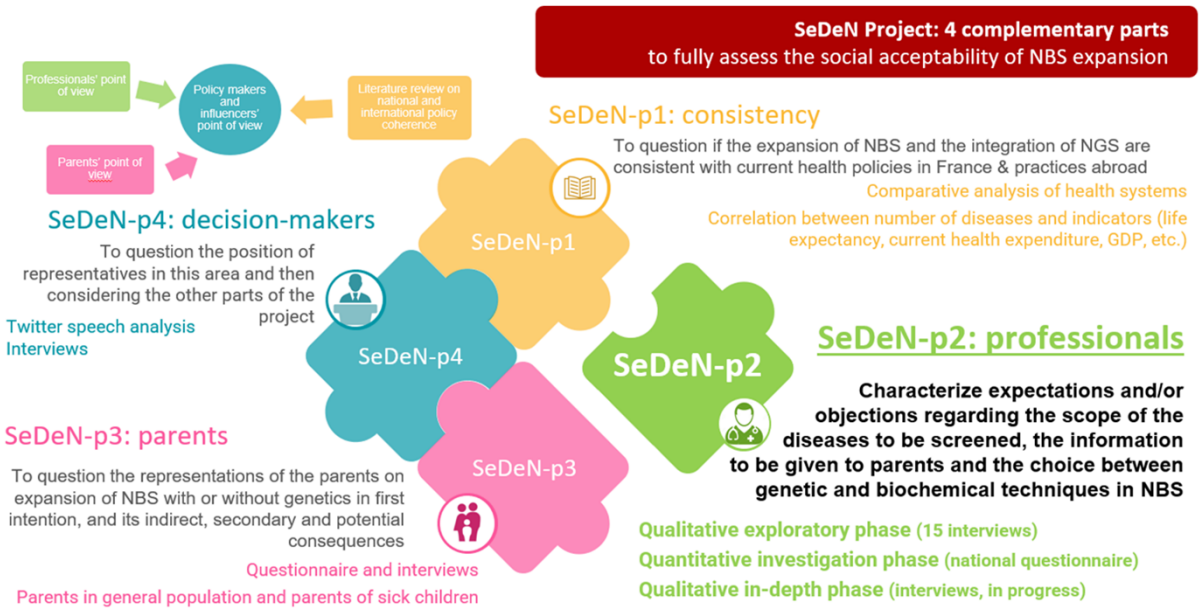
Healthcare Professionals' Views on Expanding Newborn Screening with or without Genomics in France: Results of the SeDeN-p2 Study

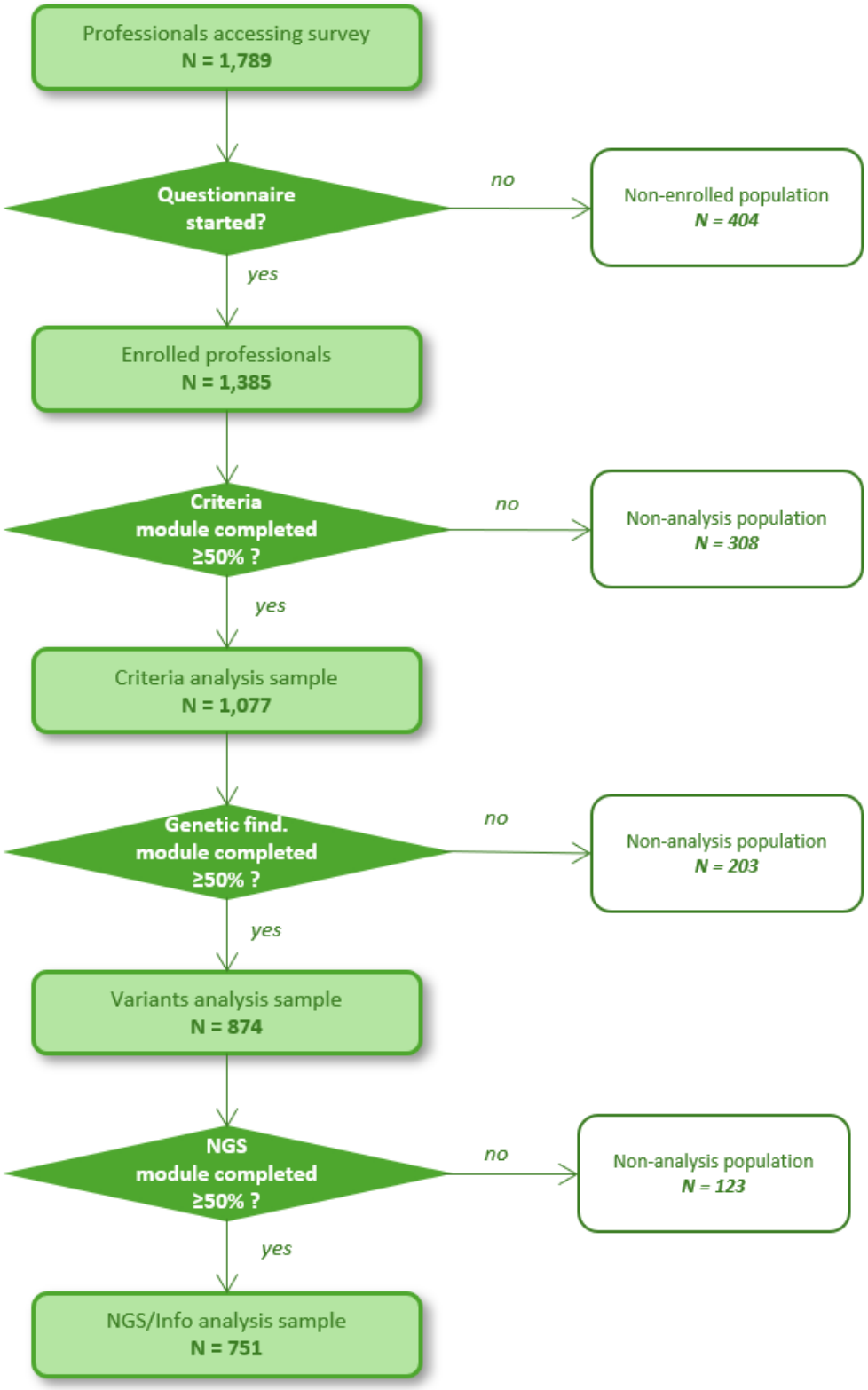
Supplementary Information

Supplemental figure 1: The SeDeN-p2 project within the SeDeN project
The SeDeN project comprises four interconnected work packages addressing different perspectives: health policies (SeDeN-p1), professionals (SeDeN-p2), parents (SeDeN-p3), and decision-makers and public discourse (SeDeN-p4). The present study focuses on SeDeN-p2, which investigates health professionals' expectations and objections regarding the scope of diseases to be screened, the information provided to parents, and the choice between genetic and biochemical screening techniques, using mixed qualitative and quantitative methods.



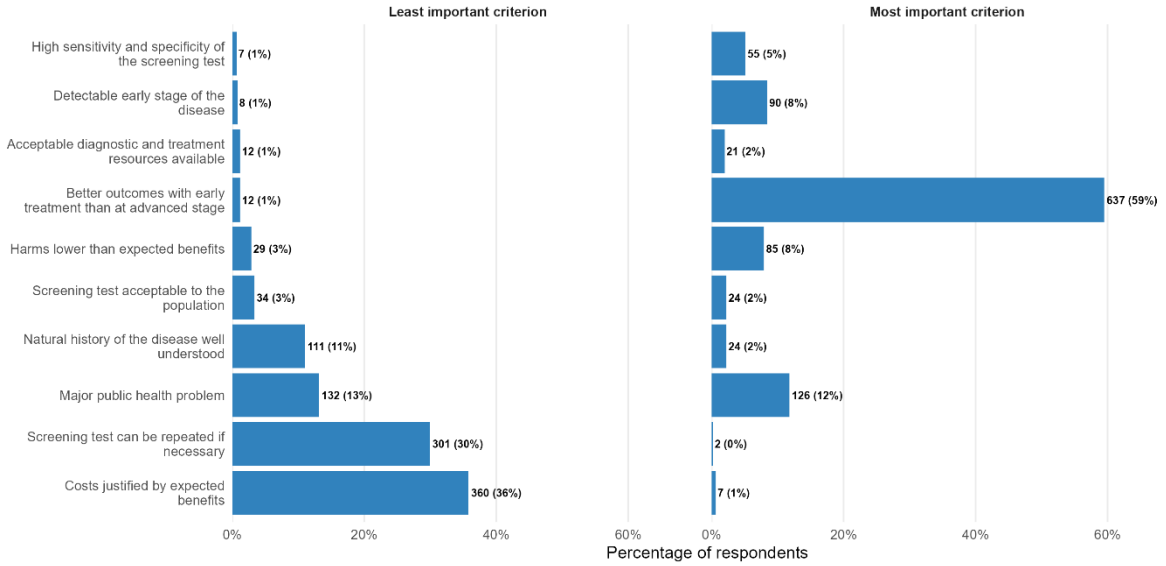
Supplemental figure 2: Flowchart of the study population and analytical samples

This flowchart describes the successive selection steps of the professional respondents included in the analyses. Among professionals accessing the survey, participants were retained in each analytical sample if they completed at least 50% of the corresponding module. This process resulted in three nested analytical samples for the criteria module, the genetic findings module, and the NGS/information module.



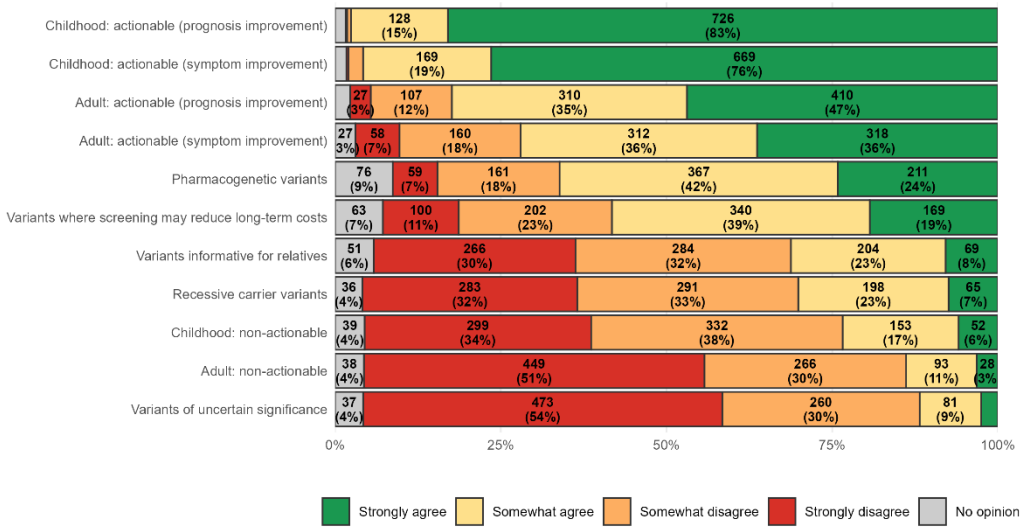
Supplemental figure 3: Most and least important Wilson–Jungner criteria selected by respondents (N=1,077)

Respondents were asked to select, among the Wilson–Jungner criteria, the single criterion they considered the most important and the single criterion they considered the least important for NBS. Bars show the percentage of respondents selecting each criterion, with counts and percentages displayed. Results are shown separately for "most important" and "least important" selections.

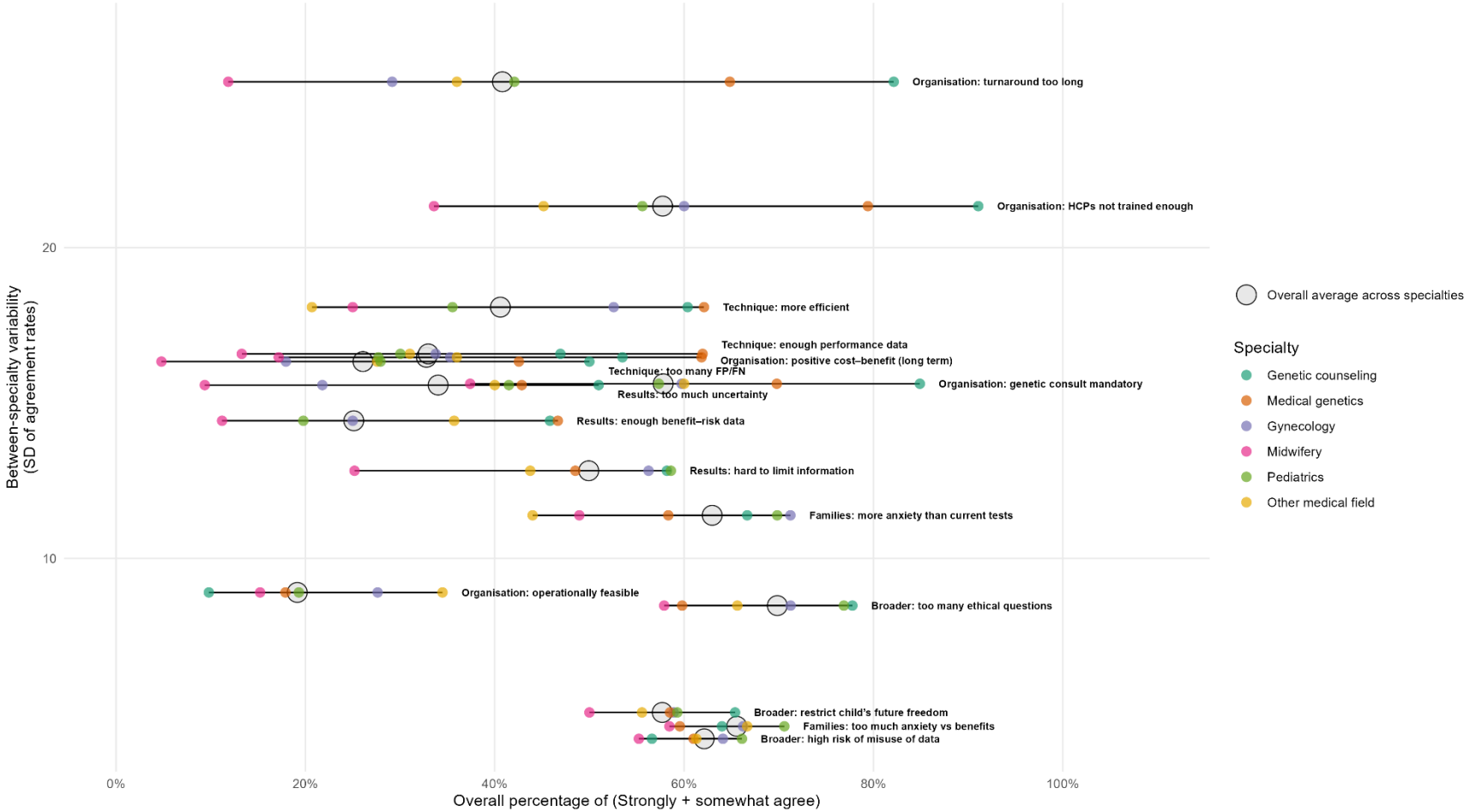


Supplemental figure 4: Professionals' views on searching for different types of genetic findings in NBS (N=874)

Respondents were asked to indicate their level of agreement with searching for different categories of genetic findings in the context of NBS. Stacked bars show the distribution of responses ("strongly agree", "somewhat agree", "somewhat disagree", "strongly disagree", "no opinion") for each genetic findings category; counts and within-category percentages are displayed inside segments when ≥3%. Categories are ordered from the highest to the lowest proportion of "strongly agree" responses. In the questionnaire, the term "variant" was used in place of "mutation".

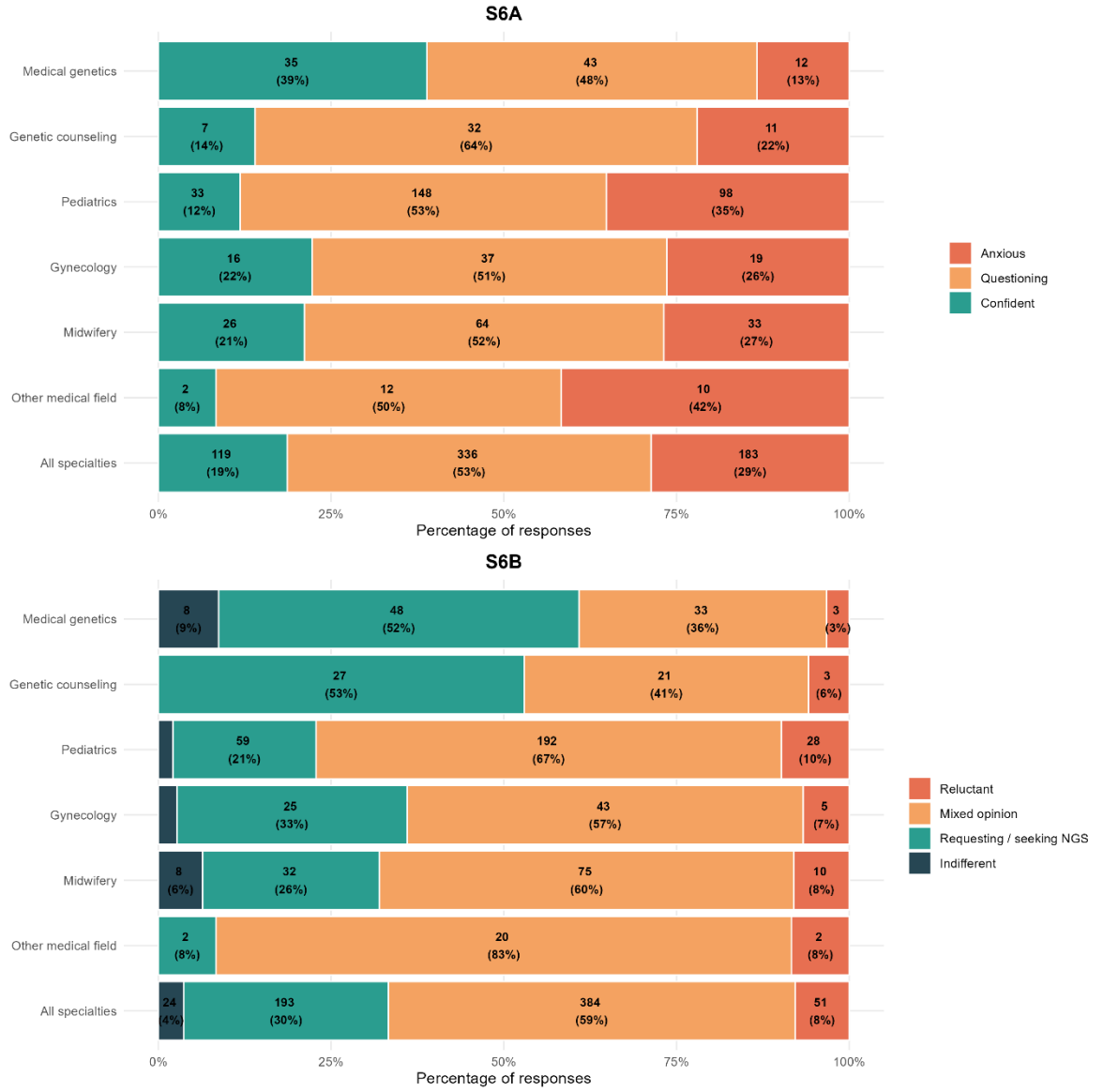


Supplemental figure 5: Overall agreement and between-specialty variability for statements related to the integration of NGS into NBS (N=751)
This figure displays, for each statement related to the integration of NGS into NBS, the overall proportion of respondents expressing agreement ("strongly agree" or "somewhat agree") on the x-axis, and the variability of agreement across professional specialties on the y-axis (expressed as the standard deviation of specialty-specific agreement rates). Coloured points represent specialty-specific agreement proportions, open circles indicate overall averages across specialties, and horizontal lines illustrate the minimum–maximum range of values across specialties. Higher values on the x-axis indicate stronger overall agreement, while higher positions on the y-axis reflect greater heterogeneity of views across specialties.



Supplemental figure 6: Anticipated parental reactions and expectations regarding the integration of NGS into NBS (N=751)

(A) Distribution of professionals' perceptions of how parents might emotionally react to the integration of NGS into NBS (confident, questioning, or anxious), by professional specialty and overall. (B) Distribution of professionals' perceptions of parental expectations regarding NGS-based screening, distinguishing active requests for testing, mixed or divided opinions, reluctance, and indifference. Stacked bars show the percentage of responses within each specialty and for all specialties combined; counts and percentages are displayed within segments.



Supplemental methods 1: Questionnaire structure and analytical module framework
This supplementary file details the structure of the questionnaire, including thematic modules, item grouping, response scales, and the predefined analytical strategy aligned with the modular design of the instrument.

The questionnaire was constructed as a modular instrument, structured into four thematic modules, each introduced by a short introductory paragraph. It comprised 101 closed-ended items and 14 open-ended questions. The first module collected sociodemographic and professional characteristics, including specialty, practice settings, involvement in NBS activities, experience with genetic testing, and exposure to rare diseases. A second module assessed the importance of criteria used to guide the selection of conditions for NBS. This module was based on the ten classical principles proposed by Wilson and Jungner[10] and the ten complementary criteria later suggested by Andermann and colleagues[11]. The French wording of the Wilson and Jungner criteria relied on a validated translation commonly used in public health contexts[12]. Respondents were asked to rate the importance of each criterion on an ordinal four-level Likert scale ranging from “Not at all important” to “Very important”, with an additional “No opinion” option. Two additional items asked respondents to identify, among these criteria, the single most important and the least important for decision-making in NBS. The second module explored views on the scope of genetic findings that could be included and reported in a NBS context. Items covered a broad range of situations, from childhood-onset diseases with direct medical benefit to adult-onset conditions, pharmacogenetic variants, carrier status, and findings with limited or uncertain clinical actionability. Agreement with each proposal was assessed using a four-level Likert scale from “Strongly disagree” to “Strongly agree”, with a “No opinion” option. The NGS module, the third module, focused on views regarding the potential integration of NGS into NBS. This module addressed different implementation modalities (e.g. targeted panels versus broader sequencing approaches), as well as technical performance, result interpretation, organisational feasibility, ethical and societal implications, and perceived impact on families. Responses were collected using a five-category scale ranging from “Strongly disagree” to “Strongly agree”, including a specific “Not my field of expertise” option to account for heterogeneous familiarity with genomic technologies. Items also explored perceptions of potential parental reactions and expectations in relation to NGS integration. Finally, the fourth module focused on information, examining professionals’ perceptions and expectations regarding the information delivered to parents about NBS. Items covered perceived adequacy of current information, awareness of the non-mandatory nature of screening, preferred timing and modalities of information delivery, and self-assessed preparedness to understand and discuss potential genomic results. Depending on the item, responses were collected using Likert-type scales or multiple-choice questions allowing multiple responses. An additional module based on clinical vignettes explored scenario-based responses to hypothetical screening situations and is reported in a separate manuscript in preparation.

As participation was voluntary and relied on professional networks, substantial attrition across questionnaire modules was observed and anticipated, reflecting both the length of the survey and the varying relevance of themes across professional groups. To address this module-specific attrition in a transparent and consistent manner, a module-based analytical strategy was defined *a priori*, aligned with the modular structure of the questionnaire and focused on preserving interpretative coherence rather than maximising sample size. For each module, a set of analytically core items corresponding to its main constructs was identified. Optional items, open-text responses, and contextual questions were not considered core. For each participant and each module, the proportion of completed core items was calculated. Respondents were included in a module’s analytical set if they had completed at least 50% of these core items, a pragmatic threshold chosen to manage attrition while maintaining coherence within each thematic block. This rule was applied independently to each module, with one exception.

Because information-related questions were positioned early in the questionnaire, attrition was lower for this module than for subsequent sections. Applying the ≥50% completion rule independently would therefore have resulted in a larger analytical set for information-related items. However, given that the objective was to interpret attitudes toward information in relation to positions on genomic integration, information-related items were analysed using the same analytical set as the NGS module. This choice avoided introducing a structurally different respondent population and ensured comparability across key analytical dimensions. To verify that this restriction did not introduce bias, response distributions for information-related variables were compared between respondents meeting the ≥50% completion criterion for the information module and those included in the NGS analytical set. Distributions were highly similar, with differences generally within ±2 percentage points (data not shown). On this basis, the NGS analytical set was retained for all analyses involving information-related items. Sociodemographic variables were described on the full available analytical set and were not subject to module-specific inclusion thresholds. This module-based analytical strategy is illustrated in Supplemental Figure 2.

Supplemental table 1: Characteristics of the population by modules

This table provides a detailed description of the sociodemographic and professional characteristics of respondents included in each module-specific analytical sample. Results are reported as absolute numbers, with percentages shown in parentheses.

	MOD1: CRITERIA	MOD2: VARIANTS	MOD3/4: NGS/INFO
Total	N = 1,077[1]	N = 874[1]	N = 751[1]
Professional profile			
Medical specialty			
Genetic counselling	66 (6.1%)	62 (7.1%)	56 (7.5%)
Gynaecology	124 (12%)	94 (11%)	83 (11%)
Medical genetics	119 (11%)	111 (13%)	102 (14%)
Midwifery	262 (24%)	195 (22%)	148 (20%)
Paediatrics	462 (43%)	375 (43%)	329 (44%)
Other	44 (4.1%)	37 (4.2%)	33 (4.4%)
Career experience			
Junior	242 (23%)	194 (22%)	169 (23%)
Mid-level	472 (44%)	379 (43%)	325 (43%)
Senior	360 (34%)	299 (34%)	256 (34%)
Missing	3	2	1
Clinical involvement			
Manages rare disease patients			
No	376 (45%)	286 (44%)	232 (42%)
Yes	453 (55%)	361 (56%)	315 (58%)
Missing	248	227	204
Role of NBS in practice			
Never	268 (26%)	220 (26%)	191 (26%)
More than once a year	123 (12%)	106 (13%)	95 (13%)
More than once per quarter	106 (10%)	92 (11%)	86 (12%)
More than once per month	172 (17%)	135 (16%)	112 (15%)
More than once per week	369 (36%)	291 (34%)	239 (33%)
Missing	39	30	28
Academic activities			
Teaching activity			
No	689 (64%)	533 (61%)	444 (60%)
Yes	381 (36%)	335 (39%)	301 (40%)
Missing	7	6	6
Research activity			
No	816 (76%)	642 (74%)	541 (73%)
Yes	254 (24%)	225 (26%)	203 (27%)
Missing	7	7	7
Practice environment			
Place of practice			
University Hospital			
No	539 (50%)	416 (48%)	357 (48%)
Yes	538 (50%)	458 (52%)	394 (52%)
Public Hospital (non-university)			
No	826 (77%)	675 (77%)	583 (78%)
Yes	251 (23%)	199 (23%)	168 (22%)
Private sector			
No	972 (90%)	796 (91%)	680 (91%)
Yes	105 (9.7%)	78 (8.9%)	71 (9.5%)
Community practice			
No	825 (77%)	683 (78%)	588 (78%)
Yes	252 (23%)	191 (22%)	163 (22%)
Other settings			
No	1,006 (93%)	818 (94%)	703 (94%)
Yes	71 (6.6%)	56 (6.4%)	48 (6.4%)

	MOD1: CRITERIA	MOD2: VARIANTS	MOD3/4: NGS/INFO
Total	N = 1,077[1]	N = 874[1]	N = 751[1]
Practice type			
Exclusively private practice	201 (19%)	148 (17%)	128 (17%)
Mixed (private and salaried)	95 (8.8%)	78 (8.9%)	65 (8.7%)
Exclusively salaried	781 (73%)	648 (74%)	558 (74%)
Main region of practice			
Paris / Île-de-France	185 (17%)	153 (18%)	128 (17%)
North-East	222 (21%)	181 (21%)	154 (21%)
North-West	160 (15%)	130 (15%)	118 (16%)
Overseas territories	61 (5.7%)	48 (5.5%)	46 (6.1%)
South-East	241 (22%)	197 (23%)	166 (22%)
South-West	208 (19%)	165 (19%)	139 (19%)
Genetics-related practice			
Experience in genetics practice			
No	450 (44%)	346 (42%)	288 (41%)
Yes	567 (56%)	477 (58%)	419 (59%)
Missing	60	51	44
Has prescribed genetic tests			
No	237 (23%)	174 (21%)	133 (19%)
Yes	780 (77%)	649 (79%)	574 (81%)
Missing	60	51	44
Personal characteristics			
Age			
Under 35	334 (31%)	260 (30%)	223 (30%)
35-49	426 (40%)	346 (40%)	297 (40%)
50+	308 (29%)	259 (30%)	224 (30%)
Missing	9	9	7
Number of children			
None	290 (28%)	234 (28%)	203 (28%)
One child	141 (14%)	104 (12%)	92 (13%)
Two children	305 (29%)	248 (29%)	205 (28%)
Three children	232 (22%)	196 (23%)	171 (24%)
More than three	75 (7.2%)	60 (7.1%)	54 (7.4%)
Missing	34	32	26
Gender			
Men	208 (20%)	180 (21%)	169 (23%)
Women	856 (80%)	684 (79%)	574 (77%)
Missing	13	10	8

[1]n (%)

Supplemental analysis 1: Additional cross-analyses by professional and individual characteristics

This supplementary file presents detailed cross-analyses according to practice setting, exposure to genetics, age, career stage, parenthood, and gender across study modules. Specialty-specific analyses are presented in the main manuscript; all other associations are reported here.

Criteria for NBS module

Prioritisation patterns varied across professional specialties and sociodemographic characteristics. Associations with professional specialty were observed for several Andermann criteria related to programme definition, governance and safeguards, including the definition of the target population ($p<0.001$), informed choice and respect for autonomy ($p<0.001$), and equity of access ($p=0.01$), as well as for Wilson and Jungner criteria related to public health relevance ($p<0.001$) and justification of costs ($p<0.01$). Experience with genetics was strongly associated with multiple Wilson and Jungner criteria, particularly those related to disease knowledge ($p<0.001$), test performance and acceptability ($p=0.03$), and perceived benefit–harm balance ($p=0.002$), as well as with several Andermann criteria related to programme structure ($p=0.002$) and quality assurance ($p<0.001$). Practice setting also played a role: working in university hospitals or being involved in research activities was associated with higher selectivity across criteria related to governance, evaluation and quality assurance, including programme effectiveness ($p=0.02$), quality assurance mechanisms ($p=0.01$), and planned evaluation ($p=0.03$). By contrast, professionals working primarily in non-university or community settings showed stronger associations with criteria emphasising programme relevance and implementation feasibility, such as programme responsiveness to recognised needs ($p=0.01$) and early intervention benefits ($p=0.04$). Age and career stage introduced an additional gradient. Associations with age group were observed for several Andermann criteria related to programme structure and evaluation (A, $p=0.003$; B, $p=0.01$; C, $p=0.006$), as well as for Wilson and Jungner criteria related to treatment effectiveness and acceptability (D, $p=0.04$; F, $p=0.02$; H, $p=0.02$). Senior professionals and those with longer experience were more frequently associated with stricter prioritisation of governance and evaluation-related criteria, whereas younger or junior respondents, particularly those under 35, showed weaker associations with these items. Finally, personal characteristics such as parenthood and gender were also associated with differences in criteria ranking, notably for criteria related to public health relevance ($p<0.001$), informed choice and autonomy ($p=0.006$), and programme acceptability ($p=0.04$), although these associations were less systematic than those observed for professional specialty and genetic expertise.

Genetic findings module

Professionals working in private or mixed practice, as well as those reporting limited experience with genetics or rare diseases, tended to express more favourable attitudes toward broader reporting, especially for adult-onset actionable findings ($p<0.05$) and variants informative for relatives ($p<0.01$). Conversely, profiles with high exposure to genetics, including professionals working in university hospitals or involved in research and teaching activities, were consistently more cautious, particularly for adult-onset non-actionable variants ($p<0.001$), carrier status ($p<0.001$), and variants of uncertain significance ($p<0.001$). Age and career stage introduced a further gradient. Younger and more junior professionals were generally more supportive of the disclosure of genetic findings, with significant associations observed for adult-onset variants ($p<0.05$), information relevant for relatives ($p<0.001$), and variants of uncertain significance ($p=0.001$). In contrast, older and more senior respondents tended to adopt more restrictive positions, particularly when findings offered limited actionability or carried higher interpretive uncertainty. Parenthood was also associated with differences in support. Respondents reporting three or more children were more likely to prioritise childhood-actionable categories, with significant associations observed for childhood non-actionable ($p=0.001$) and actionable variants

($p<0.05$), whereas no consistent pattern emerged for adult-onset findings. Gender, by contrast, was only weakly associated with responses across variation types.

Family Information module

HCPs in university hospitals reported higher confidence in parental information, while those in community or non-hospital settings felt less prepared for genomic integration. Women and more experienced professionals were also more likely to report insufficient training, whereas age showed no association.