4. Shown is an overview of physiological measures at baseline and final time points of each intervention period for all participants (intent-to-treat), in addition to mean differences calculated as final – baseline values. M = mean; SD = standard deviation; M_{diff} = mean differences; 95% CI_{diff} = 95% CI of the mean difference.

Supplementary Table 5. Maaslin ZINB results for taxon biomarkers of each treatment group.

		Log2FC	St.Error	P-value	FDR
Comparator treatment biomarkers	g__[Eubacterium]_siraeum_group; s__uncultured_bacterium	-2.12	0.263	7.21E-16	1.47E-13
	g__Barnesiella	0.433	0.0599	5.08E-13	6.61E-11
	g__Angelakisella; s__uncultured_bacterium	1.55	0.231	1.92E-11	2.11E-09
	f__Ruminococcaceae; g__uncultured; s__uncultured_organism	-2.82	0.57	7.50E-07	4.67E-05
	s__Lachnospiraceae_NK4A136_group_uncultured_Clostridium	1.85	0.377	8.93E-07	5.33E-05
	f__Lachnospiraceae	1.1	0.231	1.97E-06	0.000109
	g__[Eubacterium]_coprostanoligenes_group; s__gut_metagenome	-2.75	0.612	7.10E-06	0.000328
	f__Lachnospiraceae	-0.571	0.133	1.85E-05	0.00078
	g__Streptococcus	1.12	0.264	2.19E-05	0.00087
	g__[Eubacterium]_ventriosum_group; s__uncultured_Lachnospiraceae	2.08	0.508	4.31E-05	0.00151
	f__Ruminococcaceae; g__uncultured; s__anaerobic_digester	-1.8	0.456	7.99E-05	0.00243
	f__Ruminococcaceae; g__Subdoligranulum	-0.549	0.148	0.000209	0.00535
	f__Lachnospiraceae; g__Lachnoclostridium	0.841	0.228	0.000228	0.00553
	g__[Eubacterium]_xylanophilum_group	1.59	0.438	0.00027	0.00645
	o__Oscillospirales; f__UCG-010; g__UCG-010; s__gut_metagenome	-2.17	0.598	0.000284	0.00667
	g__Coprococcus; s__unidentified	1.83	0.521	0.000459	0.00966
	g__Campylobacter; s__Campylobacter_hominis	2.43	0.705	0.000563	0.0106
	g__[Eubacterium]_nodatum_group	-3.78	1.1	0.000579	0.0108
	f__Oscillospiraceae; g__UCG-005; s__uncultured_rumen	1.26	0.37	0.000653	0.0114
	g__Sellimonas; s__uncultured_bacterium	0.809	0.241	0.000767	0.0132
	f__Ruminococcaceae	-2.66	0.801	0.000895	0.0151
	o__Oscillospirales; f__UCG-010; g__UCG-010; s__gut_metagenome	3.26	1.04	0.00161	0.0215
	o__Rhodospirillales; f__uncultured; g__uncultured; s__uncultured_organism	-3.2	1.02	0.00175	0.0223
	g__Lachnoclostridium	-1.53	0.49	0.00174	0.0223
	f__Lachnospiraceae; g__UC5-1-2E3	-2.71	0.864	0.00173	0.0223
	c__Clostridia	1.08	0.346	0.00178	0.0225
	g__Parabacteroides	0.672	0.222	0.00244	0.0289
	f__Lachnospiraceae	1.7	0.579	0.00337	0.0369
	g__Streptococcus	0.98	0.339	0.00381	0.0401
	g__Flavonifractor; s__uncultured_bacterium	1.1	0.382	0.00395	0.041
	g__Shuttleworthia; s__uncultured_bacterium	-1.36	0.473	0.00412	0.0424
	g__Ezakiella; s__uncultured_bacterium	-1.6	0.563	0.00439	0.0449
	f__Ruminococcaceae	0.814	0.289	0.0048	0.0484

Chitin treatment biomarkers	g__Barnesiella	-0.738	0.0452	5.96E-60	8.53E-57
	g__Streptococcus	-2.17	0.271	1.20E-15	2.46E-13
	g__Clostridia_UCG-014; s__uncultured_bacterium	-3.07	0.486	2.86E-10	2.93E-08
	g__Coprococcus; s__unidentified	3.1	0.642	1.38E-06	0.000104
	f__Oscillospiraceae; g__UCG-005; s__uncultured_organism	-1.78	0.441	5.47E-05	0.0023
	o__Oscillospirales; f__UCG-010; g__UCG-010; s__gut_metagenome	1.61	0.411	9.11E-05	0.00335
	g__Clostridia_UCG-014; s__uncultured_bacterium	2.55	0.674	0.000152	0.00482
	g__[Clostridium]_methylpentosum_group	-0.926	0.245	0.000158	0.00482
	g__Streptococcus	-0.932	0.247	0.000158	0.00482
	g__Lachnoclostridium; s__uncultured_Clostridium	1.33	0.359	0.00021	0.00578
	g__[Eubacterium]_coprostanoligenes_group; s__metagenome	-0.282	0.076	0.000206	0.00578
	g__Clostridia_UCG-014; s__gut_metagenome	2.15	0.598	0.000324	0.00829
	f__Oscillospiraceae; g__UCG-005	1.24	0.346	0.000334	0.00839
	g__Negativibacillus; s__uncultured_bacterium	-1.57	0.45	0.000494	0.011
	g__Lachnospiraceae_NK4A136_group; s__uncultured_Clostridium	2.36	0.687	0.000572	0.0117
	g__Colidextribacter; s__uncultured_Clostridia	2.01	0.602	0.000867	0.0161
	g__Marvinbryantia	1.29	0.43	0.00267	0.0338
	f__Ruminococcaceae; g__uncultured; s__uncultured_organism	-1.09	0.365	0.00296	0.0365
	f__Lachnospiraceae; g__[Ruminococcus]_torques_group	-0.677	0.228	0.00301	0.0369
	g__Dialister	1.09	0.379	0.00408	0.046

Supplemental Table 5. Shown are the taxon biomarkers of the comparator treatment and the chitin treatment, which are identified by Maaslin's Zero Inflated Negative Binomial (ZINB) regression as being significantly different pre- to post-treatment for each treatment group, after controlling for false discover rate (FDR). Also shown is the effect size of the pre- to post-intervention difference, indicated by Log2 fold change (FC) values.