

Estimating indirect costs in a pediatric trial: patient diaries and interview data collection

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Abstract

Background: In France the pertinence of including indirect costs in economic evaluations of therapeutic strategies is left to author judgment. However productivity losses represent a significant amount of resources in particular for chronic pediatric conditions when caregivers are involved in addition to patients. In order to explore how best to collect indirect cost information, we investigated whether or not a patient diary provided additional information compared to retrospective investigator-led interviews and whether a diary filled intermittently produced more or less information than a continuous diary. The main objective of this study was to identify which type of data collection was most effective to obtain information on indirect costs over a 9-month study period.

Methods : Start-In! is a randomized controlled trial comparing the efficacy of three strategies of real-time continuous glucose monitoring (CGM) for 12 months in children and adolescents with type 1 diabetes. We designed an ancillary study to compare three collection methods of indirect costs: 1) retrospectively by investigators during quarterly follow up visits and prospectively with diaries filled by children or families used 2) either continuously or 3) intermittently. Were collected the amount of information on absence from school and work, and carer time for diabetes cares, and compared to the information given to the investigator during the quarterly follow up visit in the case report form.

Results: At the end of the 9-month study 42% participants had not returned their diary, less than 10% of data were collected in patients' diaries versus 82% in investigators' filled case report forms.

Conclusions: Our study only supports the hypothesis that data collection by investigators during quarterly visits would lead to fewer missing data than a diary, that it be filled up on a trimester or every three months. Diaries might represent an important additional burden to children and their families. Trial registration: Start-In! trial registry name: Study of Insulin Therapy Augmented by Real Time Sensor IN Type 1 Children and Adolescents (START-IN!). ClinicalTrials.gov Identifier: NCT00949221. Registered on July 30, 2009.

Background

In France the pertinence of including indirect costs in economic evaluations of therapeutic strategies is left to author judgment (1). However productivity losses represent a significant amount of resources in particular for chronic pediatric conditions when caregivers are involved in addition to patients. Information on absence from work or school is not collected in health insurance data bases and need to be estimated either with retrospective patients interviews by an investigator (2), or with diaries completed by the patients (3,4). Investigator-led interviews require additional work from the physicians which could be reduced by a prospective collection in diaries filled by children or families (5). But using a diary in clinical trials (paper or electronic) requires logistical management and fastidiousness from participants, especially for long lasting

studies (6). The question seemed all the more important in pediatric trials where time costs to parents may influence the uptake of an intervention (7).

In order to explore how best to collect indirect cost information, we investigated whether or not a patient diary provided additional information compared to retrospective investigator-led interviews and whether a diary filled intermittently produced more or less information than a continuous diary. We hypothesized first that a diary would enable investigators to lighten their interviews, being helped or even replaced with diaries. We assumed that patients would have a tendency to under-report their consumption. Our second hypothesis was that keeping a continuous diary was an onerous task and could lead to poor data collection over time. However, the intermittent diary, while reducing the data entry burden for patients (8), would carry the risk that patients fail to complete the diary if it is not a regular task.

The main objective of this study was to identify which type of data collection was most effective to obtain information on indirect costs over the 9-month period of a pediatric trial. The secondary objectives were to determine the patient acceptance for intermittent vs. continuous diary; and to look for a decreasing trend in the amount of data collected.

Methods

Study design

We designed an ancillary study to the Start-In! trial assessing the efficacy and cost-effectiveness of three strategies of real-time continuous glucose monitoring (RT-CGM) in type 1 diabetes children (T1D)(9). This trial was well adapted to our study objective since insulin –dependent diabetes in children is a chronic condition with major time costs to children and their parents.

Start-In! was a French multicentric trial with a randomized, controlled, prospective, open, parallel group design, comparing three therapeutic modalities in pediatric management (9).

Patients were aged from 2 to 17 years, diagnosed with T1D for more than one year, treated by intensive insulin therapy, with inadequate metabolic control. The study was conducted in 11 pediatric diabetology units with expertise in pump therapy and CGM. The primary endpoint was long term glycemic control at 12 months. The study associated two phases: all subjects wore the RT-CGM during the first three months, and thereafter were

randomized in three groups with different strategies of glucose monitoring during the next 9 months. We were interested in those 9 months patients' follow-up period.

The economic evaluation required information on on-site visits, absence from work /school due to diabetes, and daily time spent by the caregiver to provide diabetes care. This information was recorded for all patients by the investigators in the case report form (CRF) for the need of the Start-In! economic evaluation at the end of each trimester and represented the reference strategy.

In order to test whether diaries would provide additional information, patients were randomized in two groups. In the 'continuous' group, children and parents were asked to collect data in a diary without interruption during one of the 3 trimesters of the study (3 months continuously). In the 'intermittent' group, data was collected during the last month of each of the three trimesters only. To simplify the work of investigators, randomization for the ancillary study was by center and not by patient (Fig.1 and 2). Data was entered in the CRF by investigators following the same schedule: one trimester for the 'continuous' group and last month of each for the 'intermittent' group.

Figure 1: Description of the three randomizations regarding the Start-In! population.

G1, G2 and G3 represent the three randomized groups of the Start-In! trial. T1, T2 and T3 represent the three trimesters that patients from group 'continuous'.

Figure 2: Timeline of the different collections of data in diaries, depending on the randomization groups, with T0 being the end of the third month of Start-In!. Blue ovals represent the continuous groups (Gc1, Gc2 and Gc3) and orange circles represent the intermittent group (Gi).

Endpoint

The primary endpoint was the amount of information on absence from school and work, and carer time for diabetes care, collected in the diaries, compared to the information given to the investigator during the

quarterly follow up visit.

Material

Participants kept a quarterly diary for the Start-In! study. We asked them to record their absences at school and at work, the number and dates of the visits and how many parents were present at the consultation with an estimate of the daily time spent by the caregiver to provide diabetes care (blood glucose monitoring, insulin administration...).

The same information was also collected every quarter by the investigator, and entered in the CRF with the help of the diary. Diaries were collected at the same time for the Start-In! study.

Analysis

We compared the amount of information entered in the CRF in the 'continuous' vs. 'intermittent' group. As information by them-self, missing data were not addressed.

Results

A total of 151 patients were first randomized in the Start-In! trial, 52 in G1, 48 in G2 and 51 in G3. Their characteristics were similar at inclusion(9). A total of 23 patients left the study and were excluded from the analysis. 128 patients were available for analysis, 92 randomized in the 'continuous' group and 36 in the 'intermittent' group.

Primary endpoint

Half of the 128 patients in this analysis did not return diaries so their information reported to the investigators and entered in the CRF was based solely on memory.

'Continuous' group

Of the 92 patients, only 49 (53%) returned a diary. Among those, 88% (n=43) were diaries filled up for the right trimester as determined by the randomization groups (Gc1, Gc2 or Gc3), 89% (n=44) were empty, 8% (n=4) did answer that no absence occurred, and only one diary gave a date of absence at work/school.

'Intermittent' group

Of the 36 patients, only 44% (n=16) returned at least one diary. Each patient should have submitted three diaries, one by trimester, but only 38% (n=41) diaries were collected. In those 41 diaries, missing data were 97.6%, and only one diary gave a date of absence at work/school.

CRF

Regarding the same data collected retrospectively from the patients by investigators who entered them in the CRF at the trimestral follow-up visit, we took all 151 patients into account (Table 1). In the 'continuous' group, CRF were filled (partially or totally) at about 71% for patients having returned a filled diary, and at 78% for those having returned an empty or no diary. In the 'intermittent' group, the one patient who had returned a filled diary had a filled CRF. Among the others, 80% of CRF were filled.

The 'continuous' group show a tendency to have more missing data than the 'intermittent' group (24% vs. 17%).

Table 1: Frequency of data collected in the CRF depending on randomization and filling of the diary.

Type of data filled in the CRF	Group 'continuous'		Group 'intermittent' ^a	
	N=108		N=43	
	Patients with (No. (%))		Patients with (No. (%))	
	Filled diaries n=7	Diaries with no data ^b n=101	Filled diaries n=1/1/1	Diaries with no data ^b n=43/43/43
Absences from school	5 (71)	82 (81)	1/1/1 (100)	36/34/34 (81)
Absences from work	6 (86)	77 (76)	1/1/1 (100)	35/32/32 (77)
Consultations	5 (71)	85 (84)	1/1/1 (100)	36/34/34 (81)
Time for diabetes care	4 (57)	72 (71)	1/1/1 (100)	35/34/34 (79)

a: For the group 'intermittent' the data had to be collected three times: 1st/2nd/3rd.

b: 'No data' meaning that the diary was not filled or not returned.

Discussion

Our study compares three methods to document the indirect costs of T1D in children during a clinical trial including a medico-economic evaluation. The first finding was the magnitude of missing data in diaries It would appear that using diaries to collect data regarding indirect costs in a pediatric trial with a high burden for the patient and family is unsuitable.

In the CRF, the 'intermittent' group had a slightly higher rate of filled data than the 'continuous' group. It could be explained by the fact that the diaries being rarely filled, investigators can only rely on participant's memory to fill the CRF, data from the past month being easier to remember than those of the last three months.

Many research studies show a globally high concordance between self-reported and medical records of health care data in the general patient population (10,11). We were interested in the particular case of children, for whom diaries would be filled by carers, often tired parents with a chronically ill child, and probably other kids, jobs ... In fact family members of someone with diabetes seems to be at higher risk to have depression (12) and parents having a child with Tb1 can have to struggle with depression (13,14) and anxiety troubles like fear of hypoglycemia (15) which can lead to **parental emotional distress** (16). Difficulties would also be encountered with adolescent patients, with youth being more independent but having troubled relationships with parents (17), and transition issues like treatment adherence (18,19). It seems then obvious that in those conditions, the filling of non-essential data like school absences could be put in the background by the whole family. Unfortunately the patients and their carers were not asked their opinion about the different data collection, so we can only make hypothesis about the cause to so many missing data.

This study has many other limits. The amount of missing data were so important, we could not perform statistical tests nor evaluate our secondary objectives of patient acceptance and fatigue effect. And with so few data the quality of information could not be assessed, only the quantity was explored in our trial.

Conclusions

Trials that require an estimate of indirect costs rely for information on patients and families. Our study only supports the hypothesis that in the case of a pediatric chronic condition, investigator-led interviews provide

more information than diaries. Diaries might represent an important additional burden to children and their families who are already struggling with many issues.

Declarations

Ethics approval and consent to participate

The AFSSAPS (National Agency for the Safety of Medicines and Health Products) approved the protocol of the START-IN! trial. Reference number: 2007-A01330-53. Informed consent was obtained from all study participants.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests

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Competing interest

The authors declare that they have no competing interests.

Authors' contribution

ALJ wrote the manuscript. ALJ and HM carried out the analysis. IDZ supervised the methodology and statistical analysis. ALC, IDZ, SGC, CA and NTR contributed to the methodology. All authors revised the manuscript.

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Figures

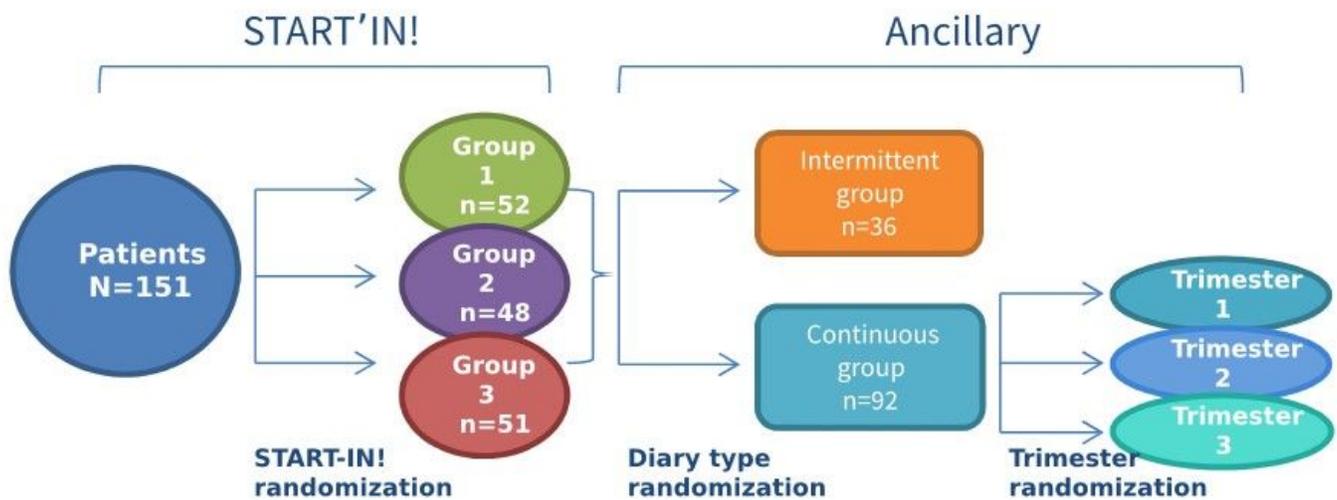


Figure 1

Description of the three randomizations regarding the Start-In! population. G1, G2 and G3 represent the three randomized groups of the Start-In! trial. T1, T2 and T3 represent the three trimesters that patients from group 'continuous'.

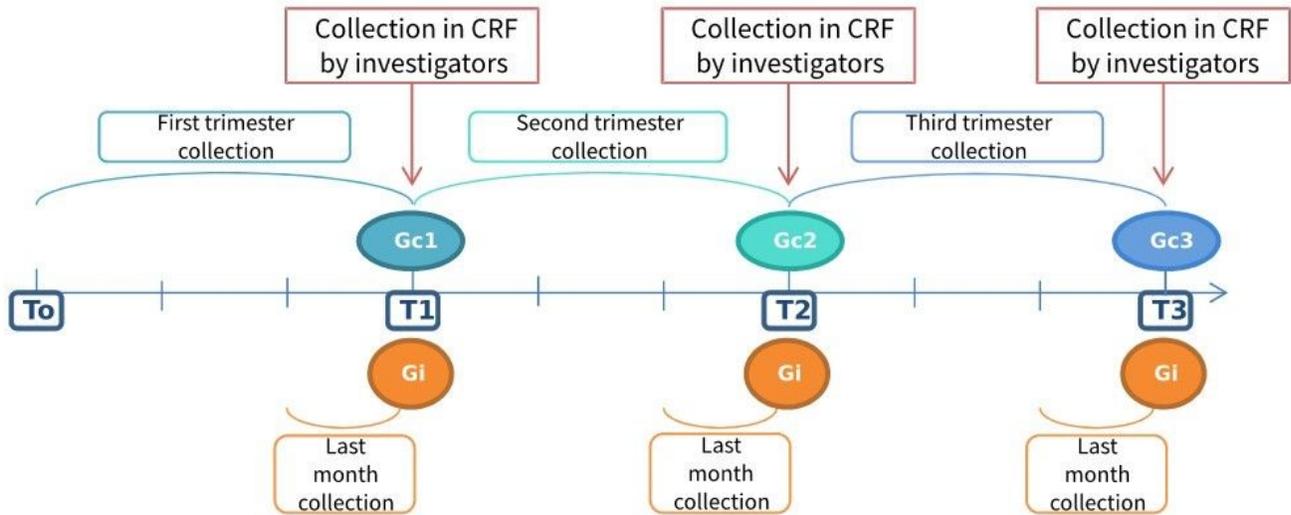


Figure 2

Timeline of the different collections of data in diaries, depending on the randomization groups, with T0 being the end of the third month of Start-In!. Blue ovals represent the continuous groups (Gc1, Gc2 and Gc3) and orange circles represent the intermittent group (Gi).

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