Review

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Somatic outcomes of young people with chronic diseases participating in transition programs: a systematic review

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Abstract:

Introduction: There is growing evidence that the health of young people with chronic health conditions deteriorates during the transfer from child-centred to adult-oriented health care. Risks include not only the deterioration of health status in general but also the occurrence of secondary diseases and adverse events. Transition programs have been implemented. However, there is a lack of evidence about whether they reduce these risks and which interventions should be principally included. Evidence-based guidelines for the transition of young people should be introduced. In this study we therefore aim to summarise actual evidence on somatic outcomes during the transition period.

Methods: A systematic literature review was conducted. Two independent reviewers searched in electronic databases (Cochrane, Embase, PubMed, Web of Science) for intervention studies that aimed to improve transition. Last update of search was October 31st 2018. Grey literature was also searched. Studies were included if they examined participants aged 11 years or older suffering from a chronic health condition and evaluated interventions aimed to improve somatic outcomes after transition. Controlled trials or studies with a measurement before and after intervention were considered. The certainty of evidence was assessed using the GRADE approach. Additionally, each study was graded using a modified grading scale based on GRADE.

Results: 28 studies met the inclusion criteria. Patients suffered from different chronic conditions such as type 1 diabetes, solid organ transplantation, inflammatory bowel disease or cystic fibrosis. Interventions had different components such as transition checklists, workshops, web-based interventions, transition plans, joint visits or transition coordinators. Outcomes included mortality and morbidity. They varied according to chronic condition. Thirteen studies showed beneficial effects in the intervention group or in post-intervention measurements. The certainty of evidence was very low.

Conclusion: A considerable number of studies evaluating transition interventions was identified. Transition interventions had some beneficial effects. Workshops, joint visits and longer or multidisciplinary appointments may be particularly effective components. Transition guidelines could be based on these results. However, due to the limitations of the included studies it is difficult to draw firm conclusions. More research is needed to further evaluate the effectiveness of transition interventions. It should address the deficits identified from prior studies, such as poor study design, short follow-up time or small sample sizes.

Keywords: adolescent; systematic review; transition; transition to adult care; transitional care; young adult; young people.

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Introduction

Adolescence is a challenging time in general due to emotional and cognitive developmental challenges as well as social and educational changes. However, adolescence also offers the opportunity to develop and establish healthy behaviour [1]. Young people (YP) become increasingly independent and need to take more responsibility for themselves. This is particularly important if they have

special health care needs or are suffering from a chronic disease, as are 13% of all children and adolescents in Germany [2]. These YP have to cope with additional challenges as they must independently achieve good adherence and engage with adult care services that are often different from the paediatric ones [3].

Transition should be a "purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems" [4]. This period lasts from multiple months to several years, unlike transfer as the one-off event of change from paediatric to adult care. Transition has a growing importance nowadays for several reasons. Due to improved health care, children formerly mostly receiving paediatric care are now surviving into adulthood and are thus in need of transition to adult care. This concerns, for example, patients suffering from cystic fibrosis (CF), where over 51% of all patients in Europe and the US are older than 18 years [5, 6]. Furthermore, more than 90% of children with congenital heart disease survive into adulthood [7].

However, patient and provider surveys showed that there are many barriers to successful transition [8]. In addition, YP with chronic diseases express a need for interventions during transition [9, 10]. Reported barriers include family and provider reluctance to end a long-standing therapeutic relationship [11], only rare opportunities for appointments without parents [12], and insufficient discussion about youth-specific topics such as sexuality, drugs or alcohol [8, 12, 13]. Only a few YP with special health care needs or chronic diseases sufficiently discuss transition with their physicians [14, 15] and many feel that services fail to meet their needs [16, 17]. Presently, 24% of YP with special health care needs in the US experience a care gap between paediatric and adult health care [18].

In the future, health care systems must adapt to the changing needs of YP. Furthermore, they should enable a smooth transition from paediatric to adult care and prevent lapses of management after transfer. Studies show that these lapses of care are common in patients suffering from congenital heart disease [19], type 1 diabetes (T1D) [9, 20, 21] or being human immunodeficiency virus (HIV)-positive [22]. Lapse of care is a major risk for unsuccessful transition, which is associated with adverse health outcomes [19, 23, 24]. Another common problem after transition is non-adherence which correlates with deterioration of somatic outcomes either [25, 26]. Improving somatic outcomes is a major goal of transitional care, as patients' health should be maintained beyond transition. However, as assessed by various studies, this is presently not the case and somatic outcomes frequently deteriorate after transfer [20, 27–29]. Concerning adolescents with T1D, the odds of having poor glycaemic control are higher for those who transfer to adult care [20, 28], and diabetes-associated complications occur more frequently [27]. Renal transplant recipients have a high risk of graft loss during transition and emerging adulthood [29, 30]. Furthermore, patients with a complex medical history and lower levels of education seem to be at particularly high risk of deteriorating health after transfer [31].

There is a lack of evidence about whether transition programs can prevent deterioration of somatic outcomes and about which interventions are best included in such programs [32, 33]. This systematic review aims to summarise existing evidence to enable the development of evidence-based guidelines and to promote seamless care for adolescents.

Methods

Structure based on PRISMA

The well-established "Preferred Reporting Items for Systematic Reviews and Meta-Analysis" (PRISMA) checklist [34] was used as the basis for this systematic review, and the PRISMA study flow chart [34] utilised (Figure 1).

Inclusion criteria

The inclusion criteria were defined on the basis of the PICO framework (Table 1). PICO points out different parts of a research question: Population, Intervention, Comparison and Outcome. It is especially useful for asking questions concerning therapy [35].

Population

All studies examining participants aged 11 years or older with chronic health conditions or special health care needs were included. Studies examining participants with psychiatric disorders or cognitive disabilities were excluded.

Intervention

All interventions aimed to improve the transition of care for YP from paediatric to adult health services were included.

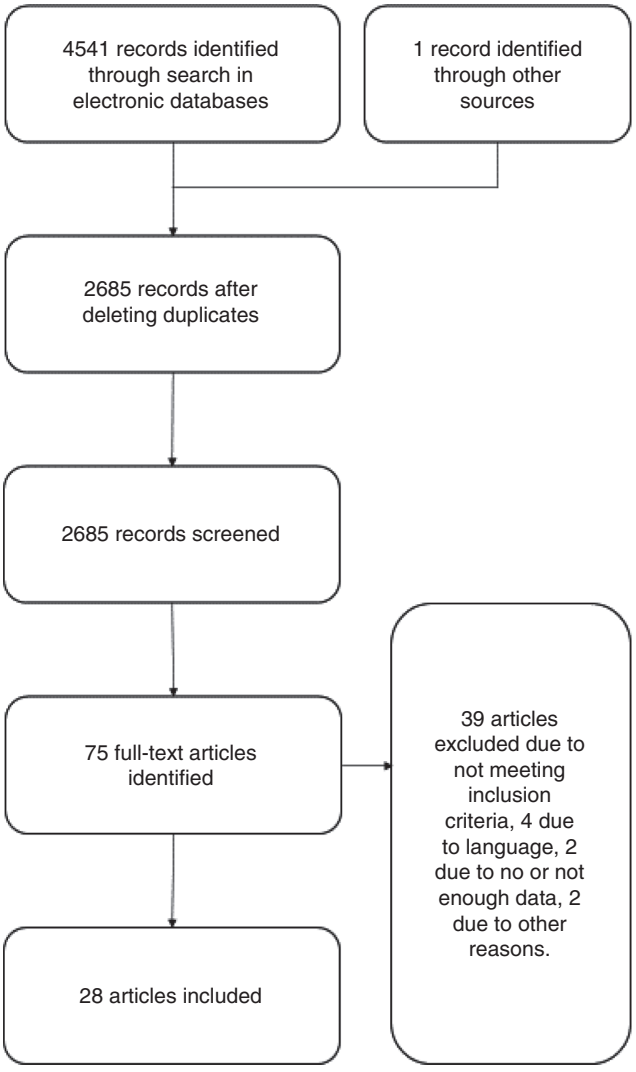

Figure 1: PRISMA study flow chart.

Table 1: PICO framework.

Can an intervention aimed to improve transition to adult care ameliorate somatic outcomes of chronically ill YPs?	
Population	11 years or older Somatic chronic diseases or health conditions
Intervention	Intervention aimed to improve transition to adult care
Comparison	Control group or comparison between two time points (before and after intervention)
Outcome	Somatic outcomes

Comparison, study design

Included were randomised controlled trials (RCTs), intervention studies with non-randomised control groups (NRCTs) and studies with measurements before and after intervention in a single group design.

Outcomes

All studies measuring somatic outcome parameters were included. Somatic outcomes include surrogate parameters that indirectly refer to or influence morbidity and mortality such as haemoglobin A1c (HbA_{1c}). Studies that exclusively examined psychosocial or behavioural outcomes, such as quality of life or transition-specific knowledge, were the subject of another review. If studies examined multiple outcome parameters, only somatic outcomes were considered. Additional psychosocial or behavioural outcomes were discounted.

Databases and other resources

The international electronic databases Cochrane Library, Embase, PubMed and Web of Science Core Collection were searched by two independent reviewers (JB, ER) for relevant studies and systematic reviews.

Reference lists of prior reviews were searched and selected experts were contacted to identify additional studies.

Search strategy

In all databases the same search terms were used. Search terms included transition- and age-specific terms. Alternative spellings and truncations were considered. Boolean operators such as 'AND' or 'OR' were used. For each database, the search strategy was adapted with database-specific keywords. To avoid bias in the review process two reviewers developed independent search strategies in advance. Final search strategies of all databases can be found in the online supplement (Supplementary tables 1–4).

Study selection

Studies with an English title and abstract, published between June 2011 and October 2018, were considered. A review from Crowley et al. with similar inclusion criteria was published in June 2011 and therefore covers older literature [33].

Title and abstract of articles identified in electronic searches and through other sources were screened after deletion of duplicates. Full texts of potentially relevant

studies were read and checked for inclusion. Disagreements were discussed to bring about consensus and authors were contacted in case of uncertainties concerning specific studies.

Certainty of evidence

The certainty of evidence was assessed by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [36]. The GRADE process was developed for the classification of recommendation strengths within the framework of guidelines and systematic reviews. The quality of evidence is thereby divided into four levels – high, moderate, low or very low – based on various criteria. Normally each outcome is graded separately [36]. However, in this review it was decided to additionally grade per study, as it was estimated that heterogeneous outcome measures would prevent outcome summaries of different studies.

In addition to GRADE, a modified grading scale based on GRADE was established. Previous reviews have suggested that studies aiming to evaluate transition interventions may have low quality of evidence. The purpose of the grading scale was to differentiate these studies from each other and asses if there are considerable differences in quality of evidence in the lower range. Therefore, quality of evidence was divided into eight levels based on the criteria shown in Table 2.

Results

Included studies

Search in electronic databases and through other sources identified 4542 records. Abstracts of 2685 studies after deleting duplicates were reviewed and full-text was obtained for 75 studies, of which 39 were excluded and are listed with reason for exclusion in the online supplement (Supplementary table 5). Twenty-eight studies met the inclusion criteria (Figure 1). Characteristics of all included studies can be found in the online supplement (Supplementary table 6).

Table 2: Modified grading scale.

Criteria	Possible score[a]
RCT	2
Controlled trial	1
No increased risk of selection bias	1
No increased risk of other biases	1
No indirectness of evidence	1
Precision based on sample size:	
n > 150 (or n > 40 if rare disease)	1
n > 100 (or n > 20 if rare disease)	1

RCT, randomised controlled trial. [a]For each criterion met, the number of points indicated in the right column will be given (8 points in total).

Study designs

Included were four RCTs, 15 NRCTs and nine intervention studies with single group design. Eight of 15 NRCTs used historic control groups.

Certainty of evidence

The certainty of evidence, using the GRADE process, was very low in all outcomes shown in Table 3. When assessing quality of evidence per study seven studies [37–43] showed low and 22 very low quality of evidence.

In the 8-point grading scale (Table 2), where one point indicates very low and eight points very good quality of evidence, none of the included studies received 7 or 8 points, 7% of them received six, 32% five, 21% four, 21% three and 14% two points. 4% of studies received one point.

We could not assess consistency and selective reporting due to small sample sizes and heterogeneity of study characteristics.

Study populations

The study population consisted of 1554 participants with the same health condition per study in all studies except one [41]. Chronic health conditions of samples are given in Figure 2. Age of the participants varied between 11 and 59 years; however, most participants were YP.

Outcome parameters

Outcome parameters varied according to disease. They included mortality, indices of morbidity and surrogate parameters such as HbA_{1c}, body mass index (BMI) or forced expiratory volume (FEV1). All outcome parameters identified are listed in the online supplement (Supplementary table 7).

Interventions

All studies used interventions which consisted of combined elements, in most cases as a dedicated transition

Table 3: Summary of findings of most frequently assessed outcomes.

Outcomes	Number of participants (studies)	Results	Certainty of Evidence (GRADE[c])	Comments
Mortality	145 (3 studies)	Beneficial effects[a] (1 study): Number of deaths: Intervention: 0/20 (0%) Control: 4/14 (28.5%) ($p < 0.01$) No effects[b] (2 studies)	Very low	
Graft rejection	179 (5 studies)	Beneficial effects (1 study): Number of rejections: Intervention: 3/33 (9.1%) Control: 7/26 (34.6%) ($p < 0.05$) No effects (1 study) Descriptive analysis only (2 studies): Number of rejections: 1) Intervention: 0/12 (0%) Control: 3/9 (33%) 2) Intervention: 2/16 (12.5%) Control: 1/16 (6.3%)	Very low	
Diabetes-associated complications	189 (3 studies)	Beneficial effects (1 study): Number of occurrences of hypoglycaemia: Intervention: 0/51 (0%) Control: 5/30 (16%) ($p = 0.02$) No effects (1 study) Descriptive analysis only (1 study): Number of diabetic ketoacidosis: 2 years prior to transition: 3/27 (11%) During intervention: 2/53 (3.8%) Number of occurrences of hypoglycaemia: 2 years prior to transition: 2/27 (7.4%) During intervention: 6/53 (11.3%)	Very low	No control groups
Haemoglobin A1c (HbA_{1c})	572 (9 studies)	Beneficial effects (5 studies): HbA_{1c} change 1) −0.7% 2) −0.93% 3) −0.9% 4) −0.77% 5) Intervention: −0.40% Control: +0.42% ($p = 0.01$) No effects (4 studies)	Very low	No control groups
Estimated Glomerular Filtration Rate (eGFR)	179 (4 studies)	Beneficial effects (1 study): Intervention: eGFR decreases by 11.3 mL/min/1.73 m^2 Control: eGFR decreases by 8.4 mL/min/1.73 m^2 ($p = 0.004$) No effects (3 studies)	Very low	
Body mass index	217 (4 studies)	Beneficial effects (1 study): Intervention: 32.5 kg/m^2 Control: 43.4 kg/m^2 ($p = 0.01$) No effects (3 studies)	Very low	
Blood pressure	176 (3 studies)	Beneficial effects (1 study): Number of patients suffering from high blood pressure: Intervention 1/31 (3.2%) Control 16/64 (25%) ($p = 0.02$) No effects (2 studies)	Very low	

[a]Beneficial effects were defined as showing a significantly better outcome in the intervention group or in measurements after intervention.
[b]No effects were defined as showing no significant differences between groups or between measurements before and after intervention.
[c]GRADE Working Group grades of evidence: High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate.

program. Of these elements, appointments with professional groups other than doctors (i.e. social workers, psychologists or nurses) or extended medical appointments were used in 43% of included studies. Web-based interventions such as websites, online computer programs or interactive online interventions (21%) were also used. 18% of studies examined joint visits, meaning that YP had appointments where both paediatric and adult provider were present. In 18% of included studies patients were transferred to adult care not necessarily by the age of 18, but according to their transition readiness or the opinion of their paediatrician.

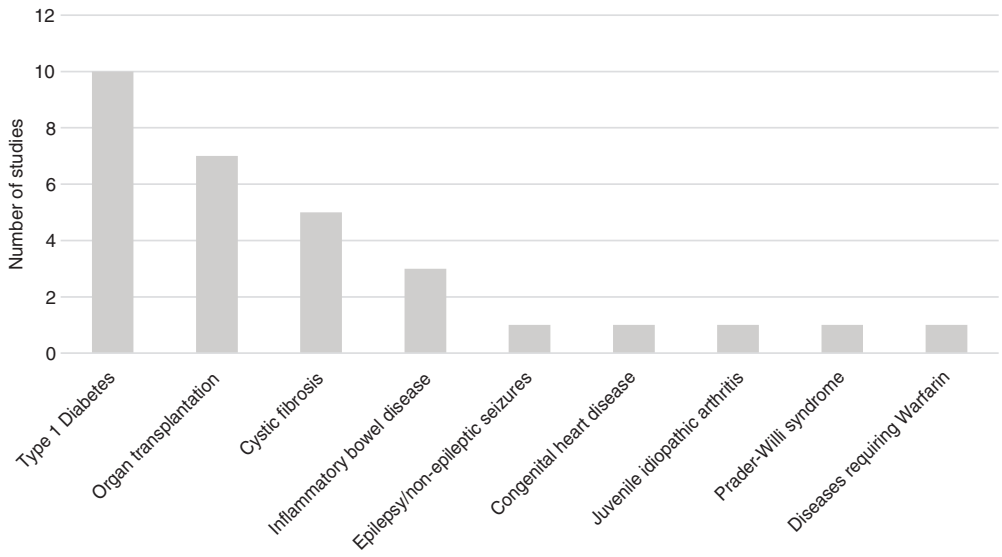

Figure 2: Number of studies that used samples with certain chronic health conditions.

Outcomes

Thirteen [24, 39, 40, 44–53] of the 28 included studies showed beneficial effects. None of the included studies demonstrated significantly better outcomes in the control group. One study [54] showed significantly worse outcomes in measurement after intervention. 56% of studies assessing HbA_{1c} showed beneficial effects [24, 44, 47, 50, 52], whereby this proportion did not exceed 25% in other outcomes like graft rejection, BMI or estimated glomerular filtration rate (eGFR) (Table 3).

Intervention components were evaluated by several studies, whereby some of them showed beneficial and others no effects (Figure 3). Beneficial effects were defined as having at least one outcome significantly better in the intervention group or in measurements after intervention. No effects were defined as showing no significant differences between groups or between measurements before and after intervention. 83% of studies that examined workshops showed beneficial effects, followed by those that assessed joint visits (60%) and extended or multidisciplinary appointments (58%). Seventeen percent

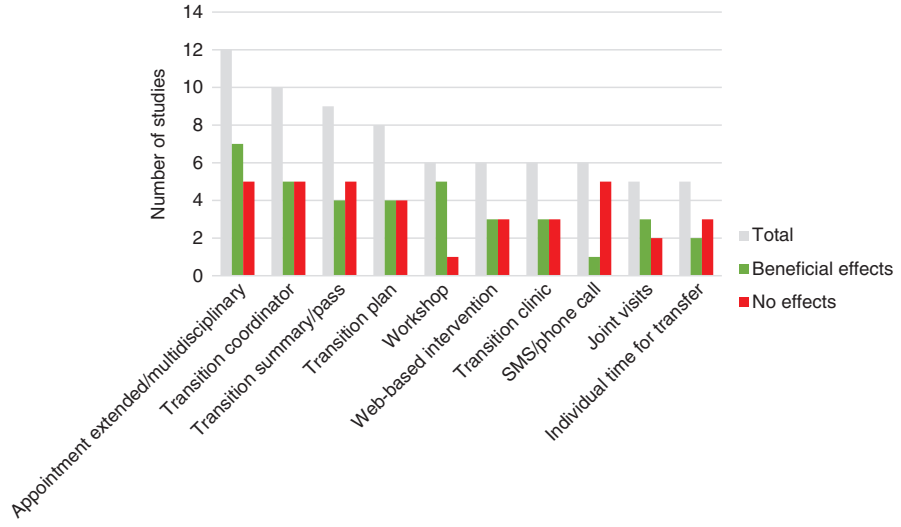

Figure 3: Number of studies that evaluated certain intervention components.
Total: Total number of studies. Beneficial effects: Number of studies showing a significantly better outcome in the intervention group or in measurements after intervention compared to the control group or measurements before intervention. No effects: Number of studies showing no significant differences between groups or between measurements before and after intervention.

of studies examining phone calls or SMS-based interventions showed beneficial effects.

Discussion

This review aimed to assess whether interventions can ameliorate somatic outcomes of YP in the transition period and determine which intervention components are particularly effective. There are reviews on this topic already [32, 33]. However, this review is a valuable contribution to prior research efforts as it covers more health conditions and transition interventions than previous reviews. This is due to available evidence consisting of 28 studies with 1554 participants.

We could show that interventions aimed to improve transition can ameliorate somatic outcomes. Generally, the effectiveness of transitional interventions on certain outcomes is difficult to infer due to varying lengths of follow-up and sample sizes. Concerning patients suffering from T1D, many studies found an improvement of HbA_{1c} values. However, findings concerning diabetes-associated complications like diabetic ketoacidosis or hypoglycaemia were inconsistent. In one NRCT [52] hypoglycaemias occurred less frequently in the intervention group compared to controls. In contrast, there were no effects observed in one RCT [55]. A reason for the inconsistency may be that severe hypoglycaemias are rare events and are therefore not to be expected given the size of sample and the length of follow-up period.

Findings were also inconsistent as to whether participation in interventions resulted in reduced mortality or graft rejection in patients who had received a liver or renal transplant. This could be due to the fact that long-term outcomes such as transplant failure or mortality can only be recorded with long follow-up periods. One of three studies examining mortality showed beneficial effects [45]. Significantly fewer deaths were observed in an intervention group compared to a historic control group. However, there may be confounding effects due to study design. Patients in the historic control group transferred at a time when the life expectancy of transplant recipients was generally still lower. Similarity of study groups cannot be assured concerning participants of the intervention group that transferred up to 17 years later than the historic control group. This is due to changes in medical care and declining mortality of transplant recipients over the past years in general [56]. Hence, results should be treated cautiously.

Across reviewed studies no effects were shown among some studies without a control group but with measurement before and after intervention [57–59]. However, this can also be considered a success, indicating that health remained stable during the transition phase.

Although findings were inconsistent concerning certain outcomes, overall evidence suggests that it is possible for transition interventions to ameliorate somatic outcomes in chronically ill YP.

Concerning the different components of transition interventions, it was observed that multidisciplinary appointments or more time at medical appointments, the use of transition coordinators and transition summaries or transition passes were most commonly described. We considered appointments as multidisciplinary if patients had appointments with social workers, psychologists, nurses or other professionals. This broad definition of multidisciplinary appointment may be a confounding effect regarding its frequent occurrence in the included studies as well as concerning the approaches, topics and qualifications of the different professional groups.

Workshops, joint visits and multidisciplinary appointments or more time at medical appointments were most successful. Studies applying one of these three components were the only ones showing rather beneficial than no effects. Of these components workshops were most effective with five out of six studies showing beneficial effects [24, 44, 46, 49, 52]. In these studies workshops were embedded in multi-component interventions.

The intervention components mentioned above were particularly beneficial and should therefore be considered for primary inclusion in transition programs.

Our findings are in line with the previous review of Crowley et al. [31]. The review, with inclusion criteria similar to our own, also showed that transition interventions have beneficial effects. The most successful transition components were transition clinics and patient education. However, only studies examining patients with T1D were identified so that effects could not be generalised to other chronic conditions. Evidence was limited due to the poor methodological quality of the included studies.

In contrast, the review of Campbell and colleagues [32] found no effects on somatic outcomes, but was limited due to the small number of studies identified (four studies; $n = 238$) and thus covered a narrow range of interventions and clinical conditions. This was due to the fact that it included RCTs only. In this review we additionally included NRCTs and intervention studies with measurements before and after intervention. However, when considering RCTs only, we must confirm that there were no beneficial effects on somatic outcomes in intervention groups when compared to controls [37, 41, 43, 55]. Future

research should ascertain whether the positive effects found for NRCTs can also be proven in RCTs.

However, there are barriers to applying a high standard of methodology in studies assessing transition interventions. For example, adequate blinding is neither meaningful nor possible for many transition interventions and there are studies that consider RCTs in the domain of transitional care to be unethical [60, 61].

Our estimate of the effectiveness of transition interventions is limited for the following reasons. Importantly, one limitation relates to the evaluation and comparison of the identified transition interventions. This is attributed to the great variety of types, intensity and duration of interventions. All interventions had different components, of which no separate evaluation was carried out. Ascertaining the effect of the components is thus difficult.

Estimate of the effect is furthermore limited due to the lack of studies with a rigorous methodology and an appropriate study design. Only four RCTs met the inclusion criteria. Many NRCTs were included but some used historic controls. It is possible that effects are biased in these studies when similarity of historic control and current study sample cannot be assured [62]. Further limitations include the frequent occurrence of bias, especially selection bias. For example, high rates of loss to follow-up as well as low response rates were common among included studies.

The risk of limitations due to imprecision varied according to study as sample sizes ranged from 18 to 120. Follow-up period was generally short, ranging from six to twelve months in most studies. It is thus not possible to judge the sustainability of outcomes. Furthermore, the full effect of interventions on somatic outcomes cannot be recorded. In particular, the long-term effects cannot be determined and may be underestimated.

Although the identified studies examined various chronic diseases, it is not certain if results can be generalised to all chronic health conditions. In our sample, rare conditions such as CF or organ transplantations were overrepresented, with seven and five studies, respectively. This could be because adherence and continuity of care is particularly important for these patients.

Using the GRADE approach, the limitations due to study designs, biases, sample sizes and follow-up data led us to judge the certainty of evidence to be very low. Therefore, we are very uncertain about the estimate.

Even though the estimate of the effectiveness of transition intervention is limited, some conclusions can be drawn. It will probably take time until results of future research, especially of high-quality RCTs, are available. However, this should not be awaited before better transition programs are initiated based on actual evidence. An important barrier to the implementation of transition programs in Germany and many other countries is a lack of adequate funding. Only joint visits are a part of one of the few structured transition programs in Germany [63] that is funded by some health insurance schemes. Future efforts should promote transition interventions that have been identified by this review as being particularly useful and ensure they are covered by health insurance funds. It is important to bear in mind that successful transition will probably reduce morbidity and mortality and thereby reduce long-term health care costs. Consequently, the allocation of financial resources for transition can lead to lower global healthcare costs overall.

Conclusion

In comparison to former reviews a much larger number of studies evaluating transition interventions was identified. Beneficial effects were observed in many of them, but findings were inconsistent concerning certain outcomes. Overall, transition interventions can be recommended. Workshops, joint visits and multidisciplinary appointments or more time at medical appointments, in particular, had beneficial effects. However, quality of evidence is low due to a lack of studies with good methodology and rigorously evaluated intervention methods. Guidelines could be based on the findings of this review, but should be supported by expert consensus. Future research should particularly focus on random assignment to study groups to prevent selection bias, whilst addressing deficits such as short follow-up time or small sample sizes identified from previous studies.

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Competing interests: We state no conflict of interest.

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