

# Can a transition clinic bridge the gap between paediatric and adult inflammatory bowel disease

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DOI:

[10.1016/j.dld.2020.02.009](https://doi.org/10.1016/j.dld.2020.02.009)

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*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Nardone, O, Iaccuci, M, Ghosh, S & Castiglione, F 2020, 'Can a transition clinic bridge the gap between paediatric and adult inflammatory bowel disease', *Digestive and Liver Disease*, vol. 52, no. 5, pp. 516-527. <https://doi.org/10.1016/j.dld.2020.02.009>

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# **CAN A TRANSITION CLINIC BRIDGE THE GAP BETWEEN PAEDIATRIC AND ADULT INFLAMMATORY BOWEL DISEASE CARE MODELS ?**

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All authors approved the final version of the manuscript

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Conflict of interest: None of the other authors have any conflict of interest to declare

MI and SG are funded by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health

No funding sources

Word count of main text: 5998

### **Abbreviations**

IBD, inflammatory bowel disease

UC, ulcerative colitis

CD, Crohn's disease

FC, faecal calprotectin

ECCO, European Crohn's and Colitis organization

AYA, adolescents and young adults

BMI, body mass index

TRAQ, Transition Readiness Assessment Questionnaire

IBDSES-A, IBD Self-Efficacy Scale for Adolescents and Young Adults

## **Abstract**

Transition care in inflammatory bowel disease is increasingly recognized as challenging given the inherent differences between paediatric and adult health care models, disease characteristics and treatment strategies. Transition is a dynamic process involving adolescents and young adults that are moving from a paediatric to an adult health care setting, and it should be flexible, continually updated and tailored to each patient. The implementation of a transition clinic is essential given the increasing incidence of the paediatric population with inflammatory bowel disease and the lifelong impact of this disease.

The key question is when and how to structure transition according to the adolescent's clinical, psychosocial, educational needs and expectations to ensure continuity of care.

In the attempt to improve the management of transition in inflammatory bowel disease and address the wide gap between adult and child care, we provide an update of the transition clinic and we propose a “treat to target” approach in transition to facilitate an effective and successful transition programme. In the changing landscape of the treatment of inflammatory bowel disease, further studies are necessary to determine the role of the transition clinic in determining the choice and strategy of therapy and its monitoring and the adoption of newer strategies such as biomarkers guided treating to target.

**Key words:** Crohn's disease; children; ulcerative colitis; healthcare

## Background

Inflammatory bowel diseases (IBD) are chronic-relapsing, heterogeneous disorders that include ulcerative colitis (UC) and Crohn's disease (CD), and are characterized by progressive bowel damage that results in relevant long-term disability in many young patients [1, 2]. Epidemiologic studies have reported a global trend towards an increased incidence of IBD in children and adolescents in the western world over the last 35 years, and 25% of patients contract the disease before the age of 18 years [3-6].

There are relevant differences between childhood-onset and adulthood-onset IBD. Recently, Chaparro et al [7] in a large cohort in the current biologics era, compared several IBD features of children  $\leq 16$  years, with those diagnosed after the age of 16 years. A total of 21 200 patients 96% adults and 4% children, diagnosed with IBD between 2007 and 2017 were included in the ENEIDA registry of the Spanish Working Group in Crohn's and Colitis (GETECCU). Both UC and CD contracted in childhood have a more extensive anatomic involvement than when contracted in adulthood. In particular, CD patients had more involvement of the upper gastrointestinal tract. At diagnosis, most patients in both age-onset categories had inflammatory behaviour, but the proportion of patients with complicated behaviour (stricturing or penetrating disease) was higher in the adulthood onset cohort at diagnosis and at the end of follow-up. The proportion of patients treated with immunomodulators and biologics was significantly higher in the childhood onset cohort, while the risk of undergoing surgery did not differ between the two groups.

Given the increasing incidence of IBD in the paediatric population and the lifelong impact of the disease, the planning of a transition program is essential to ensure continuity of care and promote self-advocacy. Classically, transition is defined as the "purposeful, planned movement of adolescents with chronic medical conditions into adult-orientated health-care systems" [8]. However, IBD transition differs significantly from most of the chronic diseases usually transferred. For example, cystic fibrosis and diabetes patients are typically diagnosed at birth or in early childhood and thus have more time to adapt to their illness, whereas the mean age at IBD diagnosis is 15 years [9]. Therefore, IBD occurs at a delicate time in a child's physical and psychosocial development and can impact on education, employment and social integration.

This review provides a state-of-art analysis of transition in IBD starting from the most relevant differences between the care system of paediatric IBD and that of the adult form. We then focus on the

structure of transition programmes and the main issues to be addressed in order to achieve a successful transition.

### **Review criteria**

A literature search using PubMed and EMBASE databases was undertaken from inception to August 2019 to identify the crucial elements to manage a IBD transition clinic. The search terms used were “transition care” OR “transition clinic” OR “transition model”. These terms were then combined with “inflammatory bowel disease” OR “IBD” OR “CD” OR “UC” and the keywords “management” OR “continuity of care” OR “outcome” OR “barriers” OR “readiness” OR “adherence”. A total of 1971 results were found. After screening titles, we narrowed down and examined full cohort and cross-sectional studies, high quality expert consensus and survey excluding duplications, studies involved transition programs for other chronic disease, irrelevant and redundant articles, and abstracts. Secondary data sources were found through a bibliographic review of the selected articles. Reviews and meta-analyses were included if considered appropriate. A total of 129 papers were retrieved and considered relevant, finally 47 provided original data.

### **Clinical distinction between paediatric and adult IBD**

Appreciation of the clinical differences between paediatric and adult IBD is an inevitable step in understanding how to manage a transition clinic. Providers involved in the transition must be aware that paediatric care differs substantially from adult care in several aspects. The paediatric health care model tends to be family-centred, and has a multidisciplinary approach, while the adult model is usually patient-centred and is often provided by a single doctor or a team in a setting in which patients should be autonomous and independent without parental involvement. [10](Table 1) Indeed, parents play a pivotal role in paediatric visits in decision-making as well as providing consent for all procedures, while in the adult setting, patients should be separated from parents to endorse independence. Understanding the changing role of parents in the transition clinic is essential to make adolescents accountable for transitioning to take responsibility and independence. This is likely to be a process in which parents are gradually less involved, especially when the patient starts living away from their parental homes.

In children with suspected IBD, a combination of upper endoscopy and ileocolonoscopy should be performed to differentiate between UC and CD and rule out upper gastrointestinal involvement in CD, on the contrary, adults not undergo upper endoscopy unless they show symptoms. [11] As reported in the recent position paper of the Porto IBD Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [12], paediatric endoscopy should be performed by a paediatric gastroenterologist, or alternatively by a gastroenterologist with specific paediatric training and/or supported by a paediatric team. Moreover, endoscopy requires deep sedation in children (some countries use general anaesthesia depending on age), while conscious sedation is generally used in adults. Indeed, it is paramount to consider the potential negative effects and the risks of repetitive deep sedation or general anaesthesia, by balancing the need of endoscopy in the decision-making process, especially in younger children with a severe disease course who are also generally reluctant to take the bowel preparation because of poor palatability, bloating or nausea [13]

Whereas the aims of mucosal healing, deep remission and improved quality of life do not differ between paediatric and adults, the major aim in paediatric patients is to ensure growth and pubertal development. In addition, adult care is focused on surveillance, sexual function, fertility and pregnancy [14, 15], while few childhood-onset colorectal cancers associated with IBD have been reported, so surveillance does not play a prominent role in paediatric care. [16]

According to the European Crohn's and Colitis organization (ECCO) and ESPGHAN guidelines [17], the first therapy recommended in children affected by active luminal CD is exclusive enteral nutrition to induce disease remission, while corticosteroids are generally avoided due to the risk of growth retardation or only suggested if there are no other options.

Notably, paediatric patients are often excluded from randomised controlled studies since most parents do not give consent to treat their child with placebo. Moreover, most research ethics boards and paediatricians consider placebo arms unethical in children. Consequently, the majority of paediatric data comes from extrapolation of adult clinical trials, supported by non-placebo controlled studies. However, if clinical equipoise exists—meaning that there is no clear evidence that active therapy is superior to the control arm—placebo can be considered. Most paediatric IBD trials have been generally conducted when

drugs have already been shown to be effective in adults, thus, clinical equipoise does not exist and thereby placebo cannot be considered. [18-20]

Currently, much attention is focusing on exit strategies and on defining what is the best time to stop treatment [21]. In paediatric care, monitoring growth and pubertal development play a pivotal role as a target and in some cases also for consideration of biologic exit strategies. Therapies should be continued for a prolonged period of time with monitoring of BMI, and not stopped until children reach the target growth, and puberty[17]

### **Transition models and timing**

Transition is a challenging phase in the management of IBD because it does not necessarily end in a single encounter during which paediatric patients meet adult providers, but it is a stepwise program, tailored for each individual. It requires a flexible structure to ensure the acquisition of behavioural skills and full responsibility for health care and management of disease. [22]

Recently, Philpott et al [23] described four models of transition to establish how to structure transition depending on the patient's behaviour and clinical history. The ideal patient is generally in remission and ready to transfer in a "typical way", while patients not completely aware of their condition and non-adherent to a scheduled appointment follow a "non-engaged model". Patients in an active phase of disease who should change their current therapy or undergo surgery are included in a "crisis transfer model" and patients with a special situation in terms of co-morbidity and low social and cultural levels require a "special need" type of transfer. These categorisations could help to assess the risk of transition failure thereby reducing the number of patients lost to follow-up. [23]

The "treat to target" paradigm [24] can be adapted to transition care. It involves a baseline risk-assessment of paediatric patients, by identifying potential barriers, selecting an initial transition programme wherein management is adjusted according to regular monitoring with non-invasive means to reach the agreed goals. [25, 26] (Figure 1). Monitoring will continue to include BMI, growth and development in addition to such other objective measures as faecal calprotectin(FC), C-reactive protein, colonoscopy and cross-sectional imaging. Transabdominal ultrasonography is especially suitable for transitioning patients because it is non-invasive, cost effective and radiation-free [27, 28]. Of note, transition patients must be responsible for such monitoring tools as FC.



Ideally, transition should take place during a phase of stable remission. [29] In many European countries and in Canada, transition generally occurs at the age of 18 years, while in the USA it may not occur until the age of 20-21 or even up to 25 years. [30] Nevertheless the timing of transfer cannot be predefined as it is not a question of chronological age and it depends on the achievement of maturity of each individual. [31] Some patients with complex issues could require more time and additional visits to the transition clinic before transfer to adult health care. In fact, a web-based survey by Wright et al showed that caregivers perceived psychological maturity and readiness as the most important factors in determining time to transition.[32] Regional health and hospital policies may also determine the age of transition.

Stollon et al reported that despite many healthcare skills were acquired between ages 12 and 14 years, self-management skills were not mastered until after age 18.[33] Hence, the time of transfer should be flexible, individually determined and be adjusted to the acquisition of the skills needed for transition. Input from IBD specialist nurses and clinical psychologists could be invaluable in the transition process. Increasingly, healthcare systems have common transition policies across several diseases.

An expert panel of nine paediatric and five adult gastroenterologists, convened by the ECCO [29], have identified the critical elements of the transition programme, and established evidence-supported messages defined as “current practice points”. They considered a joint paediatric–adult clinic, based on collaboration and interaction, the ideal model.[29] There is a wide heterogeneity in the number and the settings of joint visits among models. Moreover, the number of visits to the transition clinic has yet to be established, and similarly, it is not known whether a single appointment is more advantageous than multiple appointments. [34] Although there is no evidence regarding the benefit of an additional joint visit after the transition process, it could be useful to reduce the number patients lost to follow up and to improve the outcome of long- term disease (attendance rate, adherence, communication skills). Currently, the choice of single versus multiple visits depends on resources and feasibility. In many areas, adult and children’s hospitals are at separate sites posing logistic challenges for frequent joint clinics. However, there are no uniform recommendations, and readiness for transition as well as chronological age should both be taken into consideration, but hospital policies and the geographic location of adult and paediatric providers are also important. In situations with paediatric and adult services on the same site, a shared appointment clinic is

generally preferred, while alternatively, at least one joint meeting in the familiar paediatric environment and a second in the new adult environment is advisable. When this is not feasible, the paediatric team should provide a detailed medical report for the adult team, preferably following an agreed protocol. In addition, the paediatric team should be available to the adult team for further explanations or assistance during the immediate post-transfer period.[29] Indeed communication between providers is one of the keys of success. Moreover, it is important to create an environment in which adolescents feel free to speak about smoking, alcohol, drugs and sexuality because they may be uncomfortable to face these topics with their parents. Sexual development and maturation may be delayed in adolescents with IBD. [35] Sexual behaviour is a delicate topic and it is crucial to support sexual education and provide information about contraception, puberty and pregnancy to avoid unexpected pregnancy, reduce pregnancy-related complications, and optimise disease control for any future pregnancy. [29, 35]

### **Major skills to acquire**

The goal of the transition clinic is to foster the autonomy adolescents in terms of communication with members of the adult team, adherence and decision-making thereby maximizing their independence from their family. In this way, transition care should help patients to develop awareness of their chronic and unpredictable disease. Interestingly, autonomy skills have been considered a main marker of transition readiness. [26] Bennet et al [36] in a retrospective study surveyed two cohorts of patients; the first cohort consisted of patients who moved from paediatric to adult care through a transition service while the second cohort had not gone through a formal transition process. No significant difference was reported for occurrence of complications, perianal disease, surgery or hospitalisation in either cohort. A total of 96% patients belonging to the transition cohort and 91% of the non-transition cohort understood the importance of transition care. However, only 25 of the 46 patients of the transition group had adequate knowledge of their transition plan, whereas the majority did not feel prepared or part of the decision -making process. [36] Hence, the acquisition of specific relevant disease knowledge is a crucial component of transition readiness.

In a cross-sectional study, Gumidyala et al [37] analysed the level of IBD knowledge in 75 adolescents and young adults (AYAs) through a 12-item questionnaire. The questionnaire items were based on such relevant IBD-specific areas as medical history details, disease-management information, knowledge about IBD-related complications and health care resources. The items better known by almost all AYAs were the

type of IBD they were diagnosed with and the number and the type of surgery undergone. The areas of lower levels of knowledge were how often medications should be refilled, the effects of drugs and alcohol and how to book an appointment with their IBD provider. Of note, 17% of AYAs did not consider their IBD medications a relevant issue and could not list all of them. Factors associated with a better knowledge were older age, higher disease-management, self-efficacy, greater AYA-perceived parent autonomy granting, more frequent parent-reported transition-related communication with their medical provider, and higher AYA health care satisfaction.[37] As this study suggested, increasing age-appropriate involvement in clinic, transition-related communication and discussions before (at least one year), during and after the transition programme could improve disease knowledge.

Benchimol et al [38] developed a tool to promote patient's disease-specific knowledge called "My Health Passport for IBD", a wallet-sized card with a comprehensive summary of medical information, which allows patients and parents to answer questions about disease course, and medical and treatment history.

According to the current practise position of the ECCO , decision making and self-efficacy are crucial skills for successful transition. [29] Patients should be involved in decision-making to become aware of their disease and the related risk in order to support adherence and self-advocacy.[29] Self-efficacy involves the ability to monitor symptoms and report them to health-care providers, manage medication and handle disease flare-up. More specific and validated educational programs might foster the acquisition of skills. Currently, the application of social media plays a pivotal role in disease knowledge. A recent survey involving 109 young patients reported that only a few adolescents used social network as a source of health care information, but 31% to 41% reported that they would be interested in using cell phone applications for such tasks as reminding visits and tracking disease symptoms. In the near future, mobile technology and online networks could improve the doctor-patient communication and increase adherence. [39] However, further studies are needed to assess the feasibility of this in clinical practise.

### **Objective tools to assess patient's readiness**

Several factors might impact on the patient's readiness to transition, and different tools have been proposed to evaluate the best time of transfer but so far, none has been completely validated. The Transition Readiness

Assessment Questionnaire (TRAQ) is one of the most common and reliable measures of transition readiness used by providers; it involves questions related to appointment keeping, tracking the health care system, managing medications, knowing one's disease and medications, talking with providers, and managing daily activities. It is not disease-specific and is based on self-reporting without clinical correlation (Supplementary Table 1). [40]

Accumulating data have shown that age is a good predictor of transition readiness measured using the TRAQ. [40, 41]. In addition, Gray et al reported that a high TRAQ score corresponds to high transition readiness in older age and female gender.[42] Subsequently, Rosen et al [43] analysed the association of demographic and disease-related factors with transition readiness in a total of 95 patients: 46 belonged to the adult care setting and 49 to the paediatric setting. A low TRAQ score was associated with high rate of non-adherence. Age was the best predictor of TRAQ score: adult patients had a significantly higher TRAQ than children (median: 4.42 [IQR: 3.9–4.6] versus 4.06 [IQR: 3.4–4.4],  $P < 0.001$ ). In particular, by logistic regression analysis, age was independently associated with higher TRAQ scores (odds ratio: 1.49; 95% confidence interval, 1.1–2.02)

The self-Management and Transition to Adulthood with  $R_x = \text{Treatment}$  (STAR<sub>x</sub>) questionnaire was developed to measure self-reported transition readiness and self-management. It is not IBD-specific and involves the following factors: medication management, provider communication, engagement during appointments, disease knowledge, adult health responsibilities and resource utilization. Focusing on these aspects may help to identify needs and gaps in the patient's skills and knowledge. [44]

Recently, Izaguirre et al [45] developed, through standardized patient-reported outcome (PRO) guidelines, a self-efficacy measure, called the "IBD Self-Efficacy Scale for Adolescents and Young Adults (IBDSES-A)", to evaluate readiness of transition. It involves a 13-item disease-specific scale: managing medical care, everyday life with IBD, feelings, and the future with IBD. A total of 95 participants were recruited and the factors that moderately correlated with higher IBDSES-A scores were decreased depression and anxiety, lower IBD symptoms severity, increased health-related quality of life and self-esteem.

Consistent with these results, Carlsen et al [46] in a prospective study of 87 patients, confirmed a significant positive association between TRAQ and age. However, age was not predictive of transition readiness, while IBDSES-A and the ten-item Connor–Davidson Resilience Scale (CD-RISC), which measures the ability to

bounce back from adversity, predicted TRAQ independently of age. In the final model, only self-efficacy was significantly predictive of TRAQ [46]. Therefore, the achievement of self-efficacy could potentially improve readiness, medication adherence and managing feelings such as depression and anxiety, to reach not only a successful transition but also a better quality of life.

A recent randomized pilot study [47] analysed the effect of a targeted education intervention on adherence to medications, IBD knowledge and readiness in 13 adolescents with IBD over 4 weeks, with the intervention group having an educational meeting face-to-face with an educator in an outpatient setting compared with patients who did not received educational support. They developed an additional tool called “IBD pocket guide” to support patients’ education and self-management. Even though they reported a positive trend of improvement in IBD knowledge and adherence in the intervention group, the difference did not reach statistical significance. Therefore, studies with a larger number of patients are required to establish the feasibility of an education programme in clinical practice.

### **Perspectives and barriers to transition care**

The various participants involved in transition may have differing views and perspectives, and several studies have identified barriers to transition programs. Reluctance of patients and parents, due to their close relationship with paediatricians, is generally considered the main limitation.[29, 48-51] In a study by Bennett et al [36] a new relationship with a practitioner, a lack of communication and the patients’ own lack of understanding their disease, have been considered potential barriers to successful transition. Gray et al [51] examined the needs and concerns from the patients, parents, paediatricians and adult provider’s point of view using a structured interview. Parental perception of receiving a poorer quality of care in the new setting, financial concerns and loss of the relationship with the paediatric provider were considered the most common barriers.

Similarly, Besen et al [52] found that the attachment of patients and parents to paediatricians was the most frequent barrier to the transfer of care. Indeed, when discussing the move to an adult provider, parents compared the services offered by paediatric providers to adult providers and they were worried about the lack of a close follow-up, less interaction, difficulties with waiting time to get an appointment and bad communication. Moreover, medical adherence is considered a significant barrier due to risk-taking

behaviours, rejection of authority, cosmetic side effects, and reduced parental assistance. [53](Figure 2) The pronounced symptomology of diarrhoea and abdominal pain may favour medical adherence in adolescents with IBD, as opposed to other asymptomatic conditions.[54] It may be a challenge to achieve a “treat to target” approach by objective non-invasive monitoring using biomarkers such as FC, although that approach may be partially accepted in patients with mild symptoms.

Gray et al [55] recently analysed, through a standardized quantifiable approach, what patients, parents and paediatric providers considered important to reach a successful transition. All participants selected the top five skills from the TRAQ, which were then compared to assess the rate of agreement. Importantly, “Calling the doctor about unusual changes in health” and “taking medications correctly and independently” were selected by all participants with no significant differences among these groups. In detail, the lowest level of agreement occurred between patients and parents, with only 40% overlapped, whereas a large agreement (80%) was reported across patients and health providers. Parents and health providers overlapped on 60% of items. It is noteworthy that patients selected items representative of self-management tasks, while paediatricians were more focused on how handle disease in terms of adherence and unusual changes of symptoms, and parents paid more attention to health maintenance behaviour such as knowing how face a bad reaction to medication. However, the majority of patients enrolled were affected by CD, and it would be interesting to analyse the different perspectives between UC and CD.

In a survey developed by the Adolescent and Young Persons Section of the British Society of Gastroenterology, significant differences of perceptions were found between paediatric and adult gastroenterologists. Indeed, 80% of paediatric gastroenterologists considered a structured transition service important compared to 47% of adult gastroenterologists ( $p = 0.001$ ). A lack of time, space, funding and support services, such as IBD nurses, were identified by both paediatricians and adult gastroenterologists as the main barriers to transition care. Of note, inadequate training in adolescent care was perceived by both paediatric gastroenterologists and adult gastroenterologists. Therefore, educational programmes are required to address the lack of training and endorse a multidisciplinary approach between stakeholders. [56]

Recently, a multinational expert panel constituted by IBD nurses, and paediatric and adult gastroenterologists investigated the outcomes that reflect successful transition in IBD patients using a three rounds Delphi method. [57] Adolescent and young adult patients took part in the second stage to rate each

item previously selected in round 1. At the beginning, they identified 26 items and at the end only 10 were considered important to achieve a successful transition. The data obtained in the second stage showed that both the expert and the patient panel considered the same eight items to be important (Supplementary Table 2). In particular, six items were related to self-management skills and autonomy (e.g. independent communication and medication adherence), while the other two items were related to health-related quality of life and patient satisfaction. Finally, in the third stage, decision-making, independent communication, and patient satisfaction were the three highest ranked items among all the providers, while disease-specific items (surgery and inflammatory markers) received low grades (Table 2). However this study has several limitations, namely, only experts from Europe took part in the study, and 90% of them worked in tertiary hospitals. [57]

### **“Treat to Target” approach in transition clinic**

“Treat to target” is increasingly being adopted using FC in paediatric practice, and the concept “time to reach target FC” is being widely propagated [58]. Faecal calprotectin may be conveniently assayed with home-based kits in transition clinic populations provided the read-outs are not very high.[59] However, the adherence to home monitoring programmes remains an ambitious goal. In a recent prospective “real-life” study, Poulanne et al found a low adherence to self-monitoring activity using a combination of a rapid FC home test and a symptom questionnaire over 12 months. [60]

Non-invasive monitoring of mucosal healing and transmural healing is becoming important and is evolving using transabdominal ultrasonography and serum levels of multiple biomarkers.[27, 61] After initial therapy, there is a considerable variation in imaging and endoscopic monitoring and therefore in the transition clinic there is a need to standardized harmonized practices using non-invasive tests as much as possible. [62] As this may be different from paediatric clinics, the implementation of non invasive tests will require considerable patient engagement. Mucosal healing, transmural healing and FC results are not always concordant in paediatric IBD patients and in transition clinic. Therefore, it may be challenging to determine a treat to target strategy involving FC levels and wall thickness values for bowel ultrasonography.

In the paediatric population, the definition of the FC cut-off point is still a topic of intense debate ranging from 100 µg/g to 300 µg/g [63, 64]. Importantly, similar to adults, some studies have found a better correlation between FC and the activity of the disease in UC due to colonic involvement, while others did not

find any difference in the predictive value of FC for relapse in both diseases. [64-68] A combination of FC and CRP may be the non-invasive biomarkers in CD. Furthermore, the diagnostic accuracy of US to assess intestinal inflammation in paediatric IBD is a key issue. [69] Although it has been demonstrated that ultrasound can accurately detect CD, and that there is good agreement in disease location and activity between magnetic resonance imaging and ultrasound in paediatric IBD, sensitivity is reduced in proximal small bowel and colonic lesions. [27] However Civitelli et al showed that colonic ultrasound can assess the extent and activity of disease in children with UC and estimate the severity of a flare-up, before further invasive tests.[70]

Finally, satisfactory growth, adequate nutritional status ( body mass index [BMI] Z score adjusted for age and sex) [71] , psychosocial maturity (i.e. achievement of self-efficacy skills measured with the instruments of transition readiness mentioned above) should remain important targets of multidisciplinary management in the transition clinic and may require a different skill set of the team. These important targets should be addressed to make transition successful. (Figure 3)

### **Why do we need a transition programme? Advantages of transition**

Cole *et al* [72] in a pioneering study, evaluated the impact of a transition care on clinical outcomes in 72 IBD patients. Forty-four of them attended a transition clinic and 28 transferred directly to adult care . The rate of hospitalizations and the need for surgery were significantly higher in patients transferred without attending the transition clinic, while medication adherence and defaulting appointments were significantly improved in the transition group. Remarkably, the potential growth targets were achieved more often in the transition group than in the non-transition group. However, a limitation of this study concerned differences, although not statistically significant, in terms of duration of the disease and medical history between the two cohorts . Patients belonging to the transition group had a shorter disease duration and a higher rate of consumption of anti-TNF and thiopurine drugs that may have influenced outcomes.

A prospective study, Fu *et al* [73] evaluated the effect of transition services in terms of adherence, belief and attitude in 112 IBD patients, 59 of whom attended a transition clinic and in 53 controls. In both cohorts, self-reported adherence was poor without a significant difference between groups, while attendance at dedicated transition clinic was associated with improved beliefs and attitudes toward medicine assessed using the Beliefs in Medicine Questionnaire. Adolescents in the transition cohort had better recognition of



medical necessity, in particular, they were aware of this need even though they were still concerned about potential side effects.

Yerushalmy-Feler et al [74] reported that an organized transition process through 4 structured visits over 6 months, can impact on self-efficacy. Patients who transferred from a paediatric to an adult setting completed a questionnaire mainly focused on self-efficacy called “IBD yourself” [75] before and after a transition process. A significant improvement in self-efficacy after transition was observed ( $1.85 \pm 0.3$  before and  $1.41 \pm 0.21$  after transition,  $p < 0.0001$ ), which reflects the importance of a structured transition programme.

Recently, the advantages of participating in a transitional programme have been shown by an observational retrospective study conducted by Testa *et al* [76]. They observed in a cohort of 106 paediatric onset IBD patients, the benefit of a transition programme after 12 months of follow-up. Notably, there was significant reduction in the number of hospitalizations (pre-transition hospitalizations  $0.28 \pm 0.44$ , post-transition hospitalizations:  $0.1 \pm 0.3$ ,  $p < 0.001$ ) and flare-ups (pre-transition  $0.74 \pm 0.79$ , post-transition exacerbations:  $0.35 \pm 0.57$ ,  $p < 0.001$ ). Among the various parameters considered, the number of outpatients, growth parameters and nutritional status did not change pre- and post- transition. This result supports the importance of continuity of care in order to achieve a successful transition. [76]

A retrospective Canadian study [77] compared, in 536 patients, health service use in the 2 years before and 2 years after transition clinic conducted by adult gastroenterologists. After transition, the rate of emergency department visits (CD : relative incidence [RI] 2.12; 95% CI, 1.53-2.93; UC: [RI], 2.34; 95% CI, 1.09-5.03), outpatient visits (CD: [RI], 1.56; 95% CI, 1.42-1.72; UC: [RI], 1.48; 95% CI, 1.24-1.76) and laboratory investigations (CD: [RI], 1.43; 95% CI, 1.26-1.63; UC: [RI] 1.38; 95% CI, 1.13-1.68) were significantly increased. On the contrary, there was no change in hospitalization rate (CD: [RI], 0.70; 95% CI, 0.42-1.18; UC: [RI], 2.41; 95% CI, 0.62-9.40) because most emergency visits were not severe enough to require hospitalization. However, these results referred to differences in the organization and delivery of care between paediatric and adult gastroenterologists in Ontario where almost all paediatric gastroenterologists worked at academic centres with a dedicated multidisciplinary team to support IBD patients. Thus, patients can contact the team by phone or email, and address urgent issues without attending emergency department or outpatients clinic.[77]

Otto et al [78] in a retrospective study evaluated the impact of transitional care at one year in a group of patients transferred to the adult gastroenterologist following a transition clinic versus patients did not attend a transition clinic. Patients affected by CD transferred from the transition group had a significantly higher remission rate at 12 months than those not transferred, while the difference in remission rate was not statistically significant in UC patients. Importantly, transition significantly impacted on compliance as the attendance rates of scheduled visits were higher in patients after a transition programme.

Jeganathan et al [54], in a cross-sectional cohort study, investigated adherence to medication using the Medication Adherence Reporting Scale (MARS) in IBD-transitioned (TR) subjects and in young adolescents (YAs) who never experienced transition. No significant adherence differences were found between them. However, a slight non inferior adherence of TR patients (13.2% non-adherent) was reported in comparison to the YA group (24.4%). In addition the latter group had greater medication-related concerns assessed by the validated Beliefs about Medicines Questionnaire (BMQ). Notably, among the 17 baseline non adherents, 13 received the Inflammatory Bowel Diseases Pharmacist Adherence Counselling (IPAC) intervention, which reduced non adherence rates by 60% ( $P=0.004$ ) 6 months after baseline. Interestingly, corticosteroids, usually used for remission induction, were well accepted, whereas, aminosalicylates were predicted to have poor adherence.

Van den Brink et al [79] developed, a tool to measure the success of transition, called the “Transition Yourself Score”. It involved the following items: the time to first outpatient visit to an adult gastroenterologist, adherence to visits at the gastroenterology outpatient clinic, adherence to medication and qualitative evaluation of transition by the patients. Of note, one year after transfer, using this tool, they found that 63% of the 35 patients enrolled had a successful transition and in 31% the transition was moderately successful. The most significant finding is, that among the patients with unsuccessful transition (13/35), 80% had active disease before their transfer to adult care ( $p=0.052$ ). In contrast, clinical remission and use of medications were associated with successful transition. Further data are required to validate the Transition Yourself Score considering the small sample size and the retrospective design of the study.

In a relatively small study from Germany, structured transition of adolescents into adult health care led to relevant clinical and economic benefits. An important observation of this study was that delayed puberty was only noted in the group that transferred without structured transition. [80]

Another retrospective study conducted in the United States [81] evaluated the effect of a coordinator-led intervention on readiness and self-management skills in 135 patients with IBD. Patients seen by a transition coordinator showed a significant increase in transition readiness (pre-intervention  $68.13 \pm 14.75$  out of 100, post intervention  $74.38 \pm 14.58$ ,  $p < 0.001$ ) and acquisition of self-management skills (pre-intervention  $7.07 \pm 4.65$  out of 20 skills, post-intervention  $8.20 \pm 5.76$ ,  $p < 0.025$ ). On the contrary, no significant improvement was reported in patients who had not received the transition intervention. Thus far, this study enrolled the largest number of patients in the transition intervention group but it should be noted that there was a considerable imbalance between the intervention group and the control group. (Table 3)

A recent systematic review by Eros et al [34] summarized the impact of transition practices on clinical outcome. Notably, the articles selected were rather heterogeneous. Indeed, the measured outcomes and follow-up period differed among studies and this makes the comparison quite challenging. Moreover, most of the studies were single-centre experience and included small sample size, without either randomization or a control group. This review thus emphasizes the need for further multicentre randomized controlled trials and clear definition of the term “successful transition”.

## **Conclusion**

Given the increasing incidence and prevalence of paediatric IBD, the transition to adult care has become an important clinical issue. There is no evidence that one particular model of transitional care is more effective than others; however combined visits with a multidisciplinary approach and a good interaction between each stakeholder are potential keys of success. Importantly, transition does not necessarily end with a single appointment, but takes time, and should be initiated at least one year before the first physical appointment. It should be personalized according to the needs, personality and clinical history of the patients involved. To date, most transition studies in IBD are based on single centre experiences and on expert opinions or surveys of patients, their family, and/or on health care provider's perceptions, and did not detect any long-term effects of interventions on outcome. Thus, the next research goal is to determine the long-term impact of transition clinic on outcome by validating objective instruments to measure the success and to assess the readiness of patients as well as to adopt in clinical practice a treat to target paradigm, based on non-invasive

tools. Such studies are difficult to design as randomised studies but it may be possible to conduct cluster-randomised studies including multiple centres to determine at long-term impact.

**Figure 1. A practical strategy and plan to transition from paediatric to adult care**

The transition programme should be tailored to each patient. The main outcomes to reach are set and the best plan should be decided according to the risk assessment of difficulties and barriers related to transition.

Patients at high risk of transition failure should receive additional transition clinic visits focused on specific weaknesses compared to patients at low risk. Patient's readiness to transfer should be evaluated with the instruments currently available.

Legend: TRAQ Transition Readiness Assessment Questionnaire, IBDSSES-A, IBD Self-efficacy Scale for Adolescents and Young Adults , CD-RISC Connor-Davidson Resilience Scale

**Figure 2. Main barriers to transition from paediatric to adult IBD care**

Several factors can interact and affect each other, and might be barriers to a successful transition of care.

**Figure 3. Proposed treat to target in transition**

We propose “treat to target” approach in transition, based on objective and non-invasive tools regularly monitored every 3-6 months. Management and treatment should be adjusted when the targets are not reached. Unlike in adult patients, the tools in the transition population should be minimally invasive.

Legend: BMI, body mass index

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