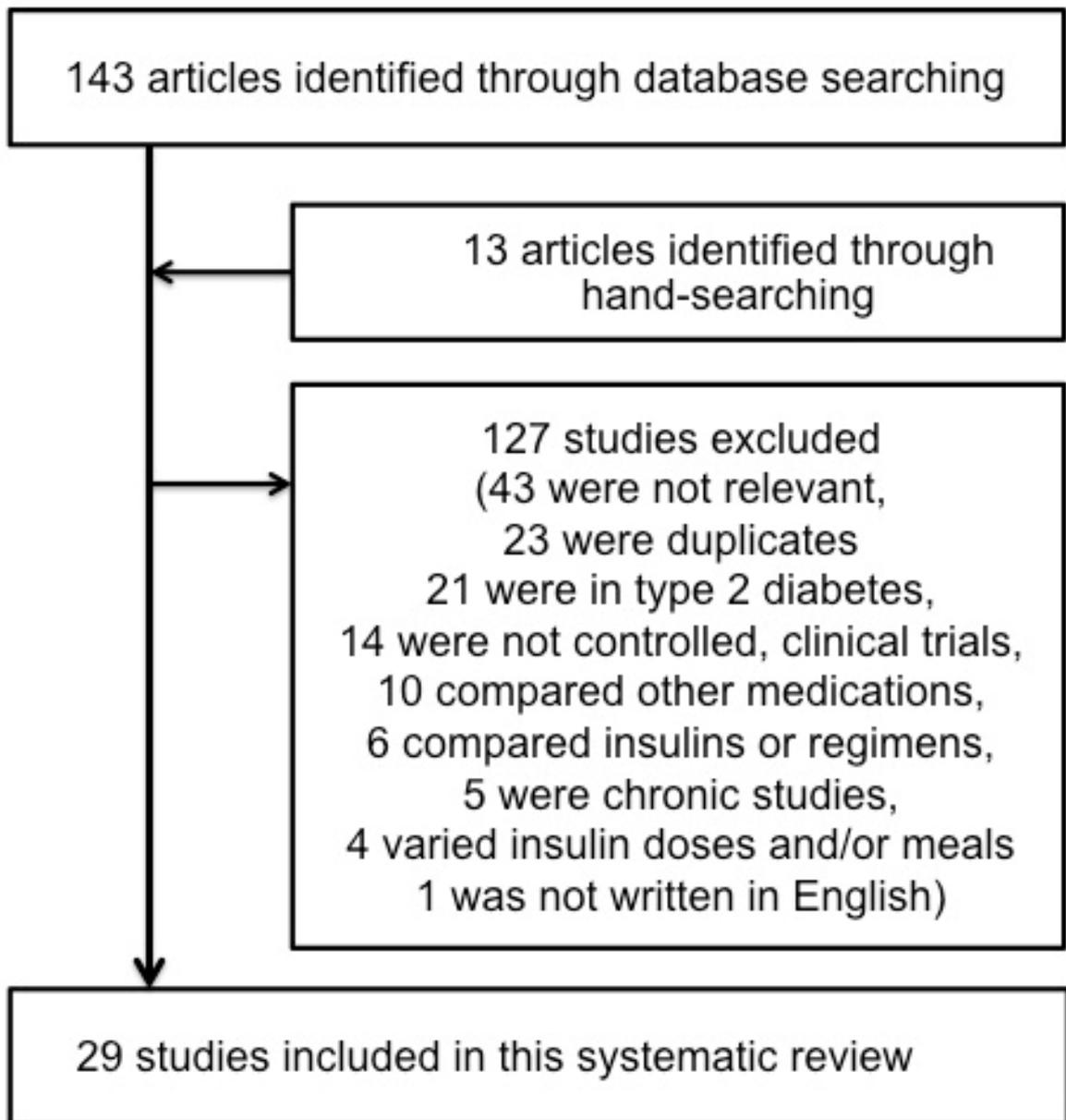


SUPPLEMENTARY DATA

Supplementary Figure 1. Flow diagram of study selection



SUPPLEMENTARY DATA

**Supplementary Table 1.** Summary of included studies examining the effects of fat, protein and GI on postprandial glycemia in type 1 diabetes

**Evidence for Effect of Glycemic Index (GI) on Postprandial Glycemia in Type 1 Diabetes**

**a) Studies using venous or capillary blood**

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Elleri et al, 2013	A: 8 B: 8	Children and adults (16-24 y)	A: 20.8 ± 3.3 y; 63% M; 24.0 ± 1.5 kg/m <sup>2</sup> ; 8.7 ± 1.5%; 7.1 y; 37% CSII.  B: 18.1 ± 4.0 y; 50% M; 22.8 ± 1.2 kg/m <sup>2</sup> ; 8.7 ± 2.0%; 7.4 y; 12% CSII.	Randomized, parallel. 2 evening meals (A: low GI, B: high GI).	Ind. CIR; normal wave	Venous; 8 h	A: 3758 B: 2571	A: 121 B: 121	A: 87 B: 45	A: 35 B: 20	A: 31 B: 9	<b>Median iAUC</b> (mmol/L/480min): A: 2.2 vs. B: 1.2. <b>Peak BG</b> (mmol/L): A: 11.7 ± 2.7 (unpronounced) vs. B: 13.8 ± 3.5 (distinct), p < 0.001 <b>Time to Peak BG</b> (min): A: 152 ± 104 vs. B: 98 ± 29, p < 0.001
LaFrance et al, 1998	9	Adults	78% M; 5.8 ± 0.2%; 44% CSII	Randomized, crossover. 2 breakfast meals (A: low GI; B: high GI)	Ind. CIR; normal wave	Venous; 5 h	A: 1718 B: 1820	A: 62 B: 66	A: 63 B: 98	A: 16 B: 16	A: 13 B: 14	<b>iAUC</b> (mmol/L/min): A: 1.1 ± 1.8 vs. B: 3.2 ± 1.4, p < 0.02.
MacDonald et al, 2009	9	Adults (18-30 y)	23.7 ± 5.6 y; 44% M; 26.0 ± 3.2 kg/m <sup>2</sup> ; 7.9 ± 0.3%; 10.0 ± 5.0 y; 91% CSII	Crossover. 4 dinner meals (A: Ham & cheese sandwich with apple; B: Thai stirfry with rice; C: Hamburger & fries; D: Creamy Pasta.	No bolus	Capillary; 3 h	A: 2316 B: 2095 C: 3354 D: 3132	A: 59.9 B: 59.7 C: 60.0 D: 60.2	A: 45 B: 109 C: 68 D: 38	A: 27.3 B: 29.6 C: 36.8 D: 32.7	A: 20.8 B: 14.2 C: 43.8 D: 42.4	<b>Median incremental BGL at 2 h</b> (mmol/L): A: 10.1, B: 10.2, C: 7.9, D: 4.0. P values compared to D, A: 0.02, B: 0.04, C: 0.04. <b>Median range in BGL over 3 h</b> (mmol/L): A: 10.1, B: 10.8, 9.2, 5.2. P values compared to D, A: 0.07, B: 0.03, C: 0.12. <b>Time to Peak BG</b> (min): A: 120, B: 180, C: 180, D: 150. <b>Median AUC</b> (mmol/L/h): A: 1325, B: 1358, C: 997, D: 593. P values compared to D, A: 0.03, B: 0.06, C: 0.07.
Mohammed et al, 2004	8	Children & adults (14-75 y)		Randomized, crossover. 5 test meals: mashed potato (A), white bread (B), spaghetti (C), barley (D) and pineapple juice	Ind. CIR; normal wave	Capillary; 4 h		A: 50 B: 50 C: 50 D: 50 E: 50	A: 83 B: 71 C: 41 D: 25 E: 46			<b>iAUC</b> (mmol/L/min): A: 672 ± 137; B: 492 ± 158; C: 223 ± 119; D: 136 ± 58; E: 359 ± 93. <b>Hypo</b> (# subjects; <3.0 mmol/L): A: 3/8; B: 3/8; C: 3/8; D: 3/8; E: 7/8; p = 0.013 between foods

SUPPLEMENTARY DATA

Parillo et al, 2011	16	Adults	36 ± 0.5 y; 24.6 ± 0.2 kg/m <sup>2</sup> ; 7.6 ± 0.2 % (56 ± 1.1 mmol/mol); 14 ± 2 y; 100% CSII	(E). Randomized, crossover. 2 test meals: low GI (A) vs. high GI (B)	Ind. CIR; normal wave	Capillary; 3 h	A: 3337 B: 3256	A: 103 B: 104	A: 59 B: 90	A: 38 B: 36	A: 28 B: 28	<b>AUC</b> (mmol/L/180min): A: 1399 ± 120 vs. B: 1757 ± 123, p = 0.006. <b>Mean BG</b> : Meal A 2.0 – 2.5 mmol/L lower than Meal B from 60 – 150 min, p < 0.05 – 0.01.
---------------------	----	--------	---	---	-----------------------	----------------	--------------------	------------------	----------------	----------------	----------------	---

b) Studies using CGM

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Nansel et al, 2008	20	Children (7-16 y)	7.4 y, 45 %M, 13.1 ± 2.6 y; 45% M; 8.3 ± 1.8%; 5.3 ± 4.5 y; 65% CSII	Randomized, crossover. 2 daylong test diets: low GI (A) vs High GI (B), including breakfast, lunch, afternoon snack, dinner and evening snack.	Ind. CIR; normal wave	CGM; 24 h	A: 7474; B: 7165	A: 264; B: 239	A: 40; B: 64	A: 108; B: 96	A: 50; B: 48	<b>Mean BGL</b> (mmol/L): A: 7.6 ± 2.0 vs. B: 10.2 ± 2.5, p < 0.001). <b>Time in Normal BGL Range</b> (3.9 – 10 mmol/L): A: 66% vs. 47%, p = 0.002. <b>Hypo</b> (Subjects with ≥ 1 episodes): A: 13 vs. B: 8, p = 0.007.
Ryan et al, 2008	20	Children (7-17 y)	13.6 ± 2.7 y; 7.4 ± 0.7%; 5.2 ± 3.8 y; 0% CSII	Randomized, crossover. 2 test meals: low GI (A) and high GI (B)	Ind. CIR; normal wave	CGM; 3 h	A: 1571 B: 1500	A: 60.1 B: 60.0	A: 48 B: 84	A: 10.6 B: 10.6	A: 9.4 B: 9.3	<b>AUC</b> (mmol/L/h): A: 2.5 (95% CI: -2.9 – 7.8) vs. B: 13.8 (95% CI: 6.4 – 21.2), p < 0.05. <b>Peak BG</b> (mmol/L): 4.6 (95% CI: 3.0-6.2) vs B: 8.1 (95% CI: 6.2-10.1), p < 0.05. <b>Time to Peak BG</b> (min): A: 70 (95% CI: 45-95) vs B: 75 (95% CI: 61-88), p < 0.05. <b>Time to Return to Fasting BG</b> (min): A: 137 (95% CI: 99-175) vs B: 179 (95% CI: 150-209).

SUPPLEMENTARY DATA

Evidence for Effect of Protein on Postprandial Glycemia in Type 1 Diabetes

a) Studies using venous or capillary blood

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
MacDonald et al, 2009	9	Adults (18-30 y)	23.7 ± 5.6 y; 44% M; 26.0 ± 3.2 kg/m <sup>2</sup> ; 7.9 ± 0.3%; 10.0 ± 5.0 y; 91% CSII	Crossover. 4 dinner meals (A: Ham & cheese sandwich with apple; B: Thai stirfry with rice; C: Hamburger & fries; D: Creamy Pasta.	No bolus	Capillary; 3 h	A: 2316 B: 2095 C: 3354 D: 3132	A: 59.9 B: 59.7 C: 60.0 D: 60.2	A: 45 B: 109 C: 68 D: 38	A: 27.3 B: 29.6 C: 36.8 D: 32.7	A: 20.8 B: 14.2 C: 43.8 D: 42.4	<b>Median incremental BGL at 2 h</b> (mmol/L): A: 10.1, B: 10.2, C: 7.9, D: 4.0. P values compared to D, A: 0.02, B: 0.04, C: 0.04. <b>Median range in BGL over 3 h</b> (mmol/L): A: 10.1, B: 10.8, 9.2, 5.2. P values compared to D, A: 0.07, B: 0.03, C: 0.12. <b>Time to Peak BG</b> (min): A: 120, B: 180, C: 180, D: 150. <b>Median AUC</b> (mmol/L/h): A: 1325, B: 1358, C: 997, D: 593. P values compared to D, A: 0.03, B: 0.06, C: 0.07.
Winiger et al, 1995	8	Adults	56 ± 3.8 y; 22.7 ± 1.1 kg/m <sup>2</sup> ; 0% CSII (but all used CSII for study)	Randomized, crossover, 2 meals (A: low protein, high fat vs. B: high protein, low fat)	Not stated (avg dose 5.6 ± 0.6U); dual wave (66:33%) (Syringe pump into vein).	Venous; 12 h	A: 2717 B: 2717	A: 58 B: 58		A: 9 B: 57	A: 43 B: 21	<b>BG Increase</b> (mmol/L): A: + 1.2 vs. + 4.3, p < 0.02 Similar BG responses for first 4 h. Meal B increases BG at a faster rate and to a significantly higher BG than Meal A.
Uthoff et al, 2010	16	Adults	44 ± 12 y; 63% M; 24 ± 3 kg/m <sup>2</sup> ; 7.5 ± 0.6%; 15 ± 12 y; 63% CSII	Crossover. (A: Fasting B: mean of 3 CHO-free test meals)	No bolus	Capillary; 4 h	A: 0 B: 2558	A: 0 B: 2.5		A: 0 B: 32.4	A: 0 B: 52.0	<b>Mean BG</b> (baseline to 4 h, mmol/L): A: 7.2 ± 2.4 to 6.8 ± 2.8 mmol/L, p = 0.461. B: 6.7 ± 2.0 to 9.8 ± 3.4 mmol/L, p < 0.0001.

SUPPLEMENTARY DATA

b) Studies using CGM

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Garcia-Lopez et al, 2013	17	Adults	24% M; 35.8 ± 8.4 y; 25.3 ± 4.0 kg/m <sup>2</sup> ; 7.7 ± 0.8%; 17.7 ± 7.7 y; 100% CSII	Randomized, crossover. 2 meals - standard (A) vs. added fat and protein (B)	Ind. CIR; normal wave	CGM; 3 h		A: 50 B: 50		A: 3.3 B: 28.9	A: 8.9 B: 37.4	<p><b>Mean BG Increase</b> (mmol/L): A: 1.2 vs. B: 1.7, NS at any time point. Mixed model analysis: BG differed at different time points after meal (p &lt; 0.001), and significant interaction time by meal (p &lt; 0.05).</p> <p><b>Time to Peak BG</b> (min): A: 60 vs. B: 90</p> <p><b>Time to Return to Fasting BG</b> (min): A: 180 vs. B: BG remained high.</p> <p><b>Hypo</b> (# subjects, &lt; 4.0 mmol/L): A: 5 vs. 5.</p>
Smart et al, 2013	33	Children (7-17 y)	12.2 ± 2.5 y, 48% M, BMI z score: 0.6 ± 0.8, 7.2 ± 0.8% (55 ± 8.7 mmol/mol), 4. ± 3.2 y, 82% CSII	Randomized, crossover. 4 meals (A: low fat, low protein; B: low fat, high protein; C: high fat, low protein; D: high fat, high protein).	Ind. CIR; normal wave	CGM; 5 h		A: 30.3 B: 30.0 C: 30.3 D: 29.8		A: 5.3 B: 40.0 C: 5.3 D: 40.0	A: 4.0 B: 3.9 C: 35.0 D: 35.2	<p><b>Mean BG Increase</b> (at 5 h, BG above Meal A, mmol/L), B: + 2.6, C: + 2.3, D: + 5.4, p &lt; 0.05.</p> <p><b>Time to Peak BG</b> (min): A: 79, B: 96, C: 126, D: 143, p &lt; 0.001</p> <p><b>Hypo</b> (# subjects): A: 14, B: 10, C: 4, D: 1, p = 0.003.</p>
Neu et al, 2014	15	Children	16.8 ± 2.9 y; 87% M; 21.1 ± 2.2 kg/m <sup>2</sup> ; 6.9 ± 0.8%; 6.9 ± 4.6 y; 40% CSII	Pseudo-randomized, crossover. 2 test meals (A: control, B: high fat, high protein)	Ind. CIR; normal wave	CGM; 12 h	A: 2341 B: 4974	A: 70 B: 70		A: 28 B: 110	A: 19 B: 52	<p><b>AUC</b> (md/dL/12 h): A: 1400 ± 580), B: 1967 ± 994, p &lt; 0.05. Delta AUC of A vs. B was 567 ± 581. Max difference in AUC occurs at 6 h (A: 5.6 ± 2.3 mmol/L), B: 10.9 ± 5.4 mmol/L)</p> <p><b>Mean BG</b>: between 4 and 12 h after the meal, p &lt; 0.05</p> <p><b>Hypo</b> (&lt; 4.4 mmol/L, % of BG values): A: 31 vs. B: 3.</p> <p><b>Hyper</b> (&gt; 8.3 mmol/L, % of BG values): A: 24 vs. B: 48.</p>
Paterson et al. 2014	27	Children & adults	55% M, range 7-40 y	Randomized, crossover. 6 protein test meals and 2 glucose comparators.	No bolus	CGM; 5 h		A: 0 B: 0 C: 0 D: 0 E: 0 F: 0 G: 10 H: 20		A: 0 B: 12.5 C: 25 D: 50 E: 75 F: 100 G: 0 H: 0	A: 0 B: 0 C: 0 D: 0 E: 0 F: 0 G: 0 H: 0	<p><b>Mean BG</b>: Meals A-D (0 – 50 g of protein) did not significantly affect BG. Meals E-F were significantly different.</p> <p><b>Peak BG</b>: Meals E &amp; F increased to the same BG as Meal H (20 g glucose).</p> <p><b>Time to Peak BG</b>: Meals E-F was at 300 mins vs. ~ 50 mins for Meal H.</p>

SUPPLEMENTARY DATA

Evidence for Effect of Fat on Postprandial Glycemia in Type 1 Diabetes

a) Studies using venous or capillary blood

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
MacDonald et al, 2009	9	Adults (18-30 y)	23.7 ± 5.6 y; 44% M; 26.0 ± 3.2 kg/m <sup>2</sup> ; 7.9 ± 0.3%; 10.0 ± 5.0 y; 91% CSII	Crossover. 4 dinner meals (A: Ham & cheese sandwich with apple; B: Thai stirfry with rice; C: Hamburger & fries; D: Creamy Pasta.	No bolus	Capillary; 3 h	A: 2316 B: 2095 C: 3354 D: 3132	A: 59.9 B: 59.7 C: 60.0 D: 60.2	A: 45 B: 109 C: 68 D: 38	A: 27.3 B: 29.6 C: 36.8 D: 32.7	A: 20.8 B: 14.2 C: 43.8 D: 42.4	<b>Median incremental BGL at 2 h</b> (mmol/L): A: 10.1, B: 10.2, C: 7.9, D: 4.0. P values compared to D, A: 0.02, B: 0.04, C: 0.04. <b>Median range in BGL over 3 h</b> (mmol/L): A: 10.1, B: 10.8, 9.2, 5.2. P values compared to D, A: 0.07, B: 0.03, C: 0.12. <b>Time to Peak BG</b> (min): A: 120, B: 180, C: 180, D: 150. <b>Median AUC</b> (mmol/L/h): A: 1325, B: 1358, C: 997, D: 593. P values compared to D, A: 0.03, B: 0.06, C: 0.07.
Lodefalk et al, 2008	7	Children	16.4 ± 0.7 y; 50% M; 23.2 ± 3.4 kg/m <sup>2</sup> ; 7.3 ± 0.7%; 3.7 ± 1.2 y; 0% CSII	Randomized, crossover. 2 meals (A: low fat, B: high fat)	Fixed CIR (7 IU); normal wave	Capillary; 4 h	A: 1338 B: 2675	Same CHO		Same protein	A: 2 B: 38	<b>4 h AUC</b> : NS <b>2 h AUC</b> : Meal A larger than Meal B, p = 0.047. <b>Time to Peak BG</b> (min): A: 120 vs. B: 210, p = 0.080.
Wolever et al, 2011	11	Adults	32.7 ± 2.4 y; 55% M; 24.0 ± 0.6 kg/m <sup>2</sup> ; 7.4 ± 0.3%; 7.6 ± 2.1 y	Randomized, crossover. 4 test meals (A: low fat/low sugar, B: low fat/high sugar, C: high fat/low sugar, D: high fat/high sugar).	Ind. CIR; normal wave	Capillary, 4 h	A: 1050 B: 950 C: 1810 D: 1690	A: 50 B: 50 C: 50 D: 50	A: 71 B: 64 C: 71 D: 64	A: 11 B: 6 C: 11 D: 6	A: 0.8 B: 0.4 C: 21 D: 20	<b>AUC</b> (mmol/L/min): A: 523 ± 133, B: 494 ± 92, C: 613 ± 144, D: 572 ± 149, NS <b>Peak BG</b> (mmol/L): A: 4.3 ± 0.9, B: 5.6 ± 0.6, C: 5.3 ± 1.0, D: 4.9 ± 0.7, NS <b>Time to Peak BG</b> (min): A: 65 ± 7, 46 ± 6, 79 ± 7, D: 52 ± 6, p < 0.05 for C & D vs. A & B.
Wolpert et al, 2013	10	Adults	55 ± 12 y; 71% M; 26.3 ± 3.6 kg/m <sup>2</sup> ; 7.2 ± 0.8%; 42 ± 6 y; 100% CSII	Randomized, crossover. 2 evening meals (A: low fat, B: high fat)	Closed loop glucose control	Venous, 18 h	A: 2299; B: 4175	A: 75 B: 75		A: 40 B: 40	A: 10 B: 60	<b>AUC above 6.7 mmol/L</b> (mg/dL*min): A: 8,350 ± 1,907 vs. B: 16,967 ± 2778, p < 0.001 <b>Infused Insulin</b> (U): A: 12.6 ± 1.9 vs. B: 9.0 ± 1.3, p = 0.01

SUPPLEMENTARY DATA

b) Studies using CGM

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals				Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	
Garcia-Lopez et al, 2013	17	Adults	24% M; 35.8 ± 8.4 y; 25.3 ± 4.0 kg/m <sup>2</sup> ; 7.7 ± 0.8%; 17.7 ± 7.7 y; 100% CSII	Randomized, crossover. 2 meals - standard (A) vs. added fat and protein (B)	Ind. CIR; normal wave	CGM; 3 h		A: 50 B: 50	A: 3.3 B: 28.9	A: 8.9 B: 37.4	<b>Mean BG Increase</b> (mmol/L): A: 1.2 vs. B: 1.7, NS at any time point. Mixed model analysis: BG differed at different time points after meal (p < 0.001), and significant interaction time by meal (p < 0.05). <b>Time to Peak BG</b> (min): A: 60 vs. B: 90 <b>Time to Return to Fasting BG</b> (min): A: 180 vs. B: BG remained high. <b>Hypo</b> (# subjects, < 4.0 mmol/L): A: 5 vs. 5.
Smart et al, 2013	33	Children (7-17 y)	12.2 ± 2.5 y, 48% M, BMI z score: 0.6 ± 0.8, 7.2 ± 0.8% (55 ± 8.7 mmol/mol), 4. ± 3.2 y, 82% CSII	Randomized, crossover. 4 meals (A: low fat, low protein; B: low fat, high protein; C: high fat, low protein; D: high fat, high protein).	Ind. CIR; normal wave	CGM; 5 h		A: 30.3 B: 30.0 C: 30.3 D: 29.8	A: 5.3 B: 40.0 C: 5.3 D: 40.0	A: 4.0 B: 3.9 C: 35.0 D: 35.2	<b>Mean BG Increase</b> (at 5 h, BG above Meal A, mmol/L), B: + 2.6, C: + 2.3, D: + 5.4, p < 0.05. <b>Time to Peak BG</b> (min): A: 79, B: 96, C: 126, D: 143, p < 0.001 <b>Hypo</b> (# subjects): A: 14, B: 10, C: 4, D: 1, p = 0.003.
Neu et al, 2014	15	Children	16.8 ± 2.9 y; 87% M; 21.1 ± 2.2 kg/m <sup>2</sup> ; 6.9 ± 0.8%; 6.9 ± 4.6 y; 40% CSII	Pseudo-randomized, crossover. 2 test meals (A: control, B: high fat, high protein)	Ind. CIR; normal wave	CGM; 12 h	A: 2341 B: 4974	A: 70 B: 70	A: 28 B: 110	A: 19 B: 52	<b>AUC</b> (md/dL/12 h): A: 1400 ± 580), B: 1967 ± 994, p < 0.05. Delta AUC of A vs. B was 567 ± 581. Max difference in AUC occurs at 6 h (A: 5.6 ± 2.3 mmol/L), B: 10.9 ± 5.4 mmol/L) <b>Mean BG</b> : between 4 and 12 h after the meal, p < 0.05 <b>Hypo</b> (< 4.4 mmol/L, % of BG values): A: 31 vs. B: 3. <b>Hyper</b> (> 8.3 mmol/L, % of BG values): A: 24 vs. B: 48.

SUPPLEMENTARY DATA

**Supplementary Table 2.** Summary of included studies investigating prandial insulin dosing strategies for fat, protein and GI in type 1 diabetes

**1. Evidence for Effect of Timing of Prandial Insulin on Postprandial Glycemia in Type 1 Diabetes**

**a) Studies using venous or capillary blood**

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Cobry et al, 2010	23	Adolescents and adults	18.3 ± 4.4 y; 52% M; 7.5 ± 0.8%; 11.3 ± 6.0 y; 100% CSII	Randomized, crossover. Standardized breakfast meal. 3 timings of bolus dose: 20 min before (Pre); Immediately before (Start); 20 min after (Post).	Ind CIR; Normal bolus	Capillary; 4 h	Same Energy	Same CHO		Same Protein	Same Fat	<p><b>AUC (mmol/L):</b> Pre: 8.9, Start: 10.3, Post: 10.3, Pre &lt; Start (p = 0.03) and Pre &lt; Post (p &lt; 0.05).</p> <p><b>Peak BGL (mmol/L):</b> Pre: 11, Start: 13.7, Post: 13.8, Pre &lt; Start (p = 0.004) and Pre &lt; Post (p &lt; 0.003).</p> <p><b>Mean BG at 1h (mmol/l):</b> Pre: 10.0, Start: 12.3, Post: 13.1, Pre &lt; Start (p = 0.003) and Pre &lt; Post (p &lt; 0.001).</p>
De Palma et al, 2011	38	Children and adolescents (6-18 y)	14.5 ± 4.3 y; 60% M; 21.9 ± 4.3 kg/m <sup>2</sup> ; 7.7 ± 0.8%; 8.0 ± 4.3 y; 100% CSII	Randomized, crossover. Pizza margherita meal. 4 test conditions: 2 bolus types (Normal or DW) and 2 timings of bolus dose (15 min before or immediately before).	Ind. CIR; Normal (N) or DW (30:70% over 6 h) and Timing (-15 min or immediately before).	Capillary; 6 h	35% of total daily kJ intake based on age.	60% E		16% E	23% E	<p><b>Mean BGL at 6 h (mmol/L):</b> N: 9.5, N (-15 min): 7.9, DW: 7.0, DW (-15 min) 6.2. P values compared to time 0, N: 0.02, N (-15min): 0.8, DW: 0.14, DW (-15 min): 0.02.</p> <p><b>Mean AUC (mmol/L/min):</b> N: 233, N (-15 min): 383, DW: 738, DW (-15 min): 106. P values compared to N (-15 min), N: &gt;0.05, DW : &gt;0.05, DW (-15 min) 0.01.</p>
Scaramuzza et al, 2010	30	Children	15.2 ± 3.9 y; 57% M; 22.4 ± 3.8 kg/m <sup>2</sup> ; 8.07 ± 4.1 y; 100% CSII	Randomized, crossover. Standardized breakfast meal. 3 timings of bolus dose: 15 min before (Pre); Immediately before (Start); just after (Post).	Ind CIR; Normal bolus	Capillary; 3 h	35% of total daily kJ intake based on age (range 6720-10500 kJ)	55%E (~95 g)		16%E (~40 g)	29%E (~28 g)	<p><b>AUC (mmol/min):</b> Pre: 1621.6, Start: 1558.3, st: 1574.7, NS.</p> <p><b>Mean BG at 1h (mmol/l):</b> Pre: 7.6, Start: 7.2, Post: 9.8, p = 0.024.</p>

SUPPLEMENTARY DATA

**b) Studies using CGM**

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Ryan et al, 2008	20	Children and adolescent: (7-17 y)	13.6 ± 2.7 y; 7.4 ± 0.7%; 5.2 ± 3.8 y; 100% MDI	Randomized, crossover. Low GI meal and 2 timings of bolus dose (Immediately before vs 15 min after commencement).	Ind. CIR; Preprandial (Pre) (immediately before) vs Postprandial (Post) (+15mins).	CGM; 3 h	1571	60	48	11	9	<p><b>Mean Glucose excursion at 1 h</b> (mmol/L): Pre: 2.9 vs Post: 5.4, p &lt; 0.05.</p> <p><b>Mean Peak Glucose</b> (mmol/l): Pre: 4.6 vs Post: 6.3, p = 0.003.</p>

SUPPLEMENTARY DATA

2. Evidence for Effect of Insulin Bolus Type on Postprandial Glycemia in Type 1 Diabetes

a) Studies using venous or capillary blood

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Chase et al, 2002	9	Children and Adults	20.3 ± 4.5 y; 22%M; 7.8 ± 0.4 %; 11.8 ± 6.1 y; 100% CSII	Randomized, crossover. Pizza and tiramisu meal. 4 bolus types: (A) Normal (B) 2 separate boluses: ½ dose prior and ½ at 90 min (C) Square wave bolus over 2 h (D) Dual wave bolus 70:30% over 2 h.	Ind. CIR administered 10 min prior to meal	Capillary; 6 h	3482	115	23	35	<p><b>Mean BG excursion at 2h (mmol/l)*:</b> A: 2.1 ± 1.1, B: 3.3 ± 1.7, C: 3.8 ± 1.4, D: -0.4 ± 1.1, p = 0.01.</p> <p><b>Mean BG excursion at 6h (mmol/l)*:</b> A: 1.2 ± 1.5, B: -0.1 ± 1.1, C: -0.1 ± 0.7, D: -0.5 ± 0.9, p = 0.23.</p> <p><b>AUC (mmol/L/hr)*:</b> A: 45.4 ± 6.3, B: 51.5 ± 7.7, C: 41.4 ± 4.3, D: 41.2 ± 3.5, p = 0.83.</p>	
Linholtm Olinder et al, 2009	15	Adolescents and young Adults	16 y (range 13-19), 0% M, 23.3 kg/m <sup>2</sup> (17.3-31.1), 6.8% (5.7- 8.9), 6.5 y (3-15), 100% CSII	Crossover. 2 pasta meals: (A): Lower fat; (B): Higher fat. 3 bolus types: Normal (N); Dual wave (DW); or Square wave (SW).	Individually standardized dose; Normal (100% immediately) or DW (60:40% over 1 h) or SW (100% over 1 h)	CGM and capillary; 3 h	2150 2272	A: 68 B: 67	A:38 B:39	A: 21 B: 20	A: 18 B: 22	<p><b>Maximal BG excursion (mmol/l)**:</b> AN: 4.0, ADW: 3.8, ASW: 5.0, BN: 2.4, BDW: 3.0, BSW: 3.7, NS.</p> <p><b>AUC (mmol/L)**:</b> AN: 1631, ADW: 1548, ASW: 1704, BN: 1451, BDW: 1312, BSW: 1515, NS.</p>
Pankowska et al, 2012	24 (12 in each group)	Children	A: 14.9 ± 2.0 y; BMI SD -0.2 ± 0.7; 6.5 ± 2.8%; 6.5 ± 2.8 y; 100% CSII  B: 15.5 ± 1.7 y; BMI SD 1.0 ± 0.5; 7.2 ± 0.9%; 6.2 ± 3.5 y; 100% CSII	Randomized, open label trial. Pizza salami meal. 2 test conditions: (A) Carb plus Fat/Protein (CFP) counting and Dual Wave; (B) Carb (CARB) counting and Normal.	CFP counting (Ind. CIR plus n Fat-Protein units x ICR/6h) versus CARB counting (Ind. CIR).  CFP resulted in additional 38% meal bolus insulin (62%:38% over 6h).	Capillary; 6 h	2398	47	25	33	<p><b>Mean BG excursion (mmol/l):</b> Mean glucose values were increased for Group B compared to Group A at 120 (p=0.003), 240 (p=0.004) and 360 (p=0.003) min.</p> <p><b>Hypo episodes (defined as BGL &lt; 2.8 mmol/l) (# Subjects):</b> A: 4 (33%) vs B: 0 (0%).</p>	

SUPPLEMENTARY DATA

b) Studies using CGM

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals				Outcomes
							Energy (kJ)	CHO (g)	Protein (g)	Fat (g)	
Jones et al, 2005	24	Adults	40 ± 10y; 27%M; 26 ± 4 kg/m <sup>2</sup> ; 6.7 ± 0.8%; 100% CSII	Randomized, crossover. Pizza margherita meal. 3 bolus types: Normal; Dual wave (50:50% over 4 h); or Dual wave (50:50% over 8 h).	Ind. CIR; Normal (N) or DW4h (50:50% over 4 h) or DW8h (50:50% over 8 h)	CGM; 12 h	2561	60	30	28	<b>Mean Glucose over 8-12 h</b> (mmol/L): N: 7.4 ± 3.0, DW4h: 8.0 ± 3.8, DW8h: 5.8 ± 2.3, p < 0.05. <b>Difference in Percent Time in Normal Glucose Range</b> (3.9 – 7.8 mmol/L): N vs.DW8h: -14%; DW4h vs. DW8h: -7%, p > 0.05.
Lee et al, 2004	10	Adults	47.9 ± 12.5 y; 33%M; 26.9 ± 5.6 kg/m <sup>2</sup> ; 7.5 ± 1.6%; 18.3 ± 12.2 y; 100% CSII	Randomized, crossover. 2 meals: (A) Bean burrito and (B) High fat, higher protein pizza. 2 bolus types: Normal and Dual wave (DW). 3 test conditions: Meal A/Normal; Meal B/Normal; and Meal B/DW.	Normal bolus: Ind. CIR versus DW: Ind. CIR plus Insulin: Protein and Insulin: Fat ratios (Both calculated as 50% CIR). DW resulted in additional 34% meal bolus insulin (66%:34% over 5.2 ± 1.4 h).	CGM; 16h	A: 2772 B: 3360	107 136	23 40	18 49	<b>Mean Glucose</b> (mmol/L): Mean glucose values were similar in each of the 3 combinations of meal and bolus types in the 3 h following the meal (p=0.64, p=0.84, p=.99). <b>Mean Glucose from 5 h to 14 h</b> (mmol/l): Mean glucose values were increased from 5 h (p=0.02) to 14 h (p=0.01) for Meal B/Normal compared to Meal A/Normal and Meal B/DW bolus.
Lopez et al, 2014	20	Children and Adults	18.0 ± 2.4 y; 50% M; 7.0 ± 0.2%; 7.4 ± 1.5 y; 100% CSII	Randomized, crossover. Standardized breakfast meal. Six bolus types: Normal bolus (N) compared to 5 different rates of square wave (SW) bolus given over 2 h.	Ind. CIR; Normal bolus (N); SW1h (100% of CIR per hour = 200% CIR total dose); SW2h (50% of CIR per h); SW3h (33% of CIR per h); SW4h (25% of CIR per h)	CGM, 2h	1346	60	10	6	<b>Mean Glucose excursion</b> (mmol/l): The mean postprandial glycemic excursion was lower at 60 minutes and 120 minutes for N compared to SWs, p<0.05. <b>Peak Glucose</b> (mmol/L): The mean peak postprandial glycemic excursion was lower for N compared to SWs, p<0.05.

SUPPLEMENTARY DATA

3. Evidence for effect of alterations in the Insulin Dose for high fat or high protein meals on Postprandial Glycemia in Type 1 Diabetes

a) Studies using venous or capillary blood

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals				Outcomes
							Energy (kJ)	CHO (g)	Protein (g)	Fat (g)	
Wolpert et al, 2013	10	Adults	55 ± 12 y; 71% M; 26.3 ± 3.6 kg/m <sup>2</sup> ; 7.2 ± 0.8%; 42 ± 6 y; 100% CSII	Randomized, crossover. 2 evening meals:(A): low fat, (B): high fat;	Closed loop glucose control. HF meal increased mean insulin requirements 42%.	Venous, 18 h	A: 2299 B: 4175	A: 75 B: 75	A: 40 B: 40	A: 10 B: 60	<b>Infused Insulin (U):</b> A: 9.0 ± 1.3 vs. B: 12.6 ± 1.9, p = 0.01 <b>AUC above 6.7 mmol/L (mg/dL*min):</b> A: 8,350 ± 1,907 vs. B: 16,967 ± 2778 despite additional insulin, p < 0.0001
Pankowska et al, 2012	24 (12 in each group)	Children	A: 14.9 ± 2.0 y; BMI SD -0.2 ± 0.7; 6.5 ± 2.8%; 6.5 ± 2.8 y; 100% CSII B: 15.5 ± 1.7 y; BMI SD 1.0 ± 0.5; 7.2 ± 0.9%; 6.2 ± 3.5 y; 100% CSII	Randomized, open label trial. Pizza salami meal. 2 test conditions: (A) Carb plus Fat/Protein (CFP) counting and Dual Wave; (B) Carb (CARB) counting and Normal.	CFP counting (Ind. CIR plus n Fat-Protein units x ICR/6h) versus CARB counting (Ind. CIR). CFP resulted in additional 38% meal bolus insulin (62%:38% over 6h).	Capillary; 6 h	2398	47	25	33	<b>Mean BG excursion (mmol/l):</b> Mean glucose values were increased for Group B compared to Group A at 120 (p=0.003), 240 (p=0.004) and 360 (p=0.003) min. <b>Hypo episodes (defined as BGL &lt; 2.8 mmol/l) (# Subjects):</b> A: 4 (33%) vs B: 0 (0%).
Bell et al, 2014	11	Adults	38 ± 17 y; 36%M; 24.6 ± 2.4 kg/m <sup>2</sup> ; 6.9 ± 0.7%; 14.4 ± 14.0 y; 100% CSII	Randomized, crossover. 6 foods: (A) Steak, (B) battered fish, (C) eggs, (D) yoghurt, (E) baked beans and (F) peanuts. 2 test conditions: Food and CARB counting; Food and FII	CARB Counting (Ind. CIR) versus FII. Mean insulin dose using CARB vs FII (units): A: 0 vs 3.7; B:1.6 vs. 3.7; C:0.1 vs 1.8; D: 5.4 vs. 6.9; E:4.3 vs. 5.9; F: 2.4 vs. 4.2.	Capillary; 3 h	A: 1350 B: 945 C: 1080 D: 1200 E: 990 F: 3900	A: 0 B: 14 C: 2 D: 45 E: 36 F: 19	A: 60 B: 12 C: 24 D: 14 E: 15 F: 40	A: 11 B: 14 C: 20 D: 6 E: 2 F: 79	<b>Mean BGL (mmol/l):</b> FII: 5.7 ± 0.2 vs CARB 6.5 ± 0.2, p = 0.003. <b>Peak BGL (mmol/L):</b> FII: -0.7 ± 0.2 vs CARB 0.1 ± 0.2, p = 0.001. <b>Hypo episodes (defined as BGL &lt; 3.6mmol/l):</b> FII: 32 (48%) versus CARB:22 (33%), NS.

SUPPLEMENTARY DATA

b) Studies using CGM

	Sample Size	Age	Population (age; gender; BMI; HbA1c; duration of diabetes; MDI/CGMS)	Study Design	Insulin Dose	Glucose Monitoring Method & Duration	Test Meals					Outcomes
							Energy (kJ)	CHO (g)	GI (%)	Protein (g)	Fat (g)	
Bao et al, 2011	28	Adults	37.8 ± 14.4 y; 24 ± 3 kg/m <sup>2</sup> ; 7.8 ± 0.9%; 19.6 ± 11.4 y; 100% CSII	Randomized, crossover. 2 meals: (A) Higher carb and (B) Lower carb. 3 test conditions: Meal A and CARB Counting (ACARB); Meal B and CARB Counting (BCARB); Meal B and FII (BFII)	CARB Counting (Ind. CIR) versus FII.	CGM; 3 h	A: 1600 B: 1600	A: 75 B: 41	A: 52 B: 53	A: 10 B: 17	A: 6 B: 17	<b>3h iAUC</b> (mmol/L/min): ACARB: 275 ± 224, BCARB: 409 ± 373, BFII: 197 ± 220, p < 0.05. <b>Time in Normal Glucose Range</b> (4.0 – 10 mmol/L) min: ACARB: 108 ± 46, BCARB: 88 ± 69, BFII: 128 ± 57, p < 0.01. <b>Peak Glucose excursion (mmol/L):</b> ACARB: 4.0 ± 2.8, BCARB: 4.1 ± 3.1, BFII: 2.4 ± 1.9, p < 0.009. <b>Hypo episodes</b> (# Subjects): ACARB: 10, BCARB: 1, BFII: 6, NS
Lee et al, 2004	10	Adults	47.9 ± 12.5 y; 33%M; 26.9 ± 5.6 kg/m <sup>2</sup> ; 7.5 ± 1.6%; 18.3 ± 12.2 y; 100% CSII	Randomized, crossover. 2 meals: (A) Bean burrito and (B) High fat, higher protein pizza. 2 bolus types: Normal and Dual wave (DW). 3 test conditions: Meal A/Normal; Meal B/Normal; and Meal B/DW.	Normal bolus: Ind. CIR versus DW: Ind. CIR plus Insulin: Protein and Insulin: Fat ratios (Both calculated as 50% CIR). DW resulted in additional 34% meal bolus insulin (66%: 34% over 5.2 ± 1.4 h).	CGM; 16h	A: 2772 B: 3360	107 136		23 40	18 49	<b>Mean Glucose</b> (mmol/L): Mean glucose values were similar in each of the 3 combinations of meal and bolus types in the 3 h following the meal (p=0.64, p=0.84, p=.99). <b>Mean Glucose from 5 h to 14 h</b> (mmol/L): Mean glucose values were increased from 5 h (p=0.02) to 14 h (p=0.01) for Meal B/Normal compared to Meal A/Normal and Meal B/DW bolus.
Kordonouri et al, 2012	42	Children and young Adults (6-21 y)	12.3 ± 3.6y; 45 %M; 5.2 ± 3.1 y; 100% CSII	Randomized, double crossover. Pizza salami meal. 4 test conditions: (A) Carb (CARB) counting and normal (B) Carb plus	CARB counting (ind. CIR) versus CFP counting (Ind. CIR plus Fat-Protein units).	CGM; 6 h	33% of total daily kJ intake based on age.	50%E		16%E	34%E	<b>AUC</b> (mmol/L/h): A: 52.9 ± 16.6, B: 43.6 ± 13.1, C: 49.9 ± 15.0, D: 40.3 ± 15.9, p < 0.05. <b>Mean Glucose</b> (mmol/L): A: 9.2 ± 3.0. B: 7.5 ± 2.3, C: 8.6 ± 2.7, D: 7.8 ± 2.8, p < 0.04).

SUPPLEMENTARY DATA

Fat/Protein (CFP) counting and normal; (C) CARB counting and DW; and (D) CFP counting and DW.

CARB Counting: DW 70:30% over 2 h. CFP Counting: DW initial bolus equal to amount of insulin for 10g carb units and prolonged bolus (over 3-6h) calculated for fat/protein units (1FPU=420kj).

**Hypo episodes** (# Subjects): A: 5 (12%), B: 12 (29%), C: 3 (7%), D: 18 (42%),  $p < 0.001$ .