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TOMADA DE DECISÃO NO DIAGNÓSTICO PRÉ-NATAL NÃO-INVASIVO: PERSPETIVAS DOS PROFISSIONAIS DE SAÚDE, DAS GRÁVIDAS E A INFLUÊNCIA DA ANSIEDADE

Dissertação de Mestrado em Psicologia Clínica

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Dissertação apresentada no Instituto Superior de Ciências da Saúde – Norte, para obtenção do grau de Mestre em Psicologia Clínica, sob orientação do Prof.Doutor José Carlos Rocha

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LISTA DE CONTEÚDOS

INTRODUÇÃO

De forma a obter o grau de Mestre em psicologia Clínica, foi realizado o presente trabalho da unidade curricular de Seminário de Investigação do 2º ano do Mestrado, em Psicologia Clínica do Instituto Superior de Ciências da Saúde – Norte, na qual, foi realizado sob orientação do Prof. Doutor José Carlos Rocha.

Este trabalho centra-se num estudo sobre a tomada de decisão no diagnóstico pré-natal não-invasivo: Perspetivas dos profissionais de saúde, das grávidas e a influência da ansiedade.

A apresentação de um estudo em formato de artigo é realizado com base nas normas requeridas pela Revista Brasileira de Ginecologia e Obstetrícia ao qual está em submissão.

A apresentação da segunda parte consiste num artigo em submissão por uma equipa do Reino Unido.

A terceira parte consiste num resumo de comunicação livre em 18th International Conference on Prenatal Diagnosis and Therapy, publicada na revista Prenatal Diagnosis.

A quarta parte trata-se de um resumo de comunicação livre nas XVI Jornadas de Psicologia do Instituto Superior de Ciências da Saúde.

PARTE I

Artigo em submissão à *Revista Brasileira de Ginecologia e Obstetrícia*

"Tomada de decisão no diagnóstico pré-natal não-invasivo: Perspetivas dos profissionais de saúde, das grávidas e a influência da ansiedade"

Tomada de decisão no diagnóstico pré-natal não-invasivo: Perspetivas dos profissionais de saúde, das grávidas e a influência da ansiedade

Decision making in noninvasive prenatal diagnosis: Perspectives of health professionals, pregnant women and anxiety influence

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Resumo

Objetivo: O teste pré-natal não invasivo (TPNNI) está cada vez mais disponível a nível mundial como resultado de desenvolvimentos tecnológicos recentes e de fortes motivações comerciais. Um projeto colaborativo internacional foi delineado para comparar as preferências das mulheres e profissionais de saúde para os principais atributos das decisões sobre os TPNNIs para a Síndrome de Down. Pretendemos clarificar os atributos relativos à amostra Portuguesa e relacionar estes com ansiedade das grávidas.

Método: Neste estudo foi utilizada um modelo de escolha discreta para obter dados sobre as preferências dos participantes perante TPNNIs de acordo com quatro atributos: precisão do diagnóstico, tempo de espera dos resultados, risco de abortamento e fornecimento de informações mais completas, incluindo resultados clinicamente pouco significativos. Os atributos foram comparados entre uma amostra de 110 mulheres grávidas e 50 profissionais de saúde. Foi também utilizada a escala de avaliação da ansiedade de Zung com vista a correlacionar os atributos com o nível de ansiedade-estado nas mulheres.

Resultados: Verificam-se diferenças significativas nas preferências entre as grávidas e os profissionais de saúde. As grávidas colocaram maior ênfase nos testes com maior segurança e com informação completa, enquanto os profissionais de saúde dão mais importância à precisão nos testes pré-natais e à segurança do teste (risco de abortamento). A ansiedade estabelece correlação significativa com a preferência por testes que oferecem mais informações sobre o feto.

Discussão: Fica clarificada a divergência entre as preferências dos profissionais e as grávidas e que pode ser tida em consideração na implementação do TPNNI, facilitando tomada de decisão, valorizando as necessidades e atributos referidos pelas grávidas. Por

outro lado, o destaque da valorização da necessidade de resultados pré-natais mais completos está associado ao nível de ansiedade da grávida, o que ajuda explicar diferenças e direciona reflexão sobre as perceções de risco da grávida no seu acompanhamento.

Palavras-chave: Diagnóstico Pré-Natal, Testes Não-invasivos, Gravidez, Tomada de Decisão, Ansiedade

Abstract

Objective: Non-invasive prenatal diagnosis (NIPD) is today much more globally available as result of recent technological advances and significant commercial drive. An international colaborative project has been defined to compare women and health professionals preferences for key attributes for Down Sindrome NIPD decisions. We aim to clarify the main attributes to Portuguese sample and correlate them with pregnant women anxiety.

Method: It was based on a discrete choice model to extract information about NIPD participant's preferences accordingly to four key attributes: accuracy, time of test, risk of miscarriage and provision of information, including less significant clinical results. Attributes have been compared between a sample of 110 pregnant women and 50 health professionals. It was also used Zung state anxiety scale envisaging correlation between choice attributes and anxiety scores.

Results: There are significant differences between women and professionals preferences. Pregnant women emphasized miscarriage risk and provision of complete information; health professionals give more value to prenatal diagnosis accuracy and

miscarriage risk. There is a significant correlation between women anxiety and the preference for prenatal diagnosis tests which provide more information about the fetus. Discussion: The divergence between professional and pregnant women concerning preferences should be considered for NIPD implementation, facilitating decision making accordingly to patients values, aware of women needs and key relevant attributes. Nevertheless, pregnant women anxiety is related to the need for more complete results from prenatal diagnosis tests, which helps to explain the differences and directs reflections to risk perception and pregnancy wellbeing.

Keywords: Prenatal diagnosis, Non-invasive Prenatal Diagnosis, Pregnancy, Decison Making and Anxiety

Introdução

A crescente disponibilidade de testes pré-natais não-invasivos com elevado teor comercial, levanta questões sobre a adequada informação da grávida e sobre se os seus reais interesses estão a ser considerados na definição dos planos nacionais. O contexto do diagnóstico pré-natal em Portugal desenvolve-se maioritariamente no sistema nacional de saúde, embora haja importantes contributos da componente privada. Existe um programa nacional de rastreio pré-natal sendo que o tipo de teste mais utilizado é o teste de rastreio pré-natal combinado. No que trata das características legislativas da interrupção voluntaria da gravidez, em Portugal, é permitida a interrupção até às 10 semanas de gestação quando se trata de motivos sociais, até às 24 semanas quando se trata de anomalia fetal ou sem limite quando se trata de um feto incompatível com a vida ou havendo risco para a mulher.

Visto a importância que este assunto tem nos nossos dias, torna-se assim relevante saber o que as pessoas envolvidas neste contexto pensam sobre o mesmo, sejam as grávidas ou os profissionais de saúde, as suas opiniões e as suas decisões face ao diagnóstico pré-natal e os seus testes. Por outro lado, há variáveis que podem explicar eventuais diferenças no modo como as grávidas decidem e valorizam os diferentes atributos. A ansiedade sentida pelas grávidas poderá ajudar a explicar o modo como pontuam os atributos de decisão perante o diagnóstico pré-natal.

Esta investigação está inserida num projeto internacional em que participam países como Dinamarca, Islândia, Itália, Portugal, Canada, Singapura, Reino Unido, Israel e Holanda e foram exploradas as preferências das mulheres e profissionais de saúde para os principais atributos dos testes pré-natais não-invasivo e invasivo para a Síndrome de Down. Aqui pretendemos clarificar os atributos relativos à amostra Portuguesa,

comparando grávidas e profissionais, e relacionar as preferências atribucionais com a ansiedade das grávidas.

A Trissomia 21 ou Síndrome de Down, acontece em cerca de 1 em 800 nascimentos. O seu diagnóstico é feito com uma amostra de material genético fetal com a amniocentese. Esse mesmo teste implica uma percentagem de 1 a 2% da grávida sofrer um abortamento espontâneo e por isso normalmente só são realizados em gravidezes de risco[1]. O grupo de risco situa-se em grávidas com idades superiores a 35 ou aquelas que tenham antecedentes familiares de malformações. A amniocentese realiza-se às 16 semanas de gravidez e consiste numa recolha de líquido amniótico.

No entanto existem novas técnicas que permitem o diagnóstico precoce da Trissomia 21 mas sem o risco de sofrer o aborto espontâneo. Essa nova técnica é chamada de Teste Não-Invasivo onde é feita uma recolha de sangue materno e filtrado o ADN do feto. As investigações começaram no final de 1990 e neste momento existem muitas clínicas onde esse teste é realizado. Apesar disso, este mesmo teste tem as suas próprias limitações no que toca ao diagnóstico pré-natal de outras perturbações, mas tornou-se bastante preciso no diagnóstico pré-natal para trissomias autossómicas fetais[2].

Tomada de decisão no DPN

Autores como Pauker e Pauker[3] falam nos seus artigos sobre estratégias prescritivas para ajudar na tomada de decisão no DPN. Com isto, produziram um guia com várias árvores de decisão que representavam o custo e os benefícios através de uma análise sucessiva de alternativas e riscos. Utilizaram modelos matemáticos para testar o modelo de apoio à decisão e propuseram que se desse especial atenção ao papel do conselheiro genético[3]. Em 1987 fizeram uma revisão dos seus trabalhos e acrescentaram evoluções teóricas sobre a decisão como a estruturação do problema e a comunicação. Acrescentaram também cálculos probabilísticos de custos-benefícios face ao DPN[4].

Depois de revisto, os autores aplicaram o seu modelo durante dez anos e publicaram os resultados da experiência com 432 casais[5]. Aqui mostram tentativas para a quantificação do valor esperado e dos atributos perante as decisões do DPN. Ilustram os seus pontos de vista com 10 casos clínicos representando outras tantas situações tipo. Concluem pela utilidade das ajudas à decisão e reportaram erros frequentes no processo de comunicação dos riscos e suas soluções.

A teoria da decisão abrange conhecimentos e diferentes técnicas analíticas foram desenvolvidas para ajudar o decisor a escolher entre um determinado número de opções perante as suas possíveis consequências[6].

Além das limitações intrínsecas às opções, outras restrições podem ser pertinentes no processo de pensamento relativo à escolha. Plous[7] faz uma listagem desenvolvida sobre algumas limitações, como as restrições percetivas, a dissonância cognitiva, os desvios promovidos pela memória e a atenção, a influência do contexto, a plasticidade e os efeitos da formulação narrativa da decisão. Vários grupos de investigadores médicos, enfermeiros e psicólogos, têm-se inclinado sobre este tipo de decisões e dão mais importância a 3 tipos de fatores que dizem ser influentes nestas decisões: 1. o contexto decisional, que dizem referir-se ao tipo de decisão (em relação a um dado procedimento, diagnóstico, tratamento ou protocolo), à seriedade das consequências (por exemplo, doar um órgão versus tomar comprimido para enxaqueca), à familiaridade com a decisão (decidir fazer exercício é mais familiar do que fazer um teste genético), aos níveis de incerteza (o rastreio bioquímico pré-natal indica um risco aproximado, enquanto um diabético sempre que não tomar insulina tem consequências); 2. o decisor em si, determinadas características do decisor como a sua idade (por exemplo, se o decisor é uma criança ou um adulto); como traços de personalidade; como a capacidade para entender a informação médica e nível de ansiedade subjacente ao conflito

decisional e à incerteza; 3. as outras influências mais genéricas como os erros percetivos, a dissonância cognitiva, a formulação do problema, a memória e a atenção[8].

Especificamente em relação ao DPN, um estudo realizado no Reino Unido, em que foi desenvolvida uma revisão da literatura e consultados os intervenientes, clarificou os seguintes atributos de tomada de decisão relevantes no DPN: a precisão do diagnóstico (podem identificar 95%, 99% ou 100% dos bebés com síndrome de Down), tempo na gravidez quando são efetuados (os testes podem obter os resultados às 10 semanas, 12 semanas ou 16 semanas de gestação) e o tempo de espera pelos resultados, o risco de abortamento (alguns testes não têm risco de aborto, outros testes têm um pequeno risco) e o fornecimento de informações mais completas, incluindo resultados clinicamente pouco significativos[9].

A ansiedade-estado é um indicador muito importante na saúde em geral e mais ainda na saúde pré-natal, uma vez que é considerado um preditor da depressão pós-parto[10], também relacionado de forma negativa com os indicadores de desenvolvimento do recém-nascido[11] e valores da ansiedade-estado elevados durante a gravidez indicam um menor peso do recém-nascido, assim como um maior risco de o parto ser antecipado. Apesar disso, o estudo da influência da ansiedade da gestante, intrinsecamente associada à perceção de risco e à incerteza face às opções, sobre os atributos de decisão do DPN ainda não oferece evidências suficientes[12].

Objetivos

1. Caracterizar as preferências das grávidas e dos profissionais de saúde para os principais atributos da decisão por um teste pré-natal não-invasivo (TPNNI) para a síndrome de Down utilizando células de ADN fetal em relação a testes invasivos.

2. Comparar as preferências e os atributos das grávidas com as dos profissionais de saúde.

3. Correlacionar os atributos dos testes com a ansiedade e com o tempo da gravidez, educação e número de filhos.

4. Comparar as preferências por fazer um teste pré-natal para a síndrome de Down entre as grávidas e os profissionais.

Método

Amostra

Os questionários foram aplicados a uma amostra completa por 160 indivíduos de ambos os sexos em que se dividem em dois grupos. Grávidas que teriam de ter o mínimo de 20 semanas de gestação e profissionais de saúde com formação na área de diagnóstico pré-natal. A idade média das grávidas é de 28,19 com um desvio padrão de 4,86. Nos profissionais a idade média situa-se nos 34,26 com desvio padrão de 7,51. Os participantes que compõem a amostra são profissionais e utentes do Hospital Padre Américo (Centro Hospitalar Tâmega e Sousa-Penafiel) em que foi obtida autorização à comissão de ética.

Materiais

Foram administrados os seguintes instrumentos: um questionário sobre opinião das mulheres e os profissionais sobre os testes de diagnóstico da Síndrome de Down (SD) durante a gravidez incorporando com quatro atributos: precisão; tempo dos resultados do teste; risco de aborto; e se os resultados deram informações simples ou completas nos dois grupos de participantes. Este questionário foi composto por três seções; 1. perguntas estruturadas sobre o teste pré-natal; 2. conjuntos de escolha do questionário; 3. questões demográficas, para as mulheres, incluíram idade, sexo, educação, experiência de testes pré-natal e número de filhos; para os profissionais de saúde estava incluído o cargo, anos na função, idade e sexo.

Na seção 1 incluiu uma pergunta pedindo aos participantes para escolher entre TPNNI, testes invasivos ou nenhum teste. TPNNI foi descrito como 99% de precisão, testando para SD, a síndrome de Edward ou síndrome de Patau e é um exame de sangue sem risco de aborto, mas se o resultado do teste tiver sido positivo, um exame invasivo que tem um risco de 1% de aborto seria recomendado. O exame invasivo foi descrito como 100% exato, testando para SD, síndrome de Edward ou síndrome de Patau e dá informações adicionais sobre doenças raras que podem causar deficiência de aprendizagem, atraso de desenvolvimento ou outros problemas de saúde. Também foi descrito como sendo invasivo com um risco de 1% de abortamento.

Nas grávidas foi também aplicado a escala de autoavaliação de ansiedade de Zung para avaliar o estado de ansiedade das mesmas. A Escala de autoavaliação de ansiedade de Zung foi desenvolvida por Zung[13] e é uma escala de autoavaliação no qual o autor se auxiliou de um critério clínico baseado nos sinais e sintomas mais característicos das manifestações de ansiedade. A escala consiste em 20 itens que traduzem sintomas, no qual a pessoa deve escolher uma das quatros opções, aquela que melhor se adequa a si: "nenhuma ou raras vezes", algumas vezes, uma boa parte do tempo, a maior parte do tempo ou totalidade do tempo. A cada uma das opções é atribuída uma pontuação que vai de 1 a 4, do menos para o mais ansioso, respetivamente. Assim, quanto mais ansioso estiver um paciente maior pontuação obtêm na escala. A pontuação da escala pode variar entre 20 a 80, dividindo a pontuação obtida pelo valor máximo possível e assim obtêm-se um índice que representa o grau de ansiedade.

Procedimento

Os instrumentos foram aplicados às grávidas de forma acompanhada no Hospital para que se pudesse responder a eventuais dúvidas das mesmas. Aos profissionais foram-lhes entregue pessoalmente cada questionário onde posteriormente me foram entregues já

preenchidos. Foi obtida a permissão para o estudo no Hospital com autorização da comissão de ética. Sendo os instrumentos preenchidos de forma completamente anónima.

Análise de dados

A análise estatística foi efetuada primariamente com vista a descrever frequências das preferências e atributos das grávidas e dos profissionais. Seguidamente, estas preferências foram comparadas entre os dois grupos utilizando para tal o teste t. Na perspetiva de estudar as relações entre a ansiedade e as pontuações de valorização dos atributos, foi utilizada o coeficiente de correlação de *Pearson*.

Resultados

Na tabela 3 podemos observar que os atributos são pontuados de 1 a 6, sendo que 1 é o mais valorizado e 6 o menos valorizado. Assim, verifica-se que o atributo mais valorizado pelas mulheres grávidas é a informação adicional nos testes pré-natais, seguindo-se por ordem decrescente pelos atributos de segurança, ou seja, com o menor risco possível de um aborto espontâneo, precisão nos testes pré-natais, antecipação no tempo em que é feito o teste, rapidez dos resultados e o custo. Na tabela 3 também observamos os atributos mais valorizados pelos profissionais, sendo estes por ordem decrescente a precisão nos testes pré-natais, a segurança, ou seja, com o menor risco possível de um aborto espontâneo, a informação adicional nos testes pré-natais, antecipação no tempo em que é feito o teste, o custo e a rapidez dos resultados.

Comparando as preferências dos dois grupos de estudo, verifica-se que há diferenças estatisticamente significativas, com um nível de significância de 0,001 nos atributos precisão dos resultados, custo e informação adicional nos testes pré-natais. A um nível

de significância de 0,05 temos os atributos de antecipação no tempo em que é feito o teste e a rapidez dos resultados.

Na tabela 4 estão os valores das Grávidas e Profissionais que não modificam as suas escolhas em relação a cada teste que escolheram. Assim, verifica-se que as grávidas apresentam uma percentagem de 42.7% nas escolhas dos testes que tinham sempre a informação completa nas opções. Já os profissionais apresentaram uma percentagem de 22.0% nesta escolha. Nas escolhas em o teste tinha sempre o fator sem risco de aborto, as gravidas apresentaram uma percentagem de 30.0% e os profissionais de 16.0%.

Na tabela 5 temos as correlações entre os atributos na decisão e Ansiedade (Zung), Tempo de Gravidez, Nível Educacional e Número de Filhos. Verifica-se que existe uma correlação negativa entre a ansiedade e a informação adicional nos testes pré-natais que nos diz que, quanto mais ansiedade as mulheres sentirem mais preferem a informação adicional. O tempo de gravidez está correlacionado positivamente com a segurança do teste, o que nos diz que quanto mais tempo de gravidez tiver a mulher menos preferem a segurança dos testes pré-natais. Existe também uma correlação negativa entre o tempo de gravidez e a informação adicional nos testes, ou seja, quanto mais tempo de gravidez mais preferência pela informação adicional dos testes pré-natais. Em relação à educação existe uma correlação positiva com o custo dos teste que diz que, quanto maior for o grau educacional da mulher menos preferem o custo do teste. Quanto as correlações com o número de filhos, existe uma correlação positiva com a precisão dos testes pré-natais, ou seja, quantos mais filhos tiverem menos preferem a precisão dos testes pré-natais.

Na tabela 6 estão descritas as percentagens sobre as preferências por fazer um teste pré-natal para a síndrome de Down. O teste 1 corresponde ao teste com 99% de precisão com informação se o bebé tem síndrome de Down, síndrome de Edward ou síndrome de

Patau. O teste é um teste de sangue e não existe qualquer risco de aborto. O teste 2 corresponde ao teste com 100% de precisão e dá informação se o bebé tem síndrome de Down, síndrome de Edward ou síndrome de Patau. Este teste também dará informações adicionais sobre condições raras que podem causar dificuldades de aprendizagem, atraso de desenvolvimento ou outros problemas de saúde. É um teste invasivo e há um risco de 1% de aborto. Verifica-se que as grávidas dão preferência ao teste 2 com uma percentagem de 59.1%. Os profissionais dão preferência também ao teste 2 com uma percentagem de 50.0%.

Discussão

O crescente uso de novas técnicas no diagnóstico pré-natal e o impacto que isso tem na vida das grávidas faz com que seja pertinente uma investigação nessa área de forma a entendermos melhor de que forma pudemos mudar para que esse impacto seja menor ou mais positivo.

Enquanto um número significante de grávidas dá mais preferência à segurança dos testes e à informação dada pelo mesmo, os profissionais estão mais centrados na precisão do teste em si, o que faz com que essa diferença seja importante num aconselhamento e informação mais profunda sobre o que cada teste pode dar a cada grávida. Com estes resultados, é importante que se desenvolvam estratégias para que se possa dar toda a informação que a grávida precisa, relativa a cada teste de diagnóstico pré-natal.

Apesar das diferenças das preferências nos atributos, na questão em que os dois grupos tinham de escolher um dos testes, ou o teste invasivo ou o não-invasivo, verificou-se que os dois grupos preferiram o teste invasivo, o que dá informações mais completas sobre o diagnóstico.

Este resultado justifica-se porque este teste dá informações mais completas sobre o diagnóstico e, por parte dos profissionais, porque representa menos custos. Este estudo pode ajudar os profissionais a clarificar os aspetos mais importantes para as grávidas.

Durante o questionário, tanto as grávidas como os profissionais, no grupo relativo às dez questões sobre os testes, apresentaram maior percentagem nos testes que tinham sempre a informação completa nas opções. O que vem contradizer um pouco o resto dos resultados do questionário no grupo dos profissionais.

Em relação a ansiedade, a correlação com a preferência de testes de diagnóstico pré-natal com informações completas, diz-nos que As grávidas mais ansiosas tendem a preferir e a valorizar a informação completa num teste de diagnóstico pré-natal.

Quanto menos ansiedade a grávida sentir, mais confortável irá ficar durante a gravidez e menos problemas poderão ter os fetos. Este aspeto da ansiedade na grávida durante a gravidez está extremamente ligado ao desenvolvimento fetal. Lobel e os seus colaboradores[14] falam de valores altos no fator que integra três indicadores de stresse: a ansiedade-estado, o stresse crónico percebido e o stresse associado a acontecimentos de vida. Estes indicadores podem provocar o baixo peso do bebé à nascença e um período de gestação mais curto.

Limitações e projetos futuros

Durante todo o estudo, existiram várias limitações. O fato de termos apenas as opiniões dos participantes de um só hospital é por si só uma limitação. Seria interessante termos mais hospitais a participar neste estudo para percebermos melhor se as diferenças que encontramos também estão presentes noutros locais do país. O hospital participante colaborou imenso com este estudo mas demoramos algum tempo a conseguir o preenchimento dos questionários das grávidas, bem como os questionários dos profissionais. Houve necessidade de falar várias vezes com os profissionais para que

nos entregassem os questionários. Era bom que os profissionais mostrassem mais interesse e gostassem mais de participar neste tipo de investigações.

Como projetos futuros deveríamos de criar mais investigações nesta área, visto que o fato de não haver muito sobre o tema nos dificultou a procura de referências bibliográficas.

Haver uma maior divulgação do DPNNI pois na nossa sociedade ainda não é muito conhecido. Deveria haver mais informação e mais disponível para todos.

Deveríamos implementar questionários das preferências dos atributos nos hospitais para as grávidas de forma a ajudar os profissionais a criar uma relação mais empática com as pacientes grávidas, assim seria mais rápido o conhecimento das suas crenças.

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Tabela 1

Valores descritivos das amostras de grávidas

	Total (*n*=110)
Idade	
Média (M)	28.2 (4.9)
Gestação	
Média (M)	34.4 (5.82)
Qualificação académica	
Baixa	34 (30.9%)
Média	55 (50.0%)
Alta	21 (19.1%)
Religião	
Sim	82 (74.6%)
Não	28 (25.5%)
Número de filhos	
Nenhum	59 (53.6%)
1	41 (37.3%)
2 ou mais	10 (9.1%)
Tem algum filho com síndrome de Down?	
Sim	0 (0%)
Não	110 (100%)
Conhece alguma criança com Síndrome de Down?	
Sim	56 (50.9%)
Não	54 (49.1%)
Vou fazer um teste de diagnóstico pré-natal.	
Concordo Totalmente / Concordo	107 (97.3%)
Discordo totalmente / Discordo	3 (2.7%)

Tabela 2

Valores descritivos das amostras dos profissionais

	Total (*n*=50)
Idade	
Média (M)	34.3 (7.5)
Profissão	
Obstetra	19 (38.0%)
Enfermeiro	26 (52.0%)
Outro	5 (10.0%)
Anos de profissão	
≤5	36 (72.0%)
6-15	11 (22.0%)
16-25	3 (6.0%)
≥26	0 (0%)
Género	
Masculino	19 (38.0%)
Feminino	31 (62.0%)

Tabela 3

Valores descritivos dos atributos preferencialmente valorizados e a comparação entre grávidas e profissionais

	Grávidas		Profissionais		*t*	*p*
Atributos	*M*	*DP*	*M*	*DP*		
Antecipação	3,58	1,18	4,08	1,37	-2,348	,020
Precisão	3,12	1,12	1,96	1,06	6,170	<,001
Custo	5,43	1,03	4,64	1,19	4,272	<,001
Segurança	2,41	1,51	2,46	1,28	-,206	,837
Informação adicional	1,91	1,17	2,72	1,34	-3,881	<,001
Rapidez resultados	4,51	1,28	5,00	1,29	-2,246	,026

Valores representados que variam entre 1 e 6, sendo que 1 é mais valorizado e 6 menos valorizado.

Tabela 4

Valores das Grávidas e Profissionais que não modificam as suas escolhas

	Grávidas (n=110)	Profissionais (n=50)
Escolheram testes com maior precisão em todas as opções	6 (5.5%)	8 (16.0%)
Escolheram testes com tempo dos resultados em todas as opções	1 (0.9%)	0 (0%)
Escolheram testes com a informação completa em todas as opções	47 (42.7%)	11 (22.0%)
Escolheram testes com sem risco de aborto em todas as opções	33 (30.0%)	8 (16.0%)
Não escolheram nenhum dos testes	0 (0%)	0 (0%)
Total	**87 (79.1%)**	**27 (54.0%)**

Tabela 5

Correlações entre os atributos na decisão e Ansiedade (Zung), Tempo de Gravidez, Nível Educacional e Número de Filhos

	Ansiedade		Tempo Gravidez		*Educação*		*Nº filhos*	
Atributos	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Antecipação	,103	,285	-,122	,205	,017	,858	-,057	,551
Precisão	-,109	,255	-,010	,919	-,182	,057	,285	,003
Custo	,057	,554	-,132	,169	,249	,009	,098	,305
Segurança	,131	,171	,233	,014	,063	,512	-,136	,157
Informação adicional	-,200	,036	-,188	,050	-,114	,236	-,073	,449
Rapidez resultados	,020	,839	,123	,200	-,035	,719	-,079	,409

Tabela 6

Preferência por fazer um teste pré-natal para a síndrome de Down

Escolha	*Profissionais*	*Grávidas*
1	21 (42.0%)	45 (40.9%)
2	25 (50.0%)	65 (59.1%)
0	4 (8.0%)	0 (0%)

PARTE II

Artigo em submissão por equipa do Reino Unido

"International preferences for prenatal tests for Down syndrome"

Running title: International preferences for prenatal tests for Down syndrome

Manuscript Title: Preferences for prenatal tests for Down syndrome: an international comparison of the views of pregnant women and health professionals

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Summary

Background: Subsequent to a significant commercial drive, non-invasive prenatal testing (NIPT) is increasingly available worldwide, with much published on potential implementation strategies. Here we compare the preferences of women and health professionals from different countries for key attributes of non-invasive and invasive prenatal tests for DS.

Methods: A discrete choice experiment was used to obtain participants' stated preference for prenatal tests that varied according to four attributes: accuracy, time of test, risk of miscarriage, and provision of information. Pregnant women and health professionals were recruited from Canada, Denmark, Iceland, Israel, Italy, the Netherlands, Portugal, Singapore and the UK.

Findings: Differences in preferences were seen between women and health professionals within and between countries. Overall, women placed greater emphasis on test safety and full information than health professionals, who emphasised accuracy and early testing. No risk of miscarriage was important for women in all countries, and the preference was highest in Iceland, the Netherlands and the UK, lowest in Italy. Women from Italy and Portugal placed a greater emphasis on full information than women from other countries. Health professionals from Italy, Israel and Portugal had a stronger preference for full information than health professionals from other countries.

Interpretation: Differences between women's and health professionals' preferences are marked between countries, suggesting that approaches to implementation and service delivery of NIPT will need to differ between countries. As all women place great emphasis on test safety when making decisions about prenatal testing, it is important that pre-test counselling for NIPT includes issues beyond safety and ensures women understand the possible implications of test results.

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Keywords

Non-invasive prenatal diagnosis (NIPT), discrete choice experiment, Down syndrome

Declaration of interests

We declare no competing interests.

Introduction

Many countries have established prenatal screening programmes for Down syndrome (DS), where an initial screening test is followed by the offer of an invasive diagnostic test for women with a "high risk" result to allow definitive diagnosis. Non-invasive prenatal testing (NIPT) which analyses cell-free fetal DNA (cffDNA) in the maternal plasma is rapidly transforming prenatal testing for DS throughout the world. NIPT can be used from 10 weeks in pregnancy to screen for DS with high sensitivity (99%) and specificity (99.5%) and can detect other common chromosomal aneuploidies (Trisomy 18, Trisomy 13 and Monosomy X).[1] NIPT allows screening for these conditions early in pregnancy with a much greater sensitivity than current screening methods and thereby significantly reduces the need for invasive testing (chorionic villus sampling (CVS) or amniocentesis) with the associated small miscarriage risk.[2] Although research is showing that comprehensive molecular karyotyping and full genome sequencing may ultimately be possible using NIPT, at present NIPT cannot provide the same level of information afforded by invasive testing for the detection of rarer chromosomal conditions.[3]

Following the first evidence in 2008 that NIPT for DS was feasible,[4, 5] this test has moved swiftly into clinical practice with testing available in the private sector since 2011. Several USA and Hong Kong/China based companies are now offering NIPT and have made their commercial tests widely available throughout the world.[6] Stakeholder viewpoints are essential to guide the widespread implementation of NIPT. We have used a discrete choice experiment (DCE) to determine the relative importance placed on specific attributes of prenatal tests by pregnant women and health professionals from different countries. By asking participants to choose between a series of hypothetical options with varying attributes, DCE's reveal which attributes influence choice behaviour, establish an individual's willingness to trade-off one attribute against another and thereby provide insight into real-life decision

making.[7] Our previous DCE looking at preferences for prenatal tests with reference to NIPT in the UK demonstrated that health professionals placed greater emphasis on test accuracy, while women prioritised test safety.[8] This study aimed to explore women's and health professional's preferences for key attributes of current prenatal screening and diagnostic tests for DS and compare findings from nine countries. The countries are culturally diverse, represent five geographical areas (Northern Europe, Southern Europe, the Middle East, Asia and North America) and have differing healthcare systems (Supplementary material: Table 1).

Methods

Study design and analysis followed standard DCE guidelines.[7, 9, 10] Nine countries participated; Canada, Denmark, Iceland, Israel, Italy, the Netherlands, Portugal, Singapore and the UK.

Ethical approval

Local ethics approval was gained by each participating research team (Supplementary material: Table 2).

Study Sample

A convenience sample of pregnant women attending maternity clinics for routine clinical care was recruited. Women were invited to complete a hard copy of the questionnaire while waiting for a clinical appointment and had the option of reading a brief information sheet that described DS and tests for DS screening (DSS) and diagnosis.

Health professionals delivering antenatal care to women who were likely to discuss options for prenatal testing were recruited. In Singapore and Iceland health professionals were invited by email and an online version of the questionnaire was utilised. In all other countries potential participants were approached in person and invited to complete a hard copy of the questionnaire.

Questionnaire Design

The questionnaire comprised three sections; 1. Structured questions about prenatal testing; 2. DCE choice sets and 3. Demographic questions. Section one included a question asking participants to choose between NIPT, invasive testing or no test. NIPT was described as 99% accurate, testing for DS, Edward's syndrome or Patau's syndrome and is a blood test with no risk of miscarriage, but if the result was

positive an invasive test which has a 1% risk of miscarriage would be recommended. The invasive test was described as 100% accurate, testing for DS, Edward's syndrome or Patau's syndrome and gives additional information about rare conditions that may cause learning disability, developmental delay or other health problems. It was also described as being invasive with a 1% risk of miscarriage.

Attributes for the DCE were those used in the previous UK DCE on prenatal tests for DS, which were developed following a literature review and consultation with stakeholders and were shown to generate plausible results.[11] The attributes cover key differences between NIPT and invasive tests and the associated levels were updated to reflect current clinically feasible ranges (Table 1). The DCE design follows the approach of Street and Burgess.[12] Two attributes had three levels and two attributes had two levels. The number of possible combinations of attributes and levels was statistically reduced from thirty two ($2^3 \times 2^2$) to nine scenarios using an orthogonal fractional main effects design.[13] A shift of one level created nine additional scenarios. The two sets of scenarios were paired to form nine choice sets. An additional choice set with one clearly superior test was included as an internal consistency check. Across the choice sets all levels of each attribute occur with equal frequency (level balance) and within each individual choice set there is no overlap in attribute levels (minimal overlap). Women were asked which test they would prefer to have and health professionals were asked which test they would prefer to offer. Participants were asked to choose between Test A, Test B or Neither (Supplementary material: Figure 1).

Demographic questions for women included age, gender, ethnicity, education, experience of prenatal tests and number of children. Demographic questions for health professionals included job title, years in role, age and gender. The questionnaires took approximately 20 minutes to complete. For non-English speaking countries the questionnaires were translated by the local research team.

Analysis

The DCE preference data were analysed for both women and health professionals using a conditional logit regression model.[14] Mean centred coding was used for accuracy and time of results and effects coding was used for risk of miscarriage and information. A constant term was included in the model to reflect the "neither" option.[15] The sign (+ or -) of the coefficients generated in the regression analysis indicates the direction of the preference for each attribute. Participants were

anticipated to prefer tests with greater accuracy, information and safety (+ coefficient) conducted early in pregnancy (- coefficient). The marginal rates of substitution (MRS) were calculated as a ratio of the coefficients of two attributes to allow direct assessment of how much of one attribute participants were willing to trade-off for more of another attribute and enable comparison of different attributes on a common scale.[9] We also determined the predicted probability that two tests from the choice set representative of NIPT and invasive testing would be selected based on the model coefficients.[9] The software package Stata 12.0 (StataCorp USA) was used to perform all analyses.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication.

Results

Participants

Overall 2707 women and 1275 health professionals were recruited from nine countries. Questionnaires were excluded if the consistency question was not answered as expected or if the respondents did not complete the choice set (women n=41, and health professionals n=30). Consequently, a total of 2666 women's and 1245 health professionals' questionnaires were included in the analysis (Supplementary material: Table 3).

Overall the sample consisted of a highly educated group of women with over half the women in seven countries having degree level education (Supplementary material: Table 4 and 5). In Italy the mean age was 36.2 years compared to 27.0–31.4 years for other countries. DSS uptake varied between countries; 90.3-97.4% in Denmark, Iceland, Italy and Portugal, 78.6-81.6% in Canada, Singapore and the UK, 69.8% in Israel and 46.0% in the Netherlands. For health professionals the mean age ranged from 34.5 years in Portugal to 47.7 years in Iceland. The training background varied widely between countries as DSS counselling is performed by different professionals. In all countries the vast majority of health professionals were women.

Direct choice between NIPT, invasive testing or no test

When asked to choose directly between having NIPT, invasive testing or no test (Figure 1) the vast majority of women in Denmark, Canada, Iceland, the Netherlands and the UK chose NIPT over invasive testing. In Italy and Portugal more women chose invasive testing than NIPT. Most countries had a sizeable proportion of women who chose not to have testing, including more than one third of women in the Netherlands and Israel. With the exception of Portugal, the majority of health professionals in each country chose NIPT as their preferred test to offer women. In Israel, Italy, Portugal, Singapore and the UK a large proportion (30% or more) chose invasive testing. The proportion of health professionals choosing no test was very small.

Regression Results

Comparison of all women and health professionals

All attributes had a significant impact on women's and health professionals' decision making; positive coefficients show participants prefer safer tests with greater accuracy and comprehensive information, while the negative coefficient indicates preference for an earlier test (Table 2). These results are consistent with *a priori* expectations, supporting the theoretical validity of the models. Comparison of women and health professional's demonstrate that women assign a relatively higher value to test safety and having comprehensive information, while health professionals place more value on accuracy and early testing (Table 2). Probability analysis suggests women and health professionals were equally likely to choose NIPT, but health professionals would be more likely to choose invasive testing than women (Table 2). The MRS confirmed women's strong preference for a test with no risk of miscarriage, as they were prepared to wait more than twice as long and accept 6% lower accuracy compared to health professionals for a test that had no risk of miscarriage (Table 3). Women were prepared to wait more than twice as long and accept 2% lower accuracy compared to health professionals for a test that gave comprehensive information.

Comparison of women and health professionals within countries

Comparison of women and health professionals identified differences in preferences within each of the countries (Table 4). With the exception of Iceland, health professionals placed more emphasis on accuracy than women. In Canada, Iceland, the Netherlands, Singapore and the UK health professionals placed more emphasis on early testing than women. With the exception of Italy, women placed more emphasis on test safety than health professionals. In Canada, the Netherlands and

Portugal women placed more emphasis on having full information than health professionals.

Comparison of women between countries

Comparison of women between countries identified differences in preferences for each test attribute ($p<0.0001$). Women in Canada, Denmark, Iceland, the Netherlands, Singapore and the UK placed greater emphasis on test accuracy than women from Italy, Israel and Portugal. Women from Denmark, Iceland, Italy and the Netherlands placed greater emphasis on early testing than women from other countries. Women from Portugal placed lower emphasis on early testing than all other countries. Women from Iceland, the Netherlands and the UK placed greater emphasis on test safety than women from other countries. Italian women placed lower emphasis on safety than all other countries. Women from Italy and Portugal placed the greatest value on having comprehensive information and women from Canada, Israel and the Netherlands placed greater emphasis on comprehensive information than women from other countries. The mean probability of choosing a test with the attributes similar to either NIPT or invasive testing suggest that women from Italy and Portugal, and to a lesser extent Israel and Singapore were more prepared to accept tests with a risk of miscarriage to gain more comprehensive information than women from other countries (Table 4).

Comparison of health professionals between countries

The preferences of health professionals also differed between countries for each attribute ($p<0.0001$). Health professionals in the Netherlands placed the greatest value on test accuracy. Health professionals from Denmark, Iceland and the Netherlands placed greater emphasis on early testing than health professionals from other countries. Health professionals from the Netherlands placed the greatest emphasis on test safety, amongst the remaining countries health professionals from Canada and the UK placed greater emphasis on test safety than health professionals from other countries. Health professionals from Israel, Italy and Portugal placed the most emphasis on having full information. For the remaining countries health professionals from Canada, Singapore and the UK placed greater emphasis on test safety than health professionals from other countries. The mean probabilities of choosing a test with the attributes similar to either NIPT or invasive testing suggest that health professionals from Israel, Italy, Portugal, and Singapore are more likely to prefer to offer tests with a risk of miscarriage to gain more comprehensive information (Table 4).

Discussion

Much has been published on NIPT with many professional bodies advocating implementation for high risk women, and others advocating that it should be used as a primary screen replacing traditional DSS. With NIPT now available through private companies in more than 60 countries[6] and evaluation of implementation in the public sector underway[16][best ref for PEGASUS and TRIDENT??] our exploration of cross-cultural variation in women's and health professional's preferences for prenatal tests is timely. Overall, women placed greater emphasis on test safety and full information than health professionals, who in turn placed more emphasis on accuracy and early testing than women. Differences were seen between women and health professionals within each country and there were clear differences between women's and health professionals' preferences between countries. These findings highlight the need for strategies for implementation of NIPT to be country specific. For example women from Italy and Portugal placed a stronger emphasis on having information on other rarer chromosomal rearrangements than women from other countries, and so there may be a greater demand for the provision of invasive testing in these countries. Ideally further targeted research into stakeholder views should be used to inform individual approaches to service delivery.

Previous DCE studies looking at prenatal testing for DS also found differences between women's and health professional's preferences. Studies conducted in the UK[8, 17], Australia[18] and the Netherlands[19] have shown similar results whereby health professionals valued accuracy and earlier timing of tests while women emphasised test safety and information. This difference is important and health professionals need to be aware that their views may differ from those of the women they are counselling. In all countries, pregnant women were willing to accept a less accurate prenatal test to access a test without risk of miscarriage. As a result, health professionals should take care not to focus solely on test safety when discussing NIPT. This is particularly pertinent as health professionals determine how tests are presented and influence test uptake,[20] and women reportedly will follow the advice of trusted health professionals.[21] The option of not having testing also needs to be highlighted to women. When asked to directly choose between NIPT, invasive testing and no test a sizable proportion of women, particularly in the Netherlands and Israel, chose no test. In Israel cultural factors may have influenced this outcome as participants included a large proportion of Orthodox Jewish women and in the Netherlands attitudes to testing and cost may influence DSS uptake which is lower than other Northern European countries.[22] Our finding mirrors the results of a

questionnaire study conducted in the US which found that even with NIPT as an option up to one third of participants would decline DSS.[23]

Our findings suggest that the value attached to key attributes of prenatal tests differ across countries for both women and health professionals. Previous research has also shown variation in women's views on prenatal testing between countries with respondents from Northern European countries more likely to value parental choice in prenatal testing than their counterparts in Southern Europe and Asia.[24] Variation in women's preferences between countries raises the question of whether differences exist between cultural groups within countries. There is some evidence suggesting that ethnic minority groups in Western countries differ in how they view and utilise prenatal screening and testing.[25-29] Further research is needed to determine whether these differences include attitudes to NIPT and, if so, how these could be addressed to improve service delivery in our increasingly multicultural societies.

Differences between countries are likely to reflect both personal decisions influenced by attitudes to prenatal testing, disability and termination and wider influences such as social and cultural contexts and healthcare policies such as the requirement for a part or full payment for prenatal testing and access to termination of pregnancy. More nuanced differences in DSS programmes and policies may also impact on preferences. Crombag et al[30] compared DSS programmes in Denmark, the Netherlands and the UK and speculate that variation in DSS uptake rates between these countries are influenced by how the offer of DSS is framed. For example in Denmark (highest uptake) DSS is free and an opt-out approach to DSS is emphasised which means that screening may be viewed as routine by women, while in the Netherlands (lowest uptake) testing must be paid for and there is a strong emphasis on the right not to know.

Limitations

A number of issues may limit the general applicability of our findings. For example, the majority (55.3%) of women who took part were highly educated and held a degree qualification or equivalent. Recruitment at individual centres may not reflect preferences across the whole country. For example DSS uptake has been shown to vary considerably between different regions in the UK[20] and in the Netherlands.[31] In addition, the study was conducted in high income countries. Low income companies will face additional challenges and focused research is needed.[6] The DCE design only considered four attributes of prenatal tests when real-life choices would also

involve other factors such as false positives, access to tests and costs and does not look into the reasoning behind the choices made or give insight into how the tests were perceived. Moreover, as in any stated-preference study, participant choices do not necessarily reflect the choices that would be made if participants were faced with a real-life decision about testing. Another potential limitation is that the questionnaire was developed in English and translation may result in the loss of culturally specific meanings.[32]

Conclusions

Differences between women's and health professionals' preferences were marked between countries, making it clear that approaches to NIPT implementation and service delivery should be country specific. Accordingly it is important that individual countries take time to research implementation strategies, gather stakeholder views and develop guidelines appropriate for their own social and screening contexts. Within each country women and health professionals differed in the value they placed on test attributes. Policies for implementation need to consider these differences to ensure needs of all stakeholders are met. As all women place great emphasis on test safety, to support informed consent it is important that pre-test counselling for NIPT thoroughly explores other attributes of NIPT, considers alternative options and reflects on the possible implications of testing so that the focus of the discussion is not just test safety.

Research in context

Systematic review

We searched PubMed with the terms "prenatal testing" AND "preferences" OR "discrete choice" for articles published in English before Mar 16, 2015. We identified several articles looking at preferences for prenatal tests using a discrete choice experiment, only two of these articles included attributes of NIPT[11, 19] and no articles had compared preferences for prenatal tests including NIPT between countries.

Interpretation

We report the results of the first study to explore cross-cultural variation in preferences for different attributes of NIPT relative to invasive testing. Our findings show clear differences in preferences between women and health professionals within and between countries, suggesting that implementation and service delivery of NIPT will need to be country specific. As all women place great emphasis on test safety when making decisions about prenatal testing, it is important that pre-test

counselling for NIPT includes issues beyond safety and ensures women understand the possible implications of test results.

Contributors

LSC conceived the study. MH, LSC, SM, SL and J-AJ developed the questionnaire. MH and SM designed the discrete choice experiment and analysed the data. MH coordinated and managed the research process and wrote the first draft of the manuscript. All authors contributed to recruitment protocols, data collection and critical revision of the manuscript. All authors approved the decision to submit the manuscript for publication.

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PARTE III

Resumo de comunicação livre no *18th International Conference on Prenatal Diagnosis and Therapy*, publicada na revista Prenatal Diagnosis

"Preferences for prenatal tests for Down syndrome: Comparing women and health professionals from nine countries"

QC metrics for Harmony generated a sex chromosome result (100%; 95% CI 99.4–100%). All samples were concordant with fetal karyotyping for fetal sex (100%; 95% CI 99.4–100%). 69 of 74 monosomy X samples classified as high-risk agreed with karyotype (sensitivity 93%; 95% CI 85.1–97.1%), with two discordant high-risk results (specificity 99.6%; 95% CI 98.6–99.9%). Six XXX samples classified as high-risk were concordant with three discordant high-risk results (sensitivity 100%; 95% CI 60.1–100% specificity 99.4%; 95% CI 98.3–99.9%). All seven XXY calls and three XYY samples were concordant (sensitivity 100%; 95% CI 64.6–100%); specificity 100%; 95% CI 99.3–100%).(sensitivity 100%; 95% CI 43–100%; specificity 100%; 95% CI 99.3–100%) respectively. CONCLUSIONS: Directed analysis of cffDNA is accurate for risk assessment of non-mosaic fetal SCA. This is the largest fetal SCA validation study to-date. This demonstrates the ability to expand Harmony to genetic conditions besides trisomies 13, 18 and 21.

2-3

Preferences for prenatal tests for Down syndrome: Comparing women and health professionals from nine countries

Melissa Hill[1], Joann Johnson[2], Sylvie Langlois[3], Hyun Lee[3], Stephanie Winsor[4], Brigid Dineley[4], Marisa Horniachek[4], Faustina Lalatta[5], Luisa Ronzoni[5], Angela Barrett[6], Mahesh Choolani[6], Ron Rabinowitz[7], Eva Pajkrt[8], Rachèl vanSchendel[9], Lidewij Henneman[9], Wieke Rommers[10], Catarina M Bilardo[10], Paula Rendeiro[11], Maria João Ribeiro[12], José Rocha[12], Ida Charlotte Bay Lund[13], Vigdís Stefánsdottir[14], Sigrun Olafsdottir[15], Helga Gottfredsdottir[15], Stephen Morris[16], Lyn Chitty[17]

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OBJECTIVES: To compare the preferences of women and health professionals from different countries for key attributes of non-invasive and invasive prenatal tests for Down syndrome. METHOD: A questionnaire incorporating a discrete choice experiment was used to obtain participants' stated preference for diagnostic tests that varied according to four attributes: accuracy, time of test, risk of miscarriage, and provision of information about Down syndrome only or Down syndrome and other conditions. Women and health professionals are being recruited from nine countries; the UK, Italy, Portugal, Iceland, Denmark, the Netherlands, Israel, Singapore and Canada. RESULTS: Preliminary data from six countries has been analysed (Singapore: n = 306 women, n = 69 health professionals; UK: n = 408 women, n = 245 health professionals; Italy: n = 300 women and n = 124 health professionals; the Netherlands n = 140 women, n = 36 health professionals; Israel: n = 83 women, n = 97 health professionals and Canada: n = 458 women, n = 286 health professionals). Differences in preferences were seen between women and health professionals in all countries with health professionals placing greater emphasis on accuracy than women. While no risk of miscarriage was the most important attribute for women in all countries, there were significant differences in the strength of this preference between countries, with a stronger preference among women in the UK and the Netherlands. In addition, women from the UK and Singapore placed a greater emphasis on accuracy than women from other countries and Italian women weighted information about conditions other than Down syndrome more highly than women from other countries. Health professionals from Italy and Israel had a stronger preference for information

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about conditions other than Down syndrome than health professionals from other countries. CONCLUSIONS: Preliminary analysis shows that differences between women's and health professionals' preferences are marked across countries. Furthermore, as there is significant variation in women's preferences for testing between countries, approaches to implementation and service delivery may need to differ between countries. As all women place great emphasis on test safety when making decisions about prenatal testing, it is important that pre-test counselling for NIPT includes issues beyond safety and ensures women understand the possible implications of test results. Analysis of data from nine countries will be presented.

2-4

PeTALS: A longitudinal study to determine the psychosocial impact following prenatal diagnosis of fetal abnormality

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OBJECTIVES: In Victoria, following prenatal diagnosis of a fetal abnormality, women and their partners are commonly offered a choice about whether to have a legally permissible abortion or continue their pregnancy. Little is known about how this is experienced by couples. The PeTALS study aims to: • explore the psychosocial impact of identifying a fetal abnormality following prenatal diagnosis and decision-making about abortion • identify professional and social supports utilised and needed around this time METHOD: This study is being conducted at three sites in Victoria including two tertiary metropolitan hospitals and a private ultrasound clinic. A longitudinal case study approach is being used to collect quantitative and qualitative data from women at three different time points – 6 weeks post definitive diagnosis of a fetal abnormality, 6–9 months later, and 2 years post-diagnosis. RESULTS: Thirty nine women were interviewed at the first time-point, regarding their experience of receiving a prenatal diagnosis (27 had various chromosomal aneuploidies, 6 had cardiac anomalies, 6 had other structural anomalies), and choosing to have an abortion (n = 33), or continue their pregnancy (n = 6). Women commonly experienced significant grief and overwhelming sadness; many described intense feelings of isolation from their partner, family and friends. Women who had an abortion described feeling negatively 'judged' and reported that their partners also experienced significant emotional impact. The level and perceived quality of support provided by individual health professionals varied both within and across the different sites. CONCLUSIONS: Women described variable and sometimes inadequate levels of follow-up bereavement care and support. There is a need for increased support and counselling for women and their partners immediately following a prenatal diagnosis. Given the expanding scope for prenatal tests to detect pathogenic DNA variations, increasingly pregnant women and their partners will be faced with these complex choices. Provision of prenatal testing and abortion in the absence of a full range of supportive options can result in significant psychological sequelae and may be considered unethical; this is an important area for ongoing research.

2-5

Germline gene therapy: Its time is nearing

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OBJECTIVES: To provide an overview of the full range of positions expressed in support or opposition to the pursuit of germline gene therapy and to outline the potential of currently available technologies and approaches toward germline gene therapy. METHOD: To analyze the primary arguments in opposition to germline therapy as well as to review the specific rationales justifying undertaking germline gene therapy; and, to assess possible technologies and approaches to germline gene therapy. RESULTS: The primary arguments in opposition to germline gene therapy are summarized into five categories: (1) uncertainty and risk; (2) 'slippery slope', particularly in regard to 'genetic enhancement'; (3) lack of consent by future generations; (4) inappropriate allocation of health resources; and (5) intrinsic immorality. There are at least four specific rationales justifying undertaking germline gene therapy: (1) medical utility; (2) medical necessity; (3) prophylactic efficiency; and (4) parental autonomy. A number of a technologies and approaches now exist that can target specific genes and theoretically could be applied to both somatic tissue and germline. CONCLUSIONS: From a utilitarian perspective, gene therapy is likely to be the most successful

PARTE IV

Resumo para Comunicação livre nas XVI Jornadas de Psicologia do Instituto Superior de Ciências da Saúde-Norte

"Tomada de decisão no diagnóstico pré-natal não-invasivo: Perspetivas dos profissionais de saúde, das grávidas e a influência da ansiedade"

Tomada de decisão no diagnóstico pré-natal não-invasivo: Perspetivas dos profissionais de saúde, das grávidas e a influência da ansiedade

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Resumo

Objetivo: O teste pré-natal não invasivo (TPNNI) está cada vez mais disponível a nível mundial decorrente de uma significativa motivação comercial. Foi desenvolvido um projeto internacional para comparar as preferências das mulheres e profissionais de saúde para os principais atributos das decisões sobre os TPNIs para a Síndrome de Down. Aqui pretendemos clarificar os atributos relativos à amostra Portuguesa e relacionar estes com ansiedade das grávidas.

Método: Neste estudo foi utilizada um modelo de escolha discreta para obter dados sobre as preferências dos participantes perante TPNNIs de acordo com quatro atributos: precisão do diagnóstico, tempo de espera dos resultados, risco de abortamento e fornecimento de informações mais completas, incluindo resultados clinicamente pouco significativos. Os atributos foram comparados entre uma amostra de 110 mulheres grávidas e 50 profissionais de saúde. Foi também utilizada a escala de avaliação da ansiedade de Zung com vista a correlacionar os atributos com o nível de ansiedade-estado nas mulheres.

Resultados: Verificam-se diferenças significativas nas preferências entre as grávidas e os profissionais de saúde. As grávidas colocaram maior ênfase nos testes com maior segurança e com informação completa, enquanto os profissionais de saúde dão mais importância à precisão nos testes pré-natais e à segurança do teste (risco de abortamento). A ansiedade estabelece correlação significativa com a preferência por testes que oferecem mais informações sobre o feto.

Discussão: Fica clarificada a divergência entre as preferências dos profissionais e as grávidas e que pode ser tida em consideração na implementação do TPNNI, facilitando tomada de decisão, valorizando as necessidades e atributos referidos pelas grávidas. Por outro lado, o destaque da valorização da necessidade de resultados pré-natais mais completos está associado ao nível de ansiedade da grávida, o que ajuda explicar diferenças e direciona reflexão sobre as perceções de risco da grávida no seu acompanhamento.

Anexo I - Normas para a publicação e submissão de artigos na revista Brasileira de Ginecologia e Obstetrícia

ISSN 0100-7203 *printed version*

ISSN 1806-9339 *on-line version*

INSTRUCTIONS TO AUTHORS

Scope and policy

The Revista Brasileira de Ginecologia e Obstetrícia (Rev Bras Ginecol Obstet., ISSN 0100 7203), a monthly publishing of scientific diffusion by Federação das Sociedades de Ginecologia e Obstetrícia (Febrasgo), is directed to obstetricians, gynaecologists, and kindred professionals, with the purpose of publishing original contributions on relevant themes about Gynaecology, Obstetrics, and related areas. It is open to Brazilian and international contributions. The journal accepts and publishes papers in Portuguese, English, and Spanish.
The material sent to analysis cannot be concurrently submitted for publication to other journals, or have been previously published. Originality, theme relevance, and quality of methodology, besides the adequacy to editorial instructions adopted by the journal, are assessed in the selection of manuscripts. Published material becomes propriety of Revista Brasileira de Ginecologia e Obstetrícia and of Febrasgo, and it can only be totally or partially reproduced with these entities' consent.

All the submitted articles are assessed by anonymous reviewers and confidentiality is maintained throughout the review process. The reviewers' evaluation and editor's instructions are sent to the authors so that they get acquainted with the alterations that should be made. The authors must return the paper with the required changes as soon as possible, accompanied by a letter that justifies, when needed, the nonacceptance of the suggestions. If the paper is not returned within a period of three months, it is assumed that the authors have no longer interest in publishing it. The authors can request at any moment of the analysis and text review process its interruption and the exclusion of the paper. The concepts and declarations stated in the articles are the authors' responsibility.

This journal publishes contributions in the following categories:

1. Original Articles, complete prospective, experimental, and retrospective studies. Manuscripts containing original results of clinical or experimental researches have priority in publication.
2. Case Reports, of great interest and well-documented from the clinical and laboratorial points of view. Authors should indicate in the submission letter the new or unexpected aspects as to the cases that have already been published. The text from Introduction and Discussion sections must be based on updated bibliographical review. The number of references may be the same of complete studies.

3. Techniques and Equipment, which are presentations of innovations in diagnosis, surgery techniques, and treatments, as long as they are not, clearly or subtly, merchandise of drugs or other products. All the standards established for complete papers should be included.
4. Review Articles, including critical and systemized literature assessment, metanalysis, or systematic reviews. The selection of themes and the invitation to authors is based on an established planning by the editors. Spontaneous contributions may be accepted. In this case, a summary or draft of the paper must be sent primarily, as well as the list of authors and respective publications on the theme. If the journal is interested, the authors are invited to write and submit the final text. All the authors must have previous publications in regular and indexed journals about the referred theme. The number of authors is limited to four, depending on the type of text and on the applied methodology. The methods and procedures adopted for the preparation of the paper must be described, and techniques to obtain updating, meta-analysis or systematic reviews can be employed. When the theme is still under investigation, the review must discuss all current tendencies and lines of investigation. It should present, besides the review text itself, abstract in Portuguese and in English, and conclusions. See the section "Preparing the manuscript" for more information on the main text, cover page, and abstracts.
5. Editorial Comments, when required by the editor.
6. Thesis Abstracts presented and approved in the last 12 months, counting from the submission date. They must contain approximately 300 words, following the requirements of the journal concerning structure, form, and content. Titles in Portuguese and English should be included and, at least, three words or keywords. There is no text review of the Thesis Abstracts. In a separated file, it should be informed the complete name of the author and advisor, members of the assessment table, date of presentation and identification of the service or department where the research was carried out and presented. It is also noteworthy that the abstract publication does not impede a posterior publication of the complete paper in any other journal.
7. Letters from the Readers to the Editor about editorial material or not, but with information that is relevant to the reader. The letters can be summarized by the editors, being highlighted the main passages. When the letters are opinions to published articles, they are sent to the authors so that their answers are simultaneously published.

Preparation of manuscripts

General information

1. This journal does not accept editorial material with commercial purposes.
2. Conflict of interests: situations that may interfere inadequately in the development and conclusions of the study must be mentioned. Among these situations, it is emphasized the participation in companies that produce drugs or equipment

cited or used in the study, as well as in contestant companies. Financial supports, subordination relations at work, consultancy, among others, are also considered as conflict sources.

3. In the text, submission and approval by the Research Ethics Committee, acknowledged by the Research Ethics National Comittee (CONEP) must be mentioned.
4. Articles that cover clinical researches on human beings must include a declaration, in the Methods section, which assures the signature of informed consent by the participants. Authors should also report that the research was carried out according to the Declaration of Helsinki, which was reviewed in 2008.
5. In the event of papers using animal experiments, authors should indicate, in the Methods sections, that the standards enrolled in the Council for International Organization of Medical Sciences (CIOMS) Ethical Code for Animal Experimentation (WHO Chronicle 1985; 39(2):51-6) and principles of the Colégio Brasileiro de Experimentação Animal - COBEA (www.cobea.org.br) were followed.
6. All randomized controlled and clinical trials submitted to publication should have a registration in a database of clinical trials. This decision was due to guidance of the International Clinical Trial Registry Platform (ICTRP) from the World Health Organization (WHO) of the International Committee of Medical Journal Editors (ICMJE). Instructions for registration are available at the website of ICMJE (http://www.icmje.org/clin_trialup.htm), and the registration can be made through the National Library of Medicine database of clinical trials, available at: http://clinicaltrials.gov/ct/gui.
7. The number of authors in each manuscript is limited to seven. Papers of collective authorship (institutional researches) must have the responsible authors indicated. Multicentric works and studies may have the number of authors compatible with the number of participant institutions (each case is assessed by the editors and reviewers). The investigators in charge for the applied protocols must be indicated. All the authors should be aware of the paper sent for publication in the journal.
8. The co-authorship concept is based on the substantial contribution for the outset and planning of the research, analysis, and interpretation of data, or for the production and critical review of the text. The inclusion of names, whose contribution does not comply with the cited criteria, or that have provided only material support, is not justifiable.
9. The authors will acknowledge receipt of the papers by e-mail. Articles that are in concordance with the Instructions to the Authors and comply with the editorial politics of the journal are submitted to analysis, by reviewers indicated by the authors. Manuscripts that do not comply with the purposes of the journal or with these instructions are returned to the authors for the necessary adaptations before the assessment by the Editorial Board or they are refused without analyses by the reviewers.
10. Together with the original files, a submission letter, in which authors should explicit the agreement with the editorial requirements, the process of review, and the conveyance of copyright to the journal should be sent.
11. The original manuscripts should not exceed 25 pages of typed text or around 30,000 characters. The number of tables and figures should be limited to what is necessary for presenting and discussing the results (as a general pattern, it should be limited to five). Case Reports should not exceed 15 pages or 18,000 characters (see "Preparation of the manuscript", "Results").
12. The paper must be submitted to the journal by the online

submission system at SciELO. The e-mail of all authors must be provided. Thus, co-authors shall receive information regarding the submission of the paper and, therefore, their signatures will not be necessary in the submission letter. The correspondence e-mail with the journal is: rbgo@fmrp.usp.br. It must be only one file of the paper, which should have the text, references, tables and figures.

Manuscript preparation

The following rules were based on the standard proposed by ICMJE and published in the article "Uniform Requirements for Manuscripts Submitted to Biomedical Journals", updated in October 2008, and available at: http://www.icmje.org/.

Text presentation

1. The papers must be double-spaced typed between lines in every section, from the cover page to the references, tables, and captions. Each page must contain approximately 25 lines in one column. The Microsoft Word® text editor is preferred, as well as the font Times New Roman, size 12. Do not highlight passages of the text, do not underline or apply bold. All pages should be numbered, starting with the cover one.
2. Do not use capital letter in names (except for the initial one) in the text or references. Do not make use of period in acronyms (DPP instead of D.P.P.). Acronyms or abbreviations should be fully written at the first time they appear in the text. Each section should begin in a new page: cover page; abstracts and keywords; text; acknowledgments; references; individual tables and images' captions.

Cover page

Present the title of the paper in English; the complete name of the authors without abbreviations; e-mails that are valid for all authors (optional, replacing the submission letter); the name of the institution where the study was carried out; institutional affiliations of the authors; information about support received by means of financing, equipment or drugs catering. It is obligatory that the address of the institution where the paper was developed, which is published in the first page of the paper, should be provided. Indicate the name, address, telephone and fax number, and e-mail of the author responsible for the correspondence. These personal information are only for contacting the journal and they should only be published if there is a request from the author(s).

Abstract

The abstract must appear in the second page. For complete papers, a structured abstract should be written and divided into identified sections: objective, methods, results, and conclusions. It should comprise approximately 300 words stating relevant information that allows the reader to have a general idea of the article. A summarized description of all employed methods and of the statistical

analysis should be included, as well as the most relevant numeric results, and not only the statistical significance. Conclusions must be based on the results of the study and not on the literature. Abbreviations, symbols, and references should be avoided.

Right after the abstract, the registry number or the identifications for randomized controlled and clinical trials should be indicated (see item 5 from the "General Information").

In the same page, at least three keywords or expressions must be cited for composing the annual index of the journal. They should be based on the Health Science Descriptors (DeCS, acronym in Portuguese), published by Bireme, which is a translation of Medical Subject Headings (MeSH) of National Library of Medicine, and is available at: http://decs.bvs.br.

The abstracts of Case Reports and Update and Review Articles do not have to be structured and are limited to 150 words.

Introduction

In the first page of introduction, the titles should be complete in Portuguese and English. In this section, show the current knowledge situation about the studied topic, divergences and lack of information that may eventually justify the development of the paper, but without an extended literature review. In Case Reports, a summary of the already presented cases, epidemiology of the reported condition, and a justification for the presentation as an isolated case must be stated. The objectives of the study should be clearly exposed.

Methods

This section should be initiated with the indication of the study setting up: if it is a prospective or retrospective, clinical or experimental trial, if the distribution of cases was randomized or not, and so on. Describe the criteria for the selection of patients or Experimental Group, including Controls. Identify the equipment and reagent used (manufacturer, city and country). If the applied methodology has already been employed, the references and a short description of the method must be indicated. Statistical methods employed and comparisons, to which each test was indicated, should also be described.

The papers that have the purpose of evaluating the efficacy or toleration of a treatment or drug must necessarily include an adequate Control Group. For additional information on the design of this kind of papers, see ICH Harmonized Tripartite Guideline - Choice of Control Group and Related Issues in Clinical Trials (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/e10_e.html), and also items 4 and 5 of "General Information".

Results

The results must be presented in logical sequence: text,

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The new and original information obtained during the investigation must be highlighted in this section. Do not repeat information already mentioned in the sections "Introduction" and "Results". Avoid citing tables and figures. Bounce the adequacy of the employed methods during investigation. Compare and relate the authors' observations to those of other researchers, commenting and explaining the differences. Provide details of the implications of the findings, as well as their limitations, and make referable recommendations. In Case Reports, the discussion must be based on extended and updated literature review. Information of already published cases should be presented for comparisons to be made.

Acknowledgments

They are directed to those who have intellectually contributed to the study, but whose contribution does not justify co-authorship, and to those who have given material support.

References

All authors and papers cited in the text must be listed in this section and vice-versa. The references must be numbered in the list by order of appearance in the text, and they should be referred to by their respective numbers when cited. Excessive number of references should be avoided, being selected only those with relevance for each statement; also, the most recent ones should be preferred. Do not cite references of difficult access, like abstracts of studies presented in congresses or publications of restrict circulation (non-indexed). Also, "non-published observations" and "personal communication" references should not be referred to. Articles that were submitted and accepted for publication should be referred to as "in press" being indicated the journal, its volume and year of publication. Papers accepted by online journals that have no indication of volume and year must be referred to as "ahead of print".

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Printed papers

- Journal articles

  Ceccarelli F, Barberi S, Pontesilli A, Zancla S, Ranieri E. Ovarian carcinoma presenting with axillary lymph node metastasis: a case report. Eur J Gynaecol Oncol. 2011;32(2):237-9.

  Jiang Y, Brassard P, Severini A, Goleski V, Santos M, Leamon A, et al. Type-specific prevalence of Human Papillomavirus infection among women in the Northwest Territories, Canada. J Infect Public Health. 2011;4(5-6):219-27.

- Articles with titles in English and text in Portuguese or other language

  Use the title in English, between brackets and by the end of the reference, indicate the language in which the article was published.
  Prado DS, Santos DL. [Contraception in users of the public and private sectors of health]. Rev Bras Ginecol Obstet. 2011;33(7)143-9. Portuguese.

  Taketani Y, Mizuno M. [Application of anti-progesterone agents for contraception]. Rinsho Fujinka Sanka. 1988;42(11):997-1000. Japanese.

- Book

  Baggish MS, Karram MM. Atlas of pelvic anatomy and gynecologic surgery. 2nd ed. Philadelphia: WB Saunders; 2006.

- Book chapter

  Picciano MF. Pregnancy and lactation. In: Ziegler EE, Filer LJ, editors. Present knowledge in nutrition. Washington (DC): ILSI Press; 1996. p. 384-95.

Electronic papers

Only official statistical information and citation of nonprinted journal are included here. For official statistics, the responsible entity, electronic address, and name of the file or entrance should be cited. The numbers of screens, date and hour of access should be included. Terms like "serial", "periodic", "homepage", and "monograph" are no longer used. All documents must be indicated only as [Internet]. For electronic documents as DOI (Digital Object Identifier), it should be mentioned at the end of it, besides the following information:

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Saúde; 2008. [cited 2007 Fev 7]. Available from: http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinasc/cnv/nvuf.def

- Monograph on the Internet or e-book

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Tables should be presented in separated pages with double space and font Arial, size 8. They must be numbered sequentially with Arabic numerals and in order of citation in the text. All tables must have a title, and all their columns should be identified with a heading. It should contain captions that allow the reader to understand the content of tables and figures, even without reading the paper integrally. Horizontal lines should be simple and limited to two in the top and one at the end of the table. Do not use vertical lines nor employ functions of table creation, justification commands, decimal or centralized tabulations. Tabulation command (Tab) should be used instead of the "space" key for separating the columns and, for a new line, the "enter" key. In the baseboard of the table, the subtitles for abbreviations and statistical tests that were employed must be presented.

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