Clinical outcomes of an integrated primary–secondary model of care for individuals with complex type 2 diabetes: a non-inferiority randomised controlled trial

Anthony W. Russell^{1,2} · Maria Donald¹ · Samantha J. Borg¹ · Jianzhen Zhang¹ · Letitia H. Burridge¹ · Robert S. Ware³ · Nelufa Begum¹ · H. David McIntyre¹ · Claire L. Jackson¹

Received: 17 April 2018 / Accepted: 5 September 2018 / Published online: 3 October 2018

© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Abstract

Aims/hypothesis The aim of the study was to determine if a Beacon model of integrated care utilising general practitioners (GPs) with special interests could achieve similar clinical outcomes to a hospital-based specialist diabetes outpatient clinic.

Methods This pragmatic non-inferiority multisite randomised controlled trial assigned individuals with complex type 2 diabetes to care delivered by a Beacon clinic or to usual care delivered by a hospital outpatient department, in a 3:1 ratio. Owing to the nature of the study, researchers were only blinded during the allocation process. Eligible participants were aged 18 or over, had been referred by their usual GP to the hospital central referral hub with type 2 diabetes and had been triaged to be seen within 30 or 90 days. The intervention consisted of diabetes management in primary care by GPs with a special interest who had been upskilled in complex diabetes under the supervision of an endocrinologist. The primary outcome was HbA_{1c} at 12 months post-recruitment. The non-inferiority margin was 4.4 mmol/mol (0.4%). Both per-protocol and intention-to-treat analyses are reported.

Results Between 27 November 2012 and 14 July 2015, 352 individuals were recruited and 305 comprised the intention-to-treat sample (71 in usual care group and 234 in the Beacon model group). The Beacon model was non-inferior to usual care for both the per-protocol (difference −0.38 mmol/mol [95% CI −4.72, 3.96]; −0.03% [95% CI −0.43, 0.36]) and the intention-to-treat (difference −1.28 mmol/mol [95% CI −5.96, 3.40]; −0.12% [95% CI −0.55, 0.31]) analyses. Non-inferiority was sustained in a sensitivity analysis at 12 months. There were no statistically or clinically significant differences in the secondary outcomes of BP, lipids or quality of life as measured by the 12 item short-form health survey (SF-12v2) and the diabetes-related quality of life (DQoL-Brief) survey. Safety indicators did not differ between groups. Participant satisfaction on the eight-item client satisfaction questionnaire (CSQ-8) was good in both groups, but scores were significantly higher in the Beacon model group than the usual care group (mean [SD] 28.4 [4.9] vs 25.6 [4.9], respectively, $p < 0.001$).

Conclusions/interpretation In individuals with type 2 diabetes, a model of integrated care delivered in the community by GPs with a special interest can safely achieve clinical outcomes that are not inferior to those achieved with gold-standard hospital-based specialist outpatient clinics. Individuals receiving care in the community had greater satisfaction. Further studies will determine the cost of delivering this model of care.

Trial registration Australian New Zealand Clinical Trials Registry ACTRN12612000380897

Funding The study was funded by the Australian National Health and Medical Research Council (GNT1001157).

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00125-018-4740-x>) contains peer-reviewed but unedited supplementary material, which is available to authorised users.

✉ Anthony W. Russell
Anthony.Russell2@health.qld.gov.au

¹ Faculty of Medicine, The University of Queensland, Level 8, Health Sciences Building, Royal Brisbane and Women's Hospital, Herston, QLD 4006, Australia

² Department of Diabetes and Endocrinology, Princess Alexandra Hospital, Brisbane, QLD, Australia

³ Menzies Health Institute Queensland, Griffith University, Brisbane, QLD, Australia

Research in context

What is already known about this subject?

- Integrated clinical models of care with close cooperation between specialists and primary care providers are fundamental to future-ready healthcare systems strained by increasing human and economic costs associated with long-term conditions, including type 2 diabetes
- To date, mixed results have been reported in terms of the effectiveness of integrated models of care on clinical outcomes for individuals with type 2 diabetes; therefore, research evidence is required before implementation into healthcare systems

What is the key question?

- Can an integrated primary–secondary model of care achieve similar clinical outcomes to a hospital-based specialist diabetes outpatient clinic?

What are the new findings?

- The model of care was non-inferior for the primary clinical outcome, HbA_{1c}
- It achieved this without harm and with greater patient satisfaction

How might this impact on clinical practice in the foreseeable future?

- Given the international focus on care integration, our innovative model offers a viable alternative to hospital-based specialist care that could make an important contribution to the management of individuals with type 2 diabetes in metropolitan settings

Keywords General practitioners with special interest · Integrated care · Non-inferiority randomised controlled trial · Primary–secondary model of care · Type 2 diabetes

Abbreviations

CSQ-8	Eight-item client satisfaction questionnaire
DBP	Diastolic BP
DNE	Diabetes nurse educator
DQoL-Brief	Diabetes-related quality of life
GP	General practitioner
GPwSI	General practitioner with a special interest
HADS	Hospital anxiety and depression scale
IDA	Insulin dose adjustment
QoL	Quality of life
SBP	Systolic BP
SF-12v2	12-item short-form health survey

Introduction

Integrated care is at the forefront of healthcare reform internationally, in part driven by growing numbers of people living with chronic disease, and the understanding that better integrated care with close cooperation between specialists and primary care providers is fundamental to future-ready healthcare systems [1, 2]. This transformation in healthcare delivery appears vitally important for diabetes care. The number of people with diabetes is expected to reach 592 million by 2035 [3] and the direct annual global cost is already estimated at US\$827 billion per year [4].

In Australia, general practitioners (GPs) are diabetes patients' primary care providers, while complex diabetes often requires referral to hospital-based specialists. This impacts on hospital outpatient services, with increased waiting lists having negative implications for cost and outcomes and resulting in system fragmentation [5]. Our previously described and evaluated Beacon model offers an alternative to standard hospital outpatient review for individuals with complex type 2 diabetes [6]. This outpatient substitution model is vertically and fully integrated with primary care providers and specialists co-located in a comprehensive service for individuals with complex diabetes [7]. Care is delivered through a community-based general practice where GPs with a special interest (GPwSIs) and advanced training in diabetes work alongside an endocrinologist and diabetes nurse educator (DNE).

The proposed advantages of such integration that refocuses specialist and primary care services in integrated community-based healthcare are threefold: patient-centredness, effectiveness and cost-efficiency. Patient benefits include improved communication, clinic accessibility and satisfaction [8]. Evidence for the effectiveness of shared or integrated care for long-term conditions including diabetes is more equivocal, with trials reporting similar improvements in metabolic control when compared with conventional hospital-based specialist care [9]. Our interest, therefore, in integrated diabetes care is

less about identifying models superior to the status quo and more about investigating models that deliver non-inferior clinical outcomes but offer alternative benefits such as patient satisfaction and efficiency. In this study, we expanded our Beacon model research using a non-inferiority randomised controlled trial and report primary and secondary outcomes, including patient-reported outcomes and satisfaction with care.

Methods

Study design This non-inferiority randomised controlled trial was conducted across two hospitals and three intervention sites in Brisbane, Australia. A third hospital withdrew early in recruitment because of low referral rates of eligible participants. As a pragmatic trial, it was implemented within routine clinical practice. It investigated an integrated primary–secondary model of care (the Beacon model) for individuals with complex type 2 diabetes as an alternative to usual hospital-based specialist outpatient care. Hospital-based research staff enrolled participants. Randomisation was achieved through a bespoke secure internet-based randomisation program, designed by the study statistician. Researchers were masked only during the allocation process. A 3:1 allocation of intervention to usual care ensured a sustainable participant load and hence financially viable business model at intervention sites. Randomisation was stratified by the enrolling hospital.

Study authorisation was granted by the University of Queensland Medical Research Ethics Committee and the Metro South Health Service District Human Research Ethics Committee. The trial was registered (Australian New Zealand Clinical Trials Registry no. ACTRN12612000380897). Participants provided written informed consent. The study protocol was published in 2013 [10].

Participants Individuals referred by their GP to the diabetes outpatient clinic of either of the participating hospitals were assessed for eligibility. Eligible individuals were 18 years or over, triaged according to local health department guidelines as category 1 (seen within 30 days) or category 2 (seen within 90 days) (electronic supplementary material [ESM] Table 1), lived inside the study's geographical catchments and were referred in the past 12 months. The last criterion was modified to account for multiple referrals exceeding 12 months. Individuals were excluded if they were on haemodialysis, pregnant, had a terminal illness with a life expectancy of less than 2 years, were a transplant recipient, had attended a study site in the previous 12 months or were unable to give informed consent.

Organisation of care The intervention arm comprised a multidisciplinary team including two GPwSIs, an endocrinologist and a DNE co-located in a community-based general practice

that hosted 4 h weekly Beacon clinics. The Beacon model builds the capacity of primary care by allowing the DNE and GPwSIs their full scope of practice, with the single endocrinologist supervising and co-consulting with GPwSIs rather than seeing individuals individually. GPwSIs undertook a 23 h online advanced diabetes care course, attended a 1 day workshop and completed an examination. The DNE is specifically skilled in case co-ordination and comfortable working independently between clinics.

Individuals receiving the intervention presented for a 45 min screening appointment at which the DNE reviewed diabetic history, assessed feet, screened for depression [11] and took anthropometric measures. DNEs also organised appropriate blood and urine testing and, where on-site equipment was available, facilitated retinal photos prior to initial medical assessment. Subsequently, individuals were assessed by a GPwSI, and an individualised diabetes management plan was developed to address blood glucose control, BP and lipid control, diabetes complications, lifestyle factors and any other participant concerns. The endocrinologist then reviewed and endorsed the management plan and, if necessary, co-consulted with the individuals and the GPwSI. The management plan included, where appropriate, referrals to other disease-specific specialists, allied health professionals or to the insulin dose adjustment (IDA) service with the DNE for insulin titration or initiation. Medical reviews, usually 3 monthly, were conducted by the GPwSI and endocrinologist over the course of treatment. Individuals were discharged to their referring GP for ongoing diabetes management once individual clinical targets were deemed to have been met or at 12 months, whichever came first. The participant's regular GP was advised to continue the usual cycle of care and given guidance about conditions for re-referral.

Individuals receiving usual care were treated at the hospital-based specialist diabetes outpatient clinic to which they were referred, and were seen by an endocrinologist working within a hospital-based multidisciplinary team. Referrals to allied health professionals, specialists or the IDA service were directed as needed. The treatment plan and participant outcomes were communicated by letter to the referring GP.

Outcomes Data from participants' clinical records and questionnaires were collected at baseline and at 6 and 12 months. The primary outcome was HbA_{1c} at 12 months. Data were analysed in accordance with current conventions for non-inferiority trials, for both per-protocol (receiving allocated treatment for 12 months or until discharge after having met HbA_{1c}, BP and lipid targets) and intention-to-treat (analysed in the randomised group, regardless of treatment compliance) samples [12]. Secondary outcomes included biochemical end-points (total cholesterol, LDL-cholesterol, HDL-cholesterol, triacylglycerol, serum creatinine and estimated [e]GFR), clinical endpoints (BMI and BP), patient-reported outcomes and

satisfaction. Patient-reported outcomes included the 12-item short-form health survey (SF-12v2) of quality of life (QoL) [13]; and the diabetes-related QoL (DQoL-Brief) survey [14]. Participant satisfaction with care was measured at follow-up using the eight-item client satisfaction questionnaire (CSQ-8) [15] and a five-item participant assessment of self-management support [16]. Questionnaire data were available for 274 (90%) participants at baseline, 210 (69%) at 6 months and 187 (61%) at 12 months.

Referring GPs provided baseline HbA_{1c} measurements as per routine referral practice, repeat blood tests were requested if more than 4 weeks had elapsed between referral and the participant's first medical appointment. All blood tests, including HbA_{1c}, were performed at pathology laboratories and sent to the treating team. The treating team determined the frequency of HbA_{1c} testing, but it was typically at 3 monthly intervals, corresponding with medical reviews. For follow-up appointments, a 6 week window either side was accepted for HbA_{1c} and secondary outcomes. For participants who withdrew or were discharged before 12 months, outcome measures were sourced from the referring GP or directly through pathology laboratories where available.

Safety endpoints included hypoglycaemic events and anxiety or depression collected as self-reported questionnaire data at 6 and 12 months. Number of deaths was also noted. Hypoglycaemic symptoms (e.g. shakiness, pale skin, dizziness, confusion, sweating, weakness, and fainting) and major hypoglycaemic events (classified as a participant requiring the emergency services or being taken to, or admitted to, hospital) were assessed using items from the Hypo Awareness Questionnaire [17]. Insulin therapy is reported and interpreted as a concomitant indicator to the hypoglycaemic safety data. A Hospital Anxiety and Depression Scale [11] score above 15 on the anxiety or depression sub-scales was reported to and followed up by the clinical team.

Additional endpoints included the proportion of participants achieving clinical targets (HbA_{1c} ≤53 mmol/mol [7.0%]; systolic [S]BP ≤140 mmHg and diastolic [D]BP ≤90 mmHg; LDL-cholesterol <2 mmol/l; and targets combined), with BP and LDL-cholesterol values in line with current international guidelines [18, 19]. Pre-specified trial registration targets for BP and LDL-cholesterol (SBP ≤130 mmHg and DBP ≤80 mmHg; LDL-cholesterol ≤2.5 mmol/l) are dual reported. Total cholesterol is reported (<4.0 mmol/l). Occasions of service data including did-not-attend rates and referral data for the IDA service are also reported.

Statistical analyses The pre-defined non-inferiority margin of 4.4 mmol/mol (0.4%) was decided by a small group of clinical experts (A.W. Russell, H.D. McIntyre and C.L. Jackson), based on what was considered a clinically meaningful reduction in HbA_{1c}, taking into account the recommendation of the US Food and Drug Administration that 0.3–0.4% is an

acceptable non-inferiority margin [20]. A margin of 0.4% has been widely used in previous trials [21].

Sample size was based on pilot study findings using an SD of 18.6 mmol/mol (1.7%), the pre-specified non-inferiority margin and a true difference between the groups in HbA_{1c} at 12 months estimated to be −1.1 mmol/mol (−0.1%). Using a 3:1 allocation ratio, $\alpha = 0.05$ and 80% power, we required 364 participants to complete the study. Assuming a 20% attrition rate, the total sample size was calculated at 456. Owing to slower than expected participant enrolment in the first 18 months of the trial, an interim analysis was undertaken solely to confirm statistics used in the sample size calculation. This analysis was not pre-specified. Based on 6 month primary outcome data from 134 participants, the SD was revised to 15.1 mmol/mol (1.38%) and attrition to 25%. The revised total sample size was 335.

To assess the adequacy of randomisation, baseline characteristics were compared, with continuous variables presented as mean (SD) and categorical variables as frequency (%). The difference in HbA_{1c} between groups was assessed using linear regression, with treatment group as a fixed factor and baseline HbA_{1c} as a linear covariate for both the per-protocol and intention-to-treat samples. A sensitivity analysis was conducted using imputation. For the intention-to-treat sample, missing data were imputed using multivariate imputation and the initial analysis was re-run. Multiple imputation was undertaken using a chained equation approach, which assumes data are missing at random. The HbA_{1c} imputation model included all variables in the analysis model, as well the demographic, biochemical, clinical and patient-reported outcome variables that were univariably identified as being associated (at $p < 0.1$), with HbA_{1c} treated as missing using logistic regression [22]. The resulting imputation model included treatment group, baseline HbA_{1c}, age, education, total cholesterol, LDL-cholesterol, HDL-cholesterol, triage category and the mental health component of the SF-12v2. Fifty iterations were performed. All non-inferiority models were also conducted for differences between baseline and 6 month follow-up.

Secondary outcomes were analysed for the intention-to-treat sample without and with imputation, using the chained equation approach. The imputation model for the secondary outcomes included all variables in the analysis model as well as all secondary outcomes. Between-group differences for the secondary biochemical and clinical outcomes and patient-reported outcomes were assessed using linear regression with treatment group as a fixed factor and the baseline value of the outcome of interest as a linear covariate. Satisfaction with care measures were compared at 12 months using unpaired *t* tests. Binary safety data were assessed using logistic regression. Occasions of service data were analysed using either linear or logistic regression, depending on the outcome. Data analyses were conducted using Stata software v14.2 (StataCorp, College Station, TX, USA).

Results

Between November 2012 and July 2015, 869 referrals were assessed for eligibility, with 254 not meeting eligibility criteria and a further 263 declining to participate. Of the 352 eligible consenting individuals, 83 and 269 were randomised to usual care and intervention, respectively (Fig. 1). A further 32 participants (six usual care, 26 intervention) were excluded from the analysis as they dropped out of the trial before any data were collected for them, and five participants (two usual care, three intervention) were excluded as they were found to be ineligible (i.e. category 3 individuals). Four participants (one usual care, three intervention) died during the treatment phase and were excluded from analyses. Six participants (three per group) moved beyond the study catchment area before receiving follow-up care at 6 months. The per-protocol population (main primary outcome analysis) was confined to individuals who completed the 12 month study protocol or were discharged having met clinical targets, yielding a sample of 55 in usual care and 185 in the intervention (discharge HbA_{1c} was used for 15 participants who met clinical targets and were discharged before 12 months). The intention-to-treat population included 71 usual care participants and 234 intervention participants.

Baseline characteristics were similar across groups (Table 1): 61% were male (usual care 67.6%, Beacon model 59.4%); mean age was 55.7 years; and average duration of diabetes was 10 years. Diabetes complications were common,

with 17.6% diagnosed with stage 3 or higher kidney disease, 22% with known cardiovascular disorders and 22.9% with retinopathy. Baseline HbA_{1c} was 79.4 mmol/mol (9.4%) in the usual care group and 80.4 mmol/mol (9.5%) in the Beacon group. Educational status differed significantly, with intervention participants less likely to have completed high school.

The mean difference in HbA_{1c} between the two groups at study completion was −0.38 mmol/mol (95% CI −4.72, 3.96) (−0.03% [−0.43, 0.36]) for the per-protocol sample and −1.28 mmol/mol (−5.96, 3.40) (−0.12% [−0.55, 0.31]) for the intention-to-treat sample. The upper limit of the 95% CI fell below the pre-defined non-inferiority margin of 4.4 mmol/mol (0.4%) for both samples, as well as for the imputed model, satisfying the hypothesis that the Beacon model is non-inferior to usual care at 12 months (Fig. 2). Non-inferiority was confirmed at 6 months, with the exception of the imputed intention-to-treat model (ESM Fig. 1). Both treatments reduced HbA_{1c} post-baseline (Fig. 3). Most gain was made between baseline and 6 month follow-up, and HbA_{1c} reduction was sustained at 12 months for both groups. The proportions of participants meeting clinical targets at 12 months were similar between groups: 23% of the usual care group and 26% of the intervention group achieved an HbA_{1c} of 53 mmol/mol (7.0%) or less (Fig. 4).

Secondary outcomes were consistent across non-imputed (ESM Table 2) and imputed models (Table 2). A significant between-group difference was reported for eGFR (mean difference 3.42 ml min^{−1} [1.73 m]^{−2} [95% CI 0.23, 6.61], *p* =

Fig. 1 CONSORT diagram of recruitment and follow-up. ^aCategory 3 individuals. ^bOnly baseline data available (withdrawn prior to 6 months of treatment). ^cIncludes participants who: had two or more did-not-attend instances (diabetes care returned to their referring GP); were too busy or ill; moved out of the study catchment after 6 months of treatment; and were no longer interested or ceased attending the clinic

Table 1 Baseline characteristics

Characteristic	Usual care <i>n</i> = 71	Beacon <i>n</i> = 234
Demographic		
Male, <i>n</i> (%)	48 (67.6)	139 (59.4)
Age, years, mean (SD)	55.4 (12.1)	55.8 (11.3)
Duration of diabetes, years, mean (SD)	9.5 (7.8)	10.2 (8.1)
Education, <i>n</i> (%) ^a		
Did not complete secondary school	20 (31.2)	100 (45.7)
Completed secondary school	33 (51.6)	91 (41.5)
Tertiary qualifications	11 (17.2)	28 (12.8)
Biochemical		
HbA _{1c} , mean (SD)		
mmol/mol	79.4 (23.9)	80.4 (19.5)
%	9.4 (2.2)	9.5 (1.8)
Triacylglycerol mmol/l, mean (SD)	2.7 (2.9)	2.7 (2.8)
Total cholesterol mmol/l, mean (SD)	4.5 (1.5)	4.6 (1.3)
LDL-cholesterol mmol/l, mean (SD)	2.3 (1.0)	2.4 (1.0)
HDL-cholesterol mmol/l, mean (SD)	1.0 (0.3)	1.0 (0.3)
Serum creatinine mmol/l, mean (SD)	88.1 (32.5)	84.0 (46.7)
eGFR, ml min ⁻¹ [1.73 m] ⁻² , mean (SD)	77.1 (19.9)	79.5 (18.7)
Clinical		
Triage category, <i>n</i> (%)		
Category 1	13 (18.3)	42 (17.9)
Category 2	58 (81.7)	192 (82.1)
BMI for all participants, kg/m ² , mean (SD)	34.6 (8.8)	34.8 (7.2)
Male	34.4 (8.5)	33.3 (6.3)
Female	35.3 (9.8)	37.0 (7.9)
SBP, mmHg, mean (SD)	134.9 (16.4)	132.2 (16.8)
DBP, mmHg, mean (SD)	79.0 (12.4)	78.6 (10.0)
Smoking, <i>n</i> (%)		
Past	21 (33.9)	55 (23.8)
Present	16 (25.8)	51 (22.1)
Never	25 (40.3)	125 (54.1)
Diabetes complications present, <i>n</i> (%)		
Microalbuminuria/macro/proteinuria	21 (37.5)	73 (38.4)
Chronic kidney disease ≥ stage 3	13 (21.3)	38 (16.7)
Retinopathy	17 (31.5)	43 (20.7)
Neuropathy	13 (20.0)	33 (14.5)
Foot ulcer ^a	3 (5.0)	11 (4.8)
Previous amputation ^a	2 (3.3)	0 (0.0)
Known cardiovascular disorders, <i>n</i> (%)		
Cardiovascular complication	18 (25.4)	49 (20.9)
CVA/mini stroke ^a	4 (5.6)	14 (6.0)
Patient-reported outcomes		
Diabetes-related QoL, mean (SD)	3.4 (0.7)	3.4 (0.7)
SF-12v2, physical component, mean (SD)	42.3 (8.3)	41.5 (10.4)
SF-12v2, mental component, mean (SD)	47.0 (10.2)	45.2 (11.2)
Safety measures		
Hypoglycaemic symptoms, past month, <i>n</i> (%)	21 (38.9)	84 (45.7)
Major hypoglycaemic event, past 6 months, <i>n</i> (%)	2 (3.5)	14 (6.6)
HADS, depression or anxiety score ≥ 15, <i>n</i> (%)	2 (3.6)	16 (8.3)

Intention-to-treat sample

Variables with missing data: 5 duration of diabetes; 12 education; 20 triacylglycerol; 14 total cholesterol; 53 LDL-cholesterol; 43 HDL-cholesterol; 58 serum creatinine; 16 eGFR; 9 BMI; 1 SBP; 1 DBP; 12 smoking; 59 microalbuminuria/macro/proteinuria; 16 chronic kidney disease; 43 retinopathy; 13 neuropathy; 14 foot ulcer; 14 previous amputation; 32 diabetes-related QoL; 35 SF-12v2 physical component; 34 SF-12v2 mental component; 48 hypoglycaemic symptoms; 37 major hypoglycaemic event past 6 months; 48 HADS

^a Expected count had fewer than five in one or more groups, Fisher's exact test used

**p* < 0.05

Fig. 2 Treatment difference, 95% CIs and non-inferiority margin for HbA_{1c} at 12 months. A 95% CI that lies entirely to the left of the non-inferiority margin of 4.4 mmol/mol (0.4%) indicates the new treatment is non-inferior. Treatment difference (95% CI): per-protocol, -0.38 (-4.72, 3.96); intention-to-treat, -1.28 (-5.96, 3.40); intention-to-treat, imputed, -0.37 (-5.06, 4.31). Error bars indicate 95% CIs. Treatment difference is intervention minus control. To convert values for HbA_{1c} to %, divide by 10.93. NI, non-inferiority

0.04). No statistical or clinical between-group differences were found for any other clinical secondary outcomes or for any patient-reported outcomes (diabetes-related QoL, physical and mental components of the SF-12v2). Both groups were mostly satisfied with the treatment received (CSQ-8), but participants in the Beacon group were significantly more satisfied (mean 28.4, SD 4.9) than the usual care group (mean 25.6, SD 4.9) ($p < 0.001$) and reported better self-management support ($p = 0.03$).

Safety indicators did not differ between the groups at either time point (Table 3). From baseline to participants' final medication adjustment (either at 12 months or discharge), use of insulin therapy (including insulin plus oral glucose-lowering agent combined therapy and insulin-only therapy) increased from 50.7% to 75.0% for usual care, and from 51.1% to 66.3% for participants in the Beacon group. Despite increases in insulin use in both groups, neither major hypoglycaemic events nor hypoglycaemic symptoms increased.

Occurrences of service data show Beacon participants had, on average, 4.1 (SD 1.4) doctor visits over the 12 month

follow-up period compared with 3.0 (SD 1.3) for the usual care group (Table 4). The mean number of DNE appointments was also greater in the Beacon model, 2.4 (SD 1.3) compared with 1.8 (SD 1.5). Duration of treatment until discharge was similar across the two treatment groups for the per-protocol sample. On average, participants receiving usual care attended 44.4 weeks of treatment and those receiving the Beacon intervention 47.0 weeks. Referrals to the IDA service were higher for the Beacon model, with 46.2% of participants referred to the service compared with 28.2% in usual care. Did-not-attend

Fig. 3 Change in mean HbA_{1c} across time. Intention-to-treat sample with imputation. Error bars indicate 95% CIs. White circles, usual care; black squares, Beacon model

Fig. 4 Percentage of participants who met clinical targets at 12 months. Intention-to-treat sample without imputation. Percentages shown represent current international clinical targets, introduced following the trial's registration: HbA_{1c} ≤53 mmol/mol (7.0%); systolic BP ≤140 mmHg + diastolic BP ≤90 mmHg; LDL-cholesterol <2 mmol/l; combined target. The proportion of participants who met the pre-defined target for BP (systolic BP ≤130 mmHg + diastolic BP ≤80 mmHg) was 34.7% for usual care and 44.7% for the Beacon model. The proportion of participants who met the pre-defined target for LDL-cholesterol (≤2.5 mmol/l) was 63.2% for usual care and 74.1% for the Beacon model. The proportion of participants who met the current international target for total cholesterol (<4.0 mmol/l) was 48.9% for usual care and 49.0% for the Beacon model. Green bars, usual care; yellow bars, Beacon model. LDL-C, LDL-cholesterol

Table 2 Secondary outcomes at 12 months

Outcome	Usual care <i>n</i> = 71	Beacon <i>n</i> = 234	Difference (95% CI)	<i>p</i> value
Biochemical, mean (SD)				
Total cholesterol (mmol/l)	4.3 (1.1)	4.2 (1.1)	−0.14 (−0.47, 0.19)	0.41
LDL-cholesterol (mmol/l)	2.3 (1.0)	2.1 (0.9)	−0.17 (−0.44, 0.09)	0.20
HDL-cholesterol (mmol/l)	1.0 (0.3)	1.0 (0.3)	0.04 (−0.03, 0.12)	0.25
Triacylglycerol (mmol/l)	2.4 (1.8)	2.4 (2.3)	0.11 (−0.68, 0.89)	0.79
Serum creatinine (mmol/l)	90.5 (35.5)	84.9 (40.9)	−2.85 (−9.53, 3.83)	0.40
eGFR (ml min ^{−1} [1.73 m] ^{−2})	74.1 (20.2)	79.2 (19.7)	3.42 (0.23, 6.61)	0.04
Clinical				
BMI (kg/m ²)	35.3 (8.3)	34.9 (6.9)	−0.70 (−1.70, 0.30)	0.17
SBP (mmHg)	131.4 (13.7)	131.3 (14.3)	−0.49 (−5.38, 4.39)	0.84
DBP (mmHg)	75.7 (9.7)	77.2 (8.7)	1.07 (−1.904, 4.04)	0.48
Patient-reported outcomes				
Diabetes-related QoL	3.6 (0.6)	3.7 (0.7)	0.12 (−0.04, 0.27)	0.14
SF-12v2, physical component	43.9 (10.4)	42.5 (11.3)	0.53 (−2.12, 3.18)	0.70
SF-12v2, mental component	46.1 (10.3)	45.6 (10.1)	−0.94 (−4.30, 4)	0.58
Satisfaction with care				
Client satisfaction questionnaire score ^a	25.6 (4.9)	28.4 (4.9)	2.73 (1.43, 4.03)	<0.001
Self-management support score ^b	69.0 (27.0)	76.4 (23.8)	7.36 (0.80, 13.92)	0.03

Intention-to-treat sample with imputation

^a Range 8–32, higher score is better^b Range 0–100, higher score is better

rates were highest (13.6%) for doctor appointments at usual care; all other did-not-attend rates were below 10%.

Discussion

The Beacon model of community-based integrated diabetes care for complex type 2 diabetes provided by upskilled GPs supported by a specialist endocrinologist was non-inferior to

usual care at specialist diabetes outpatients. Non-inferiority was achieved for the pre-specified outcome and maintained with a sensitivity analysis using a robust model for dealing with missing data. Although the mean HbA_{1c} achieved at 12 months was 67 mmol/mol (8.3%) and 68 mmol/mol (8.4%) in the Beacon model and usual care groups, respectively, this was a significant improvement from baseline and reflects the average HbA_{1c} (67 mmol/mol, SD 3.70 [8.3%, SD 1.9]) achieved in diabetes centres across Australia [23]. The

Table 3 Safety indicators by treatment group

Indicator	Usual care <i>n</i> = 71	Beacon <i>n</i> = 234	OR (95% CI)	<i>p</i> value
Hypoglycaemic symptoms, past month, <i>n</i> (%)				
6 month	22 (47.8)	76 (48.1)	1.0 (0.5, 2.0)	0.97
12 month	15 (37.5)	58 (40.9)	1.2 (0.6, 2.4)	0.70
Major hypoglycaemic event, past 6 months, <i>n</i> (%)				
6 month ^a	4 (8.7)	8 (4.9)	0.5 (0.2, 1.9)	0.34
12 month ^a	2 (5.0)	10 (7.0)	1.4 (0.3, 6.9)	0.65
Severe depression or anxiety (HADS ≥15), <i>n</i> (%)				
6 month ^a	2 (4.8)	7 (4.5)	0.9 (0.2, 4.7)	0.93
12 month ^a	2 (5.0)	9 (6.4)	1.3 (0.3, 6.3)	0.75

Variables with missing data: 101 hypoglycaemic symptoms 6 months; 123 hypoglycaemic symptoms 12 months; 97 major hypoglycaemic event 6 months; 123 major hypoglycaemic event 12 months; 103 severe anxiety or depression 6 months; 122 severe anxiety or depression 12 months

^a Expected count had fewer than five in one or more groups, Fisher's exact test used

Table 4 Occasions of service

Service	Usual care	Beacon	MD or OR (95% CI)	<i>p</i> value
Doctor visits per participant, mean (SD)	3.0 (1.3)	4.1 (1.4)	1.1 (0.7, 1.5)	<0.001
DNE visits per participant ^a , mean (SD)	1.8 (1.5)	2.4 (1.3)	0.5 (0.1, 0.9)	0.01
Average duration of treatment ^b , weeks (SD)	44.4 (18.8)	47.0 (14.5)	2.6 (−2.2, 7.3)	0.29
IDA referrals, <i>n</i> (%)	20 (28.2)	108 (46.2)	2.2 (1.2, 3.9)	0.008
DNA rate (%)				
Doctor appointments	13.6	9.0		
DNE appointments	4.8	3.6		

^a Includes screening appointment and any subsequent education^b Excludes individuals lost to follow-up

DNA, did-not-attend

difficulty in obtaining a better average HbA_{1c} indicates the complexity of individuals with long-standing diabetes and 50% insulin usage at baseline. Of the individuals in the study, 20–25% also had known cardiovascular and/or chronic kidney disease. The complexity is as expected, as ongoing management of the individuals was beyond the capacity of their usual GP, warranting referral to specialist diabetes services. We previously reported, in our non-randomised pilot study of the Beacon model, a significant improvement in HbA_{1c} compared with usual care [6]. Despite correction for differences in baseline HbA_{1c}, a greater reduction in HbA_{1c} can be obtained from a higher starting value [24]. Importantly, we have now demonstrated in a randomised controlled trial that this Beacon model of integrated care is non-inferior to the gold-standard care delivered by a hospital-based specialist diabetes outpatient clinic.

The intensification of blood glucose-lowering therapy increases the risk of hypoglycaemia. Insulin usage increased by 15.2% and 24.3% in the Beacon and usual care groups, respectively (no significant difference), with no increased rates of hypoglycaemia. There was no evidence of harm related to the Beacon model, with no increase in number of deaths (3/240 Beacon model vs 1/75 usual care) or progression of renal disease. Rather, there was a lower rate of renal decline favouring the Beacon model.

The microvascular, macrovascular and overall mortality benefits of a multifactorial intervention in type 2 diabetes management, addressing BP, lipids and glucose control, have been well documented in the Steno-2 study [25]. The Beacon model aimed to manage individuals' BP, lipids and glucose to target before discharge. At 12 months, there were no differences in BP or lipids between participants receiving usual care or the intervention. Compared with the Steno-2 study, the percentage of people achieving clinical targets in the Beacon and usual care groups was higher for HbA_{1c}, comparable for BP and lower for cholesterol [25].

Given the Beacon model has shown non-inferiority in terms of clinical outcomes, the benefits and translation of such

a model rely on demonstrating greater patient QoL, satisfaction and/or cost-effectiveness. In this study, the model of care under which participants were managed made no difference to their QoL as assessed with the SF-12v2 or DQoL-Brief. However, participants receiving the Beacon intervention reported higher satisfaction with care scores compared with usual care, although this difference was small; they also reported better self-management support. We previously explored individuals' views of the Beacon model via a qualitative sub-study [26]. Most participants found the experience enabling as it was convenient, flexible and provided prompt communication back to their usual GP. Participants also found clinicians collaborative, which improved engagement and motivation.

The average duration of treatment was similar between the Beacon model and usual care. However, occasions of service data differed between the groups. IDA referrals were more common for Beacon participants, explained in part by hospital processes whereby endocrinologists facilitated insulin stabilisation or participants undertook self-titration according to provided written algorithms, with neither of these captured as an IDA referral. The DNEs and supervising endocrinologists previously worked within the hospital outpatient clinics, ensuring consistent insulin management protocols across groups. A higher number of doctor and DNE visits with the Beacon model may reflect a more flexible model, featuring improved patient access and real-time follow-up, but also raises issues about cost. We previously reported costings of the pilot study, favouring the Beacon model despite twice the number of visits compared with usual care [27]. In other studies, integrated care in diabetes has been implemented at greater cost [28] or has been cost neutral [29]. A cost-minimisation analysis comparing the operating costs of the Beacon clinic with those of the hospital outpatient alternative is currently under way.

The World Health Organization recognises poor integration of primary, secondary and tertiary care results in reduced quality and inefficiency of healthcare as well as inconvenience to patients [30]. Evidence that integrated care leads to improved

clinical outcomes is limited, with systematic reviews inconsistently demonstrating clinical benefits [9, 31, 32]. Relevant to diabetes, three randomised controlled trials of primary–secondary integrated models have been conducted, looking at: combining upskilled GPs with practice visits by a DNE [33]; interdisciplinary diabetes team case discussions [28]; and a virtual clinic including a diabetes nurse and endocrinologist [34]. Similar to our trial, none of these integrated models demonstrated superior improvements in HbA_{1c} compared with usual care at 12–18 months' follow-up. Compared with these trials, all advanced diabetes care was managed in the Beacon clinic, and thus it is a true model of hospital outpatient avoidance.

There is no single form of integrated care; it is expressed and defined in a multitude of ways involving diverse elements and initiatives [7]. As such, disentangling the multi-components of the Beacon model and determining which aspects are most effective is difficult. It is a fully integrated vertical primary–secondary model of care that relies on co-location, co-consultation and care co-ordination. While integrated models differ in their scope and nature, one key element is the patient perspective [7]. Previous qualitative research based on patient appraisals identified the Beacon model as patient-centred and empowering, with patients valuing the supportive interpersonal communication and seeing themselves as part of the care team [26, 35].

In the UK, specialist outreach clinics improved access to specialist services and quality of healthcare, but at potentially higher cost depending on the number of individuals seen [36]. The Beacon model offers more than a specialist outreach clinic; it also emphasises the education and training of GPwSIs. Compared with the model of GPwSIs in the UK [29], the Beacon model ensures the endocrinologist continues to mentor and supervise the GPs and actively participates, where necessary, in a co-consultation with the individuals, ensuring the delivery of care remains at the quality of a specialist service. The Beacon model also amplifies skills, which the GPwSIs take back to their routine practice, so they become a referral point and source of knowledge for colleagues, potentially reducing referrals to specialist clinics.

The study has some limitations. The sustainability of the benefits is unknown, although from a clinical perspective most improvement in HbA_{1c} was achieved at 6 months and then maintained. The recruitment period was longer than expected, with an interim analysis performed to reassess the power calculations. The pragmatic nature of the trial can make it difficult to recruit and keep participants as well as to obtain all the required outcome data. There was a 57% participation rate with potential participation bias, and the response rate for the 12 month questionnaire was 61%. The primary outcome, HbA_{1c}, was not available for 15% of the intention-to-treat population, but this was managed with robust statistical modelling. The generalisability of the

results to other locations is unknown. The Beacon model is suitable for urban settings, where a relatively small number of Beacon practices can be established to serve a large population. It may be less relevant for rural and remote situations where a 'physician in the practice' model may be more feasible, with the endocrinologist holding case conferences with the GP [37].

We have published a case study on lessons learned and challenges with establishing Beacon clinics and emphasise the need for clinician leadership and adequate resourcing to facilitate the sustainability of the model [38]. Proactive planning improves GPwSI retention, and sustainability is enhanced by having a dedicated training position, in which a new GPwSI is trained every 12 months. The pilot Beacon site has now operated for more than a decade, an indication of the sustainability of the model. Sustainability is also reinforced with an appropriate business model required to fit within the local health system infrastructure, contractual and financial arrangements.

In summary, these results show a primary–secondary integrated model of care for the management of complex type 2 diabetes can be delivered in the community with similar clinical outcomes to those achieved in a hospital-based specialist diabetes outpatient clinic. It achieved this without harm but with greater patient satisfaction. Translation relies on successful implementation at other sites and application to other chronic diseases.

Acknowledgements The authors thank the clinical, administrative and managerial staff and participants at each of the study sites.

Data availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding This research was funded by the Australian National Health and Medical Research Council (NHMRC) under the Centre of Research Excellence in Quality and Safety in Integrated Primary–Secondary Care (Grant ID: GNT1001157).

Duality of interest The authors declare there is no duality of interest associated with this manuscript.

Contribution statement CLJ, AWR and HDM worked on the original idea, searched the published scientific literature and designed the methods; they were also senior clinical leads for the study implementation and contributed to data interpretation as well as revising the manuscript. MD, SJB and AWR wrote the first draft of the manuscript. MD also managed the research process and contributed to data management and interpretation. SJB also updated literature searches, undertook the data collection and contributed to data interpretation and the preparation of tables and figures. JZ and LHB contributed to research management, data collection and writing. NB conducted the data analyses supervised by the senior statistician RSW and both revised the manuscript. All authors read and approved the final submitted version. AWR is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

- Shortell SM, Addicott R, Walsh N, Ham C (2015) The NHS five year forward view: lessons from the United States in developing new care models. *BMJ* 350:h2005. <https://doi.org/10.1136/bmj.h2005>
- Winpenny EM, Miani C, Pitchforth E, King S, Roland M (2017) Improving the effectiveness and efficiency of outpatient services: a scoping review of interventions at the primary-secondary care interface. *J Health Serv Res Policy* 22:53–64. <https://doi.org/10.1177/1355819616648982>
- Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE (2014) Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract* 103:137–149. <https://doi.org/10.1016/j.diabres.2013.11.002>
- World Health Organization (2016) Global report on diabetes. WHO, Geneva
- Stainkey LA, Seidl IA, Johnson AJ, Tulloch GE, Pain T (2010) The challenge of long waiting lists: how we implemented a GP referral system for non-urgent specialist appointments at an Australian public hospital. *BMC Health Serv Res* 10(1):303. <https://doi.org/10.1186/1472-6963-10-303>
- Russell AW, Baxter KA, Askew DA, Tsai J, Ware RS, Jackson CL (2013) Model of care for the management of complex type 2 diabetes managed in the community by primary care physicians with specialist support: an open controlled trial. *Diabet Med* 30:1112–1121. <https://doi.org/10.1111/dme.12251>
- Shaw S, Rosen R, Rumbold B (2011) What is integrated care? Research report. Nuffield Trust, London
- Salisbury C, Noble A, Horrocks S (2005) Evaluation of a general practitioner with special interest service for dermatology: randomised controlled trial. *BMJ* 331:1441–1444. <https://doi.org/10.1136/bmj.38670.494734.7C>
- Smith SM, Cousins G, Clyne B, Allwright S, O'Dowd T (2017) Shared care across the interface between primary and specialty care in management of long term conditions. *Cochrane Database Syst Rev* 2:CD004910
- Zhang J, Burridge L, Baxter K, Donald M, Foster M, Hollingsworth S (2013) A new model of integrated primary-secondary care for complex diabetes in the community: a study protocol for a randomised controlled trial. *Trials* 14:382. <https://doi.org/10.1186/1745-6215-14-382>
- Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatr Scand* 67:361–370. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>
- Schumi J, Wittes JT (2011) Through the looking glass: understanding non-inferiority. *Trials* 12:106. <https://doi.org/10.1186/1745-6215-12-106>
- Saris-Baglama RN, Dewey CJ, Chisholm GB et al (2011) QualityMetric health outcomes™ scoring software 4.5 user's guide. QualityMetric Incorporated, Lincoln, RI, USA
- Burroughs TE, Desikan R, Waterman BM, Gilin D, McGill J (2004) Development and validation of the diabetes quality of life brief clinical inventory. *Diabetes Spectr* 17:41–49. <https://doi.org/10.2337/diaspect.17.1.41>
- Attkisson CC, Greenfield TK (2004) The UCSF Client Satisfaction Scales: 1. The Client Satisfaction Questionnaire-8. The use of psychological testing for treatment planning and outcome assessment. Lawrence Erlbaum Associates, Mahwah, NJ, pp 799–811
- Sequist TD, von Glahn T, Li A, Rogers WH, Safran DG (2009) Statewide evaluation of measuring physician delivery of self-management support in chronic disease care. *J Gen Intern Med* 24:939–945. <https://doi.org/10.1007/s11606-009-1033-6>
- Speight J (2010) The Hypo Awareness Questionnaire. Available from www.ahpresearch.com/. Accessed 29 Mar 2010
- de Boer IH, Bangalor S, Benetos A et al (2017) Diabetes and hypertension: a position statement by the American Diabetes Association. *Diabetes Care* 40:1273–1284. <https://doi.org/10.2337/dci17-0026>
- National Vascular Disease Prevention Alliance (2012) Guidelines for the management of absolute cardiovascular disease risk. Available from www.heartfoundation.org.au/images/uploads/publications/Absolute-CVD-Risk-Full-Guidelines.pdf. Accessed 8 Aug 2018
- U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (2008) Guidance for industry. Diabetes Mellitus: developing drugs and therapeutic biologics for treatment and prevention. Available from www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071624.pdf. Accessed 8 Aug 2018
- Johansen MY, MacDonald CS, Hansen KB et al (2017) Effect of an intensive lifestyle intervention on glycemic control in patients with type 2 diabetes. *JAMA* 318:637–646. <https://doi.org/10.1001/jama.2017.10169>
- White IR, Royston P, Wood AM (2011) Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 30:377–399. <https://doi.org/10.1002/sim.4067>
- Australian National Diabetes Audit (2016) Australian Quality Self-Management Audit final report. Available from www.nadc.net.au/wp-content/uploads/2016/04/ANDA-AQSMA-2016-Final-Report-Dec.pdf. Accessed 8 Aug 2018
- Esposito K, Chiodini P, Bellastella G, Maiorino MI, Giugliano D (2012) Proportion of patients at HbA_{1c} target <7% with eight classes of antidiabetic drugs in type 2 diabetes: systematic review of 218 randomized controlled trials with 78 945 patients. *Diabetes Obes Metab* 14:228–233. <https://doi.org/10.1111/j.1463-1326.2011.01512.x>
- Gaede P, Lund-Andersen H, Parving HH, Pedersen O (2008) Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 358:580–591. <https://doi.org/10.1056/NEJMoa0706245>
- Burridge LH, Foster MM, Donald M, Zhang J, Russell AW, Jackson CL (2017) A qualitative follow-up study of diabetes patients' appraisal of an integrated diabetes service in primary care. *Health Soc Care Community* 25:1031–1040. <https://doi.org/10.1111/hsc.12402>
- Jackson C, Tsai J, Brown C, Askew D, Russell A (2010) GPs with special interests: impacting on complex diabetes care. *Aust Fam Physician* 39:972–974
- Goderis G, Borgermans L, Grol R (2010) Start improving the quality of care for people with type 2 diabetes through a general practice support program: a cluster randomized trial. *Diabetes Res Clin Pract* 88:56–64. <https://doi.org/10.1016/j.diabres.2009.12.012>
- Nocon A, Rhodes PJ, Wright JP (2004) Specialist general practitioners and diabetes clinics in primary care: a qualitative and descriptive evaluation. *Diabet Med* 21:32–38. <https://doi.org/10.1046/j.1464-5491.2003.01063.x>
- Grone O, Garcia-Barbero M (2001) Integrated care: a position paper of the WHO European Office for Integrated Health Care Services. *Int J Integr Care* 1:e21
- Ouwens M, Wollersheim H, Hermens R, Hulscher M, Grol R (2005) Integrated care programmes for chronically ill patients: a review of systematic reviews. *Int J Qual Health Care* 17:141–146. <https://doi.org/10.1093/intqhc/mzi016>
- Martinez-Gonzalez NA, Berchtold P, Ullman K, Busato A, Egger M (2014) Integrated care programmes for adults with chronic conditions: a meta-review. *Int J Qual Health Care* 26:561–570. <https://doi.org/10.1093/intqhc/mzu071>
- Smith S, Bury G, O'Leary M et al (2004) The North Dublin randomized controlled trial of structured diabetes shared care. *Fam Pract* 21(1):39–45. <https://doi.org/10.1093/fampra/cmh109>

34. Basudev N, Crosby-Nwaobi R, Thomas S, Chamley M, Murrells T, Forbes A (2016) A prospective randomized controlled study of a virtual clinic integrating primary and specialist care for patients with type 2 diabetes mellitus. *Diabet Med* 33:768–776. <https://doi.org/10.1111/dme.12985>
35. Hepworth J, Askew D, Jackson C, Russell A (2013) ‘Working with the team’: an exploratory study of improved type 2 diabetes management in a new model of integrated primary/secondary care. *Aust J Prim Health* 19:207–212. <https://doi.org/10.1071/PY12087>
36. Bowling A, Bond M (2001) A national evaluation of specialists’ clinics in primary care settings. *Br J Gen Pract* 51:264–269
37. Moffatt J, Hossain D, Hansford G (2012) Physician in practice clinic: educating GPs in endocrinology through specialist-outreach. *Rural Remote Health* 12:2265
38. Jackson CL, Donald M, Russell AW, McIntyre HD (2017) Establishing a new model of integrated primary and secondary care based around general practice: a case study of lessons learned and challenges. *Aust Health Rev* 42:299–302