

UNIVERSITÀ DEGLI STUDI DI TRIESTE
Dipartimento Universitario Clinico di Scienze
mediche, chirurgiche e della salute



Laurea Magistrale in Medicina e Chirurgia

**Cost-effectiveness of the italian screening protocol
for international adoptees**

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Relatore
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Anno Accademico 2017/2018

*“Every single minute matters,
every single child matters,
every single childhood matters.”*

- Kailash Satyarthi, Indian children's rights activist

Abstract (Italian)

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Abstract

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Acknowledgements

To my friends *I Cazzilli*: Fede, Lorenz, Grismina and Ste, for always being worthy of being the family I chose for myself and for looking out for me day after day.

To Emme, for showing me what true compassion is and inspiring me to be a better version of myself everyday.

To Carol, the closest tea-brewing sister I could hope for. I'm truly proud of you.

To my Mom, for teaching me, among another thousand things, her own personal special way of calling somewhere "*home*".

To my Dad, for always trying to be the man he ought to be.

To the rest of my strange, enlarged family, for always supporting me in every possible way.

To Luca, my tireless desk-mate and friend, who never called himself out of an all-nighter and who always speaks a word of kindness or dedication in times of need.

To Valentina, who helped me stand in times when I couldn't stand for myself.

To Matteo, an amazing companion in this journey through pediatrics, data sets and enthusiastic English-vocabulary show off.

To dott. Monasta, for making sense of numbers that didn't seem to have any.

To prof. Barbi and prof. Ventura, for remembering me that medicine can be how i dreamed it.

And lastly, to myself, for always believing that, even when your heart's lost all its hope, after dawn there will be sunshine.

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Abbreviations

MCV **M**ean **C**orpuscular **V**alue

VBA **V**isual **B**asic for **A**pplications

Chapter 1

Introduction

Children's health has historically been a sensitive and concerning matter for human kind, both because we, as a whole species, are instinctively drawn towards the protection and care for our offspring, and because children are often struck with some of the most devastating and life-wrecking diseases, also due to the genetical marks scared onto these kids. Despite the origin, the color the skin or the culture the child bears in its lineage, human beings feel the need to raise him and safeguard him from the harms on a physical, emotional and spiritual level. This is one of the strongest biological calls to action. Thus pediatrics must care and remember that children's health and well-being must be guarded across political borders, across poverty, across starvation. This thesis, and the paper its so deeply bound to, set themselves to renew this vow.

1.1 International Adoptees

This is a kid with special needs.

If I reference here a piece of code: does it work? 5.5 at 18.

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1.1.1 International adoptions in Italy

Being a rather open-ended project, i.e. a project in which there is no strict and well-defined set of software requirement specifications, the objectives of the development have been purposefully kept wide and general, as to reflect the idea that the project could follow an exploratory approach.

Nonetheless, there are still some guidelines that have been followed from the beginning to the end of the project:

- The project shall result in a working prototype of a Virtual Reality application.
- The application shall allow the handling of CFD data; in particular, it shall provide:
 - visualization of the data,
 - interaction with the data,
 - some basic forms of manipulation of the data.
- The application shall allow the import of data from ParaView.
- The application shall run compatibly at least on Windows (version 7 or greater), and optionally on Linux.
- The application shall support a HTC Vive kit.
- The code should be designed to be maintainable, flexible and expandable.
- The application should be easy to use, being it aimed at CFD scientists with little to no prior VR experience.

1.1.1.1 Adoptions in Europe and in the world

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1.2 Health status and screening protocols

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1.2.1 Health status and screening protocols in Italy

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1.2.2 Health status and screening protocols in the world

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1.3 Illnesses and dysfunctions under exam

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1.3.0.1 Infectious diseases

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1.3.0.2 Blood count disorders and deficiency states

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1.3.0.3 Height-weight disorders

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Chapter 2

Materials and Methods

2.1 The data set

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2.1.1 The population in exam

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2.1.2 Inclusion and exclusion criteria

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2.2 Data set elaboration

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2.2.1 VBA expressions

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All VBA expression can be found in Appendix A at page 23.

2.2.2 Cut-off values

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2.2.2.1 Haemoglobin

This was a little prick.

2.2.2.2 MCV

This was ANOTHER little prick.

2.2.2.3 Circulating Iron

This was easy.

2.2.2.4 Vitamin D

Vitamin D is healthy. 25OH...

2.3 Statistical Analyses

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Chapter 3

Results

3.1 Introduction

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3.2 Risultati 1

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nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

3.3 Risultati 2

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

3.4 Risultati 3

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

Chapter 4

Discussion

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

4.1 Objectives achieved

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

4.2 Our recommendations

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

4.3 Future work

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Pellentesque nibh metus, suscipit a scelerisque sit amet, rhoncus et lectus. Mauris eget erat rutrum, euismod massa id, maximus mauris. Nulla maximus, ex sit amet lacinia consequat, enim ante mollis dui, sit amet tincidunt massa felis id magna. Aenean gravida ante nec volutpat rutrum. Cras eget ullamcorper leo. Curabitur eu volutpat tellus. Integer nec ornare sapien. Fusce ipsum justo, interdum quis libero a, mattis tristique velit. Phasellus rhoncus lorem non ultrices luctus.

Chapter 5

How to Do

This is all I know on LaTeX up to now.

5.1 Including Sections and Subsections

This is my first section.

5.1.1 I like myself

I'm nice.

5.1.2 but I'm weird

but fun.

5.1.2.1 LOST OF FUN!

Writing writing and writing.

5.1.2.2 I'm calm and shit

I write stuff in subsubsections.

And lastly this is new and amazing PARAGRAPH: You can write whatever you want and it's pretty cool and new. I still like subsubsections more.

5.2 Including references and citations

This is pretty simple to cite: developed as open-source C++ software by Rudolf Biczok [3]. We'll learn more about this as we go. Let's see if they change order [1]. They should've change [2].

5.2.1 Referencing images and tables!

So you can see figure 5.1 at page 21. AMAZING
OR you can also see the table 5.1 at page 21!

5.2.2 Referencing chapters and subchapters

You can also ref chapters, as Chapter Results 3.

5.2.3 Using footnotes

Let's try this out.¹ And another one to see if it is progressive and shit.²

¹This is my first footnote.

²CAREFUL! Don't leave any spaces before the command or they will be rendered.

I'll try now to “place them manually”. This is were the sign is.³
Somewhere else in the text. I insert what it contains.

5.3 Including quotes

This is how a quote looks.

From an evolutionary perspective, virtual reality is seen as a way to overcome limitations of standard human-computer interfaces; from a revolutionary perspective, virtual reality technology opens the door to new types of applications that exploit the possibilities offered by presence simulation.

And also in text quotes: “[by] immersing the user in the solution, virtual reality reveals the spatially complex structures in computational science in a way that makes them easy to understand and study”.

And dots...

5.4 Including URLs

We can include `https://github.com/vrcranfield/UnityApplication`.

5.5 Including code

The following code is written by Lorenzo:

³This is my footnote!

```
=IF(
  OR(
    E68 = "Russia";
    E68 = "Albania";
    E68 = "Bulgaria";
    E68 = "Ungheria";
    E68 = "Ucraina";
    E68 = "Moldavia";
    E68 = "Romania"
  );
  "Europa dell'Est";
  IF(
    OR(
      E68 = "Burkina Faso";
      E68 = "Etiopia";
      E68 = "Costa d'Avorio";
      E68 = "Congo";
      E68 = "Guinea Bissau";
      E68 = "Africa";
      E68 = "Ghana";
      E68 = "Benin"
    );
    "Africa";
    IF(
      OR(
        E68 = "Colombia";
        E68 = "Brasile";
        E68 = "Guatemala";
        E68 = "Peru";
        E68 = "Costa Rica"
      );
      "America del Sud";
      IF(
        OR(
          E68 = "Armenia";
          E68 = "India";
          E68 = "Cina";
          E68 = "Vietnam";
          E68 = "Sri Lanka";
          E68 = "Siberia";
          E68 = "Nepal";
          E68 = "Filippine"
        );
        "Asia";
        ""
      )
    )
  )
)
```

5.6 Formatting Text

This is **BOLD** *This is ITALIC* This is SANS SERIF This is TRUE TYPE

In this sentence THIS IS TINY. THIS WHOLE SENCE IS TINY.

I go back to normal.

Then I can go for large, or Large, or Larger, or Huge and even HUGE.

5.7 Including bulleted list

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nam quam tellus, venenatis a consectetur non, pretium ac nunc. Nullam eu tellus sed augue laoreet scelerisque.

- The first item of your list
- The second item of your list
- The third item of your list

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nam quam tellus, venenatis a consectetur non, pretium ac nunc. Nullam eu tellus sed augue laoreet scelerisque. Curabitur efficitur, dolor ut pretium fermentum, nisi enim pulvinar nunc, non bibendum urna odio nec neque. Cras tellus turpis, posuere in dictum vitae, vestibulum quis velit.

1. The first item of your list
2. The second item of your list
3. The third item of your list

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nam quam tellus, venenatis a consectetur non, pretium ac nunc. Nullam eu tellus sed augue laoreet scelerisque. Curabitur efficitur, dolor ut pretium fermentum, nisi enim pulvinar nunc, non bibendum urna odio nec neque. Cras tellus turpis, posuere in dictum vitae, vestibulum quis velit.

- a) The first item of your list
- b) The second item of your list
- c) The third item of your list

5.8 Including Figures

Orci varius natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam vulputate finibus malesuada. Praesent at egestas turpis. Vivamus vitae tellus malesuada, laoreet ex ac, venenatis est. Aliquam dictum tincidunt libero, cursus posuere arcu sodales non. In sed metus sit amet arcu vestibulum mollis ut vel nibh. Nam non velit tortor. Integer ac sapien a purus porta convallis. In vestibulum aliquam nunc vitae faucibus. Etiam tristique iaculis orci, vel aliquam felis accumsan et. Nulla ultricies, nisl eu malesuada lobortis, ante metus faucibus libero, vitae blandit odio enim sit amet tortor.

5.9 Including Tables

Orci varius natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam vulputate finibus malesuada. Praesent at egestas turpis. Vivamus vitae tellus malesuada, laoreet ex ac, venenatis est. Aliquam dictum tincidunt libero, cursus posuere arcu sodales non. In sed metus sit amet arcu vestibulum mollis ut vel nibh. Nam non velit tortor. Integer ac sapien a purus porta convallis. In vestibulum aliquam nunc vitae faucibus. Etiam tristique iaculis orci, vel aliquam



FIGURE 5.1: Living room as I imagine it

Source: Photo courtesy of HTC

felis accumsan et. Nulla ultricies, nisl eu malesuada lobortis, ante metus faucibus libero, vitae blandit odio enim sit amet tortor.

Day	Max Temp	Min Temp
Mon	20	13
Tue	22	14
Wed	23	12
Thurs	25	13
Fri	18	7
Sat	15	13
Sun	20	13

(A) First Week

Day	Max Temp	Min Temp
Mon	17	11
Tue	16	10
Wed	14	8
Thurs	12	5
Fri	15	7
Sat	16	12
Sun	15	9

(B) Second Week

TABLE 5.1: Max and min temps recorded in the first two weeks of July

ParaView			
VTK			
OpenGL	MPI	OpenVR	Etc.

TABLE 5.2: ParaView-VTK Architecture (simplified)

Appendix A

Data set elaboration: VBA expressions

This appendix provides all the code used in this thesis to elaborate the data set. Visual Basic for Application (VBA) is the programming language chosen for this purpose, as the most effective and manageable way of elaborating data in excel sheets. Further information can be found throughout this thesis, especially in Section 2.2 at page 8.

In the following appendix, cells are indicated as combination of a letter (identifying the column) and a number (identifying the line), as they originally were in the database. Every line represents a single child's evaluation; every column represents one of the examined parameters. The full column-parameter correspondence can be found in following Table A.1.

Column	Parameter	Unit of measure (or cell content type)	Description
<i>A</i>	First and last name	<i>text</i>	The name of
<i>B</i>	Sex	<i>text</i>	The sex of th
<i>C</i>	Age (in months)	months	The age of th

²Although registering the name of the patient posed a risk in terms of possible privacy breach, it was added nonetheless to easily identify each patient as the data set got larger through the years.

D	Age (in years)	years	*. For further
E	Nation of origin	text	*.
F	Geographic area of origin	text	*.

TABLE A.2: Column-parameter correspondence

A.1 Age (in months)

This VBA expression checks the *Age (in months)* column (C) and, if it's not empty, it divides it's value by 12, rounding it down, just as age works. The `ROUNDOWN` function was implemented in order to avoid overestimating child's age.

```
=IF(  
  C2 <> "" ;  
  ROUNDDOWN(  
    C2 / 12;  
    0  
  );  
  ""  
)
```

A.2 Geographic area of origin

To further understand how geographic origin influenced the results of our screening program, every nation was grouped up in 4 major continents or areas with the following excel expression.

```
=IF(  
  OR(  
    ...
```

```
E2 = "Russia";
E2 = "Albania";
E2 = "Bulgaria";
E2 = "Hungary";
E2 = "Ukraine";
E2 = "Moldavia";
E2 = "Romania"
);
"Eastern Europe";
IF(
    OR(
        E2 = "Burkina Faso";
        E2 = "Ethiopia";
        E2 = "Ivory Coast";
        E2 = "Congo";
        E2 = "Guinea Bissau";
        E2 = "Africa";
        E2 = "Ghana";
        E2 = "Benin"
    );
    "Africa";
    IF(
        OR(
            E2 = "Colombia";
            E2 = "Brazil";
            E2 = "Guatemala";
            E2 = "Peru";
            E2 = "Costa Rica"
        );
        "South America";
        IF(
            OR(
                E2 = "Armenia";
                E2 = "India";
                E2 = "China";
                E2 = "Vietnam";
                E2 = "Sri Lanka";
                E2 = "Siberia";
                E2 = "Nepal";
                E2 = "Philippines"
            );
            "Asia";
            ""
        )
    )
)
```

A.3 Pathological values

The data set contained numerical values for many laboratory analyses. Cut-off values for these results were established via the most recent literature review, as explained in Section 2.2.2. In the following sections, the code used to establish which ones were pathological and which were not, is displayed and shortly explained.

A.3.1 Weight and height

These parameters, since they had already been converted to percentile values, were easily implemented with the following simple VBA expression:

```
=IF(  
    H2 <> "";  
    IF(  
        H2 <= 10;  
        1;  
        0  
    );  
    ""  
)
```

A.3.2 Haemoglobin

Hemoglobin required a more complicated and sophisticated expression, in order to be stratified, because hemoglobin pathological cut-offs depend on various factors, as described in Section 2.2.2.1. Moreover mild, moderate and severe anemias had to be separated in order to properly evaluate the child's health status; each one had an arbitrary value of 1 (*mild*), 2 (*moderate*) or 3 (*severe*) associated to it.

```
=IF(  
    L2 <> "";  
    IF(  
        H2 <= 10;  
        1;  
        0  
    );  
    ""  
)
```



```

        C2 >= 132;
        C2 < 168
    );
    IF(
        L2 >= 12;
        0;
        IF(
            AND(
                L2 < 12;
                L2 >= 11
            );
            1;
            IF(
                AND(
                    L2 < 11;
                    L2 >= 8
                );
                2;
                3
            )
        )
    )
)
);
""
)

```

A.3.3 MCV

As just described for haemoglobin, MCV required more complicated techniques in order to be stratified, because of its variability (through age, sex, ecc...), as described in Section 2.2.2.2. Moreover, boolean results couldn't be accepted for this parameter, so arbitrary values were used to appropriately identify microcytic (1) and macrocytic (2) anemias.

```

=IF(
    N2 <> "";
    IF(
        B2 = "F";
        IF(
            AND(

```



```
        C2 >= 0;  
        C2 < 60  
    );  
    IF(  
        N2 > 85;  
        2;  
        IF(  
            AND(  
                N2 <= 85;  
                N2 >= 69  
            );  
            0;  
            1  
        )  
    );  
    IF(  
        AND(  
            C2 >= 60;  
            C2 < 120  
        );  
        IF(  
            N2 > 89;  
            2;  
            IF(  
                AND(  
                    N2 <= 89;  
                    N2 >= 75  
                );  
                0;  
                1  
            )  
        );  
        IF(  
            AND(  
                C2 >= 120;  
                C2 < 168  
            );  
            IF(  
                N2 > 92;  
                2;  
                IF(  
                    AND(  
                        N2 <= 92;  
                        N2 >= 78  
                    );  
                    0;  
                    1  
                )  
            )  
        )  
    )
```

```
)  
)  
);  
IF(  
    B2 = "M";  
    IF(  
        AND(  
            C2 >= 0;  
            C2 < 60  
        );  
        IF(  
            N2 > 85;  
            2;  
            IF(  
                AND(  
                    N2 <= 85;  
                    N2 >= 71  
                );  
                0;  
                1  
            )  
        );  
        IF(  
            AND(  
                C2 >= 60;  
                C2 < 120  
            );  
            IF(  
                N2 > 88;  
                2;  
                IF(  
                    AND(  
                        N2 <= 88;  
                        N2 >= 76  
                    );  
                    0;  
                    1  
                )  
            );  
            IF(  
                AND(  
                    C2 >= 120;  
                    C2 < 168  
                );  
                IF(  
                    N2 > 90;  
                    2;  
                    IF(  
                        AND(  

```

```
        N2 <= 90;  
        N2 >= 76  
    );  
    0;  
    1  
    )  
    )  
    )  
    )  
    );  
    ""  
    )  
    );  
    ""  
    )
```

A.3.4 Circulating iron

The following VBA expression was used to establish whether circulating iron levels were insufficient.

```
=IF(  
    P2 <> "";  
    IF(  
        AND(  
            P2 >= 16;  
            P2 <= 129  
        );  
        0;  
        1  
    );  
    ""  
)
```

A.3.5 Ferritin

The following VBA expression was used to identify pathological ferritin values. These were, again, stratified for *mild* (1), *moderate* (2) and *severe* (3) deficiencies.

```
=IF(  
  R2 <> " ";  
  IF(  
    R2 >= 20;  
    0;  
    IF(  
      AND(  
        R2 < 20;  
        R2 >= 15  
      );  
      1;  
      IF(  
        AND(  
          R2 < 15;  
          R2 >= 10  
        );  
        2;  
        IF(  
          R2 < 10;  
          3  
        )  
      )  
    )  
  );  
  ""  
)
```

A.3.6 Vitamin D

The following VBA expression was used to establish whether Vitamin D (serum 25-hydroxycholecalciferol) values were *insufficient* (1), *deficient* (2) or *severely deficient* (3). The predictive choice for this marker is explained at Section 2.2.2.4.

```
=IF(  

```

```
AA2 <> " ";  
IF(  
    AA2 >= 50;  
    0;  
    IF(  
        AND(  
            AA2 < 50;  
            AA2 >= 25  
        );  
        1;  
        IF(  
            AND(  
                AA2 < 25;  
                AA2 >= 10  
            );  
            2;  
            IF(  
                AA2 < 10;  
                3  
            )  
        )  
    )  
);  
""  
)
```

Column	Parameter	Unit of measure (or cell content type)	Description
A	First and last name	<i>text</i>	The name of the kid. ¹
B	Sex	<i>text</i>	The sex of the kid.
C	Age (in months)	months	The age of the kid.
D	Age (in years)	years	*. For further information, see Section A.1.
E	Nation of origin	<i>text</i>	*.
F	Geographic area of origin	<i>text</i>	*.
G	Residency time in Italy (in months)	months	*.
H	Weight	percentile	*.
I	Pathological weight	<i>boolean</i>	*.
J	Height	percentile	*.
K	Pathological height	<i>boolean</i>	*.
L	Haemoglobin	g/dl	*.
M	Pathological haemoglobin	<i>boolean</i>	*.
N	MCV	fl	*.
O	Pathological MCV	<i>boolean</i>	*.
P	Circulating iron	µg/dl	*.
Q	Pathological circulating iron	<i>boolean</i>	*.
R	Ferritin	ng/ml	*.
S	Pathological ferritin	<i>boolean</i>	*.

TABLE A.1: Column-parameter correspondence

Bibliography

- [1] Totaro C, Bortone B, Putignano P, Sollai S, Galli L, De Martino M, Chiappini E. *Internationally adopted children: not only infectious diseases!*. Journal of Travel Medicine, Brief Communication, pp. 1–5. 2008. doi: 10.1093/jtm/-tay036
- [2] Totaro C, Bortone B, Putignano P, Galli L, De Martino M, Chiappini E. *Bambino adottato: non pensiamo solo alle infezioni!*. Medico e Bambino, Vol. 37, No. 5/2018, pp. 307–3012. May 2018. Available at: https://www.medicoebambino.com/?id=1805_307.pdf [accessed July 2018]
- [3] *Nomenclatore tariffario di specialistica ambulatoriale*. Regione Autonoma Friuli Venezia Giulia. May 2018. Available at: <http://www.regione.fvg.it/rafvig/cms/RAFVG/salute-sociale/sistema-sociale-sanitario/FOGLIA51/> [accessed July 2018]