

Article title: Diagnostic and management practices for phenylketonuria in 19 countries of the South and Eastern European Region: survey results

Journal: European Journal of Pediatrics

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Online resource 2

Summary of answers to questions not presented in main results section of manuscript

Survey on PKU care in Eastern Europe and neighbouring countries

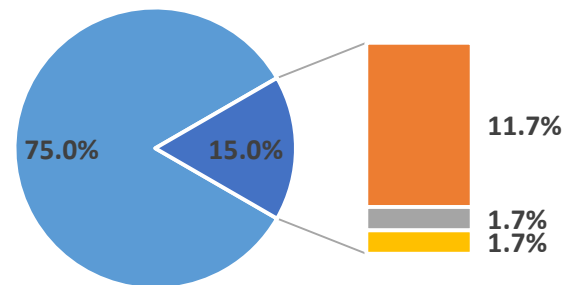
1d. With which group(s) of PKU patients are you involved? (multiple answers possible)

| Answer Options | Response Percent | Response Count |
|---|------------------|----------------|
| All patients with PKU | 75.0% | 45 |
| Only newborns, children and teenagers | 11.7% | 7 |
| Only newborns, children and teenagers and PKU patients with intellectual disability | 1.7% | 1 |
| Only adults and maternal PKU | 1.7% | 1 |
| <i>answered question</i> | 90.0% | 54 |
| <i>skipped question</i> | 10.0% | 6 |
| <i>total</i> | 100.0% | 60 |

1d: With which group(s) of PKU patients are you involved?

N=61

- All patients with PKU
- Only newborns, children and teenagers
- Only newborns, children and teenagers and PKU patients with intellectual disability
- Only adults and maternal PKU



Survey on PKU care in Eastern Europe and neighbouring countries

1e. How many centres or clinics offer a PKU service in your country? (leave blank if you do not know)

| Answer Options | Total (combined answers from single country) | median | min | max | Response Percent | Response Count |
|--------------------------------|--|--------------------------|-----|-----|------------------|----------------|
| Number of centres and clinics: | 45 | 4 | 1 | 11 | n/a | 27 |
| | | <i>answered question</i> | | | 87.1% | 27 |
| | | <i>skipped question</i> | | | 12.9% | 4 |
| | | <i>total</i> | | | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

1f. Approximately how many PKU patients (treated and untreated) are there in your country? (leave blank if you do not know)

| Answer Options | Total (combined answers from single country) | median | min | max | Response Percent | Response Count |
|---------------------|---|--------------------------|-----|--------|---------------------|-------------------|
| Number of patients: | 15,732 | 350 | 6 | 10,000 | n/a | 21 |
| | | <i>answered question</i> | | | 67.7% | 21 |
| | | <i>skipped question</i> | | | 32.3% | 10 |
| | | <i>total</i> | | | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

1i. Please approximate the distribution of all PKU patients followed over the course of a typical (i.e. average) year at your clinic/centre, as follows: (leave blank if you do not know)

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|--|------------------|------|--------|-----|--------------------------|------------------|----------------|
| Percentage of children (<18 years of age): | 75.4 | 17.8 | 80 | 40 | 100 | 87.1% | 27 |
| Percentage of adults (≥18 years of age): | 24.6 | 17.8 | 20 | 0 | 60 | 87.1% | 27 |
| | | | | | <i>answered question</i> | 87.1% | 27 |
| | | | | | <i>skipped question</i> | 12.9% | 4 |
| | | | | | <i>total</i> | 100.0% | 31 |

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| 0 | 12.9% | 4 |
| 1-10 | 12.9% | 4 |
| 11-25 | 22.6% | 7 |
| 26-50 | 32.3% | 10 |
| ≥51 | 6.5% | 2 |
| <i>answered question</i> | 87.1% | 27 |
| <i>skipped question</i> | 12.9% | 4 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

1m. Approximately what is the average distance (km) that PKU patients currently have to travel to your centre? (leave blank if you do not know)

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|-----------------------|------------------|-------|--------|-----|-----|--------------------------|----------------|
| Number of kilometers: | 136.8 | 114.3 | 110 | 10 | 500 | n/a | 26 |
| | | | | | | <i>answered question</i> | 83.9% |
| | | | | | | <i>skipped question</i> | 16.1% |
| | | | | | | <i>total</i> | 100.0% |
| | | | | | | | 26 |
| | | | | | | | 5 |
| | | | | | | | 31 |

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| 1-10 | 6.5% | 2 |
| 11-50 | 19.4% | 6 |
| 51-100 | 16.1% | 5 |
| 101-200 | 29.0% | 9 |
| ≥201 | 12.9% | 4 |
| <i>answered question</i> | 83.9% | 26 |
| <i>skipped question</i> | 16.1% | 5 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

1n. Approximately how many PKU patients at your centre are followed in another country? (leave blank if you do not know)

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|---------------------|------------------|-----|--------|-----|--------------------------|------------------|----------------|
| Number of patients: | 2.6 | 4.0 | 1 | 0 | 20 | n/a | 28 |
| | | | | | <i>answered question</i> | 90.3% | 28 |
| | | | | | <i>skipped question</i> | 9.7% | 3 |
| | | | | | <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

| 2a-ii If yes, is the programme public or private? | | |
|---|------------------|----------------|
| Answer Options | Response Percent | Response Count |
| Public | 96.8% | 30 |
| Private | 0.0% | 0 |
| Partially public, partially private | 0.0% | 0 |
| <i>answered question</i> | 96.8% | 30 |
| <i>skipped question</i> | 3.2% | 1 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

| 2a-iii If yes, does it exist at a regional or national level? | | |
|---|------------------|----------------|
| Answer Options | Response Percent | Response Count |
| At a regional level: | 6.5% | 2 |
| At a national level: | 87.1% | 27 |
| <i>answered question</i> | 93.5% | 29 |
| <i>skipped question</i> | 6.5% | 2 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

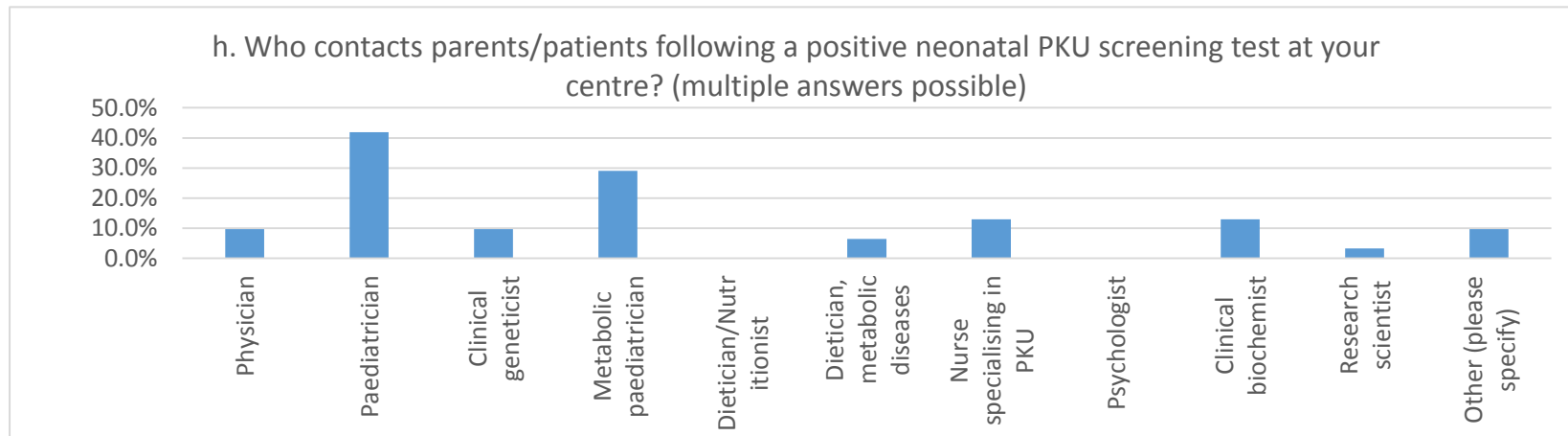
2b. When was neonatal screening implemented? (please provide year as YYYY; eg. 2013)

| Answer Options | | Response Average | SD | median | min | max | Response Percent | Response Count | |
|---------------------------------|----------------|------------------|----------------|--------|------|------|---------------------------------|----------------|-----------|
| At a regional level: | | 1982 | 13.6 | 1985 | 1964 | 2009 | 54.8% | 17 | |
| At a national level: | | 1989 | 12.5 | 1986 | 1975 | 2011 | 90.3% | 28 | |
| | | | | | | | <i>answered question</i> | 96.8% | 30 |
| | | | | | | | <i>skipped question</i> | 3.2% | 1 |
| | | | | | | | <i>total</i> | 100.0% | 31 |
| Regional | Answer Options | Response Percent | Response Count | | | | | | |
| | 1960s | 12.9% | 4 | | | | | | |
| | 1970s | 9.7% | 3 | | | | | | |
| | 1980s | 16.1% | 5 | | | | | | |
| | 1990s | 12.9% | 4 | | | | | | |
| | 2000s | 3.2% | 1 | | | | | | |
| | 2010s | 0.0% | 0 | | | | | | |
| <i>answered question</i> | | 54.8% | 17 | | | | | | |
| <i>skipped question</i> | | 45.2% | 14 | | | | | | |
| <i>total</i> | | 100.0% | 31 | | | | | | |
| National | Answer Options | Response Percent | Response Count | | | | | | |
| | 1960s | 0.0% | 0 | | | | | | |
| | 1970s | 25.8% | 8 | | | | | | |
| | 1980s | 29.0% | 9 | | | | | | |
| | 1990s | 9.7% | 3 | | | | | | |
| | 2000s | 19.4% | 6 | | | | | | |
| | 2010s | 6.5% | 2 | | | | | | |
| <i>answered question</i> | | 90.3% | 28 | | | | | | |
| <i>skipped question</i> | | 9.7% | 3 | | | | | | |
| <i>total</i> | | 100.0% | 31 | | | | | | |

Survey on PKU care in Eastern Europe and neighbouring countries

2h. Who contacts parents/patients following a positive neonatal PKU screening test at your centre? (multiple answers possible)

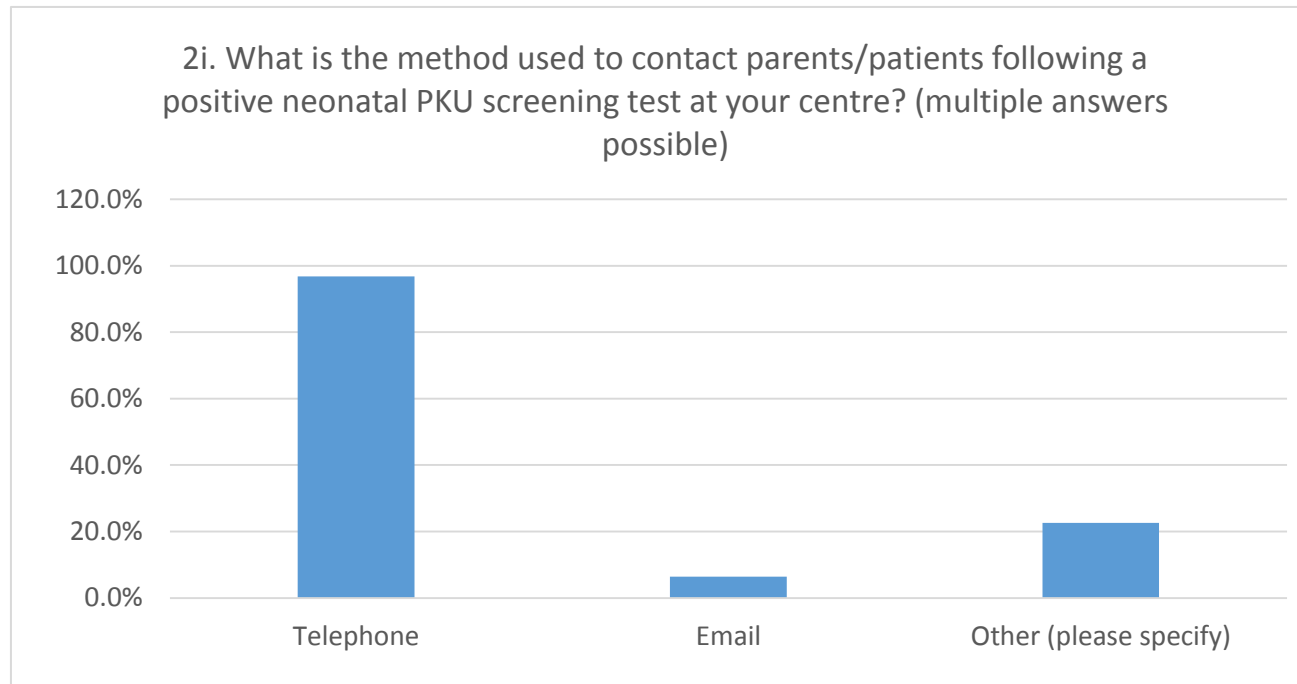
| Answer Options | Response Percent | Response Count |
|-------------------------------|------------------|----------------|
| Physician | 9.7% | 3 |
| Paediatrician | 41.9% | 13 |
| Clinical geneticist | 9.7% | 3 |
| Metabolic paediatrician | 29.0% | 9 |
| Dietician/Nutritionist | 0.0% | 0 |
| Dietician, metabolic diseases | 6.5% | 2 |
| Nurse specialising in PKU | 12.9% | 4 |
| Psychologist | 0.0% | 0 |
| Clinical biochemist | 12.9% | 4 |
| Research scientist | 3.2% | 1 |
| Other (please specify) | 9.7% | 3 |
| <i>answered question</i> | 93.5% | 29 |
| <i>skipped question</i> | 6.5% | 2 |
| <i>total</i> | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

2i. What is the method used to contact parents/patients following a positive neonatal PKU screening test at your centre? (multiple answers possible)

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Telephone | 96.8% | 30 |
| Email | 6.5% | 2 |
| Other (please specify) | 22.6% | 7 |
| <i>answered question</i> | 96.8% | 30 |
| <i>skipped question</i> | 3.2% | 1 |
| <i>total</i> | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

2j. Is the confirmatory diagnosis of PKU and introduction of treatment performed for in-patients or out-patients at your centre? (multiple answers possible)

| Answer Options | Response Percent | Response Count |
|--|------------------|----------------|
| In-patients (i.e. patients admitted to the | 71.0% | 22 |
| Out-patients (i.e. patients attending a clinic | 35.5% | 11 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

2o. If your centre performs BH4 loading tests, are they generally done before starting with a low-phenylalanine (Phe) diet?

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Yes | 38.7% | 12 |
| No | 35.5% | 11 |
| <i>answered question</i> | 74.2% | 23 |
| <i>skipped question</i> | 25.8% | 8 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

2r-ii If yes, what is the method used for pterins analysis? (multiple answers possible)

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| in urine | 32.3% | 10 |
| in dry blood spot | 19.4% | 6 |
| <i>answered question</i> | 45.2% | 14 |
| <i>skipped question</i> | 54.8% | 17 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

2t If yes, would the information be included in the BIOPKU database (www.biopku.org)?

| Answer Options | Response Percent | Response Count |
|---------------------------------|------------------|----------------|
| Yes | 19.4% | 6 |
| No | 35.5% | 11 |
| I am not aware of this database | 16.1% | 5 |
| <i>answered question</i> | 71.0% | 22 |
| <i>skipped question</i> | 29.0% | 9 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

3d. Does your centre allow breastfeeding in neonates and infants with PKU?

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Yes | 96.8% | 30 |
| No | 3.2% | 1 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

3h. BH4 treatment is:

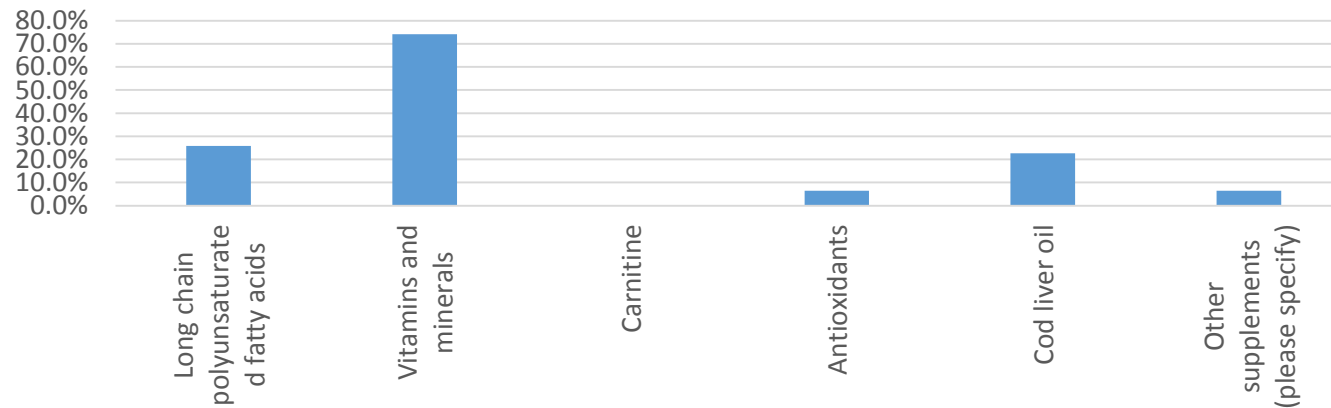
| Answer Options | Response Percent | Response Count |
|---|------------------|----------------|
| Available at all PKU centres in your country | 48.4% | 15 |
| Available at your centre, but not necessarily | 0.0% | 0 |
| Not available at your centre, but might be | 6.5% | 2 |
| Not available anywhere in your country | 38.7% | 12 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

3j. Do PKU patients at your centre take any of the additional supplements (besides in Phe-free protein substitutes) on the following list? (Multiple answers are possible; if the

| Answer Options | Response Percent | Response Count |
|--|------------------|----------------|
| Long chain polyunsaturated fatty acids | 25.8% | 8 |
| Vitamins and minerals | 74.2% | 23 |
| Carnitine | 0.0% | 0 |
| Antioxidants | 6.5% | 2 |
| Cod liver oil | 22.6% | 7 |
| Other supplements (please specify) | 6.5% | 2 |
| <i>answered question</i> | 80.6% | 25 |
| <i>skipped question</i> | 19.4% | 6 |
| <i>total</i> | 100.0% | 31 |

3j. Do PKU patients at your centre take any of the additional supplements (besides in Phe-free protein substitutes) on the following list? (Multiple answers are possible; if the answer is no, leave blank)



Survey on PKU care in Eastern Europe and neighbouring countries

4e. Approximately what is the average return time of routine Phe control results to your patients, after blood sampling?

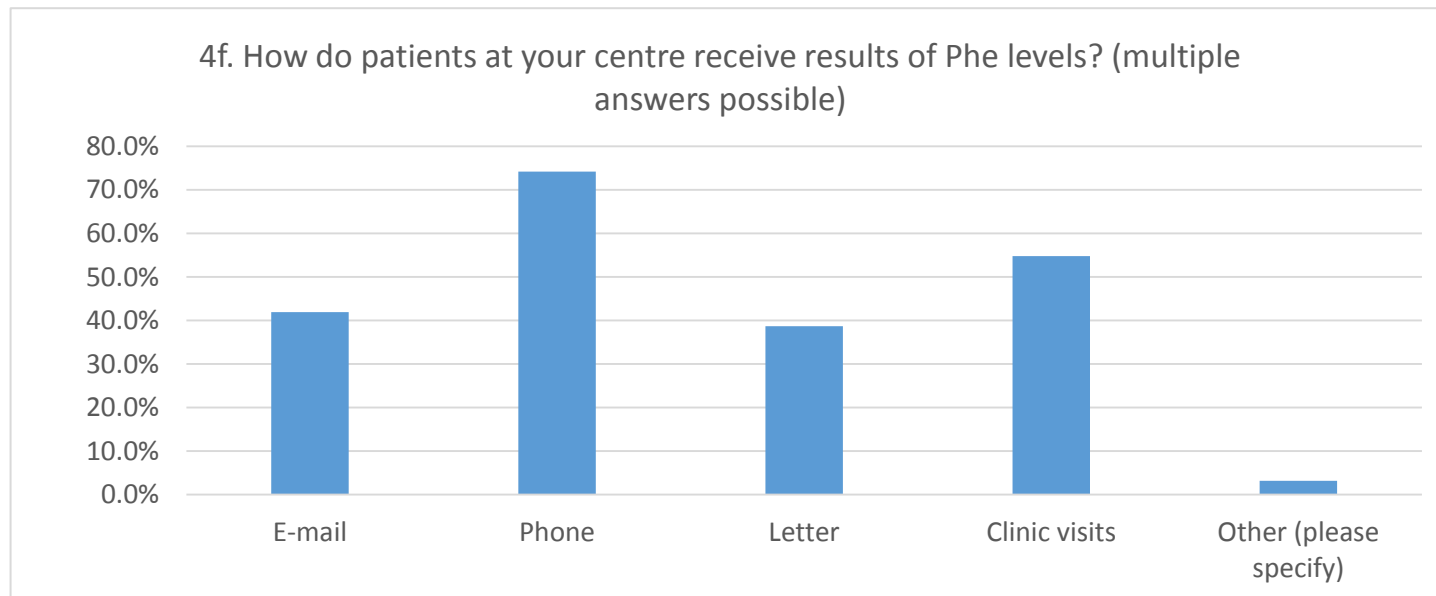
| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|-----------------|------------------|-----|--------|-----|-----|--------------------------|----------------|
| Number of days: | 3.8 | 2.1 | 3 | 1 | 8 | n/a | 30 |
| | | | | | | <i>answered question</i> | 96.8% |
| | | | | | | <i>skipped question</i> | 3.2% |
| | | | | | | <i>total</i> | 100.0% |
| | | | | | | | 30 |
| | | | | | | | 1 |
| | | | | | | | 31 |

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| 1-2 | 25.8% | 8 |
| 3-4 | 35.5% | 11 |
| 5-6 | 16.1% | 5 |
| 7-8 | 19.4% | 6 |
| <i>answered question</i> | 96.8% | 30 |
| <i>skipped question</i> | 3.2% | 1 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

4f. How do patients at your centre receive results of Phe levels? (multiple answers possible)

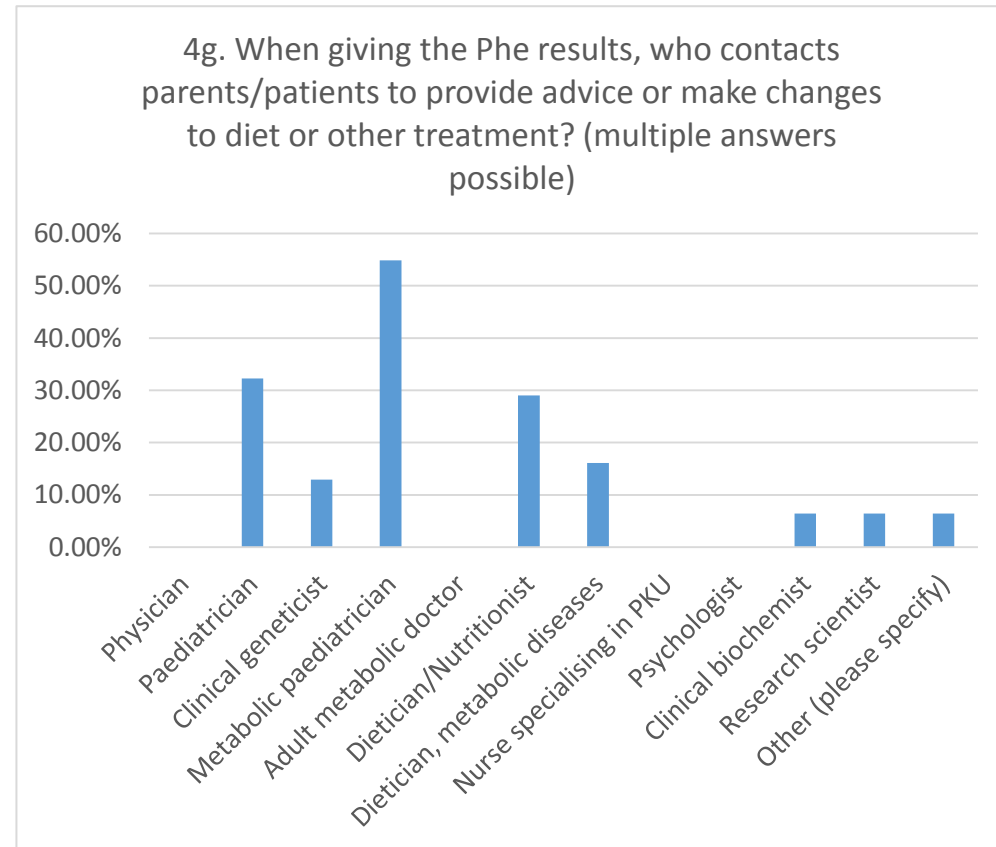
| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| E-mail | 41.9% | 13 |
| Phone | 74.2% | 23 |
| Letter | 38.7% | 12 |
| Clinic visits | 54.8% | 17 |
| Other (please specify) | 3.2% | 1 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

4g. When giving the Phe results, who contacts parents/patients to provide advice or make changes to diet or other treatment? (multiple answers possible)

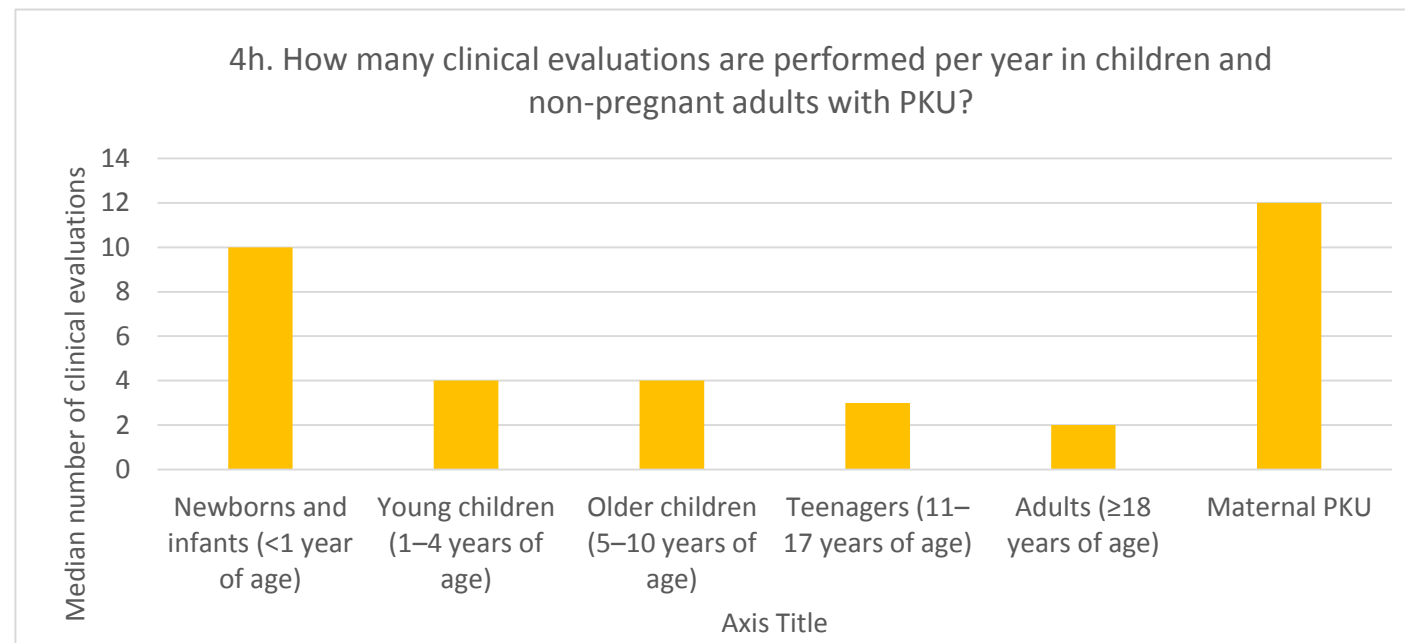
| Answer Options | Response Percent | Response Count |
|---------------------------------|------------------|----------------|
| Physician | 0.0% | 0 |
| Paediatrician | 32.3% | 10 |
| Clinical geneticist | 12.9% | 4 |
| Metabolic paediatrician | 54.8% | 17 |
| Adult metabolic doctor | 0.0% | 0 |
| Dietician/Nutritionist | 29.0% | 9 |
| Dietician, metabolic diseases | 16.1% | 5 |
| Nurse specialising in PKU | 0.0% | 0 |
| Psychologist | 0.0% | 0 |
| Clinical biochemist | 6.5% | 2 |
| Research scientist | 6.5% | 2 |
| Other (please specify) | 6.5% | 2 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

4h. How many clinical evaluations are performed per year in children and non-pregnant adults with PKU?

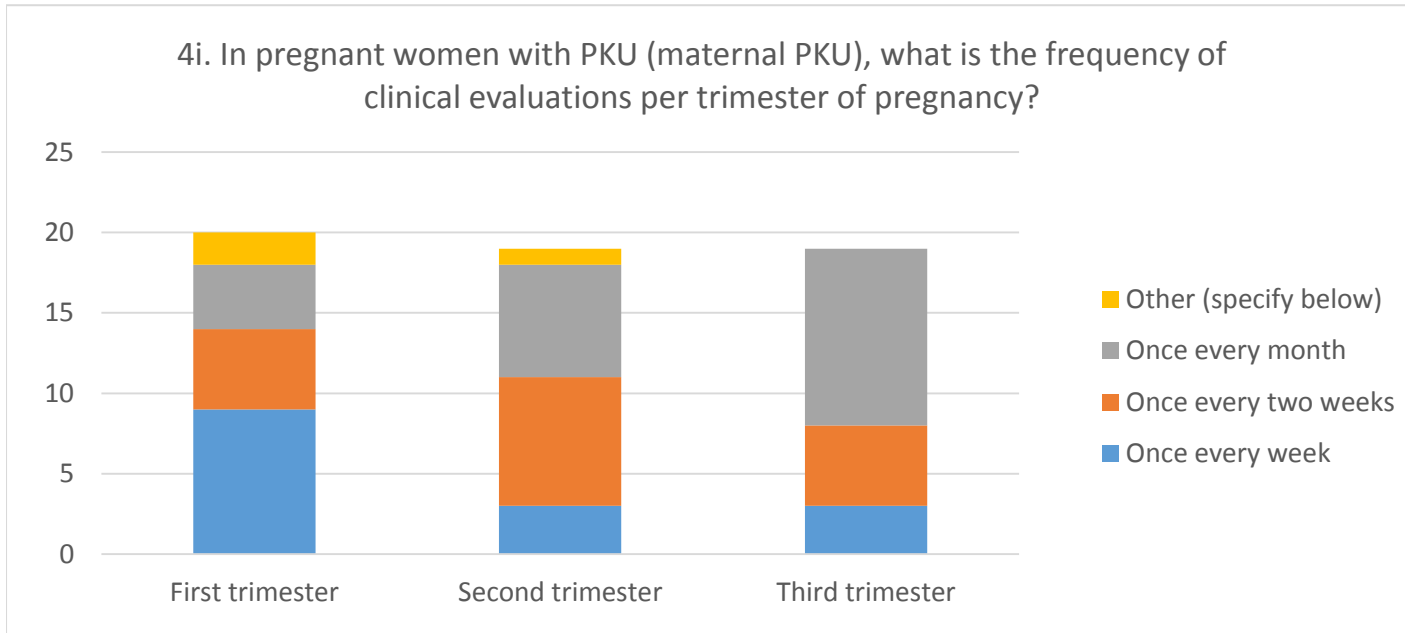
| Answer Options | Response Average | SD | Median | Min | Max | Response Percent | Response Count |
|---------------------------------------|------------------|------|--------|-----|-----|------------------|----------------|
| Newborns and infants (<1 year of age) | 11.76 | 9.76 | 10 | 4 | 24 | 93.5% | 29 |
| Young children (1-4 years of age) | 7.34 | 9.49 | 4 | 2 | 12 | 93.5% | 29 |
| Older children (5-10 years of age) | 4.52 | 4.80 | 4 | 1 | 10 | 93.5% | 29 |
| Teenagers (11-17 years of age) | 3.66 | 3.07 | 3 | 1 | 15 | 93.5% | 29 |
| Adults (≥18 years of age) | 3.13 | 4.85 | 2 | 1 | 25 | 77.4% | 24 |
| Maternal PKU | 10.45 | 6.39 | 12 | 1 | 25 | 64.5% | 20 |
| answered question | | | | | | 93.5% | 29 |
| skipped question | | | | | | 6.5% | 2 |
| total | | | | | | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

4i. In pregnant women with PKU (maternal PKU), what is the frequency of clinical evaluations per trimester of pregnancy?

| Answer Options | Once every week | Once every two weeks | Once every month | Other (specify below) | Response Percent | Response Count | |
|---|-----------------|----------------------|------------------|-----------------------|------------------|----------------|-----------|
| First trimester | 9 | 5 | 4 | 2 | 64.5% | 20 | |
| Second trimester | 3 | 8 | 7 | 1 | 61.3% | 19 | |
| Third trimester | 3 | 5 | 11 | 0 | 61.3% | 19 | |
| <i>answered question</i> | | | | | 16 | 67.7% | 21 |
| <i>skipped question</i> | | | | | 13 | 32.3% | 10 |
| <i>total</i> | | | | | 100.0% | 31 | |
| Question totals | | | | | | 5 | |
| <i>Specify here if other frequencies are used in each trimester</i> | | | | | | | |



Survey on PKU care in Eastern Europe and neighbouring countries

5a. Are you aware of published guidelines or protocols for PKU diagnosis and treatment?

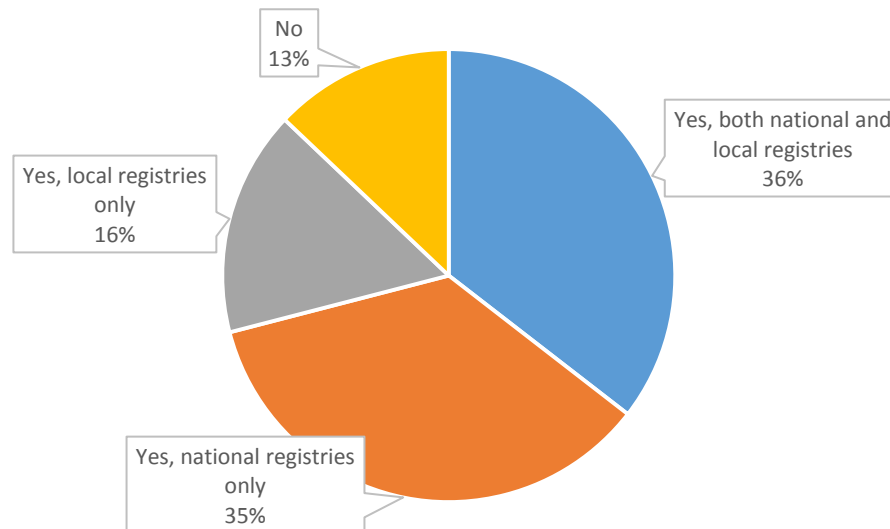
| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Yes | 80.6% | 25 |
| No | 12.9% | 4 |
| <i>answered question</i> | 93.5% | 29 |
| <i>skipped question</i> | 6.5% | 2 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

5c. Do you have a local or national PKU patient registry?

| Answer Options | Response Percent | Response Count |
|---|------------------|----------------|
| Yes, both national and local registries | 35.5% | 11 |
| Yes, national registries only | 35.5% | 11 |
| Yes, local registries only | 16.1% | 5 |
| No | 12.9% | 4 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |

5c. Do you have a local or national PKU patient registry?



Survey on PKU care in Eastern Europe and neighbouring countries

5d. Are there any organisations (eg. scientific societies, groups of interest, or others) dedicated to professionals involved in PKU treatment in your country?

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Yes | 58.1% | 18 |
| No | 41.9% | 13 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |

Survey on PKU care in Eastern Europe and neighbouring countries

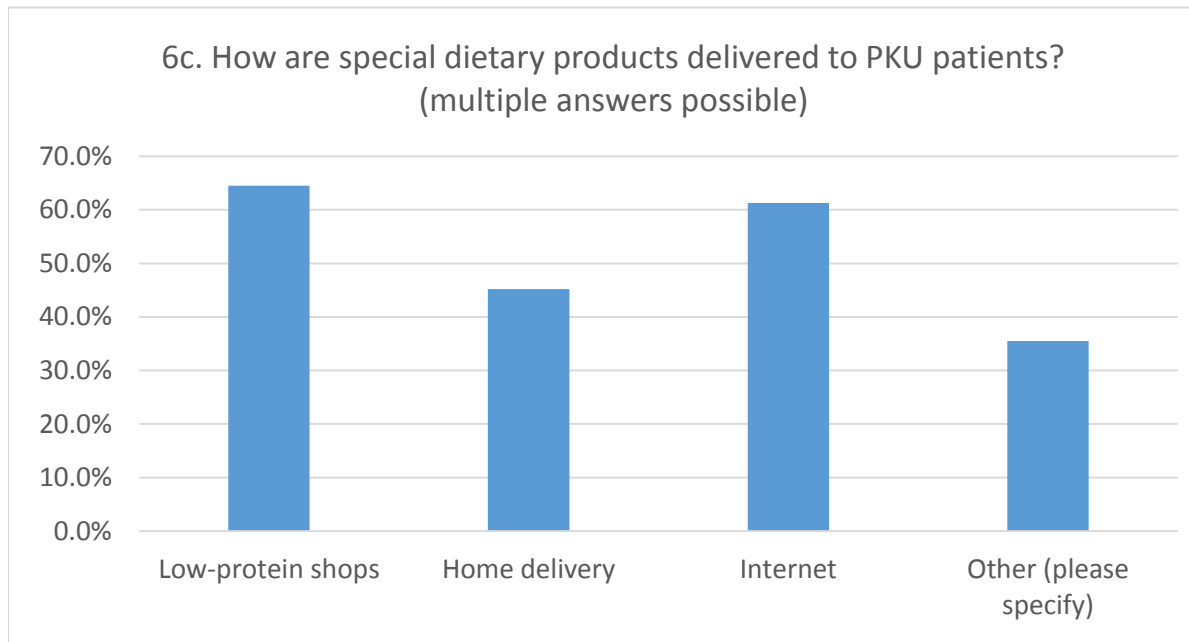
6a. How many kinds of Phe-free protein substitutes are available in your country?

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count | |
|--|--------------------------|-------------------------|-----------------------|-----|-----|--------------------------|----------------|-----------|
| Number of different Phe-free protein substances: | 14.4 | 21.2 | 6 | 1 | 100 | n/a | 28 | |
| | | | | | | <i>answered question</i> | 90.3% | 28 |
| | | | | | | <i>skipped question</i> | 9.7% | 3 |
| | | | | | | <i>total</i> | 100.0% | 31 |
| | Answer Options | Response Percent | Response Count | | | | | |
| | 1-5 | 45.2% | 14 | | | | | |
| | 6-10 | 19.4% | 6 | | | | | |
| | 11-20 | 6.5% | 2 | | | | | |
| | 21-100 | 19.4% | 6 | | | | | |
| | <i>answered question</i> | 90.3% | 28 | | | | | |
| | <i>skipped question</i> | 9.7% | 3 | | | | | |
| | <i>total</i> | 100.0% | 31 | | | | | |

Survey on PKU care in Eastern Europe and neighbouring countries

6c. How are special dietary products delivered to PKU patients? (multiple answers possible)

| Answer Options | Response Percent | Response Count |
|--------------------------|------------------|----------------|
| Low-protein shops | 64.5% | 20 |
| Home delivery | 45.2% | 14 |
| Internet | 61.3% | 19 |
| Other (please specify) | 35.5% | 11 |
| <i>answered question</i> | 100.0% | 31 |
| <i>skipped question</i> | 0.0% | 0 |
| <i>total</i> | 100.0% | 31 |



Survey on PKU care in Eastern Europe and neighbouring countries

6d. How many pharmaceutical companies supply Phe-free protein substitutes in your country? (leave blank if you do not know)

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|-------------------------------------|------------------|-----|--------|-----|-----|--------------------------|----------------|
| Number of pharmaceutical companies: | 2.6 | 1.0 | 3 | 0 | 4 | n/a | 26 |
| | | | | | | <i>answered question</i> | 83.9% |
| | | | | | | <i>skipped question</i> | 16.1% |
| | | | | | | <i>total</i> | 100.0% |
| | | | | | | | 26 |
| | | | | | | | 5 |
| | | | | | | | 31 |

| Answer Options | Response Percent | Response Count |
|----------------|--------------------------|----------------|
| 0 | 3.2% | 1 |
| 1 | 9.7% | 3 |
| 2 | 16.1% | 5 |
| 3 | 41.9% | 13 |
| 4 | 12.9% | 4 |
| | <i>answered question</i> | 83.9% |
| | <i>skipped question</i> | 16.1% |
| | <i>total</i> | 100.0% |

Survey on PKU care in Eastern Europe and neighbouring countries

6e. How many companies supply low-protein foods in your country? (leave blank if you do not know)

| Answer Options | Response Average | SD | median | min | max | Response Percent | Response Count |
|--------------------------|------------------|----------------|--------|-----|-----|--------------------------|----------------|
| Number of companies: | 4.3 | 4.0 | 4 | 1 | 20 | n/a | 23 |
| | | | | | | <i>answered question</i> | 74.2% |
| | | | | | | <i>skipped question</i> | 25.8% |
| | | | | | | <i>total</i> | 100.0% |
| | | | | | | | 23 |
| | | | | | | | 8 |
| | | | | | | | 31 |
| Answer Options | Response Percent | Response Count | | | | | |
| 1-2 | 25.8% | 8 | | | | | |
| 3-5 | 35.5% | 11 | | | | | |
| 6-10 | 9.7% | 3 | | | | | |
| 11-20 | 3.2% | 1 | | | | | |
| <i>answered question</i> | 74.2% | 23 | | | | | |
| <i>skipped question</i> | 25.8% | 8 | | | | | |
| <i>total</i> | 100.0% | 31 | | | | | |