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Revisiting the incidence of schizophrenia: learning about the other half

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Summary and general discussion

Summary of findings

We started our thesis (chapter 1) by highlighting the burden of disease caused by schizophrenia and stressing the importance of valid incidence estimates for researchers and health policy makers. We explained that detecting all incident cases of schizophrenia in a population is difficult since the onset is often gradual. Then, we described the current standard method to estimate the treated incidence of schizophrenia: the *First Contact (FC) design*. We pointed out that the FC design was not originally intended to determine the treated incidence, but that in the 1990s, a research practice arose which used the design for that purpose. We identified three unspoken assumptions underlying that practice. We then introduced another approach based on data from The Hague's electronic Psychiatric Case Register. A unique opportunity presented itself to compare both approaches in one population. This provided the basis for our main research question:

Which method (ePCR or FC) should be used to estimate the treated incidence of schizophrenia?

We broke that question down into three subquestions:

First, we asked: *do the ePCR and FC methods agree?* In chapter 2, we compared the results from both methods in exactly the same study population and study period. The ePCR estimate was about three times higher than the FC estimate (69 vs 21 per 100 000 person years, respectively).

Second, we asked: if they disagree, why? To answer that question, we tested three assumptions that underly the use of the FC method to estimate the treated incidence of schizophrenia, with the following results:

Assumption (a) was tested in chapter 3. There, we examined retrospectively which initial diagnoses were made at first contact with psychiatric services, for 1753 subjects aged 18–35 years diagnosed with any psychotic disorder between 2005–2009. For all types of psychoses, 56% (985/1753) had been treated in secondary mental health services prior to the onset of psychosis. For the subset of 355 subjects diagnosed specifically with schizophrenia, 62% (222/355) were diagnosed at first contact, but 38% (133/355)[4] first got another diagnosis of non-psychotic mental disorder. This finding contradicts assumption (a).

4 Subjects first diagnosed with another type of psychosis but ultimately diagnosed with schizophrenia were not included in that figure, so 38% is a lower bound.

Assumption (b) was tested in chapter 4. There, we used the ePCR to estimate the incidence and lifetime morbid risk of schizophrenia by age and sex, among citizens of The Hague aged 20–79 years between 1997–2012. Nearly half (46%) of onsets were diagnosed after age 40 years. This finding contradicts assumption (b).

Assumption (c) was tested in chapter 5. There, we used the data from chapter 2 to calculate age and sex adjusted incidence rate ratios (IRR) for the three largest migrant groups, relative to the Native Dutch population. The FC method was relatively more inclusive for migrants presenting at earlier ages or with shorter durations of prior treatment (DPT) than the native Dutch. Finding differential sampling in the FC method contradicts assumption (c).

Third, we asked: *how do our findings fit into the existing evidence?* In chapter 6, we first introduced a framework to classify the various study designs that have been used in different studies, along three dimensions (i.e. *coverage* of mental health services, *time frame* of the diagnosis, and *accuracy* of the diagnosis). In chapter 7, we then reviewed all studies published between 2008–2019 that reported the treated incidence of schizophrenia in general populations in Northern Europe (like ours). In a meta-regression, our framework of study design (chapter 6) explained 67% of between-study variation. A *full* model—i.e. also accounting for differences between study populations in age and urbanicity—explained 91% of between study variation. According to that model, studies conducted in general psychiatric services reported similar estimates to those conducted in specialized services (incidence rate ratio 1.12 with 95% confidence interval 0.88 to 1.43). But studies applying a cumulative time frame to diagnosis reported fourfold higher estimates (4.04; 3.14 to 5.2) than those applying a first contact time frame. And studies based on clinical diagnoses reported lower estimates (0.55; 0.43 to 0.72) than those based on standardized research diagnoses. In chapter 8, we summarized the vulnerabilities of the FC method. We then proposed a hybrid design that incorporates the ePCR method's benefit of inclusive case finding with the FC method's diagnostic standardization.

Interpretation

The findings from chapters 2, 5 and 7 allow us to explain why the FC and ePCR methods' estimates diverged by a factor three (chapters 2 and 5). The approaches were different in three ways: First, in contrast to the FC-design, the ePCR applies a cumulative time frame—which, according to our meta-analysis, may have increased the estimate fourfold on average. Second, it was based on clinical diagnoses—which may have reduced it by half. And finally, its coverage of services was slightly better—which again may have increased the estimate somewhat.

Our meta-analysis (chapter 7) explains why previous studies (Jongsma et al., 2019; Kirkbride, Errazuriz, et al., 2012; Stafford et al., 2018; van der Werf et al., 2012; Vassos et al., 2012) measured vastly different incidence rates in otherwise similar populations: different designs yield different results.

We are not the first to investigate the effect of study design on incidence estimates [5]. In their meta-analyses of incidence studies, McGrath et al. (2004) and van der Werf et al. (2012) included only studies with a first contact sampling frame and *within that category* observed no other differences by design. Jongsma et al. (2019) later did include several studies with a cumulative time frame (including our study from chapter 2, and *pooling two types of register studies (with both FC and cumulative time frames)* observed that register-based studies reported higher rates than FC-studies. Our studies add to the literature by explicitly separating and quantifying the different factors.

Revision of the framework introduced in chapter 6

The framework formulated in chapter 6 (Figure 9.1a) sought to untangle the opposite effects of three dimensions of study design. But the findings in the meta-analysis (chapter 7) require us to update it somewhat.

In our initial version of the framework (chapter 6), we expected that researchers would be more conservative in diagnosing schizophrenia than clinicians.

Edwards et al. (2019) followed our framework but noted that not every case meeting diagnostic criteria is recognized as such by clinicians and/or receives care. As a result, they anticipated that studies reporting clinical diagnoses (in their words,) would produce lower estimates than studies reporting study diagnoses (in their terms).

We quantified the relative effect of each of these dimensions on the incidence estimate in our meta-analysis (chapter 7). Our meta-analysis results generally confirmed our initial framework (chapter 6), but—as Edwards et al. (2019) predicted—studies based

5 The question drew a lot of attention when the need for standardized diagnosis became clear (Cooper, 1972; Kendell et al., 1968), and it was centered on the seminal WHO first contact studies (Jablensky et al., 1992; Sartorius et al., 1974). Kendell et al. (1993) outlined in detail the difficulties of estimating the incidence of schizophrenia. It has been consistently been shown that covering more types of facilities results in higher incidence rates (Amminger et al., 2006; Anderson et al., 2018; Jörgensen et al., 2010). Similarly, the notion that a longer time frame for diagnosis results in higher incidence rates (Amminger et al., 2006; Bresnahan et al., 2000; Kleinhaus et al., 2011), as well as the idea that the first contact design can result in selection bias, were discussed several times (Aleman et al., 2003; Kleinhaus et al., 2011).

on clinical diagnoses appear to yield lower estimates than studies based on standardized research diagnoses.

Figure 9.1b shows a *new illustration of our revised framework*. In response to a reviewer's suggestion, we changed the name of the axis from 'accuracy' to 'reliability' of the diagnosis. We reordered the values on that axis to (1) clinical, (2) science, and (3) non-standardized diagnosis. As a consequence, the relative sizes of the boxes representing the two approaches in the diagram have changed.

Systematic comparison of both methods

Before answering the main research question, we will compare the pros and cons of each method in terms of the updated framework (i.e. *coverage*, *time frame*, *reliability*), and in terms of *generalisability* and *feasability*.

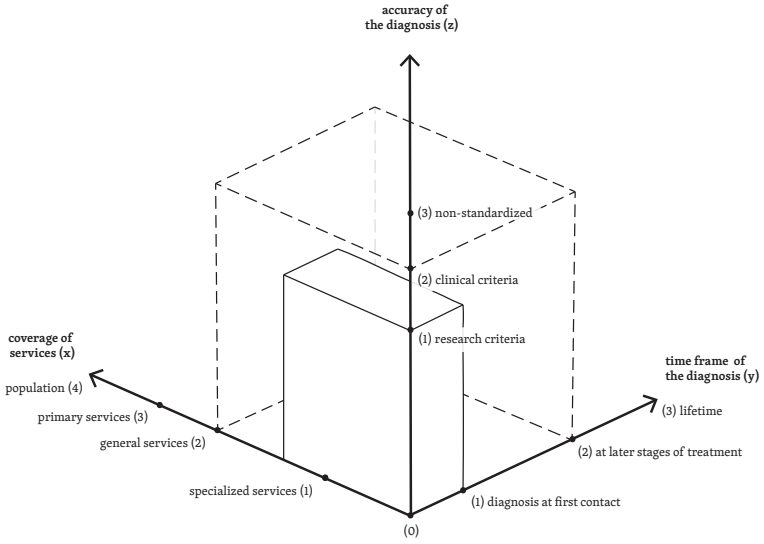
In terms of *service coverage*, the FC method is typically restricted to a (specialized) subset of the psychiatric services, whereas the ePCR method covers all services.

Also, the FC method is typically restricted to younger cases, usually aged <40 years (i.e. early onsets), whereas the ePCR method potentially covers the entire lifespan (i.e. also late and very-late onsets).

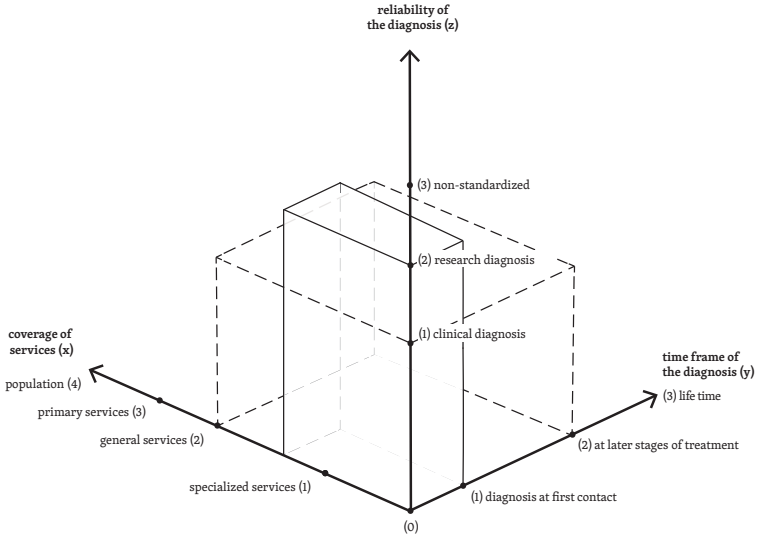
In terms of *time frame to diagnosis*, the FC method (i.e. using a first contact time frame) is restricted to initial diagnoses, whereas the ePCR method (i.e. using a cumulative time frame) covers the entire diagnostic history over the lifespan, and so can work with ultimate diagnoses.

Together, these characteristics imply that the ePCR method should be able to capture most incident cases of treated schizophrenia, whereas *by design* the FC method will capture only a special *subset*, i.e. younger patients who manifest schizophrenia-like symptoms at first contact with (specialized) services.

Service coverage appears to be less important than time frame or reliability among these factors (chapter 7). This means that if the time frame for diagnosis is long enough, full coverage of all psychiatric services might not be required. Most patients will likely be referred to specialized services when they are diagnosed with schizophrenia, and can then be counted.



(a) Initial illustration



(b) Revised illustration

Figure 9.1 Revision of the framework's illustration

The volume of the solid box represents the incidence as estimated in a FC study and the volume of the dotted box the incidence as estimated in an ePCR study.

In terms of *reliability of the diagnosis*, the prototype FC approach (Jablensky et al., 1992; Veling et al., 2007) is based on standardized study diagnoses. But in reality, many FC studies have used clinical diagnoses made in services for Early Detection of Psychosis (chapter 7). The ePCR approach is fully based on clinical (administrative) diagnoses.

So, are standardized research diagnoses better than clinical diagnoses? *If* a clinician decides to formally diagnose schizophrenia, that diagnosis is probably accurate (Dalman et al., 2002; Ekholm et al., 2005; Fusar-Poli et al., 2016; Ludvigsson et al., 2011; Uggerby et al., 2013) and stable [chapter 2, and Fusar-Poli et al. (2016)]. It seems the problem is rather that clinicians often *don't* diagnose schizophrenia when standardized procedures (and DSM criteria) suggest they should (chapter 7). We speculated (chapter 7) that they may be reluctant to formally diagnose schizophrenia due to the stigma associated with the diagnosis. This implies that underestimation (missing true cases) is more likely than overestimation (incorrectly including non-cases) when using clinical diagnoses in either FC or ePCR methods.

The degree to which each approach's study samples represent the overall schizophrenia population is referred to as *generalisability*. Can the FC approach be used to determine risk factors for schizophrenia even though it underestimates the incidence? The issue is that the FC design requires subjects to present to facilities *in a particular way* in order to be counted [6]. The problem is that many risk factors for schizophrenia also affect how people present to facilities. Men and women, migrants and natives, the elderly and the young, for example, have vastly different coping mechanisms, social support, attitudes toward medical care, help-seeking actions, clinical presentation, and so on. They may not be subjected to the same degree of stress or stigma, and they do not break down in the same way or at the same rate. As a result, they do not take the same routes to and from psychiatric care [7]. To put it another way, selection bias is built into the design. The results in chapters 2 and 5 showed that the FC approach does indeed produce a biased sample. We may conclude that risk factors identified in FC studies inform us about a subset of schizophrenia cases that present to services in a particular way, while risk factors identified in ePCR studies can inform us about cases with a broader range of clinical presentations.

6 This way, the FC has requirements stricter than the DSM. Whereas the DSM doesn't require a minimum age of onset, the FC approach does. Also, whereas the DSM does not stipulate which route to and through care a subject should take, the FC approach demands that subjects have psychotic symptoms precisely when they seek help for the first time in their life. Subjects meeting these additional conditions above and beyond the DSM criteria are exceptions: they correspond to subjects with an acute onset, who are often genetically (strongly) predisposed to psychosis and so on.

7 In technical jargon: the FC approach creates a causal structure known as *conditioning on a common effect of two variables* (Hernán et al., 2004).

With *feasability*, we mean the preconditions and costs associated with each method. We will review separately two types of efforts: those to (a) identify all cases, and those to (b) exclude all non-cases.

To (a) identify all cases, an FC study requires a massive effort to include all entry points in the system in the study, and a lot of manpower to monitor and interview subjects with schizophrenia-like symptoms who present at relevant entry points. But it requires no electronic Health Administrative Dataset (eHAD). Creating an eHAD-based ePCR from scratch would be prohibitively expensive. Arguably, eHADs have arisen in advanced economies over the past decade, among other reasons because health insurers have forced a culture of detailed and secure registration for financing purposes. Some of these eHADs can be repurposed as an ePCR. In practice, FC studies are typically short-term initiatives, whereas ePCR studies may be ongoing.

With respect to (b) the efforts to exclude all non-cases, the issue is that known (prevalent) cases can migrate into the catchment area, or return to psychiatric services after dropping out for many years or receiving care outside of the catchment area. In population based studies, such cases have to be identified and excluded from the counts.

In the FC method, researchers can simply ask participants about their diagnostic history and date of settlement during the face-to-face interviews. It is then straightforward to exclude known cases who settled into the area less than six months ago (Jablensky et al., 1992) and known cases from the area who return to psychiatric services. Here, the FC strategy is simple and effective.

In contrast, in the ePCR method, the algorithm queried the history of zipcodes and diagnoses to identify instances of in-migration or returning cases. But because the period at risk extends from childhood to old age, the algorithm requires records reaching back for up to 60 years to be complete. So a key problem with *young* ePCRs [8] is that they cannot distinguish new cases from known cases of schizophrenia unless they have accumulated many decades of data [9].

8 i.e. running on a few decades of data only.

9 To the best of our knowledge, no ePCR currently provides full coverage for the entire period at risk (ages 10 to 100). However, Scandinavian ePCRs, especially those from Denmark, may be very close to that point (Ludvigsson et al., 2011; Mors et al., 2011). Since they are typically national registers, internal migration is not an issue. In addition, they use social security numbers to link municipal databases to the ePCR. That way, they can identify people who have recently arrived in the country. Their ePCRs may also recognise identified cases returning to treatment from as far back as the 1970s, which is ten years earlier than our ePCR.

The good news is that the problem of data scarcity is self-limiting. Within 10 to 20 years several ePCRs will have accumulated data covering service use and diagnostic histories over the entire at risk period. From that point onwards, in-migration and known patients returning to services can be identified with high accuracy. Meanwhile, there are several work-arounds for young ePCRs waiting for data to accumulate. First, it is possible to estimate (and adjust for) the bias introduced by this problem by obtaining data from outside the eHAD, e.g. by consulting municipal data on (re)settlement histories (as we did in chapter 2), or by examining case-notes (as we did in chapter 4). Second, it can be solved completely by contacting cases identified by the ePCR to ask them directly (as done in the FC method, and in the hybrid method proposed in chapter 8).

Answer to the main research question

So *which method (ePCR or FC) should be used to estimate the treated incidence of schizophrenia?* The treated incidence should account for every first onset of schizophrenia. The difficulty is that subjects who are originally diagnosed with another medical condition can later be diagnosed with schizophrenia. That can happen anywhere in the mental health system, while under treatment for another disorder, and after any history of previous diagnoses. Such cases should be counted too, but the FC approach was not designed to detect them. Our answer is nevertheless, that *as long as their respective strengths and limitations are taken into account, both methods can be used*.

We have summarized the pro's and con's of each method in Table 9.1. In short, the FC method does not require an eHAD infrastructure but relies on intensive collaboration between clinicians on a project-like basis. First contact diagnoses at their best are based on standardized research procedures, in practice they are often based on clinical diagnoses. The FC methods has a simple and effective solution for identifying false positives. Inclusion typically stops if the onset is before 40 years of age. Because case finding is restricted to initial diagnoses (i.e. first contact time frame) *the FC approach provides the incidence rate and risk factors of a special subset consisting of roughly one third of the schizophrenia case population*: young subjects presenting schizophrenia-like symptoms at first contact.

The ePCR method requires a data warehouse containing accurate and complete health administrative records from all relevant psychiatric services within a defined catchment area. The database should have accumulated enough data to trace back the entire diagnostic history. If these preconditions are met, ongoing registration of incident cases of schizophrenia is straightforward, and vastly cheaper than any analog FC study. The ePCR can then identify onsets of schizophrenia anywhere in the mental health system, at any stage of treatment and after any history of prior diagnoses. It can still underestimate

Table 9.1 Pro's and con's of each method

		FC	ePCR	hybrid
coverage	services	specialized	general	general
time	diagnosis	initial	ultimate	ultimate
reliability	procedure using	research diagnosis interview	clinical diagnosis decades of data	both interview
generalizability	sample age	subset early onset	all treated entire lifespan	all treated entire lifespan
feasability	requires duration	manpower project	eHAD ongoing	both project

the treated incidence, however, because it relies on clinicians' diagnoses, who tend to be more conservative than researchers (chapter 7). It can provide reliable estimates of the treated incidence over the entire lifespan but—especially for late (LOS) and very-late onset (VLOS) cases—that use requires multiple decades of data to identify and exclude all instances of known cases migrating into the area or returning to psychiatric services after dropping out.

General strengths and limitations of this thesis

The strengths and limitations specific to each primary study (chapters 2, 5) and the meta-analysis (chapter 7) are discussed in each respective chapter.

Our general strategy was to compare both methods directly in a medium sized city in Northern Europe (The Hague, Netherlands 1997–2012) along three dimensions of study design (i.e. service coverage, time frame for diagnosis, and accuracy of diagnosis). We also confirmed our observations by reviewing all incidence studies conducted in Northern Europe and published between 2008 and 2019, applying a regression model that differentiated the impact of variations along the same three dimensions of study design, while also accounting for true differences between study populations (i.e. age and urbanicity).

In our primary studies, both methods were performed according to the highest standards. The data for the FC method were extracted from a first contact study that emulated the

WHO Ten-Country study, and that was classified by others in several meta-analyses (Bourque et al., 2010; Jongsma et al., 2019) as meeting high quality standards. The data for the ePCR method were based on a case register with just over 30 years of electronic health administrative records, covering all general, specialized (i.e. tertiary, emergency or outreaching) psychiatric services in the catchment area. From these data, service pathways and diagnostic histories could be reconstructed, and onsets of schizophrenia could be detected at any stage of treatment anywhere in the mental health system. The clinical diagnoses used in the ePCR were made by well trained clinicians. Once made, they were carefully audited and stable over time (chapter 2) [10].

Our catchment area for the ePCR was population based (city of The Hague) and strictly defined (by zip code). The municipality provided accurate census numbers by year, age (in 5-year brackets), sex and ethnicity. It was representative of medium sized cities in Northern Europe. The studies included in the meta-analysis were also performed in Northern Europe (i.e. United Kingdom, France, Netherlands, Denmark, Sweden, and Finland). We have assumed that these populations were similar enough to our own study population—in terms of organization of psychiatric services, health insurance coverage and help-seeking behavior—to be used for a replication of our findings.

We note three limitations that afflict *all* currently available methods to estimate the incidence of schizophrenia. First, the schizophrenia construct itself is problematic (Blom, 2004; Boyle, 1990; Guloksuz & Os, 2017). Second, only subjects treated for schizophrenia are counted [11]. Third, we do not know if our findings apply outside Northern Europe. Health services are different in the United States, Canada and Australia, but attitudes towards help-seeking seem the same as in Europe. Findings from ePCR studies from these countries also point in the same direction as our studies (Anderson et al., 2018). Our study did not cover schizophrenia incidence estimates from Low and Middle Income countries (LMIC) and we can therefore not make any judgment on replicability in these countries.

10 One could argue that diagnostic criteria have changed over time. This is not a problem here, because the criteria (DSM-IV at the time) did not change during our entire study period. Cases classified under DSM-III criteria during the 1980s were treated as 'known cases' and not counted.

11 According to Guloksuz & Os (2017), the true natural history of schizophrenia cannot be determined from a treated population because that sample only contains people with the most extreme manifestations of the condition and ignores those with milder forms who do not need treatment. This phenomenon is known as 'Berkson's bias' or 'outcome bias.' It arises when a disorder and the need for treatment (for example, arising from co-morbidity and other complicating) *concur*, i.e. together increase the likelihood of being included in the study sample. It can create spurious correlations and confound true risk factors. This bias is arguably greater in the FC approach since it detects only a subset of treated subjects. However, despite covering all paths of care, the ePCR approach is limited to subjects receiving treatment and thus also suffers from "outcome bias".

The degree to which our conclusions can be applies to other types of psychosis, the general population, or LMICs is restricted by these three general limitations. However, within this context (schizophrenia, treated incidence, Northern Europe), they do not invalidate our comparison of two approaches or our observations about the impact of differences in study design.

One limitation is specific for this thesis. The ePCR we used was relatively *young*, in the sense that it had not yet accumulated enough data to cover the entire period at risk for schizophrenia of each subject it monitored. How much could this have affected our findings? The ePCR used in this study had accumulated just over 30 years of data at the time of this thesis. According to sensitivity tests (chapters 2 and 4), up to the age of 40, distortions from in-migration or returning cases were minor (roughly 5 percent). However, beyond that age, the reliability of our ePCR decayed: the number of false positives increased to approximately 15% between the ages of 40–59 years, and even 40% between the ages of 60–79 years (chapter 7). We have adjusted for the bias resulting from this problem with several methods (discussed on page), but some remaining cases may either have been counted that should have been excluded (i.e. misclassification by confusing incident and prevalent cases), or counted correctly, but under the wrong age of onset group (i.e. misclassification by age). Any remaining distortions are arguably minor and inadequate to explain the major (2–5 fold) design-related effects found in this thesis.

Implications

The differences uncovered in this thesis between the FC and ePCR approaches have practical implications for researchers, clinicians, and policymakers.

Implications for policy makers

For policy makers, our findings imply that two to four times more persons develop schizophrenia every year than current incidence models assume. These subjects are already under treatment, so there is no need to expand general psychiatric services. But the provision of care for schizophrenia should be adjusted for the fact that the majority of new cases of schizophrenia are found among patients *already under treatment* for another mental disorder. This other half (chapter 8) may have other needs than subjects with an early/acute psychosis type of onset.

At a national and global scale, the calculations of the *global burden of disease* from schizophrenia need to be adjusted. Currently, they largely seem to be based on FC studies, which

implies a serious underestimation by a factor two or more (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators & Murray, 2018).

Implications for researchers

Whereas the FC design can be considered as the first solution to the limitations of traditional case registers for epidemiological research, psychiatric case registers based on modern electronic health administrative data sets now offer a second—much easier, much cheaper—solution to the same problem. ePCRs solve several limitations of the first contact method, adding the possibility to reconstruct individual pathways (both treatment and diagnostic) over time, across all psychiatric services within a catchment area. This way, they can provide a longitudinal perspective on the dynamics of psychosis over time.

We are aware that for many areas, especially in Low and Middle Income countries (LMIC) the ePCR method is not yet an option as it requires electronic health administrative data. These need to be complete, extensive and of high quality. It will take considerable time before such data will become more widely available. Until that time, the lack of ePCRs will restrict the value of international comparisons. In LMIC countries, the FC method may remain the only option for now, with the risk of systematically underestimating the incidence of schizophrenia.

If researchers have no other option than to use a FC method, they should be aware of its limitations, as the FC method seriously underestimates the incidence, and its selection bias distorts its risk factor estimates. They may want to make additional efforts, deviating from the original FC design, to identify cases at older ages, and at later stages of treatment.

We should also untangle the *relationship between risk factors and time*. The FC method covers only a short section of the at risk period for schizophrenia. As such, it cannot distinguish between factors that *cause* the onset of schizophrenia (i.e. among subjects which would have otherwise never developed the disorder), and factors that *accelerate* its onset (i.e. among subjects who would have otherwise developed the disorder later). The former factors raise the lifetime morbid risk (LMR), whereas the latter don't [12].

12 In general, a finer-grained study of the natural history of schizophrenia is needed (Os & Kapur, 2009). Such an analysis should take into account the complex dynamics that occur as single psychotic symptoms (Guloksuz & Os, 2017) progress (for some) into severe psychosis and chronic disability: as individuals first seek help, and some then percolate through successive filters and layers (Goldberg, 1992), ever deeper into the mental health system, sometimes in a straight line, but often with false starts and other diagnoses along the way.

We have argued in chapter 8 that a *hybrid* approach is possible, which combines the best of each method. In this hybrid, any subject with a first administrative diagnosis of psychosis (any type) would undergo standardized diagnostic protocols to arrive at a research diagnosis. This solution would be optimal in terms of coverage (complete), time frame to diagnosis (cumulative) and reliability (research diagnosis). It would require a high quality eHAD covering all services, but would not require multiple decades of data, because false-positives could be identified easily during the interviews.

Implications for clinical practice

Finally, our findings challenge the *textbook stereotype* of schizophrenia as a "devastating disorder with acute onset in the second or third decade of life" (National Institute of Mental Health, 2020). It has become clear that there is wide variation in how schizophrenia emerges. The onset is usually insidious, and in western societies most cases seek care for other disorders long before the onset of psychosis. Most new cases of schizophrenia can be found among subjects who are already under treatment. Onset after age 40 is common. Well-known risk factors for schizophrenia (gender, migrants, socio-economic status) are probably correct for cases with early (acute) onset, but their applicability to schizophrenia in general is unclear.

So we should *get to know the other half* of the schizophrenia population. What kind of care do they require? The older patient with late-onset schizophrenia, in particular, has received little attention (Cohen et al., 2000). In comparison to subjects with early onset schizophrenia (EOS), subjects with late onset schizophrenia (LOS) may have had more time to complete their education, find a career, and/or settle with partners and children before becoming ill. They would most likely need assistance to preserve what has been accomplished. Several scholars (Clay et al., 2018; Greenfield et al., 2016; Lappin et al., 2016) have recently suggested expanding Early Psychosis programs to include cases with LOS. Our findings support this development.