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Feasibility of Safety System within a Novel Personalised Decision Support Tool

The Patient Empowerment Through Predictive Personalised Decision Support (PEPPER) Study

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Declaration of Interest

- No conflicts of interest

- Project Funding: European Union's Horizon 2020 (Grant No 689810)

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Type 1 Diabetes

- Globally, 400 million people with diabetes; 5-10% with Type 1 diabetes
- Insulin treatment:
  - MDI (Basal-bolus regime) or
  - CSII (Insulin pump)

- In UK, structured education with CHO counting effective, but only ~27% achieve HbA1c <58mmol/mol
- Complex insulin dose calculation at mealtimes

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Patient Empowerment Through Predictive Personalised Decision Support (PEPPER)

- Six European partners
- €3.8m European Union Horizon H2020 project
- Multidisciplinary (clinicians, nurses, engineers, computer scientists)

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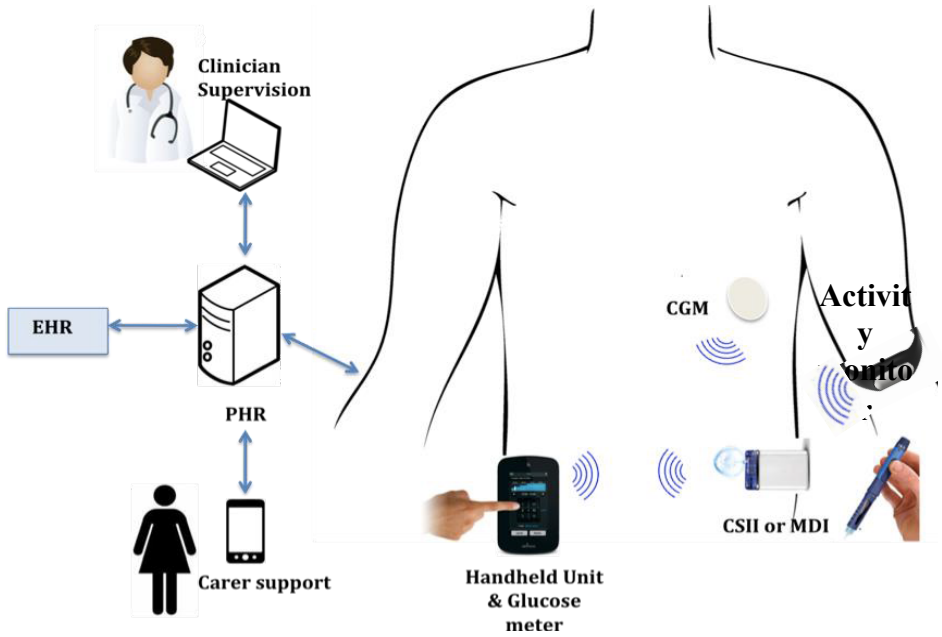
PEPPER Architecture



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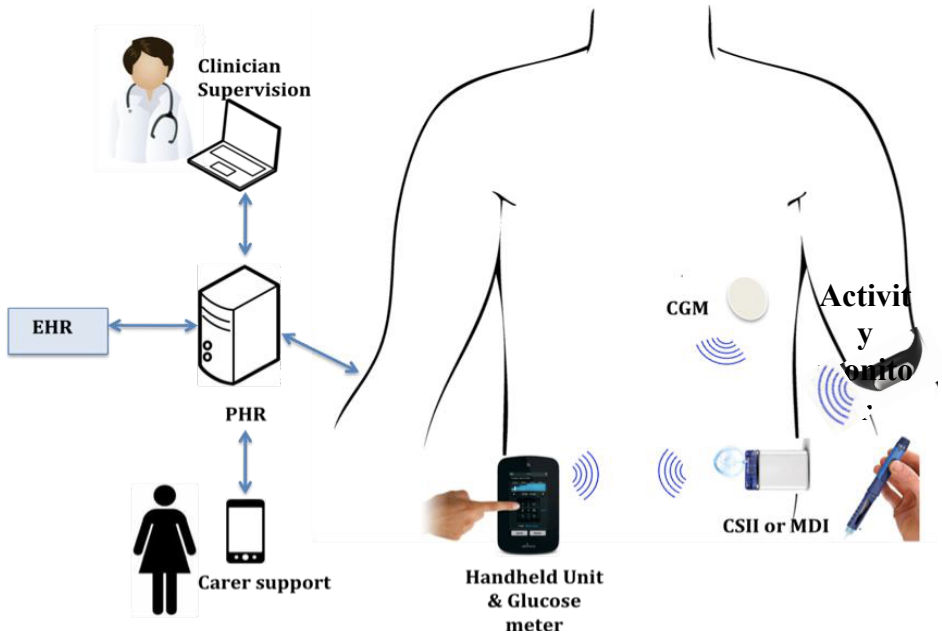
PEPPER Architecture



Two components:

- Safety system
- Intelligent insulin bolus calculator based on artificial intelligence

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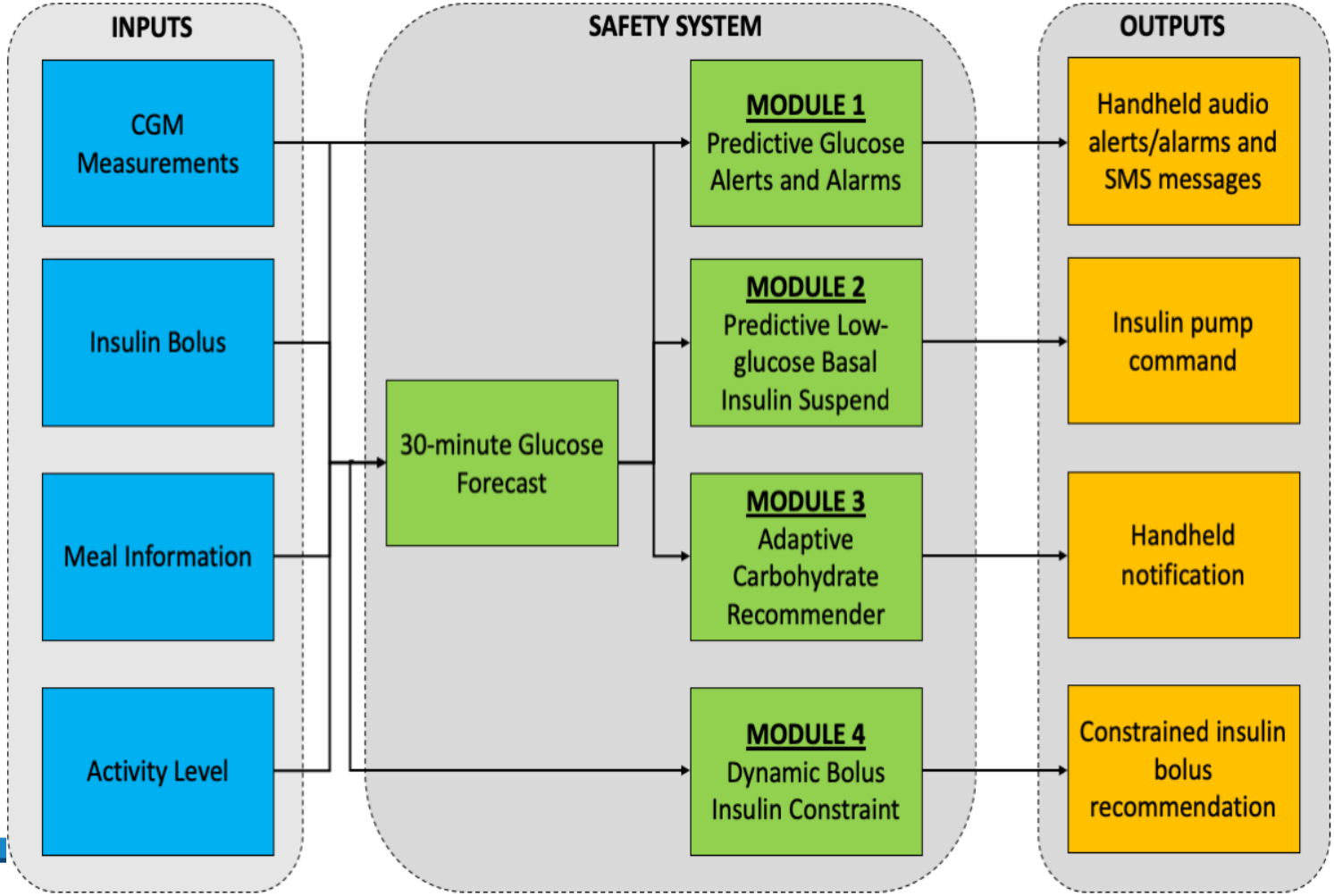
PEPPER: Safety System



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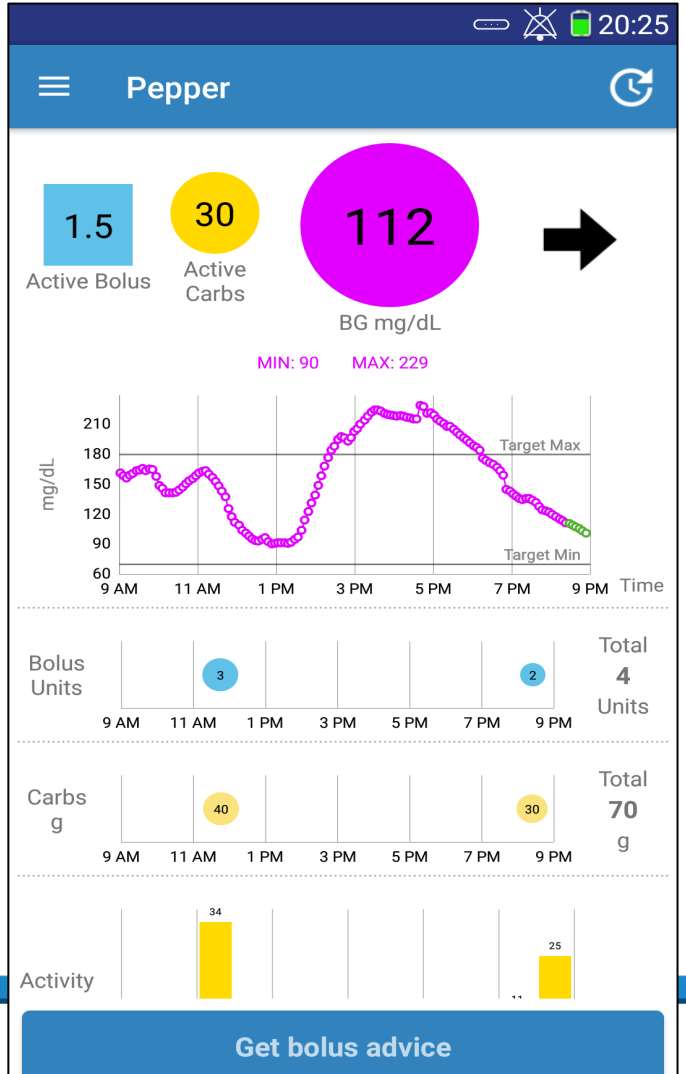

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PEPPER Clinical Platform

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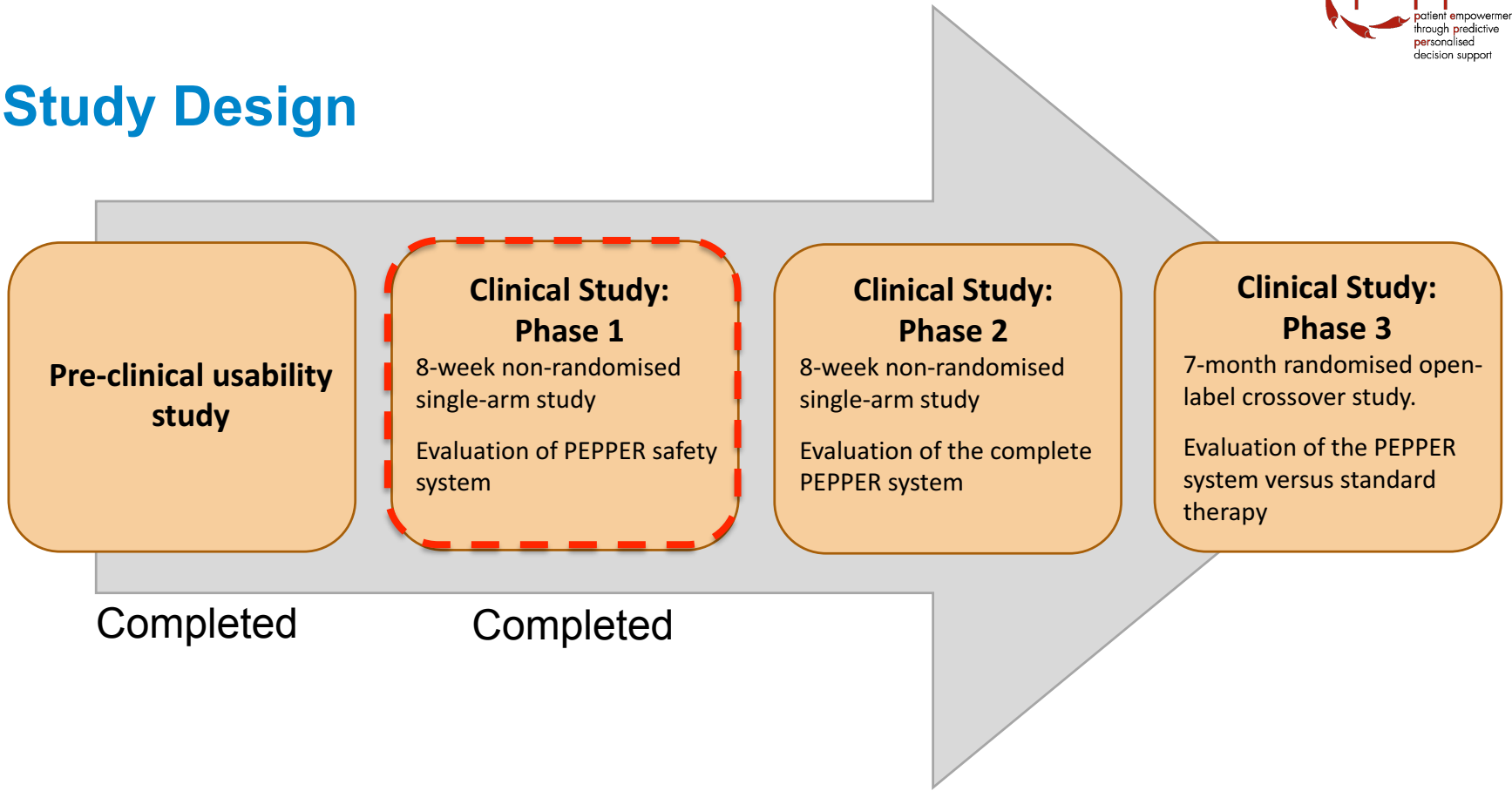
Study Design



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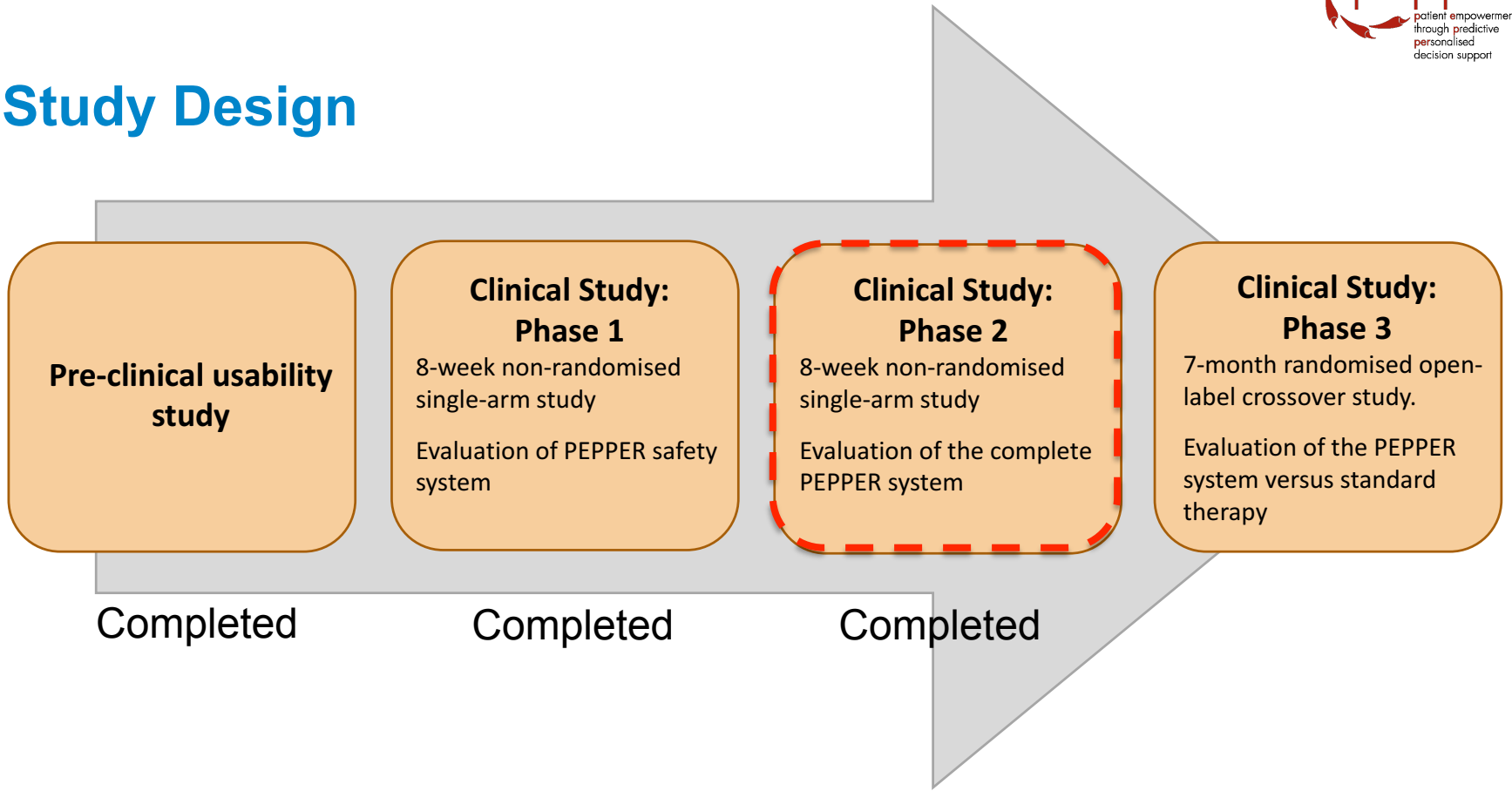

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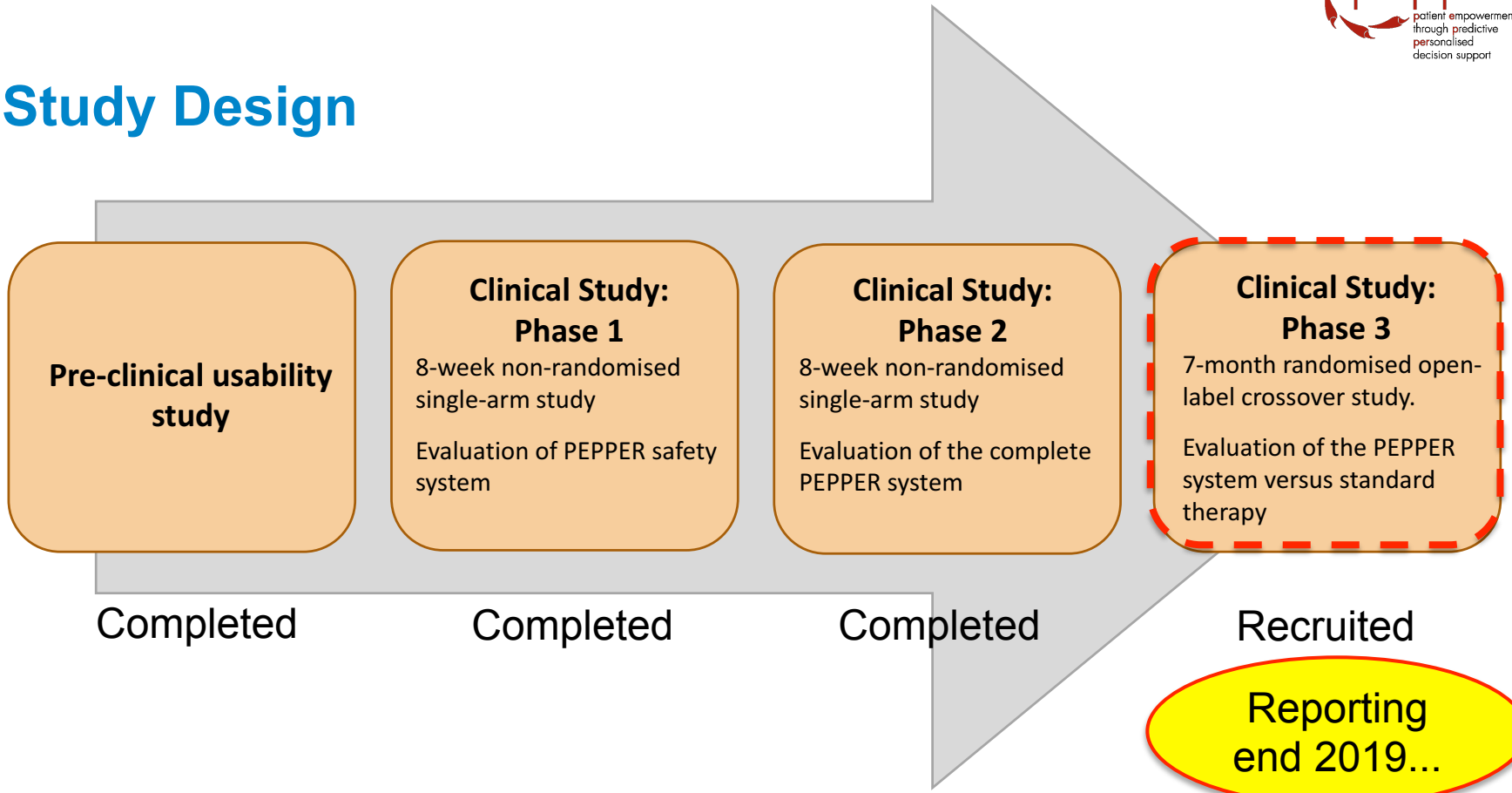

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Phase 1: Aims & Objectives

Non-randomised, open label study (8 weeks)
n=15 pump and MDI (ICL & IDIBGI participants)

Aim: To assess the safety and usability of the PEPPER system.

Primary outcome: % time in hypoglycaemia ($<3.9 mmol/l$)

Secondary outcomes:
Other glycaemic outcomes
Safety system outcomes
Quality of life (QoL) questionnaire scores

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Inclusion Criteria

- >18 years of age
- Type 1 diabetes > 1 years
- On MDI or CSII > 6 months
- HbA1c: 48-86mmol/mol
- Structured education

Exclusion Criteria

- Severe hypoglycaemia in last 6 months
- DKA in last 6 months
- Use of regular acetaminophen
- Pregnant or planning pregnancy
- Breastfeeding
- Enrolled in other clinical trials
- Have active malignancy or under investigation for malignancy
- Severe visual impairment
- Reduced manual dexterity

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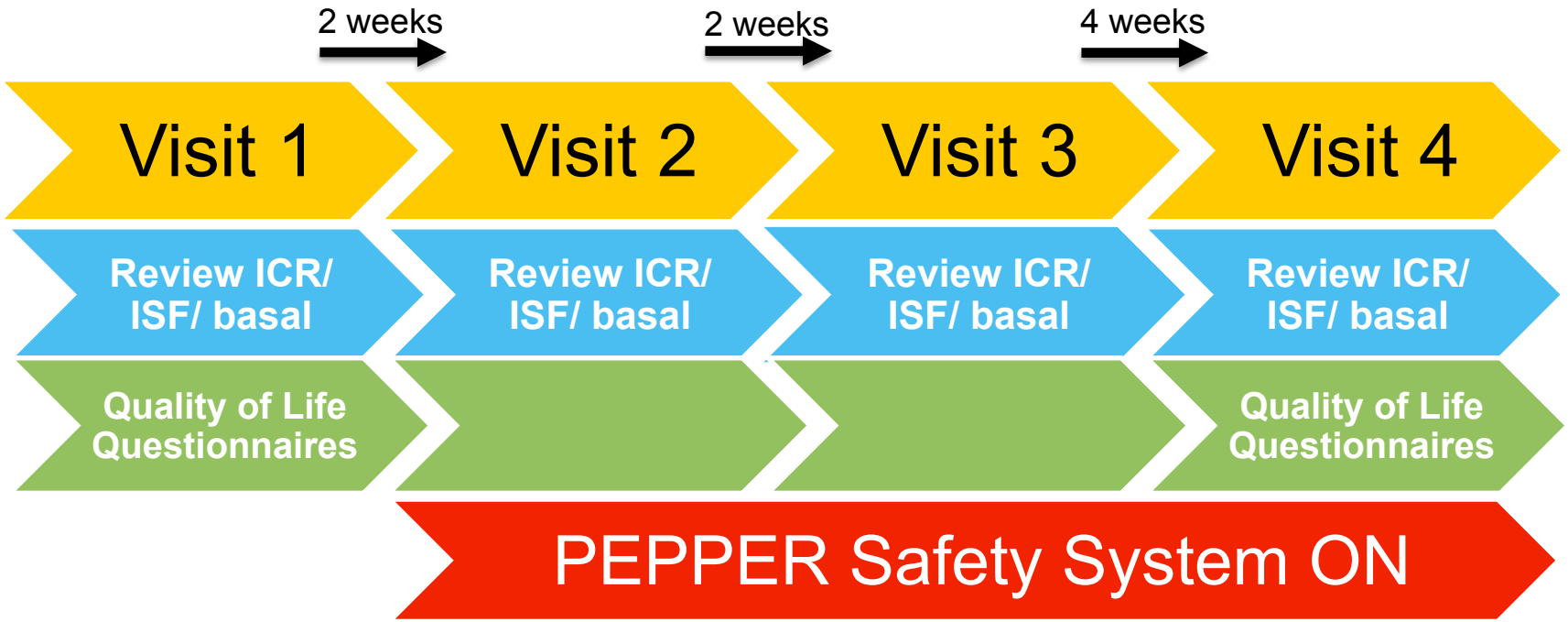
Methods



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Feasibility data for Phase 1 in MDI participants

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Baseline characteristics

Demographics	Median (IQR) (n=8)
Gender (male:female)	3:5
Age (years)	37.5 (31.8-53.3)
BMI (kg/m^2)	23.8 (23.2-27.5)
Duration of diabetes (years)	22.5 (18.0-26.5)
Gold score	2.0 (1.75-2.25)
HbA1c (mmol/mol)	63 (57-66)
Number of CBG measurements per day	3.5 (2-5)

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Glycaemic outcomes

	Run-in (n=6) Weeks 1 & 2	Endpoint (n=6) Weeks 7 & 8	P-value
% time in hypoglycaemia			
<3.9mmol/l	3.7 (1.6 - 6.4)	2.7 (0.9 - 7.3)	0.15
<3.3mmol/l	1.8 (0.7 - 3.6)	0.8 (0.0 - 1.5)	0.05
<3.0mmol/l	0.8 (0.1 - 4.8)	0.3 (0.0 - 0.9)	0.02

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% time in target			
3.9-10.0mmol/l	52.8 (38.3 - 61.5)	61.3 (47.5 - 71.7)	0.03

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% time in target			
3.9-10.0mmol/l	52.8 (38.3 - 61.5)	61.3 (47.5 - 71.7)	0.03
% time in hyperglycaemia			
>10.0mmol/l	44.3 (37.3 - 57.8)	33.8 (27.5 - 49.2)	0.09

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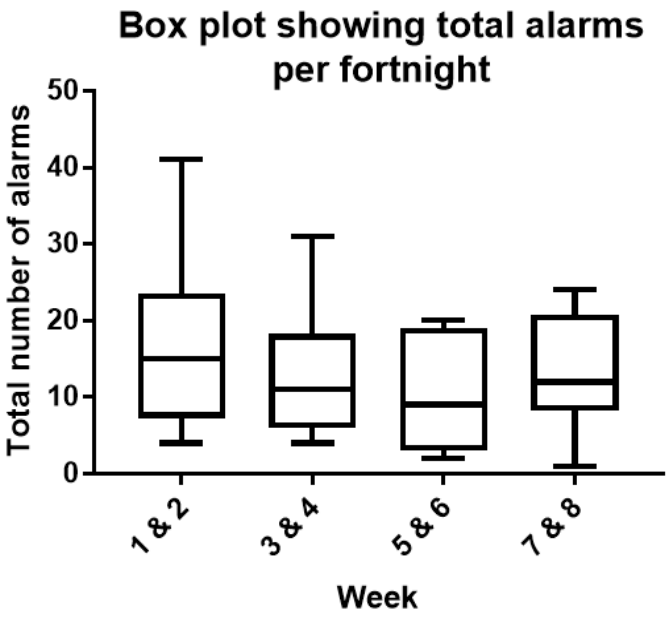
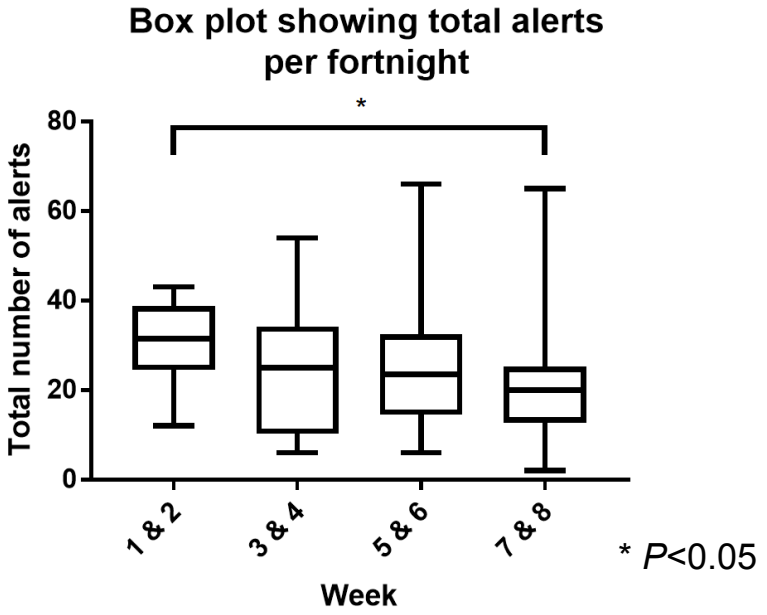
Safety System outcomes





* $P<0.05$

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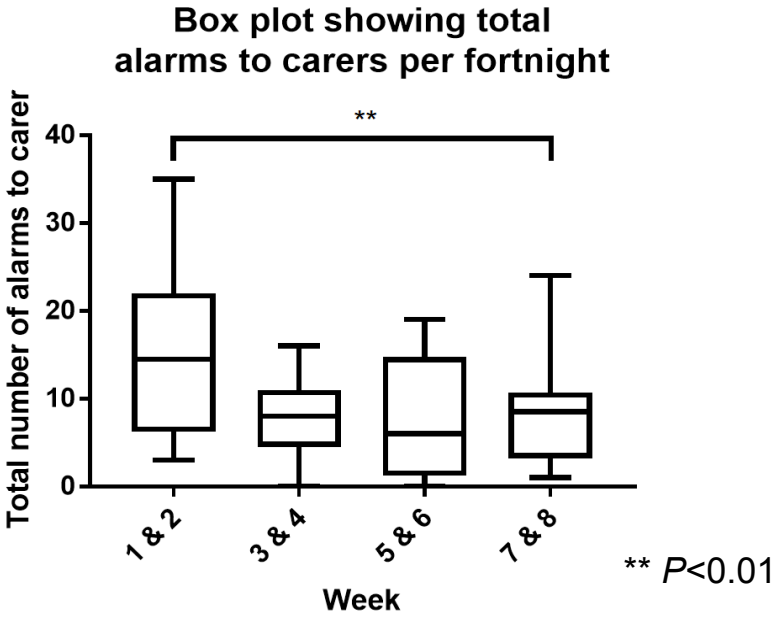

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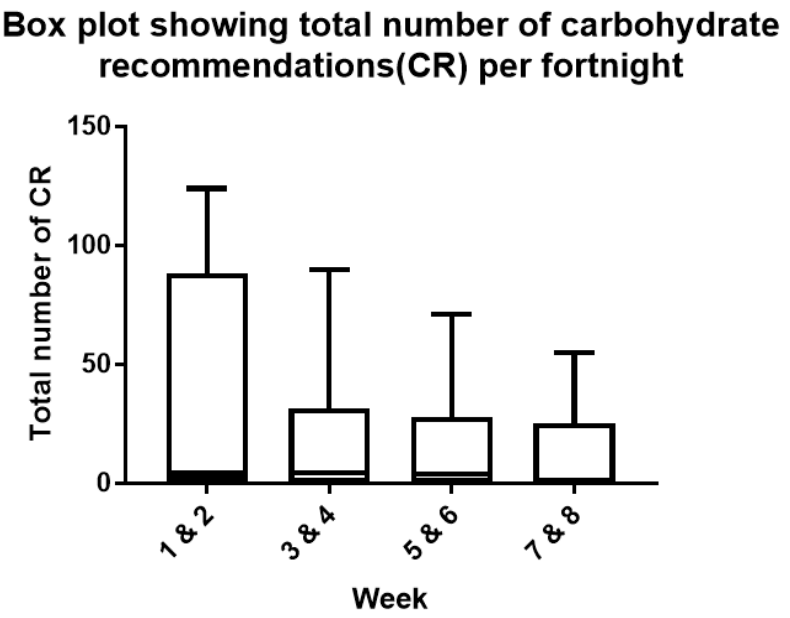

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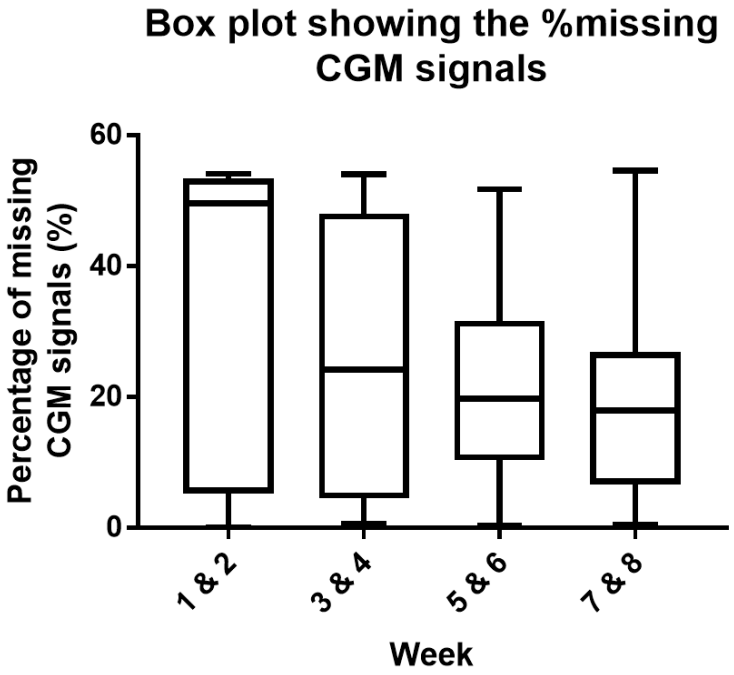
Data loss



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Quality of Life

Quality of life questionnaire	Baseline score	Endpoint score	P-value
PAID	30.6 (22.8-50.0)	38.1 (25.0-52.3)	0.84
DQOL	34.1 (28.7-47.3)	33.3 (32.0-50.8)	0.20

PAID: Problem Area in Diabetes
DQOL: Diabetes Quality of Life

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Discussion

Glycaemic outcomes

- Reduction % time in hypoglycaemia
- Significant increase in % time in target

Safety system

- Significant reduction in number of alerts
- Reduction in number of carbohydrate recommendations, alarms to carers
- Reduction in % of missing CGM data

Quality of Life questionnaires

- No significant change

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Study Limitations

- Small participant numbers
- Selection bias
- Short follow up period
- CGM effect
- CGM data loss
- Alert thresholds changed during the study

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Conclusion

- Proof of concept study
- Feasibility and safety of the PEPPER safety system in MDI participants
- Data suggests PEPPER safety system has the potential to enable improvements in hypoglycaemia and time in range.

- Future directions:
  - Phase 2: assess artificial intelligence component
  - Phase 3: assess PEPPER system vs. standard therapy

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Phase 1 Pump Glycaemic Outcomes

	Run-in Weeks 1 & 2	SS – Low Glucose Weeks 3 & 4	SS + Low Glucose Weeks 7 & 8	P-value
% time in hypoglycaemia				
<3.9mmol/l	3.8 (3.7 – 4.0)	1.4 (1.3 - 2.3)	0.6 (0.6 – 1.9)	**0.04**
<3.3mmol/l	0.9 (0.8 – 1.2)	0.5 (0.5 – 0.8)	0.4 (0.2 – 0.7)	0.08
<3.0mmol/l	0.5 (0.4 – 0.9)	0.4 (0.3 - 0.5)	0.3 (0.2 - 0.5)	0.15
% time in target				
3.9-10.0mmol/l	77.3 (75.6 – 85.4)	74.3 (65.2 – 84.3)	76.1 (66.1 - 84.7)	1.00
% time in hyperglycaemia				
>10.0mmol/l	18.5 (11.0 – 20.0)	24.3 (14.4 – 32.5)	23.3 (14.7 - 32.0)	0.77

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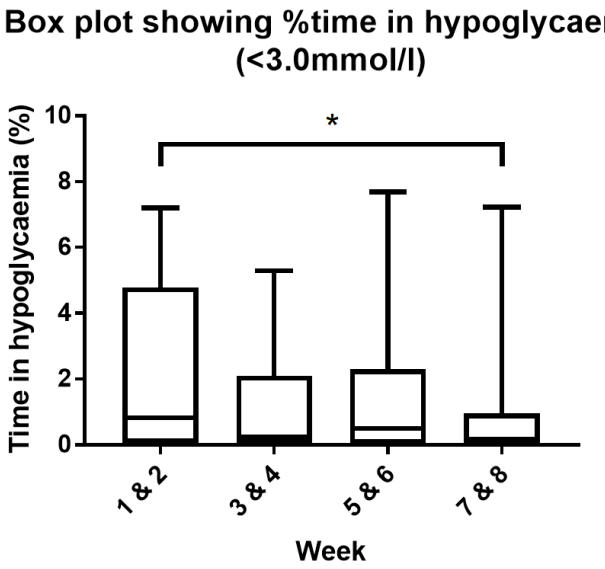
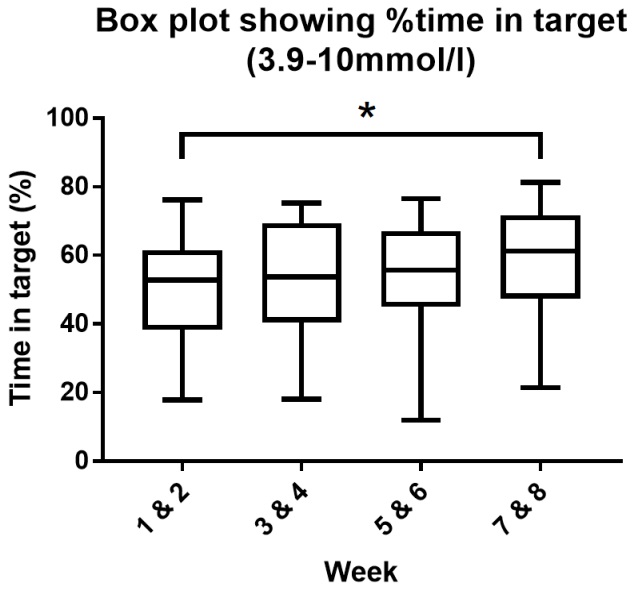
Glycaemic outcomes





* *P*<0.05