

BACKGROUND AND AIMS

Diabetic ketosis (DK) is a risk factor or precursor for diabetic ketoacidosis (DKA), a potentially life-threatening condition. In this prospective analysis, we analysed risk and protective factors for the incidence of DK in a sample of people with type 1 diabetes.

Furthermore, we performed two meta-analyses to evaluate the role of structured diabetes self-management education as a risk mitigation strategy for DK and DKA.

MATERIALS AND METHODS

Risk and protective factors for diabetic ketosis

We combined data from four prospective educational studies examining the efficacy of an education programme for type 1 diabetes (PRIMAS) and for insulin pump users (INPUT), respectively. Two randomised controlled trials tested the education programmes against a control condition and two comparative effectiveness research trials tested the education programmes in real world settings. We prospectively analysed the incidence of DK 6 months after the end of the education phase and determined risk and protective factors for occurrence of DK by using univariate tests and a multivariable logistic regression model. DK was assessed by Case Report Forms and via interview.

Meta-analyses

To further analyse the impact of structured diabetes education on DK and DKA, we performed a literature search and conducted two meta-analyses. First, we analysed whether participation in structured education could reduce the number of persons who experienced at least one event. Second, we analysed whether participation in structured education could reduce the event rate of DKA.

RESULTS

Risk and protective factors for diabetic ketosis

- Analyses were based on 760 participants with type 1 diabetes (see Table 1).
- At baseline, only 8.4% of participants reported at least one DK-event. During the follow-up period, the self-reported incidence of DK was 38 events per 100 patient years; but only 5.5% of the sample reported at least one DKA event, which indicated a highly skewed distribution.
- In univariate tests, people reporting DK were significantly more frequent on insulin pump therapy, did not participate in the education programmes PRIMAS or INPUT, had a higher baseline depression score, and reported more frequently DK events before baseline (Figure 1).
- In a multivariable logistic regression analysis, only participation in diabetes education (OR = 0.51; 95% CI 0.26 - 0.99) and previous DK (OR = 6.3 95% CI 3.08 - 13.09) were independent baseline predictors of DK during the follow-up period (Figure 2).

Meta-analyses

- The literature search yielded 24 studies of which three studies reported the number of people experiencing at least on DKA event (1-3), and six studies reported the event rate of DKA (1,2,4-7).
- We added data from the four studies described above and included the number of people experiencing at least one DK event before and after participation in the structured intervention (8-11).
- Figure 3 shows that structured self-management education could reduce the number of people experiencing at least one DK/DKA event by 56%. This could be shown for DKA and DK with slightly higher effects of diabetes education on DKA.
- Figure 4 shows that also the number of DKA events could be significantly reduced by 61% after participation in structured diabetes education.

CONCLUSION

Experiencing an event of DK was a significant risk factor for a recurrent episode. Interestingly, participation in a structured self-management education programme was associated with a reduced risk for a DK event. However, assessing DK via Case Report Form and interview is clearly a limitation of this study.

Nevertheless, mean incidence rate and percentage of study participants affected by DK clearly indicates the existence of risk groups for DK. A better understanding of risk factors for DK or for DKA is needed to identify persons at risk and to employ risk mitigation strategies for these risk groups.

The meta-analyses demonstrated the importance of structured diabetes education as a risk mitigation strategy. Not only the number of affected people was reduced by diabetes education but also the number of DKA events.

In summary, structured self-management education is a potent protective factor for the development of diabetic ketosis and ketoacidosis.

Studies included in the meta-analyses

- Muhlhauser I, Bruckner I, Berger M, et al. Evaluation of an intensified insulin treatment and teaching programme as routine management of type 1 (insulin-dependent) diabetes. The Bucharest-Dusseldorf Study. Diabetologia 1987; 30(9): 681-90.
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- Speight J, Holmes-Truscott E, Harvey DM, et al. Structured type 1 diabetes education delivered in routine care in Australia reduces diabetes-related emergencies and severe diabetes-related distress: The OzDAFNE program. Diabetes Res Clin Pract 2016; 112: 65-72.
- Tankova T, Dakovska G, Koev D. Education of diabetic patients—a one year experience. Patient Educ Couns 2001; 43(2): 139-45.
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- Lemozy-Cadroy S, Crognier S, Gourdy P, et al. Intensified treatment of type 1 diabetes: prospective evaluation at one year of a therapeutic patient education programme. Diabetes & metabolism 2002; 28(4 Pt 1): 287.
- Humayun MA, Jenkins E, Knott J, et al. Intensive structured education for type 1 diabetes management using BERTIE: Long-term follow-up to assess impact on glycaemic control and quality of life indices. Diabetes Res Clin Pract 2018; 143: 275-81.
- Hermanns N, Kulzer B, Ehrmann D, Bergis-Jurgan N, Haak T. The effect of a diabetes education programme (PRIMAS) for people with type 1 diabetes: Results of a randomized trial. Diabetes Res Clin Pract 2013; 102(3): 149-57.
- Ehrmann D, Bergis-Jurgan N, Haak T, Kulzer B, Hermanns N. Comparison of the Efficacy of a Diabetes Education Programme for Type 1 Diabetes (PRIMAS) in a Randomised Controlled Trial Setting and the Effectiveness in a Routine Care Setting: Results of a Comparative Effectiveness Study. PLoS One 2016; 11(1): e0147581.
- Ehrmann D, Kulzer B, Schipfer M, Lippmann-Grob B, Haak T, Hermanns N. Efficacy of an Education Program for People With Diabetes and Insulin Pump Treatment (INPUT): Results From a Randomized Controlled Trial. Diabetes Care 2018.
- Bergis D, Ehrmann D, Albrecht C, Haak T, Kulzer B, Hermanns N. Comparison of the efficacy of an education program for people with diabetes and insulin pump treatment (INPUT) in a randomized controlled trial setting and the effectiveness in a routine care setting: Results of a comparative effectiveness study. Patient Educ Couns 2019.

Table 1: Sample characteristics

Data are mean (SD) or n (%)	All	Without Ketosis	With Ketosis	p
N	760 (100%)	718 (94.5%)	42 (5.5%)	
Age (years)	45.0 (14.0)	45.1 (14.0)	44.0 (14.0)	0.644
Sex				0.726
Male	342 (45%)	322 (44.9%)	20 (47.6%)	
Female	418 (55%)	396 (55.1%)	22 (52.4%)	
Education (years)	11.6 (2.5)	11.6 (2.5)	11.7 (2.7)	0.727
BMI (kg/m²)	27.1 (5.3)	27.0 (5.3)	27.9 (5.5)	0.284
Insulin therapy				0.006
Multiple insulin injections	278 (37%)	270 (37.6%)	8 (19%)	
Insulin pump therapy	482 (63%)	448 (62.4%)	34 (81%)	
Duration of diabetes (years)	20.5 (13.6)	20.5 (13.7)	20.5 (12.1)	0.989
HbA1c (central laboratory)				0.244
mmol/mol	65 (13.1)	65 (12.0)	67 (14.2)	
%	8.1 (1.2)	8.1 (1.1)	8.3 (1.3)	
Previous ketosis				<0.001
No	696 (91.6%)	669 (93.2%)	27 (64.3%)	
Yes	64 (8.4%)	49 (6.8%)	15 (35.7%)	
Depressive symptoms (range: 0 – 60)	14.5 (9.0)	14.3 (8.9)	17.3 (9.6)	0.036
Participation in self-management education program				0.030
No	199 (26.2%)	182 (25.3%)	17 (40.5%)	
Yes	561 (73.8%)	536 (74.7%)	25 (59.5%)	

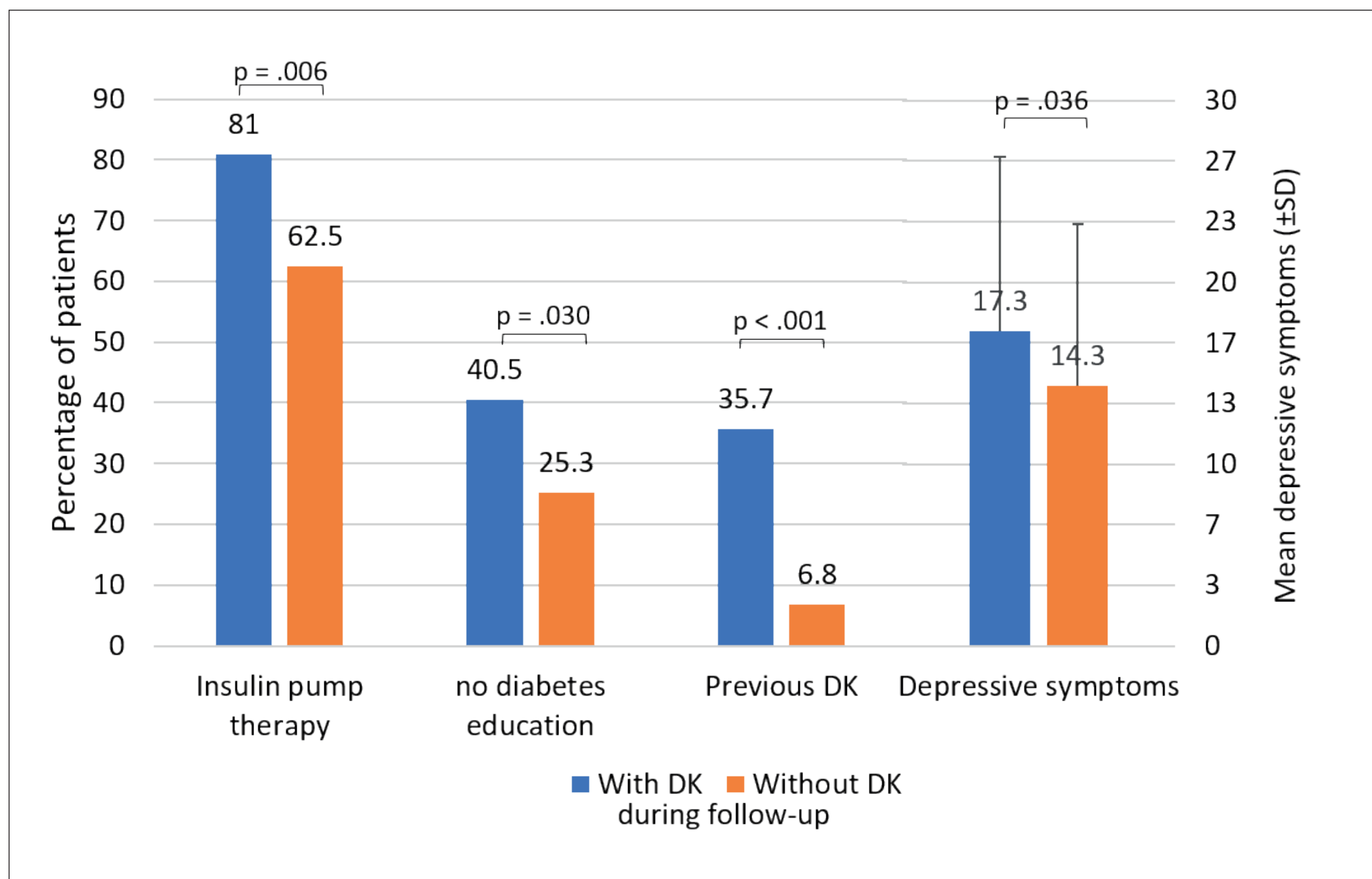


Figure 1: Differences between participants with a diabetic ketosis during follow-up vs. without diabetic ketosis at follow-up

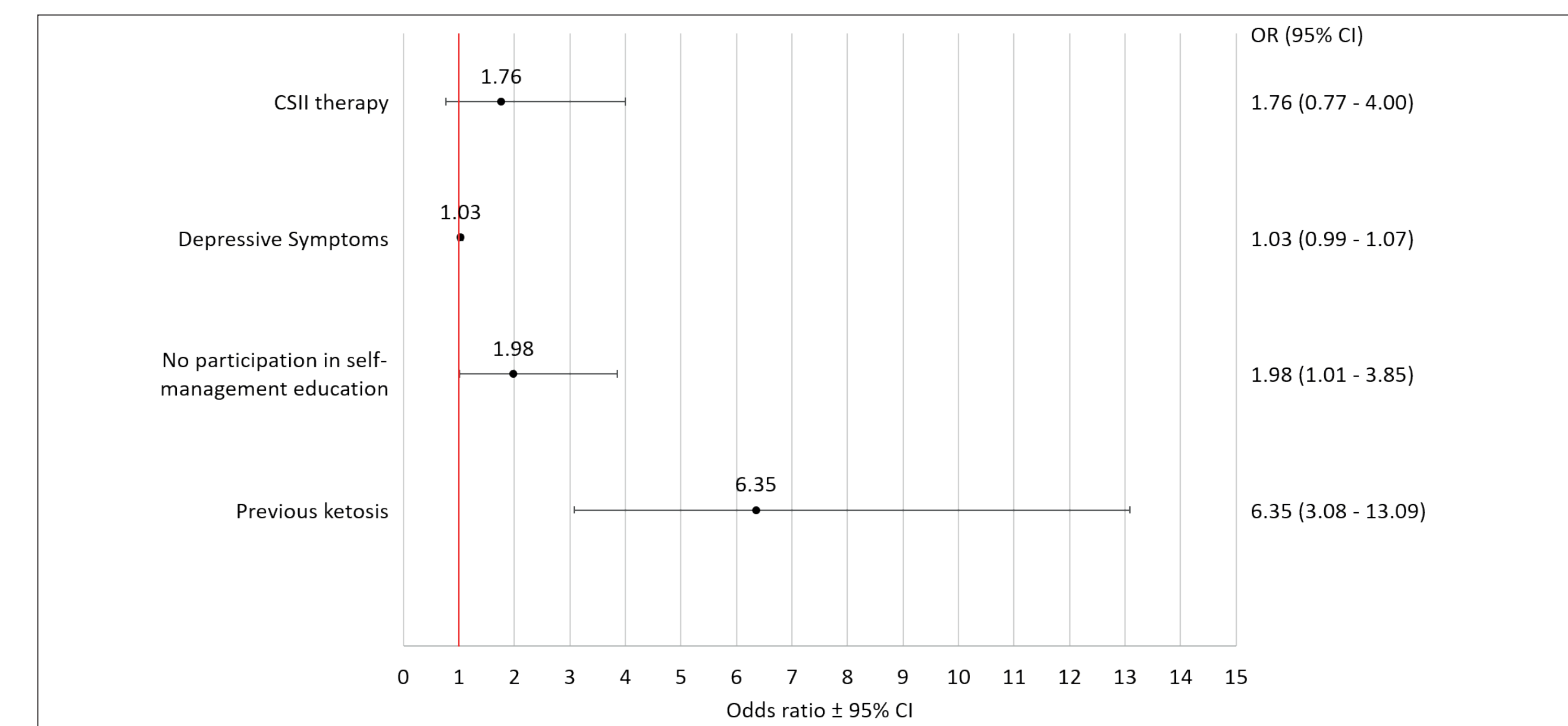


Figure 2: Logistic regression analysis on prediction of diabetic ketosis during follow-up

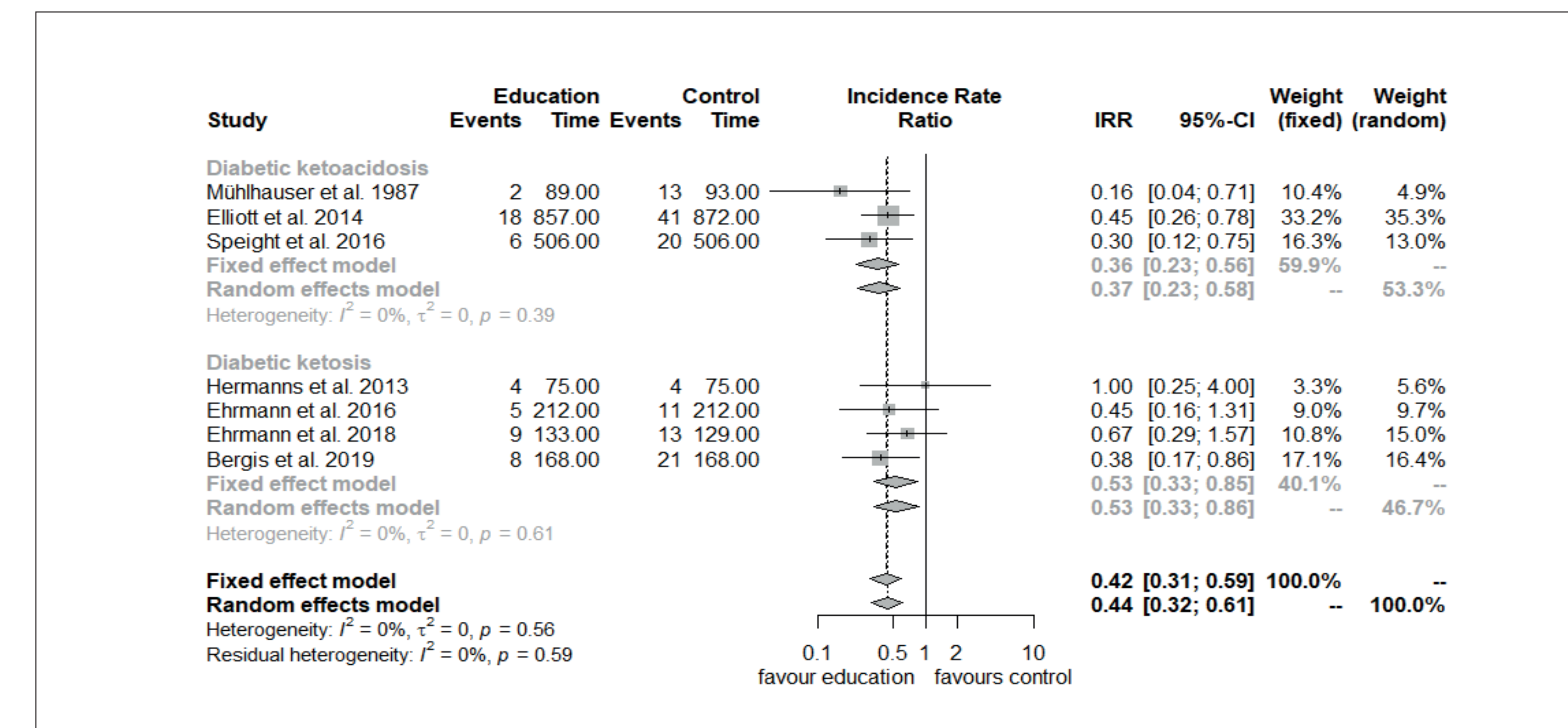


Figure 3: Meta-analysis of number of affected persons and the effect of structured diabetes education (Events refers to persons ≥ 1 event; time refers to number of persons in total; Fixed effect model: Mantel-Haenszel; Random effects model: DerSimonian-Laird; IRR = Incidence Rate Ratio; CI Confidence interval)

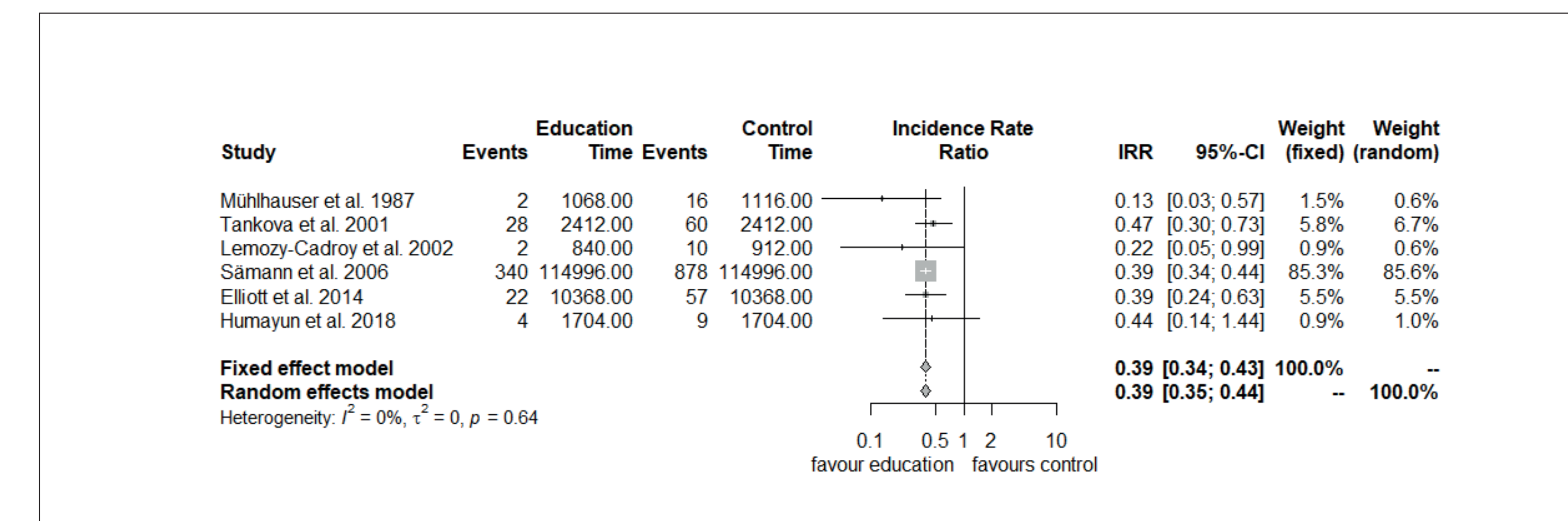


Figure 4: Meta-analysis of incidences of diabetic ketoacidosis and the effect of structured diabetes education (time refers to person-months; Fixed effect model: Mantel-Haenszel; Random effects model: DerSimonian-Laird; IRR = Incidence Rate Ratio; CI Confidence interval)

Contact Information

FIDAM - Diabetes Research Institute
Prof. Dr. Bernhard Kulzer
97980 Bad Mergentheim, Germany
kulzer@fidam.de

