Genetic counseling/testing practices for late-onset neurodegenerative disease: systematic review

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ABSTRACT

Objective: To understand current genetic counseling and testing practices for late-onset neurodegenerative diseases (LONDs), and identify whether practices address the goals of genetic counseling.

Methods: We performed a literature search using CINAHL, MEDLINE, PsycINFO, and EMBASE, for articles published from 2009 to 2020. Any peer-reviewed research articles in English that reported research and clinical genetic counseling and testing practices for LONDs were included. We used narrative synthesis to describe different practices and map genetic counseling activities to the goals of genetic counseling: interpretation, counseling, education, and support. Risk of bias was assessed using the Qualsyst tool. The protocol was registered with PROSPERO (CRD42019121421).

Results: Sixty-one studies sourced from 68 papers were included. Most papers focused on predictive testing (58/68) and Huntington's disease (41/68). There was variation between papers in study design, study population, outcomes, interventions, and settings. Although there were commonalities, novel or inconsistent genetic counseling practices were identified. Eighteen papers addressed all four goals of genetic counseling.

Conclusion: Current practices are varied and informed by local laws and protocols, resources, and the availability of different health providers. There was an emerging focus on flexible, multidisciplinary, client- and family-centered care. As genetic testing becomes a routine part of care for patients with LONDs (and their relatives), health providers must balance their limited time and resources with ensuring that clients are safely and effectively counseled. Areas of further research include diagnostic and reproductive genetic counseling/testing practices, evaluations of novel approaches to care, and the role and use of different health providers in practice.

INTRODUCTION

Late-onset neurodegenerative diseases (LONDs) highlight the complexities and challenges of genetic and genomic testing for patients and relatives [1, 2]. Genetic counseling facilitates and supports individuals through the process of decision-making about testing [1, 2]. Genetic counselors are allied health providers trained to provide this specialized care, however, the international shortage of genetic counselors requires other health providers to assume the role [3]. Health providers from outside of genetics are often unprepared to integrate genetic and genomic health information into routine clinical care due to a lack of resources and guidelines, low confidence in initiating genetics discussions, and concerns about discrimination and psychological harm [4]. Examining current genetic counseling practices for individuals undergoing diagnostic, predictive, and reproductive testing for LONDs is therefore important to understand whether these practices adequately address genetic counseling goals.

Genetic counseling is a communication process that aims to help individuals understand and adapt to the medical, psychological, familial, and reproductive implications of the genetic contribution to specific health conditions [5-7]. Adequate knowledge and time allocated to provide genetic counseling is vital to maximize the health benefits of genetic testing while minimising harm to the client and their relatives [1, 2, 8]. According to the Human Genetics Society of Australasia and the United States of America (USA)'s National Society of Genetic Counselors, the activities of genetic counseling should integrate the following four goals:

1. Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence [5, 6].
2. Education about the natural history of the condition, inheritance pattern, testing, management, prevention, support resources, and research [5, 6].

3. Counseling to promote informed choices in view of risk assessment, family goals, ethical and religious values [5-7].
4. Support to encourage the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder [5, 7].

Genetic counseling for different LONDs may be similar given their shared genetic and phenotypic characteristics as progressive diseases that can affect movement, cognition, behavior, personality, or communication, with few treatment or preventative options available to stop or slow progression [9, 10]. Genetic testing, through next-generation sequencing, allows multiple LOND genes to be screened concurrently at lower cost and greater speed, and is becoming more common in neurology clinics [1, 11]. There are three main categories of genetic testing available for LONDs: diagnostic, predictive, and reproductive testing. When a pathogenic variant (mutation) is identified in an affected patient through diagnostic testing, predictive or reproductive testing becomes available to biological relatives. Predictive (or pre-symptomatic) testing identifies whether an asymptomatic relative has inherited a pathogenic variant, which implies a future risk of disease (hereafter described as predictive testing). Reproductive testing provides the option to prevent inheritance of a pathogenic variant through testing a pregnancy (prenatal diagnosis) or *in vitro* fertilisation (IVF, pre-implantation genetic diagnosis). Individuals who do not wish to know their status as a pathogenic variant carrier may be able to undergo reproductive testing through exclusion or non-disclosure testing [12].

Guidelines and protocols for genetic testing have been developed for a range of LONDs [13-19] and are informed by the HD predictive and reproductive testing guidelines [13, 14, 20, 21]. However, guidelines are not always translated into practice [22, 23]. The primary aim of this review was to establish a comprehensive understanding of the evidence for current genetic counseling and testing practices for LONDs. The secondary aim was to identify to what

extent current practices address the established goals of genetic counseling. The findings will inform the development of a genetic counseling and testing model of service delivery for LONDs.

METHODS

Protocol and registration

The systematic review protocol was registered on 01/20/2019 with the International Prospective Register of Systematic Reviews (PROSPERO, CRD42019121421) and was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [24].

Eligibility criteria

The inclusion and exclusion criteria are listed in Table 1 and were developed using the PICOS framework [24]. We wished to find commonalities in genetic counseling practices for different LONDs. Therefore, condition-specific aspects of genetic testing, such as anticipation in triplet repeat disorders, were not considered. Although the goal of genetic counseling is not necessarily to promote undergoing testing, we elected to refer to genetic counseling that involved situations where a genetic test is available. We included articles published since 2009 as we expected this would include current practices used since the advent of next-generation sequencing technology [11].

Literature search strategy

We searched four electronic databases (CINAHL, MEDLINE, PsycINFO, and EMBASE) with terms related to the target disease group and intervention (Table 2). Searches were combined and de-duplicated using Endnote X9. Further references were elicited through backward-searching the reference lists of included papers, and forward-searching using the Web of Science database. The searches were re-run before the final analysis on 27 May 2020.

Study selection

The primary (AC) and secondary reviewer (ROS) piloted the inclusion criteria. AC then screened all references against the criteria at the title and abstract and full-text screening stage, and ROS independently assessed 10% of titles and abstracts and 20% of full texts. After each stage, disagreements were resolved through discussion. Where no agreement was reached, the decision to include or exclude was made by a third reviewer (AM). Inter-rater reliability after title and abstract and full-text screening, respectively, demonstrated a level of agreement of 96.8% and 91.5%, and at least strong agreement using the prevalence-adjusted bias-adjusted kappa (PABAK=0.94 and 0.83) [25, 26]. The study selection process and reasons for exclusion are summarized in Figure 1.

Data extraction and quality assessment

AC completed data extraction and critical appraisal forms for each included paper, then ROS checked, verified, and validated these. Data items were related to the research question (e.g. genetic testing type, health provider role and involvement, number of appointments, requirement of a support person, and activities involved). The activities involved in genetic counseling practice were extracted, grouped in key topic areas, and mapped against the four goals of genetic counseling [5-7].

The Qualsyst tool [27] was used to critically appraise the quality of included studies, as it allows for assessment of quantitative and qualitative research across a broad range of study designs, and has previously been used in genetic counseling and testing research [28-30].

Narrative synthesis

A systematic narrative synthesis was performed to describe variation between practices and activities [31]. Narrative synthesis is a textual approach to synthesis and relies on the use of words and text to summarize and explain findings [31]. A meta-analysis was not possible due to

the heterogeneity of included studies. No papers were excluded based on a quality threshold, but the methodological quality and potential biases between and within studies were assessed.

Data availability statement

Complete searches, data extraction tables and references are available in the supplemental data.

RESULTS

Study characteristics and quality appraisal

Sixty-eight papers representing 61 studies were included (Table 3, further details in Table e-2). Several studies focused on more than one condition or testing type. The most commonly studied condition was Huntington's disease (HD) (41/68), followed by spinocerebellar ataxias (SCAs) (12/68) and amyotrophic lateral sclerosis (ALS)/frontotemporal dementia (FTD) (11/68). The majority of papers focused on predictive testing (58/68). Fewer papers focused on diagnostic (17/68) or reproductive (11/68) testing. Only 4/68 focused just on diagnostic testing, and 5/68 papers focused just on reproductive testing. Genetic counseling practices were reported from studies of clinical experience (32/68), novel practices trialed in clinical settings (6/68), and recommendations for practice from research (30/68).

Twenty-four papers reported qualitative methods. Thirteen included papers used two different study types: qualitative and quantitative methods (8/13) or a combination of cohort study, case series, or case study (5/13). There were no randomized control trials. The total number of included participants is not easily comparable between studies given the variability in study design, study population, outcomes, interventions, and settings. Sixty papers (60/68) achieved a Qualsyst score of 0.80 or higher, indicating sound methodological quality for their study type.

Narrative synthesis: genetic counseling practices for LONDs

Genetic counseling and testing practices varied between the health providers involved and the requirement for a neurological or psychiatric/psychological assessment. The requirement for a support person and the minimum number of appointments before and after testing also varied. Thirty-nine papers reported specifically on at least one of these aspects (Table 4) and included 6/39 on diagnostic testing, 35/39 on predictive testing, and 5/39 on reproductive testing.

Findings from the narrative synthesis are further summarized under the following topics related to understanding current genetic counseling and testing practices for LONDS and the extent they address the established goals of genetic counseling: the involvement and role of health providers, the number of appointments, the requirement of a support person, barriers to accessing genetic counseling and testing, the activities involved in genetic counseling practice, and addressing the goals of genetic counseling. Due to the limited available papers on diagnostic and reproductive testing, the focus is on predictive testing. However, diagnostic and reproductive testing practices are reported where available.

(i) The involvement and role of health providers

A multidisciplinary team of two or more health providers were involved in the genetic counseling practice in 33 papers (Table 4). The specific role of each health provider within the team was not always clearly described and varied between practices. Twenty-nine papers mentioned the role of neurologists, psychiatrists, and psychologists in assessing symptoms of disease or risk factors for coping. In some practices, clients were required to complete structured psychological or psychosocial surveys [e5, e8, e11, e13, e15, e20, e33, e36, e44, e45, e49], or disease-specific neurological or objective knowledge measurement tools [e8, e10] in addition to, or instead of a formal neurological or psychiatric/psychological assessment. In diagnostic and reproductive testing, neurological assessments were described once each [e29, e37], and

psychological assessments were described in reproductive testing only [e37]. In reproductive testing, these assessments were performed if an individual was symptomatic at the time of reproductive testing discussions [e37].

Where symptoms were identified as part of the neurological or psychiatric/psychological assessment, the response varied. A Cuban protocol eliminated symptomatic individuals from their predictive testing protocol [e43, e44], while other teams proceeded with predictive testing if clients perceived themselves as asymptomatic [e8, e11, e21, e25, e34, e43, e45]. Testing was deferred in some studies if high risk of future clinical distress [e5, e11, e13, e21, e34, e36, e44, e49, e65], problematic motivation [e5, e22, e26, e30, e65], or the absence of a support system [e5, e49, e65] were identified. One case series highlighted three situations where individuals still proceeded with predictive testing despite having high-risk psychopathology [e26]. The testing process included close interaction with the clients' psychiatric care team, and the outcome was successful in two of three cases [e26]. In the one study that discussed neurological and psychological assessments in reproductive testing, a couple's request for IVF could be rejected if symptoms were present in a parent and the couple seemed unable to provide a stable home environment [e37].

Five studies highlighted the need for increased training for those working in primary care [e19, e24, e67], psychiatry [e16, e25], and neurology [e16]. The value of having certain providers in the team was formally evaluated in three studies [e5, e8, e35]. In one study, most clients were satisfied with their neurologist appointment, particularly those who consulted a neurologist before, compared to after, receiving predictive testing results [e35]. Although instruments to assess anxiety, depression, and other psychopathology informed risk of post-test distress [e13, e20, e36], formal psychiatric testing provided more information than a questionnaire in one study [e5]. In one practice trialed in a clinical setting, a psychologist or psychiatrist was involved in a clinical case conference where they never met the client but discussed the case in detail

before testing and results disclosure [e8]. This supported both the client and clinician throughout the predictive testing process [e8].

(ii) The number of appointments

Up to four pre-testing appointments were required in some predictive testing protocols, and one study each reported a minimum of one appointment pre-testing for diagnostic [e68] and reproductive testing [e21] (Table 4). After predictive testing results disclosure, additional appointments to further educate about the condition, and discuss risk perception and beliefs was recommended in two studies [e1, e32]. Sixteen studies encouraged the client to attend short or longer-term psychological follow-up sessions, either if a pathogenic variant was confirmed [e24, e25, e47], regardless of the result [e8, e11, e12, e15, e21, e28, e34, e36, e42, e44, e45, e61, e67], or if requested or required based on pre-test discussions [e22, e33, e34]. Acceptance of follow-up varied with up to 80% of participants choosing to proceed with post-test psychological follow-up in two studies on predictive testing [e22, e47], and none proceeding in two other studies in predictive [e11] and reproductive testing [e7].

In two studies, clients provided positive feedback about the counseling, support, and information received throughout the structured protocol [e34, e36]. However, negative feedback was provided in nine studies [e10-e12, e14, e21, e28, e34, e36, e67]. Some clients were deterred by the length, complexity, rigidity, or content of the protocol (including total duration and number of consultations) [e10-e12, e14, e21, e28, e34, e36, e67], particularly if they had already decided to proceed with testing [e10, e14]. Others were concerned that the psychological assessments pre-testing were unnecessary or that testing would be withheld based on the clients' psychological state [e11, e21, e28, e36]. Consequently, fourteen papers suggested predictive testing be conducted in a more individual, flexible way by adapting the protocol to the specific needs, information processed and decision-making of the client [e12, e15, e17, e22, e27, e28, e33, e34, e42, e43, e45, e51, e61, e62]. Adaptations included reducing the number of appointments [e27, e34, e43, e51, e61], tailoring the

content [e27, e28, e34, e51, e61] or adapting the psychological support provided to each individual's needs [e33, e34]. Still, no papers examined whether the number of pre- and post-test counseling sessions made a difference to outcomes. One UK series of studies trialed a new practice of support post-testing, with a novel standalone genetic counseling narrative group approach for individuals with a negative HD predictive test result [e38] and a positive HD predictive test result [e39, e40], as well as their partners [e40]. The majority of participants were positive about the group session being a safe way to share experiences in a structured way [e40], discuss difficult emotions, highlight coping resources and felt a sense of community [e38, e39].

(iii) The requirement of a support person

Variations regarding the requirement of a support person throughout the testing process were reported in 14 papers (Table 4). Some papers cautioned that the support person might require attention, support, or information, particularly if their first attendance is at the client's results appointment [e7, e19, e21, e24, e25, e65]. One study suggested that support should not be sought from a relative who is having predictive testing concurrently, as this could create further anxiety [e12]. A support person may also adopt the decision-making role, as described by one case study of a patient with ALS and a family history of HD, whose wife was given decision-making capacity regarding HD predictive testing given his terminal condition [56]. No included studies formally evaluated the effect of having a support person (or not). Clients in one study provided negative feedback on the mandatory requirement of having a support person present at the results appointment [e28].

(iv) Barriers to accessing genetic counseling and testing

Eleven studies described travel distance and time as barriers to accessing genetic counseling or testing [e11, e12, e18, e23, e27-e29, e36, e62, e64] or adequate support throughout the process [e28]. Geographical barriers were addressed by conducting sessions by telephone or telehealth as part of a regular protocol or depending on client preference [e15, e21, e37, e48, e49, e53]. In other

studies, home visits [e23] or satellite clinics [e29] were conducted, a local health provider was upskilled so that remote testing and counseling would be available [e15, e28], or multiple appointments were arranged on the same day for one client [e18] or multiple relatives [e23, e62]. No adverse effects of these modifications were reported, but only two studies evaluated these practices. In one, those who received results by telephone and experienced difficulty afterwards suggested it would not have helped to attend in person [e48]. In the other, there were no significant differences concerning the quality of care, information, counseling, and support provided during the predictive testing process between those who used telehealth with a local health provider and those who attended an in-person appointment [e15].

Clients experienced difficulty accessing appropriate support or information in seven studies [e18, e23, e41, e45, e49, e62, e64]. To address this barrier, educational materials were developed with the community in their preferred language [e18, e41, e62], clients were given funding support to attend appointments [e18], and the team met with local physicians to educate about genetic risk and health resources [e62]. No studies evaluated the differences in access to or uptake of testing before and after implementing these new practices. One educational website was piloted with at-risk individuals, health providers and other stakeholders, and positive feedback was received [e41].

Eight studies noted different laws were present that may be a barrier for accessing genetic counseling and testing. This included discrimination based on genetic testing results [e42, e49], access to termination of pregnancy for genetic disorders [e43, e45], access to direct, exclusion or non-disclosure reproductive testing [e37] and obligations to inform relatives about genetic results or family medical information (before or after death) [e22, e42, e50, e56].

Client-specific barriers to accessing predictive or reproductive testing included the presence of an intervening at-risk relative [e21, e30, e42, e60] or where there were identical twins [e42]. Three practices explicitly excluded individuals at 25% risk from their predictive testing protocol if

the intervening relative was available for testing [e42, e43, e45]. Others used strategies to encourage relatives to consider testing, including: suggesting the client discuss testing with their relative with the hope that they proceed first [e21, e30, e42, e60]; offering to meet the relative to involve them in the pre-test counseling and ensure they are aware of the consequences of the client having testing first [e30]; or to undergo testing alongside their twin sibling [e42]. These strategies were useful in two cases [e42]. Where these strategies were unsuccessful, clients signed a confidentiality agreement to ensure non-disclosure (to maintain the intervening relative's right not to know) [e42, e60]. To minimize adverse outcomes in a case where the intervening relative believed they would commit suicide if they knew they were affected, grandparental blood samples were also collected for use in reproductive testing before revealing the test outcome [e60]. The possible adverse effect of testing clients at 25% risk was highlighted in one study: of four intervening at-risk relatives who had been informed of their positive status, three became depressed, and one committed suicide after the result was disclosed [e30].

(v) The activities involved in genetic counseling practice

The activities involved in current genetic counseling and testing practice for LONDs are summarized in Table 5. The activities are divided between the four defined goals of genetic counseling [5-7]. Some activities only concerned certain types of genetic testing, while others were consistent across multiple testing settings. All reported activities were performed in one or more predictive testing practices (35/35), whereas fewer were reported in diagnostic (23/35) and reproductive testing (19/35).

(vi) Addressing the goals of genetic counseling

Eighteen papers included activities that addressed all four goals of genetic counseling (Table 6). The education goal was the most commonly included goal across all papers (52/68), closely followed by the counseling (49/68) and support (45/68) goals. There were no major

differences between the goals addressed and testing types, with the number and type of goals addressed spread evenly across each testing type.

DISCUSSION

Our primary aim of this systematic review was to establish a comprehensive understanding of current genetic counseling and testing practices for LONDs. We identified 61 different studies published in 68 papers from 19 countries that described genetic counseling and testing practices for LONDs over the past decade. Studies varied greatly in setting and design. HD was the most common condition studied, and predictive testing was examined more frequently then diagnostic or reproductive testing. Although some practices had shared aspects, there were many novel or inconsistent approaches to genetic counseling for LONDs. For predictive testing, a multidisciplinary care approach was taken in most studies with neurologists, geneticists and psychologists being the most common health providers involved. Health provider decision-making about genetic testing varied in the presence of ethical issues, high-risk psychopathology, and neurological symptoms. In some predictive testing protocols, up to four pre-test counseling sessions were required. Attendance at follow-up sessions post-testing was variable. Overall, there was an emerging focus on a client- or family-centered, flexible approach to genetic counseling for LONDs to address negative feedback, barriers to accessing testing and possible harms. However, few innovative modifications to practice were evaluated. Our secondary aim was to identify to what extent current practices address the established goals of genetic counseling. Our findings indicate that current genetic counseling practices rarely address the four published genetic counseling goals.

Given most studies focused on predictive testing, it is difficult to draw any firm conclusions regarding genetic counseling practices for diagnostic and reproductive testing. There are

several possible explanations for fewer studies in these two areas. In diagnostic testing, those undergoing testing will demonstrate some symptoms suggestive of a LOND. Therefore, both patients and their health providers may think a genetic test may guide medical management and access to emerging targeted clinical trials [32, 33]. Still, as the diagnostic testing guidelines for HD note, the confirmation of a disease diagnosis may affect both the patient and their family [19]. Therefore, genetic counseling is an essential part of diagnostic testing**.** Depending on the needs and expectations of the patient and their family, they may need to be informed of hereditary risks, assisted with adjusting to the diagnosis and familial risk, or provided with access to predictive or reproductive testing, further support, information, and resources [19, 34]. One crucial difference between LONDs is that for entirely heritable conditions, like HD, a diagnosis would only be confirmed if a pathogenic variant was detected. For partially heritable conditions, like FTD, genetic testing may be performed separately to the diagnosis of the LOND [35]. Therefore, different genetic counseling practices may be required depending on the patient's diagnostic status and the likelihood of confirming a pathogenic variant [18, 19]. The low number of studies on reproductive testing may be explained by its low uptake rate overall, as clients may choose other family planning options like conceiving naturally or choosing not to conceive [e54, 36]. There may also be legal barriers to accessing reproductive testing or termination of pregnancy [e37, e43, e45]. Further investigation in both diagnostic and reproductive testing for LONDs is warranted.

The involvement of a multidisciplinary team was consistent across predictive testing practices, which is supported by the current guidelines [13, 15-18]. The low number of studies including genetic counselors suggests this health professional group may be under-utilized. An explanation could be local barriers to incorporating genetic counselors in practice (health-care system disparities, cultural differences, or the global shortage of genetic counselors) [3, 30]. The involvement and role of different health providers were difficult to distinguish in many

studies. Only three studies evaluated certain specialist health providers, highlighting the benefits of neurologists, psychiatrists, or psychologists in a predictive testing team [e5, e8, e35]. Where reported, neurological and psychiatric/psychological assessments in predictive testing were more commonly mandatory, which contrasts with the HD predictive testing guidelines, where these assessments are considered important but not required in a predictive testing protocol [13]. In the presence of high-risk psychopathology, neurological symptoms, or ethical issues in predictive testing, health provider decision-making about proceeding with testing varied. There was no apparent trend to suggest that responses differed between health provider specialty types. Further research is required to compare the provision of genetic counseling for LONDs between different health providers and to assess whether this has any effect on patient outcomes and testing decision-making.

In some predictive testing protocols, up to four pre-testing appointments were required, and the protocol length was frustrating for some clients [e11, e12, e21, e28]. The success and uptake of follow-up post-testing varied between studies, despite being encouraged. Many studies highlighted the need for an individualized, flexible, client-centered approach to genetic counseling practice given that a client who attends for genetic testing and counseling has a unique lived experience and motivation for proceeding with testing [e19, e21, e26, e42, e44, e51, e54, e60, e64]. Financial, geographical, or language barriers to accessing testing or appropriate support and information may also need addressing [e18, e23, e41, e45, e49, e62, e64]. Therefore, clients may or may not require a neurological or psychological/psychiatric assessment, a support person at appointments, multiple pre- or post-testing consultations, or further resources, support, or information. Genetic counseling practices should also consider the possible implications of genetic testing for the client's family, given the potential risk of harm for relatives [e30, e60]. Client and family-centered considerations are reflected in the current HD predictive testing guidelines [13]. Predictive testing performed within an integrated counseling protocol is

considered safe in several studies, with few major adverse events reported in clients [e34, 12, 37]. Pre-test discussions are thought to protect against negative psychological effects post-testing [e14, e21, e67]. Few included studies assessed the effectiveness and safety of a modified versus more traditional genetic counseling protocol, highlighting an area of necessary evaluation in the future that is supported by a previous quality assessment on genetic counseling for predictive testing of LONDs [38].

Of the studies that did assess innovative genetic counseling practices, there was evidence to support telephone or telehealth consultations for clients to access more flexible testing and support locally [e15, e48]. In contrast, the predictive HD testing guidelines, published in 2013, state that results should [13]. Perhaps this recommendation requires review, given emerging data on the provision of telehealth during the ongoing pandemic [39, 40]. Health providers' time may become more limited if a clinical trial for asymptomatic patients becomes available, and interest in predictive testing increases [e29, e57]. Additional novel practices, such as using an educational website pre-testing [e41] or group sessions post-testing [e38-e40], may also help manage health provider time. Other innovative approaches to genetic counseling practice should be considered and evaluated, with client safety at the forefront.

All genetic counseling activities were identified in one or more predictive testing study. In comparison, less activities were identified in diagnostic and reproductive testing (although fewer studies were in these areas). The majority of current practices did not meet all four genetic counseling goals, raising the possibility that current practices do not fulfill the required goals, or that the goals need to be adapted to align with the specific practices required for LONDs. Firm conclusions or implications for practice are premature, given that some study objectives assessed one aspect of genetic counseling practice only (e.g. knowledge, or motivations to undergo testing), few practices were formally evaluated, practices were inconsistently reported, and the overall strength of evidence is low. Findings

do, however, highlight gaps in our knowledge and considerations for further research in genetic counseling and testing for LONDs. The identified genetic counseling activities may provide a basis for the possible activities required in a model of genetic counseling service delivery for LONDs, addressing all four genetic counseling goals.

Limitations

Limitations exist regarding the individual articles and study selection methodology. Although several genetic counseling practices were identified, few were formally trialed or evaluated. The inclusion criteria resulted in the omission of works published in different languages, before 2009 and presented outside peer-reviewed journals. Consequently, our findings may have been affected by selection and publication bias. No randomized control trials were identified, and we did not exclude eight low-quality studies, affecting the robustness of the synthesis. We grouped LONDs due to their shared similarities, and therefore condition-specific issues were likely present but not extracted.

Overall, the strength of evidence in these studies was low. There was considerable heterogeneity across the included studies in terms of study design, populations (and response rate), and outcomes, which became a critical issue in making sound conclusions regarding implications for practice. The authors AC and ROS used their knowledge as experienced genetic counselors to combine and allocate genetic counseling activities amongst the four genetic counseling goals, which may have led to a bias toward presenting the aspects of practice considered important to a genetic counselor. We assessed whether included practices addressed the goals of genetic counseling, and we could not definitively know whether certain practices omitted certain activities due to outcome reporting bias.

Conclusion

Current genetic counseling and testing practice for LONDs is varied and informed by local laws and practices, resources, and the availability of different health providers. Few practices addressed all four goals of genetic counseling. A flexible, multidisciplinary approach to genetic counseling that is adaptable to the client and their family's needs continues to emerge. Evaluations of novel approaches to care are limited and provide an opportunity for further evaluation. Possible future study areas should focus on diagnostic and reproductive genetic testing and counseling practices, and the role and use of different health providers. As genetic and genomic testing becomes a routine part of care for patients with LONDs (and their relatives), health providers must balance their limited time and resources with ensuring that clients can be safely and effectively counseled. Increased involvement of genetic counselors or innovative approaches to providing genetic counseling may fulfill this need.

LIST OF TABLES AND FIGURES

ADDITIONAL FILES

PRISMA 2009 checklist.pdf.

e-References

TABLES

Table 1 Inclusion and exclusion criteria

INCLUSION	EXCLUSION
Population	
• Health providers of genetic testing and/or counseling for late-onset neurodegenerative diseases (LONDs*) **OR** • Adults with or at risk of a LOND, or medical guardians of adults with a LOND	• Childhood-onset, lower penetrance, autosomal recessive or X-linked inherited diseases • Included population not easily stratified from excluded population (e.g. if there are multiple diseases or ages included)
Intervention	
• Any aspect of genetic counseling practice, both before, during, or after genetic testing. This includes diagnostic testing, predictive or pre-symptomatic testing, and reproductive testing	• Laboratory methods • Research genetic testing where the result is never disclosed to the individual
Comparator	
No comparator	
Outcomes	
• Key components and activities of the genetic testing or counseling process including the role and involvement of health providers • Goals of genetic counseling or testing including experience, outcomes, and recommendations that inform practice (Goals include any of the four goals of genetic counseling: interpretation, education, counseling, support)	• Outcomes not specific to the genetic counseling or testing process • Likelihood of detecting a pathogenic variant, population frequencies, phenotypic data, uptake rate of testing, and family communication, without any information on clinical genetic testing or counseling practices
Study design and context	
• Any method of peer-reviewed research **AND** • Published after 1 January 2009	• Non-peer-reviewed papers, editorials, grey literature, non-systematic reviews, book chapters or dissertations • Practice recommendation or guideline papers

AND • Published in English, from worldwide	that do not explicitly stem from research or clinical experience

*****LONDs that were included in this study were expected to have similar potential psychological sequelae to each other as they had the following characteristics: mostly adult-onset, neurodegenerative, high penetrance, and autosomal dominant inheritance. This included (but was not limited to) Huntington's disease, amyotrophic lateral sclerosis, frontotemporal dementia, Alzheimer's disease, genetic prion diseases, CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), muscular dystrophies, hereditary spastic paraplegias, spinocerebellar ataxias or neuropathies (including Charcot-Marie-Tooth disease).

Table 2 Search strategy used

Search terms[#]				
Genetic counsel* OR gene* test* OR gene* screen*	**AND**	Alzheimer* disease OR Huntington* disease OR chorea OR prion disease OR CADASIL OR muscular dystroph* OR hereditary spastic paraplegia OR cerebellar ataxia OR Charcot Marie Tooth OR familial amyloid* neuropathy OR degenerative disease OR neurodegenerative disease OR Amyotrophic Lateral Sclerosis OR motor neuron* disease OR Frontotemporal Dementia OR Frontotemporal Lobar Degeneration (OR other associated terms)	**AND**	Year 2009 - present

[#]Complete list of search terms available in Table e-1

*Denotes truncations of key terms to broaden our search and include various word endings and spellings.

Table 3 Summary of included papers

Characteristics	Number of papers	References
Conditions investigated*#		
Huntington's disease (HD)	41	e1-e41
Spinocerebellar ataxias (SCAs- all subtypes)	12	e8-e12, e36, e42-e47
Amyotrophic lateral sclerosis/Frontotemporal dementia (ALS/FTD)	11	e26, e27, e48-e56
Familial amyloid polyneuropathy (TTR-FAP)	7	e9-e13, e33, e36
Unspecified disease type or included >6 LONDs	5	e57-e61
Alzheimer's disease (AD)	3	e62-e64
Prion disease	2	e65, e66
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)	2	e36, e67
Facioscapulohumeral muscular dystrophy (FSHD)	1	e68
Intervention type#		
Diagnostic genetic testing	17	e3, e17, e19, e23, e27, e29, e32, e50, e52, e53, e55, e56, e58, e62, e63, e65, e68
Predictive genetic testing	58	e1-e6, e8-e15, e17-e19, e21-e36, e38-e45, e47-e52, e55, e57, e59-e62, e64-e68
Reproductive genetic testing	11	e4, e7, e16, e21, e37, e42, e43, e46, e54, e55, e60
Unspecified genetic testing type	1	e20
Main author location(s)#		
Europe	33	e4, e5, e7-e10, e12-e14, e17, e22, e24, e25, e30, e33-e40, e45, e47, e50-e52, e56-e58, e61, e66, e67

North America	29	e1-e3, e6, e15, e16, e19-e21, e23, e26-e29, e31, e32, e41-e44, e46, e48, e49, e53, e54, e62-e65
South America	2	e11, e45
Asia	2	e59, e68
Africa	1	e18
Australia	2	e55, e60
Source of genetic counseling practice		
Practice sourced from clinical experience	32	e4, e16, e18, e21-e23, e26, e27, e29-e31, e34, e36, e37, e42-e45, e47, e50-e53, e55, e56, e58-e60, e62, e65, e67, e68
Practice trialed in clinical setting	6	e8, e15, e20, e38-e40
Practice recommended from clinical research	20	e1, e2, e5-e7, e9-e14, e24, e25, e33, e35, e48, e49, e57, e63, e66
Practice recommended from non-clinical research	10	e3, e17, e19, e28, 32, e41, e46, e54, e61, e64
Study type[#]		
Qualitative	24	e1-e3, e7, e9, e10, e12, e14, e17, e19, e24, e25, e28, e30, e32, e38-e41, e48, e54, e57, e64, e66
Case series	21	e4, e8, e9, e11, e18, e21, e22, e26, e29, e30, e42-e45, e49, e51, e58, e63, e66-e68
Cohort study	14	e1, e5, e6, e11, e13-e15, e20, e33, e34, e36, e37, e47, e67
Case study	11	e23, e27, e45, e50, e51, e55, e56, e60, e62, e65, e68
Cross-sectional survey	9	e16, e31, e35, e41, e46, e52, e53, e59, e64
Delphi survey	1	e61
Before and after study	1	e38
Risk of Bias assessment		
>0.90	50	e3-e13, e15-e17, e19-e21, e23-e27, e29, e31-e33, e35-

		e40, e42-e47, e50, e52, e53, e55-e57, e59-e61, e65, e67, e68
0.80-0.89	10	e1, e14, e18, e34, e41, e48, e54, e58, e62, e64
0.70-0.79	5	e2, e22, e28, e49, e63
0.60-0.69	1	e30
0.50-0.59	2	e51, e66

*Only data on conditions of interest extracted, #some papers included multiple categories

Table 4 Variations among genetic counseling and testing practices for LONDs

Aspects of genetic counseling practice	**Number of papers**	**References for each testing type**		
		Diagnostic testing	**Predictive testing**	**Reproductive testing**
Health providers involved within testing team				
Neurologist	24	e29, e53, e56, e58, e68	e6, e8, e12, e14, e18, e22, e26, e27, e29, e34, e35, e42-e45, e47-e49, e56, e59, e67, e68	e42
Geneticist	23	e56, e58, e68	e8, e11, e14, e18, e21, e22, e30, e34, e35, e42, e44, e45, e48, e49, e51, e59, e61, e66-e68	e37, e42
Psychologist	21	e56, e58	e8, e11, e14, e15, e18, e21, e22, e30, e34, e42-e45, e47, e51, e59, e61, e66, e67	e42
Genetic counselor	15	e29, e53, e68	e15, e21, e26, e27, e29, e42-e45, e48, e49, e59, e61, e68	e42
Psychiatrist	7	e29	e5, e8, e22, e26, e29, e45, e59	
Nurse	7	e29, e53	e18, e22, e29, e30, e59, e61	
Social worker	6	e53	e22, e26, e42, e45, e61	e42
Molecular biologist/ Laboratory geneticist	3		e8, e22, e61	
Family physician	2		e8, e43	
Medical doctor (other or unspecified)	2		e42, e61	e42
Obstetrician/ gynaecologist	2			e21, e37
Bioethicist	1		e42	e42
Neuropsychiatrist	1	e29	e29	

Neurological assessment					
Mandatory		11	e29	e6, e8, e29, e34-e36, e42-e44, e47, e67	
As needed		5		e11, e21, e22, e45	e37
Offered		1		e35	
Where possible		2		e15, e28	
Psychiatric/ psychological assessment[#]					
Mandatory		16		e5, e8, e11, e12, e14, e21, e26, e30, e42-e44, e47, e51, e57, e66, e67	
As needed		9		e11, e13, e21, e22, e45, e48, e49, e65	e37
Minimum recommended number of appointments					
Pre-test	1	5	e68	e48, e49, e51, e68	e21
	1 + reflection time	3		e14, e21, e22	
	2	7		e8, e12, e15, e28, e30, e34, e45	
	3	4		e14, e18, e21, e36	
	4	4		e11, e45, e47, e67	
Post-test	1	17	e68	e14, e18, e45, e48, e49, e51, e68	
	1 + follow-up encouraged	19		e1, e8, e11, e12, e15, e21, e24, e25, e28, e32, e34, e36, e42, e44, e45, e47, e61, e67	e7
Support person[+] at appointments					
At results appointment		6		e11, e12, e15, e28, e45, e67	
Strongly encouraged		5	e27, e56	e12, e21, e28	
Optional		3		e11, e21, e49	
Involvement of both members		3			e37, e43, e54

of a couple				
Mandatory	1		[e45]	
[#]Psychological and psychiatric assessments have been combined as many studies were unclear about which health provider was involved, [+]A support person may be a family member or peer				

Table 5 Activities involved in genetic counseling and testing practices for LONDs in accordance with the four defined goals of genetic counseling, and divided between testing types

Genetic counseling activity	**Number of papers**	**References for each testing type**		
		Diagnostic testing	**Predictive testing**	**Reproductive testing**
Goal of genetic counseling 1: Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence				
Assess risk of client and other relatives carrying a pathogenic variant, incorporating family- and variant-specific information, penetrance and pathogenicity in risk assessment	17	e19, e27, e53, e56, e62, e65, e68	e4, e19, e24, e25, e27, e30, e42, e44, e45, e49, e51, e62, e65, e67, e68	e4, e42
Gather family history and any relevant family genetic testing reports	15	e3, e23, e53, e58, e62, e63, e68	e3, e8, e15, e21, e23, e27, e30, e44, e57, e62, e65, e68	
Gather personal medical history including previous testing results	14	e23, e56, e58, e62	e8, e15, e23, e26, e27, e44, e57, e62, e65, e67, e68	e37
Engage in interdisciplinary discussion and literature review	9	e58	e8, e22, e26, e27, e42, e49, e59, e61	e42
Goal of genetic counseling 2: Education about the natural history of the condition, inheritance pattern, testing, management, prevention, support, resources and research				
Provide condition-specific information about: - natural history (main clinical symptoms, early and late manifestations, prognosis, mode of inheritance, all possible genetic testing results) - uncertainties (variable age at onset, severity, progression, penetrance, mostly	27	e23, e32, e50, e53, e55, e56, e58, e68	e5, e8, e9, e11, e15, e21, e23, e26, e28, e32, e35, e36, e41, e45, e49, e51, e55, e57, e61, e64, e65, e67, e68	e55

limited prevention and treatment options)				
Discuss the use, privacy and storage of results now and in future (e.g. whether they would form part of the medical record, able to be shared in case of death) and distinguish between research and clinical care	17	e50, e56, e58, e62, e65	e11, e21, e22, e27, e31, e42-e45, e49, e50, e57, e61, e62, e65	e43
Advise that knowledge about the condition could inform family planning and detail all of the reproductive testing options available	13	e68	e41, e43, e45, e49, e51, e57, e65, e67, e68	e7, 16, e37, e46
Detail the genetic testing process and protocol	12		e12, e15, e36, e41, e43-e45, e48, e49, e57, e61, e67	e43
Review possible clinical implications of testing on other relatives	12	e53, e56, e68	e24, e28, e30, e41, e42, e49, e57, e60, e68	e7, e42
Provide information in oral, visual and written format, including online information	12	e3, e62	e3, e14, e18, e21, e22, e30, e41, e57, e61, e62	e37, e46
Gain informed consent in writing	11	e50, e56, e58, e68	e8, e21, e22, e27, e44, e49, e68	e37
Identify and address informational misconceptions, myths and prejudgments	11	e3, e23, e32	e3, e10, e12, e23, e27, e32, e36, e45, e57, e64, e65	
Ensure all potential consequences of testing understood by client	7	e3	e1, e3, e12, e26, e27, e51, e67	
Discuss possible other implications of testing for the client and relatives (e.g. risk of discrimination in insurance, misattributed paternity)	7	e65, e68	e21, e28, e42, e49, e51, e65, e68	
Review limitations of currently available genetic testing	5	e55, e68	e4, e49, e55, e57, e68	e4, e55

Review the results of any risk assessment performed as part of the workup	4	e68	e11, e45, e57, e68	
Provide information about possible research studies available	1		e41	
Goal of genetic counseling 3: Counseling to promote informed choices in view of risk assessment, family goals, ethical and religious values.				
Discuss motivations for proceeding with testing, including decision-making process, and clarify expectations where required	20	e32	e5, e6, e8, e9, e14, e21, e22, e26, e29, e32-e34, e36, e44, e45, e49, e51, e57, e65, e67	
Assess psychosocial readiness to undergo testing and ability to cope with testing process and/or either possible result, including adaptation mechanisms, psychological history, current substance abuse/ stressors/ changes in mood/ cognitive functioning	20	e3	e3, e5, e8, e11, e13, e15, e21, e26, e33, e34, e36, e44, e45, e47, e49, e51, e65-e68	
Assess and address family dynamics and communication (e.g. whether the client plans to communicate any type of result with relatives, suggesting further family discussion before proceeding with testing and/or supporting the client in familial communication)	16	e50, e62, e65	e8, e9, e21, e22, e26, e27, e42, e44, e45, e49, e51, e57, e61, e62, e65	e42
Confirm the client is making an autonomous choice	13		e2, e5, e8, e11, e14, e15, e21, e24, e34, e42, e49, e51, e57	e21, e42
Review lived experience of disease (e.g. time elapsed since awareness of family diagnosis, whether the client has direct experience and understanding of the disease)	12	e17	e8, e17, e21, e22, e24, e26, e34, e49, e51, e57, e67	e54
Discuss the voluntary nature of undergoing testing including the right to opt-out at any time and alternative options (e.g. DNA banking, deferring testing, undergoing testing but not receiving the results)	10		e8, e11, e21, e22, e27, e34, e45, e48, e49, e67	

Assess access to social support within and outside the family	10		e13, e15, e26, e28, e42, e45, e47, e49, e51, e57	e42
Encourage the client to consider possible responses and effects of testing on other individuals (e.g. support person, partners, family members) including the possibility of various results scenarios between different family members	9	e3	e3, e24-e26, e49, e51, e57, e61	e7
Review the timing of testing, perceived advantages and disadvantages of proceeding (or not)	8		e9, e12, e24, e26, e44, e45, e49, e57	
Review common emotional responses and possible psychological effects of testing	8		e26, e34, e36, e41, e47, e49, e65	e7
Ensure all potential consequences have been considered	7	e3	e3, e12, e25-e27, e51, e67	
Discuss attitudes and values towards family planning options including termination of pregnancy	4		e60	e7, e21, e43, e60
Provide additional consultations when requested and space for the client to raise questions, doubts or concerns	3		e36, e48, e49	
Goal of genetic counseling 4: Support to encourage the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder				
Offer counseling or psychological support to client, other family members and support person both pre-, during and post-testing to facilitate adjustment, integrate results into daily life and minimize potential adverse effects	30	e3, e19, e65, e66	e1, e3, e6, e11, e13, e15, e19, e21, e22, e24-e26, e30, e33, e34, e38-e40, e42, e43, e45, e47-e49, e51, e61, e65-e67	e7, e21, e43

Offer support or information resources throughout (e.g. online information, contact details or referral to relevant organisations)	10	e3, e23, e62, e65	e3, e14, e15, e23, e30, e41, e49, e61, e62, e65	
Provide an opportunity for the client to express and explore their emotional reaction to the result	7		e12, e15, e21, e24, e26, e51, e65	
Offer medical follow-up to pathogenic variant carriers	7		e13, e21, e25, e43, e45, e61, e67	
Preferably the same health provider(s) meet client post-testing	5		e8, e11, e22, e57, e67	
Request for feedback on the process (e.g. satisfaction with the protocol, general suggestions, if they would recommend it to other persons)	2		e5, e36	

Table 6 Genetic counseling goals addressed in included studies

Characteristics	Number of papers	References for each testing type[#]			
		Diagnostic testing	Predictive testing	Reproductive testing	Unspecified testing type
Goal of genetic counseling addressed in study[#]					
Interpretation	32	e3, e19, e23, e27, e29, e52, e53, e55, e56, e58, e62, e63, e65, e68	e3, e4, e8, e15, e19, e21-e23, e26-e30, e35, e42-e45, e49, e52, e55, e57, e60-e62, e65, e68	e4, e21, e37, e42, e43, e55, e60	
Education	52	e3, e19, e23, e29, e32, e50, e53, e55, e56, e58, e62, e65, e68	e1, e3-e5, e8-e12, e14, e15, e18, e19, e21-e24, e26-e32, e35, e36, e41-e45, e48-e51, e55, e57, e60-e62, e64, e65, e67, e68	e4, e7, e16, e21, e37, e42, e43, e46, e54, e55, e60	
Counseling	49	e3, e17, e29, e32, e50, e56, e58, e62, e65	e2, e3, e5, e6, e8, e9, e11-e15, e17, e21, e22, e24-e30, e32-e34, e36, e41-e45, e47-e49, e51, e57, e59-e62, e65-e68	e7, e21, e42, e43, e54, e60	e20
Support	45	e3, e17, e19, e23, e58, e62, e65	e1, e3, e5, e6, e8, e11-e15, e17, e19, e21-e26, e28, e30, e33, e34, e36, e38-e45, e47-e49, e51, e57, e59, e61, e62, e65-e67	e7, e21, e42, e43	e20
Number of goals of genetic counseling addressed in study[#]					
4	18	e3, e58, e62, e65	e3, e8, e15, e21, e22, e26, e28, e30, e42-e45, e49, e57, e61, e62, e65	e21, e42, e43	
3	18	e19, e23, e29, e56	e5, e11, e12, e14, e19, e23, e24, e27, e29, e36, e41, e48, e51, e60, e67, e68	e7, e60	
2	21	e17, e32, e50, e53, e55, e68	e1, e4, e6, e9, e13, e17, e25, e32-e35, e47, e50, e55, e59, e66	e4, e37, e54, e55	e20
1	13	e27, e52, e63	e2, e10, e18, e31, e38-e40, e52,	e16, e46	

			e64		

#Some studies had a different number of goals addressed for each testing type, so more than one option could be selected

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Figure 1 Summary of study selection process, as recommended by PRISMA [24]

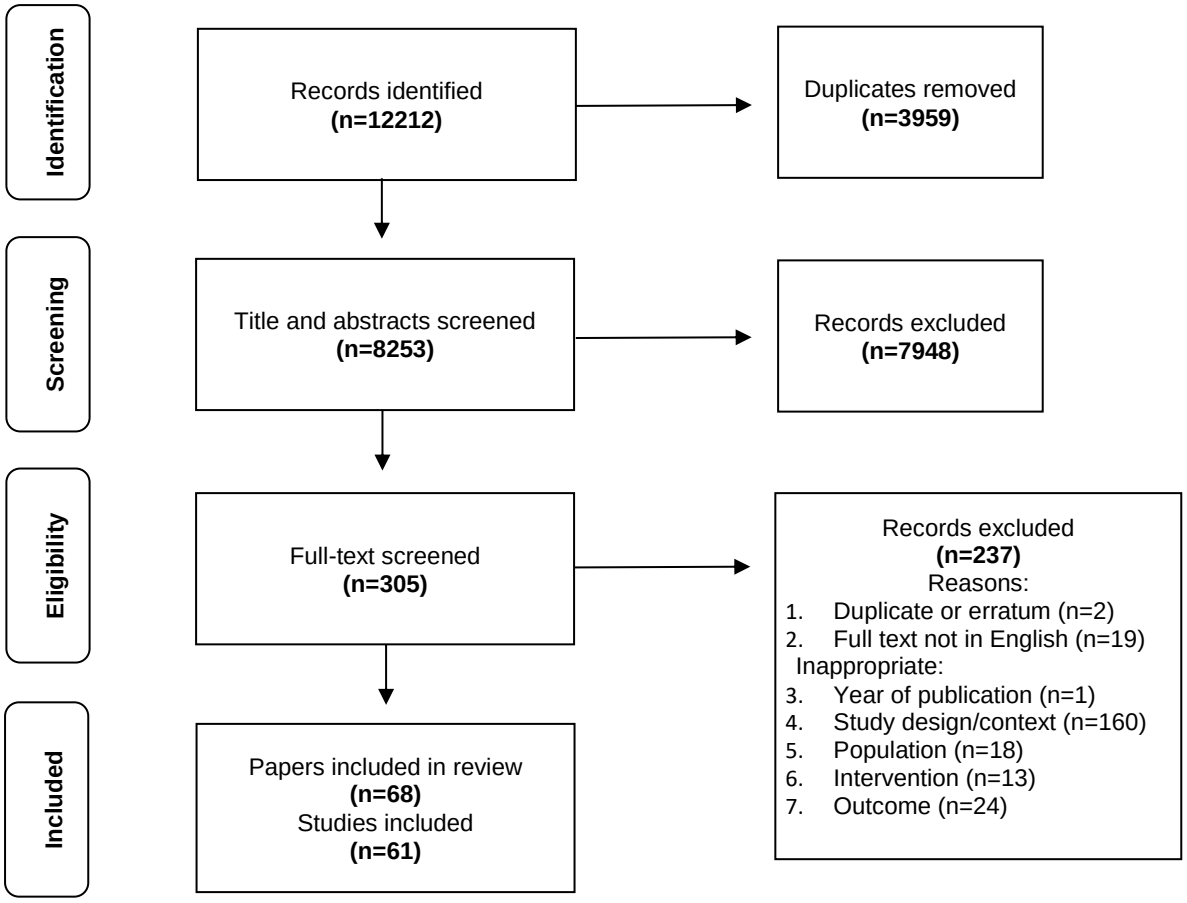

Table e- 1 Search terms used

Search terms	Medline	Embase	CINAHL	PsycINFO
1. Genetic counsel*	Genetic Counseling/	genetic counselling/	TI genetic counsel* OR AB genetic counsel*	TI genetic counsel* OR AB genetic counsel*
	Genetic counsel*.tw.	Genetic counsel*.tw.	(MH "Genetic Counseling")	DE "Genetic Counseling"
2. Genetic testing : Gene* test OR Genetic test* OR gene test*	(gene* test or gene* test or genetic test* or genetic test* or gene test* or gene test*).tw.	(gene* test or gene* test or genetic test* or genetic test* or gene test* or gene test*).tw.	TI gene* test OR AB gene* test OR TI genetic test* OR AB genetic test* OR TI gene test* OR AB gene test*	TI gene* test OR AB gene* test OR TI genetic test* OR AB genetic test* OR TI gene test* OR AB gene test*
	Genetic Testing/			DE "Genetic Testing"
3. Genetic screening: Gene* screen OR genetic screen* OR gene screen*	(gene* screen or gene* screen or genetic screen* or genetic screen* or gene screen* or gene screen*).tw.	(gene* screen or gene* screen or genetic screen* or genetic screen* or gene screen* or gene screen*).tw.	TI gene* screen OR AB gene* screen OR TI genetic screen* OR AB genetic screen* OR TI gene screen* OR AB gene screen*	TI gene* screen OR AB gene* screen OR TI genetic screen* OR AB genetic screen* OR TI gene screen* OR AB gene screen*
		Genetic screening/	(MH "Genetic Screening")	
4. Amyotrophic Lateral Sclerosis	Amyotrophic Lateral Sclerosis/	amyotrophic lateral sclerosis/	TI amyotrophic lateral sclerosis OR AB amyotrophic lateral sclerosis	TI amyotrophic lateral sclerosis OR AB amyotrophic lateral sclerosis
	Amyotrophic Lateral Sclerosis.tw.	Amyotrophic Lateral Sclerosis.tw.	(MH "Amyotrophic Lateral Sclerosis")	DE "Amyotrophic Lateral Sclerosis"
5. motor neuron* disease	Motor Neuron Disease/	motor neuron disease/	(MH "Motor Neuron Diseases")	TI motor neuron* disease OR AB motor neuron* disease
	motor neuron* disease.tw.	motor neuron* disease.tw.	TI motor neuron* disease OR AB motor neuron* disease	
6. lou gehrig* disease	lou gehrig* disease.tw.	lou gehrig* disease.tw.	TI lou gehrig* disease OR AB lou gehrig* disease	TI lou gehrig* disease OR AB lou gehrig* disease
7. Frontotemporal Dementia	Frontotemporal Dementia/	frontotemporal dementia/	(MH "Frontotemporal Dementia")	TI frontotemporal dementia OR AB frontotemporal dementia
	Frontotemporal Dementia.tw.	Frontotemporal Dementia.tw.	TI frontotemporal dementia OR AB frontotemporal dementia	
8. Frontotemporal Lobar Degeneration	Frontotemporal Lobar Degeneration/	Frontotemporal Lobar Degeneration.tw.	(MH "Frontotemporal Lobar Degeneration")	TI frontotemporal lobar degeneration OR AB frontotemporal lobar degeneration
	Frontotemporal Lobar Degeneration.tw.		TI frontotemporal lobar degeneration OR AB frontotemporal lobar degeneration	
9. Dementia	DEMENTIA/	Dementia/	(MH "Dementia")	DE "Dementia"
	Dementia.tw.	Dementia.tw.	TI dementia OR AB dementia	TI dementia OR AB dementia
10. semantic dementia	semantic dementia.tw.	Semantic dementia/		DE "Semantic Dementia"

		semantic dementia.tw.	TI semantic dementia OR AB semantic dementia	TI semantic dementia OR AB semantic dementia
11. presenile dementia	presenile dementia.tw.	Presenile dementia/	(MH "Dementia, Presenile")	DE "Presenile Dementia"
		presenile dementia.tw.	TI presenile dementia OR AB presenile dementia	TI presenile dementia OR AB presenile dementia
12. Pick* disease	"Pick Disease of the Brain"/	Pick* disease.tw.	(MH "Pick Disease of the Brain")	DE "Picks Disease"
	Pick* disease.tw.		TI pick* disease OR AB pick* disease	TI pick* disease OR AB pick* disease
13. Pick* dementia	Pick* dementia.tw.	Pick presenile dementia/	TI pick* dementia OR AB pick* dementia	TI pick* dementia OR AB pick* dementia
		Pick* dementia.tw.		
14. Tauopath*	Tauopathies/	Tauopathy/	TI tauopath* OR AB tauopath*	TI tauopath* OR AB tauopath*
	Tauopath*.tw.	Tauopath*.tw.		
15. Pallidopontonigral degeneration	Pallidopontonigral degeneration.tw.	Pallidopontonigral degeneration.tw.	TI Pallidopontonigral degeneration OR AB Pallidopontonigral degeneration	TI Pallidopontonigral degeneration OR AB Pallidopontonigral degeneration
16. pallido ponto nigral degeneration	pallido ponto nigral degeneration.tw.	pallido ponto nigral degeneration.tw.	TI Pallido ponto nigral degeneration OR AB Pallido ponto nigral degeneration	TI Pallido ponto nigral degeneration OR AB Pallido ponto nigral degeneration
17. Alzheimer* disease	ALZHEIMER DISEASE/	Alzheimer disease/	(MH "Alzheimer's Disease")	DE "Alzheimer's Disease"
	Alzheimer* disease.tw.	Alzheimer* disease.tw.	TI Alzheimer* disease OR AB Alzheimer* disease	TI alzheimer* disease OR AB alzheimer* disease
18. Huntington* disease	HUNTINGTON DISEASE/	Huntington* disease.tw.	(MH "Huntington's Disease")	DE "Huntingtons Disease"
	Huntington* disease.tw.		TI huntington* disease OR AB huntington* disease	TI huntington* disease OR AB huntington* disease
19. Huntington* chorea	Huntington* chorea.tw.	Huntington chorea/	TI huntington* chorea OR AB huntington* chorea	TI huntington* chorea OR AB huntington* chorea
		Huntington* chorea.tw.		
20. huntington disease like	huntington disease like.tw.	Huntington disease like syndrome/	TI huntington disease like OR AB huntington disease like	TI huntington disease like OR AB huntington disease like
		huntington disease like.tw.		
21. Corticobasal degeneration	Corticobasal degeneration.tw.	Corticobasal degeneration/	TI corticobasal degeneration OR AB corticobasal degeneration	DE "Corticobasal Degeneration"
		Corticobasal degeneration.tw.		TI corticobasal degeneration OR AB corticobasal degeneration
22. Progressive supranuclear palsy	Supranuclear Palsy, Progressive/	Progressive supranuclear palsy/	(MH "Supranuclear Palsy, Progressive")	DE "Progressive Supranuclear Palsy"
	Progressive supranuclear palsy.tw.	Progressive supranuclear palsy.tw.	TI progressive supranuclear palsy OR AB progressive supranuclear palsy	TI Progressive Supranuclear Palsy OR AB Progressive Supranuclear Palsy

23. prion disease	Prion Diseases/	Prion disease/	(MH "Prion Diseases")	TI prion disease OR AB prion disease
	prion disease.tw.	prion disease.tw.	TI prion disease OR AB prion disease	
24. creutzfeldt jakob	Creutzfeldt-Jakob Syndrome/	Creutzfeldt Jakob disease/	(MH "Creutzfeldt-Jakob Syndrome")	DE "Creutzfeldt Jakob Syndrome"
	creutzfeldt jakob.tw.	creutzfeldt jakob.tw.	TI creutzfeldt jakob OR AB creutzfeldt jakob	TI creutzfeldt jakob OR AB creutzfeldt jakob
25. Gerstmann-Straussler-Scheinker	Gerstmann-Straussler-Scheinker Disease/	Gerstmann Straussler Scheinker syndrome/	(MH "Gerstmann-Straussler-Scheinker Syndrome")	TI Gerstmann-Straussler-Scheinker OR AB Gerstmann-Straussler-Scheinker
	Gerstmann-Straussler-Scheinker.tw.	Gerstmann-Straussler-Scheinker.tw.	TI Gerstmann-Straussler-Scheinker OR AB Gerstmann-Straussler-Scheinker	
26. fatal familial insomnia	Insomnia, Fatal Familial/	Fatal familial insomnia/	TI fatal familial insomnia OR AB fatal familial insomnia	TI fatal familial insomnia OR AB fatal familial insomnia
	fatal familial insomnia.tw.	fatal familial insomnia.tw.		
27. CADASIL	CADASIL/	CADASIL/	(MH "CADASIL")	TI cadasil OR AB cadasil
	CADASIL.tw.	CADASIL.tw.	TI cadasil OR AB cadasil	
28. muscular dystroph*	Muscular Dystrophies/	Muscular dystrophy/	(MH "Muscular Dystrophy")	DE "Muscular Dystrophy"
	muscular dystroph*.tw.	muscular dystroph*.tw.	TI muscular dystroph* OR AB muscular dystroph*	TI muscular dystroph* OR muscular dystroph*
29. hereditary spastic paraplegia	Spastic Paraplegia, Hereditary/	hereditary spastic paraplegia.tw.	(MH "Spastic Paraplegia, Hereditary")	TI hereditary spastic paraplegia OR AB hereditary spastic paraplegia
	hereditary spastic paraplegia.tw.		TI hereditary spastic paraplegia OR AB hereditary spastic paraplegia	
30. spinocerebellar ataxia	Spinocerebellar Ataxias/	spinocerebellar ataxia.tw.	(MH "Spinocerebellar Ataxias")	TI spinocerebellar ataxia OR AB spinocerebellar ataxia
	spinocerebellar ataxia.tw.		TI spinocerebellar ataxia OR AB spinocerebellar ataxia	
31. Spinocerebellar degeneration	Spinocerebellar Degenerations/	Spinocerebellar degeneration/	(MH "Spinocerebellar Degenerations")	TI spinocerebellar degeneration OR AB spinocerebellar degeneration
	Spinocerebellar degeneration.tw.	Spinocerebellar degeneration.tw.	TI spinocerebellar degeneration OR AB spinocerebellar degeneration	
32. cerebellar ataxia	Cerebellar Ataxia/	Cerebellar ataxia/	(MH "Cerebellar Ataxia")	TI cerebellar ataxia OR AB cerebellar ataxia
	cerebellar ataxia.tw.	cerebellar ataxia.tw.	TI cerebellar ataxia OR AB cerebellar ataxia	
33. Charcot Marie Tooth	Charcot-Marie-Tooth Disease/	Charcot Marie Tooth.tw.	(MH "Charcot-Marie-Tooth Disease")	DE "Charcot-Marie-Tooth Disease"

	Charcot Marie Tooth.tw.		TI charcot marie tooth OR AB charcot marie tooth	TI charcot marie tooth OR AB charcot marie tooth
34. familial amyloid* polyneuropathy	familial amyloid* polyneuropathy.tw.	Familial amyloid polyneuropathy/ familial amyloid* polyneuropathy.tw.	TI familial amyloid* polyneuropathy OR AB familial amyloid* polyneuropathy	TI familial amyloid* polyneuropathy OR AB familial amyloid* polyneuropathy
35. Familial amyloid* neuropathy	Amyloid Neuropathies, Familial/ Familial amyloid* neuropathy.tw.	Familial amyloid* neuropathy.tw.	(MH "Amyloid Neuropathies, Familial") TI Familial amyloid* neuropathy OR AB Familial amyloid* neuropathy	TI Familial amyloid* neuropathy OR AB Familial amyloid* neuropathy
36. Familial Amyloidosis	Familial Amyloidosis.tw.	Familial Amyloidosis.tw.	(MH "Amyloidosis, Familial") TI familial amyloidosis OR AB familial amyloidosis	TI familial amyloidosis OR AB Familial amyloidosis
37. familial transthyretin amyloidosis	familial transthyretin amyloidosis.tw.	familial transthyretin amyloidosis.tw.	TI Familial Transthyretin Amyloidosis OR AB Familial Transthyretin Amyloidosis	TI Familial Transthyretin Amyloidosis OR AB Familial Transthyretin Amyloidosis
38. hereditary motor sensory neuropathy	"Hereditary Sensory and Motor Neuropathy"/ hereditary motor sensory neuropathy.tw.	Hereditary motor sensory neuropathy/ hereditary motor sensory neuropathy.tw.	(MH "Neuropathies, Hereditary Motor and Sensory") TI hereditary motor sensory neuropathy OR AB hereditary motor sensory neuropathy	TI hereditary motor sensory neuropathy OR AB hereditary motor sensory neuropathy
39. degenerative disease	degenerative disease.tw.	Degenerative disease/ degenerative disease.tw.	TI degenerative disease OR AB degenerative disease	TI degenerative disease OR AB degenerative disease
40. neurodegenerative disease	Neurodegenerative Diseases/ neurodegenerative disease.tw.	neurodegenerative disease.tw.	(MH "Neurodegenerative Diseases") TI neurodegenerative disease OR AB neurodegenerative disease	DE "Neurodegenerative Diseases" TI neurodegenerative disease OR AB neurodegenerative disease
41. 1 or 2 or 3				
42. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40				
43. 41 and 42				
44. Limit 43 to 2009-present				
*Note: MESH headings and DE subjects used where available. Search limited to text word (.tw) and 'all subheadings included' in Medline and Embase. Search limited to title or abstract in CINAHL and PsycINFO.				

Table e- 2 Detailed summary of included papers

Study	Paper reference and author location	Condition(s) investigated[#]	Objectives	Sample characteristics*	Study type	Testing type	Main findings relevant to the systematic review	Genetic counseling goal(s) addressed	Qualsyst result (Total score/ total possible score) and quality issues
	Genetic counseling practice sourced from clinical experience								
1	Eno et al. (2020) [e31] USA	HD	Report the use of the electronic health record (EHR) for presymptomatic HD GT across different HD Centers (i.e. how the HD gene analysis is ordered, resulted and stored)	23 clinical care teams (HDSA Centers of Excellence) (53% response rate)	Cross-sectional survey	Predictive	Most teams have developed their own practices and there was much variation in whether the following were recorded in the EHR: encounters, notes, results, GT ordered, and whether pathology received by laboratory	Education	0.93 (13/14) Question/objective not clearly described
2	Bardakjian et al. (2019) [e29] USA	HD	Report the experience of a new HD Center since its inception, estimating the capture of the population served, describing the care provided and measuring changes in client behavior in response to release of research-related information	266 unique HD clients seen in HD Center 145 seen in 2018: 88 with manifest HD, 28 premanifest mutation carriers, 12 who underwent predictive GT and did not carry an expanded allele, 8 who requested but did not complete predictive GT, 7 who decided against predictive GT, 2 phenocopies with negative GT	Retrospective case series	Diagnostic Predictive	New center demonstrated high demand for in-clinic multidisciplinary care Neurologist and nurse involved in 100% of encounters, followed by psychiatrist and genetic counselor Demand for predictive GT significantly increased following the press announcement of successful completion of clinical trial	Interpretation Education Counseling	0.92 (11/12) Results not sufficiently described
3	Bonnard et al. (2019) [e30] France	HD	Compare the age, motivations, and time required before deciding to have GT performed between 25% at-risk and 50% at-risk individuals Compare outcomes in 25% at-risk individuals, between those who are	1611 individuals requested predictive GT between 1992-2016 1456 at 50% risk: 73% underwent predictive GT 155 at 25% risk: 60% underwent GT,	Consecutive case series	Predictive	Most common motivation in 50% risk and 25% risk group was “to know” Four adverse reactions when individual at 25% risk underwent GT and informed intervening	Interpretation Education Counseling Support	0.60 (18/30) Quantitative results well described Qualitative study design, and data collection not clearly described

			variant positive or variant negative Observe whether revealing the parent's status adversely affected the parent–child relationship Understand the familial context that led them to request GT before their at-risk parent	14/94 were variant positive 9 variant positive individuals at 25% risk and 9 age-matched variant negative individuals. Four participated in further semi-structured interview (2/4 reported as case studies).	Qualitative study		relative: 3 intervening relatives became depressed, 1 suicide 1 month after the result had been disclosed		Theoretical framework/ wider body of knowledge, data analysis, verification procedures and reflexivity of the account not described Conclusions not well supported
4	Crook et al. (2019) [e55] Australia	ALS	Present the case of an ALS patient who underwent GT through our motor neurone disease clinic Highlight current limitations to analysing and interpreting C9orf72 expansion GT results and describe how this resulted in discordant reports of pathogenicity between GT laboratories that confounded the GC process	1 ALS patient who received discordant C9orf72 expansion results and interpretation	Case study	Diagnostic Predictive Reproductive	Discordant results confounded GC process, highlighted difficulties in GT and interpreting C9orf72 results Discordant results have associated potential psychological and legal risks for the client and health provider	Interpretation Education	0.90 (9/10) Question/ objective not clearly described
5	Klepek et al. (2019) [e53] USA	ALS	Characterize clinician practices regarding GT and GC, perceived challenges, and attitudes and other factors that may be associated with the offer of ALS GT Compare clinician attitudes towards GT to attitudes of persons with ALS	80 ALS clinicians and members of the Northeast ALS Consortium (response rate 31.4%) 96.2% were neurologists	Cross-sectional survey	Diagnostic	Lack of consensus in ALS GT practices: 92.3% offered GT to patients with familial ALS, 57% to sporadic ALS with family history of dementia, 36.9% to sporadic ALS Divergent views between clinicians and patients: clinicians less likely to have GT themselves, or see value in GT for relatives	Interpretation Education	1.00 (16/16)
6	Paneque et al. (2019) [e36]	LONDs including:	To describe the profile of the population seeking	1498 requested predictive GT, 240	Retrospective cohort study	Predictive	45% did not follow up after receiving GT	Education Counseling	1.00 (22/22)

	Portugal	HD TTR-FAP SCA3, SCA2, SCA7 CADASIL (dentatorubral-pallidoluysian atrophy)	presymptomatic GT, while also reflecting on the experience and conducting the protocol of multidisciplinary sessions since 1996	withdrew, 28 were excluded 1230 underwent predictive GT, 680 non-carriers, 550 carriers			results, 29.6% were seen a year post-GT Most common reason for GT to reduce uncertainty (41.7%)	Support	
7	Tibben et al. (2019) [e4] The Netherlands	HD	Describe four cases in which the couples and clinicians involved were confronted with an unexpected outcome of prenatal GT	4 couples in which expanded CAG repeats were observed in (or stemming from) the presumed non-HD side	Non-consecutive case series	Predictive Reproductive	Population risks of HD should be a required discussion to ensure comprehensively informed reproductive GT and GC	Interpretation Education	1.00 (10/10)
8	Olszewska et al. (2018) [e58] Ireland	>6 LONDs	Perform a retrospective chart review/ cohort analysis of the Neurogenetics clinic over 12 months, reviewing symptoms and work up data	27 individuals who attended a pilot neurogenetics clinic	Consecutive case series	Diagnostic	Benefits of multidisciplinary team to address gap in service delivery Identification of pathogenic variants directed screening, treatment and facilitated onward GC	Interpretation Education Counseling Support	0.80 (8/10) Question/ objective not clearly described Conclusions not well supported
9	Charles et al. (2017) [e23] USA	HD	Highlight the difficulties involved with care of an extended family with HD living on a small island nation due to their low socioeconomic status, barriers to accessing medical care and geographical isolation	1 family with HD who live on several resource-limited Caribbean Islands	Case study	Diagnostic Predictive	Genetic and clinical diagnosis can be impeded by lack of resources and lack of access to specialty care Definitive diagnosis positively impacted family by facilitating GC, community outreach, and dispelling disease myths.	Interpretation Education Support	1.00 (10/10)
10	Goldman et al. (2017) [e26] USA	HD ALS/FTD	Demonstrate the complex nature of GC and GT in the presence of psychiatric symptoms, whether emanating from the disease itself or the	4 individuals with psychiatric symptoms who requested predictive GT	Non-consecutive case series	Predictive	Psychiatric symptoms may emanate from the disease itself, or living in an affected family Health providers must still prepare clients for	Interpretation Education Counseling support	1.00 (10/10)

			results of living in an affected family				positive and negative results Protocol may need to proceed slowly to foster positive outcome		
11	Mandich et al. (2017) [e34] Italy	HD	Report the sociodemographic characteristics of predictive GT applicants, their motivations and expectations, and the outcomes of the GC protocol during two decades of direct HD GT.	299 individuals who applied for predictive GT between 1993-2014	Retrospective cohort study	Predictive	Protocols completed more in men (68.5% vs 53.5%), those over 25 (63.4% vs 48.1%) Factors influencing the decision-making process differed between males and females	Counseling Support	0.82 (18/22) Analytic methods, results and likely confounders not sufficiently described
12	Mantero et al. (2017) [e56] Italy	ALS/FTD (Parkinson's disease)	Discuss the issues that arose in family GC for likely sporadic ALS and parkinsonism-dementia complex (ALS-PDC)	1 individual with likely sporadic ALS-PDC	Case study	Diagnostic	GC important for family even if low recurrence risk, to provide support and discuss limitations	Interpretation Education Counseling	1.00 (10/10)
13	Vajda et al. (2017) [e52] Ireland/ UK	ALS	Determine the degree of consensus among clinicians on the clinical use of GT in ALS and the factors that determine decision-making	167 ALS clinicians from 21 different countries 86.8% were neurologists	Cross-sectional survey	Diagnostic Predictive	90.2% offer GT to patients defined as having familial ALS, 49.4% to sporadic ALS 42% never off presymptomatic GT Responses varied between ALS specialists and non-specialists and based on number of new patients seen	Interpretation	1.00 (16/16)
14	Clift et al. (2016) [e65] USA	Prion disease	Present an example case which discusses the psychosocial issues encountered and the role of GC in presymptomatic GT for incurable neurodegenerative conditions	1 individual who sought predictive GT after familial CJD was confirmed in her mother on post-mortem GT	Case study	Diagnostic Predictive	Multidisciplinary approach key to GC care for the family Clinicians should be aware of GC resources	Interpretation Education Counseling Support	0.90 (9/10) Question/ objective not clearly described
15	Stark et al. (2016) [e60] Australia	Unspecified LOND	Explore a complex case where the GT wish of one family member was in direct conflict to that of	1 family at risk of an unspecified LOND: the client at 25% risk requested	Case study	Predictive Reproductive	Approach described to balancing competing rights in a family	Interpretation Education Counseling	1.00 (10/10)

			another, assess the potential benefits and harms from acceding to or denying such a request, and present an approach to balancing competing rights of individuals within families	predictive GT, the intervening relative did not wish to know and would commit suicide if mutation positive			Magnitude of risks for client and relatives should be considered and every effort made to limit adverse outcomes in GT process		
16	Clement et al. (2015) [e22] France	HD	Review the historical context of guidelines and good clinical practice, the experiences of our team covering more than 20 years of predictive GT for HD in France, and the new French legislation, all factors that regulate presymptomatic GT	1705 persons at risk of HD who requested GC between 1992 and 2013.	Consecutive case series	Predictive	47% withdrew from predictive GT protocol demonstrating that request for GT does not imply client wants to know New legislation of health providers to disclose family medical information may impact on predictive GT uptake, due to concerns about confidentiality Benefit of a multidisciplinary approach	Interpretation Education Counseling Support	0.70 (7/10) Subject characteristics and results not sufficiently described Conclusions not well supported
17	Cruz-Marino et al. (2015) [e43] Cuba	SCA2	Review the 13-year experience of the SCA2 predictive GT program in Cuba, describing different ethical, psychosocial, and technical challenges that led to major changes in the predictive GT protocol	1193 individuals who requested predictive GT within a 13-year period	Consecutive case series	Predictive Reproductive	895 completed the protocol: 43.4% uptake of predictive GT, 23.9% uptake of reproductive GT (10/33 couples carried test-positive fetus to term) Some withdrew due to protocol length Benefit of multidisciplinary team and practices at the community level demonstrated	Interpretation Education Counseling Support	1.00 (10/10)
	Cruz-Marino et al. (2013) [e44] Cuba	SCA2	Review the 11-year experience of predictive GT for SCA2, including the pre-GT opinions about different aspects of	1050 individuals who requested predictive GT between 2001-2011	Consecutive case series	Predictive	768 completed the protocol, predictive GT uptake 24.91% 31 symptomatic individuals were	Interpretation Education Counseling Support	1.00 (10/10)

			the protocol and the profile of at-risk individuals who underwent GT				eliminated from the predictive GT protocol at their first appointment (neurological assessment)		
18	Mandich et al. (2015) [e50] Italy	ALS	Report several issues in GC for ALS	2 siblings with ALS who had discordant GT results	Case study	Diagnostic Predictive	One sibling may have phenocopy Benefits highlighted around exploring the complexity and pitfalls of GT and GC, the unexpected consequences for relatives pre-GT, and using multidisciplinary team	Education Counseling	1.00 (10/10)
19	Klitzman et al. (2014) [e16] USA	HD AD (Tay Sachs, CF, autism, sex selection)	Survey attitudes and practices to understand whether providers in neurology and psychiatry discuss PND and PGD with clients, and if so, how frequently, when, how and what factors are involved	535 health providers: 163 neurologists 372 psychiatrists	Cross-sectional survey	Reproductive	24.9% of neurologists, and 31.9% of psychiatrists had discussed PND 95.3% didn't feel comfortable discussing PGD	Education	1.00 (18/18)
20	Schuler-Faccini et al. (2014) [e45] Brazil, Portugal	SCA3	Present our experience from two programs conducting predictive GT for SCA3 in Porto, Portugal and Porto Alegre, Brazil from 1999-2012 Report an illustrative GC case	329 individuals who sought predictive GT for SCA3, 263 from Brazil 1 family case example	Consecutive case series Case study	Predictive	50% from Brazil, 77% from Portugal underwent GT Benefit of multidisciplinary team demonstrated	Interpretation Education Counseling Support	1.00 (10/10)
21	Smith et al. (2014) [e27] USA	ALS HD	Describe the challenges and lessons learned from a case in which an individual with a fatal condition was at risk for a second fatal condition and had difficulties with communication	1 individual with ALS at 50% risk of HD	Case study	Diagnostic Predictive	GC challenges inherent in this case: difficulty communicating due to disease progression, diagnostic consideration of two fatal conditions, complex risk information, personal	Interpretation Education Counseling	1.00 (10/10)

							and familial implications		
22	Tanaka et al. (2013) [e59] Japan	>6 LONDs	Present the results of a follow-up nationwide survey on predictive GT for LONDs in Japan	60 institutional members of Japan's National Liaison Council for Clinical Sections or Medical Genetics (response rate 67.4%)	Cross-sectional survey	Predictive	301 clients interested in predictive GT over 5 year period, 93 underwent GT Lack of non-MD counseling staff was apparent, clinical geneticists predominantly involved	Counseling Support	1.00 (14/14)
23	Gonzalez et al. (2012) [e47] Portugal	SCA3	Assess the following in individuals who had 5 years prior received positive results from predictive GT for SCA3: the psychological well-being, family satisfaction/ occurrence of familial changes, and the role played by a number of factors, such as presence of symptoms, in general psychological wellbeing and family satisfaction	47 individuals from the Azores archipelago who had positive predictive GT results approximately 5 years prior and attended their 4th post-GT psychological evaluation session, representing nearly 80% of the total number of individuals who tested positive	Retrospective cohort study	Predictive	More than half demonstrated moderate (28.9%) or severe (23.7%) stress Most (59.6%) had high familial satisfaction Development of first symptoms negatively impacted psychological state	Counseling Support	0.95 (21/22) Conclusions not well supported
24	Reyes et al. (2012) [e67] France	CADASIL	Analyse the profiles and motivations of individuals at risk of CADASIL who requested predictive GT between 2003-2010 Identify the neurological, cognitive and psychological modifications observed in applicants who received a positive result	33 individuals who requested predictive GT 11 completed neuro and psychological examination after receiving results and 18 months later	Consecutive case series Prospective cohort	Predictive	63% dropped out pre-GT High overall quality of life reported in those who could be followed up Multidisciplinary and multistep practice through to protect from harm	Education Counseling Support	1.00 (20/20)
25	Van Rij et al. (2012) [e37] The Netherlands Belgium France	HD	Provide a comparative overview of PGD approaches and technical workup for HD between 1995-2008 across 3 European centers	331 couples received GC	Prospective cohort study	Reproductive	68% requested direct PGD GT, 32% requested exclusion PGD 257 started PGD workup, 29 were	Interpretation Education	1.00 (22/22)

			Study differences in the populations who apply for PGD and their reproductive histories Compare PGD results between the centers and compare them with literature data				rejected, 61 refrained from PGD Overall delivery rate of couples starting ≥1 PGD cycle 37.4% (65/174)		
26	Yanoov-Sharav et al. (2012) [e68] Israel	FSHD	Present our experience of GT and GC for FSHD between 2000 -2006 Present a case study which highlights a unique example of GC for dominant, relatively late-onset disease	66 individuals who underwent GT for FSHD (59 diagnostic GT, 7 predictive GT) 1 family case example	Consecutive case series Case study	Diagnostic Predictive	< 60% received pre-GT GC, <30% received post-GT GC Pre-GT GC and multidisciplinary care emphasized due to complexities of LONDs and molecular GT	Interpretation Education Counseling	1.00 (10/10)
27	Dufrasne et al. (2011) [e21] Canada	HD	Report and analyse the uptake, reasons given for requesting predictive GT, social and demographic characteristics, GT outcomes, and emotional reactions of individuals who proceeded with HD predictive GT and explore how best to fulfill participants' perceived needs	181 individuals who requested predictive GT between 1994 and 2008	Consecutive case series	Predictive Reproductive	135 completed GT >1 reason for predictive GT usually mentioned, most common eliminating uncertainty Prenatal GT not frequently requested	Interpretation Education Counseling Support	1.00 (18/18) Described as retrospective cohort study
28	Cruz Marino et al. (2011) [e42] Cuba	SCA2 (Friedrich's Ataxia)	Describe some of the ethical dilemmas that arose in predictive GT for hereditary ataxias in Cuba Explore the GC process and the decisions made during predictive GT and prenatal diagnosis	4 case examples with ethical dilemmas: identical twins, GT an individual at 12.5% risk, GT a foetus at 25% risk and misattributed paternity	Non-consecutive case series	Predictive Reproductive	Complexities of predictive GT are apparent and expanded guidelines required to address these ethical issues	Interpretation Education Counseling Support	1.00 (12/12)
29	Butler et al. (2011) [e62] Canada	AD	Identify GC challenges and describe our specific GC approach for members of a geographically remote	1 family with early-onset familial Alzheimer disease (EOFAD) caused by PSEN1 in a North	Case study	Diagnostic Predictive	Alternative approaches to disseminating genetic information and ensuring appropriate, confidential and	Interpretation Education Counseling Support	0.80 (8/10) Question/ objective and study design not clearly described

			and culturally distinct community	American Aboriginal community			accessible GC services described		
30	Futter et al. (2009) [e18] South Africa	HD	Compile a comprehensive profile of the participants who had undergone predictive GT for HD in the West Cape region of South Africa to inform changes to improve GC services	36 individuals who had undergone predictive GT between 1995-2005 27 participated in interviews	Consecutive Case series Qualitative study not reported	Predictive	Uptake of GT in those with mixed ancestry was significantly lower Possible barriers: limited access to GT due to low income or education	Education	0.86 (12/14) Only quantitative data assessed Analytic methods and results not sufficiently described
31	Riedijk et al. (2009) [e51] The Netherlands	FTD	Unclear. Assumed objectives: To report predictive GT uptake and outcomes between 1999-2008 To present a case study and propose the idea of separation-individuation	100-180 individuals from familial FTD families and at 50% risk	Consecutive case series Case study	Predictive	13 requested GC between 1999 and 2002, 13 underwent GC between 2003 and 2008 , 1 underwent PND Low acceptance of GT hypothesized due to theoretical framework of separation-individuation	Education Counseling Support	0.50 (5/10) Question/ objective and results not sufficiently described Study design not described Conclusions not well supported
	Genetic counseling practice trialed in clinical setting								
32	Spiers et al. (2020) [e39] UK	HD	Evaluate participants' experience with a GC narrative group session to determine whether participating in a single GC narrative group is perceived as helpful	12 individuals who had tested positive on predictive GT and had participated in one of three GC group sessions between December 2017 and March 2018	Qualitative	Predictive	Group had a positive impact of being able to meet and empathize with others in a similar situation, increased disclosure to others and improved mood and future outlook	Support	1.00 (20/20)
	Stopford et al. (2020) [e40] UK	HD	Explore presymptomatic individuals' (and their partners) experiences of a structured narrative group session to understand the value and feasibility of integrating narrative practices within a GC session	8 individuals who were purposively selected and attended a single narrative group sessions, 6 mutation positive, 2 male partners (not at risk of HD)	Qualitative	Predictive	Positive feedback received, highlighting importance of time and space for structured sharing of experiences	Support	1.00 (20/20)
	Macleod et al. (2018) [e38] UK	HD	Explore the feasibility of offering narrative group sessions in the context of a predictive GT follow-up clinic	9 individuals who had tested negative on predictive GT	Uncontrolled before and after study	Predictive	Group sessions were seen as safe and enjoyable, and benefits included feeling less isolated,	Support	0.95 (38/40) Qualitative: analytic methods and reflexivity of the

			Determine how participants experienced the session and whether they would recommend participation to others		Qualitative		being inspired by other's stories and connecting as a group		account not clearly described
33	Esplen et al. (2013) [e20] Canada	HD (cancer, haemochro-matosis)	Develop a brief, reliable and valid instrument to screen psychosocial risk among those who are undergoing GT for adult-onset hereditary diseases	31 individuals from HD families undergoing GT participated (4% of total participants)	Prospective cohort	Unspecified	5 (23.8%) demonstrated distress 1 month post-GT Screening tool developed for further investigation in clinic or research	Counseling Support	0.95 (21/22) Likely confounders not described
34	Hawkins et al. (2013) [e15] Canada	HD	Report the predictive GT undertaken between January 2011- January 2012 using telehealth and usual care Examine whether telehealth improves access to HD predictive GT while maintaining quality of care and support	41 individuals referred for predictive GT, 28 requested telehealth (15 attended at least one session, 14 completed survey, 10 received results, 8 completed 2nd survey) 13 who utilized usual care (11 received results and completed 2nd survey)	Prospective cohort	Predictive	No significant differences between individuals undergoing GT in person or by telehealth with respect to quality of care, information, counseling and support Majority were satisfied with GC process in both groups	Interpretation Education Counseling Support	0.91 (20/22) Question/ objective and subject characteristics not clearly described
35	Mariotti et al. (2010) [e8] Italy	HD SCA1 SCA2 SCA3 SCA17	Define a well-framed, structured and easy procedure for GC in subjects at risk for LONDs, in which psychological support is intended both for the client and the health provider Verify feasibility and effectiveness of this procedure and compare possible differences in the impact of predictive GT in subjects with SCAs and HD	92 individuals undergoing predictive GT GC 60 at risk of HD, 32 at risk for SCAs	Consecutive case series	Predictive	72 (78%) proceeded with program, 55 (60%) received GT result, 38 (41%) completed entire program The need for psychological support was recognized for 5 mutation carriers and a non-carrier Clinical conference supported client and health provider	Interpretation Education Counseling Support	1.00 (22/22)
	Genetic counseling practice recommended from clinical research								

36	Oosterloo et al. (2020) [e35] The Netherlands	HD	Provide an overview of the experiences of Dutch persons at risk of HD in consulting a neurologist before or after DNA analysis Make a recommendation if and at what moment in the GT procedure the judgment of a neurologist is desirable	71 individuals at risk of HD who visited one of 4 Dutch GC clinics, 32 saw a neurologist before GT, 12 after GT, 27 did not see a neurologist. 68 completed predictive GT (29% response rate)	Cross-sectional survey	Predictive	41/44 felt visit to neurologist was positive 59 desired consulting a neurologist, even those who did not have the gene expansion, suggesting consultation before GT may be beneficial	Interpretation Education	0.95 (19/20) Outcome measures partially reported
37	Schwartz et al. (2019) [e66] France	Prion disease	Understand the feelings of at risk individuals towards predictive GT, their decision-making, and the long-term consequences Understand specific issues raised by PRNP-related disease	30 individuals who consulted the genetic department regarding predictive GT between 2004-2017 3/8 mutation carriers, 10/12 non-carriers and 6/10 who declined GT	Case series Qualitative (including psychological instruments)	Predictive	Anxiety rates high in non-carriers and untested subjects, highlighting psychological burden of living in a family with inherited prion disease	Counseling support	0.57 (17/30) Case series and qualitative study: question/ objective and study design not clearly described Qualitative study: data collection methods not clearly described. Theoretical framework/ wider body of knowledge, data analysis, verification procedures and reflexivity of the account not described
38	Ledo et al. (2018) [e13] Portugal	HD TTR-FAP	Investigate long-term consequences of predictive GT to identify variables that may predict middle and long-term psychological disturbance due to predictive GT	196 individuals who had previously undergone predictive GT (28.6% response rate) 167 at risk of TTR-FAP, 29 at risk of HD	Prospective cohort	Predictive	Psychopathological assessment pre-GT can inform those who may need psychological support several years later Result of predictive GT not a relevant predictor	Counseling Support	1.00 (20/20)

39	Stuttgen et al. (2018) [e1] USA	HD	Analyse long term changes in risk perception, and investigate factors that contributed to changes in risk perception	186 individuals who underwent predictive GT and had provided risk perception values before and after GT 39 had concurrent research clinic notes and semi-structured interviews, 27 referred to risk perception in interviews	Retrospective cohort Qualitative	Predictive	27% had unexpected changes in risk perception after GT results disclosure, particularly in those with repeat expansions Risk perception influenced by more than just results of predictive GT	Education Support	0.85 (34/40) Quantitative analytic methods and variance estimates not clearly described Theoretical framework and reflexivity of the account not described
	Stuttgen et al. (2018) [e2] USA	HD	Examine opinions on the importance of autonomy in the decision to be tested for HD, whether a formal HD GT protocol is necessary, whether a physician ordering HD GT in the absence of a formal HD protocol is acceptable, whether ordering presymptomatic GT for HD online via a direct-to-consumer (DTC) website is acceptable, and whether incidental/ secondary findings of HD should be returned in the context of whole exome/ genome sequencing	39 recent interviews with individuals who underwent predictive GT between 1986-1998 15 expansion carriers, 21 non-carriers, 3 who dropped out before GT result disclosure	Qualitative	Predictive	Most supported individual's right to decide whether and when to pursue HD GT (31/38), use of a formal HD GT protocol (22/37), and returning medically actionable secondary findings (34/36) Most were opposed to physician ordering (28/35) and DTC HD GT (24/31) in the absence of a formal protocol and returning a secondary finding of an expanded HD allele (18/37)	Counseling	0.75 (15/20) Question/ Objective not clearly described Theoretical framework and reflexivity of the account not described
40	Ibisler et al. (2017) [e14] Germany	HD	Prospectively follow the decision-making process of individuals at risk in our center Explore their experiences following the decision as well as the impacts of GT results	72 individuals who participated in at least one of three surveys 31 participated in telephone interview	Prospective cohort Qualitative	Predictive	93.4% had already sought information via the internet before the first GC session More participants with an affected mother (56.9%) than an affected father (31%) sought GC	Education Counseling Support	0.86 (36/42) Theoretical framework/ wider body of knowledge and verification procedures not described Data analysis and reflexivity of the account not clearly described

41	Leite et al. (2017) [e9] Portugal	TTR-FAP HD SCA3 (haemochro-matosis)	Understand why subjects at-risk of LONDs want to undergo predictive GT Compare results with the motivations of subjects at-risk for hereditary haemochromatosis	213 individuals at risk of 3 LONDS (174 TTR-FAP, 34 HD, 5 SCA3)	Qualitative Case series (unclear whether consecutive or non-consecutive)	Predictive	Most common motivations: reasons related to the future, reasons related to others and curiosity and the need to know - all reasons external and unrelated to the characteristics of the disease	Education Counseling	0.93 (37/40) Quantitative and qualitative analytic methods, and reflexivity of the account not clearly described
	Leite et al. (2017) [e10] Portugal	TTR-FAP HD SCA3 (haemochro-matosis)	Investigate what subjects at risk for TTR-FAP, HD, and SCA3 know about these 3 diseases in comparison with the knowledge that subjects at risk for HH have about the conditions	213 individuals at risk of 3 LONDS (174 TTR-FAP, 34 HD, 5 SCA3)	Qualitative	Predictive	References to the disease, references to the family and metaphors were mentioned more by subjects at risk of a LOND	Education	0.90 (18/20) Analytic methods and reflexivity of the account not clearly described
42	Quaid et al. (2017) [e6] USA	HD	Examine factors associated with the decision of research participants who changed their minds and opted to undergo presymptomatic HD GT, compared with those who still chose not to be tested	1001 individuals at risk of HD who are a part of the PHAROS observational study, 104 underwent predictive GT after initially declining	Prospective cohort	Predictive	Baseline behavioral scores (especially apathy) were more strongly associated with later GT than motor and chorea scores Following GT, 56% of those who tested negative had less depression compared to prior, depression stayed the same or increased for 64% of those with repeat expansion	Counseling Support	1.00 (22/22)
43	Andersson et al. (2016) [e25] Sweden	HD	Describe a couple's long-term experiences (from 6 months after result disclosure) and the consequences of predictive GT	1 couple interviewed separately on 9 occasions over a 2.5 year period	Qualitative - longitudinal descriptive case	Predictive	Long-term consequences of GT devastating for both members of the couple: anxiety, repeated suicide attempts, financial difficulties and divorce Long-term support recommended for both client and partner	Counseling Support	1.00 (20/20)

	Andersson et al. (2013) [e24] Sweden	HD	Describe the prospective experience of a client undergoing a presymptomatic GT for HD, and her husband in order to obtain an understanding of the client's perspective and the effect on the couple	1 couple interviewed separately on 9 occasions over a 15 month period	Qualitative – longitudinal descriptive case	Predictive	Throughout pre- and post-GT, need to acknowledge needs of client and partner, particularly important at time of results and symptom onset	Education Counseling Support	1.00 (20/20)
44	Benatar et al. (2016) [e49] USA	ALS	Highlight clinically relevant aspects of the genetic complexity of ALS and present an approach to predictive GT that we have developed and refined over the last 8 years in the pre-FALS study	317 GC sessions with 161 individuals at 50% risk of familial ALS who are part of the pre-fALS study 75 post-GT sessions with 63 individuals with familial ALS	Consecutive case series	Predictive	Clients may be interested in research participation without results being disclosed Pre-GT GC requires detailed discussion and careful consideration of potential pitfalls of proceeding	Interpretation Education Counseling Support	0.70 (7/10) Study design and results not sufficiently described Conclusions not well supported
	Fanos et al. (2011) [e48] USA	ALS	Explore the basis for participants' decision to learn results of presymptomatic GT or not, understand the psychosocial impact of the decision and assess attitudes toward receiving results by telephone or in person	20 individuals at 50% risk of familial ALS, who are part of the pre-fALS study 14 elected to receive results (8 mutation carriers, 6 non-carriers)	Qualitative	Predictive	Telephone counseling as option for those who can't easily access in person counseling Those who decline GT may change their mind in future Clients adapted well in the short-term	Education Counseling Support	0.80 (16/20) Theoretical framework and reflexivity of the account not described
45	Paneque et al. (2015) [e57] Portugal	All LONDs tested for in Portugal	Explore professionals' views of relevant quality indicators in their own GC practice concerning predictive GT for LONDs Examine current assessment of such GC practice in Portuguese genetic services	18 genetic health professionals (85% of total eligible interviewees)	Qualitative	Predictive	Core components of GC identified Challenges specific to LONDs: ambiguity of health/ illness status, time burden for health professionals Health professionals associated quality with non-directiveness, information given and comprehension pre-GT, decision-making facilitated based on consultands' motivations	Interpretation Education Counseling Support	0.90 (18/20) Reflexivity of the account not described

46	Guimaraes et al. (2013) [e12] Portugal	TTR-FAP HD SCA3	From the client's perspective, recognize aspects relevant across the predictive GT and GC process that might indicate an effective practice Analyse aspects of current protocols that might be relevant for a successful practice	22 individuals undergoing predictive GT 13 for TTR-FAP, 6 for HD, 3 for SCA3	Qualitative	Predictive	Highlight the need of health providers to be armed with personal and professional skills to GC safely and effectively, and provide flexible client-centered care Further training and clinical supervision may help	Education Counseling Support	0.90 (18/20) Data analysis and reflexivity of the account not clearly described
47	Ledo et al. (2013) [e33] Portugal	HD TTR-FAP	Compare the behavior symptoms inventory (BSI) psychopathological indices observed before and one year after completion of predictive GT Identify differences between the psychological impact depending on type of risk disease, carrier or non-carrier status and demographic variables (age, gender, marital status) included in the general protocol.	53 individuals who underwent predictive GT (40 for TTR-FAP and 13 for HD) and completed psychological evaluations one year later	Retrospective cohort	Predictive	BSI levels across the time points were higher in both those who tested negative and positive, compared to controls Average BSI levels decreased post-GT regardless of the result, and condition	Counseling Support	1.00 (20/20)
48	Uhrova et al. (2013) [e5] Czech Republic	HD	Characterize the differences in psychiatric examination and psychometric measures between people at risk who were recommended to postpone predictive GT, and those who proceeded	52 individuals who underwent psychiatric examination as part of the HD predictive GT protocol: 41 continued with GT (19 tested positive, 22 tested negative), 11 were recommended to postpone	Retrospective Cohort	Predictive	Psychiatric examination provides more significant information regarding whether to consider postponing GT than formalized psychiatric screening tools Motivations must be assessed pre-GT, postponing may be required if problematic	Education Counseling Support	1.00 (18/18)
49	Van Rij et al. (2013) [e7] The Netherlands	HD	Create a better understanding of the motives and experiences of couples opting for exclusion PND or PGD	17 couples who had undergone reproductive GT with exclusion	Qualitative	Reproductive	7 couples had terminated 11 pregnancies, none showed regret. Some elected to have PGD	Education Counseling Support	0.95 (19/20) Reflexivity of the account not clearly described

			Study the acceptability of exclusion PGD among candidates	13 PND with exclusion 6 PGD with exclusion (2 couples experienced both)			with exclusion to avoid another termination Adequate professional and psychological support required before, during and after PND/PGD		
50	Rodrigues et al. (2012) [e11] Brazil	SCA3 HD TTR-FAP SCA1 SCA2 SCA6 SCA7	Describe the Brazilian public health system experience of a predictive GT program, run in accordance with the international guidelines for HD, SCAs and TTR-FAP between 1999-2009 Conduct a subsequent survey of the psychological characteristics of individuals who sought predictive GT, to detect differences between groups	183 individuals who commenced predictive GT (147 at risk for SCA3, 22 for HD, 8 for TTR-FAP, 6 for other SCAs) 31 participated in a follow-up interview and 15 had also completed psychological survey pre-GT	Consecutive case series Retrospective cohort Qualitative study not reported	Predictive	Low uptake of post-GT psychological evaluation, reason remains unknown Authors suggest adjustments necessary to provide adequate follow-up	Education Counseling Support	1.00 (18/18) Only quantitative data assessed
51	Alexander et al. (2011) [e63] Canada	AD	Assess the effectiveness, outcomes and costs of requesting medical records for the confirmation of client–reported family histories of dementia	275 medical record requests during the 24-month period of January 1, 2005–December 31, 2006	Consecutive case series	Diagnostic	Useful medical records obtained from 92 (33.5%) requests: 77 supported, 15 did not support patient-reported information Patient-reported family history was accurate in 84% Almost 500 hours of GC time spent	Interpretation	0.75 (15/20) Question/ objective, study design and results not sufficiently described Variance estimates not described
	Genetic counseling practice recommended from non-clinical research								
52	Cahn et al. (2020) [e46] USA	SCA1, 2, 3, 6, 7, 8, 14, 17, 35	Assess knowledge of genetic risk and perceptions of reproductive options in individuals with a diagnosis of spinocerebellar ataxia	94 individuals with or at risk of SCA, 77 symptomatic	Cross-sectional survey	Reproductive	39.8% would consider PGD, less PND (number unclear) 79.8% would not consider donated embryos, 63-74% would not consider donated gametes	Education	1.00 (18/18)

							Most common decision-making factors: child will not inherit SCA, cost and risk to mother or child		
53	Withers et al. (2019) [e64] USA and Mexico	Alzheimer's disease	Examine cultural beliefs about Alzheimer's disease and genetic screening among at risk populations of Mexican heritage	123 individuals from families living in Mexico and California in which Alzheimer's disease mutations were known to run 13 (plus an additional 5) participated in in-depth interviews	Cross-sectional survey Qualitative	Predictive	Few respondents understood their risk of inheriting a pathogenic variant causing Alzheimer's disease in their family Family myths and stigma also present in the family	Education	0.87 (33/38) Method of subject selection, sampling strategy and theoretical framework/ wider body of knowledge not clearly described Reflexivity of the account not described
54	Hagen (2018) [e17] Sweden	HD	Explore the intersections between genes, the body and the lived experience of a genetic disease to contribute to a deeper understanding of the lived experience of genetic diseases	11 individuals from HD families 2 affected, 1 presymptomatic carrier, 2 tested negative, 1 untested and at risk, 5 unrelated relatives	Qualitative	Diagnostic Predictive	Lived experience is fluid and dynamic and must be addressed as part of GC process both pre- and post-GT	Counseling Support	0.95 (19/20) Reflexivity of the account not clearly described
55	Hartzfeld et al. (2015) [e54] USA	ALS	Learn how familial ALS influences reproductive decisions, the potential influence of others, factors considered during the decision-making process, and participants' overall experience regarding reproductive choices	10 individuals from familial ALS families who were aware of the risk of the disease when they had children	Qualitative	Reproductive	Those who decided to have children always planned on having children, hoped for a cure and compared ALS favourably to other diseases Those who chose not to have children had extensive experience of ALS and caretaking, saw ALS as inevitable tragedy and avoided serious relationships	Education Counseling	0.80 (16/20) Theoretical framework/ wider body of knowledge not clearly described Conclusions not well supported Reflexivity of account not described
56	Paneque et al. (2015) [e61] Portugal	LONDs	Identify quality aspects of effective GC practice in presymptomatic GT for	45 experts with extensive experience of GC from 11 countries, 29 completed round	Delphi	Predictive	High quality professional standards; service standards; the consultand-centered	Interpretation Education Counseling Support	1.00 (16/16)

			late-onset neurological disorders	1 (64.4%), 13 completed round 2 (31.1%) and 17 competed round 3 (37.7%)			practice; and protocol standards were developed Most relevant quality indicators were related to consultand-centered practice, and advanced counseling/ interpersonal skills		
57	Hawkins et al. (2013) [e28] Canada	HD	Understand the obstacles to GT in terms of accessibility of services in Vancouver, as well as exploring the mechanisms by which this issue may be addressed	33 participants recruited based on a non-probability sample 24 tested, 9 rural, 15 non-rural 9 not tested, 3 rural, 6 non-rural	Qualitative	Predictive	Barriers to accessibility of GT: distance (time and travel, financial and opportunity costs, stress of travel) and inflexibility of the GT process	Interpretation Education Counseling Support	0.75 (15/20) Theoretical framework/ wider body of knowledge, data analysis and reflexivity of the account not clearly described Verification procedures not described
58	Hawkins Virani et al. (2013) [e41] Canada	HD	Develop a patient-friendly, comprehensive, accessible Web-based tool to provide accurate information about predictive GT for HD Pilot the content and test usability of the website, and modify the website	33 individuals from HD families, 9 had not had predictive GT, 24 had with 17 tested positive and 7 tested negative 10 individuals who had participated in above study, 5 genetic counselors across North America, 10 HD researchers and experts and 10 lay individuals invited, 23 completed survey (response rate 65.7%)	Qualitative Web-based cross-sectional survey	Predictive	Effective website included unbiased overview of important factors to be considered before undergoing predictive GT, interactive diagrams, video documentaries, and personal stories Website considered an effective counseling tool to support informed decision-making	Education Counseling Support	0.86 (31/36) Subject characteristics, outcome measures, quantitative analytic methods, theoretical framework/wider body of knowledge and reflexivity of the account not clearly described
59	Etchegary (2011) [e19] Canada	HD	Explore the healthcare experiences of families affected by HD, and elicit their suggestions for improvement in the	24 individuals from HD families 2 affected, 3 presymptomatic carriers, 5 tested	Qualitative	Diagnostic Predictive	Participants experienced difficulty accessing appropriate healthcare and support, and were	Interpretation Education Support	0.95 (19/20) Reflexivity of the account not clearly described

			quality of care provided to them.	negative, 2 tested - intermediate result, 2 tested – results not received, 6 untested and at risk, 4 spouses			frustrated by lack of knowledge of family physicians Regular follow-up and increased education of health professionals recommended		
60	Klitzman (2010) [e32] USA	HD (Alpha-1 antitrypsin deficiency, breast cancer)	Investigate the range of possible misunderstandings related to genetics that clients may have, the reasons why these may persist, and the implications that these may have.	21 individuals with or at risk of HD, 15 asymptomatic, 6 symptomatic, 14 had undergone GT, 10 were positive, 10 were negative	Qualitative	Diagnostic Predictive	Participants experienced various misconceptions/ misunderstandings about GT: that they could control disease onset, beliefs about inheriting mutations and physical traits together or that more biological material was inherited from one parent	Education Counseling	0.95 (19/20) Reflexivity of the account not clearly described
61	Schwartz (2010) [e3] USA	HD	Explore the unique issues surrounding being diagnosed with a chronic, progressive, genetic disorder through a narrative inquiry approach	10 individuals diagnosed with HD within the past year	Qualitative	Diagnostic Predictive	Lived experience of HD had the following key chapters in the narrative: discovering the existence of HD, confirming the diagnosis, revealing the diagnosis to others, and experiencing the reverberations of HD	Interpretation Education Counseling Support	0.95 (19/20) Reflexivity of the account not clearly described

[#]Conditions not of interest in brackets; *Only population of interest included

KEY: AD: Alzheimer's disease, ALS= amyotrophic lateral sclerosis, CADASIL= cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, FSHD= Facioscapulohumeral muscular dystrophy, FTD= frontotemporal dementia, GC= genetic counseling, GT= genetic testing, HD= Huntington's disease, PGD= preimplantation genetic diagnosis with in vitro fertilisation, PND= prenatal diagnosis, SCA: spinocerebellar ataxia, TTR-FAP= Familial amyloid polyneuropathy; USA= United States of America

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APPENDICES

Appendix 1 Authors

Name	Location	Role	Contribution
Ms Ashley Crook MGenCouns	University of Technology Sydney, Graduate School of Health, Ultimo, Australia; Centre for MND research, Department of Biomedical Science, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia; Department of Clinical Medicine, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia	Lead researcher	• Study concept or design • Major role in the acquisition of data • Analysis and interpretation of data • Drafting and revision of the manuscript for content
Dr Chris Jacobs PhD	University of Technology Sydney, Graduate School of Health, Ultimo, Australia	Co-supervisor	• Study concept or design • Revision of the manuscript for content
A/Prof Toby Newton-John PhD	University of Technology Sydney, Graduate School of Health, Ultimo, Australia	Co-supervisor	• Study concept or design • Revision of the manuscript for content
Ms Rosie O'Shea MGenCouns	University of Technology Sydney, Graduate School of Health, Ultimo, Australia	Second reviewer	• Acquisition and analysis of data • Revision of the manuscript for content
A/Prof Alison McEwen PhD	University of Technology Sydney, Graduate School of Health, Ultimo, Australia	Primary supervisor, third reviewer	• Study concept or design • Analysis of data • Revision of the manuscript for content