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Prospective, Exploratory Pilot Study on Integrating Genetic Profiling with AI Algorithm and Phenotype Questionnaire in Personalized Skincare

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Abstract

The rapid transition toward real-world personalized skincare strategies is based on the integration of molecular pathway analysis, laboratory skin models, advanced technologies, clinical data, (epi)genomics testing, and AI. In this perspective, we designed a prospective, exploratory, uncontrolled pilot study with an educational component, integrating genetic testing of relevant skin-aging biomarkers and telomere length with AI and a phenotypic questionnaire to provide individualized skincare guidance. Our study also aimed to implement an innovative academic teaching method based on this integrative patient-centered skin health; therefore, we enrolled 44 students from the Faculty of Pharmacy Iasi. We present the genetic profiling of all 44 subjects according to genetic biomarkers for extrinsic and intrinsic skin aging (*ASIP* and *SOD2* polymorphisms, respectively), while a telomere length analysis was conducted only for 20 enrolled participants due to financial constraints at the study's initiation. Based on the possible combination of these polymorphisms, we performed a genetic stratification of the study cohort. After the integration of the genetic results with the individual responses, and with Perfect AI assessment performed for the whole cohort, we provided optimized skincare counselling to all 44 enrolled subjects; here, we selected some case reports as examples of personalized skincare routines and cosmetic ingredients for each genotype segment. Our pilot exploratory study finished up with a follow-up questionnaire and a satellite workshop on ethical aspects. Finally, we compared the design and insights of our pilot study with those of other cosmetic clinical trials that focus on integrative patient-tailored skincare.

Keywords: personalized skincare; cosmetogenomics; *ASIP*; *SOD2*; telomere length; integrative cosmetics; skin aging; photo-aging; cosmetic education; artificial intelligence

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1. Introduction

Personalized dermatology and cosmetology represent the future of aesthetic and anti-aging medicine, able to integrate genetic predisposition, epigenetic status, environmental exposures, and lifestyle factors in order to develop tailored interventions rather

than applying standardized, "one size fits all" treatment protocols. Cosmetogenomics is regarded as a distinct and complementary dimension within precision dermatology due to its promising preservation and enhancement of skin health and aesthetic outcomes. Cosmetogenomics is able to predict, identify, and monitor subtle changes in skin dynamics (such as skin texture, pigmentation, firmness, elasticity, hydration, wrinkles, and skin aging), thus enabling the implementation of early and adaptive skincare strategies [1–3]. Several studies highlight the transition from chronological age assessment toward biological age evaluation through genetic and epigenetic biomarkers [4,5]. Epigenetic modifications are increasingly recognized as critical regulators of aging processes, providing insight into how environmental exposures influence gene expression over time [6]. The emergence of epigenetic clocks has enabled more accurate assessments of biological aging and offers opportunities for personalized prevention and intervention strategies. Similarly, genetic profiling studies demonstrate that single-nucleotide polymorphisms (SNPs) influence key skin characteristics, including collagen degradation, pigmentation patterns, oxidative stress responses, and inflammatory tendencies [7,8]. Variants in genes like matrix metalloprotease (*MMP1*), superoxide dismutase (*SOD2*), tyrosinase (*TYR*), and interleukin *IL-6* can explain why individuals respond differently to cosmetic and dermatological treatments [9]. Complementing these findings, investigations into genetic signatures of skin aging suggest that combining multiple genetic markers may facilitate individualized risk assessment and treatment planning [5,8]. Therefore, the development of personalized skin strategies should integrate genomics, molecular biology, and other multi-omics approaches within the emerging field of "skinomics" [10].

In addition, artificial intelligence (AI) tools enable virtual real-time skin analysis, and AI-based platforms integrate imaging-based skin measurements, clinical parameters, multi-omics data, environmental and lifestyle influences, and client behaviors and preferences, thereby enabling personalized skincare treatment protocols to be suggested [11,12]. Therefore, AI-powered technologies are able to connect and translate the genomic and cosmetic perspectives into real-world implementation by providing tailored skincare products and regimens to the final beneficiary. AI-driven platforms could facilitate the standardization of relevant aspects of precise, patient-centered, and highly efficacious prophylactic and therapeutic skincare in aesthetic medicine and cosmetology. For instance, in laser dermatology, the integration of AI Generative Adversarial Networks and Virtual Try-On tools into energy-based devices assesses skin vascularity, hydration level, and melanin content in real time; facilitates the selection and adjustment of the treatment parameters; monitors the effects over time; and accordingly, customizes the regimens. Thus, they optimize the efficacity and minimize the risk of excessive collagen remodeling or post-inflammatory hyperpigmentation in highly sensitive patients due to genetic predisposition [9,13]. Moreover, in injectable therapies, AI-predictive analytics allow the pretreatment selection of the most efficacious and optimal collagen-stimulating interventions, hyaluronic acid fillers, and toxin injectable sites; at the same time, they also reduce the adverse events due to early detection of biomarkers of inflammatory reactions, delayed hypersensitivity, or vascular compromise. However, the increasing integration of AI-driven platforms into contemporary and future cosmetogenomics will greatly depend on solid clinical validation and enlarged proof-of-concept studies [8,9,12,13].

We designed a prospective, exploratory, uncontrolled pilot study with an educational component, integrating genetic testing of relevant skin-aging biomarkers and telomere length with an AI algorithm and a phenotypic questionnaire to illustrate and convince students from the Faculty of Pharmacy, pursuing either the long academic curriculum as pharmacists or the 3-year cosmetology and cosmetic product technology specialty, of the importance of the innovative implementation of genetics and AI in cosmetic counselling of

their future patients. Our study design did not include a control group, randomization, blinded assessment, or a standardized skincare intervention, as in conventional clinical trials; instead, it is mainly meant to invite our students to explore the current benefits and obstacles of this integrative paradigm in their professional practice, with particular emphasis on the identification of skin conditions and care needs; the selection of optimal skincare ingredients and regimens tailored to each patient; the monitoring of improvements in the initial skin signs and symptoms after a follow-up period; as well as sensitive ethical issues associated with the interpretation of genomics, clinical, and AI data.

2. Materials and Methods

2.1. Study Design

The exploratory longitudinal study enrolled a total of 44 female students (age 18–55 years) from which 20 belonged to the short academic specialty (3 years) of cosmetology and cosmetic product technology within the Faculty of Pharmacy and 24 were from the long academic curriculum (5 years) of the Faculty of Pharmacy at the University of Medicine and Pharmacy "Grigore T. Popa" Iasi, Romania. The inclusion criteria were voluntary participants who were interested in the topic and objectives of the investigations and who signed the written informed consent after they got all the information about the study from the trial's investigators. The exclusion criteria were age under 18 years old; subjects diagnosed with severe diseases (oncological, neuropsychiatric, dermatologic, hypersensitivity, etc.), which might have an increased risk of developing adverse events; and subjects who refused to sign the informed consent and to observe the study's requirements. Each of the 44 enrolled subjects responded to an in-house phenotypic questionnaire elaborated on by the investigators, performed the genetic testing for hereditary predisposition to skin extrinsic and intrinsic aging, and measured skin matrix parameters using the Perfect AI algorithm. Only the 20 cosmetology students underwent the genetic analysis for telomere length due to limited financial resources available at the time of initiating this study. After the analysis of the collected samples in accredited outsourced genetic testing laboratories, each subject received a Genetic Testing Report for the respective analyses. The genetic testing results provide indicative information regarding skin predispositions to aging and the average telomere length as an estimative marker among the complexity of interactions affecting the skin's epigenetic age (in comparison to a standard telomere length), which were then interpreted by the investigators of this study in correlation with the questionnaires and skin matrix measurements made by the Perfect AI algorithm.

2.2. Telomere Length and Skin-Aging Genetic Predisposition

Telomere length and skin-aging genetic predisposition were analyzed by outsourcing to specialized laboratories (Fagron Genomics S.L.U., C/ de les Cosidores, 150, Terrassa, Barcelona, Spain; Cromogenetic, Oradea, Romania; EDL Lab, Endeavor DNA, 60 Lansdowne Place, Hove, East Sussex, BN3 1FG, UK) which have certified Quality Management System and use Gentras Tracing DNA Technologies. The oral mucosal cell samples for each subject were collected, preserved, and delivered according to these laboratories' strict indications. The samples were collected non-invasively (saliva/light buccal swab; 1–2 min) according to the instructions provided with the laboratory collection kits and do not involve blood sampling. Afterwards, the isolated DNA from these samples was quantitatively assessed by the Absolute Human Telomere Length Quantification qPCR Assay Kit (AHTLQ). The quantitative polymerase chain reaction-based method PCR (qPCR) is extensively applied, particularly in high-throughput studies for rapid and precise quantification measurement of telomere length in relation to various biomarkers of environmental exposures and diseases [14].

2.3. In-House Phenotypic Questionnaire

Volunteer subjects who willingly agreed to participate in this study, after signing the informed consent, completed a questionnaire elaborated on by the investigators. The questionnaire takes approximately 20 min to complete, mainly by clicking on appropriate responses and, for a few questions, by providing short descriptions. The received filled-out questionnaires were anonymized through a unique code and analyzed exclusively for the purposes of this study. The in-house elaborated questionnaire was structured as follows:

- Demographic data (age and sex); skin phototype (Fitzpatrick scale/how the skin reacts to sun exposure without protection); and skin type (dry/oily/combination/sensitive/normal);
- Current skincare routine—dermato-cosmetic products and/or main active ingredients already used in the skincare routine (e.g., alpha-hydroxy acids/beta-hydroxy acids/retinoids/antioxidants/peptides/vitamins, etc.); the frequency of application (daily/several times a day or per week/rarely/never) for each step of the skincare routine, such as cleansing, exfoliation, moisturizing, use of SPF (sun protection) products; and how easily they follow the skincare routine;
- Skin concerns (multiple choices)—for example: wrinkles, redness, itching (pruritus), rashes, acne, rosacea, hyperpigmentation/dark spots, and skin allergies; any signs of recent skin sensitivity or irritation; acne-related concerns and tendency to develop acne scars or post-inflammatory marks (post-acne pigmentation); as well as the subjective perception of how skin concerns affect the self-esteem during day-to-day life;
- Two primary skincare goals—e.g., skin tone uniformization; reduction in excess oil (sebum) production; improved hydration and skin comfort; better skin tolerance/fewer irritations; anti-aging (fine lines, wrinkles, and firmness); and other (to be specified);
- Previous dermatological/cosmetic treatments (type of treatment and approximate date);
- Types of interventions acceptable at this time—e.g., changes in skincare routine and/or cosmetic products only; minimally invasive procedures; preferences for cosmetic products (e.g., compounded/custom-made, natural, or commercially manufactured products) and for changes to current skincare routine; expectations regarding cosmetic treatment effectiveness; and product tolerability;
- Current lifestyle habits: average hours of sleep per night, stress level, smoking status, alcohol consumption (never/occasional/frequent), type of diet (balanced/high in refined sugars/high fat/high protein/dairy-rich/vegetarian/raw vegan), daily liquid intake, physical activity (type and frequency per week), UV exposure/artificial tanning and sun exposure (average daily exposure during warmer months), occupational exposures (hazardous substances and pollutants), time spent in dry or air-conditioned environments, and frequency of travel;
- Hormonal/endocrine status: menstrual status (regular/irregular/amenorrhea/early menopause), pregnancy/breastfeeding, known endocrine pathology (thyroid disorders/polycystic ovary syndrome/diabetes, etc.). and hormonal medication (contraceptives, steroids, and anti-androgens);
- Medical conditions and medications relevant to skin health: metabolic disorders, dermatological conditions, allergies (to medications, cosmetics, and foods), and autoimmune diseases;
- Medications with potential effects on the skin: retinoids—isotretinoin, adapalene, tretinoin; antibiotics—tetracyclines, macrolides; and other photosensitizing medications (like non-steroid anti-inflammatory drugs (NSAIDS), thiazide diuretics, and amiodarone).

2.4. Perfect AI Algorithm

The web link and the instructions for performing Perfect AI algorithm measurements were clarified to all the enrolled subjects (https://www.perfectcorp.com/business/showcase/skincare/live-diagnostics, accessed on 10 February 2026). Each enrolled participant obtained a skin matrix assessment with different scores for cutaneous parameters such as firmness, texture, radiance, pores, wrinkles, hydration/moisture, oiliness, redness, acne, eyebags, dark circles, and droopy lower/upper eyelid. The investigators strongly emphasized that within this study, the Perfect AI algorithm has not been used and validated as a stand-alone diagnosis and clinical decision-support tool.

2.5. Follow-Up of the Study

The interpretation and correlation of all these data served as a guide for cosmetic individualized counselling, and this study will also validate an innovative educational model for the students of the Faculty of Pharmacy in Iasi, either as future pharmacists or cosmetic specialists. Each subject received an individualized skincare routine plan and recommendations in order to complete and modify some routine skincare principles and dermato-cosmetic products, as well as lifestyle factors, which were greatly adapted and optimized for each subject's skin problems. They applied all these recommendations for 3 months, and finally, they responded to a concise online satisfaction questionnaire (4–5 min), depicted in Figure 1.

2.6. Statistical Analyses

Statistical analyses were performed using JASP Statistics 0.98.1. and R version 4.6.1 (https://www.r-project.org/). Descriptive statistics were used to summarize the study data. The distribution of telomere length was evaluated using Q–Q plots. Because telomere length deviated from normality, associations between telomere length, chronological age, and estimated biological age were assessed using Spearman's rank correlation coefficient (ρ). The association between *ASIP* rs4911414 and *SOD2* rs4880 genotypes was evaluated using a contingency table. Pearson's chi-square (χ^2) test and Cramer's V with its confidence interval were calculated as effect size measures. Because the expected cell frequencies did not satisfy the assumptions required for the chi-square test, the Fisher-Freeman–Halton exact test was additionally performed. All statistical tests were two-sided, and p-value < 0.05 was considered statistically significant.

2.7. Confidentiality and Ethical Aspects

Before initiating this study, the investigators submitted all the required documentation to the Ethical Committee for Scientific Research of University of Medicine and Pharmacy "Grigore T Popa" Iasi. This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of University of Medicine and Pharmacy "Grigore T. Popa" Iasi, Romania (Protocol code 664/approved 28 October 2025). All data collected within the study (questionnaires, genetic tests, and Perfect AI measurements) were strictly anonymized (coded, with no names on the kits); analyzed in accredited research laboratories abroad that specialized in genetic analysis; and finally reported according to the assigned code, without direct identification of the subject. Data was anonymized from the moment of collection (unique codes without name/personal identification number/address), stored separately from any correspondence list, and accessible only to the investigators; reporting was carried out exclusively by code. The investigators protected and kept the obtained data confidential. National laws and regulations regarding the protection of personal data were strictly observed. Information resulting from participation in the study may be made available to the institution hosting the research, the Ethics Committee,

or other persons/institutions if required by law. Access to data complies with the GDPR (EU Regulation 679/2016).

Feedback Questionnaire on Participation in the Personalized Cosmetic Product and Skincare Study

1. To what extent did you follow the recommended cosmetic skincare plan?
2. How comfortable were you with implementing the personalized skincare recommendations?
3. To what extent did you follow the recommended dietary and lifestyle modifications?
4. How comfortable were you with implementing the personalized lifestyle recommendations?
5. What factors made it difficult for you to follow the recommendations? (Open-ended question)
6. How would you rate the improvement in your skin concerns (e.g., acne, wrinkles, dehydration, hyperpigmentation, excess sebum) after following the personalized recommendations?
7. How would you rate your skin tolerance to the recommended cosmetic ingredients?
8. Overall, how would you rate the usefulness of the personalized recommendations?
9. To what extent do you consider the inclusion of genetic testing to have been necessary for a better understanding of your individual skin profile?
10. To what extent do you consider the inclusion of Perfect AI in skin assessments to have been necessary for a better understanding of your individual skin profile?
11. To what extent do you consider that combining all assessment methods (genetic testing, Perfect AI, and questionnaires) was necessary for personalizing the cosmetic skincare plan
12. To what extent do you consider that participation in this study was beneficial from an educational perspective for the development of your professional skills?
13. Additional comments (Please provide any additional comments regarding your experience and satisfaction following your participation in this study)

Figure 1. Study follow-up questionnaire.

3. Results

All 44 enrolled volunteer participants strictly adhered to the study's protocol without any deviation, so the drop-out rate was 0. Below, we briefly present the statistically analyzed results for the genetic tests (telomere length for 20 enrolled participants due to financial constraints; biomarkers of photo-aging and intrinsic aging—performed for the whole cohort of 44 enrolled subjects), the stratification of participants based on their combined genotype for *ASIP* and *SOD2* polymorphisms, some examples of optimized skincare solutions for participants classified into each genotypic segment, and the follow-up feedback after the implementation of the tailored cosmetic guidance.

3.1. Telomere Length Genetic Reports

Telomeres are specialized repetitive DNA sequences at the end of eukaryotic chromosomes with a protective role against chromosomal fusion and damage. Telomeres progressively shorten as cells undergo successive divisions, and when they reach a

critical length, the cell cycle arrests, a process known as replicative senescence. Therefore, telomeres are regarded as a cellular life clock, a pivotal indicator of cellular aging and strongly associated with the onset and progression of various age-related diseases [14,15].

We have applied the genetic analysis to determine the telomere length for 20 enrolled participants (due to limited financial resources available at the initiation of this study). The telomere analysis reports indicate the average length of telomeres of all chromosomes from a comparison with a control sample with a known telomere length (reference sample). Biological age estimation, i.e., the degree of aging based on a patient's telomere length vs. standard/control is recorded as the average telomere length (expressed in kilobases kb) and also graphically illustrated. The approximate biological age is estimated following statistical models endorsed by scientific publications, as well as by internal validations [16–18]. Repeatability and reproducibility of the test used in our study demonstrate validity greater than 99%. In comparison to other methods such as telomere end restriction fragment analysis (TRF) and single-stranded telomere length analysis (STELA), which measure the absolute telomere's length, qPCR offers relative quantification or changes in telomere length, like the fluorescent in situ hybridization (FISH) method [14,15].

Out of 20 tested participants, 19 subjects (95.0%) were classified according to their biological age as very aged/high risk and only 1 participant (5.0%) as aged/medium risk, in comparison to their real age. No low-risk samples were identified within our enrolled cohort. Regarding the segment of high risk/very aged subjects, the average telomere length varies within 0.77–1.84 kb, with an average of 1.33 $\pm$ 0.59 kb and an estimated biological age within the interval of 35–42 ($\pm$1) years, while the aging was within the range of 14–21 years above the real age of the tested participants (20, 21, or 23 years old) (Figure 2). For instance, a subject belonging to the very aged category in comparison to their real age (21 years old) recorded an average telomere length of 0.81 kb. Thus, the estimated biological age is 42 $\pm$ 1 years, meaning that the biological age showed a marked aging rate with respect to the subject's chronological age, since the cells have a telomeric length that is much shorter than expected. For the single tested subject within the group estimated as aged (medium risk category) in comparison to the real age (21 years), the average telomere length is 3.51 kb, with an estimated biological age of 24 $\pm$ 1 years, having an aging rate of 4 years in comparison to their real age (20 years old).

The Spearman correlations among telomere length, chronological age, and biological age remain qualitatively similar without the outlier, and the Q–Q plot confirms that the distribution of telomere length deviated from normality (Figure 2). This study revealed there was no significant association observed between telomere length and chronological age ($\rho = 0.143$, $p = 0.549$). Biological aging is therefore the result of cumulative processes at the molecular and cellular levels, largely independent of chronological age in the studied cohort.

3.2. Skin-Aging Genetic Testing

This genetic test aimed to evaluate the risk of skin aging with respect to some extrinsic and intrinsic factors.

3.2.1. Relevance of rs4911414 *ASIP* Polymorphism as an Extrinsic Skin-Aging Biomarker

We investigated the genetic susceptibility to photo-aging by analyzing *ASIP* rs4911414 polymorphism in the study cohort (all 44 enrolled subjects), and the results are presented in Table 1. According to their genetic profile of *ASIP* rs4911414, subjects could be stratified into the following genotype segments: homozygous for wild-type (major, normal, or protective) allele G, heterozygous with a single risk allele T (genotype GT), and homozygous for

the risk allele (genotype TT). Carriers of one or both of the risk allelic variants (T)—i.e., the GT or TT genotypes—for rs4911414 *ASIP* have an "unfavorable" genetic profile for photo-aging.

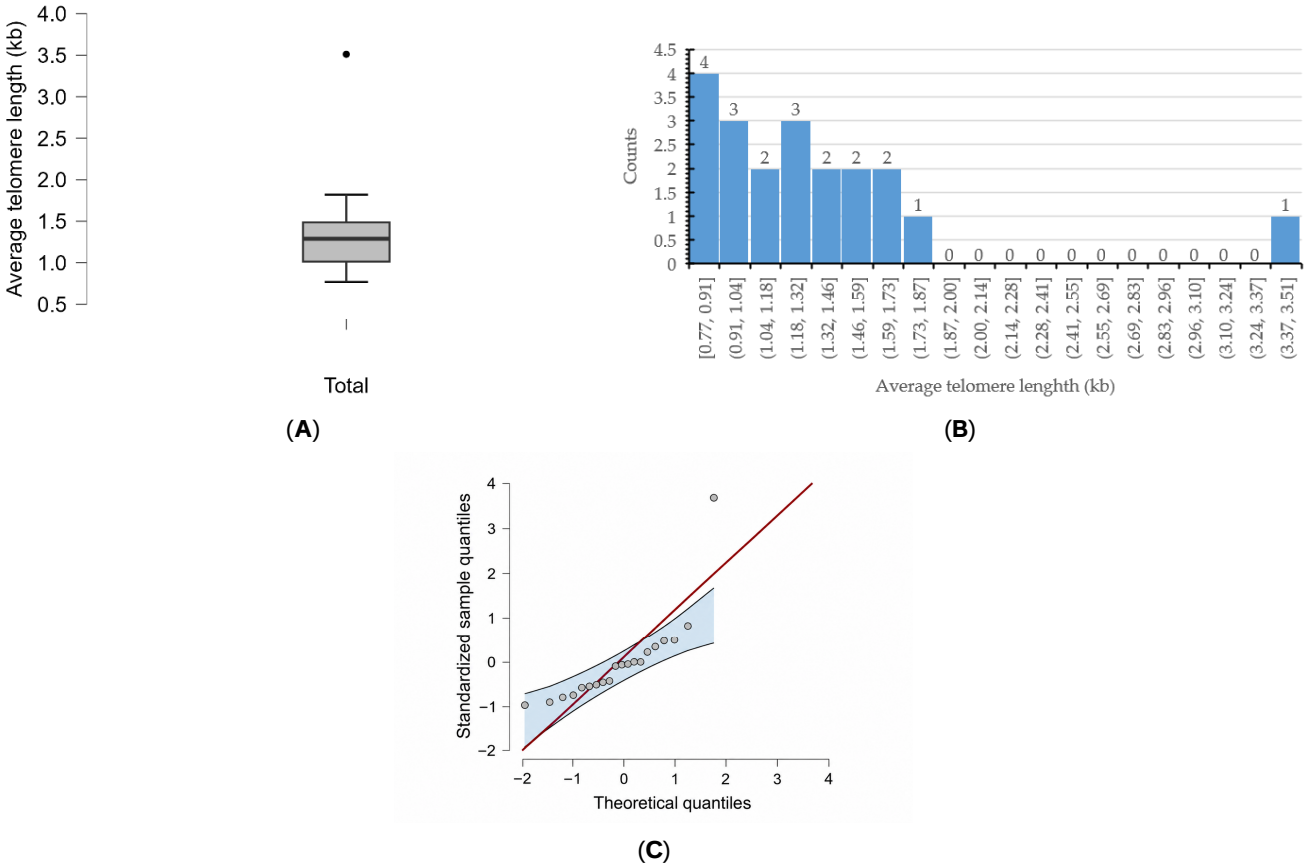


Figure 2. Average telomere length (kb) including the outlier value (**A**), the distribution of telomere lengths (**B**) (n = 20), and a Q–Q plot of the average telomere length (kb) (**C**), where Gray circles represent the observed sample quantiles, the red diagonal line represents the theoretical normal reference line, and the light-blue shaded area represents the 95% confidence envelope; the black lines indicate its boundaries.

Table 1. Distribution of genetic polymorphisms of *ASIP* and *SOD2* as extrinsic and intrinsic skin-aging biomarkers, respectively, within the enrolled cohort.

Analyzed Gene Polymorphism as Biomarker for Skin Aging	Wild-Type Allele/ Risk Allele	Genetic Profile Significance	Genotype Stratification	Number of Identified Subjects from the Total Enrolled Cohort (44)
Photo-aging/ extrinsic skin-aging *ASIP* rs4911414	G/ T	unfavorable	homozygous TT	4
			heterozygous GT	23
		favorable	homozygous GG	17
Intrinsic aging *SOD2* c.47C>T (Ala16Val) SNP (rs4880)	T/ C	unfavorable	homozygous CC	9
		favorable	heterozygous TC	23
			homozygous TT	12

The results indicated a distribution of *ASIP* genotypes, with 17 cases (38.6%) being GG carriers, 23 (52.3%) GT carriers, and 4 (9.1%) having TT alleles. There is a lower prevalence of the homozygous TT genotype; however, because heterozygous carriers also possess the risk allele, 61.4% of the participants exhibited inherited susceptibility to UV-induced skin aging and would benefit from photoprotective skincare routines.

3.2.2. Relevance of *SOD2* Polymorphism as an Intrinsic Skin-Aging Biomarker

We investigated the genetic predisposition by analyzing the *SOD2* c.47C>T SNP (rs4880) for the whole cohort of 44 enrolled subjects, and the results are presented in Table 1 and Figure 3. The genotype stratification for subjects is a "favorable" antioxidant capacity for carriers of TT or TC genotypes and a "unfavorable" genetic predisposition for carriers homozygous for risk/less functional C alleles (genotype CC). For the *SOD2* polymorphism, the studied cohort comprised 12 (27.3%) out of the 44 participants who were carriers of the TT genotype, 23 (52.3%) who carried the TC genotype, and 9 (20.5%) who carried the CC genotype (Figure 3), so 79.5% of the subjects carried the favorable genotype and 20.5% presented an unfavorable genetic predisposition, and the latter segment would greatly benefit from early implemented strategies to support the antioxidant activity of epithelial cells with targeted antioxidative nutrients and food supplements, as well as cosmeceutical creams with antioxidative ingredients.

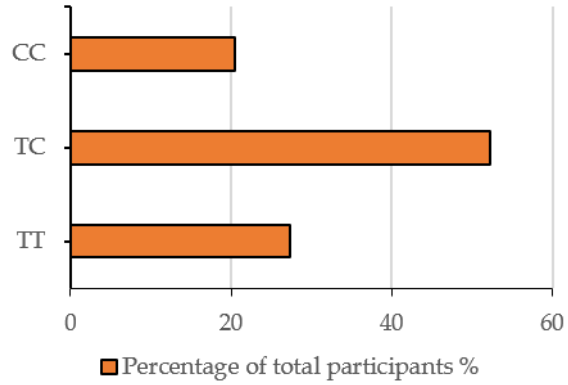


Figure 3. Genotype stratification upon *SOD2* c.47C>T SNP (rs4880) as an intrinsic aging biomarker.

3.3. Perfect AI Skin Analysis

The AI integration within the study design has enabled the voluntary participants to discover the opportunities, usefulness, limitations, ethical considerations, and economic implications of AI algorithms in the personalized, preventive, and therapeutic cosmetic counselling and monitoring of the effects of the skincare recommendations which they will provide to their future patients. For each of the 44 enrolled subjects, we have integrated the results of the skin-aging genetic tests with the information provided by Perfect AI's cutaneous parameters and with their answers to the phenotypic questionnaire in order to provide each participant optimized solutions and changes in comparison to their currently used skincare routine and cosmetic ingredients. However, in this current study, Perfect AI has neither been used nor validated as a stand-alone diagnostic tool for personalized skincare-decision making.

3.4. Stratification of Study Cohort Based on Analyzed Genetic Biomarkers of Skin Aging

Stratification of genotyped subjects based on their genetic susceptibility to skin aging according to each participant's combination of risk alleles for both photo-aging and intrinsic skin aging is illustrated in Table 2.

The results indicate that the heterozygous genotype was the most prevalent for both polymorphisms, whereas the homozygous risk genotype was less frequent. The most frequent genotype combinations were GG/TC and GT/TC, each accounting for 27.3% of the study population. In contrast, the double homozygous combination that is associated with an unfavorable profile (TT/CC) was observed in only two participants (4.5%). To assess whether genetic susceptibility to photo-aging (*ASIP*) was associated with susceptibility to intrinsic aging (*SOD2*), Pearson's chi-square test was performed, and no statistically

significant association was identified between the two polymorphisms (χ^2 = 4.755, df = 4, p = 0.313). Furthermore, the effect size, estimated using Cramer's V, was 0.232 (95% CI: 0.000–0.383), indicating only a weak association between the two genetic biomarkers. Six of the nine expected cell frequencies were below 5; therefore, the chi-square test needed further confirmation. The Fisher–Freeman–Halton exact test confirmed that the association was not statistically significant (two-sided exact p = 0.267). These results suggest that the investigated polymorphisms independently contribute to susceptibility to skin aging in the present cohort (Figures 4 and 5).

Table 2. Stratification of enrolled cohort according to the combined genetic predisposition to extrinsic and intrinsic aging based on analyzed *ASIP* and *SOD2* gene polymorphisms.

Stratification Based on Genetic Profile of Skin Aging	Genetic Susceptibility to Photo-Aging: *ASIP* rs4911414 as Biomarker	Genetic Susceptibility to Intrinsic Aging: *SOD2* c.47C>T (rs4880) as Biomarker	Number of Participants from the Whole Cohort of Tested Subjects (44)
FAVORABLE	Favorable GG	Favorable TT or TC	14 subjects of 44 enrolled, from which 2 are homozygous for both SNPs carrying GG and, respectively, TT alleles; 12 persons are carriers of GG alleles for *ASIP* and TC alleles for *SOD2* SNPs
UNFAVORABLE	Unfavorable TT or GT	Unfavorable CC	6 subjects from a cohort of 44, from which 2 participants are homozygous for the risk alleles of both SNPs; 4 subjects are carriers of genotype GT for *ASIP* and, CC alleles for *SOD2* SNPs, respectively
COMBINED PROFILE	Favorable GG	Unfavorable CC	3 homozygous carriers of favorable/protective alleles for the *ASIP* biomarker (genotype GG) and for the risk allele C for the *SOD2* SNP (genotype CC), from all 44 enrolled
	Unfavorable TT or GT	Favorable TT or TC	21 subjects from a total of 44 enrolled, from which 1 homozygous for both genetic biomarkers—for the risk allele (genotype TT) for *ASIP* SNP and for favorable allele T for *SOD2* SNP (genotype TT); 12 heterozygous for both genetic biomarkers, i.e., with GT genotype for *ASIP* SNP and TC genotype for *SOD2* SNP; 7 heterozygous (GT genotype) for *ASIP* SNP as a photo-aging biomarker and homozygous for favorable/wild-type allele T for *SOD2* SNP relevant for intrinsic aging; 1 homozygous for the unfavorable allele (genotype TT) of *ASIP* SNP and heterozygous (genotype TC) for *SOD2* SNP as an intrinsic aging biomarker.

3.5. Personalized Skincare Strategy Based on Integrated Genetic Predisposition, AI Algorithm, and Phenotypic Questionnaire

A great majority of the tested subjects were completely unaware of their increased susceptibility to photo-aging and/or accelerated intrinsic aging until the genetic test results were known, thus exposing themselves to damaging environmental factors and lifestyle behaviors, as well as to inappropriate or even harmful cosmetic procedures and ingredients.

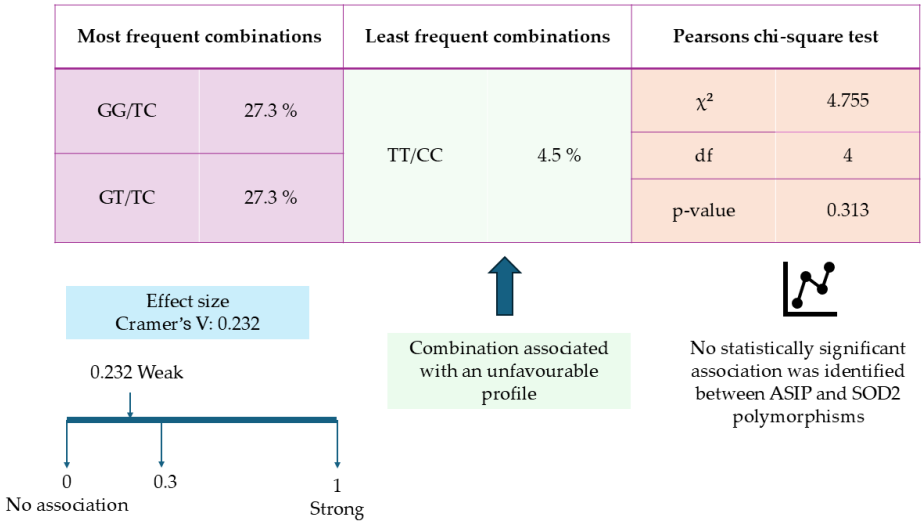


Figure 4. Description of the association of the two analyzed polymorphisms of *ASIP* and *SOD2* (χ^2, chi-square statistic; df, degrees of freedom).

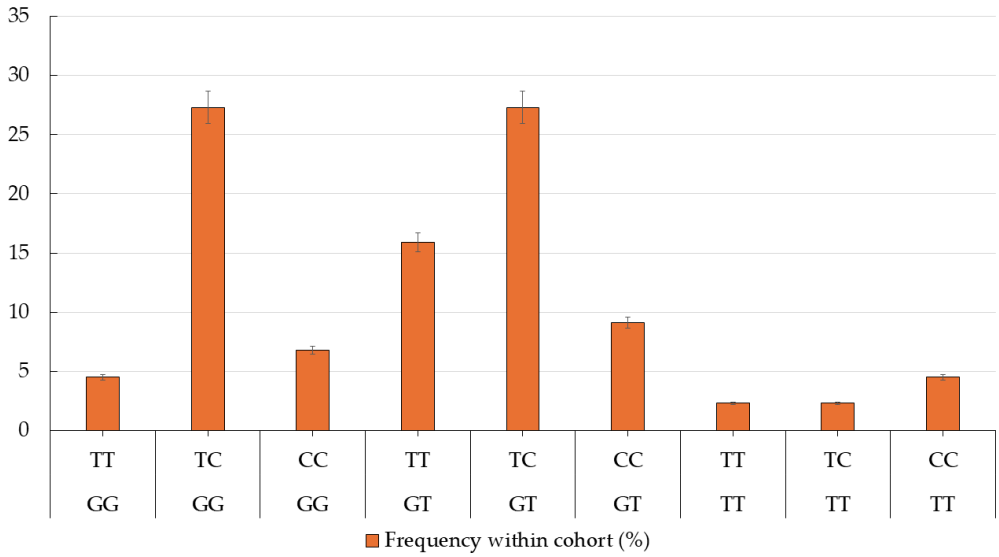


Figure 5. Association of analyzed *ASIP* and *SOD2* polymorphisms in the studied cohort (n = 44).

In order to illustrate the personalized counselling based on the integration of the summary of performed tests (genetic profile, Perfect AI assessment, and relevant responses in the questionnaires) and greatly taking into account the current skincare ingredients and attitudes reported by each subject, we exemplify below some optimized reports sent by investigators to enrolled subjects belonging to each of the four segments (A–D) derived from the stratification of cohort study based on analyzed genetic biomarkers of skin aging (Section 4.4 and Supplementary Materials). Each report included as final notes the following paragraph: "The genetic polymorphisms analysed in these reports indicate a susceptibility or predisposition and do not establish, confirm, or replace a formal medical diagnosis made by a healthcare professional. As a general recommendation, cosmetic skincare should prioritise product tolerability, monitor the skin's response over time, and adjust products according to clinical outcomes and individual tolerance. Before introducing any new cosmetic product, it is advisable to perform a patch test by applying the product to a discreet yet sensitive area of skin, such as the inner forearm, behind the ear, or along the jawline, in order to assess cutaneous tolerance and minimise the risk of irritation or allergic reactions."

CASE REPORTS as examples of individualized guidance and optimized skincare ingredients and routines have been selected for each genotype segment and are presented as Supplementary Materials.

3.6. Participants' Satisfaction and Feedback on Pilot Study Goals After 3 Months of Applied Personalized Counselling

The questions addressed in the follow-up feedback questionnaire are depicted in Figure 1 and they are the level of adherence and implementation of the personalized counselling (questions Q1–Q5), the improvement in clinical outcomes (Q6–Q8), as well as the perceived value of the study and the benefits of the integrative approach (genetic testing, AI, and phenotypic self-assessment questionnaires) to the development of the students' professional abilities and expertise (Q9–Q12). The results are presented in Figures 6–8.

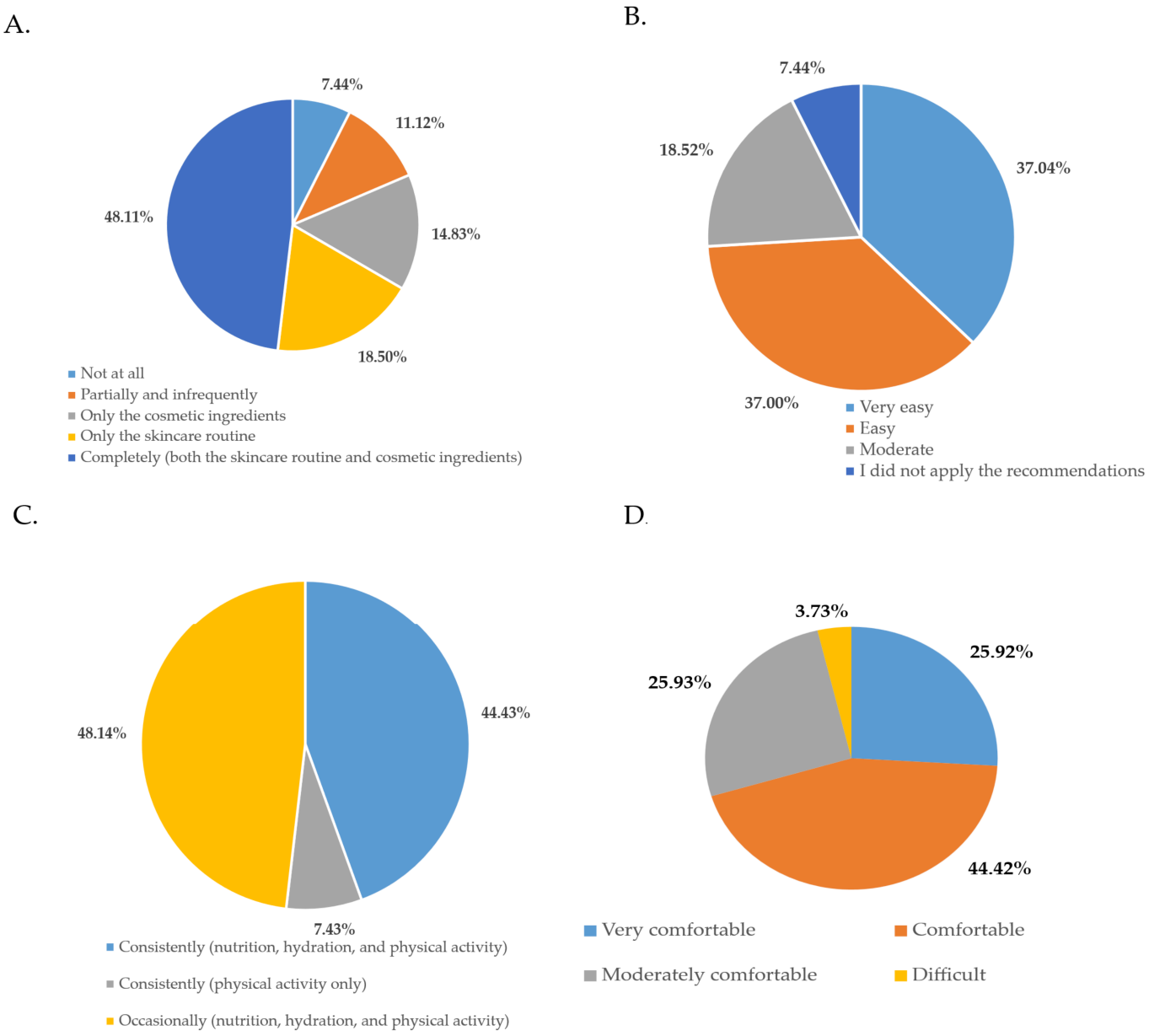


Figure 6. Compliance and implementation: (**A**) answers for Q1; (**B**) answers for Q2; (**C**) answers for Q3; (**D**) answers for Q4.

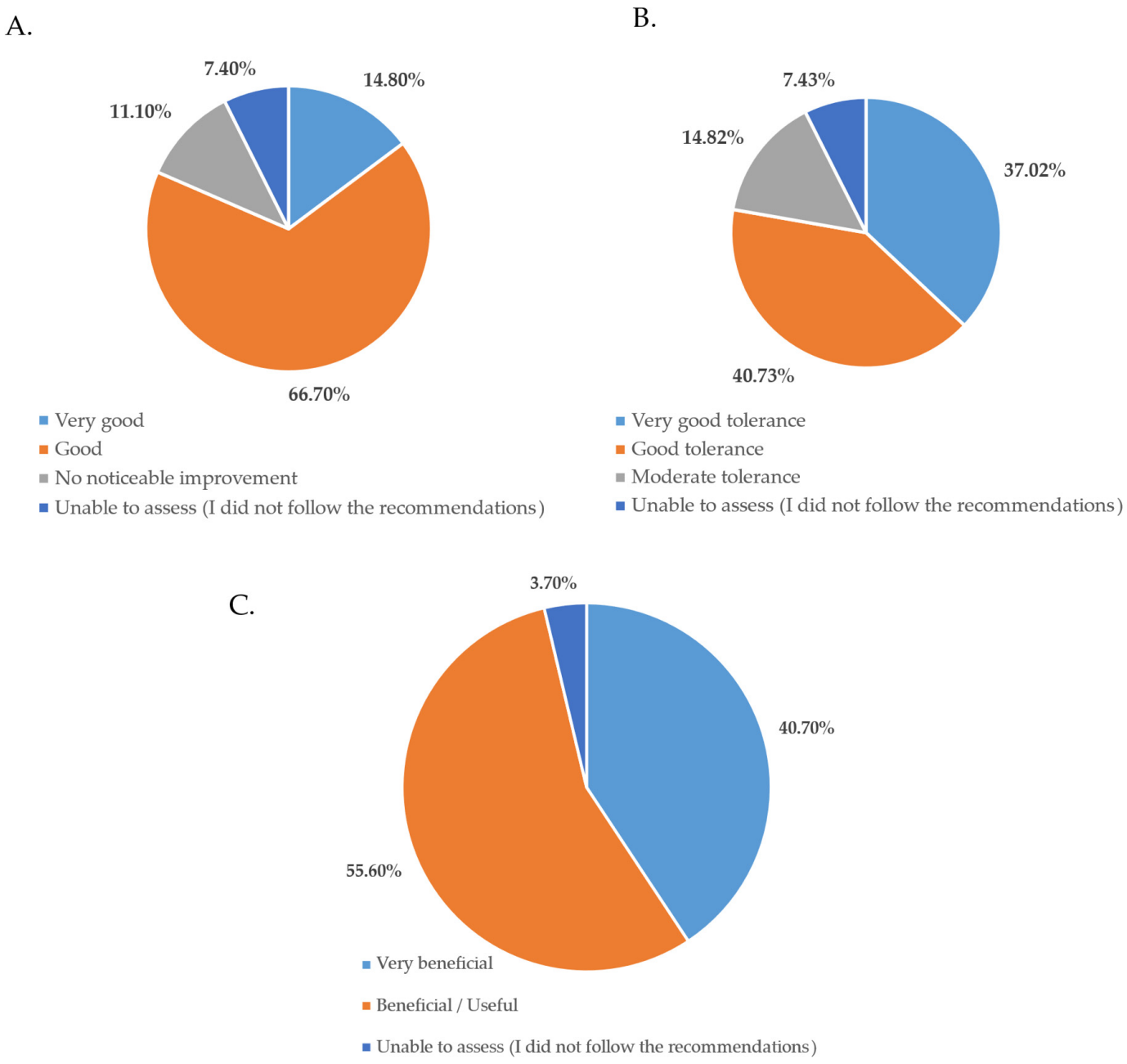


Figure 7. Diagrams illustrating the level of clinical improvements: (**A**) answers for Q6; (**B**) answers for Q7; (**C**) answers for Q8.

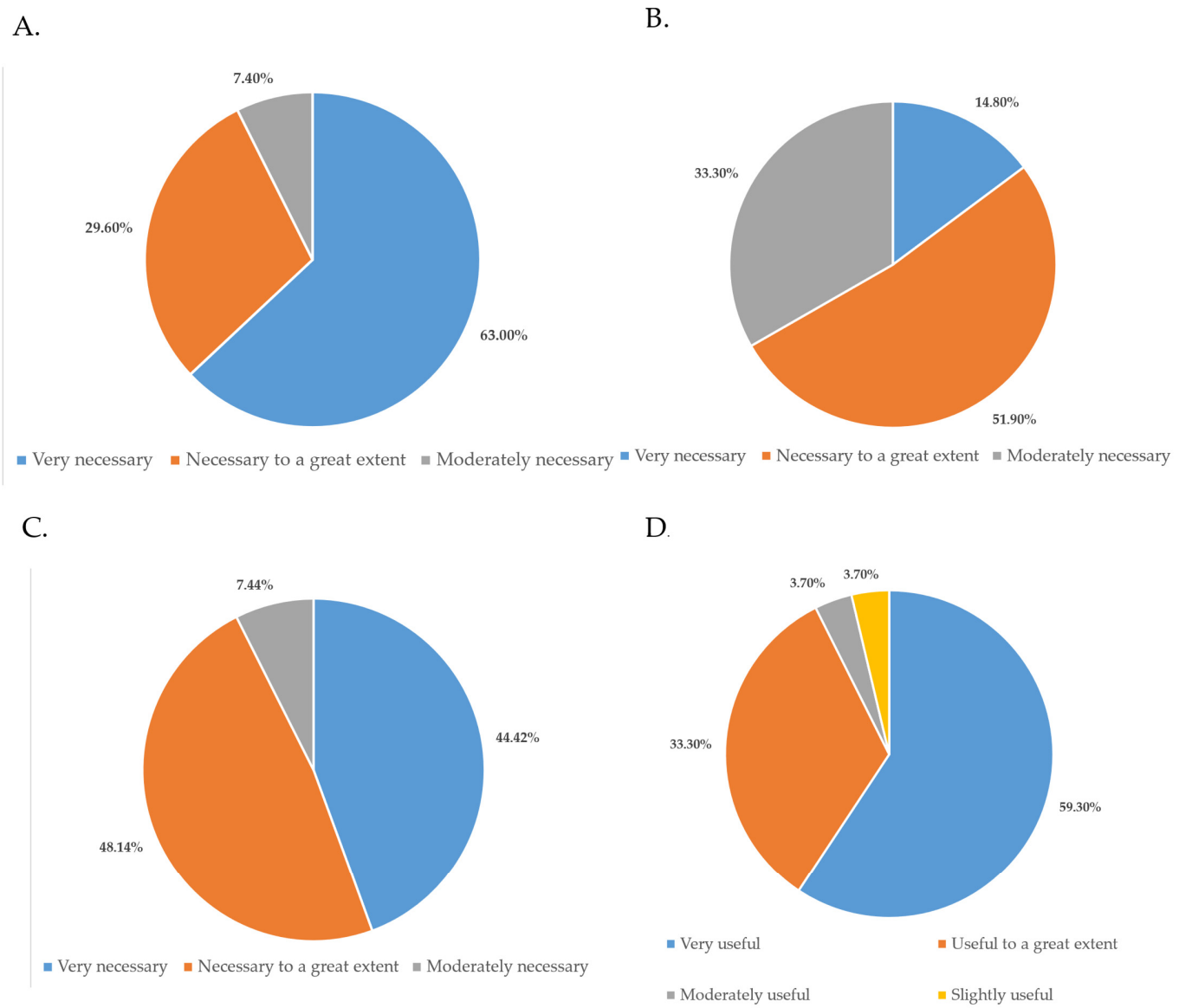


Figure 8. Satisfaction on development of professional abilities: (**A**) answers for Q9; (**B**) answers for Q10, (**C**) answers for Q11; (**D**) answers for Q12.

4. Discussion

4.1. Telomere Length Genetic Reports

The length and ability of the telomeres to remain protected are determined by genetic factors (which can contribute to approximately 40% of the variance in telomere length) and also by some behaviors and environmental conditions (for example: stress, diet, sedentarism, overweight, depressed mood, living in environments with high levels of pollution, etc.). There might be a complex association between telomere's stability and skin aging [16], or the risk of skin malignancy [17].

Moreover, telomere biology should be placed as a nodal event into an integrative approach with a multi-mechanistic framework of skin-aging model, interconnected to epigenetic, inflammatory, and cellular metabolic pathways. In this complex model, telomere attrition may serve as a downstream biomarker rather than a trigger/driver of aging, taking into account that oxidative stress and mitochondrial dysfunction often precede telomere attrition, telomere-associated DNA damage might also occur independently, and telomerase activity correlates with body mass but not to lifespan in many rodent studies [18–21].

Recent research has revealed that telomere length has emerged as a valuable, pivotal predictive biomarker in multiple skin anti-aging and rejuvenating strategies, that could be modulated by controlling some environmental factors and lifestyle choices. Although human telomeres shorten during the aging process, the speed of this process varies for each person. Knowing the situation of an individual's telomeres and being able to track their shortening provides very valuable information to improve and customize anti-aging therapies [20,22–24].

Telomere length was estimated from the genetic testing performed in only 20 participants from the whole 44 enrolled cohort (due to financial constraints at the initiation of the study); thus, it does not provide a definitive, validated assessment of the skin biological age because of the complex influences (genetic, environmental, metabolic, and lifestyle) of this genetic biomarker. The statistical analysis of our results showed no significant association between telomere length and skin chronological age in this subgroup. However, the factors that are most easily accessible for slowing down the rate of telomere shortening for our enrolled students, within the current study protocol, appear to be lifestyle-related.

Correlating the demographic and lifestyle data declared by the subjects (i.e., age, gender, height, weight, nutrition, stress, and physical activity) with the marked aging for the great majority of the tested subjects, we noticed an association with high calory food intake, especially highly processed, hypercaloric, and junk food as a nutrition style; insufficient daily hydration; and a rather sedentary life within the very aged subgroup. Therefore, the investigators strongly advised the enrolled subjects to adhere to a much healthier lifestyle that will be beneficial for reducing the aging rate by (a) performing moderate physical activity, according to their preferences and aligned to possible co-existing pathological conditions; (b) reducing the intake of calories from high carbohydrate and junk food; (c) increasing the proportion of antioxidant and anti-inflammatory nutrients in their diet (such as: omega 3; coenzyme Q10; resveratrol; polyphenols; and vitamins A, B, C, D, and E, found in a lot of vegetables, nuts, and fruits); and (d) eventually starting on adjuvant food supplements with rejuvenating effects at the cellular level [23–26].

All these suggestions to adopt a healthier lifestyle and diet, including consuming a nutritionally balanced diet and daily hydration (2 L/day), foods rich in omega-3, nutrients with anti-inflammatory potential, vitamins, and antioxidants; reducing the consumption of ultra-processed/"junk food" and refined sweets; engaging in moderate physical activity; reducing smoking; and alleviating insomnia, are in accordance with recent published scientific proofs which demonstrated the strong positive impact of lifestyle and epigenetic interventions on both telomere length, and skin health and aesthetics [17,20,22,24]. For instance, powerful and statistically significant associations among telomere length and aging rate with lifestyle interventions encompassing moderate or vigorous physical activity, a balanced diet, smoking cessation, and good sleep habits have been revealed by a comprehensive systematic review and meta-analysis from 20 independent trials with a total of 2995 enrolled subjects, in comparison to control groups. In addition, the combination of intense physical exercises with endurance training yielded better improvements in telomere length than either type of exercise alone [16,20–22].

4.2. Skin-Aging Genetic Testing

4.2.1. Relevance of Testing the rs4911414 *ASIP* Polymorphism as an Extrinsic Skin Aging Biomarker

Photo-aging or extrinsic skin aging is mainly caused by inherited sensitivity to the harmful effects of ultraviolet (UVA and UVB) radiation, which is considered the major driver of extrinsic aging, triggering reactive oxygen species (ROS) formation, DNA damage, and epigenetic alterations (e.g., hypermethylation of tumor suppressor genes and hypomethylation of oncogenes), also increasing the risk of skin cancer [27]. Many large-

scale studies have identified genetic variations that increase sensitivity to the sun and the tendency to suffer from sunburn (erythema). Some people's skin is therefore 3–4 times more vulnerable than the general population to sun damage and their repeated exposure to UVA and UVB causes premature skin aging. The effect is achieved through DNA damage in epidermal cells, oxidative stress, and persistent and chronic inflammation. The pivotal role of lifestyle and environmental circumstances in modulating these epigenetic changes is well documented, since smoking, poor nutrition, insomnia, and long and/or unprotected sun exposure impair skin regeneration and exacerbate oxidative stress and inflammaging [7,27,28].

Genetic factors modulate individual susceptibility to environmental exposures (especially UV radiation, smoking, and air pollution), while lifestyle factors contribute to inter-individual variations in the aging rate/speed despite similar environmental histories [27,29]. Recent reviews consider pigmentation genes among the most reproducible genetic contributors to skin-aging phenotypes. According to Wong et al. (2025) [30], pigmentation-related loci repeatedly emerge in both genome-wide association studies (GWASs) and candidate-gene studies, suggesting that pigmentation pathways represent a genuine biological component of skin-aging susceptibility. Independent studies evidenced the strong association of Agouti signaling protein (*ASIP*)-related pigmentation pathways with extrinsic skin aging [30]. In photo-aging, *ASIP* plays a crucial role acting as an antagonist to the melanocortin-1 receptor (MC1R) in skin cells, by competing with the binding of the alpha-MSH (melanocyte-stimulating hormone) to MC1R. By blocking this receptor, *ASIP* shifts melanin production from protective eumelanin (black/brown) to less protective pheomelanin (red/yellow), which significantly increases the skin's vulnerability to damages caused by UV-induced ROS [30,31]. In addition, this spike in ROS leads to mitochondrial DNA damage in fibroblasts, which triggers enzymes like matrix metalloproteinases (MMPs) responsible for the break-down of collagen and also causes solar elastosis (wrinkling and loss of elasticity).

Therefore, the biological rationale for *ASIP* genetic testing resides on the regulatory role of the *ASIP* gene in melanogenesis, specifically influencing the balance between eumelanin, correlated to relatively strong photoprotection, and pheomelanin, associated with UV sensitivity and lighter pigmentation phenotypes [30,32]. Since pigmentation is one of the strongest biological determinants of UV susceptibility, *ASIP* genetic variants can influence an individual's inherited vulnerability to photo-aging. Variations in the *ASIP* gene expression act as a dominant genetic factor in reducing human pigmentation. Specific genetic variations, mostly SNPs of the *ASIP* gene, are strongly associated with an increased number of facial pigmented spots (freckles) and a higher overall risk of photo-aging and skin cancer [31,32]. Based on the current evidence, *ASIP* rs4911414 polymorphism is reported as one of the loci repeatedly and intensely associated with skin-aging phenotypes. The *ASIP* rs4911414 polymorphism is an intergenic/upstream variant located roughly 120 kb away from the actual coding region of the *ASIP* gene, and it is considered one of the strongest candidates within the *ASIP* pigmentation-associated regulatory pathway, besides the *ASIP* rs1015362 and *MC1R* gene variants [6,28,30,32,33]. The *ASIP* rs4911414 polymorphism is strongly linked to variability in hyperpigmentation, reduced tanning ability, increased freckling, and sun/UV sensitivity. All these traits are established risk factors for cumulative UV-induced skin damage and subsequent accelerated photo-aging [30].

There is a high prevalence (55%) in the European population of carriers of these unfavorable genotypes, a percentage that sustains the practical importance of the genetic analysis: identify them early and applying the protective anti-aging strategies to the

subjects who are more sensitive to environmental insults, primarily solar radiation and UV emissions from tanning lamps [30–32].

The potential clinical benefits of testing the rs4911414 *ASIP* polymorphism include useful information regarding a predisposition to UV sensitivity, the likelihood of developing hyperpigmentation-related photo-aging, the need for aggressive photoprotection strategies, and personalized prevention programs. From a preventive cosmetic and dermatologic perspective, the identification of a risk-associated *ASIP* genotype could support recommendations for daily broad-spectrum sunscreen use, earlier implementation of anti-photo-aging interventions, increased UV avoidance, and more frequent dermatologic monitoring [29–31].

However, critical expert opinions consistently emphasize that *ASIP* testing alone provides only a partial assessment of photo-aging risk because of several important limitations, such as (a) the limited predictive value of the *ASIP* genetic test as a stand-alone biomarker, since it represents only one pathway/polymorphism among many identified loci associated within the complexity of the genetic architecture underlying skin-aging phenotypes; (b) the strong predominance of environmental factors (particularly UV radiation, smoking, and pollution) upon extrinsic aging, which could be modified, but not at all replaced, by the genetic susceptibility [27]; and (c) the increasing preference for polygenic risk models rather than single-gene testing, since multiple biological pathways contribute to skin aging, including pigmentation, DNA repair mechanisms, extracellular matrix remodeling, and regenerative and developmental pathways, and they also provide more informative risk assessment than *ASIP* alone [6,30,33]. Furthermore, expert consensus emerging from recent systematic reviews indicates that rs4911414 *ASIP* polymorphism contributes a small proportion of total aging variability, since environmental exposures remain the dominant determinants of photo-aging [5,6,28,32,34,35]. In addition, a brief comparative analysis of the clinical relevance of *ASIP* among other genetic tests points out that other genetic biomarkers are regarded stronger than *ASIP* due to their robust associations with photo-aging, skin color determination, UV sensitivity, and photo-carcinogenesis. In this regard, we could exemplify *MC1R* (melanocortin 1 receptor gene), regulating melanin synthesis [2,5,28,30,35,36]; *IRF4* (interferon regulatory factor 4 gene), involved in pigmentation regulation and immune signaling [4,30,37]; *MMP1* (matrix metalloprotease gene), involved in collagen degradation and more directly associated with wrinkle formation than *ASIP* [6,30,34,38,39]; *XRCC1* (X-ray repair cross-complementing 1 gene), potentially more directly related to DNA repair after UV-induced damage and to cumulative photo-damage than pigmentation genes [2,4,5]; *TYR* (tyrosinase gene), encoding a crucial copper-containing enzyme responsible for the first and rate-limiting step of melanin production and therefore more directly involved in melanin production [6,28,30,32]; and *OCA2* (oculocutaneous albinism II gene), involved in melanin synthesis, skin color determination, and pigmentation-related aging risk [6,30,32,37].

In view of the above, our study on rs4911414 *ASIP* testing would be best interpreted as one component of a future broader polygenic assessment of skin-aging susceptibility, rather than as a single definitive predictor of photo-aging. In this regard, our study represents a very first step of future more comprehensive trials, and it is greatly meant to encourage our faculty's students to design and perform multiple genes cosmetogenomics endeavors (integrating pigmentation, DNA repair genes, oxidative stress, and extracellular matrix genes) in pursuit of personalized skin anti-aging and rejuvenating solutions.

4.2.2. Relevance of *SOD2* Polymorphism Testing as an Intrinsic Skin-Aging Biomarker

The antioxidant activity of the cells of the epidermis is the main way in which they defend themselves from damage from UV radiation, other environmental factors (such as air pollutants and smoke), and free radicals that are normally produced within the cells

themselves. Antioxidant activity depends on various genes, among which *SOD2* stands out, which is expressed in the mitochondria—the energy center of the cells where the majority of intrinsic free radicals are produced. *SOD2* is so important that life is not possible in its absence [32,40].

The *SOD2* gene encodes mitochondrial manganese superoxide dismutase (MnSOD), the primary antioxidant enzyme responsible for detoxifying superoxide radicals generated during oxidative phosphorylation. Because mitochondrial oxidative stress is a central mechanism and hallmark of intrinsic (chronological) skin aging, *SOD2* has attracted interest as a candidate genetic biomarker of aging susceptibility [6,8]. The evidence supporting *SOD2* biological relevance as a skin-aging genetic biomarker includes the following: (a) Velarde et al. (2012) demonstrated that *SOD2* deficiency in mouse skin promotes oxidative stress, cellular senescence, epidermal thinning, and other aging-like phenotypes, as well as the adaptive changes in *SOD2* expression during skin aging and fibroblast senescence, reinforcing its role in cutaneous aging biology [41]. (b) Weyemi et al. (2012) further showed that reduced *SOD2* activity accelerates skin-aging characteristics in vivo [42]. (c) Rinnerthaler et al. (2015) identified oxidative stress and mitochondrial dysfunction as key drivers of intrinsic skin aging, providing mechanistic support for antioxidant-gene biomarkers such as *SOD2* [43]. (d) Mansoor et al. (2025), showed the predictive value of *SOD2* polymorphisms profiling and the efficacy of an antioxidant treatment to a patient with poor defense capacity against oxidative stress applied 6 weeks before the fractional CO_2 laser procedure, since the follow-up monitoring proved amplified healing and diminished erythema [44]. For patients with reduced *SOD2* activity due to SNP variations, cosmetic dermatologists can proactively introduce antioxidant-rich skincare regimens and recommend treatments which minimize oxidative stress. In laser therapy, for example, previously knowing a patient's *SOD2* profile can guide the application of post-treatment antioxidants to optimize recovery and protect against further damage. Moreover, SNP profiling shows promise in managing adverse effects associated with cosmetic procedures. For instance, variations in the *SOD2* gene can predispose individuals to oxidative stress following certain cosmetic treatments. Patients with these variations may be more vulnerable to post-treatment inflammation and tissue damage [5,6,28,32].

The analysis of point mutations of the *SOD2* gene allows us to understand whether it will have correct localization and action in the mitochondria; as a consequence, it is an indication of greater or lesser activity. Individuals with lower functional *SOD2* activity (with half the efficiency) than the general population will consequently be more exposed to damage from free radicals, which are produced in a physiological way by all the cells of their organism. This will have a "visible" effect, especially at the epidermis level, with a greater tendency towards skin aging, presenting thin, atrophic, pale, loose skin; extensively furrowed by wrinkles; and inelasticity [45].

The most studied *SOD2* genetic variant is *SOD2* c.47C>T SNP (rs4880). This cDNA change c.47T>C is translated at the protein level into a Val16Ala (V16A, Ala16Val) change, having as a functional consequence an alteration in mitochondrial targeting and import efficiency of the MnSOD enzyme, which influences the antioxidant defense capacity. Functional studies suggest that different alleles affect mitochondrial ROS handling, DNA damage accumulation, and cellular senescence pathways associated with accelerated skin aging. Therefore, *SOD2* c.47C>T SNP rs4880/Val16Ala (V16A, Ala16Val) represents the overwhelmingly standard choice as a genetic biomarker in skin intrinsic aging, antioxidant defense, nutrigenomics, and wellness panels because it is the functional mitochondrial targeting polymorphism with the strongest scientific evidence [5,6,28,32,45]. If *ASIP* and MC1R derive much of their predictive value from pigmentation and UV-response genetic pathways, which overlap substantially with photo-aging, *SOD2* is regarded as one of the

strongest mechanistic biomarkers of intrinsic aging. Within a multigene panel specifically targeting intrinsic aging, *SOD2* polymorphism may deserve a higher weighting than its position would suggest when considering all skin-aging phenotypes together [6,28,35,46,47].

However, despite strong mechanistic plausibility, *SOD2* rs4880 SNP currently remains a moderately relevant rather than a definitive intrinsic skin-aging biomarker, because (a) most evidence links *SOD2* to general aging, oxidative stress, and cellular senescence, rather than directly to validated human skin-aging phenotypes such as wrinkle severity, dermal thinning, elasticity loss, or skin-age scores; (b) human association studies have produced inconsistent findings regarding longevity and age-related outcomes; and (c) recent systematic reviews of skin-aging genetics identify numerous loci involved in pigmentation, extracellular matrix remodeling, inflammation, and oxidative stress, suggesting that skin aging is polygenic and unlikely to be predicted exclusively by *SOD2* polymorphisms alone [5,6,28,30,32,48].

Therefore, *SOD2* testing is biologically justified as a marker of susceptibility to oxidative stress-driven intrinsic aging, but its predictive value would be substantially improved when interpreted within a multi-gene aging panel rather than as a stand-alone biomarker. For instance, a genetic skin-aging panel might comprise, besides *SOD2* rs4880, also SNPs of genes like *MMP1* rs1799750 (-1607 1G/2G) and *MMP3* rs3025058 (5A/6A) associated with collagen degradation, connective tissue aging, and wrinkle susceptibility, thus having strong skin-specific relevance [28,34,38,39]; *COL1A1* (pro-alpha1 protein chain of type I collagen) rs1800012 (Sp1 binding site), associated with collagen synthesis, connective tissue quality, and matrix structural integrity and therefore more directly linked to dermal aging than *SOD2* [32,48]; *ELN* (tropoelastin synthesis), more directly and relevant to loss of skin elasticity and dermal resilience [10,28,48]; *CAT* (catalase) rs1001179 (-262C>T), which is complementary to *SOD2* due to its role in hydrogen peroxide detoxification in skin and systemic aging [28,32]; *GPX1* (glutathione peroxidase) rs1050450 (Pro198Leu), with similar relevance to *SOD2* due to its glutathione-dependent ROS detoxification in age-related phenotypes [5,28,32,49]; *MC1R* (various SNPs: R151C, R160W, D294H, etc.), involved in pigmentation, DNA damage response, and oxidative stress protection and thus having strong associations with perceived facial age and skin-aging phenotypes in humans [35,37,50]. Within such genetic panels, *SOD2* would be best viewed as an oxidative stress susceptibility biomarker, whereas *MMP*-, collagen-, elastin-, and pigmentation-related SNPs often show more direct relationships with observable skin-aging phenotypes [5,28,30,34,35,37–39,49,50].

In view of the above and in line with the partial conclusion on rs4911414 *ASIP* as a photo-aging biomarker, our focus on *SOD2* rs4880 (Val16Ala) testing has also mainly aimed to emphasize the relevance of cosmetogenomics testing within modern individualized skin anti-aging strategies and to stimulate the scientific curiosity of our students in performing the next level of the enlarged polygenic assessment of skin-aging susceptibility.

4.3. Perfect AI Skin Analysis

We have chosen the Perfect AI Skin Analysis algorithm because it demonstrates several advantages over conventional skin assessment algorithms and hardware-based systems. Recent clinical studies conducted in collaboration with dermatology researchers from Wake Forest School of Medicine reported high concordance with physician evaluations, excellent test–retest reliability (ICC > 0.90/95% reproducibility), and up to 20 times faster analysis compared with traditional imaging devices. Unlike many AI dermatology systems that show reduced performance across diverse skin tones, Perfect AI was validated on heterogeneous populations and under variable lighting conditions, improving its robustness and real-world usability. The platform is also trained on more than 70,000 medical-grade images and can quantify up to 14–15 skin parameters, enabling highly personalized and

scalable skin evaluation [51–54]. In this exploratory study, Perfect AI has neither been used nor validated as a unique, stand-alone diagnostic tool.

4.4. Stratification of Study Cohort Based on Analyzed Genetic Biomarkers of Skin Aging

We stratified the whole enrolled cohort based on the genetic susceptibility to skin aging according to each participant's combination of risk alleles for both photo-aging and intrinsic skin aging as follows: (A) carriers of favorable genetic profiles for both extrinsic and intrinsic skin aging (no risk alleles detected), comprising the subjects identified as having the favorable genotype GG for *ASIP* for photo-aging and genotype TT or TC for *SOD2* SNP for oxidative stress defense capacity; (B) participants with unfavorable genetic profile for both types of aging, identified by the presence of risk alleles for the TT or GT genotype for *ASIP* polymorphism, and CC for *SOD2* SNP; (C) persons with a combined genetic profile due to protective alleles for photo-aging, but an unfavorable genotype for skin intrinsic aging; and (D) carriers with a combined genetic profile having unfavorable genetic predisposition to photo-aging (homozygous TT or heterozygous GT—for *ASIP* analyzed as a biomarker) but no genetic susceptibility for accelerated intrinsic skin aging (carriers of TT or TC genotypes for *SOD2* SNP as a biomarker).

The results revealed a predominance of heterozygous genotypes for both investigated polymorphisms *ASIP* and *SOD2*, and most young adults who participated in this study present a genetic susceptibility profile and would benefit from preventive cosmetic strategies (these should therefore not be limited only to individuals carrying homozygous risk variants). These early interventions are beneficial to individuals who are exposed to UV-radiation, smoking, unbalanced nutrition, or chronic stress [28]. Since our study did not demonstrate a significant association between *ASIP* and *SOD2* polymorphisms, it is important to evaluate both biomarkers; otherwise, the individual skin-aging profile would be incomplete.

4.5. Personalized Skincare Strategy Based on Integrated Genetic Predisposition, AI Algorithm, and Phenotypic Questionnaire

Following genetic testing, the carriers of unfavorable/susceptible genetic profiles in relation to photo-aging were advised to topically apply high-protection creams and SPF50+ filters, limit the daily duration of exposure to the sun, prefer bathing in the sun in the first part of the morning or the second part of the afternoon, and protect the area around the eyes very well using sunglasses. On the other hand, the carriers of unfavorable/susceptible genetic profiles in relation to intrinsic aging were strongly advised to adhere to daily and continuous oral intake of strong antioxidant nutraceuticals, in particular, alpha tocopherol and lipoic acid as they have a well-documented effect as scavengers of oxygen radicals produced at the respiratory chain level. For instance, a healthy and balanced diet recommends the intake of many foods rich in antioxidants such as fruit and vegetables; in particular, the intake of vitamins A, C, and E and beta carotene is essential. The best foods against free radicals are blueberries and red fruits, rich in vitamins A and C, and anthocyanin glycosides; carrots, rich in beta carotene and vitamin C; kiwi and citrus fruits, rich in vitamin C; beets, rich in vitamins B9 and C, and potassium; goji berries, real antioxidant superfoods; dark chocolate, rich in flavonoids; green tea and white tea, rich in polyphenols and catechins; oilseeds; and nuts [23–26]. For the subgroup of 20 participants enrolled from the cosmetology specialty who also benefited from telomere length measurement in addition to the skin-aging (extrinsic and chronological) genetic testing; the Perfect AI skin analysis; and an in-house questionnaire, which was also performed for the entire cohort of 44 subjects, the study investigators strongly emphasized the importance of quick and continuous adherence to a much healthier lifestyle (nutrition, hydration, physical exercise, sleep habits, and balance in lifestyle) since 19 subjects were identified as very

aged and just one as aged in comparison to their real age. These highly recommended behavioral changes are integrated with individualized cosmetic ingredients and skincare routines. In the Supplementary Materials, we selected some optimized guidance sent by the investigators to enrolled subjects belonging to each of the four segments (A–D) derived from the stratification of the cohort study based on integration of the genetic, questionnaire, and orientative AI data.

4.6. Participants' Satisfaction and Feedback on Pilot Study Goals After 3 Months of Applied Personalized Counselling

The compiled responses to the structured questions within the feedback questionnaire (depicted in Figure 1) are illustrated as diagrams in Figures 6–8. The diagrams in Figure 6 show that the great majority of the enrolled participants have succeeded in consistently and successfully implementing the personalized skincare and lifestyle recommendations; the remaining, a very small proportion, who encountered some difficulties in pursuing the individualized plan evoked a stressful daily schedule as the main reason. Regarding the self-assessment of clinical improvements, the results illustrated in Figure 7 point out that, overall, above 93% of participants reported "very good or good" clinical outcomes and skin tolerance, and they appreciated the received personalized skincare guidance noting that it was "very beneficial or beneficial"; the rest, approximately 3.7–7.4% subjects, partially and/or inconsistently applied the individualized skincare products and cosmetic routine or lifestyle recommendations. Concerning the satisfaction with the development of their professional abilities, the responses complied in diagrams in Figure 8 have emphasized that almost all the participants appreciated the learning experience and the innovative integrative approach of incorporating the genetic tests, AI algorithms, and self-assessment questionnaire in order to guide the personalized cosmetic counselling, noting that it was "very useful/useful to a great extent". Once again, the exception of 7.4% subjects comes from those who have inadequately applied or did not apply the recommendations.

4.7. Comparative Insights on Our Pilot Study vs. Other Similar Clinical Trials

Our prospective and exploratory design pilot study has focused on the importance of the integration of cosmetogenomics and AI tools within a classical phenotypic questionnaire and clinical data in order to achieve more efficient personalized skin health, thus significantly contributing to a new educational paradigm within academic curricula—patient-centered cosmetic counselling. Therefore, our pilot study has aligned with the modern major paradigm shift in cosmetology and skin-aging research, moving from generalized approaches toward precision, mechanism-based, and personalized interventions, due to the growing role of (epi)genetics in deciphering individual skincare trajectories and treatment responses. Since the outcomes of SNP-based skincare personalization are influenced by environmental exposures, lifestyle factors, and epigenetic modifications, our study integrated also these perspectives and it can contribute to the elaboration of future standardized protocols and multi-center validation trials, in line with similar recently published clinical trials in modern cosmetology [1–4,6–8,10,28]. Due to its major educational focus, our study protocol did not involve a control group, randomization, or blinded assessment, as in conventional clinical trials implying standardized skincare intervention or testing new cosmetic products. Another limitation of our study derives from financial constraints at the study's initiation phase, which enabled us to perform the telomere length genetic testing in only 20 participants instead of the whole cohort of 44 enrolled subjects on whom we succeeded in analyzing their *ASIP* and *SOD2* genetic polymorphisms.

Our data demonstrated that early genetic susceptibility identification has greatly improved the adoption of antioxidative cosmeceuticals and nutrition, and optimized cosmetic ingredients; sun-protective habits; and other lifestyle changes relevant to photo-aging, intrinsic

aging and medium-term skin appearance improvements among pharmacists students and those of the cosmetology specialization. A very high proportion of the participants enrolled in the study who received personalized skincare and lifestyle recommendations based on genetic predisposition information have successfully and completely adhered to them and offered follow-up feedback, thus demonstrating an improved engagement in preventive behaviors (such as increased sunscreen use, more skin examinations, and reduced sun exposure, particularly among genetically higher-risk individuals), adoption of personalized cosmetic products, healthier diet, and physical exercise practice. As clearly mentioned in each final feedback report, our students have become aware that (a) an analysis of genetic polymorphisms estimates a susceptibility/predisposition and does not establish or replace a definitive specialist diagnosis; (b) lifestyle recommendations (diet and physical activity) should also be adapted and individualized according to personal preferences, known allergies or intolerances, and any existing medical conditions; and (c) the cosmetic care should be consistent and balanced with attention to tolerability, by monitoring the skin's evolution and making product adjustments according to the clinical response.

Our study has focused on genetic, AI, and behavioral endpoints for a substantial cohort of 44 participants, thus being a starting point for future larger cohorts so as to expand the generalizability potential. Our trial has also demonstrated the real-world feasibility and consumer applicability of genomics-based patient-centered skincare personalization. These strength points are obvious, although the study's investigators aimed neither to assess new cosmetic products or original aesthetic invasive procedures nor to comply with a randomized or blinded design (based on a control arm in parallel to the tested arm) or to standardized outcome measures.

Our study is in line with other recently published trials evaluating SNP-associated skin responses to UV radiation and oxidative stress, which emphasize potential benefits of genomics-informed personalized skincare interventions over standard regimens targeting skin hydration, elasticity, and pigmentation. For instance, Haykal et al. (2025) [6], in a systematic review conducted by aggregating 22 randomized controlled trials (RCTs, level I evidence), 35 observational studies (level II), and 17 conceptual or expert opinion papers (level III), involving human subjects or ex vivo skin models, published between January 2012–April 2025, concluded that genomics enhanced treatment efficacy and long-term skin health patient satisfaction, and the integration of genetic, environmental, and lifestyle factors can generate evidence-based predictive and personalized recommendations. In addition, AI-driven cosmetogenomics would be complementary to precision dermatology [6]. However, all these studies have also pointed out that stronger and broader validation in more diverse study populations; inclusion of more pertinent evidence-based studies not predominantly derived from exploratory ones; more transparent and standardized methodologies; and expanded and harmonized ethical and regulatory safeguards, especially concerning genetic discrimination risks, data ownership, and cross-border data transfer, are required to ensure a widespread clinical translation [2,4,6,36].

Genomics-informed individualization has been associated with statistically significant improvements in multiple aesthetic skin parameters compared to non-personalized regimens, despite the mentioned disadvantages like high heterogeneity across trials and limited transparency on trial designs and outcomes. Other in silico and biomarker-driven investigations had a preclinical or computational focus and explored genetic pathways and SNP associations relevant to skin inflammation and cosmetic ingredient response [36], which identified genetic pathways influencing skin aging and treatment response and offered mechanistic insight to guide future clinical trial design and ingredient personalization. In comparison to these studies, our study has chosen some essential validated SNPs most relevant to photo-aging and intrinsic aging predictability, and it used these individual

genomic signatures to guide lifestyle recommendations and to select the cosmetic ingredient formulations already approved and with a long history within the network of local community pharmacies. From this point of view, our study is similar to that mentioned by Mun S. et al., 2025 [55].

Another original part of our pilot study resides in this learning-by-doing method of teaching and academic education. As the satisfaction feedback questionnaires have pointed out, this experiential learning has also provided our enrolled students with increased self-esteem and confidence in their professional abilities, a very pleasant learning journey, and also an equilibrated wellbeing status. The design of our pilot study assigns to our enrolled students the role of future patients, and in this way, they could better appreciate the importance of patient empowerment and engagement in their cosmetic care plan, thus further enhancing the collaborative relationship in modern cosmetology.

The optimized recommendations formulated by the investigators for the enrolled students of the Faculty of Pharmacy from different specializations provided an informative guide for the selection of personalized dermato-cosmetic products based on genetic and integrative skin evidence, a guide that supports an innovative educational and training model promoted by the Faculty of Iasi. Correlating the questionnaire responses with the results of these genetic skin tests and with the cutaneous parameters measured using the Perfect AI algorithm would enable undergraduate students from the Pharmacy Faculty specializations to select individualized cosmetic products, to develop a skincare plan, and to recommend lifestyle modifications which are tailored and optimal for the particular needs of each future patient. This educational approach would substantially increase the competitiveness of future pharmacists, cosmetology specialists, and beneficiaries of other undergraduate academic programs within the faculty on the national and European labor market.

Our study could be viewed in this alignment of global interest in precision dermato-cosmetology with both educational and clinical–aesthetic translational relevance. AI-assisted cosmetology enhanced precision, safety, and predictive modeling, especially in non-invasive dermato-cosmetological interventions, marking a contributory shift from reactive to proactive and preventive cosmetology in the new paradigm of the modern AI-driven genomics era. Although the applied Perfect AI is not a properly sophisticated AI-driven digital twin [56], it has enabled us to easily and comfortably measure cutaneous skin parameters and to illustrate the AI integration into preventive, predictable, and targeted cosmetics for our students, based on individual susceptibility to aging, chronic inflammation, collagen and elastin alterations, oxidative stress, cutaneous barrier dysfunctions, and hormonal fluctuations. A digital twin is a virtual and dynamically updated representation of an individual's skin, using a much broader range of information such as genetic and multi-omics profiling (genomics, proteomics, transcriptomics, metabolomics, and microbiomics), real-world lifestyle variables, and environmental exposures (UV radiation, sun exposures, and pollutants) [56].

Integrating genetic data and AI into cosmetology raises ethical challenges related to data privacy and ownership; algorithmic transparency; bias; potential risk of discrimination in employment or insurance contexts if information is misused; consent for scientific dissemination or secondary use without explicit patient approval; or collection for commercial purposes and control by different stakeholders, regulatory bodies, and jurisdictional variations in case of cross-border data transfer (e.g., GDPR in Europe and HIPAA in the United States). It is generally agreed that these ethical issues must be supported by robust and harmonized regulatory frameworks and policy, in order to sustain the real-practice adoption of cosmetogenomics and AI-driven tools within patient-centered dermato-cosmetology [2,9,57,58]. In order to address the applicable ethical concerns in our study, the investigators implemented all precautious rules and actions by providing all

required explanations, transparency, and confidentiality about all personal information concerning the study's participants, including also a clearly written paragraph in the informed consent about the possibility of withdrawing from the study without any consequences. The study design and protocol, the informed consent, and all questionnaires completed by the participants were previously approved by The Ethics Committee for Research at our university (as stated in Section 2.7).

Moreover, starting from the Perfect AI implementation in our pilot study and from the critical analysis of the recent literature on this topic [9,51], we have organized a satellite workshop where we have discussed and debated in mocked role-play with the student volunteers enrolled in this study the potential of the AI-assisted systems to improve diagnostic accuracy, predict treatment responses, analyze complex genetic datasets, facilitate individualized therapeutic recommendations, and create hybrid models of skincare for delivering highly personalized treatment plans, as well as challenges related to the abovementioned ethical considerations, data privacy, algorithmic transparency, harmonized legislation, and regulatory oversight.

Future perspectives of AI-assisted cosmetogenomics would enable real-time optimized skincare and treatment plans by dynamically adjusting both at-home dermato-cosmeceutical ingredients and in-clinic aesthetic interventions based on monitoring skin assessments [2,4,6,7,9]. However, these promising perspectives must address some current limitations, such as the high cost and restrained accessibility of SNPs and multi-omics analysis, the lack of standardized and harmonized regulations and protocols for AI-powered cosmetogenomic field, challenges in data reproducibility, and clinical validation, before it becomes not only an essential and evolving frontier but also a truly implemented personalized skincare paradigm.

5. Conclusions

Our pilot study highlights an innovative educational and training model that integrates genetic research into the teaching process and provides current and future graduates of the Faculty of Pharmacy with new skills and competitive advantages on today's competitive job market. This integrative professional approach for future specialists in pharmacy and cosmetology would greatly contribute to a new fundamental educational paradigm based on personalized scientific evidence in cosmetic counselling.

This educational model demonstrates and convincingly emphasizes, through direct experiential learning, the importance of continuous and integrative education based on the latest genetic and AI technological advances in dermato-cosmetology for cosmetology specialists, pharmacists, and students/graduates of other academic programs within the Faculty of Pharmacy in Iași. These advances should be reflected in the formulation, recommendation, and selection of dermato-cosmetic products tailored to the skin needs and lifestyle characteristics of each subject/future patient.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/cosmetics13050241/s1, Supplementary File S1: CASE REPORTS as examples of individualized guidance, and optimized skincare ingredients and routines are selected for each genotype segment.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

AI	Artificial intelligence
ASIP	Agouti signaling protein
BMI	Body mass index
CAT	Catalase
COL1A1	Pro-alpha1 protein chain of type I collagen
DNA	Deoxyribonucleic acid
ELN	Tropoelastin
FISH	Fluorescent in situ hybridization
GPX1	Glutathione peroxidase
GWAS	Genome-wide association studies
IL	Interleukin
IRF4	Interferon regulatory factor 4
kb	Kilobases
MC1R	Melanocortin-1 receptor
MMP	Matrix metalloprotease
MnSOD	Manganese superoxide dismutase
NSAIDS	Non-steroid anti-inflammatory drugs
OCA2	Oculocutaneous albinism II
PCOS	Polycystic ovary syndrome
qPCR	Quantitative polymerase chain reaction-based method
ROS	Reactive oxygen species
SNP	Single-nucleotide polymorphisms
SOD2	Superoxide dismutase type 2
STELA	Single-stranded telomere length analysis
TRF	Telomere end restriction fragment analysis
TYR	Tyrosinase
UVA, UVB	Ultraviolet radiation
XRCC1	X-ray repair cross-complementing 1

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