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SUPPLEMENTAL DATA

Table S1. Defining the excluded studies and the reason for their exclusion from the final abundance dataset.

References	Segments and Transporters Quantified	Reason for Exclusion
Absolute analysis studies		
(Wisniewski et al., 2015)	Colon; ABCB1; ABCC2; ABCC3; ABCC4; SLCO2B1; SLC22A3; SLC16A1	Primary: Diseased samples (Cancer; Adenoma); Secondary: Non total membrane fraction
(Miyachi et al., 2016)	Jejunum; ABCC1; ABCC4; ABCG2; SLCO2B1; SLC2A2; SLC10A2; SLC15A1; SLC16A1; SLC22A1; SLC22A3; SLC22A4; SLC51A; SLC51B;	Diseased samples (Morbidly obese)
(Nakamura et al., 2016)	Jejunum; ABCB1; ABCC2; ABCC3; ABCC4; ABCG2; SLCO2B1; SLC10A2; SLC15A1; SLC16A1; SLC22A1; SLC22A3; SLC22A4; SLC51A	Primary: Pooled samples Secondary: Non-Total Membrane
(Olander et al., 2016)	Jejunum; SLCO2B1	Non total membrane fraction
(Bruck et al., 2017)	Jejunum; ABCB1; ABCC2; ABCC3; ABCG2; SLCO2B1; SLC10A2; SLC15A1; SLC22A1; SLC22A3	Duplicated samples with another published study (Drozdik et al., 2014)
(Vaessen et al., 2017)	Jejunum; ABCB1; ABCC1; ABCC2; ABCG2; SLCO2B1; SLC15A1	Non total membrane fraction
Relative analysis studies		

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(Hinoshita et al., 2000) ^a	Colon; ABCC1; ABCC3	Primary: Non-Caucasian (Japanese) Secondary: Diseased samples (Cancer)
(Herrera-Ruiz et al., 2001)	Duodenum; Jejunum; Ileum & Colon; SLC15A1	Pooling of samples (cDNA-commercial source)
(Landowski et al., 2003)	Duodenum; SLC15A1	No normalization to housekeeping gene
(Seward et al., 2003)	Small Intestine (generically labelled) & Colon; SLC51A; SLC51B	Pooling of samples (cDNA)
(Jung et al., 2004)	Ileum; SLC10A2; SLC15A1	Could not be digitized (No densitometry results)
(Nishimura and Naito, 2005)	Small Intestine (generically labelled) & Colon; ABCC1; ABCC3; ABCC4; SLCO2B1; SLC2A2; SLC10A2; SLC15A1; SLC22A1; SLC22A3; SLC22A4	Pooled samples
(Terada et al., 2005) ^a	Duodenum; Jejunum; Ileum & Colon; SLC15A1; SLC22A1; SLC22A3; SLC22A4	Non-Caucasian (Japanese)
(Kim et al., 2007)	Duodenum; ABCC1; ABCC3; ABCC4; SLC2A2; SLC15A1; SLC16A1; SLC22A4	No normalization to housekeeping gene
(Hilgendorf et al., 2007)	Jejunum; ABCC1; ABCC3; SLCO2B1; SLC10A2; SLC15A1; SLC16A1; SLC22A1; SLC22A4	Duplicated samples with another published study (Seithel et al., 2006)
(Thibault et al., 2007)	Colon; SLC16A1	Diseased samples (Crohns; Ulcerative Colitis)

Consideration of OATP1A2

(Tamai et al., 2000; Hilgendorf et al., 2007; Meier et al., 2007; Groer et al., 2013; Drozdik et al., 2014; Wisniewski et al., 2015; Nakamura et al., 2016)

Samples processed for the Jejunum, Ileum, Colon or generically the ‘small intestine’ without further disclosure of the specific region

OATP1A2 was not included in the final database as the weight of evidence suggests absence or negligible expression. The references in column 1 highlight the limited evidence of mRNA or protein expression in the intestine. In one study mRNA expression as via a blot analysis, however semi-quantitative values were not presented hence, even this study would not have provided values to incorporate into a weighted mean meta-analysis (Glaeser et al., 2007)

^a Our aim was to generate a ‘clean as possible’ baseline for healthy Caucasian (and possible healthy Japanese/Chinese/Korean) subjects, hence the Asian samples were excluded from the analysis

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Table S2A. The complete database, including excluded sample measurements, for the absolute abundance dataset.

Gene (Protein)	Anatomical Intestinal Segment (No. of Sample Measurements)				References
	Duodenum	Jejunum	Ileum	Colon	
SLC2A2 (GLUT2)	0	0	0	0	N/A
SLC10A2 (ASBT/IBAT)	6	14 ^a	15	6	(Groer et al., 2013; Drozdziak et al., 2014; Nakamura et al., 2016) ^a
SLC15A1 (PEPT1)	6	17 ^a	19	6	(Groer et al., 2013; Oswald et al., 2013; Drozdziak et al., 2014; Nakamura et al., 2016; Vaessen et al., 2017)
SLC16A1 (MCT1)	0	5 ^a	0	24	(Wisniewski et al., 2015; Nakamura et al., 2016; Vaessen et al., 2017)
SLCO2B1 (OATP2B1)	6	23 ^{a, b}	19	20	(Groer et al., 2013; Oswald et al., 2013; Drozdziak et al., 2014; Wisniewski et al., 2015; Nakamura et al., 2016; Olander et al., 2016; Vaessen et al., 2017)
SLCO4C1 (OATP4C1)	0	0	0	0	N/A
SLC22A1 (OCT1)	6	18 ^a	15	6	(Groer et al., 2013; Drozdziak et al., 2014; Nakamura et al., 2016; Vaessen et al., 2017)

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SLC22A3 (OCT3)	6	14 ^a	15	25	(Groer et al., 2013; Drozdik et al., 2014; Wisniewski et al., 2015; Nakamura et al., 2016; Vaessen et al., 2017)
SLC22A4 (OCTN1)	0	1 ^a	0	0	(Nakamura et al., 2016)
SLC51A (OST- α)	0	2 ^a	1	0	(Harwood et al., 2015; Nakamura et al., 2016)
SLC51B (OST- β)	0	3	1	0	(Harwood et al., 2015)
ABCB1 (P-gp)	20	25 ^a	20	30	(Tucker et al., 2012; Groer et al., 2013; Oswald et al., 2013; Drozdik et al., 2014; Harwood et al., 2015; Wisniewski et al., 2015; Nakamura et al., 2016; Vaessen et al., 2017)
ABCC1 (MRP1)	0	4	0	24	(Wisniewski et al., 2015; Vaessen et al., 2017)
ABCC2 (MRP2)	20	25 ^a	19	26	(Tucker et al., 2012; Groer et al., 2013; Oswald et al., 2013; Drozdik et al., 2014; Harwood et al., 2015; Nakamura et al., 2016; Vaessen et al., 2017)
ABCC3 (MRP3)	6	14 ^a	15	30	(Groer et al., 2013; Drozdik et al., 2014; Wisniewski et al., 2015; Nakamura et al., 2016)
ABCC4 (MRP4)	0	1 ^a	0	24	(Wisniewski et al., 2015; Nakamura et al., 2016)
ABCG2 (BCRP)	20	25 ^a	19	6	(Tucker et al., 2012; Groer et al., 2013; Oswald et al., 2013; Drozdik et al., 2014; Harwood et al., 2015; Nakamura et al., 2016; Olander et al., 2016; Vaessen et al., 2017)

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^a for Nakamura et al., 2016, although 13 samples were pooled it is classed as a single sample and variability cannot be obtained, only experimental precision is available (i.e. replicates of same sample); ^b, for Olander et al., 2016, sample n was not disclosed so assumed a value of n=1. N/A is No [sample] Available for meta-analysis inclusion.

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Table S2B. The complete database, including excluded sample measurements, for the relative abundance dataset.

Protein	Anatomical Intestinal Segment (No. of Sample Measurements)					References
	Small Intestine ^a	Duodenum	Jejunum	Ileum	Colon	
SLC2A2 (GLUT2)	1	36 ^b	0	0	1	(Nishimura and Naito, 2005; Kim et al., 2007; Wilder-Smith et al., 2014)
SLC10A2 (ASBT/IBAT)	1	30	17	122	57	(Jung et al., 2004; Nishimura and Naito, 2005; Hruz et al., 2006; Hilgendorf et al., 2007; Meier et al., 2007; Renner et al., 2008; Wojtal et al., 2009; Bourguine et al., 2012; Drozdik et al., 2014)
SLC15A1 (PEPT1)	1	67	39	105	82	(Herrera-Ruiz et al., 2001; Ziegler et al., 2002; Landowski et al., 2003; Jung et al., 2004; Nishimura and Naito, 2005; Terada et al., 2005; Englund et al., 2006; Seithel et al., 2006; Hilgendorf et al., 2007; Kim et al., 2007; Meier et al., 2007; Wojtal et al., 2009; Bourguine et al., 2012; Drozdik et al., 2014)
SLC16A1 (MCT1)	0	23	18	20	59	(Gill et al., 2005; Englund et al., 2006; Seithel et al., 2006; Hilgendorf et al., 2007; Kim et al., 2007; Thibault et al., 2007; Bourguine et al., 2012)
SLCO2B1 (OATP2B1)	1	30	26	75	59	(Nishimura and Naito, 2005; Englund et al., 2006; Seithel et al., 2006; Hilgendorf et al., 2007; Meier et

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						al., 2007; Wojtal et al., 2009; Bourguine et al., 2012; Drozdik et al., 2014; Mooij et al., 2014)
SLCO4C1 (OATP4C1)	0	0	0	3	3	(Bourguine et al., 2012)
SLC22A1 (OCT1)	1	33	41	48	50	(Nishimura and Naito, 2005; Terada et al., 2005; Englund et al., 2006; Seithel et al., 2006; Hilgendorf et al., 2007; Wojtal et al., 2009; Bourguine et al., 2012; Drozdik et al., 2014)
SLC22A3 (OCT3)	1	19	31	25	27	(Nishimura and Naito, 2005; Terada et al., 2005; Seithel et al., 2006; Bourguine et al., 2012; Drozdik et al., 2014)
SLC22A4 (OCTN1)	1	35	32	67	65	(Nishimura and Naito, 2005; Terada et al., 2005; Hilgendorf et al., 2007; Kim et al., 2007; Meier et al., 2007; Wojtal et al., 2009; Bourguine et al., 2012; Girardin et al., 2012; Drozdik et al., 2014)
SLC51A (OST- α)	1	6	12	49 ^b	7	(Seward et al., 2003; Renner et al., 2008; Drozdik et al., 2014)
SLC51B (OST- β)	1	6	12	49 ^b	7	(Seward et al., 2003; Renner et al., 2008; Drozdik et al., 2014)
ABCC1 (MRP1)	1	37	20	43	96	(Hinoshita et al., 2000; Nishimura and Naito, 2005; Zimmermann et al., 2005; Englund et al., 2006; Seithel et al., 2006; Hilgendorf et al., 2007; Kim et al., 2007; Bourguine et al., 2012; Drozdik et al., 2014)

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ABCC3 (MRP3)	1	35	26	38	81	(Fromm et al., 2000; Hinoshita et al., 2000; Albermann et al., 2005; Zimmermann et al., 2005; Berggren et al., 2007; Blokzijl et al., 2007; Hilgendorf et al., 2007; Kim et al., 2007; Bourguine et al., 2012; Drozdik et al., 2014)
ABCC4 (MRP4)	1	21	12	25	20	(Nishimura and Naito, 2005; Zimmermann et al., 2005; Kim et al., 2007; Bourguine et al., 2012; Drozdik et al., 2014)
ABCB1 (P-gp) ^c	0	36	26	58	28	(O., 2000; Mouly and Paine, 2003; Troutman and Thakker, 2003; Dietrich et al., 2004; Albermann et al., 2005; Zimmermann et al., 2005; Englund et al., 2006; Seithel et al., 2006; Berggren et al., 2007; Hilgendorf et al., 2007)
ABCC2 (MRP2) ^c	0	91	4	41	26	(Fromm et al., 2000; Glaeser., 2003; Dietrich et al., 2004; Albermann et al., 2005; Zimmermann et al., 2005; Oswald et al., 2006; Seithel et al., 2006; Urquhart et al., 2008)
ABCG2 (BCRP) ^c	0	55	14	45	35	(Dietrich et al., 2004; Albermann et al., 2005; Gutmann et al., 2005; Englund et al., 2006; Seithel et al., 2006; Canaparo et al., 2007; Hilgendorf et al., 2007; Urquhart et al., 2008)

^a Articles did not define the region from which the sample was selected and abundance quantified in; ^b Includes measurements using mRNA-based RT-PCR and protein-based Western Blotting (Renner et al., 2008; Wilder-Smith et al., 2014); ^c Includes measurements using relative expression analysis previously performed and reported (Harwood et al., 2013).

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Table S3. The final transporter abundance database separating samples quantified by absolute and relative methods^a.

Transporter	Method	ADAM model segment (Sample No. given in parentheses)							
Gene (Protein)		Duodenum	Jejunum I	Jejunum II	Ileum I	Ileum II	Ileum III	Ileum IV	Colon
ABCB1 (P-gp)	Relative	0.51	1	1.46	1.5	1.51	1.52	1.51	0.57
	Absolute	0.57	1	1.86	1.78	1.78	2.18	2.06	0.36
ABCC1 (MRP1)	Relative	0.45	1	0.88	0.86	0.86	0.89	0.89	0.93
	Absolute	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A
ABCC2 (MRP2)	Relative	1.41	1	1	0.6	0.6	0.6	0.6	0.02
	Absolute	0.30	1	0.89	0.89	0.89	0.92	0.92	1.65
ABCC3 (MRP3)	Relative	1.52	1	1.47	1.19	1.19	1.15	1.15	4.38
	Absolute	1.45	1	0.81	1.01	1.01	1.17	1.17	2.60
ABCC4 (MRP4)	Relative	1.02	1	1.22	1.71	1.71	1.20	1.20	1.76
	Absolute	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A
ABCG2 (BCRP)	Relative	0.47	1	1.00	0.59	0.59	0.59	0.59	0.13
	Absolute	0.63	1	2.47	0.94	0.94	0.87	1.14	0.44
SLC2A2 (GLUT2)	Relative	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b	1 ^b

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	Absolute	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A
SLC10A2 (IBAT)	Relative	0.81	1	0.25	3.71	3.71	4.02	4.02	0.04
	Absolute	1.00	1	4.00	38.27	38.27	100.94	100.94	2.00
SLC15A1 (PepT1)	Relative	0.74	1	1.31	0.94	0.94	0.93	0.93	0.02
	Absolute	0.70	1	1.11	1.33	1.33	1.36	1.36	0.07
SLC16A1 (MCT1)	Relative	1.25	1	1.00	1.29	1.29	1.29	1.29	4.72
	Absolute	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A
SLCO2B1 (OATP2B1)	Relative	0.71	1	0.95	1.30	1.30	1.33	1.33	1.04
	Absolute	1.06	1	0.91	0.89	0.89	0.91	0.91	1.19
SLCO4C1 (OATP4C1)	Relative	1 ^b	1 ^b	1 ^b	1	1	1	1	0.55
	Absolute	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A
SLC22A1 (OCT1)	Relative	0.93	1	0.90	0.74	0.74	0.63	0.63	1.38
	Absolute	1.03	1	0.87	1.07	1.07	1.11	1.11	0.73
SLC22A3 (OCT3)	Relative	0.87	1	1.47	1.74	1.74	1.86	1.86	1.25
	Absolute	1.19	1	1.11	1.07	1.07	1.26	1.26	2.25
SLC22A4 (OCTN1)	Relative	0.46	1	0.63	0.78	0.78	0.80	0.80	0.24

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	Absolute	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
SLC51A	Relative	0.56	1	1.94	1.08	1.08	0.93	0.93	0.71
	Absolute	N/A ^b	N/A ^b	1	N/A ^b	N/A ^b	N/A ^b	0.6	N/A ^b
SLC51B	Relative	0.50	1	0.82	0.85	0.85	0.84	0.84	0.27
	Absolute	N/A ^b	N/A ^b	1	N/A ^b	N/A ^b	N/A ^b	0.66	N/A ^b

N/A – data not available or did not meet with the inclusion criteria in the final database.

^a for references see Tables S2 and S3.

Table S4. Mean simulated transporter abundances and population variability in each intestinal segment in 2000 North European Caucasians in Simcyp Simulator Version 17-Released.

Intestinal Segment Transporter Abundance in pmol (CVs are given in parentheses)								
Proteins	Duodenum	Jejunum I	Jejunum II	Ileum I	Ileum II	Ileum III	Ileum IV	Colon
ABCB1 (P-gp)	28.40	216.29	315.78	217.12	218.57	220.02	218.57	24.12
	(106)	(119)	(119)	(119)	(119)	(119)	(119)	(77)
ABCC2 (MRP2)	174.26	486.54	486.54	195.37	195.37	195.37	195.37	1.89
	(118)	(131)	(131)	(131)	(131)	(131)	(131)	(87)
ABCC3 (MRP3)	176.62	320.10	284.89	329.90	329.90	342.75	342.75	378.33
	(105)	(117)	(117)	(117)	(117)	(117)	(117)	(74)
ABCG2 (BCRP)	22.75	190.78	190.78	75.33	75.33	75.33	75.33	4.81
	(101)	(111)	(111)	(111)	(111)	(111)	(111)	(71)
SLC10A2 (ASBT/IBAT)	23.39	5.53	22.10	364.01	364.01	403.72	399.36	1.20
	(89)	(106)	(106)	(106)	(106)	(106)	(106)	(54)
SLC15A1 (PepT1)	491.94	2048.56	2171.48	1686.28	1686.28	1699.99	1699.99	12.10

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	(85)	(104)	(104)	(104)	(104)	(104)	(104)	(53)
SLCO2B1 (OATP2B1)	41.91	224.58	211.10	192.38	192.38	192.38	192.38	46.73
	(111)	(123)	(123)	(123)	(123)	(123)	(123)	(83)
SLC22A1 (OCT1)	99.62	376.92	327.92	325.40	325.40	327.92	327.92	200.20
	(100)	(111)	(111)	(111)	(111)	(111)	(111)	(61)
SLC22A3 (OCT3)	9.63	31.67	35.16	22.89	22.89	26.07	26.07	11.83
	(102)	(116)	(116)	(116)	(116)	(116)	(116)	(81)
SLC51A/B (OST- α/β)	38.02	256.78	485.31	185.59	185.59	159.81	159.81	37.05
	(137)	(136)	(136)	(136)	(136)	(136)	(136)	(104)

Transporters where there was no data available that met the study exclusion criteria (*ABCC1* (MRP1); *SLC2A2* (GLUT2); *SLC16A1* (MCT1); *SLCO4C1* (OATP4C1); *SLC22A4* (OCTN1)) are not shown. Simulated variability (CV) is a function of the inter-individual variability associated with the transporter abundance and that of the membrane protein yield per segment and segmental surface area of the individual.

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Total Membrane Protein Yield

This section describes the assumptions and specific corrections to enable translation of Total Membrane (TM) protein yield for the small intestine (TMePPI) and colon (TMePPC) in milligrams, from yields reported as μg TM protein/ cm^2 of mucosa (Tucker et al., 2012; Harwood, 2015) or μg TM protein/mg mucosal protein personal communication with Dr Stefan Oswald, University of Greifswald based on the Drozdziak *et al*, 2014 study. The terms ‘Total’ or ‘Crude’ membrane are assumed equivalent matrices.

A: Assumptions and Corrections applied for TM protein yield from Tucker *et al.*, 2012:

- TMePPI was generated from mucosal scraping information in duodenum only (n=14). TM protein was prepared using differential centrifugation.
- The TM protein per cm^2 of duodenum mucosa was reported. This enabled the calculation of duodenum TM protein yield calculated based on the duodenum surface area of a representative ‘Healthy Individual’ based on the duodenum surface area defined from the ADAM model in the Simcyp Simulator Version 16.
- To obtain scalars for the jejunum and ileum, segments which were not studied specifically by Tucker *et al.*, 2012, several assumptions were required.
 - Calculations relied on duodenal microsomal yields per cm^2 for jejunum and ileum microsomal yields.
 - The yield of microsomal protein per cm^2 was calculated for each segment by dividing the scraped mucosal mass using the segmental mucosal mass yield as a reference (Paine et al., 1997) by the segmental surface area of each ADAM region (duodenum, jejunum and ileum) for the representative ‘Healthy Individual’.
 - Corrections for the greater yield per cm^2 in the duodenum as estimated for Paine *et al.*, 1997 was applied to these data to obtain jejunum and ileum microsomal yield.
 - The sum of the regions gave a total membrane protein yield for the intestine (TMePPI).

B: Assumptions and Corrections applied for TM protein yield from Drozdziak *et al.*, 2014 via personal communication with Dr Stefan Oswald (University of Greifswald):

- TM protein was prepared after crushing the mucosa using a commercial membrane extraction kit.

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- The TM protein yield of the small intestine (not attributed to specific segments) and that for the colon was communicated to the authors as μg TM protein/ mg mucosal protein.
- The estimation of TMePPI required the yield of mucosal masses for the duodenum, jejunum and ileum to be known, which were not provided in Drozdik *et al.*, 2014. The duodenum, jejunum and ileum mucosal mass values from Paine *et al.*, 1997 were employed. As there were no such data available for colon mucosal mass, this was estimated using the calculated terminal ileum (a one of 4 ileum segments in the ADAM model) mass/cm² and scaling this value to the colon surface area from a representative ‘Healthy Individual’ from the ADAM model.
- The key assumptions for the scaling approach proposed for Drozdik *et al.*, 2014 are;
 - There is 100% extraction by the kit and no contamination in the total membrane fraction for other cell types (i.e., non-enterocytes)
 - Mucosal masses are similar for Drozdik *et al.*, 2014 and Paine *et al.*, 1997, but Drozdik *et al.*, 2014 uses stripped mucosal tissue mass for the reported yield while Paine *et al.*, 1997 uses a scraping technique to obtain mucosal mass.

C: Assumptions and Corrections applied for TM protein yield from Harwood 2015:

- TM protein was prepared using differential centrifugation after enterocyte were eluted.
- The TM protein per cm² of jejunum, ileum and colon mucosa was reported. This enabled the calculation of jejunum, ileum and colon TM protein yield calculated based on the respective segmental surface areas of a representative ‘Healthy Individual’ as defined from the ADAM model in the Simcyp Simulator Version 16.
- A recovery correction factor of 8.82 was applied to correct for procedural losses of TM protein during the fractionation process. This was obtained via quantification of the enterocyte membrane marker protein Villin and the plasma membrane protein marker Na⁺ K⁺-ATPase abundances by targeted LC-MS/MS, and applying a mathematical framework describing recovery correction factors generation for fractionated matrices (Harwood et al., 2014).
- To obtain scalar for the duodenum which was not studied specifically by Harwood 2015, several assumptions were required.
 - Calculations relied on a single proximal jejunum sample where TM protein yield per cm² obtained was obtained as a surrogate for duodenal yield calculations which scaled to the duodenal surface area.

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- Corrections for the greater mucosal mass per cm² in the duodenum compared to jejunum as estimated for Paine *et al.*, 1997, and using the ratio of the ADAM model duodenum-to-jejunum surface area was applied to obtain duodenal TM protein yield in milligrams.
- The sum of the duodenum, jejunum and ileum yields gave the TeMPPI (mg) value.

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