SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO DETERMINAZIONE

AOO: AOO000

REGISTRO: Determinazione

NUMERO: 0000356

DATA: 05/03/2024 15:53

OGGETTO: Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari esocio-assistenziali con codice progetto PNRR-MAD- dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosisprevention". Affidamento del Servizio di Analisi, presso l'impresa AMOLAB, con metodologia REMS dei dataset ricevuti dall'Azienda e costruzione del database di riferimento e del calcolo delle corrispondenti curve di riferiemento per feti e neonati, fornendo in output all' azienda i risultati di queste elaborazioni in un formato idoneo alla divulgazione scientifica in ambito medico - Determina a contrarre

SOTTOSCRITTO DIGITALMENTE DA:

Michela Boschi

ADOTTATO DA:

S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici

CLASSIFICAZIONI:

- [01-08-07]

DESTINATARI:

- Collegio sindacale: collegiosindacale@ao.pr.it
- S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici

DOCUMENTI:

File	Firmato digitalmente da	Hash
DETE0000356_2024_determina_firmata.pdf	Boschi Michela	481A29102E492010E19B25BB472F922868 0DDF658C3417FBAEAE407DA15A2812

File	Firmato digitalmente da	Hash
DETE0000356_2024_Allegato1.pdf:		668DD37571A6CFC4B44DDEB9F21E2CB CCDA419B98BC97DDC9F85DCD16328E4 32
DETE0000356_2024_Allegato2.pdf:		5972F8B6A4D61A31E66D6AEE9E660CDE A4C40D1974909D2A73051C2518C73591
DETE0000356_2024_Allegato3.pdf:		13754EFB484EDEA9FFA2881E51667082E 777F925B294082D8BCAD6F99A1DF02A
DETE0000356_2024_Allegato4.pdf:		976414C5B93F7BE6560489A37DCD36D19 D81E43A74D5A4E39E89E3F9A6E914D6
DETE0000356_2024_Allegato5.pdf:		382B875E767D56F39273460FAE92676CF D91C9229A82405DDCC12EBE460BAAEA
DETE0000356_2024_Allegato6.pdf:		A375D2C28C0E660D6C7316939DABA169 00F4651305BD78EBE43AE5EDA144DE08
DETE0000356_2024_Allegato7.pdf:		1E5F9CE5BE528069CA364769304DD5A5 8E37A2B1A99084F309E9AD33598728DF

S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici

DETERMINAZIONE

OGGETTO: Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari esocio-assistenziali con codice progetto PNRR-MAD- dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosisprevention". Affidamento del Servizio di Analisi, presso l'impresa AMOLAB, con metodologia REMS dei dataset ricevuti dall'Azienda e costruzione del database di riferimento e del calcolo delle corrispondenti curve di riferiemento per feti e neonati, fornendo in output all'azienda i risultati di queste elaborazioni in un formato idoneo alla divulgazione scientifica in ambito medico - Determina a contrarre

IL DIRETTORE

RICHIAMATO
l'atto deliberativo n. 366 del 27/09/2016 avente oggetto "Istituzione del Dipartimento Interaziendale "Tecnico e Logistica" tra l'Azienda Unità Sanitaria Locale di Parma e l'Azienda Ospedaliero - Universitaria di Parma in attuazione del processo di integrazione delle funzioni di area tecnico- amministrativa e di staff - Articolazione organizzativa - Approvazione della specifica convenzione attuativa - ", competente in materia di acquisizione di beni, servizi e per l'esecuzione dei lavori pubblici;

VISTA la propria competenza ad adottare il presente atto;

CONSIDERATO CHE

- con nota prot. 336 del 17/05/2023, che si allega, si comunicava l' Attivazione del Progetto di Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- , dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)" – Principal Investigator Prof.ssa Serafina Perrone dell'U.O. di Neonatologia dell'Azienda Ospedaliero Universitaria di Parma;
- nella predetta nota si rappresentava la necessità di attivare un contratto di servizi conto terzi finalizzato al proseguio delle attività previste dal progetto di ricerca anzidetto, ammesso a

finanziamento (utilizzo della tecnologia REMS nella popolazione fetale e neonatale per la costruzione preliminare di un database di riferimento), per l'esecuzione di un Servizio di Analisi, con metodologia REMS dei dataset ricevuti dall'Azienda e costruzione del database di riferimentio e del calcolo delle corrispondenti curve di riferiemento per feti e neonati, fornendo in output all'azienda i risultati di queste elaborazioni in un formato idoneo alla divulgazione scientifica in ambito medico;

DATO ATTO CHE, per le esigenze rappresentate nel progetto, veniva selezionato l'operatore economico AMOLAB con sede in via Raffaello Sanzio 18, 73100 Lecce, C.F. e P.IVA 04401310752, rappresentata dall' Ing. Salvatore Calcagnile in qualità di Amministratore Unico, così come indicato nella nota n. 49109 del 04/12/2023;

PRESO ATTO CHE, per il servizio de quo, è prevista una spesa complessiva per l'anno 2024 pari ad euro 33.606,56 oltre IVA (euro Trentatremilaseicentosei/56 oltre IVA di legge) che troverà copertura su budget n. 1018977 – Codice 1000456 – Descrizione: *-PRG- 1000008-2023/ 137-1000122-2023/137- Budget effettivo 870.000,00 – Codice progetto 2023/137 – Nome progetto: PNRR-MAD- 2022-12376819;

INDIVIDUATO: quale responsabile unico del progetto, ai sensi dell'art. 15 D.lgs 36/2023, la Prof.ssa Serafina Perrone in qualità di P.I., che nominava come da allegata nota, la sottoscritta Dott.ssa Michela Boschi, quale responsabile di fase per la procedura di affidamento

PRESO ATTO dell'inesistenza nei confronti del RUP di cause di incompatibilità, astensione ed esclusione in particolare di non trovarsi in alcuna delle situazioni, anche potenziali, di conflitto di interesse, rispetto ai soggetti coinvolti nel procedimento, come da allegata dichiarazione;

Determina

per le ragioni di cui in premessa,

- di stipulare un contratto di servizi conto terzi finalizzato al proseguio delle attività previste dal progetto di ricerca in oggetto, ammesso a finanziamento (utilizzo della tecnologia REMS nella popolazione fetale e neonatale per la costruzione preliminare di un database di riferimento) per l'esecuzione di un Servizio di Analisi, con metodologia REMS dei dataset ricevuti dall'Azienda e costruzione del database di riferimentio e del calcolo delle corrispondenti curve di riferiemento per feti e neonati, fornendo in output all'azienda i risultati di queste elaborazioni in un formato idoneo alla divulgazione scientifica in ambito medico;

- Che la spesa complessiva per l'anno 2024, pari ad euro 33.606,56 oltre IVA (euro Trentatremilaseicentosei/56 oltre IVA di legge), troverà copertura su budget n. 1018977 – Codice 1000456 – Descrizione: *-PRG- 1000008-2023/ 137-1000122-2023/137- Budget effettivo 870.000,00 – Codice progetto 2023/137 – Nome progetto: PNRR-MAD- 2022-12376819;

- di dare atto che responsabile unico del progetto, ai sensi dell'art. 15 D.lgs 36/2023, è la Prof.ssa Serafina Perrone in qualità di P.I., che nominava come da allegata nota, la sottoscritta Dott.ssa Michela Boschi, quale responsabile di fase per la procedura di affidamento

Responsabile del procedimento ai sensi della L. 241/90:
Serafina Perrone

Firmato digitalmente da:
Michela Boschi

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO PROTOCOLLO GENERALE

AOO: AOO000

REGISTRO: Protocollo generale

NUMERO: 0009298

DATA: 27/02/2024

OGGETTO: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione subcontratto.

CLASSIFICAZIONI:

DOCUMENTI:

File	Hash
PG0009298_2024_Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto.pdf.pdf:	BCD4F4A0DBAFEF730D1C55381DBB59B331412E2ACFA835A8D5CC50956556AC6B

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Parma
Azienda Ospedaliero - Universitaria di Parma

Simona Pattacini <spattacini@ao.pr.it>

Fwd: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto

1 messaggio

Aureliana Maggio <aumaggio@ausl.pr.it> 27 febbraio 2024 alle ore 10:10
A: spattacini <spattacini@ao.pr.it>

---------- Forwarded message ---------
Da: Rossella Zucchelli <rzucchelli@ao.pr.it>
Date: gio 22 feb 2024 alle ore 11:37
Subject: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto
To: Perrone, Serafina <serafina.perrone@unipr.it>
Cc: Michela Boschi <mboschi@ao.pr.it>, Malanca, Michele <mmalanca@ao.pr.it>

Gent.ma Prof.ssa Perrone,
in relazione al progetto PNRR-MAD-2022-12376819 per il quale sono stata individuata "Responsabile unico del progetto" ai fini del corretto monitoraggio e rendicontazione tramite piattaforma ReGis, la presente è per delegarla a RUP (Responsabile Unico del Procedimento), ai sensi del vigente Codice degli Appalti, per l'attuazione del Subcontratto previsto sia nelle attività progettuali sia nel piano finanziario accettato dal Ministero della Salute.
Cordiali saluti

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Dott.ssa Rossella Zucchelli

Azienda Ospedaliero-Universitaria di Parma

Grant Office

Via Gramsci, 14 - 43126 Parma

Tel. +39 0521 703686

e-mail: rzucchelli@ao.pr.it

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO DELIBERAZIONE

AOO: AOO000

REGISTRO: Deliberazione

NUMERO: 0000633

DATA: 13/09/2023 14:53

OGGETTO: Nomina RUP Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1 valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention". - PI Prof.ssa Serafina Perrone.

SOTTOSCRITTO DIGITALMENTE DA:

Il presente atto è stato firmato digitalmente da Fabi Massimo in qualità di Direttore Generale
Con il parere favorevole di Rossi Sandra - Direttore Sanitario FF
Con il parere favorevole di Ventura Antonio - Direttore Amministrativo

Su proposta di Teresa Coppola - Area Gestione Giuridica Amministrativi Studi che esprime parere favorevole in ordine ai contenuti sostanziali, formali e di legittimità del presente atto

CLASSIFICAZIONI:

- [01-02-04]

DESTINATARI:

- Collegio sindacale
- Direzione Sanitaria
- S.S.D.I. Ingegneria Clinica
- S.C.I. Servizio Economico Finanziario e aspetti economici dell accesso alle prestazioni sanitarie
- S.C. Ricerca Clinica ed Epidemiologica
- S.C.I. Internal Auditing

DOCUMENTI:

File	Firmato digitalmente da	Hash
DELI0000633_2023_delibera_firmata.pdf	Coppola Teresa; Fabi Massimo; Rossi Sandra; Ventura Antonio	13D708C0046B17D87584A09F62496A088EF52AA7AB09E12BBFE594D4634E79D5

DELIBERAZIONE

OGGETTO: Nomina RUP Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1 valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention". - PI Prof.ssa Serafina Perrone.

IL DIRETTORE GENERALE

RICHIAMATE:

- Il Regolamento (UE) 2021/241 del Parlamento europeo e del Consiglio del 12 febbraio 2021 che istituisce il dispositivo per la ripresa e la resilienza dell'Unione Europea;
- Il Piano nazionale di Ripresa e Resilienza (PNRR) valutato positivamente con Decisione del Consiglio ECOFIN del 13 luglio 2021, notificata all'Italia dal Segretariato generale del Consiglio con nota LT 161/21, del 14 luglio 2021, ed in particolare la Missione 6, Componente 2, Investimento 2.1 "Valorizzazione e potenziamento della ricerca biomedica del SSN", che consiste nel "rafforzare il sistema della ricerca biomedica tramite due linee di intervento: a) il finanziamento di progetti Proof of Concept (PoC), sostenendo lo sviluppo di tecnologie con un basso grado di maturità tecnologica e promuovendo il trasferimento di tecnologie verso l'industria; b) il finanziamento di programmi o progetti di ricerca nel campo delle malattie rare e dei tumori rari e di altre malattie altamente invalidanti;
- Il decreto del Presidente del Consiglio dei ministri 9 luglio 2021 recante l'individuazione delle amministrazioni centrali titolari di interventi previsti nel PNRR, ai sensi dell'art. 8, comma 1, del decreto legge 31 maggio 2021, n. 77, convertito con modificazioni, dalla legge 29 luglio 2021, n. 108;
- Il Decreto del Ministro dell'economia e delle finanze del 6 agosto 2021 relativo all'assegnazione delle risorse in favore in favore di ciascuna Amministrazione titolare degli interventi PNRR e corrispondenti milestone e target;
- Il Decreto del Ministro della salute, di concerto con il Ministro dell'economia e delle finanze 15 settembre 2021, di istituzione dell'Unità di Missione del Ministero della salute titolare di interventi PNRR, si sensi dell'articolo 8 del citato decreto legge n. 77 del 2021;
- L'atto di indirizzo del Ministro del 12 ottobre 2021 con il quale sono stati individuati i relativi Soggetti Attuatori nell'ambito degli interventi e sub-interventi di investimento del PNRR a titolarità del Ministero della salute;

- Le Linee Guida per lo svolgimento delle attività connesse al monitoraggio del PNRR, predisposte dal Servizio Centrale per il PNRR, presso il Ministero dell'economia e delle finanze (MEF) – Dipartimento Ragioneria generale dello Stato (RGS) che descrivono le funzionalità del sistema informativo " *ReGIS*";
- Le "Linee Guida per lo svolgimento delle attività di controllo e rendicontazione delle Misure PNRR di competenza delle Amministrazioni centrali e dei Soggetti attuatori", che contengono indicazioni procedurali per un corretto espletamento delle attività di controllo e rendicontazione delle spese e di Milestone &Target;
- Il 1° Avviso pubblico per la presentazione e selezione di progetti di ricerca da finanziare nell'ambito del PNRR, pubblicato sul sito web del Ministero della salute il 20 aprile 2022 e sulla G.U. della Repubblica Italiana;
- Il messaggio del Ministero della Salute tramite il WorkFlow della ricerca del 13 dicembre 2022 con cui è stato comunicato che la valutazione della proposta progettuale "Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone, ha avuto esito positivo e che, pertanto, la stessa è stata ammessa a finanziamento;

VISTA la comunicazione del 15.12.2022 con cui il Soggetto attuatore/beneficiario, Regione Emilia Romagna, ha inoltrato la Convenzione relativa al Progetto PRNN-MAD- 2022-12376819, già sottoscritta dal Direttore dell'Ufficio 3, Direzione Generale della ricerca e dell'innovazione in sanità del Ministero della salute e per la Regione Emilia Romagna, dall'Ing. Luca Baldino, legale rappresentante, e successivamente sottoscritta anche dal Principal Investigator, prof.ssa Serafina Perrone, come da nota prot. n. 1232480 del 15.12.2022 con cui la Convenzione è stata inviata al Soggetto attuatore/beneficiario, Regione Emilia Romagna;

PRECISATO che per la realizzazione delle attività del progetto, della durata di 24 mesi, l'importo ammesso a finanziamento è pari a € 870.000,00;

RILEVATO che tale progetto, di cui l'Azienda Ospedaliero-Universitaria di Parma è capofila, viene realizzato in partnership con l'Azienda Ospedaliero-Universitaria di Messina (UO 2), per la quale è previsto il finanziamento di € 348.000,00;

RICHIAMATA la deliberazione n. 336 del 17.05.2023 con cui è stata attivato il Progetto in questione, approvato definitivamente dal Comitato Etico AVEN nella seduta del 04.04.2023;

RILEVATO che le attività progettuali hanno avuto inizio il 20.05.2023, come da comunicazione della Prof.ssa Serafina Perrone, trasmessa alla Regione Emilia Romagna con nota prot. n. 15507 del 07.04.2023;

ACQUISITO il codice CUP del Progetto: F53C22001880001;

PRESO ATTO della richiesta della Regione Emilia Romagna di notificare il nominativo dell'utente da profilare nel Sistema ReGIS e della comunicazione inviata alla Regione stessa con nota prot. n. 11341/2023 con cui si anticipava, in riferimento all'Azienda Ospedaliero Universitaria di Parma, l' individuazione della dott.ssa Rossella Zucchelli, in quanto presta le proprie attività presso l'Area Grant Office, che ha il mandato di gestire i progetti finanziati, come da delibere n. 61/2021 e n. 637/2021;

RILEVATO che come da "Linee Guida per la governance del PNRR nelle Aziende Sanitarie di Parma" i RUP (Responsabile Unico del Procedimento) sono nominati con specifici atti del Direttore Generale e sono responsabili della realizzazione operativa dei progetti e dei connessi adempimenti di monitoraggio, rendicontazione e controllo e devono conferire al sistema ReGIS tutti i dati relativi ai progetti di propria competenza nel rispetto delle tempistiche previste;

RITENUTO, pertanto, di nominare la Dott.ssa Rossella Zucchelli, quale RUP per il Progetto PNRR-MAD-2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone;

Delibera

Per le motivazioni esposte in premessa e che si intendono qui integralmente richiamate:

- di nominare la Dott.ssa Rossella Zucchelli, quale RUP per il Progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone;
- di inviare il presente atto di nomina alla Regione Emilia Romagna – Settore Innovazione nei servizi sanitari e sociali;
- di comunicare il presente atto alla Struttura Interaziendale Internal Auditing

Responsabile del procedimento ai sensi della L. 241/90:
Teresa Coppola

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO PROTOCOLLO GENERALE

AOO: AOO000

REGISTRO: Protocollo generale

NUMERO: 0009306

DATA: 27/02/2024

OGGETTO: Invio documenti Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto.

CLASSIFICAZIONI:

DOCUMENTI:

File	Hash
PG0009306_2024_Documenti Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto.pdf.pdf:	DD196BA2488E39FD326996E13CA511ACC77417651B5BF50822D5D4B19303DFE1
PG0009306_2024_DELI0000633_2023_nomina RUP.pdf.pdf:	86629BF0AC05E7EAB775304E1C4D4A0E4D7E642F8EE4801621CE37E4CDC3AA88
PG0009306_2024_2_conflitto interessi versione estesa.pdf.pdf:	DD7A6982F39ED54D4F4FADD04CBA2B7B2EB63795B1BCD134A4E64135F68A0352
PG0009306_2024_Nomina responsabile di fase 24-02.pdf.pdf:	D78AB595B47F698AD3E040550AE4A508F9D3D68F701DFD0B903FDCABD683D935

Fwd: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto

1 messaggio

Aureliana Maggio <aumaggio@ausl.pr.it> 27 febbraio 2024 alle ore 10:09
A: spattacini <spattacini@ao.pr.it>

---------- Forwarded message ---------
Da: Serafina PERRONE <serafina.perrone@unipr.it>
Date: sab 24 feb 2024 alle ore 15:18
Subject: R: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto
To: Maggio, Aureliana <aumaggio@ausl.pr.it>
Cc: Michela Boschi <mboschi@ao.pr.it>, Zucchelli, Rossella <rzucchelli@ao.pr.it>

Carissima;
a seguito della mail della Dott.ssa Zucchelli,
sono dunque a inviare i documenti richiesti:
-assenza di conflitto di interessi firmato
-nomina di fase completato nelle parti mancanti
-atto di delibera di nomina del RUP
-mail in calce di delega della Dott.ssa Zucchelli.

Mi fate sapere se, a questo punto, può andar tutto bene?
in particolare, vi occorre firma digitale?
Resto a disposizione per altro adempimento.
Vi ringrazio
A presto
Serafina

Prof. S. Perrone, MD, PhD

Professore Associato di Pediatria

Dpt. di Medicina e Chirurgia,

Università degli Studi di Parma

UOC Neonatologia

Tel: 0521-903821-703518

Da: Rossella Zucchelli <rzucchelli@ao.pr.it>
Inviato: giovedì 22 febbraio 2024 11:36
A: Serafina PERRONE <serafina.perrone@unipr.it>
Cc: Michela Boschi <mboschi@ao.pr.it>; Malanca, Michele <mmalanca@ao.pr.it>
Oggetto: Progetto PNRR-MAD-2022-12376819 - delega a RUP per attivazione Subcontratto

Gent.ma Prof.ssa Perrone,
in relazione al progetto PNRR-MAD-2022-12376819 per il quale sono stata individuata "Responsabile unico del progetto" ai fini del corretto monitoraggio e rendicontazione tramite piattaforma ReGis, la presente è per delegarla a RUP (Responsabile Unico del Procedimento), ai sensi del vigente Codice degli Appalti, per l'attuazione del Subcontratto previsto sia nelle attività progettuali sia nel piano finanziario accettato dal Ministero della Salute.

Cordiali saluti

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Dott.ssa Rossella Zucchelli

Azienda Ospedaliero-Universitaria di Parma

Grant Office

Via Gramsci, 14 - 43126 Parma

Tel. +39 0521 703686

e-mail: rzucchelli@ao.pr.it

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3 allegati

Nomina responsabile di fase 24-02.docx
164K

DELI0000633_2023_nomina RUP.pdf
162K

2_conflitto interessi versione estesa.pdf
314K

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO DELIBERAZIONE

AOO: AOO000

REGISTRO: Deliberazione

NUMERO: 0000633

DATA: 13/09/2023 14:53

OGGETTO: Nomina RUP Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1 valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention". - PI Prof.ssa Serafina Perrone.

SOTTOSCRITTO DIGITALMENTE DA:

Il presente atto è stato firmato digitalmente da Fabi Massimo in qualità di Direttore Generale
Con il parere favorevole di Rossi Sandra - Direttore Sanitario FF
Con il parere favorevole di Ventura Antonio - Direttore Amministrativo

Su proposta di Teresa Coppola - Area Gestione Giuridica Amministrativi Studi che esprime parere favorevole in ordine ai contenuti sostanziali, formali e di legittimità del presente atto

CLASSIFICAZIONI:

- [01-02-04]

DESTINATARI:

- Collegio sindacale
- Direzione Sanitaria
- S.S.D.I. Ingegneria Clinica
- S.C.I. Servizio Economico Finanziario e aspetti economici dell accesso alle prestazioni sanitarie
- S.C. Ricerca Clinica ed Epidemiologica
- S.C.I. Internal Auditing

DOCUMENTI:

File	Firmato digitalmente da	Hash
DELI0000633_2023_delibera_firmata.pdf	Coppola Teresa; Fabi Massimo; Rossi Sandra; Ventura Antonio	13D708C0046B17D87584A09F62496A088EF52AA7AB09E12BBFE594D4634E79D5

DELIBERAZIONE

OGGETTO: Nomina RUP Progetto PNRR Missione 6 - Componente 2 - Investimento 2.1 valorizzazione e potenziamento della ricerca biomedica del SSN. Progetto "Malattie Croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention". - PI Prof.ssa Serafina Perrone.

IL DIRETTORE GENERALE

RICHIAMATE:

- Il Regolamento (UE) 2021/241 del Parlamento europeo e del Consiglio del 12 febbraio 2021 che istituisce il dispositivo per la ripresa e la resilienza dell'Unione Europea;
- Il Piano nazionale di Ripresa e Resilienza (PNRR) valutato positivamente con Decisione del Consiglio ECOFIN del 13 luglio 2021, notificata all'Italia dal Segretariato generale del Consiglio con nota LT 161/21, del 14 luglio 2021, ed in particolare la Missione 6, Componente 2, Investimento 2.1 "Valorizzazione e potenziamento della ricerca biomedica del SSN", che consiste nel "rafforzare il sistema della ricerca biomedica tramite due linee di intervento: a) il finanziamento di progetti Proof of Concept (PoC), sostenendo lo sviluppo di tecnologie con un basso grado di maturità tecnologica e promuovendo il trasferimento di tecnologie verso l'industria; b) il finanziamento di programmi o progetti di ricerca nel campo delle malattie rare e dei tumori rari e di altre malattie altamente invalidanti;
- Il decreto del Presidente del Consiglio dei ministri 9 luglio 2021 recante l'individuazione delle amministrazioni centrali titolari di interventi previsti nel PNRR, ai sensi dell'art. 8, comma 1, del decreto legge 31 maggio 2021, n. 77, convertito con modificazioni, dalla legge 29 luglio 2021, n. 108;
- Il Decreto del Ministro dell'economia e delle finanze del 6 agosto 2021 relativo all'assegnazione delle risorse in favore in favore di ciascuna Amministrazione titolare degli interventi PNRR e corrispondenti milestone e target;
- Il Decreto del Ministro della salute, di concerto con il Ministro dell'economia e delle finanze 15 settembre 2021, di istituzione dell'Unità di Missione del Ministero della salute titolare di interventi PNRR, si sensi dell'articolo 8 del citato decreto legge n. 77 del 2021;
- L'atto di indirizzo del Ministro del 12 ottobre 2021 con il quale sono stati individuati i relativi Soggetti Attuatori nell'ambito degli interventi e sub-interventi di investimento del PNRR a titolarità del Ministero della salute;

- Le Linee Guida per lo svolgimento delle attività connesse al monitoraggio del PNRR, predisposte dal Servizio Centrale per il PNRR, presso il Ministero dell'economia e delle finanze (MEF) – Dipartimento Ragioneria generale dello Stato (RGS) che descrivono le funzionalità del sistema informativo " *ReGIS*";
- Le "Linee Guida per lo svolgimento delle attività di controllo e rendicontazione delle Misure PNRR di competenza delle Amministrazioni centrali e dei Soggetti attuatori", che contengono indicazioni procedurali per un corretto espletamento delle attività di controllo e rendicontazione delle spese e di Milestone &Target;
- Il 1° Avviso pubblico per la presentazione e selezione di progetti di ricerca da finanziare nell'ambito del PNRR, pubblicato sul sito web del Ministero della salute il 20 aprile 2022 e sulla G.U. della Repubblica Italiana;
- Il messaggio del Ministero della Salute tramite il WorkFlow della ricerca del 13 dicembre 2022 con cui è stato comunicato che la valutazione della proposta progettuale "Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali con codice progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone, ha avuto esito positivo e che, pertanto, la stessa è stata ammessa a finanziamento;

VISTA la comunicazione del 15.12.2022 con cui il Soggetto attuatore/beneficiario, Regione Emilia Romagna, ha inoltrato la Convenzione relativa al Progetto PRNN-MAD- 2022-12376819, già sottoscritta dal Direttore dell'Ufficio 3, Direzione Generale della ricerca e dell'innovazione in sanità del Ministero della salute e per la Regione Emilia Romagna, dall'Ing. Luca Baldino, legale rappresentante, e successivamente sottoscritta anche dal Principal Investigator, prof.ssa Serafina Perrone, come da nota prot. n. 1232480 del 15.12.2022 con cui la Convenzione è stata inviata al Soggetto attuatore/beneficiario, Regione Emilia Romagna;

PRECISATO che per la realizzazione delle attività del progetto, della durata di 24 mesi, l'importo ammesso a finanziamento è pari a € 870.000,00;

RILEVATO che tale progetto, di cui l'Azienda Ospedaliero-Universitaria di Parma è capofila, viene realizzato in partnership con l'Azienda Ospedaliero-Universitaria di Messina (UO 2), per la quale è previsto il finanziamento di € 348.000,00;

RICHIAMATA la deliberazione n. 336 del 17.05.2023 con cui è stata attivato il Progetto in questione, approvato definitivamente dal Comitato Etico AVEN nella seduta del 04.04.2023;

RILEVATO che le attività progettuali hanno avuto inizio il 20.05.2023, come da comunicazione della Prof.ssa Serafina Perrone, trasmessa alla Regione Emilia Romagna con nota prot. n. 15507 del 07.04.2023;

ACQUISITO il codice CUP del Progetto: F53C22001880001;

PRESO ATTO della richiesta della Regione Emilia Romagna di notificare il nominativo dell'utente da profilare nel Sistema ReGIS e della comunicazione inviata alla Regione stessa con nota prot. n. 11341/2023 con cui si anticipava, in riferimento all'Azienda Ospedaliero Universitaria di Parma, l' individuazione della dott.ssa Rossella Zucchelli, in quanto presta le proprie attività presso l'Area Grant Office, che ha il mandato di gestire i progetti finanziati, come da delibere n. 61/2021 e n. 637/2021;

RILEVATO che come da "Linee Guida per la governance del PNRR nelle Aziende Sanitarie di Parma" i RUP (Responsabile Unico del Procedimento) sono nominati con specifici atti del Direttore Generale e sono responsabili della realizzazione operativa dei progetti e dei connessi adempimenti di monitoraggio, rendicontazione e controllo e devono conferire al sistema ReGIS tutti i dati relativi ai progetti di propria competenza nel rispetto delle tempistiche previste;

RITENUTO, pertanto, di nominare la Dott.ssa Rossella Zucchelli, quale RUP per il Progetto PNRR-MAD-2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone;

Delibera

Per le motivazioni esposte in premessa e che si intendono qui integralmente richiamate:

- di nominare la Dott.ssa Rossella Zucchelli, quale RUP per il Progetto PNRR-MAD- 2022-12376819 dal titolo "Getting bone health right from the start: innovative technology and new mechanism of mother-fetus cross talk for osteopenia and osteoporosis prevention", il cui PI è la Prof.ssa Serafina Perrone;
- di inviare il presente atto di nomina alla Regione Emilia Romagna – Settore Innovazione nei servizi sanitari e sociali;
- di comunicare il presente atto alla Struttura Interaziendale Internal Auditing

Responsabile del procedimento ai sensi della L. 241/90:
Teresa Coppola

DICHIARAZIONE SOSTITUTIVA ATTO DI NOTORIETA' ATTESTANTE ASSENZA DI CONFLITTO DI INTERESSI

La sottoscritta: Prof.ssa Serafina Perrone

Titolare del Seguente Incarico: Responsabile Scientifico progetto PNRR-MAD- , dal titolo "Getting bone health right from the 2022-12376819 start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE

OGGETTO: **MISSIONE 6 SALUTE (M6) – PIANO NAZIONALE DI RIPRESA E RESILIENZA (PNRR) – COMPONENTE 2 (C2) INVESTIMENTO 2.1. VALORIZZAZIONE E POTENZIAMENTO DELLA RICERCA BIOMEDICA DEL SSN. – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- , dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)" – P.I. Prof.ssa Serafina Perrone**

CIG A01DA56008

Consapevole delle sanzioni penali previste dall'art. 76 del D.P.R. n. 445/2000 e s.m.i. per le ipotesi di falsità in atti e dichiarazioni mendaci, nonché delle conseguenze di cui all'art. 75, comma 1, del medesimo D.P.R., sotto la mia personale responsabilità, ai fini di quanto previsto dagli articoli 5, 6, 7 e 13 del D.P.R. n. 62/2013 e s.m.i. del Codice di Comportamento "Per il personale operante presso le Aziende Sanitarie AUSL e Azienda Ospedaliero Universitaria di Parma" approvato da Azienda USL Parma con deliberazione n. 348 del 29 maggio 2018" (Allegato 6 al Piano per la Prevenzione della Corruzione e la Trasparenza AUSL/AOU Parma 2022/2024)

MI OBBLIGO

• a conformare la mia condotta ai principi di correttezza, buon andamento ed imparzialità dell'azione amministrativa, agendo in posizione di indipendenza ed imparzialità ed astenendomi in caso di conflitto di interessi.

A tal fine

DICHIARO

1. che l'incarico da me ricevuto

X **non coinvolge**
☐ **coinvolge**
alcun mio personale interesse, ovvero interessi di miei parenti, affini entro il secondo grado, coniuge, conviventi, oppure di persone con le quali ho rapporti di frequentazione abituale – art. 7 del D.P.R. n. 62/2013 e s.m.i. (Codice di Comportamento dei Dipendenti pubblici) e del Codice di Comportamento;

2. di

X **non avere**
☐ **avere**
comunque nessuna situazione di conflitto di interessi di cui al D.P.R. n. 62/2013 e s.m.i. (Codice di Comportamento dei Dipendenti pubblici) e del Codice di Comportamento, o di cui all'art. 42 del Codice dei Contratti Pubblici*

IN PARTICOLARE :

X di **NON AVERE AVUTO** negli ultimi tre anni, **rapporti diretti o indiretti, di collaborazione con soggetti privati in qualunque modo retribuiti**, che svolgono attività di interesse rispetto alla funzione istituzionale esercitata

OPPURE

☐ di **AVERE AVUTO** negli ultimi tre anni, **rapporti diretti o indiretti, di collaborazione con soggetti privati in qualunque modo retribuiti**, che svolgono attività di interesse rispetto alla funzione istituzionale esercitata e che tali soggetti privati coi quali ho avuto i suddetti rapporti di collaborazione, per quanto a conoscenza del sottoscritto:

☐ **avere** interessi in attività o decisioni inerenti la struttura organizzativa/servizio di assegnazione del sottoscritto per quanto riguarda le funzioni allo stesso affidate (art. 6 – D.P.R. n. 62/2013 e s.m.i.)

☐ **non avere** interessi in attività o decisioni inerenti la struttura organizzativa/servizio di assegnazione del sottoscritto per quanto riguarda le funzioni allo stesso affidate (art. 6 – D.P.R. n. 62/2013 e s.m.i.)

Parma, lì 22-02-2024

In fede __Serafina Perrone ____

INFORMATIVA
Ex artt. 4/5/6 del Codice di Comportamento

Art. 4 Conflitto di interessi e obbligo di astensione

1. Il conflitto di interessi è una condizione in cui il destinatario del Codice è portatore di interessi della propria sfera privata che, anche solo potenzialmente, possono influenzare negativamente e compromettere l'imparzialità e l'indipendenza richieste nelle attività svolte per conto dell'Azienda. Il conflitto può riguardare interessi di qualsiasi natura, anche non patrimoniali, come ad esempio quelli derivanti dall'intento di voler assecondare pressioni politiche, sindacali o dei superiori gerarchici o comunque di voler ricavare utilità propria o di terzi in modo indebito.

2. Il destinatario si astiene dal partecipare all'adozione di decisioni o ad attività in situazioni di conflitto di interessi, anche potenziale, e in situazioni che possano coinvolgere interessi propri, ovvero di suoi parenti, affini entro il secondo grado, del coniuge o di conviventi, oppure di persone con le quali abbia rapporti di frequentazione abituale, ovvero di soggetti od organizzazioni con cui egli o il coniuge abbia causa pendente o grave inimicizia o rapporti di credito o debito significativi, ovvero di soggetti od organizzazioni di cui sia tutore, curatore, procuratore o agente, ovvero di enti, associazioni anche non riconosciute, comitati, società o stabilimenti di cui sia amministratore o gerente o dirigente, ovvero quando esistano importanti ragioni di convenienza.

3. L'astensione va comunicata per iscritto al soggetto competente individuato al successivo comma 5, anche attraverso modalità informatizzate, e in tempo utile per la trattazione della pratica o lo svolgimento dell'attività, specificando le ragioni. Il responsabile decide sull'astensione, fornendo una risposta scritta tempestiva, anche attraverso modalità informatizzate.

4. Il dipendente fornisce, all'atto della prima assegnazione al servizio e in caso di ogni successivo trasferimento o diverso incarico, e aggiorna annualmente, una dichiarazione avente ad oggetto tutti i rapporti che lo stesso abbia o abbia avuto negli ultimi tre anni, a qualsiasi titolo, con soggetti esterni dai quali possa derivare un conflitto di interessi anche potenziale e/o comunque in qualunque modo retribuiti. Detta dichiarazione specifica per ciascun rapporto tutti gli eventuali emolumenti percepiti e/o benefici goduti, sia direttamente che indirettamente, e inoltre: a) se in prima persona, o suoi parenti o affini entro il secondo grado, il coniuge o il convivente abbiano ancora rapporti finanziari con il soggetto con cui ha avuto i predetti rapporti; b) se siano intercorsi o intercorrano con soggetti che abbiano interessi in attività o decisioni inerenti al servizio, limitatamente alle attività a lui affidate. La dichiarazione, resa ai sensi degli artt. 46 e 47 del DPR 445/2000, è rilasciata in forma completa, utilizzando il modulo predisposto dalle Aziende, anche attraverso modalità informatizzate. Le previsioni del presente comma si applicano anche ai direttori.

5. La valutazione circa la sussistenza di una situazione di conflitto di interessi spetta:
- per i dipendenti, al superiore gerarchico
- per il direttore amministrativo, sanitario e socio-sanitario al Direttore Generale
- per il direttore scientifico si rinvia alla normativa nazionale di settore
- per il Direttore Generale al Direttore Generale Cura della Persona, Salute e Welfare
- per gli altri destinatari, al superiore gerarchico secondo le procedure aziendali.

6. L'adozione delle decisioni conseguenti rispetto alla valutazione di cui al comma precedente avviene secondo le procedure definite dalle Aziende o dalla Regione per il Direttore Generale.

7. Il dipendente non accetta incarichi di collaborazione da soggetti privati che abbiano, o abbiano avuto nel biennio precedente, un interesse economico significativo in decisioni o attività inerenti all'ufficio di appartenenza.

Art. - 6 Partecipazione ad associazioni e organizzazioni

1. I destinatari del codice, nel rispetto della disciplina vigente del diritto di associazione, non assumono incarichi in associazioni e organizzazioni che possano porli in conflitto di interessi con l'attività svolta all'interno delle Aziende, incluse le associazioni di volontariato e/o senza fini di lucro.

2. Al fine della valutazione del conflitto di interessi, i dipendenti e i direttori comunicano tempestivamente, anche attraverso modalità informatizzate, al proprio superiore gerarchico l'adesione o l'appartenenza ad associazioni od organizzazioni, anche senza fini di lucro, specificando il ruolo ricoperto, i cui ambiti di interessi possano interferire con lo svolgimento dell'attività del servizio di appartenenza, nonché quelle in ambito sanitario, socio sanitario, di ricerca e di tutela della salute. Il presente comma non si applica all'adesione a partiti politici o a sindacati.

3. In ogni caso, per i dipendenti e per i direttori è vietata l'adesione o l'appartenenza ad associazioni o organizzazioni con la previsione di un corrispettivo e/o compenso, ferma restando la possibilità di effettuare attività extraistituzionali secondo le modalità previste dalla normativa vigente.

4. I destinatari non esercitano pressioni, promettendo vantaggi o prospettando svantaggi di carriera o di altra natura, nei confronti di colleghi e altri operatori o utenti dei servizi con i quali vengano in contatto durante l'attività professionale, al fine di agevolare l'adesione ad associazioni o organizzazioni.

INFORMATIVA

Dlgs n. 165 /2001 "Testo Unico sul Pubblico Impiego"

Ex Art. 53, comma 16 ter

16-ter. I dipendenti che, negli ultimi tre anni di servizio, hanno esercitato poteri autoritativi o negoziali per conto delle pubbliche amministrazioni di cui all'articolo 1, comma 2, non possono svolgere, nei tre anni successivi alla cessazione del rapporto di pubblico impiego, attivita' lavorativa o professionale presso i soggetti privati destinatari dell'attivita' della pubblica amministrazione svolta attraverso i medesimi poteri. I contratti conclusi e gli incarichi conferiti in violazione di quanto previsto dal presente comma sono nulli ed e' fatto divieto ai soggetti privati che li hanno conclusi o conferiti di contrattare con le pubbliche amministrazioni per i successivi tre anni con obbligo di restituzione dei compensi eventualmente percepiti e accertati ad essi riferiti.

D. Lgs 50/2016 Codice dei contratti pubblici

Art. 4 (Conflitto di interesse)

1. Le stazioni appaltanti prevedono misure adeguate per contrastare le frodi e la corruzione nonché per individuare, prevenire e risolvere in modo efficace ogni ipotesi di conflitto di interesse nello svolgimento delle procedure di aggiudicazione degli appalti e delle concessioni, in modo da evitare qualsiasi distorsione della concorrenza e garantire la parità di trattamento di tutti gli operatori economici.

2. Si ha conflitto d'interesse quando il personale di una stazione appaltante o di un prestatore di servizi che, anche per conto della stazione appaltante, interviene nello svolgimento della procedura di aggiudicazione degli appalti e delle concessioni o può influenzarne, in qualsiasi modo, il risultato, ha, direttamente o indirettamente, un interesse finanziario, economico o altro interesse personale che può essere percepito come una minaccia alla sua imparzialità e indipendenza nel contesto della procedura di appalto o di concessione. In particolare, costituiscono situazione di conflitto di interesse quelle che determinano l'obbligo di astensione previste dall'articolo 7 del decreto del Presidente della Repubblica 16 aprile 2013, n. 62.

3. Il personale che versa nelle ipotesi di cui al comma 2 è tenuto a darne comunicazione alla stazione appaltante, ad astenersi dal partecipare alla procedura di aggiudicazione degli appalti e delle concessioni. Fatte salve le ipotesi di responsabilità amministrativa e penale, la mancata astensione nei casi di cui al primo periodo costituisce comunque fonte di responsabilità disciplinare a carico del dipendente pubblico.

4. Le disposizioni dei commi da 1, 2 e 3 valgono anche per la fase di esecuzione dei contratti pubblici.

5. La stazione appaltante vigila affinché gli adempimenti di cui ai commi 3 e 4 siano rispettati.

Oggetto: **MISSIONE 6 SALUTE (M6) – PIANO NAZIONALE DI RIPRESA E RESILIENZA (PNRR) – COMPONENTE 2 (C2) INVESTIMENTO 2.1. VALORIZZAZIONE E POTENZIAMENTO DELLA RICERCA BIOMEDICA DEL SSN. – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- , dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE – Dichiarazione assenza conflitto di interessi e nomina del responsabile di fase ai sensi e per gli effetti dell'art. 15, co. 4 d.lgs. 36/2023 e allegato I.2**

PREMESSO che l'Azienda Ospedaliero Universitaria di Parma intende avviare la procedura per l'affidamento diretto finalizzato al prosieguo delle attività previste dal progetto di ricerca di cui in oggetto ammesso a finanziamento (utilizzo della tecnologia REMS nella popolazione fetale e neonatale per la costruzione preliminare di un database di riferimento) nel progetto PNRR-MAD-, dal titolo "Getting bone health right from the 2022-12376819 start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE;

DATO ATTO che la sottoscritta Prof.ssa Serafina Perrone, Principal Investigator del predetto progetto, veniva delegata dal RUP per la fase di affidamento diretto, e che il RUP è stato nominato da parte del Direttore Area Gestione Giuridica Amministrativi Studi (Dott.ssa Teresa Coppola) con l'allegato atto 'Delibera aziendale: n. 0000633 del 13-09-2023';

CONSIDERATO che, giusta la nomina anzidetta, si rilascia l'allegata dichiarazione di assenza del conflitto di interessi in capo alla sottoscritta;

RICHIAMATO l'art. 15, comma 4, del d.lgs. 36/2023 il quale prevede, che "Fermo restando l'unicità del RUP, le stazioni appaltanti e gli enti concedenti, possono individuare modelli organizzativi, i quali prevedano la nomina di un responsabile di procedimento per le fasi di programmazione, progettazione ed esecuzione e un responsabile di procedimento per la fase di affidamento. Le relative responsabilità sono ripartite in base ai compiti svolti in ciascuna fase, ferme restando le funzioni di supervisione, indirizzo e coordinamento del RUP";

VERIFICATO, a tal fine, che la Dott.ssa Michela Boschi, Direttore della S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici è idonea e disponibile ad assumere l'incarico *de quo* per la fase di affidamento del servizio;

RITENUTO, pertanto, di assegnare alla predetta la responsabilità della fase dell'affidamento dell'appalto in oggetto;

CONSIDERATO che, fatta salva l'assegnazione di singoli procedimenti ai responsabili di fase, restano ferme le funzioni di supervisione, indirizzo e coordinamento da parte del RUP, il quale può avocare a sé i procedimenti assegnati;

DISPONE

1) l'individuazione della Dott.ssa Michela Boschi, Direttore della S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici quale responsabile per la fase di affidamento dell'appalto in oggetto;

2) di rendere noto il nominativo del responsabile di fase negli atti dell'affidamento.

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO DELIBERAZIONE

AOO: AOO000

REGISTRO: Deliberazione

NUMERO: 0000336

DATA: 17/05/2023 16:36

OGGETTO: Attivazione del Progetto di Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- 2022-12376819, dal titolo “Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)” – Principal Investigator Prof.ssa Serafina Perrone dell’U.O. di Neonatologia dell’Azienda Ospedaliero Universitaria di Parma.

SOTTOSCRITTO DIGITALMENTE DA:

Il presente atto è stato firmato digitalmente da Fabi Massimo in qualità di Direttore Generale
Con il parere favorevole di D'Abbiero Nunziata - Direttore Sanitario FF
Con il parere favorevole di Ventura Antonio - Direttore Amministrativo

Su proposta di Teresa Coppola - Area Gestione Giuridica Amministrativi Studi che esprime parere favorevole in ordine ai contenuti sostanziali, formali e di legittimità del presente atto

CLASSIFICAZIONI:

- [01-02-04]

DESTINATARI:

- Collegio sindacale
- S.C. Farmacia e Governo Clinico del Farmaco
- S.C.I. Servizio Economico Finanziario e aspetti economici dell accesso alle prestazioni sanitarie
- S.C. Ricerca Clinica ed Epidemiologica
- Area Gestione Giuridica Amministrativi Studi
- Direzione Sanitaria
- S.S.D.I. Ingegneria Clinica

DOCUMENTI:

File	Firmato digitalmente da	Hash
DELI0000336_2023_delibera_firmata.pdf	Coppola Teresa; D'Abbiero Nunziata; Fabi Massimo; Ventura Antonio	A8DFABAD0B4F514B8877BBB2F8365E84463A2E81041DF80A8908F38B8D1DA5AD
DELI0000336_2023_Allegato1.pdf:		D0995046454EAC23909DB074735A4F4027B9EF9D24408B830EBE203D55099962

DELIBERAZIONE

OGGETTO: Attivazione del Progetto di Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- 2022-12376819, dal titolo “Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)” – Principal Investigator Prof.ssa Serafina Perrone dell’U.O. di Neonatologia dell’Azienda Ospedaliero Universitaria di Parma.

IL DIRETTORE GENERALE

RICHIAMATE:

la Delibera del Direttore Generale n. 192 del 12/03/2018 Recepimento del Regolamento “Regolamentazione degli aspetti procedurali, amministrativi ed economici per la conduzione di ricerche e sperimentazioni cliniche nelle Aziende Sanitarie/IRCCS dell’Area Vasta Emilia Nord (AVEN)” elaborato in sede AVEN;

la Delibera del Direttore Generale n. 215 del 20/03/2018 Indicazioni inerenti la delibera n. 192 del 12 marzo 2018 ad oggetto “Recepimento del Regolamento “Regolamentazione degli aspetti procedurali, amministrativi ed economici per la conduzione di ricerche e sperimentazioni cliniche nelle Aziende Sanitarie /IRCCS dell’Area Vasta Emilia Nord (AVEN)” elaborato in sede AVEN”;

la Delibera del Direttore Generale n. 371 del 23/05/2018 Regolamento UE 2016/679 relativo alla protezione delle persone fisiche con riguardo al trattamento dei dati personali - Designazione del DATA PROTECTION OFFICER e ricognizione delle prime attività di adeguamento;

la Delibera del Consiglio dell’Autorità Nazionale Anticorruzione n. 831 del 3 agosto 2016 Determinazione di approvazione definitiva del Piano Nazionale Anticorruzione 2016, in particolare il paragrafo nominato “Sperimentazioni cliniche. Proposta di ripartizione dei proventi derivanti da sperimentazioni cliniche”;

la Delibera della Giunta Regionale n.1207 del 29 luglio 2016 “Approvazione schema nuovo Protocollo di Intesa tra la Regione Emilia-Romagna e le Università di Bologna, Ferrara, Modena-Reggio Emilia e Parma, in attuazione dell'art. 9 della L.R. 23 dicembre 2004, n. 29” in particolare l’art. 17 “Attività di ricerca, sperimentazione clinica e prestazioni conto terzi”;

la Legge Regionale 1 giugno 2017, n. 9 “Fusione dell’Azienda Unità sanitaria locale di Reggio Emilia e dell’ Azienda Ospedaliera Arcispedale Santa Maria Nuova. Altre disposizioni di adeguamento degli aspetti

organizzativi in materia sanitaria" in particolare l'art.7 "Nullaosta alle sperimentazioni cliniche" che attribuisce al Direttore Generale della struttura sanitaria in cui è condotta l'attività di ricerca il rilascio del nullaosta alla conduzione degli studi;

la Convenzione tra Azienda Ospedaliero-Universitaria di Parma e l'Università degli Studi di Parma in tema di sperimentazione clinica di cui alla delibera n. 125 del 17/05/2013;

RICHIAMATI, altresì,

- il decreto del Ministro dell'economia e delle finanze del 6 agosto 2021 relativo all'assegnazione delle risorse in favore di ciascuna Amministrazione titolare degli interventi PNRR e corrispondenti milestone e target;
- il decreto del Ministro della salute, di concerto con il Ministro dell'economia e delle finanze 15 settembre 2021, di istituzione dell'Unità di Missione del Ministero della salute titolare di interventi PNRR, ai sensi dell'articolo 8 del citato decreto legge n. 77 del 2021;
- l'atto di indirizzo del Ministro del 12 ottobre 2021 con il quale sono stati individuati i relativi

Soggetti Attuatori nell'ambito degli interventi e sub-interventi di investimento del piano Nazionale di ripresa e resilienza (PNRR) a titolarità del Ministero della salute;

PREMESSO che il Ministero della Salute in data 13 dicembre 2022 ha comunicato che la valutazione della proposta progettuale ha avuto esito positivo e che, pertanto, la stessa è stata ammessa a finanziamento e precisamente: "Codice progetto PNRR-MAD- 2022-12376819, dal titolo "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)" **;**

ATTESO che per tale progetto, presentato dalla Prof.ssa Serafina Perrone, l'Azienda Ospedaliero-Universitaria di Parma aveva manifestato, con nota del 18.05.2023, in caso di ammissione al finanziamento, la disponibilità a garantire il supporto logistico organizzativo affinché il ricercatore possa condurre la ricerca per tutta la durata del progetto, prevedendo altresì come richiesto dal bando ministeriale, l'attribuzione di una borsa di studio per la medesima finalità di realizzazione del progetto;

VISTA inoltre la comunicazione, pervenuta per le vie brevi, con cui il Soggetto attuatore/beneficiario, la Regione Emilia-Romagna, ha comunicato i Progetti vincitori del Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali, fra cui il progetto in oggetto;

RICHIAMATA la comunicazione del 15.12.2022, con cui il Soggetto attuatore/beneficiario, Regione Emilia-Romagna, ha inoltrato la Convenzione progetto PNRR-MAD- 2022-12376819, già firmata digitalmente dal Direttore dell'Ufficio 3, Direzione generale della ricerca e dell'innovazione in sanità del Ministero stesso, e per la Regione Emilia-Romagna dall'Ing. Luca Baldino (Legale rappresentante), da sottoscrivere digitalmente da parte del Principal Investigator Prof.ssa Serafina Perrone;

RICHIAMATA, altresì, la nota prot.n. 1232480 del 15.12.2022 con cui la convenzione del Ministero della Salute, controfirmata dal Principal Investigator Prof.ssa Serafina Perrone, è stato inviata al Soggetto attuatore/beneficiario, Regione Emilia-Romagna, al fine di perfezionare i dettagli contrattuali relativi allo studio in oggetto;

CONSIDERATO che l'Azienda Ospedaliero-Universitaria di Parma, per il progetto di ricerca in oggetto, ha ottenuto un finanziamento pari ad € 870.000,00, in qualità di Azienda Capofila di Progetto;

ACQUISITO, il piano dei costi, a cui si rinvia per approfondimenti, ed accertata la compatibilità dello stesso con il progetto autorizzato dal Ministero della Salute;

ATTESO che, il finanziamento dovrà essere utilizzato per le finalità di progetto, nel rispetto delle modalità in esso indicate e concordate nel Budget a cui si rinvia per approfondimenti;

ATTESO, altresì, che le acquisizioni dei beni e servizi e di quant'altro necessario all'espletamento del progetto, verranno formalizzati e disposti dai competenti Servizi aziendali;

ACQUISITO inoltre, il parere unico favorevole condizionato del Comitato Etico AVEN rilasciato nella seduta del 10/01/2023 e il parere definitivo espresso nella seduta del 04.04.2023 sciogliendo le riserve precedentemente espresse comunicato con nota n. 15386 del 06.04.2023;

ACQUISITA infine la nota da parte del PI, Prof.ssa Serafina Perrone, che dichiara quale data di inizio delle attività progettuali il 20.05.2023, trasmessa al Soggetto attuatore/beneficiario, Regione Emilia-Romagna, assieme alla documentazione richiesta, con nota prot. n. 15507 del 07/04/2023;

ACQUISITO anche il numero del codice unico del progetto (CUP) di cui alla legge 16 **,** gennaio 2003, n. F53C22001880001;

DATO ATTO che la durata del progetto in oggetto è pari a 24 mesi , prorogabile eventualmente di ulteriori 6 mesi, come previsto dall'articolo 4 della convenzione, a cui si rinvia per approfondimenti;

DATO ATTO, altresì, che il Principal Investigator, Prof.ssa Serafina Perrone, è colui che coordina e conduce la ricerca e ne ha il controllo e la responsabilità sullo svolgimento, garantendo l'osservanza del protocollo di studio approvato dal Comitato Etico AVEN, e di eventuali emendamenti valutati ed approvati dal Comitato Etico medesimo;

VISTA la comunicazione del Ministero della Salute, agli atti prot. n. 19382 del 08.05.2023, di rilascio del nulla osta all'inizio delle attività del Progetto;

DATO ATTO, quindi, della legittimità del presente provvedimento;

RICHIAMATA l'istruttoria procedimentale effettuata ai sensi e per gli effetti della delibera n. 79 del 06 febbraio 2017;

RICHIAMATA, infine, la delibera n. 238 del 10 marzo 2021;

Delibera

Per le motivazioni esposte in premessa:

1. di autorizzare l'attivazione del Progetto di Ricerca Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- 2022-12376819, dal titolo "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)"" – Principal Investigator Prof.ssa Serafina Perrone dell'U.O. di Neonatologia dell' Azienda Ospedaliero Universitaria di Parma;
2. di dare atto che lo studio in argomento comporterà per l'Azienda un introito pari a euro € 870.000,00, in qualità di Azienda Capofila di Progetto;
3. di prendere atto che il piano dei costi presentato dal Principal Investigator, a cui si rinvia per approfondimenti, è conforme al programma di spesa di durata biennale presentato al Ministero della Salute;
4. di dare atto che per procedere alla rendicontazione delle spese effettuate nell'ambito di questo progetto, è stata attribuita allo stesso una sigla identificativa che corrisponde a "PNRR-MAD- 2022-12376819" che dovrà essere riportata su tutte le richieste ed i giustificativi di spesa aziendali su proposta del Principal Investigator del progetto, Prof.ssa Serafina Perrone, in conformità al piano dei costi a cui si rinvia per approfondimenti e nel rispetto della normativa vigente e del vincolo di destinazione;
5. di designare quale Delegato al trattamento dei dati personali, relativamente allo studio in oggetto il Principal Investigator, Prof.ssa Serafina Perrone, come da documento allegato, che costituisce parte integrante e sostanziale del presente atto;

Responsabile del procedimento ai sensi della L. 241/90:
Teresa Coppola

Allegato

ATTO DI DESIGNAZIONE A

DELEGATO AL TRATTAMENTO DEI DATI

nell’ambito degli STUDI e delle SPERIMENTAZIONI CLINICHE

Titolo dello studio: Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD-2022-12376819, dal titolo “Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)”

L’Azienda Ospedaliero-Universitaria di Parma (di seguito “Azienda”), con sede in Via Gramsci 14 – Parma, nella persona del Direttore Generale, legale rappresentante, Titolare del trattamento dei dati personali,

DESIGNA

DELEGATO AL TRATTAMENTO DEI DATI PERSONALI

ai sensi degli artt. 29 e 32, par. 4, del Regolamento (UE) 2016/679 e 2-quaterdecies del D. Lgs. 30 giugno 2003, n. 196

la Prof.ssa Serafina Perrone

in qualità di Responsabile Scientifico **nell’ambito dello studio sopra riportato** effettuato con strumenti elettronici o comunque automatizzati o con strumenti diversi, per l’ambito di funzioni e competenze attribuite.

Il Delegato risulta essere stato individuato per esperienza, capacità ed affidabilità tali da fornire idonea garanzia del pieno rispetto delle vigenti disposizioni in materia di protezione dei dati personali, ivi compreso il profilo relativo alla sicurezza, ed ha il compito e la responsabilità di adempiere a tutto quanto necessario per il rispetto delle disposizioni vigenti in materia e di osservare scrupolosamente quanto in esse previsto, nonché osservare le istruzioni impartite dal Titolare.

I dati personali vengono trattati, nell'ambito del suddetto studio per il perseguimento dei fini istituzionali dell'Azienda in conformità al vigente "Manuale aziendale in materia di trattamento dei dati personali", in cui sono indicati i profili di responsabilità in tema di protezione dei dati personali e le modalità di designazione dei soggetti Autorizzati ad eseguire operazioni di trattamento dei dati personali.

Istruzioni operative per il trattamento dei dati da parte del DELEGATO

Nello svolgimento della delega attribuita la S.V. dovrà attenersi alle seguenti disposizioni:

- **trattare** i dati personali solo su istruzione del Titolare del trattamento e garantire la corretta applicazione del Regolamento generale per la protezione dei dati (GDPR) e del D.Lgs. 196/2003, come modificato dal D.Lgs. 101/2018, nonché la conformità alle indicazioni dell'Autorità Garante per la protezione dei dati personali;
- **designare** i propri collaboratori quali Autorizzati al trattamento dei dati personali per i trattamenti di dati di propria competenza, in modalità scritta (modulo Autorizzati) e secondo livelli differenziati, conservando il relativo atto presso l'Investigator Site File (secondo quanto previsto dalle GCP);
- **fornire** agli Autorizzati istruzioni conformi alle disposizioni aziendali circa le corrette modalità da seguire e le misure di sicurezza da adottare per il trattamento dei dati personali, e richiedendo, se del caso, il rilascio delle credenziali per l'accesso ai software di competenza utilizzando la modulistica in uso, come da procedura Aziendale;
- **verificare** periodicamente che i dati personali oggetto di trattamento nello specifico ambito di competenza siano esatti, aggiornati, pertinenti e non eccedenti e che questi siano conservati in una forma che consenta l'identificazione dell'interessato per un periodo di tempo non superiore a quello necessario agli scopi per i quali essi sono stati raccolti o successivamente trattati;

- osservare e fare osservare dai collaboratori designati Autorizzati:
    a. le istruzioni (Manuale aziendale in materia di protezione dei dati personali; Istruzioni operative per i Delegati al trattamento dei dati; Manuale ad uso

degli autorizzati), linee di indirizzo (es. La cartella clinica – Linee di indirizzo per la corretta gestione), regolamenti (es. Regolamento per l'utilizzo dei sistemi informatici dell'Azienda Ospedaliero – Universitaria di Parma Regolamento per la gestione del Dossier Sanitario Elettronico all'interno dell'Azienda Ospedaliero-Universitaria di Parma), circolari e procedure aziendali (es. Procedura per la gestione dei Data Breach), specificamente ma non esclusivamente in materia di protezione dei dati personali, e i loro aggiornamenti, anche al fine di scongiurare possibili incidenti di sicurezza;

b. le istruzioni di carattere generale impartire dal Titolare a tutti i soggetti autorizzati al trattamento (es. Istruzioni operative sul corretto trattamento dei dati rivolte a tutti i dipendenti/collaboratori);
c. eventuali ulteriori specifiche istruzioni predisposte dallo stesso Delegato in relazione agli specifici ambiti di competenza, anche per gruppi omogenei di funzioni.

- **verificare** che i dati oggetto di trattamento siano esatti, aggiornati, pertinenti e non eccedenti rispetto alle finalità per cui vengono trattati;
- **attenersi** alle indicazioni di sicurezza dettate dal Titolare del trattamento e compatibilmente con l'ambito di attività, adottare le misure di sicurezza tecniche e organizzative adeguate, al fine di proteggere i dati da trattamenti non autorizzati o illeciti, dal rischio di perdita, di distruzione o di danno accidentale;
- **partecipare** ai momenti formativi organizzati dall'Azienda ed assicurare la partecipazione dei propri autorizzati;
- **fornire** le informazioni richieste da Servizi aziendali (U.O. Ricerca e Innovazione; U.O. Servizio Informativo Aziendale; Gruppo Aziendale Privacy ecc.), segnalare ogni questione rilevante in materia e trasmettere tempestivamente istanze e reclami degli interessati al DPO anche per il tramite del Gruppo Aziendale Privacy;
- **collaborare** con i competenti servizi per la compilazione e l'aggiornamento del Registro dei trattamenti aziendale;
- **non** porre in essere trattamenti di dati diversi e ulteriori senza la preventiva autorizzazione del Titolare del trattamento;
- **segnalare** senza ritardo al Titolare del trattamento, in conformità alla vigente procedura aziendale, ogni violazione di dati personali (c.d. Data Breach) di cui si

abbia conoscenza nell'ambito delle attività di ricerca e collaborare alla istruttoria del caso al fine di sottoporre al DPO ogni utile e opportuna determinazione in merito.

- **Vigilare che gli Autorizzati:**
  - **trattino** dati personali, qualora necessari e pertinenti, nel rispetto dei principi di liceità, correttezza e trasparenza, e con specifici accorgimenti e modalità tali da garantire la tutela della dignità e delle libertà individuali dell'interessato e la confidenzialità nelle comunicazioni;
  - **rispettino** il segreto d'ufficio e il segreto professionale o altri obblighi equivalenti di segretezza;
  - **rispettino** le adeguate misure di sicurezza organizzative e tecniche impartite dall'Azienda e dal Delegato per proteggere i dati personali;
  - **non comunichino** e/o diffondano i dati personali, neppure ricorrendo a sistemi di comunicazione digitale (tipo social network o messaggistica), a soggetti non autorizzati, e non li utilizzino per fini personali, anche attraverso la loro acquisizione tramite dispositivi personali, come ad esempio telefono cellulare, memoria USB, pc, ecc...;
  - **utilizzino** la documentazione cartacea, nonché i supporti rimovibili su cui sono memorizzati i dati personali (qualora autorizzati), osservando le istruzioni operative impartite dell'Azienda Ospedaliero Universitaria di Parma e/o dal Responsabile della Protezione dei dati personali (c.d. Rpd o DPO), custodendoli con modalità tali da evitare accessi non autorizzati e trattamenti non consentiti dei dati.
  - **provvedano** a distruggere ogni eventuale copia della documentazione o dei dati personali acquisiti per lo studio.

La S.V. dovrà altresì verificare che:

- Siano impiegate specifiche misure e accorgimenti tecnici per incrementare il livello di sicurezza dei dati trattati per l'esecuzione dello studio, sia nella fase di memorizzazione o archiviazione, sia nella fase successiva di elaborazione delle informazioni, nonché nella successiva fase di trasmissione dei dati, individuando la categoria dei dati personali trattati: ovvero se trattasi di dati comuni o particolari (relativi alla salute, origine razziale o etnica, genetici, biometrici…) o giudiziari in

modo da assegnare un adeguato livello di sicurezza (pseudonimizzazione, tecniche di cifratura, …).

- Siano adottati, in particolare:

a. accorgimenti adeguati a garantire la qualità dei dati e la corretta attribuzione agli interessati;

b. idonei accorgimenti per garantire la protezione dei dati dello studio dai rischi di accesso abusivo ai dati, furto o smarrimento parziali o integrali dei supporti di memorizzazione o dei sistemi di elaborazione portatili o fissi (ad esempio, attraverso l'applicazione parziale o integrale di tecnologie crittografiche a file system o database, oppure tramite l'adozione di altre misure che rendano inintelligibili i dati ai soggetti non legittimati) nelle operazioni di registrazione e archiviazione dei dati;

c. canali di trasmissione protetti, tenendo conto dello stato dell'arte della tecnologia, nei casi in cui si renda necessaria la comunicazione dei dati raccolti nell'ambito dello studio a una banca dati centralizzata dove sono memorizzati e archiviati oppure ad un promotore o a soggetti esterni di cui lo stesso promotore si avvale per la conduzione dello studio. Laddove detta trasmissione sia effettuata mediante supporto ottico (CD-ROM) è designato uno specifico autorizzato della ricezione presso il promotore ed è utilizzato, per la condivisione della chiave di cifratura dei dati, un canale di trasmissione differente da quello utilizzato per la trasmissione del contenuto;

d. tecniche di etichettatura, nella conservazione e nella trasmissione di campioni biologici, mediante codici identificativi, oppure altre soluzioni che, considerato il numero di campioni utilizzati, li rendono non direttamente riconducibili agli interessati, permettendo di identificare questi ultimi solo in caso di necessità;

e. con specifico riferimento alle operazioni di elaborazione dei dati dello studio memorizzati su in una banca dati centralizzata, è necessario adottare:

- idonei sistemi di autenticazione e di autorizzazione per il personale preposto al trattamento in funzione dei ruoli e delle esigenze di accesso e trattamento, avendo cura di utilizzare credenziali di validità limitata alla durata dello studio e di disattivarle al termine dello stesso;

- procedure per la verifica periodica della qualità e coerenza delle credenziali di autenticazione e dei profili di autorizzazione assegnati ai soggetti designati al trattamento;

- sistemi di controllo degli accessi al database e per il rilevamento di eventuali anomalie.

In ordine al salvataggio dei dati, il Delegato dovrà:

- valutare con il supporto tecnico, il tipo di supporto/dispositivo su cui salvare i dati personali trattati e che siano attive politiche adeguate di backup dei dati sia nel caso in cui gli stessi vengano memorizzati su sistemi di storage dell'Azienda o che siano salvati sui sistemi del gruppo di ricerca;

-assicurarsi che i dati personali non vengano salvati dai collaboratori su unità di memoria esterne (hard disk, chiavette, DVD) a meno che non siano autorizzati e dotati di appositi sistemi di cifratura (in modo da proteggere i dati anche nel caso in cui tali unità di memoria vengano smarrite o rubate);

-verificare con il supporto tecnico la completa cancellazione dei dati in caso di dismissione/riparazione/riutilizzo di hardware o dispositivi contenente i dati stessi.

In ordine alle procedure di Autenticazione ed Autorizzazione il Delegato dovrà:

-individuare i soggetti autorizzati a trattare i dati personali, definendo con il supporto tecnico le corrette autorizzazioni di accesso ai dispositivi e alle aree ove i dati sono trattati/conservati; qualora non sussistano più le ragioni per l'accesso ai dati (ad es. uscita di un ricercatore dal team di ricerca, conclusione del progetto di ricerca) procedere a far rimuovere tempestivamente le relative autorizzazioni;

-adottare meccanismi di autenticazione (pin, password e dati biometrici) per l'accesso al dato e/o ai sistemi che trattano il dato, attivando meccanismi di crittografia dei supporti fisici per tutti i sistemi.

Con la delibera di autorizzazione della Direzione Aziendale il Responsabile Scientifico dello studio acquista la qualifica di Delegato al trattamento dei dati personali.

La presente designazione, che potrà essere oggetto di revisione, ha efficacia per la sola durata dello studio e fino ad una successiva ed ulteriore delega o fino alla risoluzione del rapporto di lavoro o collaborazione per qualsiasi causa oppure fino alla revoca da parte del Titolare.

Il Titolare del trattamento dei dati personali Azienda
Ospedaliero-Universitaria di Parma

Prof.ssa Serafina Perrone
UO Neonatologia - AOU PARMA

Silvia Orzi - S.C.I. Esecuzione Contratti per Fornitura di Beni

Cristina Gazzola - S.C.I. Servizio Economico Finanziario e aspetti economici dell accesso alle prestazioni sanitarie

Michela Boschi - S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici

Alessandra Zanardi - S.C. Farmacia e Governo Clinico del Farmaco

Giulia De Luca - S.C. Farmacia e Governo Clinico del Farmaco

Marco Brambilla - Servizio Interaziendale Tecnologie dell'Informazione

Matteo Berghenti - S.S.D.I. Ingegneria Clinica

Michela Guasti - S.C.I. Area Giuridica

Laura Oddi - S.C.I. Area Economica

Antonio Ventura - Direttore Amministrativo

Nunzia D'Abbiero - Direttore Sanitario

OGGETTO: Indicazioni per la gestione economico/amministrativa dello studio autorizzato con Delibera n .336/2023

Con la presente si comunica che, in seguito all'autorizzazione all'avvio del Progetto di Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- , dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis

prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)" – Principal Investigator Prof.ssa Serafina Perrone dell' U.O. di Neonatologia di questa Azienda, sono stati attribuiti i seguenti:

- **Commessa** (codice identificativo progetto): PNRR-MAD- 2022-12376819
- **ID Budget:** 1018977
- **Combinazione:** *-PRG-PROGETTI DI RICERCA-PNRR-MAD- 2022-12376819-2023/137 PNRR-MAD- 2022-12376819-2023/137 PNRR-MAD- 2022-12376819-_-_-_-_-_-_-_-

I sopracitati codici, dovranno essere indicati in tutte le richieste di acquisizione di beni, servizi e personale, da inoltrare ai competenti Servizi Aziendali.
Inoltre, per garantire la tracciabilità e la corretta rendicontazione delle prestazioni aggiuntive (esami strumentali o di laboratorio, procedure mediche o assistenziali), la commessa è registrata sul sistema AREAS (gestione degenze), dove alla pagina dedicata agli studi clinici occorre segnalare tutte le prestazioni aggiuntive erogate al paziente ai fini dello studio.
Si ricorda che, in conformità alla normativa vigente e al regolamento aziendale, costituisce uno specifico dovere del Responsabile scientifico comunicare all'Azienda la tipologia e il volume dei costi aggiuntivi effettivamente sostenuti, utili agli addebiti a carico dello Sponsor. E' inoltre sua responsabilità assicurarsi che venga trasmessa al Comitato Etico competente e all'Azienda un rapporto sullo stato di avanzamento dello studio al termine di ogni anno solare e al termine dello studio stesso, descrittivo dello stato di avanzamento (pazienti arruolati e costi sostenuti localmente per tipologia).

Ringraziando per la collaborazione, si inviano cordiali saluti

Firmato digitalmente da:
Teresa Coppola

Responsabile procedimento:
Rossella Zucchelli

Grant Office
Area Gestione Giuridica Amministrativi Studi
Tel. 0521/703686/3609

Azienda Ospedaliero - Universitaria di Parma
Via Gramsci, 14 - 43126 Parma
T. +39.0521.702111 - 703111
Partita Iva 01874240342
PEI: protocollo@cert.ao.pr.it

1 - General information

Project code: PNRR-MAD-2022-12376819

Project topic: C1) Malattie croniche non trasmissibili, ad alto impatto sui sistemi sanitari e socio-assistenziali: fattori di rischio e prevenzione

Applicant Institution: Emilia-Romagna

PI / Coordinator: Perrone Serafina

Istitution that perform as UO for UO1: Azienda Ospedaliero Universitaria di Parma

Call section: Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali

Proposal title: Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention

Duration in months: 24

MDC primary: Ostetricia e Ginecologia

MDC secondary: Pediatria

Project Classification IRG: Musculoskeletal, Oral and Skin Sciences

Project Classification SS: Skeletal Biology Development and Disease - SBDD

Project Keyword 1: Studies involving diseases of the skeleton and mineral metabolism in humans and animal models such as osteogenesis imperfecta; Paget¿s disease of bone; chondrodystrophies, osteodystrophies; diseases of mineral ion homeostasis associated with abnormalities of parathyroid hormone, Vitamin D, calcitonin and other hormonal and paracrine factors.

Project Request: **Animals:** ☐ **Humans:** ☒ **Clinical trial:** ☐

Project total financing request to the MOH: € 870.000

Free keywords: Bone mineral Density, oxidative stress, Endocrine discruiptors, environment, fetus, newborns, children, osteoporosis

Declarations

In case of a Synergy grant application 'Principal Investigator'(PI) means 'corresponding Principal Investigator on behalf of all Principal Investigators', and 'Host Institution' means 'corresponding Host Institution'.

1) The Principal Investigator declares to have the written consent of all participants on their participation and on the content of this proposal, as well as of any researcher mentioned in the proposal as participating in the project (either as other PI, team member or collaborator).	X
2) The Principal Investigator declares that the information contained in this proposal is correct and complete.	X
3) The Principal Investigator declares that all parts of this proposal comply with ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct).	X
4) The Principal Investigator is only responsible for the correctness of the information relating to his/her own organisation. Each applicant remains responsible for the correctness of the information related to him and declared above.	X

Personal data protection

The assessment of your grant application will involve the collection and processing of personal data (such as your name, address and CV), which will be performed pursuant to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Unless indicated otherwise, your replies to the questions in this form and any personal data requested are required to assess your grant application in accordance with the specifications of the call for proposals and will be processed solely for that purpose. Details concerning the purposes and means of the processing of your personal data as well as information on how to exercise your rights are available in the privacy statement. Applicants may lodge a complaint about the processing of their personal data with the European Data Protection Supervisor at any time.

Abstract

Maximization of bone mass during skeletal growth has become the goal of primary prevention of osteopenia and osteoporosis. Any factor that might influence peak bone mass attained at skeletal maturity is important in determining the individual¿s risk of developing osteoporosis later in life. Bone health begins with maternal health and nutrition, which influences skeletal mass and bone density in the fetus. Peak bone mass acquisition is also under a genetic influence from both parents. To date, some evidences suggests that the risk of osteoporosis later in life may be determined by environmental influences during intrauterine or early postnatal life. The mechanisms underlying the long term effect of the intrauterine environment on bone health are currently unknown but definitely include ``fetal programming¿¿ of oxidative stress and endocrine systems that influence skeletal growth and development in utero and thereafter. Osteopenia is recognized with increasing frequency in low-birth weight newborn infants. Intrauterine growth restriction also increases the risk of obesity and metabolic syndrome which dramatically affect bone quality. Micro RNA and long non coding RNA have recently come into the spotlight due to their ability to control gene expression at the post-transcriptional level providing epigenetic modification and targeting the growth plate.
These considerations highlight that the evaluation of skeletal status from perinatal period is essential for both the early detection of the conditions characterized by defects in bone mass or mineralization and for the monitoring of the bone development process.
It is still unknow if and how fetal bone mineral density varies according to maternal nutritional factors, if and how it impacts on some outcomes at childbirth (eg spontaneous clavicle or skull fractures during operative birth) and on the long term bone mineralization.
Radiofrequency Echographic Multi Spectrometry (REMS) technology has proven to be useful in the assessment of bone mineral denisity in pregnant women. Very few studies have reported that transmission ultrasound can be used for the assessment of bone status in newborns. The attractiveness of REMS technology in fetus and newborns stands in the lack of ionizing radiation, ease of use and, above all, the possibility to perform longitudinal studies on REMS patterns from

intrauterine to extrauterine life and during the first year of life. New challenge relies in - development of transducers and software tspecific for fetus and newborns. which will be part of this project.
Starting from the mother¿s exposome information, the project will unravel the effect of environmental contaminants, and in particular of endocrine disruptors, of oxidative stress and of miRNAs within the field of epigenetics on bone health .
The aims of the present study are:

A) To determine the feasibility of the use of REMS, as assessed by a new measurement approach to evaluate skeletal status in fetuses, newborns and children as a precise and innovative technology.
B To assess how mother's REMS patterns, and her anthropometric and gestational data influence REMS parameters in the fetus, newborn and during the first year of life.
C) To unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health

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In order to best review your application, do you agree that the above non-confidential proposal title and abstract can be used, without disclosing your identity, when contacting potential reviewers? Yes

2 - Participants & contacts

Operative Units

Institution that perform as UO	CF Institution	Department / Division / Laboratory	Role in the project	Southern Italy	SSN
1 - Azienda Ospedaliero Universitaria di Parma	01874240342	Department of Mothers Infants and Children	Coordinator		X
2 - Sicily	03051890832	Department of Human Pathology of adulthood and childhood	Collaborator	X	X

Principal Research Collaborators

Key Personnel Name	Operative Unit	Role in the project
1 - Ghi Tullio	Azienda Ospedaliero Universitaria di Parma	Co-PI (Gynecologist for mother and fetal data)
2 - STREET MARIA ELISABETH	Azienda Ospedaliero Universitaria di Parma	Research Collaborator Pediatrician
3 - WASNIEWSKA MALGORZATA GABRIELA	Sicily	Research Collaborator Pediatrician Southern Italy
4 - Aversa Tommaso	Sicily	Research Collaborator Pediatrician Southern Italy
5 - DALL'ASTA ANDREA	Azienda Ospedaliero Universitaria di Parma	Under 40 (Gynecologist for mother and fetal data)
6 Under 40 - CORICA DOMENICO	Sicily	Under 40 (Pediatrician)
7 Under 40 - DI PASQUO ELVIRA	Azienda Ospedaliero Universitaria di Parma	Under 40 (Gynecologist for mother and fetal data)

Project Code: PNRR-MAD-2022-12376819	**Call section:** Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e
Applicant Institution: Emilia-Romagna	**Applicant/PI Coordinator:** Perrone Serafina

Key Personnel Name	Co-PI	Resp. CE	Resp. Animal	Birth Date	Gender
1 - Ghi Tullio	X			28/04/1973	M
2 - STREET MARIA ELISABETH				21/02/1967	F
3 - WASNIEWSKA MALGORZATA GABRIELA				17/09/1959	F
4 - Aversa Tommaso				31/01/1980	M
5 - DALL'ASTA ANDREA				22/11/1985	M
6 Under 40 - CORICA DOMENICO				31/12/1987	M
7 Under 40 - DI PASQUO ELVIRA				04/08/1986	F

Additional research collaborators under 40 to hire

Key Personnel Name	Operative Unit	Birth Date	Gender	Role in the project	Degree	Actual Pos. and Inst.
0 - Pepe Giorgia	Sicily	23/04/1990	F	Patient enrollment, samples collection	Master Degree	
1 - MURA REBECCA	Azienda Ospedaliero Universitaria di Parma	18/06/1993	F	Patient enrollment, samples collection	Master Degree	
2 - cannavò Laura	Sicily	16/08/1990	F	Patient enrollment, samples collection	Master Degree	

2.1 Administrative data of participating

Operative Unit Number 1:

Address: Viale Antonio Gramsci, 14, 43126 Parma PR
PEC: protocollo@cert.ao.pr.it

Operative Unit Number 2:

Address: Via Consolare Valeria, 1, 98124 Messina ME
PEC: protocollo@pec.polime.it

Operative Unit Number 3:

Address: NA
PEC: NA

Operative Unit Number 4:

Address: NA
PEC: NA

Operative Unit Number 5 (self financing):

Address: NA
PEC: NA

2.2 Principal Investigator (PI) Profile

Last Name: Perrone
First Name: Serafina
Last name at birth:
Gender: F

Title: Principal investigator
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 23/07/1968
Place of Birth: San Pietro Vernotico

Official H index (Scopus or Web of Science): 32.0

Scopus Author Id:7004420322 **ORCID ID:**0000-0001-5478-5657 **RESEARCH ID:**AAC-2592-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci 14, Parma
Postcode / Cedex: 43126
Town: Parma
Phone:+393388704211
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Siena	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine, vote of 110/110 cum laude	1988	1993
University of Siena	Specialization / Specializzazione	Specialization in Pediatrics (address Neonatology and Neonatal Pathology), vote 70/70 cum laude	1993	1997
University of Siena	PhD	Doctor of Research (PhD) in "Growth Factors"	1998	2001
Istituto Superiore Sant'Anna of Pisa	Master's Degree / Laurea Magistrale	Master II levels: Managerial High Training Course for the Director of Complex Structure	2017	2018
University of Siena	Master's Degree / Laurea Magistrale	Master II levels. Intensive and Subintensive Therapy of the Pediatric age (0-18 years) with advanced simulation	2018	2019

Personal Statement:

The main goal of the project is to get insight on previously unexplored aspects of bone system improving the approach used in bone mineral density assessment, and thereby reducing the frequency of osteopenia, with better quality of life.
The project aims to unravel mechanisms of mother-fetus cross talk focusing on perinatal exposure to oxidative stress (OS) and endocrine disruptors.
PI has long experience on markers of OS in the early identification of the newborn at high risk and in evaluating new protective clinical strategies. More recently her research may provide insight into the pathogenesis and effects of fetal programming and infants outcomes. Data are in line with fetal programming hypothesis of health from birth toward

adulthood

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma and Azienda Ospedaliera Universitaria di Parma	Department of Medicine and Surgery; Neonatal Intensive Care Unit and Neonatal Unit	Parma, Italy	Associate Professor of Pediatrics and Medical Manager position (Head of Neonatology Unit)	2019	2222
University Hospital of Siena (Azienda Ospedaliera Universitaria Senese)	Neonatal Intensive Care Unit	Siena, Italy	Medical manager position	2000	2019

Other awards and honors

2002: Winner of the ¿Ubaldo di Mita¿ National Award for the best graduation thesis in Pediatrics, issued by Italian Society of Neonatology
2014: Oral Presentation Arward at 4th International Congress of UENPS, Athens, Greece 2014: Long-term impact of VLBW on psyco-neurological development in young adults: a single center population linkage study
2016: Best Abstract Arward at 6th International Congress of UENPS, Valencia Spain 2016:
Newborn metabolic profile mirrors that of mother in pregnancy

Other CV informations

Coordinator and Head of the Clinical Biochemistry Study Group (Italian Society of Neonatology).
Deputy President of the Bachelor of Health Professions in Nursing, University of Parma
Appointment as Regional Referent for Rare Diseases
Invited as Expert Revisor for AIFA experimental project, (Italian Drug Agency) and for Research proposal submitted to the executive Government agency of National Science Centrum of Poland
Guest Editor of Special issue ¿Oxidative stress in the Newborn¿ in ¿Antioxidants¿ (2021)
Lead Guest Editor of Special issue ¿Biomarkers on Oxidative stress in the neonatal period¿ in ¿Journal of Pediatric Biochemistry¿ (2016).
Guest Editor of Special issue ¿Oxidative stress in the Newborn¿ in ¿Oxidative Medicine and Cellular Longevity (2015)

Selected peer-reviewed publications of the PI valid for minimum expertise level

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
The clinical course of SARS-CoV-2 positive neonates	Review	1462-1469	40	2020	10.1038/s41372-020-0715-0	32632198	21	L
Biomarkers of oxidative stress in the fetus and in the newborn	Review	23-31	142	2019	10.1016/j.freeradbiomed.2019.03.034	30954545	21	F
Breast milk: To each his own. From metabolomic study, evidence of personalized nutrition in preterm infants	Article	158-161	62	2019	10.1016/j.nut.2018.12.015	30921551	14	F
C reactive protein in healthy term newborns during the first 48 hours of life	Article	F163-F166	103	2018	10.1136/archdischild-2016-312506	28667188	30	F

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Identification of a panel of cytokines in neonates with hypoxic ischemic encephalopathy treated with hypothermia	Article	119-124	111	2018	10.1016/j.cyto.2018.08.011	30142532	10	F
Early prediction of hypoxic-ischemic brain injury by a new panel of biomarkers in a population of term newborns	Article	NOT_FOUND	2018	2018	10.1155/2018/7608108	30050660	21	L
The free radical diseases of prematurity: From cellular mechanisms to bedside	Review	NOT_FOUND	2018	2018	10.1155/2018/7483062	30140369	32	F
Oxidative Stress Biomarkers: Establishment of Reference Values for Isoprostanes, AOPP, and NPBI in Cord Blood	Article	NOT_FOUND	2017	2017	10.1155/2017/1758432	28512386	16	F
Oxidative Stress as a Physiological Pain Response in Full-Term Newborns	Article	NOT_FOUND	2017	2017	10.1155/2017/3759287	28133505	10	F
Oxidative Stress Biomarkers: Establishment of Reference Values for Isoprostanes, AOPP, and NPBI in Cord Blood	Article	NOT_FOUND	2017	2017	10.1155/2017/1758432	28512386	16	L
Maternal obesity and perinatal oxidative stress: The strength of the association	Article	221-227	31	2017	NOT_FOUND	28337896	18	L
Oxygen Use in Neonatal Care: A Two-edged Sword	Review	NOT_FOUND	4	2017	10.3389/fped.2016.00143	NOT_FOUND	47	F
Placental histological examination and the relationship with oxidative stress in preterm infants	Article	72-78	46	2016	10.1016/j.placenta.2016.08.084	27697224	23	F
Brain susceptibility to oxidative stress in the perinatal period	Review	2291-2295	28	2015	10.3109/14767058.2013.796170	23968388	46	F
Lipid and protein oxidation in newborn infants after lutein administration	Article	NOT_FOUND	2014	2014	10.1155/2014/781454	24876916	34	F
Biomarkers of oxidative stress in fetal and neonatal diseases	Review	2575-2578	25	2012	10.3109/14767058.2012.718004	22876862	39	F
Oxidative injury in neonatal erythrocytes	Review	104-108	25	2012	10.3109/14767058.2012.715471	23025782	36	F
New pharmacologic and therapeutic approaches for hypoxic-ischemic encephalopathy in the newborn	Review	83-88	25	2012	10.3109/14767058.2012.663168	22309153	25	F
May oxidative stress biomarkers in cord blood predict the occurrence of necrotizing enterocolitis in preterm infants?	Article	128-131	25	2012	10.3109/14767058.2012.663197	22339378	51	F
Perinatal outcome and placental histological characteristics: A single-center study	Article	110-113	25	2012	10.3109/14767058.2012.664344	22348288	33	F

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

Selected peer-reviewed publications of the PI for the evaluation CV

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**
The use of melatonin in hypoxic-ischemic brain damage: An experimental study	Article	119-124	25	2012	10.3109/14767058.2012.663232	NOT_FOUND	62
Oxidative stress and antioxidant strategies in newborns	Review	63-65	23	2010	10.3109/14767058.2010.509940	20807155	103

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**
Whole body hypothermia and oxidative stress in babies with hypoxic-ischemic brain injury	Article	236-240	43	2010	10.1016/j.pediatrneurol.2010.05.009	20837300	51
Oxygen toxicity: Chemistry and biology of reactive oxygen species	Review	186-190	15	2010	10.1016/j.siny.2010.04.003	20494636	204
Early identification of the risk for free radical-related diseases in preterm newborns	Article	241-244	86	2010	10.1016/j.earlhumdev.2010.03.008	20466493	89
Free iron, total F2-isoprostanes and total F4-neuroprostanes in a model of neonatal hypoxic-ischemic encephalopathy: Neuroprotective effect of melatonin	Article	148-154	46	2009	10.1111/j.1600-079X.2008.00639.x	19141088	71
Melatonin protects from the long-term consequences of a neonatal hypoxic-ischemic brain injury in rats	Article	157-164	44	2008	10.1111/j.1600-079X.2007.00503.x	18289167	132
Association between oxidative stress in pregnancy and preterm premature rupture of membranes	Article	793-797	40	2007	10.1016/j.clinbiochem.2007.03.004	17442295	92
Early oxidative stress in amniotic fluid of pregnancies with Down syndrome	Article	177-180	40	2007	10.1016/j.clinbiochem.2006.10.019	17208212	67
Non protein bound iron as early predictive marker of neonatal brain damage	Article	1224-1230	126	2003	10.1093/brain/awg116	12690060	94

** Autocertificated

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
University of Parma in collaboration with Azienda USL and AOU Parma	University Hospital of Parma	2022-2024	Network on the prevention and fight against the "Sudden Infant Death Syndrome" (SIDS) in the province of Parma period 2022/2024"	Coordinator	15.000,00	Local Protocol
University of Parma in collaboration with Azienda U.S.L. and Azienda Ospedaliero Universitaria of Parma	University of Parma	2019-2021	Network on the prevention and fight against the "Sudden Infant Death Syndrome" (SIDS) in the province of Parma period 2019/2021	Coordinator	15.000,00	Local Protocol

2.3 CO-PI Profile

Last Name: Ghi
First Name: Tullio
Last name at birth:
Gender: M

Title: Co-PI (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 28/04/1973
Place of Birth: Cosenza

Official H index (Scopus or Web of Science): 39.0

Scopus Author Id:6602157913 **ORCID ID:**0000-0003-1823-1096 **RESEARCH ID:**AAC-6832-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Viale Antonio Gramsci 14
Postcode / Cedex: 43100
Town: Parma
Phone:+393385070025
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Bologna	Specialization / Specializzazione	Obstetrics and Gynecology	1997	2002
University of Bologna	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	1991	1997

Personal Statement:

The project aims to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate and correlate maternal bone characteristics with those observed in the fetus and in the newborn. As Co-PI of the project, Tullio Ghi will coordinate and supervise the researcher group involved in the project and will provide expertise

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
King's College Hospital	Harris Birthright Centre Fetal Medicine Unit	London	Clinical fellowship in Fetal Medicine and fetal cardiology	2000	2001
Ospedale Sant¿Orsola Malpighi	Dipartimento di Ostetricia e Ginecologia	Bologna	Consultant in Obstetrics and Gynecology	2003	2014
Università degli Studi di Parma	Department of Medicine and Surgery	Parma	Associate Professor of Obstetrics and Gynecology	2014	2021
Università degli Studi di Parma	Department of Medicine and surgery	Parma	Director of the Residency School of Obstetrics and Gynecolo	2020	2022
Azienda Ospedaliero-Universitaria di Parma	Obstetrics and Gynecology department	Parma	Head of Obstetrics and Gynecology at the University Hospital of Parma	2021	2022
Università degli Studi di Parma	Dipartimento di Medicina e Chirurgia	Parma	Full Professor of Obstetrics and Gynecology	2021	2022

Other awards and honors

He is in board of the Italian Society of Ultrasound in Obstetrics and Gynecology and is the past president of the Italian Society of Preeclampsia (AIPE)
In 2019 he has founded the ISLANDS group (International Society of Labor and Delivery Sonography).
Best oral presentation at II Congress Research and developments in fetal medicine, London, 2002.
Best oral presentation and oral poster at XVII ISUOG Congress, Florence, October, 2007.
Best oral poster at XXVI ISUOG Congress, Rome, 2016

Other CV informations

Following his residence in Ob-Gyn at the S.Orsola Hospital of Bologna, from 2000 until 2001 Prof.Ghi was at King's College Hospital for a fellowship in Fetal Medicine. He has a phD in fetal Medicine at the University of Milan (2002-2005). Since 2014 he is based at the Department of Medicine and Surgery of the University of Parma, where he has been appointed as Full Professor of Obstetrics and Gynecology, Director of the Residency School in Obstetrics and Gynecology at the University Hospital of Parma. His main field of research is on obstetrics, ultrasound in labor and prenatal diagnosis of congenital anomalies. He has published more than 200 articles and 3 books

Selected peer-reviewed publications of the Co-PI valid for minimum expertise level

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Customized Fetal Growth Charts for Parents' Characteristics, Race, and Parity by Quantile Regression Analysis: A Cross-sectional Multicenter Italian Study	Article	83-92	35	2016	10.7863/ultra.15.03003	26643757	22	F
Narrow subpubic arch angle is associated with higher risk of persistent occiput posterior position at delivery	Article	511-515	48	2016	10.1002/uog.15808	26565728	22	F
Agreement between two- and three-dimensional transperineal ultrasound methods for assessment of fetal head-symphysis distance in active labor	Review	183-188	43	2014	10.1002/uog.13204	24006290	24	L

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
The "occiput-spine angle": A new sonographic index of fetal head deflexion during the first stage of labor	Article	84.e1-84.e7	215	2016	10.1016/j.ajog.2016.02.020	26880733	29	F
Development of customized fetal growth charts in twins	Article	514.e1-514.e17	216	2017	10.1016/j.ajog.2016.12.176	28065816	32	F
Sonographic pattern of fetal head descent: Relationship with duration of active second stage of labor and occiput position at delivery	Article	82-89	44	2014	10.1002/uog.13324	24496823	41	F
Intrapartum transperineal ultrasound assessment of fetal head progression in active second stage of labor and mode of delivery	Article	430-435	41	2013	10.1002/uog.12379	23288706	59	F
ISUOG practice guidelines: Invasive procedures for prenatal diagnosis	Review	256-268	48	2016	10.1002/uog.15945	27485589	61	F
Fetal head-symphysis distance: A simple and reliable ultrasound index of fetal head station in labor	Article	419-424	41	2013	10.1002/uog.12335	23124698	77	L
ISUOG Practice Guidelines: intrapartum ultrasound	Review	128-139	52	2018	10.1002/uog.19072	29974596	104	F

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
Università di Parma	Department of Medicine and Surgery	2022	Womb wise. Prenatal development of multisensory integration: a 4D ultrasound study	Coordinator	50.975,00	Local Protocol

2.3 Research Collaborators n. 2

Last Name: STREET
First Name: MARIA ELISABETH
Last name at birth:
Gender: F

Title: Research Collaborator Pediatrician
Country of residence: ITALY
Nationality: ITALIANA
Country of Birth: UNITED KINGDOM
Date of birth: 21/02/1967
Place of Birth: Regno Unito

Official H index (Scopus or Web of Science): 25.0

Scopus Author Id:7006191926 **ORCID ID:**0000-0001-8427-8971 **RESEARCH ID:**B-7099-2011

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci, 14
Postcode / Cedex: 43126
Town: Parma
Phone:3332076294
Phone 2: 3332076294

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	Master's Degree / Laurea Magistrale	II level University Master in ¿Management of Endocrine and Eating Disorders in Pediatrics	2003	2004
University of Parma	PhD	Paediatric Gastro-Endocrinology	1997	2000
University of Parma	Specialization / Specializzazione	Paediatric Residency (rotatory), Department of Paediatrics, University of Parma, Italy (Diploma cum Laude)	1992	1996
University of Parma	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	1986	1992

Personal Statement:

The overall goal of the project is to unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother's nutrition as part of the in utero exposome, and subsequent body composition and bone health
Prof Street has a strong expertise in endocrinology in pediatric patients. She ensures quality of the follow-up of newborn infants
She also will give a substantial contribution in collecting data, interpreting result and supervising the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma	Department of Paediatrics	Parma, Italy	Research Associate	1999	2003
Parma University Hospital	Department of Paediatrics	Paediatric Endocrine Clinic, Parma	Honorary Clinical Fellow, supervision and teaching to paediatric residents.	1996	2002
Parma University Hospital	Department of Paediatrics	Parma, Italy.	Hospital contracts and Research Fellow	2002	2007
University Hospital of Parma	Department of Paediatrics	Parma, Italy.	clinical permanent position	2007	2014
AUSL-IRCCS di Reggio Emilia	Division of Paediatric Endocrinology and Diabetology	Reggio Emilia, Italy	Head Division of Paediatric Endocrinology and Diabetology and director research Laboratory-Dept of Mother and Child	2014	2021
University Hospital of Parma, P. Barilla Children¿s Hospital, Parma, Italy	Department of Medicine and Surgery	University Hospital of Parma	Researcher University of Parma and Head Clinical and Research Centre for Paediatric Endocrinology	2021	2022

Other awards and honors

2000: Travel Grant awarded by the European Society for Paediatric Endocrinology for the ESPE Meeting in Bruxelles
2003: Travel Grant¿ awarded by the European Society for Paediatric Endocrinology for the ESPE Meeting in Ljubjana
2005: Best scientific contributions to the XV National Meeting of the Italian Society for Pediatric Endocrinology and Diabetology
2008: Top rated basic abstract ESPE meeting, Istanbul
2013 Best oral communication basic science XIX ISPED National meeting Bari

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
UE- Horizon 2020	Reggio Emilia Hospital	2019-2024	Mother and Infant dyads: lowering the impact of endocrine disrupting chemicals in milk for a healthy life -LIFE MILCH-LIFE18 ENV/IT/0004601 MILCH	Collaborator	492.000,00	www.lifemilch.eu
MERCK	Reggio Emilia Hospital	2017-2021	International competitive GRANT FOR GROWTH INNOVATION (GGI): MicroRNAs as a New Tool To Predict Growth Response to Growth Hormone Treatment	Coordinator	60.000,00	Local Protocol

2.4 Research Collaborators n. 3

Last Name: WASNIEWSKA
First Name: MALGORZATA GABRIELA

Last name at birth:
Gender: F

Title: Research Collaborator Pediatrician Southern Italy
Country of residence: ITALY
Nationality: Italiana
Country of Birth: POLAND
Date of birth: 17/09/1959
Place of Birth: Koszalin

Official H index (Scopus or Web of Science): 28.0

Scopus Author Id:7004045267 **ORCID ID:**0000-0001-9090-2574 **RESEARCH ID:**AFJ-4491-2022

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Dipartimento di Patologia Umana dell'adulto e dell'età evolutiva, Azienda Ospedaliera "G. Martino" di Messina, Università degli Studi di Messina
Postcode / Cedex: 98125
Town: Messina
Phone:+393286522425
Phone 2: 3286522425

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	PhD	Pediatric Gastroendocrinology	1999	2003
University of Messina	Specialization / Specializzazione	Residency in Pediatrics (1st grade in Poland-1987; 2nd grade in Poland-1991; in Italy, University of Messina-1999	1995	1999
Warsaw Academy of Medicine	Master's Degree / Laurea Magistrale	Degree in Medicine at Warsaw Academy of Medicine , acknowledgement of Degree in Medicine in Italy (1994);	1978	1983

Personal Statement:

The overall goals of the project are -to unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother's nutrition as part of the in utero exposome, and subsequent body composition and bone health
Prof Wasniewska has a long experience in pediatric endocrinology. She will ensure quality of the follow-up of newborn infants
She also will give a substantial contribution in collecting data, interpreting result and supervising the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Human Pathology of adulthood and childhood "	Messina, Italy	Full Professor of Pediatrics and Medical manager Position	2022	2022
University of Messina	Department of Human Pathology of adulthood and childhood	Messina, Italy	Associate Professor of Pediatrics and Medical manager position	2015	2022
University of Messina	Pediatric Clinic	Messina, Italy	Clinical Researcher	2004	2015
National Research Institute of Mother and Child	Pediatric Clinic	Warsaw ; Poland	Assistant and First Assistant	1983	1993

Other awards and honors

Coordinator of the Didactic Commission of Italian Society of Pediatric Endocrinology (2021-23)
- national coordinator (2007-09 and 2012-2013) of the Study Group ¿Endocrine diseases due to altered function of the Gs¿ protein¿ of Italian Society of Pediatric Endocrinology and Diabetology
- national coordinator (2013-2015) of the Study Group ¿Turner Syndrome¿ of Italian Society of Pediatric Endocrinology and Diabetology
-Referent of pediatric endocrinology in the Sicily region (2017-2021).

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
ESPE Research Unit Grant	University of Messina	2018-2019	Personalised approach to non-syndromic childhood obesity using multi-omics disease signature Head of The Italian Research Unit.	Coordinator	130.000,00	ESPE website and local protocol
Pfizer	University of Messina	2021-2023	Pfizer Global Grant: ADHERENCE TO GROWTH HORMONE THERAPY AND QUALITY OF LIFE IN PEDIATRIC PATIENTS: NEW STRATEGIES OF EVALUATION AND INTERVENTION	Coordinator	65.000,00	Pfizer web site and local protocol
Sicily Region	University of Messina	2022-2024	0-6 EpPOI- Educate to prevent childhood obesity	Coordinator	100.000,00	Local protocol

2.5 Research Collaborators n. 4

Last Name: Aversa
First Name: Tommaso
Last name at birth:
Gender: M

Title: Research Collaborator Pediatrician Southern Italy
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 31/01/1980
Place of Birth: Messina

Official H index (Scopus or Web of Science): 19.0

Scopus Author Id:16199757000 **ORCID ID:**0000-0002-1754-6822 **RESEARCH ID:**O-2490-2014

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Via Consolare Valeria 1
Postcode / Cedex: 98125
Town: Messina
Phone:+393495103397
Phone 2: 3495103397

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Department of Clinical and Experimental Medicine and Pharmacology, University of Messina	PhD	Experimental Endocrinological and Metabolic Sciences (XXV cycle)	2010	2012
University of Messina	Specialization / Specializzazione	Pediatrics	2004	2009
University of Messina	Master's Degree / Laurea Magistrale	Master degree in Medicine and Surgery	1998	2004

Personal Statement:

The aim of the project is
Aversa Tommaso is a pediatrician with experience in gastroendocrinology, particularly in endocrinological and metabolic aspects of children born small for gestational age, the pathogenesis and molecular biology of GH deficiency. The role of Prof Aversa will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Associate Professor of Pediatrics	2021	2022
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Assistant Professor of Pediatrics	2018	2021
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Research Associate of Pediatrics	2013	2018
Azienda Ospedaliera Universitaria Policlinico ¿Gaetano Martino¿	Pediatric Clinic	Messina, Italy	Pediatric Consultant with a special interest in Pediatric Endocrinology	2014	2022

Other awards and honors

Junior Member of Sicilian Regional Council of the Italian Society of Pediatrics (SIP) for the period 2020-2023
Delegate of the College of Young Pediatricians at the National Executive Council of the SIP for the period 2021-2023
Chair of the study group for Thyroid Disease in Childhood of the SIEDP/ISPED for the period 2017-2019
Chair of the study group for Turner Syndrome of SIEDP/ISPED for the period 2021-2023

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
Pfizer	University of Messina	2021-2023	ADHERENCE TO GROWTH HORMONE THERAPY AND QUALITY OF LIFE IN PEDIATRIC PATIENTS: NEW STRATEGIES OF EVALUATION AND INTERVENTION	Collaborator	65.000,00	Pfizer web site and local protocol
Sicily Region	University of Messina	2022-2024	0-6 EpPOI- Educate to prevent childhood obesity	Collaborator	100.000,00	Local Protocol

2.6 Research Collaborators n. 5

Last Name: DALL'ASTA
First Name: ANDREA
Last name at birth:
Gender: M

Title: Under 40 (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 22/11/1985
Place of Birth: Cremona

Official H index (Scopus or Web of Science): 16.0

Scopus Author Id:57150758200 **ORCID ID:**0000-0001-7201-0206 **RESEARCH ID:**K-4774-2018

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci 14
Postcode / Cedex: 43126
Town: Parma
Phone:+393332700919
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	PhD	Medical Sciences	2017	2020
University of Parma	Specialization / Specializzazione	Obstetrics and Gynecology	2011	2016
University of Parma	Master's Degree / Laurea Magistrale	Medicine and Surgery	2005	2010

Personal Statement:
The aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Prof Dall'Asta is among the authors of a recent publication on the use of this technology in assessing the Bone mineral density (BMD) in a group of healthy pregnant women. The role of Prof Dall'Asta will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma	Department of Medicine and Surgery	University Hospital of Parma	Associate Professor of Obstetrics and Gynecology, medical doctor	2021	2022
Azienda Ospedaliero Universitaria di Parma	Obstetrics and Gynecology Unit	Parma, Italy	Mediacal Manager position	2019	2022
Imperial College London	Queen Charlotte¿s and Chelsea Hospital	London	Fellowship in Obstetrics and Feto-Maternal Medicine	2018	2019
Imperial College London	Queen Charlotte¿s and Chelsea Hospital	London	Fellowship in Obstetrics and Feto-maternal Medicine	2015	2016

Other awards and honors

ISUOG World Congress 2018: Best oral presentation -Transabdominal and transperineal intrapartum ultrasound and mode of delivery in prolonged second stage of labor

ISUOG World Congress 2018: Best oral presentation -The cervical sliding sign: a new ultrasound tool in the assessment of threatened preterm labor

ISUOG World Congress 2015: Best oral presentation -Late amniocentesis: is our counselling up to date?

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
University of Parma	University of Parma	2017	Mobilità Dottorandi - Contributo Aggiuntivo di supporto all attività scientifica presso una sede estera	Coordinator	1.000,00	Parma University web-site and local protocol
Imperial College London	Imperial College London	2018	NIHR Imperial Biomedical Research Centre Imaging	Collaborator	60.000,00	Local protocol

2.7 Research Collaborators n. 6 - Under 40

Last Name: CORICA
First Name: DOMENICO
Last name at birth:
Gender: M

Title: Under 40 (Pediatrician)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 31/12/1987
Place of Birth: Messina

Official H index (Scopus or Web of Science): 12.0

Scopus Author Id:55572465600 **ORCID ID:**0000-0002-3628-1612 **RESEARCH ID:**AAC-7112-2021

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Dipartimento di Patologia Umana dell'Adulto e dell'Età evolutiva "G. Barresi", Azienda Ospedaliera Universitaria Policlinico "G. Martino", via Consolare Valeria 1
Postcode / Cedex: 98125
Town: Messina
Phone:+393403919824
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Messina	PhD	Medical and Surgical Biotechnologies	2018	2021
University of Messina	Specialization / Specializzazione	Pediatrics	2013	2018

Personal Statement:

A main objective of the projectis to incvestiogate changes in body composition, metabolism, changes in bone features and development in relationship with early exposure to EDCs and OS.
Dr Domenico Corica is a Pediatrician. He will evaluate bone mineral density in infants during the follow-up of the enrolled population.
He has a ontract for medical assistance activities, including on-call shifts during the day and on holidays, as paediatrician in the in-patient ward at the Clinic of Paediatrics , and at the Paediatric Endocrinology outpatient clinic with Day Service and Day Hospital,

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University Hospital ¿G. Martino¿ of Messina	Department of Adult and Adolescent Human Pathology "G. Barresi"	Messina	Pediatric Consultant with a special interest in Pediatric Endocrinology	2022	2022

Other awards and honors

- Coordinator of the Italian Society of Paediatric Endocrinology (ISPED) Study Group 'Endocrine diseases due to impaired function of the Gs¿ protein function" for the two-year period 2021-2023.
- Member of the ISPED Youth Commission for the two-year period 2019-2021.
- Coordinator of the ISPED Journal Club for 2019-2021.

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.8 Research Collaborators n. 7 - Under 40

Last Name: DI PASQUO
First Name: ELVIRA
Last name at birth:
Gender: F

Title: Under 40 (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 04/08/1986
Place of Birth: Agnone

Official H index (Scopus or Web of Science): 8.0

Scopus Author Id:55232384700 **ORCID ID:**0000-0002-4405-418 **RESEARCH ID:**AAA-8246-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Viale Gramsci 14
Postcode / Cedex: 43100
Town: parma
Phone:+393296080182
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Università Cattolica del Sacro Cuore di Roma	Specialization / Specializzazione	Specialization in Obstetrics and Gynecology	2012	2017
Università Cattolica del Sacro Cuore di Roma	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	2006	2011

Personal Statement:

The aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Elvira di Pasquo is among the authors of a recent publication on the use of this technology in assessing the Bone mineral density (BMD) in a group of healthy pregnant women. The role of Elvira di Pasquo will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
Azienda Ospedaliero-Universitaria di Parma	Obstetrics and Gynecology Unit	Parma	Position: Consultant Obstetrician and Gynecologist	2018	2022
Fondazione Policlinico Gemelli	Department of Mother and Child	Rome	Consultant Obstetrician and Gynecologist	2017	2018

Other awards and honors

Best oral presentation ISUOG World Congress 2019, Berlin
Best oral presentation ISLANDS 2022, Rome

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.9 Additional Research Collaborators n. 2 - Under 40 to hire

Last Name: Pepe
First Name: Giorgia
Last name at birth: Pepe
Gender: F

Title: Patient enrollment, samples collection
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 23/04/1990
Place of Birth: Reggio Calabria

Official H index (Scopus or Web of Science): 5.0

Scopus Author Id:0000-0003-1130-829 **ORCID ID:**57202775155 **RESEARCH ID:**AAP-8204-2020

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: AOU POliclinico G. Martino , via C. Valeria 1
Postcode / Cedex: 98128
Town: Messina
Phone:+393286961402
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Messina	Specialization / Specializzazione	Postgraduate degree in Pediatrics	2015	2020
University of Messina	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine and Surgery	2009	2014

Personal Statement:

The Research Project brings together multidisciplinary competencies, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
Dr Pepe Giorgia will contribute to ernoll poluatuion and to follow the babies with clinical and instrumental visits, according to the time line of the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Biomedical Sciences and Dental and Functional Images	Messina	PhD student in ¿Translational molecular medicine and surgery¿	2020	2022

Other awards and honors

- 2021: The paper ¿Prospective evaluation of autoimmune and non-autoimmune subclinical hypothyroidism in Down syndrome children" was selected as the ¿TOP 5 PAPER¿ produced by the SIEDP (Italian Society for Pediatric Endocrinology and Diabetology) Study Groups .
- 2020: Successful application to the ESPE (European Society for Pediatric Endocrinolgy) Summer School 2020-2021, in England (Lake Windermere)
- 2016: Award of merit for Women Doctors by the Italian Association ¿Associazione Mogli Me

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
European Society for Pediatric Endocrinolog	University of Messina	2021	Grant ESPE (the European Society for Pediatric Endocrinology) for the abstracts submitted for the 59th meeting ESPE.	Coordinator	500,00	ESPE web site

2.10 Additional Research Collaborators n. 3 - Under 40 to hire

Last Name: MURA
First Name: REBECCA

Last name at birth:
Gender: F

Title: Patient enrollment, samples collection
Nationality: italiana
Date of birth: 18/06/1993

Country of residence: ITALY
Country of Birth: ITALY
Place of Birth: brescia

Official H index (Scopus or Web of Science): 0.0

Scopus Author Id:NA **ORCID ID:**NA **RESEARCH ID:**NA

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: via Gramsci 14
Postcode / Cedex: 43126
Town: Parma
Phone:+393470749631
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine and Surgery	2015	2020

Personal Statement:
One of the aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Dr Mura Rebecca will provide expertise and actively recruit cases for bone evaluation.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
Univarsity of Parma	Department of Medicine and Surgery	Parma	Postgarduate Student-Specialization training in Radiology	2020	2022

Other awards and honors
NA

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.11 Additional Research Collaborators n. 4 - Under 40 to hire

Last Name: cannavò
First Name: Laura
Last name at birth: Messina
Gender: F

Title: Patient enrollment, samples collection
Country of residence: ITALY
Nationality: italiana
Country of Birth: ITALY
Date of birth: 16/08/1990
Place of Birth: Messina

Official H index (Scopus or Web of Science): 4.0

Scopus Author Id:57193996033 **ORCID ID:**0000-0002-4464-9421 **RESEARCH ID:**NA

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Via Consolare Valeria 1
Postcode / Cedex: 98123
Town: Messina
Phone:+393400029733
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Univesiry of Messina	Specialization / Specializzazione	Pediatrics	2016	2021
University of Messina	Master's Degree / Laurea Magistrale	University Master II Level: endocrinologia della donna dell'infanzia e dell'adolescente	2015	2016
University of Messina	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master degree Medicine and surgery	2009	2015

Personal Statement:

The Research Project brings together multidisciplinary competencies, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
Dr Laura Cannavò will contribute to ernoll poluatuion and to follow the babies with clinical and instrumental visits, according to the time line of the project. She has a particular expertise in Oxidative stress related diseases of newborn infant

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Biomedical Sciences and Dental and Functional Images	Messina	PhD student in ¿Translational molecular medicine and surgery¿	2021	2022

Other awards and honors

Prize 'Onore al merito', by University of Messina

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.17 Expertise Research Collaborators

Selected peer-reviewed publications of the Research Group / Collaborators

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
cannavò Laura	Potential benefits of melatonin to control pain in ventilated preterm newborns: An updated review	Review	NOT_FOUND	NOT_FOUND	2021	10.1111/papr.13069	NOT_FOUND	0	F
Pepe Giorgia	Minipuberty in born small for gestational age infants: A case control prospective pilot study	Article	NOT_FOUND	NOT_FOUND	2022	10.1007/s12020-022-03003-0	35142975	0	F
CORICA DOMENICO	Meal-Related Asprosin Serum Levels Are Affected by Insulin Resistance and Impaired Fasting Glucose in Children With Obesity	Article	NOT_FOUND	12	2022	10.3389/fendo.2021.805700	NOT_FOUND	1	F
CORICA DOMENICO	Prospective assessment of liver stiffness by shear wave elastography in childhood obesity: a pilot study	Article	59-69	75	2022	10.1007/s12020-021-02828-5	34302259	2	F
cannavò Laura	Oxidative stress and respiratory diseases in preterm newborns	Review	NOT_FOUND	22	2021	10.3390/ijms222212504	34830385	2	F
Pepe Giorgia	The metabolic syndrome in pediatrics: Do we have a reliable definition? A systematic review	Review	265-278	185	2021	10.1530/EJE-21-0238	34061767	1	O
Aversa Tommaso	Pubertal induction in girls with Turner Syndrome	Review	469-480	46	2021	10.23736/S2724-6507.20.03285-X	33435643	1	F
Pepe Giorgia	Bone Maturation as a Predictive Factor of Catch-Up Growth During the First Year of Life in Born Small for Gestational Age Infants: A Prospective Study	Article	NOT_FOUND	11	2020	10.3389/fendo.2020.00147	NOT_FOUND	2	F
cannavò Laura	Ventilation, oxidative stress and risk of brain injury in preterm newborn	Review	NOT_FOUND	46	2020	10.1186/s13052-020-00852-1	32703261	7	F
Pepe Giorgia	Prospective evaluation of autoimmune and non-autoimmune subclinical hypothyroidism in down syndrome children	Article	385-392	182	2020	10.1530/EJE-19-0823	31999620	7	F
cannavò Laura	In children with acquired hypothyroidism levothyroxine requirements may be significantly conditioned by the etiology of thyroid failure	Review	252-255	67	2020	10.1007/s12020-019-01965-2	31270749	3	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
STREET MARIA ELISABETH	Endocrine-disrupting chemicals in human fetal growth	Review	NOT_FOUND	21	2020	10.3390/ijms21041430	32093249	41	F
CORICA DOMENICO	Precocious Preclinical Cardiovascular Sonographic Markers in Metabolically Healthy and Unhealthy Childhood Obesity	Review	NOT_FOUND	11	2020	10.3389/fendo.2020.00056	NOT_FOUND	13	F
WASNIEWSKA MALGORZATA GABRIELA	Subclinical hypothyroidism in children: When a replacement hormonal treatment might be advisable	Article	NOT_FOUND	10	2019	10.3389/fendo.2019.00109	NOT_FOUND	28	L
DALL'ASTA ANDREA	Prediction of spontaneous vaginal delivery in nulliparous women with a prolonged second stage of labor: the value of intrapartum ultrasound	Article	642.e1-642.e13	221	2019	10.1016/j.ajog.2019.09.045	31589867	25	F
DI PASQUO ELVIRA	Outcome of non-visualization of fetal gallbladder on second-trimester ultrasound: cohort study and systematic review of literature	Review	582-588	54	2019	10.1002/uog.20252	30809885	12	F
Aversa Tommaso	Phenotypic expression of autoimmunity in children with autoimmune thyroid disorders	Article	NOT_FOUND	10	2019	10.3389/fendo.2019.00476	NOT_FOUND	17	F
CORICA DOMENICO	Could AGE/RAGE-related oxidative homeostasis dysregulation enhance susceptibility to pathogenesis of cardio-metabolic complications in childhood obesity?	Review	NOT_FOUND	10	2019	10.3389/fendo.2019.00426	NOT_FOUND	12	F
DALL'ASTA ANDREA	Cerebroplacental ratio assessment in early labor in uncomplicated term pregnancy and prediction of adverse perinatal outcome: prospective multicenter study	Article	481-487	53	2019	10.1002/uog.19113	29900608	34	F
STREET MARIA ELISABETH	Diagnosis, treatment and prevention of pediatric obesity: Consensus position statement of the Italian Society for Pediatric Endocrinology and Diabetology and the Italian Society of Pediatrics	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0525-6	30064525	70	O
CORICA DOMENICO	Does family history of obesity, cardiovascular, and metabolic diseases influence onset and severity of childhood obesity?	Review	NOT_FOUND	9	2018	10.3389/fendo.2018.00187	NOT_FOUND	24	F
Ghi Tullio	ISUOG Practice Guidelines: intrapartum ultrasound	Review	128-139	52	2018	10.1002/uog.19072	29974596	104	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Pepe Giorgia	Peculiarities of precocious puberty in boys and girls with McCune-Albright syndrome	Review	NOT_FOUND	9	2018	10.3389/fendo.2018.00337	NOT_FOUND	7	O
Aversa Tommaso	Epidemiological and clinical aspects of autoimmune thyroid diseases in children with Down's syndrome	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0478-9	29562915	9	F
STREET MARIA ELISABETH	Current knowledge on endocrine disrupting chemicals (EDCs) from animal biology to humans, from pregnancy to adulthood: Highlights from a national italian meeting	Review	NOT_FOUND	19	2018	10.3390/ijms19061647	29865233	108	F
Aversa Tommaso	Atypical phenotypic aspects of autoimmune thyroid disorders in young patients with Turner syndrome	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0447-3	29343299	7	F
DALL'ASTA ANDREA	Antiphospholipid antibody profile based obstetric outcomes of primary antiphospholipid syndrome: the PREGNANTS study	Article	525.e1-525.e12	216	2017	10.1016/j.ajog.2017.01.026	28153662	104	O
DALL'ASTA ANDREA	Qualitative evaluation of Crystal Vue rendering technology in assessment of fetal lip and palate	Article	549-552	49	2017	10.1002/uog.17346	27804201	15	F
WASNIEWSKA MALGORZATA GABRIELA	Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2016 Cincinnati International Turner Syndrome Meeting	Review	G1-G70	177	2017	10.1530/EJE-17-0430	28705803	461	O
WASNIEWSKA MALGORZATA GABRIELA	Autoimmune comorbidities in Hashimoto's thyroiditis: Different patterns of association in adulthood and childhood/adolescence	Article	133-141	176	2017	10.1530/EJE-16-0737	27913607	55	L
Ghi Tullio	Development of customized fetal growth charts in twins	Article	514.e1-514.e17	216	2017	10.1016/j.ajog.2016.12.176	28065816	32	F
DI PASQUO ELVIRA	Efficiency of prenatal diagnosis in Pierre Robin sequence	Review	1169-1175	37	2017	10.1002/pd.5162	28950416	13	F
WASNIEWSKA MALGORZATA GABRIELA	The Evolution of Thyroid Function after Presenting with Hashimoto Thyroiditis is Different between Initially Euthyroid Girls with and Those without Turner Syndrome	Article	403-409	86	2016	10.1159/000452722	27866202	10	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
STREET MARIA ELISABETH	Di-(2-ethylhexyl) phthalate metabolites in urine show age-related changes and associations with adiposity and parameters of insulin sensitivity in childhood	Article	NOT_FOUND	10	2015	10.1371/journal.pone.0117831	25706863	41	C
STREET MARIA ELISABETH	Parma consensus statement on metabolic disruptors	Review	NOT_FOUND	14	2015	10.1186/s12940-015-0042-7	26092037	117	O
DI PASQUO ELVIRA	Is there any role for the hydroxychloroquine (HCQ) in refractory obstetrical antiphospholipid syndrome (APS) treatment?	Review	760-762	14	2015	10.1016/j.autrev.2015.04.010	25936295	26	O
WASNIEWSKA MALGORZATA GABRIELA	Five-year prospective evaluation of thyroid function in girls with subclinical mild hypothyroidism of different etiology	Article	801-808	173	2015	10.1530/EJE-15-0484	26374873	35	F
DI PASQUO ELVIRA	Fondaparinux in pregnancy: Could it be a safe option? A review of the literature	Review	1049-1051	135	2015	10.1016/j.thromres.2015.04.001	25912931	30	O
Ghi Tullio	ISUOG practice guidelines: Invasive procedures for prenatal diagnosis	Review	256-268	48	2016	10.1002/uog.15945	27485589	61	F
Ghi Tullio	Intrapartum transperineal ultrasound assessment of fetal head progression in active second stage of labor and mode of delivery	Article	430-435	41	2013	10.1002/uog.12379	23288706	59	F
Ghi Tullio	Fetal head-symphysis distance: A simple and reliable ultrasound index of fetal head station in labor	Article	419-424	41	2013	10.1002/uog.12335	23124698	77	L

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

3 - Ethics

1. HUMAN EMBRYOS/FOETUSES	
Does your research involve Human Embryonic Stem Cells (hESCs)?	No
Does your research involve the use of human embryos?	No
Does your research involve the use of human foetal tissues / cells?	No

2. HUMANS	
Does your research involve human participants?	Yes
Does your research involve physical interventions on the study participants?	No
3. HUMAN CELLS / TISSUES	
Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses?	No
4. PERSONAL DATA	
Does your research involve personal data collection and/or processing?	Yes
Does your research involve further processing of previously collected personal data (secondary use)?	No
5. ANIMALS	
Does your research involve animals?	No
6. ENVIRONMENT & HEALTH and SAFETY	
Does your research involve the use of elements that may cause harm to the environment, to animals or plants?	No
Does your research deal with endangered fauna and/or flora and/or protected areas?	No
Does your research involve the use of elements that may cause harm to humans, including research staff?	No
7. DUAL USE	
Does your research involve dual-use items in the sense of Regulation 428/2009, or other items for which an	No
8. EXCLUSIVE FOCUS ON CIVIL APPLICATIONS	
Could your research raise concerns regarding the exclusive focus on civil applications?	No
9. MISUSE	
Does your research have the potential for misuse of research results?	No
10. OTHER ETHICS ISSUES	
Are there any other ethics issues that should be taken into consideration? Please specify	Yes

I confirm that I have taken into account all ethics issues described above and that, if any ethics issues apply, I will complete the ethics self-assessment and attach the required documents. [X]

4 - Call-specific questions

Eligibility	
I acknowledge that I am aware of the eligibility requirements for applying as specified in the Call-PNRRXXXX_M6/C2, and certify that, to the best of my knowledge my application is in compliance with all these requirements. I understand that my proposal may be declared ineligible at any point during the evaluation or granting process if it is found not to be compliant with these eligibility criteria.	X
I confirm that the proposal that I am about to submit draws substantially don't repeat on an existing or recently finished GRANT funded.	X
Data-Related Questions and Data Protection (Consent to any question below is entirely voluntary. A positive or negative answer will not affect the evaluation of your project proposal in any form and will not be communicated to the evaluators of your project.)	
For communication purposes only, the MoH asks for your permission to publish,in whatever form and medium, your name, the proposal title, the proposal acronym, the panel, and host institution, should your proposal be retained for funding.	X
Some national and regional public research funding authorities run schemes to fund MoH applicants that score highly in the MoH's evaluation but which can not be funded by the MoH due to its limited budget. In case your proposal could not be selected for funding by the MoH do you consent to allow the MoH to disclose the results of your evaluation (score and ranking range) together with your name, non- confidential proposal title and abstract, proposal acronym, host institution and your contact details to such authorities?	X
The MoH is sometimes contacted for lists of MoH funded researchers by institutions that are awarding prizes to excellent researchers. Do you consent to allow the MoH to disclose your name, non-confidential proposal title and abstract, proposal acronym, host institution and your contact details to such institutions?	X
The Ministry of Health occasionally could contacts Principal Investigators of funded proposals for various purposes such as communication campaigns, pitching events, presentation of their project's evolution or outcomes to the public, invitations to represent the Ministry of Health in national and international forums, studies etc. Should your proposal be funded, do you consent to the Ministry of Health staff contacting you for such purposes?	X
For purposes related to monitoring, study and evaluating implementation of MoH actions, the MoH may need that submitted proposals and their respective evaluation data be processed by external parties. Any processing will be conducted in compliance with the requirements of Regulation 45/2001.	

5 – Description Project

Summary description

Any factors influencing peak bone mass, attained at skeletal maturity, are important in determining the individual¿s risk of developing osteoporosis in later life. Bone health begins with maternal health and nutrition, which influences skeletal mass and bone density already in utero.
The mechanisms underlying the effect of the intrauterine environment on bone health are currrently unknown but definitely include ``fetal programming¿¿ of oxidative stress and endocrine systems as these influence skeletal growth and development thereafter.

For the prevention of bone health, challenges rely 1) in the need for the new technology and software specific and applicable to the fetus and newborn; 2) in establishing the effect of environmental contaminants, and in particular of endocrine disruptors oxidative stress, and subsequent epigenetic changes in the mothers, and subsequently on the fetus, newborns and infant

Background / State of the art

Bone health begins with maternal health and nutrition, which influence skeletal mass and bone density in the fetus. Peak bone mass acquisition is also under a genetic influence from both parents. Evidence suggests that the risk of osteoporosis later in life may be determined by environmental influences during intrauterine or early postnatal life. The mechanisms underlying the long term effect of the intrauterine environment on bone health are currrently unknown but definitely include 'fetal programming' of oxidative stress and endocrine systems that influence skeletal growth and development. Osteopenia is recognized with increasing frequency in low-birth weight newborns. Intrauterine growth restriction also increases the risk of obesity and metabolic syndrome which dramatically affect bone quality. Micro RNAs have recently come into the spotlight due to their ability to control gene expression at the post-transcriptional level providing epigenetic modification and targeting the growth plate. Radiofrequency Echographic Multi Spectrometry (REMS) technology has proven to be useful in the assessment of bone mineral denisity (BMD) in pregnant women. Very few studies have reported that transmission ultrasound can also be used for the assessment of BMD in newborns. The attractiveness of REMS technology in fetus and newborns in its lack of ionizing radiation, ease of use and, above all, the possibility to perform longitudinal studies from intrauterine to extrauterine life

Description and distribution of activities of each operating unit

UO1 will perform: -assessment of the bone mineral density of the femur in low risk pregnant women at term gestation (>37 weeks) with REMS technology, -development of an ultrasound based software for the antenatal assessment of the bone mineral density of the femur in the fetus at term gestation (>37 weeks), -postnatal assessment of the bone mineral density of the femur in newborns and infants with REMS technology at birth and at 1 month and 3 months of life.
-postnatal assessment of biomarkers involved in bone mineral density (calcium phosforous metabolism, oxidative stress profile and lipid mediators involved in oxidative stress, endocrine disruptors)
- long term outcome of all enrolled babies (at 3-6-12 months clinical and auxological evaluation)

UO2 will perform a study to validate measurements and reproducibility of findings from UO-1. In particular, they will enrol 100 mothers and newborns.. Blood and urine will be drawn at time points as specified above. Specimens will be centralised for miRNA, for biomarkers of oxidative stress and for endocrine disruptors assays. Complete auxological measurements, and BMD evalution will be taken as in UO1

UO 1 and UO 2 will ensure that the subject¿s parents/legal representatives are given full and adequate oral and written information (subject¿s parents¿/legal representatives¿ information) about the nature, purpose, consequences and possible risk of the clinical study. Subjects¿ parents/legal representatives will be informed that they are free to withdraw the subject from the study at any time without any resulting disadvantages, how personal and health-related data of the subject and the parents will be collected and used during the study, and that the subject identity and medical information will not be disclosed. The subject¿s parents/legal representatives will be given the opportunity to ask questions and should be allowed sufficient time to consider the information provided. The subject¿s parents¿/legal representatives¿ signed and dated informed consent will be obtained before conducting any study specific procedure. A copy of the signed and dated informed consent form will be given to the subject¿s parent)/legal representatives, along with a copy of the insurance conditions.

5.4 Specific Aims and Experimental Design

Specific aim 1

To use antepartum the REMS technology to assess the BMD of the femur in a group of low risk pregnancies at term gestation
To develop an ultrasound based algorithm to assess in this population the bone mineral density of the fetal femur at term gestation.
To use after birth the REMS technology to evaluate the BMD of the femur in the same group of infants at serial follow up scans
To establish the reliability of the fetal evaluation performed with the new dedicated software in respect with the values obtained immediately after birth with the use of the previously validated REMS technology
REMS processes the raw, unfiltered ultrasound signals acquired during an echographic scan of the axial site (femur).
REMS will be used to measure BMD in fetus and neborns at 14 hours and 1 month of life.

Specific aim 2

To assess how mother's REMS patterns, and her anthropometric and gestational data influence BMD in the fetus, newborn and during the first year of life.
A specific questionnaires administered to the mothers will establish the possible exposure based nutrition, clothing and use of cosmetics and detergents, upholstery, etc in the houses.

Time points of sample collections:
At birth: Maternal urine and blood, Cord blood
48 hours of life: neonatal blood and urine
3th month of life: urine
6 months of life: urine and blood
12 months of life: urine

To assess bone biomarkers profile, the following parameters will be investigated:

MicroRNAs: In cord serum at birth (artery) total RNA will be extracted, and by TaqMan Advanced miRNA assays (Applied Biosystems) miRNAs will be quantified and normalized using hsa-miR-16-5p (Assay ID: 477860_mir) as endogenous control. Among a group of 8-10 candidate miRNAs, in particular miR-199a-5p, miR-335-5p, and miR-494-3p will be studied as it has benn recently shown that they vary in relationship to GH status, and are related to growth response. All three target genes in the growth plate
Endocrine disruptors (EDCs): A specific mix of endocrine disupting chemicals will be assayed. Thirteen different EDCs are assayed, namely: Di(2-ethylhexyl) phthalate and its oxidised metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP), Bisphenol (BP) A, BPS, BPF, polyciclic aromatic hydrocarbons, polychorodibenzophuranes and polichorodibenzo-p-dioxins, perfluoro-alchilic substances, gliphosate, and its main metabolite, parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid), piretroid insecticides,heavy metals (Pb, Cr)
Oxidative stress (OS) profile and lipid mediators involved in oxidative stress: will be evaluated both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA) . A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). To this end, highly specific and sensitive methods, such as high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed: HPLC to detect MDA, vitamin E, glutathione, GSH, and AA. The involvement of fatty acid and lipid metabolism will be also investigated by evaluating specialized pro-resolving lipid mediators (Resolvin D1, by ELISA test)
Standard biochemical tests: calcium, phosphorus, alkaline phosphatase, PTH, vitamin D (25 OH), and IGF-I.

Maternal and Cord blood: OS, EDCs markers, miRNA expression profiling (in cord blood).
48 hours of life: OS markers in blood. Urine EDCs markers
3 month of life: urine EDCs markers.
6 months of life: urine EDCs markers. Blood: OS and EDCs markers, standard biochemical tests for bone status evaluation. If changes will be present, these assays will be repeated at 12 months of age after adequate supplementation with vitamin D if necessary
12 months of life: urine EDCs markers

Specific aim 3

To unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health

A long term outcome of all enrolled babies will be also performed: at 3-6-12 months of age, the infants will be placed under clinical and auxological evaluation (head circumference, length, weight, skinfolds, pubertal stages, and ano-genital distances, measurement of fontanels, arm span) in order to relate these measurements with those of BMD, assessed by ultrasound paramenters. The findings of BMD will be related to mothers height, weight gain in pregnancy, BMI at start of pregnancy. All measurements will be related with the miRNAs in cord serum, with the EDCs in mothers urine and in cord serum, and with the biomarkers of oxidative stress in serum. BMD during extrauterine life will be related with fetal measurements. Data in adeguate for gestational age infants (AGA), small for gestational age infants (SGA) and large for gestational age infants (LGA) will be compared

Experimental design aim 1

This is a multicentric longitudinal single group pilot study, whose primary aim is to confirm the feasibility of the use of REMS technology for the evaluation of the bone health status in mothers, fetuses, in newborns (14 hours after life) and in infants (until 1 year of life) and to assess the reliability and predictability of BMD serial measurements from the 37th gestational week to all subsequent timepoints until 1 year of life.
Asthe novel application of REMS technology in the fetal and neonatal population proposed in this project requires the preliminary construction of a reference database (from which the corresponding reference curves will be in turn extracted), population-based data will be gathered (i.e., without adopting exclusion criteria based on possible bone-related disorders), which is the approach adopted in the National Health and Nutrition Examination Survey (NHANES) III database (Looker et al., Osteoporos Int 1998, 8:468¿489), and is considered also as the best way to collect reference data in the field of bone densitometry (Engelke and Gluer 2006, Osteoporos Int 2006, 17: 1283¿1292).
The first 100 enrolled fetuses will be included in the reference database. . The same approach will be applied to the newborns, for which, obviously, the first 100 acquired cases will correspond to the first 100 enrolled fetuses.
The size of the sample to be included in the reference database (100 for the fetal database and 100 for the newborn one) was calculated taking into account the conclusions of the work by Hou et al. (Osteoporos Int 2008, 19:71¿78), according to whom, a suitable reference database can be obtained from a population of 458 women of the same ethnicity aged 6¿85 y , in which the most populated age interval includes 44 patients. We considered the fetuses as corresponding to an age interval and each considered newborn/infant age (14 h, 1 month, 3 months, 6 months, 12 months) as corresponding to a different age interval. Then, according to the methodology adopted in the construction of the reference database for REMS technology application in adults (Conversano et al., Ultrasound Med Biol 2015, 41:281-300), we rounded off this value (44) to 50 and multiplied it by a safety factor of 2.
The clinical personnel of the participating OUs will perform all the mentioned echographic acquisitions on fetuses and newborns at each established age by employing dedicated REMS devices provided in a customized research configuration and will take care toanonymize the corresponding datasets. These datasets will be transferred to the subcontractor, whose

researchers will adapt the REMS configuration already available for paediatric applications to recognize the target bone structures in fetuses and newborns and to provide the corresponding densitometric output. In this way, for each considered ¿age interval¿, a BMD value will be associated to each acquisition and from the first 100 values of each group mean value and standard deviation will be extracted, in order to obtain a 6-point reference curve of BMD as a function of age including fetuses (age ¿0¿) and newborns (age from 14 h to 12 months). The availability of such a curve will allow the expression of the densitometric result in terms of a statistically significant Z-score, which represents the most effective way to assess the bone growth. The whole process will be repeated separately for the male and female cases, in order to obtain a dedicated curve for each sex

Experimental design aim 2

As a natural extension of the primary aim of the study, we will also try to explore the association between mother's REMS patterns / anthropometric and gestational data and BMD values in the fetus and in the newborn during the first year of life.
A specific questionnaires wil be administered to the mothers to establish any possible exposure to endocrine disrupting chemicals (EDC) related with nutrition, clothing and use of cosmetics and detergents, upholstery, etc in their houses.
In the mothers, height, weight, and weight gain during pregnancy will be recorded. Body mass index (BMI) at the beginning of pregnancy will be calculated accordingly (Kg/m2).
To assess bone biomarker profiles, the following parameters will be investigated
-MicroRNAs: In cord serum at birth (artery) , miR-199a-5p, miR-335-5p, and miR-494-3p, mir-369-3p, mir-374-5p, mir-379-5p, and mir-503-5p, miR-140, and Lin28a (Let-7 family)
will be studied. Some vary in relationship to GH status, and are all related with longitudinal growth and gene regulation in the growth plate . All miRNAs will have target genes of importance in the growth plate
-Endocrine disruptors (EDCs): A specific mix of endocrine disupting chemicals will be assayed. Thirteen different EDCs will be assayed, namely: Di(2-ethylhexyl) phthalate and its oxidised metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP), Bisphenol (BP) A, BPS, BPF, polyciclic aromatic hydrocarbons, polychorodibenzophuranes and polichorodibenzo-p-dioxins, perfluoro-alchilic substances, gliphosate, and its main metabolite, parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid), piretroid insecticides,heavy metals (Pb, Cr)
-Oxidative stress (OS) profile and lipid mediators involved in oxidative stress: will be evaluated both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA) . A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). To this end, highly specific and sensitive methods, such as high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed: HPLC to detect MDA, vitamin E, glutathione, GSH, and AA. The involvement of fatty acid and lipid metabolism will be also investigated by evaluating specialized pro-resolving lipid mediators (Resolvin D1, by ELISA test)
-Standard biochemical tests: calcium, phosphorus, alkaline phosphatase, PTH, vitamin D (25 OH), ostecalcin IGF-I, glucose will be assayed to assess bone metabolim with LH, FSH, and Estradiol (E2) in females and Testosterone (T) in males to assess minipuberty that will have an effect on bone.

Time points of miRNAS, EDCs, OS and biochemical markers of bone metabolism and hormone measurements, auxological evaluation and pubertal staging
Mothers: EDCs markers.
Birth (cord blood): miRNAs, EDCs and OS markers, standard biochemical tests for bone status evaluation, standard anthropometric measurements of newborns
48 hours of life: OS markers in blood. Urine EDCs markers

3 month of life: urine EDCs markers. Complete auxological evaluations and pubertal staging
6 months of life: urine EDCs markers. Blood: miRNAs, OS and EDCs markers, standard biochemical tests for bone status evaluation, hormones for minipuberty assessment. If changes will be present, these assays will be repeated at 12 months of age after adequate supplementation with vitamin D if necessary. Complete auxological evaluations and pubertal staging
12 months of life: urine EDCs markers Complete auxological evaluations and pubertal staging

Experimental design aim 3

This is a nested longitudinal study with the aim to evaluate the long term outcome observed until 1 year of age of the newborns.
A long term outcome of all enrolled babies will be performed to unravel the relationships among early exposure to endocrine disruptors, miRNA expression, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health will be related with mothers height, weight gain in pregnancy, BMI at start of pregnancy, and biochemical data.
At 1, 3-6-12 months of age, length of newborns and infants will be taken on a horizontal harpenden stadiometer, and weight on an electronic scale. Body mass index (BMI) will be calculated accordingly (Kg/m2)and evaluated according to WHO standards (WHO website -https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). Head circumference, arm span, diameters of fontanels and pubertal stages will be recorded.
Skinfold thickness will be measured using a Holtain skinfold calliper at the triceps, biceps, subscapular and suprailiac sites. Specific validated algorithms for age will be used to describe subcutaneous body fat distribution.
Specific questionaires to mothers will be administered at the time of enrollment and the clinical evaluation of the newborn infants-at follow-up
Questionnaires 1 and 2 (mother life-style) and 3 (mother-to-child) are an adaptation of validated questionnaires (mother-child) within the previous project "Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases "(LIFE PERSUADED) LIFE13 ENV / IT / 000482, coordinated by the Istituto Superiore di Sanità. They have therefore been reworked on the basis of the recent report commissioned by the European Parliament (https://www.europarl.europa.eu/RegData/etudes/STUD/2019/608866/IPOL_STU (2019) 608866_EN.pdf) and current scientific literature, in order to identify possible sources of EDC release (foreseen in the project analyzes) in the usual environment of the mother-child couples recruited for the study (Martina et al. 2012; Wong et al. 2017; Mitro et al. 2016; Geens et al 2012; Serrano et al. 2014; Morgan et al. 2012; Tang et al. 2017; Phillips 1999; Borowska et al. 2015). When possible, an e-survey with partially assisted administration will be used for the administration of the Mother and Child questionnaires. The questionnaires will be built as a Google Form (Google Form): this structure allows you to build a questionnaire made available through the URL of the page, without the need to install it on a single server.
Any possible relationships among BMD established using the REMS technique, biochemical markers of bone metabolism measured in the mothers just before birth, and in the infants at 6 months of age, and anthropometric measurements will be studied
All measurements will be related with the miRNAs in cord serum, with the EDCs in mothers urine and in cord serum, and with the biomarkers of oxidative stress in serum. BMD during extrauterine life will be related with fetal measurements. Data in adeguate for gestational age infants (AGA), small for gestational age infants (SGA) and large for gestational age infants (LGA) will be compared

Picture to support preliminary data

Project- Picture.pptx

Hypothesis and significance

The Research Project brings together multidisciplinary competencies of excellence, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
A 2021 cross-sectional study of in-hospital births reported a prevalence rate increase by 23% (from 25.3 to 31.1 per 1000 hospital births). Scalp injuries composed 80% of all birth traumas and increased yearly from 19.87 to 26.46 per 1000 hospital births. Major birth trauma was associated with higher odds of hypoxic-ischemic encephalopathy, seizures, need for mechanical ventilation, meconium aspiration, and sepsis. Length of stay was increased by 56%, and total charges were almost doubled for major birth trauma.
The clinical diagnosis of osteoporosis relies heavily on bone mineral density (BMD) measured at the femoral neck, and although BMD has excellent predictive value for future fractures, the assessment of fracture risk has evolved over the years, resulting in the birth of fracture prediction tools. Fracture risk factors not currently present in these instruments are being studied for the inclusion of environmental factors that affect bone quality even before birth. The data from the knowledge of endocrine molecules and associated pathways triggered by oxidative stress are helping us to understand how to best manage patients from the earliest stages of life.
Understanding and improving the current data are critical to setting priorities for action and for tracking progress
An integrated, coordinated effort to address the unmet, significant research and development needs is required to identify causes and prevention strategies.
A prevailing theme is notable: more research and improved access to safe, timely health care are desperately needed if we are to achieve the goals of improving neonatal and child health outcomes.
Rather, bone mineral density comprises a set of interrelated factors of influence. Because of this complexity, a collaborative effort is imperative to both understand the relevant factors and design thoughtful, successful interventions.

5.5 Methodologies and statistical analyses

Methods of data collection

A traning course will be performed in Parma, to share and be familiar with the new REMS technology and to reach a common standard of bone assessment in pregnant women, fetuses, newborns and infants.
We will set up the research guidelines regarding both methodology of BMD scan and storage and shipment of urine, cord blood and peripheral blood. In addition, a common computerized data sheet will be kept for the description of clinical, biochemical, instrumental and auxological data.
Women will be enrolled andand gestational history, clinical maternal conditions, pharmacological therapy, demographic and anthropometric parameters will be recorded, and a specific questionnaire will be administered to establish any possible exposure to endocrine disrupting chemicals (EDC) related with nutrition, clothing and use of cosmetics and detergents.
The following data will be considered when available: measurement of cranial circumference and femur length of the fetus; measurement of the amniotic fluid index; active foetal movements; utero-placental hemodynamics; feto-placental hemodynamics; fetal hemodynamics (Doppler ultrasounds)
The BMD assessment by REMS technology will be scheduled as follows.
- Maternal and fetal BMD assessment: 37 weeks of gestation
- Neonatal assessment: 14 hours after birth and at 1-3-6-12 months of life

As depicted in Figure 1, samples (urine and blood) will be collected according to the following scheme:

- Maternal sample: at birth 3 mL of blood + urine
- Umbilical cord: l 4 ml of cord blood (0,5 ml + 1 ml +1 ml + 1,5 ml for measurement of OS, EDCs, standard biochemical tests, microRNAs, respectively)
- Neonate/infant:
0,5 ml of peripheral blood and 2 mL of urine at 48 hours of life (OS biomarkers)
4 ml of peripheral blood+ 2 mL of urine at 6 months (standard biochemical tests, EDCs, OS biomarkers
2 mL of urine at 12 months

Real-Time qRT-PCR will be used forthe specific candidate miRNAs: miR-199a-5p, miR-335-5p, and miR-494-3p, mir-369-3p, mir-374-5p, mir-379-5p, and mir-503-5p, miR-140, and Lin28a (Let-7 family)
Thirteen different EDCs will be assayed: 1) LC-MS for di(2-ethylhexyl) phthalate (DEHP) and its metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP); bisphenol A and polycyclic aromatic hydrocarbons (PAHs); polychlorodibenzofurans (PCDFs) and polychlorodibenzo-p-dioxins (PCDDs), Glyphosate and its major metabolite aminomethylphosphonic acid; Parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid); the pyrethroid insecticide. 2) ICP-MS for Heavy metals (i.e, Pb).
Oxidative stress profile will be analyzed both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA). A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). For these assays high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed.
Calcium, phosphorus, alkaline phosphatase and blood glucose will be measured on the Atellica CH Analyzer.
IGF-I, vitamin D (25 OH), PTH, osteocalcin, LH, FSH, E2, T levels will be measured using immunoassay on the LIAISON Analyzer Diasorin.

Data collection will be carried out using the REDCap platform (Research Electronic Data Capture, www.project-redcap.org) installed at the AOUPR and reachable at the URL: https://redcap.ao.pr.it:8443/ through which a specific computerized data collection form (eCRF, electronic Case Report Form) will be prepared. The system will be accessible only and exclusively to authorized personnel at each participating center

Statistic plan

According to primary objective we would evaluate the BMD density of the femur in the fetus at term gestation (>37 weeks)

with REMS technology to predict his change at 1 month of life.
Sample size was determined by performing a simulation using a one sided (alpha= 0.025) confidence intervals for Linear Regression Slope test, in which 300 newborns will allow to test if the regression coefficient, which represent the association degree between baseline and the 1 month BMD value, will be at least equal to 1.1 with a lower limit precision distance equal to 0.094. Higher thresholds of coefficient regression were evaluated showing a relative increase of the precision interval. This result was obtained by assuming a correlation value for the covariance matrix of the residual equal to 0.8. Alpha was set to 0.025 to allow a secondary key evaluation with an intermediate time point at 14 hours after birth.

Statistical analysis

Main descriptive statistics will be adopted to summarize the sample size characteristics in terms of mean and standard deviation for continuous variables and absolute and relative (percentage) frequencies for qualitative variable.
The main hypothesis will be firstly evaluated by means of linear regression model in which the dependent variable is the BMD value at 1 month and the independent regressor is the BMD value at baseline. More complex models comprehensive of mixed effects and repeated measures (MMRM) analysis will be implemented to evaluate the within and between variability components and the evolution of BMD values over time. Multivariable models will be applied to identify independent factors associated (MicroRNAs, Endocrine disruptors, Oxidative stress biomarkers and Standard biochemical tests, questionnaire items on nutrition, clothing and use of cosmetics and etc., detailed in previous section) with the outcome.
To take care of the multicollinearity issue generated in the multivariable model, a LASSO regression will be performed in order to shrink the regression coefficients toward zero by penalizing the regression model with a penalty term.
To further test the ability of significant regressors to predict an increase of BMD values over time, receiver operating characteristics (ROC) curve will be employed categorizing the outcome as a binary variable (BMD increased vs. BMD not increased).
Similar modeling will be implemented for long term outcomes detailed in aim 3 and Propensity score Matching will be adopted to enrobust the comparisons described in aim 2 section.
Due to the explorative nature of the study, we would not exclude at priori any additional hypothesis testing and unsupervised clustering analysis approach that could help to identify systematic patterns of patients with similar characteristics.
All the statistical analyses will be centralized to the unit of Clinical and Epidemiological Research Unit at U.O.1 performed using R-project and STATA statistical softwares.

Timing of analysis data

Study duration: 24 months
Protocol set up and Preparation of documents for the Ethical Committee submission: first 2 months:
1. Panel meeting of all project participants, elucidation of the critical points (recruitment of cases, sample collection, storage and shipping, common standards of care, and measurements) and related issues
2. Set-up of REMS evaluation of fetal and neonatal bone mineral density.
3. Training course for REMS evaluation of BMD in pregnant women and newborns for all the participants in the project during the 3rd month

Patient recruitment: from month 3 to 8.
1. Start recruiting patients.
2. Set up of REMS algorithm. Start bone health evaluation in mothers, fetuses and newborns.
3. Construction of REMS reference curve for fetuses and newborns. (At month 8 from project start, the available REMS

reference curve will include three ¿age points¿, i.e. ¿0¿ corresponding to the fetus, ¿14 h¿ and ¿1 month¿, then this curve will progressively extended up to the case of 12-month newborns during the clinical follow-up on the enrolled newbornsMeeting of all staff of researchers: verifying the correctness of procedures and resolve any issues arising
4. Meeting of all research staff to verify the correctness of procedures and resolve any issues arising

Follow up: from month 5 until month 20 (duration of follow up for each patient: 12 months)
Laboratory test and analysis of samples: from month 7 until month 21: two time-points for analyses (month 15 and month 21)

Data set revision: month 17 to 21

Statistical data analysis, interpretation and dissemination from month 21 to 24
1. Setting-up of the biophysical and biochemical profile of bone mineral density in fetus, newborn and child
2. Establishment of the role of the generated profile in predicting bone mineral density in childhood
3. Report of obtained data at scientific workshop and meetings.
4. Exploitation of the main results through press conferences.
5. Preparation of a full paper for ¿open access¿ submission to an international scientific journal.

5.6 Expected outcomes

When the project will be concluded, we expect to have achieved significant innovative tools for the early identification of bone health status in the fetuses and newborns. In this way, we will be able to identify which mother-fetus-newborn-infant will benefit from intervention (i.e. vit D supplementation and/or nutritional program), thereby reducing both birth fracture risk and long term adverse outcomes related to low bone density.

In particular, the following objectives will be reached:

1. Understanding of the bone mineral density values in fetus, newborn, infant and child, and of their temporal evolution;
2. Understanding the mother fetus cross-talk regarding bone mineral density;
3. Standardization of REMS technology as a tool for bone heath assessment starting from intrauterine life;
4.Recognition of microiRNAs pathway as biomarkers to assess bone health status and potential new targets for interventional therapy;
5. Verification of the oxidative stress following EDC exposome;
7. Enabling early assessment of bone mineral density in the neonatal population;
8. Developing marketable tools to bring these goals into clinical perinatal care practice;
9. Unifying standards of perinatal care.

The combined efforts of joint multidisciplinary expertise in this project will get insight on previously unexplored aspects of bone system allowing to follow bone health status from pregnancy to early childhood

5.7 Risk analysis, possible problems and solutions

Description of risk (level of likelihood: Low -L /Medium-M/ High-H)
Risk #1: Insufficient competence and effectiveness (L)
Solution #4: The project team is highly complementary and gathers the requested skills and responsibility for the main streams of research development.
Moreover, the engineering-technical skills will be acquired through appropriate sub-contracting.
Risk #2: Delays in the tasks (M)
Solution #2: All the involved staff members, and in particular the PI and the Co-PI, have significant experience both in the conduction of clinical studies involving pregnant women, fetuses and newborns and in the management of research projects. Therefore, they will adopt in advance all the typical experience-driven contingency measure to avoid possible delays. This will involve in particular some specific project activities which efficient development requires strong peculiar skills, such as protocol set up, preparation of the documentation for Ethical Committee, preparation of the statistical analysis plan, data set revision, scientific writing, etc.
Risk #3: No information sharing between members of the team (L)
Solution #3: A clear management structure with a defined meeting schedule and clear lines of authority/reporting will be established. Moreover, the staff members of the two participating UO already used to collaborate with each other and the 2-year pandemic period has further increased their ability of collaborating in the distance (Cannavò L, Perrone S, et al. Int J Mol Sci. 2021;22(22):12504; . Cannavò L, Perrone S, et al. Pain Pract. 2022;22:248-254)
Risk #4: Loss of research data due to technical problems (M)
Solution #4: A dedicated database for the storage of the data acquired during the present project will be specifically developed by an external supplier, and this will include all the most recent solutions to avoid data loss (e.g., automated backup on different hard-disks, advanced cybersecurity settings, etc.). The corresponding cost has been included in the project budget.
Risk #5: Not enough patients in clinical study (L).
Solution #5: This is actually unlikely to happen thanks to the reputation of the key opinion leaders involved as staff members, who will directly promote the project clinical study. However, specific local sensibilization campaigns will be set up, highlighting the importance of knowing in advance the bone health status of fetuses/newborns and the non-invasiveness of the proposed approaches.

5.8 Significance and Innovation

The main innovative aspect is to use REMs technology for bone health assessment, starting from fetuses. The project will provide the knowledge of mechanisms involved in perinatal bone growth and mineralization, using, for the fisrt time, a combined clinical and strumental strategy designed, on the one hand, to identify and evaluate bone status and possible etiopathogenetic factors of birth fracture in neonate and, on the other hand, to verify and confirm the role of such mechanisms in the instrumental evaluation of bone mineral density. Furthermore, we intend to ascertain the reliability and predictivity of these new markers in our population by clinical and auxological follow up.
Understanding the effects of changes in miRNAS, oxidative stress and endocrine disruptors
on the development of bone mineral densisty may lead to further research improving preventative and therapeutic measures that can fight osteoporosis, a main important contributor to morbidity and mortality worldwide

5.9 Bibliography

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5.10 Timeline / Deliverables / Payable Milestones

The Research team has been constructed in order to optimise enrolment of patients, appropriate timing of the research, and to have proper validation of the new technique emplyed for the bone study. All participants in the present project will join together with the aim of optimising the research to be conducted.
A traning course will be performed in Parma, to share and be familiar with the new REMS technology and to reach a common standard of bone assessment in pregnant women, fetuses, newborns and children.
This clinical study will be evaluated by the reference Ethics Committee before inclusion of the first subject.
Derivelables:
1)Enrolment of mathers and infants will be concluded at month 8
2)Bone status assessmet through REMS in mothers, fetus and neonate
3)Follow up (clinical and instrumental evaluations) concluded at month 20
4) Data analysiis interpration and data pubblication

Milestones 12 month

Enrollment of mothers and their children: concluded
First three months instrumental evaluation of BMD:
Preliminary data on pregnant women, fetus, newborns, and infants at 48 hours, 1 and three months of life
Preliminary results on short term perinatal outcome following birth

First and second questionnaire completed
Samples collection of enrolled mothers (urine and Blood)
Samples collection of all newbors and infants until three months of life (cord blood, peripheral blood and urine at 46 hours, 1 and 3 months of life)

Milestones 24 month

Instrumental, biochemical and clinical follow up concluded
Validation of REMS technology to assess bone mineral density from birth to infancy
Final statistical analysis of then relationships between, exposeme, oxidative stress and bone mineral density in the enrolled populaton enrolled
Knowledge on auxological data, endocrine parameters and bone mineral density in 1- years old children
Establishment of frequency of birth fractures
Report of obtained data at scientific workshops and meetings.
Exploitation of the main results through press conferences.
Submission of at least 1 full paper on the main results of the project to an international scientific journal focused on the relevant medical fields.

Gantt chart

Gantt-diagram.jpg

5.11 Equipment and resources available

Facilities Available

UO1 and UO2 have the facilities to perform patients enrolment and sample collection based on personnel with demonstrated capability, in strict observance of any relevant protocols at all times.
UO1 also provide the availability of use the infrastructure and technical equipment to measure:
- oxidative stress biomarkers: Trace GC and PolarisQ, Thermo/Finnigan; Waters 600 E System Controller HPLC equipped with a dual absorbance UV-visible detector); -80 ultra low temperature freezer
- microRNAs: Real time PCR machine; Real-Time Thermocycler 7900HT Fast PCR system (Applied Biosystems); PCR workstation; PCR hood and micro-centrifuge
-ECDs: ICP-MS and HP 1100 LC-MSD instruments (Agilent)
The suitability of the infrastructures is documented by the relevant funded projects and research activities conducted in recent years by the personnel involved in the project
Furthermore, UO1 has technical support, office space and maintenance, library, networking, high-speed computing, and administrative services. UO1 activities will be performed through integrated bioinformatics and molecular expertises.
UO2 will participate as recruiting center. The long lasting attention to studies and research activities is demonstrated by institutional repository IRIS. In addition, the PI has a long experience in endocrinology
Both, UO1 and UO2 will be equipped with 2 REMS devices with a convex probe operating at the nominal frequency of 3.5 MHz and operators will be trained to follow a standard procedure to acquire femur images and elaborate them by means of REMS algorithm.
The quality of the data will be guaranteed through the implementation of a series of automated controls in the phase of data entry in the eCRF (pre-calculated fields, branching logic, self-validations) and in the management of the data entered (deletion, display and filtering)

Subcontract

The novel application of REMS technology in the fetal and neonatal population requires the preliminary construction of a reference database (from which the corresponding reference curves will be in turn extracted).
The accomplishment of this task requires specific engineering-technical skills that are not available in the staff of the participant UOs and are essential in order to ensure the correct and rigorous application of the signal and image processing procedures detailed in the papers describing the principles of the technology that has later been identified as REMS (UMB 2015, 41:281; UMB 2016, 42:1337).

5.12 Desc. of the complementarity and sinergy of secondary collab. researchers

The consortium created for this project will integrate the expertises of each Research Units (UO) for successfully concluding all the programmed objectives.

Two Research Units are provided:
UO-1 AO-Parma
UO-2 AO-Messina

The role of each secondary collaborator researchers is complementary, according to an integrated vision of the project, in which the specific skills of each UO are highly coordinated. Gynecologists, Neonatologists and Pediatricians will ensure clinical and instrumental follow-up of the babies from birth until 1 year of life
The patient enrollment and the management of sample collection will be carried out by the UO-1 and UO-2.
UO-1 will prepare a detailed database to share with all the other collaborator researchers, including the general characteristics, the clinical data of pregnant women and their respective newborns, and laboratory results.

UO-1 collaborator researchers will perform:
- Patients enrolment and samples collection
- bone mineral density evaluation longitudinally from fetus to childhood (REMS technology)
- auxological outcome of newborn infant at 1, 3, 6 12 months of life
- OS, EDCs concentrations, miRNA in cord blood and plasma of newborn/infants
- EDCs concentrations in urine of newborns infants
-statistical analysis by experts bio-statisticians

UO-2 collaborator researchers will perform:
- patients enrolment and samples collection
- bone mineral density evaluation longitudinally from fetus to childhood (REMS technology)
- auxological outcome of newborn infant at 1, 3, 6 and 12 months of life

5.13 Translational relevance and impact for the national health system (SSN)

What is already know about this topic?

The amount of bone gained during growth and its consequent rate of loss is strictly related to the skeletal mass in adulthood (Heaney RP, 1995).
Bone health begins with maternal heath and nutrition (Godfrey K 2001).
The risk of osteoporosis later in life may be determined environmental influences during intrauterine or early postnatal life [Bocheva G, 2011; Holroyd C, 2012].
Oxidative stress in pregnancy impacts on fetal growth development and newborn infants are especially prone to oxidative

stress harmuful effects (Perrone S, 2016)
Exposure to EDCs at critical ages has been related with the development of obesity and metabolic syndrome, that are related with changes in bone composition (Street 2020; Predieri B 2021)
Radiofrequency Echographic Multi Spectrometry (REMS) technology is useful in the assessment of Bone mineral density in pregnant women (De Gennaro V, 2021)

Details on what is already know about this topic

REMS has been validated for BMD evaluation in a population of low-risk pregnant women at term of gestation. Change in bone mass density/composition involves mechanisms and pathways that aren¿t currently well defined and could be influenced by early exposure to EDCs. The action of endocrine disrupting chemicals during fetal and neonatal life is mainly exercised via epigenetic regulation of metabolic and endocrine pathways. Among these, oxidative stress and regulatory mechanisms of gene expression, the miRNA network, are of upmost importance (bocheva 2012). The molecular mechanisms by which miRNAs exert their regulatory role in longitudinal bone growth are involved with the regulation of cell growth, particularly of chondrocytes (Holroyd C 2012)
Studies performed by Basu S (2001) establish a biochemical link between increased oxidative stress and reduced bone density and provide a rational for this project investigating the role of pro- and antioxidants in bone mineral density

What this reasearch adds?

Understanding of the frequency of birth fractures at the centers participating in the study
Identification of REMs patterns characteristic of bone mineral density from prenatal to postnatal life
Recognition of changes in body composition, metabolism, changes in bone features and development in relationship with early exposure to EDCs and OS.
Validation of lipid peroxidation biomarkers as markers of perinatal oxidative stress involved in BMD
Standardization of the various endocrine disruptors and evaluation of their prognostic significance.
Unifying standards of BMD evaluation (biochemical and biophysical parameters) from early stage of life
Identification of targeted campaigns for osteopenia and osteoporosis prevention

Details on what this reasearch adds

This study project is pioneering in developing and standardize an ultrasound-based technique to assess the BMD from perinatal to post-natal life. The results from the project are expected to clarify important physio-pathological mechanism which may be implicated in the variation in individual bone mass or fracture risk.
As a first point, it is expected that this study will add important knowledge on the existing crosstalk between the maternal and the fetal bone and on how the exposure to EDCs and OS may interfere on this process since the intrauterine life.
Secondly, the post-natal longitudinal assessment is expected to clarify how the antenatal bone mineral status, the biochemical markers and the exposure to EDCs and to the OS correlate with the auxological evaluation and with the bone mineral status during the first year of life. The identification of a specific panel of biomarkers may anticipate the risk of future osteopenia or osteoporosis in the adulthood

What are the implications for public health, clinical practice, patient care?

This project may generate new knowledge on the nature-nurture interactions occurring in human infants - during a highly plastic period of development - and the focus on fetus may furthermore highlight how precocious exposures to OS and EDCs can be embedded into the biology of the human infant. The results will provide the information needed to organise specific and correct prevention campaigns to improve public health and in line with principle of the developmental origins of health and disease.
This project be beneficial to clinicians and to policy makers to further advance the quality of interventions based on scientific evidence. Studying the perinatal factors impacting bone health, setting up new technology, easy to use, for the assessment

of BMD will be effective in improvements in the quality of care that clinician deliver to infants and their parents.
The impact on economic cost reduction (prevention of birth fracture, osteopenia and osteoporosis) is equally relevant.

Details on what are the implications for public health, clinical practice, patient care

The understanding of the bone status before birth will allow a stratification of the specific risk of bone fractures at birth and during the early post-natal life
On one side this will represent a field of interest for the obstetricians which may tailor the type of obstetric interventions during delivery on the specific risk of fractures (eg. Type of operative delivery if needed, type of manouvres for the shoulder dystocia) and for the neonatologist/pediatrics which may develop specific programs on those neonates/infants with a suboptimal bone mineral status
At last, the increase in life expectancy more particularly in the developed countries, has made osteoporosis and associated fragility fractures of unusual economic interest. It has been estimated that, acresso 27 countries in the European Union, by 2025 the social costs of this disease will reach 120,000 million Euros

6 - Budget

Total proposed budget (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	110.047,00	110.047,00	not permitted	0,00
2 Researchers' Contracts	280.000,00	0,00	280.000,00	32,18
3a.1 Equipment (Leasing -	300.000,00	100.000,00	200.000,00	22,99
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	212.000,00	0,00	212.000,00	24,37
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts *	41.000,00	0,00	41.000,00	4,71
5 Patient Costs	30.000,00	0,00	30.000,00	3,45
6 IT Services and Data Bases	23.000,00	0,00	23.000,00	2,64
7 Travels	9.000,00	0,00	9.000,00	1,03
8 Publication Costs	9.000,00	0,00	9.000,00	1,03
9 Dissemination	9.000,00	0,00	9.000,00	1,03
10 Overheads *	57.000,00	0,00	57.000,00	6,55
11 Coordination Costs	0,00	0,00	0,00	0,00
Total	1.080.047,00	210.047,00	870.000,00	100,00

* percentage calculated as average value between all the Operating Units.

Report the Co-Funding Contributor:

Co-Funding will be granted by each UO, notably with an overall proportion of 19.4% (detailed: UO1 18.8%; UO2 20.3%)

Budget Justification

1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Researchers
2 Researchers' Contracts	2 Researchers for 2 years (80 kEuro each); 3 data scientists (2-year scholarships, 40 kEuro each)
3a.1 Equipment (Leasing - Rent)	Leasing of 4 echographic devices for REMS acquisitions provided in "open configuration" for research purposes 2 devices for each UO: in each UO, 1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborns).
3a.2 Equipment (buying)	NA

3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, paper, sterile needles, protection disposables, masks, gloves, disinfectant) Kits for biological sample tests (Kit elisa, kit for real time PCR, consumable for HPLC, GS-MS and ICP-MS, etc)
3c Model Costs	NA
4 Subcontracts	REMS data analysis, reference database construction and reference curve calculation for fetuses and newborns + statistical analyses of acquired REMS datasets
5 Patient Costs	Patient insurance
6 IT Services and Data Bases	NAS support at each center for networked data flow. A dedicated database for the storage of the data acquired during the present project will be specifically developed, and this will include all the most recent solutions to avoid data loss
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Communications at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Proposed total budget UO1 Institution: Azienda Ospedaliero Universitaria di Parma (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	71.170,00	71.170,00	not permitted	0,00
2 Researchers' Contracts	160.000,00	0,00	160.000,00	30,65
3a.1 Equipment (Leasing - Rent)	150.000,00	50.000,00	100.000,00	19,16
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	120.000,00	0,00	120.000,00	22,99
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts	41.000,00	0,00	41.000,00	7,85
5 Patient Costs	30.000,00	0,00	30.000,00	5,75
6 IT Services and Data Bases	23.000,00	0,00	23.000,00	4,41
7 Travels	5.000,00	0,00	5.000,00	0,96
8 Publication Costs	5.000,00	0,00	5.000,00	0,96
9 Dissemination	5.000,00	0,00	5.000,00	0,96
10 Overheads	33.000,00	0,00	33.000,00	6,32
11 Coordination Costs	0,00	0,00	0,00	0,00
Total	643.170,00	121.170,00	522.000,00	100,00

Budget Justification

1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Research
2 Researchers' Contracts	1 Researcher for 2 years (80 kEuro); 2 data scientists (2-year scholarships, 40 kEuro each)
3a.1 Equipment (Leasing - Rent)	Leasing of 2 echographic devices for REMS acquisitions provided in "open configuration" for research purposes (1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborn-infants).
3a.2 Equipment (buying)	NA
3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, paper, sterile needles, protection disposables, masks, gloves, disinfectant) Kits for biological sample tests (Kit elisa, kit for real time PCR, consumable for HPLC, GS-MS and ICP-MS, etc)
3c Model Costs	NA
4 Subcontracts	REMS data analysis, reference database construction and reference curve calculation for fetuses and newborns + statistical analyses of acquired REMS datasets
5 Patient Costs	Patient insurance
6 IT Services and Data Bases	NAS support at each center for networked data flow. A dedicated database for the storage of the data acquired during the present project will be specifically developed, and this will include all the most recent solutions to avoid data loss
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Communicatios at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Proposed total budget UO2 Institution: Sicily (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	38.877,00	38.877,00	not permitted	0,00
2 Researchers' Contracts	120.000,00	0,00	120.000,00	34,48
3a.1 Equipment (Leasing - Rent)	150.000,00	50.000,00	100.000,00	28,74
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	92.000,00	0,00	92.000,00	26,44
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts	0,00	0,00	0,00	0,00
5 Patient Costs	0,00	0,00	0,00	0,00
6 IT Services and Data Bases	0,00	0,00	0,00	0,00
7 Travels	4.000,00	0,00	4.000,00	1,15
8 Publication Costs	4.000,00	0,00	4.000,00	1,15
9 Dissemination	4.000,00	0,00	4.000,00	1,15
10 Overheads	24.000,00	0,00	24.000,00	6,90
11 Coordination Costs	not permitted	not permitted	not permitted	0,00
Total	436.877,00	88.877,00	348.000,00	100,00

Budget Justification	
1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Research
2 Researchers' Contracts	1 Researcher for 2 years (80 kEuro); 1 data scientist (2-year scholarships, 40 kEuro)
3a.1 Equipment (Leasing - Rent)	Leasing of 2 echographic devices for REMS acquisitions provided in "open configuration" for research purposes (1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborn-infants
3a.2 Equipment (buying)	NA
3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, sterile needles, protection disposables, disinfectant). Kit elisa, solvents, syringes, pipettes, sieroplast test tubes, urine tubes, reagents, chemistry and immunoassay tests.
3c Model Costs	NA
4 Subcontracts	NA
5 Patient Costs	NA
6 IT Services and Data Bases	NA
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Abstracts at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Principal Investigator Data

Cognome: Perrone
Nome: Serafina
Genere: F
Codice fiscale: PRRSFN68L63I119M
Documento: Carta d'identità, Numero: AS5134422
Data di nascita: 23/07/1968
Luogo di nascita: San Pietro Vernotico
Provincia di nascita: BR
Indirizzo lavorativo: Via Gramsci 14, Parma
Città: Parma
CAP: 43126
Provincia: PR
Email: saraspv@yahoo.it
Altra email: serafina.perrone@unipr.it
Telefono: +393388704211
Qualifica: Professore Universitario
Struttura: Unità Operativa Complessa di Neonatologia
Istituzione: Azienda Ospedaliero Universitaria di Parma
Datore/ente di lavoro? Yes
Datore/ente di lavoro SSN? No
Nome datore/ente di lavoro non SSN: Università
Nome istituzione SSN: Azienda Ospedaliera Universitaria di Parma
Tipo contratto: Lavoro Subordinato a Tempo Indeterminato

Con l'invio della presente proposta si dichiara che la stessa o parti significative di essa non sono oggetto di altri finanziamenti pubblici o privati e che di conseguenza vi è assenza del c.d. doppio finanziamento ai sensi dell'art. 9 del Regolamento (UE) 2021/241, ossia che non ci sia una duplicazione del finanziamento degli stessi costi da parte di altri programmi dell'Unione, nonché con risorse ordinarie da Bilancio statale.

By submitting this proposal, I declare that no significant part or parts of it are recipient of any other public or private funding and that consequently there isn't any so-called double financing pursuant to art. 9 of Regulation (EU) 2021/241, i.e. that there is no duplication in the financing of the same costs by other Euopean Union programs or any other ordinary resources from the State budget.

Project validation result

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

FRONTESPIZIO PROTOCOLLO GENERALE

AOO: AOO000

REGISTRO: Protocollo generale

NUMERO: 0049109

DATA: 04/12/2023

OGGETTO: Contratto PNRR-REMS-Bone ammesso a finanziamento.

CLASSIFICAZIONI:

DOCUMENTI:

File	Hash
PG0049109_2023_perrone.msg.msg:	2DE0E0ABFA4D11E5C0418751AF507D11FEE0D7E0B66814E50CE8DC91FFD12816
PG0049109_2023_Contratto ricerca AMOLAB_OSPEDALEPARMA_PNRR REMS.doc.pdf:	9325B4241CE913C73D8060D9DFC38D64FD77574109C383E8F40D0F1A878B3508
PG0049109_2023_PNRR-PERRONE-completo-12376819.pdf.pdf:	A375D2C28C0E660D6C7316939DABA16900F4651305BD78EBE43AE5EDA144DE08
PG0049109_2023_All.3-Amministrazione-PG0022130_2023_lettera.pdf.pdf:	382B875E767D56F39273460FAE92676CFD91C9229A82405DDCC12EBE460BAAEA
PG0049109_2023_perrone_testo.txt.pdf:	6AAF3941BCA1339E15203035695B65637F75615A69C162286CB35D39B5367715

----- Messaggio inoltrato -----
Da: "Serafina PERRONE" <serafina.perrone@unipr.it>
A: "Maggio, Aureliana" <aumaggio@ausl.pr.it>
Cc: "Boschi, Michela" <MBoschi@ao.pr.it>, "Iaria, Maria" <maiaria@ao.pr.it>, "Zucchelli, Rossella" <rzucchelli@ao.pr.it>
Inviato: Sabato, 25 novembre 2023 19:19:07
Oggetto: Oggetto: Contratto- PNRR-REMS-Bone ammesso a finanziamento

Gent.ma,
chiedo di poter attivare un contratto di servizi conto terzi finalizzato al proseguio delle attività previste dal progetto di ricerca di cui in oggetto ammesso a finanziamento (utilizzo della tecnologia REMS nella popolazione fetale e neonatale per la costruzione preliminare di un database di riferimento).
L'impresa AMOLAB, con sede operativa a Lecce, Campus Ecotekne, dimostra le eccellenze e le competenze tecnico-ingegneristiche specifiche che non sono disponibili nel personale delle U.O. partecipanti al Progetto vinto e sono essenziali per garantire la corretta e rigorosa applicazione delle procedure di elaborazione dei segnali ultrasonici e delle immagini ecografiche.
L'importo del servizio è di circa 33.660 euro + IVA.
A tal proposito mi permetto di allegare:
-bozza di contratto
-progetto completo ammesso a finanziamento (in pag 53 troverà i dettagli del budget, alla voce 'subcontracts)'
-all.3 (delibera per la gestione economico amministrativa dello studio) Resto a disposizione per eventuali, ulteriori adempimenti.
Cordiali saluti
S. Perrone

_____

Prof. S. Perrone, MD, PhD

Professore Associato di Pediatria

Dpt. di Medicina e Chirurgia,

Università degli Studi di Parma

UOC Neonatologia

Tel: 0521-903821-703518

perrone.msg.
Anteprima non disponibile.
Probabilmente il file non è convertibile in pdf ed è necessario quindi scaricarlo.
Ai fini di una eventuale pubblicazione sull'Albo On Line: questo file non sarà pubblicato e sarà mostrato questo messaggio al cittadino.

CONTRATTO DI SERVIZI CONTO TERZI

TRA

L'Azienda Ospedaliero-Universitaria di Parma con sede legale in Parma, Via Gramsci, 14, Codice Fiscale e Partita IVA n. 01874240342, nella persona del del suo Direttore Generale, Dott. Massimo Fabi domiciliato per la carica presso la sede legale di cui sopra (d'ora innanzi denominato/a semplicemente "Azienda") ;

da una parte,

e

l'impresa **AMOLAB SRL** (di seguito denominata AMOLAB), con sede legale in via Raffaello Sanzio 18, 73100 Lecce, C.F., numero di iscrizione al Registro Imprese e P.IVA 04401310752, rappresentata dall'Ing. Salvatore Calcagnile in qualità di Amministratore Unico,

di seguito singolarmente/collettivamente anche "la parte"/"le parti";

PREMESSO CHE:

1. L'Azienda è risultata vincitrice di un progetto PNRR di cui al Bando M6/C2_CALL 2022, della durata di 24 mesi e finanziato dall'Unione Europea per un importo complessivo di 870.000 Euro (Codice progetto: PNRR-MAD-2022-12376819; Topic: Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali; Titolo: "Getting bone health right from the start: innovative technology and new mechanisms of mother-fetus cross talk for osteopenia and osteoporosis prevention" Coordinatore: Prof.ssa Serafina PERRONE);

2. Lo Studio sarà condotto in accordo alla normativa vigente in materia;

3. Lo Studio, per quanto applicabile, è finalizzato a determinare lo sviluppo

ottimale della massa ossea durante la crescita scheletrica per la prevenzione primaria dell'osteopenia e osteoporosi;

4. Lo Studio prevede di: 1) verificare l'efficacia della tecnologia REMS come nuovo approccio preciso e innovativo di valutazione dello stato scheletrico nei feti, nei neonati e nei bambini; 2) valutare la eventuale correlazione tra i parametri REMS della madre e i suoi dati antropometrici e gestazionali, e quelli feto e del neonato durante il primo anno di vita;

5. L'Azienda ha individuato, nell'ambito nazionale, nell'impresa AMOLAB, le eccellenze e le competenze tecnico-ingegneristiche specifiche che non sono disponibili nel personale delle U.O. partecipanti al Progetto vinto e sono essenziali per garantire la corretta e rigorosa applicazione delle procedure di elaborazione dei segnali ultrasonici e delle immagini ecografiche, dettagliate nei lavori che descrivono i principi della tecnologia che è stata successivamente identificata come REMS, e le dotazioni strumentali idonee all'esecuzione delle verifiche e valutazioni di cui al punto precedente. Il tutto finalizzato all'utilizzo della tecnologia REMS nella popolazione fetale e neonatale per la costruzione preliminare di un database di riferimento (da cui verranno a loro volta estratte le corrispondenti curve di riferimento).

Tutto ciò premesso, quale parte integrante e sostanziale, tra le parti

SI CONVIENE E SI STIPULA QUANTO SEGUE:

Art. 1 - Premesse

Le premesse sono parte integrante del contratto.

Art. 2 – Oggetto

AMOLAB analizzerà con impiego della metodologia REMS i dataset ricevuti dall'Azienda e si occuperà della costruzione del database di riferimento e del

calcolo delle corrispondenti curve di riferimento per feti e neonati, fornendo in output all'azienda i risultati di queste elaborazioni in un formato idoneo alla divulgazione scientifica in ambito medico. Tutte le attività di competenza di AMOLAB di cui al presente articolo saranno svolte presso la sede operativa di AMOLAB sita a Lecce all'interno del Campus Ecotekne (via per Monteroni), con impegno ad eseguirle in tempi congrui e con modalità scientificamente corrette.

Art. 3 - Responsabili

L'Azienda identifica nella Prof.ssa Serafina PERRONE (email: serafina.perrone@unipr.it) il Responsabile Scientifico per l'esecuzione dello studio.

AMOLAB identifica nella Dott.ssa Maria Giovanna DI TRANI (email: ditrani@amolab.it) il responsabile per l'esecuzione di quanto innanzi.

Art. 4 – Durata

Il contratto avrà decorrenza dalla data di sottoscrizione e terminerà in data **30 aprile 2025**.

Art. 5 - Pagamenti e Fatturazioni

L'Azienda si impegna a corrispondere ad AMOLAB, per l'effettuazione delle attività previste all. Art. 2, un importo complessivo di euro **33.606,56 + IVA (euro Trentatremilaseicentosei/56 oltre IVA di legge),** così suddiviso:

- **Una prima quota a titolo di anticipazione di € 26.885,24 (**Euro Ventiseimilaottocentoottantacinque/24) + IVA di legge, dietro emissione di regolare fattura elettronica da parte di AMOLAB, entro 30 giorni dalla stipula del presente;

- **Una seconda ed ultima quota a saldo di € 6.721,31 (**Euro Seimilasettecentoventuno/31) + IVA di legge, dietro emissione di regolare fattura elettronica da parte di AMOLAB, previa valutazione positiva da parte del responsabile scientifico dell'Azienda delle attività svolte da AMOLAB e documentate in apposita relazione tecnico-scientifica, entro 30 giorni dall'emissione della fattura.

Tutte le comunicazioni propedeutiche al pagamento del dovuto tra la parte Committente ed AMOLAB dovranno avvenire a mezzo PEC ai seguenti indirizzi:

per l'Azienda: protocollo@cert.ao.pr.it

per AMOLAB: amolab@pec.it

Le fatture elettroniche, emesse da AMOLAB, dovranno riportare il Codice destinatario, il CIG, il numero e la data di emissione, riferimenti normativi IVA e le note descrittive di dettaglio del servizio fatturato, utilizzando la dicitura specifica "Contratto PNRR-MAD-2022-12376819 tra Azienda Ospedaliera PARMA e AMOLAB".

Il pagamento delle fatture elettroniche è effettuato a mezzo bonifico bancario entro e non oltre il termine di trenta giorni dalla data di ricevimento della fattura emessa da AMOLAB.

Art. 6 - Tracciabilità

AMOLAB si assume tutti gli obblighi di tracciabilità dei flussi finanziari di cui all'art. 3 della legge 13 agosto 2010 n. 136 e successive modifiche.

Il mancato utilizzo del bonifico bancario o postale ovvero degli altri strumenti

di incasso o pagamento idonei a consentire la piena tracciabilità delle operazioni costituisce causa di risoluzione del contratto ai sensi dell'art. 3, comma 9 bis, della L. 136/2010.

Art. 7 - Conto di evidenza

AMOLAB comunica i seguenti estremi del conto corrente dedicato alle commesse pubbliche per tutti i movimenti finanziari relativi al presente contratto, nonché le generalità ed il codice fiscale delle persone delegate ad operare sullo stesso:

IBAN: IT30 Y030 6916 0281 0000 0005 961

SWIFT/BIC: BCITITMM

Intestato ad: AMOLAB SRL

Generalità e codice fiscale delle persone delegate ad operare su di esso:

- Santina Corvino nata a Francavilla Fontana (BR) il 20/12/1987 c.f.: CRVSTN87T60D761U.

Art. 8 - Contributo scientifico

L'Azienda garantisce la citazione del contributo di AMOLAB nelle sedi o nelle riviste scientifiche in cui i risultati saranno riportati o stampati.

Art. 9 - Risultati

L'Azienda garantisce che a seguito della presente contratto non verrà fatto alcun uso dei risultati diverso da quanto previsto dai meccanismi propri della comunicazione di risultati scientifici alla comunità scientifica nazionale o internazionale.

Art. 10 - Protezione dei dati personali dei soggetti

Con riferimento al trattamento dati personali e relativi alla salute dei pazienti, le parti prendono atto dei contenuti del Regolamento Europeo sulla

protezione dei dati personali n. 679/2016, del D.L.gs. 196/2003 come novellato con D.L.gs. 10/08/2018 n. 101 e delle indicazioni del Garante Privacy. Resta pertanto inteso che ciascuno per gli ambiti di propria competenza:

a) Titolare del trattamento dei suddetti sarà l'Azienda Ospedaliera di Parma, nell'ambito dei trattamenti che allo stesso competono, in particolare per le finalità di ricerca.

AMOLAB, limitatamente ai compiti delegati per iscritto, anche tramite il presente contratto, e per il periodo in esso determinato, si impegna ad adottare le misure di sicurezza, sia tecniche sia organizzative, per proteggere i dati e ridurre al minimo i rischi di distruzione o perdita, anche accidentale, dei dati stessi, di accesso non autorizzato o di trattamento non consentito o non conforme alle finalità della raccolta.

Le parti si impegnano a rispettare le finalità dello studio e ad osservare quanto previsto dal Regolamento Europeo sulla protezione dei dati personali n. 679/2016, dal D.L.gs. 196/2003 come novellato con D.L.gs. 10/08/2018 n. 101 e delle indicazioni del Garante Privacy e si danno reciprocamente atto di aver adottato adeguate misure di sicurezza.

L'Azienda dichiara di avere adempiuto a tutte le disposizioni previste dalla normativa suddetta per quanto concerne il trattamento dei dati personali.

I dati saranno trattati unicamente per le finalità connesse all'esecuzione del presente Accordo.

Gli obblighi di riservatezza dei dati si cui al presente articolo continueranno ad essere pienamente validi ed efficaci anche a seguito della risoluzione o cessazione per qualsiasi causa del presente Accordo, per un periodo massimo

di sette anni.

Le parti si danno atto che l'Azienda Ospedaliero-univeristaria di Parma è autonomo Titolare del trattamento riguardante i dati personali contenuti e conservati nelle cartelle cliniche dei pazienti.

Art. 11 – Disciplina anticorruzione

Le parti sono obbligate all'osservanza della Legge 6 Novembre 2012, n. 190.

L'Azienda, AMOLAB e il Responsabile dello studio dichiarano di non essere a conoscenza dell'esistenza di alcun conflitto di interessi (ai sensi della regolamentazione emanata dall'Autorità Nazionale Anticorruzione e dei regolamenti interni adottati al riguardo presso la propria struttura) che possa precludere la sottoscrizione del presente Contratto.

Le Parti si impegnano a svolgere le attività e ad adempiere agli obblighi previsti nel Contratto nel rispetto della normativa e regolamentazione vigente in materia di prevenzione e repressione della corruzione, così come previsto dalla regolamentazione emanata dall'Autorità Nazionale Anticorruzione, in particolare in materia di codici di comportamento negli enti del servizio sanitario nazionale e obblighi di pubblicità, trasparenza e diffusione di informazioni, nonché da eventuali piani e linee guida regionali adotatte in materia.

AMOLAB e il Responsabile dello studio dichiarano:

- che il Contratto non contrasta in alcun modo con i principi contenuti all'interno del proprio Piano Aziendale di prevezione della corruzione (o regolamenti assimilabili).

AMOLAB, l'Azienda e il Responsabile dello studio rispettivamente dichiarano:

- di non aver (direttamente o indirettamente) offerto, corrisposto, ricevuto ovvero autorizzato l'offerta, corresponsione o accettazione di denaro, beni o qualsiasi utilità – e si impegnano ad astenersi dall'offrire, corrispondere, ricevere ovvero autorizzare l'offerta, corresponsione o accettazione di denaro, beni o qualsiasi utilità ovvero dal compiere qualsiasi altra attività – con l'obiettivo di influenzare impropriamente o indebitamente l'attività di un dipendente pubblico o di qualunque altro soggetto, col fine di ottenerne un indebito vantaggio o beneficio personale.

La violazione di quanto previsto da questo articolo costituisce grave inadempimento del presente Contratto ai sensi e per gli effetti di cui all'art. 1456 c.c., risultando pregiudicato il rapporto di fiducia tra le Parti.

Art. 12 - Controversie

Il presente contratto è regolato dalla vigente legge italiana; nel caso di controversie derivanti dal contratto, qualora le stesse non vengano definite in via di composizione amichevole, il Foro competente è quello di Parma.

Art. 13 - Risoluzione

Qualora una delle parti si renda inadempiente di una delle obbligazioni di cui all'accordo economico e non ponga rimedio a tale inadempimento entro 30 giorni dal ricevimento della diffida ad adempiere trasmessa con PEC, ai sensi dell'art. 1454 cc il presente contratto si intenderà risolto, con riconoscimento solamente delle attività correttamente svolte fino a tal momento. Ciascun contraente ha il diritto di recedere dal presente contratto con un preavviso scritto di almeno trenta giorni.

Art. 14 - Modificazioni

Ogni modifica del presente contratto dovrà essere formalizzata per iscritto di

comune accordo fra le parti.

Art. 15 – Oneri

Il presente contratto viene redatto in un unico originale in formato digitale. L'imposta di bollo è assolta in modo virtuale dall'Azienda Ospedaliera di Parma. Il presente contratto è assoggettato a registrazione solo in caso d'uso. Le spese di registrazione sono a carico esclusivo della parte che la richiede.

Letto, confermato, sottoscritto digitalmente.

Parma/Lecce, lì

Per l'Azienda Ospedaliera di Parma	Per AMOLAB
Il Direttore Generale	L'Amministratore Unico
Dott. Massimo FABI	Ing. Salvatore CALCAGNILE

1 - General information

Project code: PNRR-MAD-2022-12376819

Project topic: C1) Malattie croniche non trasmissibili, ad alto impatto sui sistemi sanitari e socio-assistenziali: fattori di rischio e prevenzione

Applicant Institution: Emilia-Romagna

PI / Coordinator: Perrone Serafina

Istitution that perform as UO for UO1: Azienda Ospedaliero Universitaria di Parma

Call section: Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali

Proposal title: Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis prevention

Duration in months: 24

MDC primary: Ostetricia e Ginecologia

MDC secondary: Pediatria

Project Classification IRG: Musculoskeletal, Oral and Skin Sciences

Project Classification SS: Skeletal Biology Development and Disease - SBDD

Project Keyword 1: Studies involving diseases of the skeleton and mineral metabolism in humans and animal models such as osteogenesis imperfecta; Paget¿s disease of bone; chondrodystrophies, osteodystrophies; diseases of mineral ion homeostasis associated with abnormalities of parathyroid hormone, Vitamin D, calcitonin and other hormonal and paracrine factors.

Project Request: **Animals:** ☐ **Humans:** ☒ **Clinical trial:** ☐

Project total financing request to the MOH: € 870.000

Free keywords: Bone mineral Density, oxidative stress, Endocrine discruiptors, environment, fetus, newborns, children, osteoporosis

Declarations

In case of a Synergy grant application 'Principal Investigator'(PI) means 'corresponding Principal Investigator on behalf of all Principal Investigators', and 'Host Institution' means 'corresponding Host Institution'.

1) The Principal Investigator declares to have the written consent of all participants on their participation and on the content of this proposal, as well as of any researcher mentioned in the proposal as participating in the project (either as other PI, team member or collaborator).	X
2) The Principal Investigator declares that the information contained in this proposal is correct and complete.	X
3) The Principal Investigator declares that all parts of this proposal comply with ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct).	X
4) The Principal Investigator is only responsible for the correctness of the information relating to his/her own organisation. Each applicant remains responsible for the correctness of the information related to him and declared above.	X

Personal data protection

The assessment of your grant application will involve the collection and processing of personal data (such as your name, address and CV), which will be performed pursuant to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Unless indicated otherwise, your replies to the questions in this form and any personal data requested are required to assess your grant application in accordance with the specifications of the call for proposals and will be processed solely for that purpose. Details concerning the purposes and means of the processing of your personal data as well as information on how to exercise your rights are available in the privacy statement. Applicants may lodge a complaint about the processing of their personal data with the European Data Protection Supervisor at any time.

Abstract

Maximization of bone mass during skeletal growth has become the goal of primary prevention of osteopenia and osteoporosis. Any factor that might influence peak bone mass attained at skeletal maturity is important in determining the individual¿s risk of developing osteoporosis later in life. Bone health begins with maternal health and nutrition, which influences skeletal mass and bone density in the fetus. Peak bone mass acquisition is also under a genetic influence from both parents. To date, some evidences suggests that the risk of osteoporosis later in life may be determined by environmental influences during intrauterine or early postnatal life. The mechanisms underlying the long term effect of the intrauterine environment on bone health are currently unknown but definitely include ``fetal programming¿¿ of oxidative stress and endocrine systems that influence skeletal growth and development in utero and thereafter. Osteopenia is recognized with increasing frequency in low-birth weight newborn infants. Intrauterine growth restriction also increases the risk of obesity and metabolic syndrome which dramatically affect bone quality. Micro RNA and long non coding RNA have recently come into the spotlight due to their ability to control gene expression at the post-transcriptional level providing epigenetic modification and targeting the growth plate.
These considerations highlight that the evaluation of skeletal status from perinatal period is essential for both the early detection of the conditions characterized by defects in bone mass or mineralization and for the monitoring of the bone development process.
It is still unknow if and how fetal bone mineral density varies according to maternal nutritional factors, if and how it impacts on some outcomes at childbirth (eg spontaneous clavicle or skull fractures during operative birth) and on the long term bone mineralization.
Radiofrequency Echographic Multi Spectrometry (REMS) technology has proven to be useful in the assessment of bone mineral denisity in pregnant women. Very few studies have reported that transmission ultrasound can be used for the assessment of bone status in newborns. The attractiveness of REMS technology in fetus and newborns stands in the lack of ionizing radiation, ease of use and, above all, the possibility to perform longitudinal studies on REMS patterns from

intrauterine to extrauterine life and during the first year of life. New challenge relies in - development of transducers and software tspecific for fetus and newborns. which will be part of this project.
Starting from the mother¿s exposome information, the project will unravel the effect of environmental contaminants, and in particular of endocrine disruptors, of oxidative stress and of miRNAs within the field of epigenetics on bone health .
The aims of the present study are:

A) To determine the feasibility of the use of REMS, as assessed by a new measurement approach to evaluate skeletal status in fetuses, newborns and children as a precise and innovative technology.
B To assess how mother's REMS patterns, and her anthropometric and gestational data influence REMS parameters in the fetus, newborn and during the first year of life.
C) To unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health

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In order to best review your application, do you agree that the above non-confidential proposal title and abstract can be used, without disclosing your identity, when contacting potential reviewers? Yes

2 - Participants & contacts

Operative Units

Institution that perform as UO	CF Institution	Department / Division / Laboratory	Role in the project	Southern Italy	SSN
1 - Azienda Ospedaliero Universitaria di Parma	01874240342	Department of Mothers Infants and Children	Coordinator		X
2 - Sicily	03051890832	Department of Human Pathology of adulthood and childhood	Collaborator	X	X

Principal Research Collaborators

Key Personnel Name	Operative Unit	Role in the project
1 - Ghi Tullio	Azienda Ospedaliero Universitaria di Parma	Co-PI (Gynecologist for mother and fetal data)
2 - STREET MARIA ELISABETH	Azienda Ospedaliero Universitaria di Parma	Research Collaborator Pediatrician
3 - WASNIEWSKA MALGORZATA GABRIELA	Sicily	Research Collaborator Pediatrician Southern Italy
4 - Aversa Tommaso	Sicily	Research Collaborator Pediatrician Southern Italy
5 - DALL'ASTA ANDREA	Azienda Ospedaliero Universitaria di Parma	Under 40 (Gynecologist for mother and fetal data)
6 Under 40 - CORICA DOMENICO	Sicily	Under 40 (Pediatrician)
7 Under 40 - DI PASQUO ELVIRA	Azienda Ospedaliero Universitaria di Parma	Under 40 (Gynecologist for mother and fetal data)

Project Code: PNRR-MAD-2022-12376819	**Call section:** Malattie Croniche non Trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e
Applicant Institution: Emilia-Romagna	**Applicant/PI Coordinator:** Perrone Serafina

Key Personnel Name	Co-PI	Resp. CE	Resp. Animal	Birth Date	Gender
1 - Ghi Tullio	X			28/04/1973	M
2 - STREET MARIA ELISABETH				21/02/1967	F
3 - WASNIEWSKA MALGORZATA GABRIELA				17/09/1959	F
4 - Aversa Tommaso				31/01/1980	M
5 - DALL'ASTA ANDREA				22/11/1985	M
6 Under 40 - CORICA DOMENICO				31/12/1987	M
7 Under 40 - DI PASQUO ELVIRA				04/08/1986	F

Additional research collaborators under 40 to hire

Key Personnel Name	Operative Unit	Birth Date	Gender	Role in the project	Degree	Actual Pos. and Inst.
0 - Pepe Giorgia	Sicily	23/04/1990	F	Patient enrollment, samples collection	Master Degree	
1 - MURA REBECCA	Azienda Ospedaliero Universitaria di Parma	18/06/1993	F	Patient enrollment, samples collection	Master Degree	
2 - cannavò Laura	Sicily	16/08/1990	F	Patient enrollment, samples collection	Master Degree	

2.1 Administrative data of participating

Operative Unit Number 1:

Address: Viale Antonio Gramsci, 14, 43126 Parma PR
PEC: protocollo@cert.ao.pr.it

Operative Unit Number 2:

Address: Via Consolare Valeria, 1, 98124 Messina ME
PEC: protocollo@pec.polime.it

Operative Unit Number 3:

Address: NA
PEC: NA

Operative Unit Number 4:

Address: NA
PEC: NA

Operative Unit Number 5 (self financing):

Address: NA
PEC: NA

2.2 Principal Investigator (PI) Profile

Last Name: Perrone
First Name: Serafina
Last name at birth:
Gender: F

Title: Principal investigator
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 23/07/1968
Place of Birth: San Pietro Vernotico

Official H index (Scopus or Web of Science): 32.0

Scopus Author Id:7004420322 **ORCID ID:**0000-0001-5478-5657 **RESEARCH ID:**AAC-2592-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci 14, Parma
Postcode / Cedex: 43126
Town: Parma
Phone:+393388704211
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Siena	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine, vote of 110/110 cum laude	1988	1993
University of Siena	Specialization / Specializzazione	Specialization in Pediatrics (address Neonatology and Neonatal Pathology), vote 70/70 cum laude	1993	1997
University of Siena	PhD	Doctor of Research (PhD) in "Growth Factors"	1998	2001
Istituto Superiore Sant'Anna of Pisa	Master's Degree / Laurea Magistrale	Master II levels: Managerial High Training Course for the Director of Complex Structure	2017	2018
University of Siena	Master's Degree / Laurea Magistrale	Master II levels. Intensive and Subintensive Therapy of the Pediatric age (0-18 years) with advanced simulation	2018	2019

Personal Statement:

The main goal of the project is to get insight on previously unexplored aspects of bone system improving the approach used in bone mineral density assessment, and thereby reducing the frequency of osteopenia, with better quality of life.
The project aims to unravel mechanisms of mother-fetus cross talk focusing on perinatal exposure to oxidative stress (OS) and endocrine disruptors.
PI has long experience on markers of OS in the early identification of the newborn at high risk and in evaluating new protective clinical strategies. More recently her research may provide insight into the pathogenesis and effects of fetal programming and infants outcomes. Data are in line with fetal programming hypothesis of health from birth toward

adulthood

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma and Azienda Ospedaliera Universitaria di Parma	Department of Medicine and Surgery; Neonatal Intensive Care Unit and Neonatal Unit	Parma, Italy	Associate Professor of Pediatrics and Medical Manager position (Head of Neonatology Unit)	2019	2222
University Hospital of Siena (Azienda Ospedaliera Universitaria Senese)	Neonatal Intensive Care Unit	Siena, Italy	Medical manager position	2000	2019

Other awards and honors

2002: Winner of the ¿Ubaldo di Mita¿ National Award for the best graduation thesis in Pediatrics, issued by Italian Society of Neonatology
2014: Oral Presentation Arward at 4th International Congress of UENPS, Athens, Greece 2014: Long-term impact of VLBW on psyco-neurological development in young adults: a single center population linkage study
2016: Best Abstract Arward at 6th International Congress of UENPS, Valencia Spain 2016:
Newborn metabolic profile mirrors that of mother in pregnancy

Other CV informations

Coordinator and Head of the Clinical Biochemistry Study Group (Italian Society of Neonatology).
Deputy President of the Bachelor of Health Professions in Nursing, University of Parma
Appointment as Regional Referent for Rare Diseases
Invited as Expert Revisor for AIFA experimental project, (Italian Drug Agency) and for Research proposal submitted to the executive Government agency of National Science Centrum of Poland
Guest Editor of Special issue ¿Oxidative stress in the Newborn¿ in ¿Antioxidants¿ (2021)
Lead Guest Editor of Special issue ¿Biomarkers on Oxidative stress in the neonatal period¿ in ¿Journal of Pediatric Biochemistry¿ (2016).
Guest Editor of Special issue ¿Oxidative stress in the Newborn¿ in ¿Oxidative Medicine and Cellular Longevity (2015)

Selected peer-reviewed publications of the PI valid for minimum expertise level

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
The clinical course of SARS-CoV-2 positive neonates	Review	1462-1469	40	2020	10.1038/s41372-020-0715-0	32632198	21	L
Biomarkers of oxidative stress in the fetus and in the newborn	Review	23-31	142	2019	10.1016/j.freeradbiomed.2019.03.034	30954545	21	F
Breast milk: To each his own. From metabolomic study, evidence of personalized nutrition in preterm infants	Article	158-161	62	2019	10.1016/j.nut.2018.12.015	30921551	14	F
C reactive protein in healthy term newborns during the first 48 hours of life	Article	F163-F166	103	2018	10.1136/archdischild-2016-312506	28667188	30	F

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Identification of a panel of cytokines in neonates with hypoxic ischemic encephalopathy treated with hypothermia	Article	119-124	111	2018	10.1016/j.cyto.2018.08.011	30142532	10	F
Early prediction of hypoxic-ischemic brain injury by a new panel of biomarkers in a population of term newborns	Article	NOT_FOUND	2018	2018	10.1155/2018/7608108	30050660	21	L
The free radical diseases of prematurity: From cellular mechanisms to bedside	Review	NOT_FOUND	2018	2018	10.1155/2018/7483062	30140369	32	F
Oxidative Stress Biomarkers: Establishment of Reference Values for Isoprostanes, AOPP, and NPBI in Cord Blood	Article	NOT_FOUND	2017	2017	10.1155/2017/1758432	28512386	16	F
Oxidative Stress as a Physiological Pain Response in Full-Term Newborns	Article	NOT_FOUND	2017	2017	10.1155/2017/3759287	28133505	10	F
Oxidative Stress Biomarkers: Establishment of Reference Values for Isoprostanes, AOPP, and NPBI in Cord Blood	Article	NOT_FOUND	2017	2017	10.1155/2017/1758432	28512386	16	L
Maternal obesity and perinatal oxidative stress: The strength of the association	Article	221-227	31	2017	NOT_FOUND	28337896	18	L
Oxygen Use in Neonatal Care: A Two-edged Sword	Review	NOT_FOUND	4	2017	10.3389/fped.2016.00143	NOT_FOUND	47	F
Placental histological examination and the relationship with oxidative stress in preterm infants	Article	72-78	46	2016	10.1016/j.placenta.2016.08.084	27697224	23	F
Brain susceptibility to oxidative stress in the perinatal period	Review	2291-2295	28	2015	10.3109/14767058.2013.796170	23968388	46	F
Lipid and protein oxidation in newborn infants after lutein administration	Article	NOT_FOUND	2014	2014	10.1155/2014/781454	24876916	34	F
Biomarkers of oxidative stress in fetal and neonatal diseases	Review	2575-2578	25	2012	10.3109/14767058.2012.718004	22876862	39	F
Oxidative injury in neonatal erythrocytes	Review	104-108	25	2012	10.3109/14767058.2012.715471	23025782	36	F
New pharmacologic and therapeutic approaches for hypoxic-ischemic encephalopathy in the newborn	Review	83-88	25	2012	10.3109/14767058.2012.663168	22309153	25	F
May oxidative stress biomarkers in cord blood predict the occurrence of necrotizing enterocolitis in preterm infants?	Article	128-131	25	2012	10.3109/14767058.2012.663197	22339378	51	F
Perinatal outcome and placental histological characteristics: A single-center study	Article	110-113	25	2012	10.3109/14767058.2012.664344	22348288	33	F

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

Selected peer-reviewed publications of the PI for the evaluation CV

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**
The use of melatonin in hypoxic-ischemic brain damage: An experimental study	Article	119-124	25	2012	10.3109/14767058.2012.663232	NOT_FOUND	62
Oxidative stress and antioxidant strategies in newborns	Review	63-65	23	2010	10.3109/14767058.2010.509940	20807155	103

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**
Whole body hypothermia and oxidative stress in babies with hypoxic-ischemic brain injury	Article	236-240	43	2010	10.1016/j.pediatrneurol.2010.05.009	20837300	51
Oxygen toxicity: Chemistry and biology of reactive oxygen species	Review	186-190	15	2010	10.1016/j.siny.2010.04.003	20494636	204
Early identification of the risk for free radical-related diseases in preterm newborns	Article	241-244	86	2010	10.1016/j.earlhumdev.2010.03.008	20466493	89
Free iron, total F2-isoprostanes and total F4-neuroprostanes in a model of neonatal hypoxic-ischemic encephalopathy: Neuroprotective effect of melatonin	Article	148-154	46	2009	10.1111/j.1600-079X.2008.00639.x	19141088	71
Melatonin protects from the long-term consequences of a neonatal hypoxic-ischemic brain injury in rats	Article	157-164	44	2008	10.1111/j.1600-079X.2007.00503.x	18289167	132
Association between oxidative stress in pregnancy and preterm premature rupture of membranes	Article	793-797	40	2007	10.1016/j.clinbiochem.2007.03.004	17442295	92
Early oxidative stress in amniotic fluid of pregnancies with Down syndrome	Article	177-180	40	2007	10.1016/j.clinbiochem.2006.10.019	17208212	67
Non protein bound iron as early predictive marker of neonatal brain damage	Article	1224-1230	126	2003	10.1093/brain/awg116	12690060	94

** Autocertificated

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
University of Parma in collaboration with Azienda USL and AOU Parma	University Hospital of Parma	2022-2024	Network on the prevention and fight against the "Sudden Infant Death Syndrome" (SIDS) in the province of Parma period 2022/2024"	Coordinator	15.000,00	Local Protocol
University of Parma in collaboration with Azienda U.S.L. and Azienda Ospedaliero Universitaria of Parma	University of Parma	2019-2021	Network on the prevention and fight against the "Sudden Infant Death Syndrome" (SIDS) in the province of Parma period 2019/2021	Coordinator	15.000,00	Local Protocol

2.3 CO-PI Profile

Last Name: Ghi
First Name: Tullio
Last name at birth:
Gender: M

Title: Co-PI (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 28/04/1973
Place of Birth: Cosenza

Official H index (Scopus or Web of Science): 39.0

Scopus Author Id:6602157913 **ORCID ID:**0000-0003-1823-1096 **RESEARCH ID:**AAC-6832-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Viale Antonio Gramsci 14
Postcode / Cedex: 43100
Town: Parma
Phone:+393385070025
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Bologna	Specialization / Specializzazione	Obstetrics and Gynecology	1997	2002
University of Bologna	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	1991	1997

Personal Statement:

The project aims to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate and correlate maternal bone characteristics with those observed in the fetus and in the newborn. As Co-PI of the project, Tullio Ghi will coordinate and supervise the researcher group involved in the project and will provide expertise

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
King's College Hospital	Harris Birthright Centre Fetal Medicine Unit	London	Clinical fellowship in Fetal Medicine and fetal cardiology	2000	2001
Ospedale Sant¿Orsola Malpighi	Dipartimento di Ostetricia e Ginecologia	Bologna	Consultant in Obstetrics and Gynecology	2003	2014
Università degli Studi di Parma	Department of Medicine and Surgery	Parma	Associate Professor of Obstetrics and Gynecology	2014	2021
Università degli Studi di Parma	Department of Medicine and surgery	Parma	Director of the Residency School of Obstetrics and Gynecolo	2020	2022
Azienda Ospedaliero-Universitaria di Parma	Obstetrics and Gynecology department	Parma	Head of Obstetrics and Gynecology at the University Hospital of Parma	2021	2022
Università degli Studi di Parma	Dipartimento di Medicina e Chirurgia	Parma	Full Professor of Obstetrics and Gynecology	2021	2022

Other awards and honors

He is in board of the Italian Society of Ultrasound in Obstetrics and Gynecology and is the past president of the Italian Society of Preeclampsia (AIPE)
In 2019 he has founded the ISLANDS group (International Society of Labor and Delivery Sonography).
Best oral presentation at II Congress Research and developments in fetal medicine, London, 2002.
Best oral presentation and oral poster at XVII ISUOG Congress, Florence, October, 2007.
Best oral poster at XXVI ISUOG Congress, Rome, 2016

Other CV informations

Following his residence in Ob-Gyn at the S.Orsola Hospital of Bologna, from 2000 until 2001 Prof.Ghi was at King's College Hospital for a fellowship in Fetal Medicine. He has a phD in fetal Medicine at the University of Milan (2002-2005). Since 2014 he is based at the Department of Medicine and Surgery of the University of Parma, where he has been appointed as Full Professor of Obstetrics and Gynecology, Director of the Residency School in Obstetrics and Gynecology at the University Hospital of Parma. His main field of research is on obstetrics, ultrasound in labor and prenatal diagnosis of congenital anomalies. He has published more than 200 articles and 3 books

Selected peer-reviewed publications of the Co-PI valid for minimum expertise level

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Customized Fetal Growth Charts for Parents' Characteristics, Race, and Parity by Quantile Regression Analysis: A Cross-sectional Multicenter Italian Study	Article	83-92	35	2016	10.7863/ultra.15.03003	26643757	22	F
Narrow subpubic arch angle is associated with higher risk of persistent occiput posterior position at delivery	Article	511-515	48	2016	10.1002/uog.15808	26565728	22	F
Agreement between two- and three-dimensional transperineal ultrasound methods for assessment of fetal head-symphysis distance in active labor	Review	183-188	43	2014	10.1002/uog.13204	24006290	24	L

Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
The "occiput-spine angle": A new sonographic index of fetal head deflexion during the first stage of labor	Article	84.e1-84.e7	215	2016	10.1016/j.ajog.2016.02.020	26880733	29	F
Development of customized fetal growth charts in twins	Article	514.e1-514.e17	216	2017	10.1016/j.ajog.2016.12.176	28065816	32	F
Sonographic pattern of fetal head descent: Relationship with duration of active second stage of labor and occiput position at delivery	Article	82-89	44	2014	10.1002/uog.13324	24496823	41	F
Intrapartum transperineal ultrasound assessment of fetal head progression in active second stage of labor and mode of delivery	Article	430-435	41	2013	10.1002/uog.12379	23288706	59	F
ISUOG practice guidelines: Invasive procedures for prenatal diagnosis	Review	256-268	48	2016	10.1002/uog.15945	27485589	61	F
Fetal head-symphysis distance: A simple and reliable ultrasound index of fetal head station in labor	Article	419-424	41	2013	10.1002/uog.12335	23124698	77	L
ISUOG Practice Guidelines: intrapartum ultrasound	Review	128-139	52	2018	10.1002/uog.19072	29974596	104	F

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
Università di Parma	Department of Medicine and Surgery	2022	Womb wise. Prenatal development of multisensory integration: a 4D ultrasound study	Coordinator	50.975,00	Local Protocol

2.3 Research Collaborators n. 2

Last Name: STREET
First Name: MARIA ELISABETH
Last name at birth:
Gender: F

Title: Research Collaborator Pediatrician
Country of residence: ITALY
Nationality: ITALIANA
Country of Birth: UNITED KINGDOM
Date of birth: 21/02/1967
Place of Birth: Regno Unito

Official H index (Scopus or Web of Science): 25.0

Scopus Author Id:7006191926 **ORCID ID:**0000-0001-8427-8971 **RESEARCH ID:**B-7099-2011

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci, 14
Postcode / Cedex: 43126
Town: Parma
Phone:3332076294
Phone 2: 3332076294

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	Master's Degree / Laurea Magistrale	II level University Master in ¿Management of Endocrine and Eating Disorders in Pediatrics	2003	2004
University of Parma	PhD	Paediatric Gastro-Endocrinology	1997	2000
University of Parma	Specialization / Specializzazione	Paediatric Residency (rotatory), Department of Paediatrics, University of Parma, Italy (Diploma cum Laude)	1992	1996
University of Parma	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	1986	1992

Personal Statement:

The overall goal of the project is to unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother's nutrition as part of the in utero exposome, and subsequent body composition and bone health
Prof Street has a strong expertise in endocrinology in pediatric patients. She ensures quality of the follow-up of newborn infants
She also will give a substantial contribution in collecting data, interpreting result and supervising the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma	Department of Paediatrics	Parma, Italy	Research Associate	1999	2003
Parma University Hospital	Department of Paediatrics	Paediatric Endocrine Clinic, Parma	Honorary Clinical Fellow, supervision and teaching to paediatric residents.	1996	2002
Parma University Hospital	Department of Paediatrics	Parma, Italy.	Hospital contracts and Research Fellow	2002	2007
University Hospital of Parma	Department of Paediatrics	Parma, Italy.	clinical permanent position	2007	2014
AUSL-IRCCS di Reggio Emilia	Division of Paediatric Endocrinology and Diabetology	Reggio Emilia, Italy	Head Division of Paediatric Endocrinology and Diabetology and director research Laboratory-Dept of Mother and Child	2014	2021
University Hospital of Parma, P. Barilla Children¿s Hospital, Parma, Italy	Department of Medicine and Surgery	University Hospital of Parma	Researcher University of Parma and Head Clinical and Research Centre for Paediatric Endocrinology	2021	2022

Other awards and honors

2000: Travel Grant awarded by the European Society for Paediatric Endocrinology for the ESPE Meeting in Bruxelles
2003: Travel Grant¿ awarded by the European Society for Paediatric Endocrinology for the ESPE Meeting in Ljubjana
2005: Best scientific contributions to the XV National Meeting of the Italian Society for Pediatric Endocrinology and Diabetology
2008: Top rated basic abstract ESPE meeting, Istanbul
2013 Best oral communication basic science XIX ISPED National meeting Bari

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
UE- Horizon 2020	Reggio Emilia Hospital	2019-2024	Mother and Infant dyads: lowering the impact of endocrine disrupting chemicals in milk for a healthy life -LIFE MILCH-LIFE18 ENV/IT/0004601 MILCH	Collaborator	492.000,00	www.lifemilch.eu
MERCK	Reggio Emilia Hospital	2017-2021	International competitive GRANT FOR GROWTH INNOVATION (GGI): MicroRNAs as a New Tool To Predict Growth Response to Growth Hormone Treatment	Coordinator	60.000,00	Local Protocol

2.4 Research Collaborators n. 3

Last Name: WASNIEWSKA
First Name: MALGORZATA GABRIELA

Last name at birth:
Gender: F

Title: Research Collaborator Pediatrician Southern Italy
Country of residence: ITALY
Nationality: Italiana
Country of Birth: POLAND
Date of birth: 17/09/1959
Place of Birth: Koszalin

Official H index (Scopus or Web of Science): 28.0

Scopus Author Id:7004045267 **ORCID ID:**0000-0001-9090-2574 **RESEARCH ID:**AFJ-4491-2022

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Dipartimento di Patologia Umana dell'adulto e dell'età evolutiva, Azienda Ospedaliera "G. Martino" di Messina, Università degli Studi di Messina
Postcode / Cedex: 98125
Town: Messina
Phone:+393286522425
Phone 2: 3286522425

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	PhD	Pediatric Gastroendocrinology	1999	2003
University of Messina	Specialization / Specializzazione	Residency in Pediatrics (1st grade in Poland-1987; 2nd grade in Poland-1991; in Italy, University of Messina-1999	1995	1999
Warsaw Academy of Medicine	Master's Degree / Laurea Magistrale	Degree in Medicine at Warsaw Academy of Medicine , acknowledgement of Degree in Medicine in Italy (1994);	1978	1983

Personal Statement:

The overall goals of the project are -to unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother's nutrition as part of the in utero exposome, and subsequent body composition and bone health
Prof Wasniewska has a long experience in pediatric endocrinology. She will ensure quality of the follow-up of newborn infants
She also will give a substantial contribution in collecting data, interpreting result and supervising the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Human Pathology of adulthood and childhood "	Messina, Italy	Full Professor of Pediatrics and Medical manager Position	2022	2022
University of Messina	Department of Human Pathology of adulthood and childhood	Messina, Italy	Associate Professor of Pediatrics and Medical manager position	2015	2022
University of Messina	Pediatric Clinic	Messina, Italy	Clinical Researcher	2004	2015
National Research Institute of Mother and Child	Pediatric Clinic	Warsaw ; Poland	Assistant and First Assistant	1983	1993

Other awards and honors

Coordinator of the Didactic Commission of Italian Society of Pediatric Endocrinology (2021-23)
- national coordinator (2007-09 and 2012-2013) of the Study Group ¿Endocrine diseases due to altered function of the Gs¿ protein¿ of Italian Society of Pediatric Endocrinology and Diabetology
- national coordinator (2013-2015) of the Study Group ¿Turner Syndrome¿ of Italian Society of Pediatric Endocrinology and Diabetology
-Referent of pediatric endocrinology in the Sicily region (2017-2021).

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
ESPE Research Unit Grant	University of Messina	2018-2019	Personalised approach to non-syndromic childhood obesity using multi-omics disease signature Head of The Italian Research Unit.	Coordinator	130.000,00	ESPE website and local protocol
Pfizer	University of Messina	2021-2023	Pfizer Global Grant: ADHERENCE TO GROWTH HORMONE THERAPY AND QUALITY OF LIFE IN PEDIATRIC PATIENTS: NEW STRATEGIES OF EVALUATION AND INTERVENTION	Coordinator	65.000,00	Pfizer web site and local protocol
Sicily Region	University of Messina	2022-2024	0-6 EpPOI- Educate to prevent childhood obesity	Coordinator	100.000,00	Local protocol

2.5 Research Collaborators n. 4

Last Name: Aversa
First Name: Tommaso
Last name at birth:
Gender: M

Title: Research Collaborator Pediatrician Southern Italy
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 31/01/1980
Place of Birth: Messina

Official H index (Scopus or Web of Science): 19.0

Scopus Author Id:16199757000 **ORCID ID:**0000-0002-1754-6822 **RESEARCH ID:**O-2490-2014

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Via Consolare Valeria 1
Postcode / Cedex: 98125
Town: Messina
Phone:+393495103397
Phone 2: 3495103397

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Department of Clinical and Experimental Medicine and Pharmacology, University of Messina	PhD	Experimental Endocrinological and Metabolic Sciences (XXV cycle)	2010	2012
University of Messina	Specialization / Specializzazione	Pediatrics	2004	2009
University of Messina	Master's Degree / Laurea Magistrale	Master degree in Medicine and Surgery	1998	2004

Personal Statement:

The aim of the project is
Aversa Tommaso is a pediatrician with experience in gastroendocrinology, particularly in endocrinological and metabolic aspects of children born small for gestational age, the pathogenesis and molecular biology of GH deficiency. The role of Prof Aversa will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Associate Professor of Pediatrics	2021	2022
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Assistant Professor of Pediatrics	2018	2021
University of Messina	Department of Human Pathology of Adulthood and Childhood ¿G. Barresi¿	Messina	Research Associate of Pediatrics	2013	2018
Azienda Ospedaliera Universitaria Policlinico ¿Gaetano Martino¿	Pediatric Clinic	Messina, Italy	Pediatric Consultant with a special interest in Pediatric Endocrinology	2014	2022

Other awards and honors

Junior Member of Sicilian Regional Council of the Italian Society of Pediatrics (SIP) for the period 2020-2023
Delegate of the College of Young Pediatricians at the National Executive Council of the SIP for the period 2021-2023
Chair of the study group for Thyroid Disease in Childhood of the SIEDP/ISPED for the period 2017-2019
Chair of the study group for Turner Syndrome of SIEDP/ISPED for the period 2021-2023

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
Pfizer	University of Messina	2021-2023	ADHERENCE TO GROWTH HORMONE THERAPY AND QUALITY OF LIFE IN PEDIATRIC PATIENTS: NEW STRATEGIES OF EVALUATION AND INTERVENTION	Collaborator	65.000,00	Pfizer web site and local protocol
Sicily Region	University of Messina	2022-2024	0-6 EpPOI- Educate to prevent childhood obesity	Collaborator	100.000,00	Local Protocol

2.6 Research Collaborators n. 5

Last Name: DALL'ASTA
First Name: ANDREA
Last name at birth:
Gender: M

Title: Under 40 (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 22/11/1985
Place of Birth: Cremona

Official H index (Scopus or Web of Science): 16.0

Scopus Author Id:57150758200 **ORCID ID:**0000-0001-7201-0206 **RESEARCH ID:**K-4774-2018

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Via Gramsci 14
Postcode / Cedex: 43126
Town: Parma
Phone:+393332700919
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	PhD	Medical Sciences	2017	2020
University of Parma	Specialization / Specializzazione	Obstetrics and Gynecology	2011	2016
University of Parma	Master's Degree / Laurea Magistrale	Medicine and Surgery	2005	2010

Personal Statement:
The aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Prof Dall'Asta is among the authors of a recent publication on the use of this technology in assessing the Bone mineral density (BMD) in a group of healthy pregnant women. The role of Prof Dall'Asta will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Parma	Department of Medicine and Surgery	University Hospital of Parma	Associate Professor of Obstetrics and Gynecology, medical doctor	2021	2022
Azienda Ospedaliero Universitaria di Parma	Obstetrics and Gynecology Unit	Parma, Italy	Mediacal Manager position	2019	2022
Imperial College London	Queen Charlotte¿s and Chelsea Hospital	London	Fellowship in Obstetrics and Feto-Maternal Medicine	2018	2019
Imperial College London	Queen Charlotte¿s and Chelsea Hospital	London	Fellowship in Obstetrics and Feto-maternal Medicine	2015	2016

Other awards and honors

ISUOG World Congress 2018: Best oral presentation -Transabdominal and transperineal intrapartum ultrasound and mode of delivery in prolonged second stage of labor

ISUOG World Congress 2018: Best oral presentation -The cervical sliding sign: a new ultrasound tool in the assessment of threatened preterm labor

ISUOG World Congress 2015: Best oral presentation -Late amniocentesis: is our counselling up to date?

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
University of Parma	University of Parma	2017	Mobilità Dottorandi - Contributo Aggiuntivo di supporto all attività scientifica presso una sede estera	Coordinator	1.000,00	Parma University web-site and local protocol
Imperial College London	Imperial College London	2018	NIHR Imperial Biomedical Research Centre Imaging	Collaborator	60.000,00	Local protocol

2.7 Research Collaborators n. 6 - Under 40

Last Name: CORICA
First Name: DOMENICO
Last name at birth:
Gender: M

Title: Under 40 (Pediatrician)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 31/12/1987
Place of Birth: Messina

Official H index (Scopus or Web of Science): 12.0

Scopus Author Id:55572465600 **ORCID ID:**0000-0002-3628-1612 **RESEARCH ID:**AAC-7112-2021

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Dipartimento di Patologia Umana dell'Adulto e dell'Età evolutiva "G. Barresi", Azienda Ospedaliera Universitaria Policlinico "G. Martino", via Consolare Valeria 1
Postcode / Cedex: 98125
Town: Messina
Phone:+393403919824
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Messina	PhD	Medical and Surgical Biotechnologies	2018	2021
University of Messina	Specialization / Specializzazione	Pediatrics	2013	2018

Personal Statement:

A main objective of the projectis to incvestiogate changes in body composition, metabolism, changes in bone features and development in relationship with early exposure to EDCs and OS.
Dr Domenico Corica is a Pediatrician. He will evaluate bone mineral density in infants during the follow-up of the enrolled population.
He has a ontract for medical assistance activities, including on-call shifts during the day and on holidays, as paediatrician in the in-patient ward at the Clinic of Paediatrics , and at the Paediatric Endocrinology outpatient clinic with Day Service and Day Hospital,

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University Hospital ¿G. Martino¿ of Messina	Department of Adult and Adolescent Human Pathology "G. Barresi"	Messina	Pediatric Consultant with a special interest in Pediatric Endocrinology	2022	2022

Other awards and honors

- Coordinator of the Italian Society of Paediatric Endocrinology (ISPED) Study Group 'Endocrine diseases due to impaired function of the Gs¿ protein function" for the two-year period 2021-2023.
- Member of the ISPED Youth Commission for the two-year period 2019-2021.
- Coordinator of the ISPED Journal Club for 2019-2021.

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.8 Research Collaborators n. 7 - Under 40

Last Name: DI PASQUO
First Name: ELVIRA
Last name at birth:
Gender: F

Title: Under 40 (Gynecologist for mother and fetal data)
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 04/08/1986
Place of Birth: Agnone

Official H index (Scopus or Web of Science): 8.0

Scopus Author Id:55232384700 **ORCID ID:**0000-0002-4405-418 **RESEARCH ID:**AAA-8246-2022

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: Viale Gramsci 14
Postcode / Cedex: 43100
Town: parma
Phone:+393296080182
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Università Cattolica del Sacro Cuore di Roma	Specialization / Specializzazione	Specialization in Obstetrics and Gynecology	2012	2017
Università Cattolica del Sacro Cuore di Roma	Master's Degree / Laurea Magistrale	Master Degree in Medicine and Surgery	2006	2011

Personal Statement:

The aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Elvira di Pasquo is among the authors of a recent publication on the use of this technology in assessing the Bone mineral density (BMD) in a group of healthy pregnant women. The role of Elvira di Pasquo will be to provide expertise and actively recruit cases for analysis.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
Azienda Ospedaliero-Universitaria di Parma	Obstetrics and Gynecology Unit	Parma	Position: Consultant Obstetrician and Gynecologist	2018	2022
Fondazione Policlinico Gemelli	Department of Mother and Child	Rome	Consultant Obstetrician and Gynecologist	2017	2018

Other awards and honors

Best oral presentation ISUOG World Congress 2019, Berlin
Best oral presentation ISLANDS 2022, Rome

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.9 Additional Research Collaborators n. 2 - Under 40 to hire

Last Name: Pepe
First Name: Giorgia
Last name at birth: Pepe
Gender: F

Title: Patient enrollment, samples collection
Country of residence: ITALY
Nationality: Italiana
Country of Birth: ITALY
Date of birth: 23/04/1990
Place of Birth: Reggio Calabria

Official H index (Scopus or Web of Science): 5.0

Scopus Author Id:0000-0003-1130-829 **ORCID ID:**57202775155 **RESEARCH ID:**AAP-8204-2020

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: AOU POliclinico G. Martino , via C. Valeria 1
Postcode / Cedex: 98128
Town: Messina
Phone:+393286961402
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Messina	Specialization / Specializzazione	Postgraduate degree in Pediatrics	2015	2020
University of Messina	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine and Surgery	2009	2014

Personal Statement:

The Research Project brings together multidisciplinary competencies, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
Dr Pepe Giorgia will contribute to ernoll poluatuion and to follow the babies with clinical and instrumental visits, according to the time line of the project

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Biomedical Sciences and Dental and Functional Images	Messina	PhD student in ¿Translational molecular medicine and surgery¿	2020	2022

Other awards and honors

- 2021: The paper ¿Prospective evaluation of autoimmune and non-autoimmune subclinical hypothyroidism in Down syndrome children" was selected as the ¿TOP 5 PAPER¿ produced by the SIEDP (Italian Society for Pediatric Endocrinology and Diabetology) Study Groups .
- 2020: Successful application to the ESPE (European Society for Pediatric Endocrinolgy) Summer School 2020-2021, in England (Lake Windermere)
- 2016: Award of merit for Women Doctors by the Italian Association ¿Associazione Mogli Me

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
European Society for Pediatric Endocrinolog	University of Messina	2021	Grant ESPE (the European Society for Pediatric Endocrinology) for the abstracts submitted for the 59th meeting ESPE.	Coordinator	500,00	ESPE web site

2.10 Additional Research Collaborators n. 3 - Under 40 to hire

Last Name: MURA
First Name: REBECCA

Last name at birth:
Gender: F

Title: Patient enrollment, samples collection
Nationality: italiana
Date of birth: 18/06/1993

Country of residence: ITALY
Country of Birth: ITALY
Place of Birth: brescia

Official H index (Scopus or Web of Science): 0.0

Scopus Author Id:NA **ORCID ID:**NA **RESEARCH ID:**NA

Contact address

Current organisation name: Azienda Ospedaliero Universitaria di Parma
Current Department / Faculty / Institute / Laboratory name: Department of Mothers Infants and Children
Street: via Gramsci 14
Postcode / Cedex: 43126
Town: Parma
Phone:+393470749631
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
University of Parma	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master Degree in Medicine and Surgery	2015	2020

Personal Statement:
One of the aim of this project is to validate the use of the Radiofrequency Echographic Multi Spectrometry (REMS) technology to investigate the correlation between the maternal bone characteristics and those observed in the fetus and in the newborn. Dr Mura Rebecca will provide expertise and actively recruit cases for bone evaluation.

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
Univarsity of Parma	Department of Medicine and Surgery	Parma	Postgarduate Student-Specialization training in Radiology	2020	2022

Other awards and honors
NA

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.11 Additional Research Collaborators n. 4 - Under 40 to hire

Last Name: cannavò
First Name: Laura
Last name at birth: Messina
Gender: F

Title: Patient enrollment, samples collection
Country of residence: ITALY
Nationality: italiana
Country of Birth: ITALY
Date of birth: 16/08/1990
Place of Birth: Messina

Official H index (Scopus or Web of Science): 4.0

Scopus Author Id:57193996033 **ORCID ID:**0000-0002-4464-9421 **RESEARCH ID:**NA

Contact address

Current organisation name: Sicily
Current Department / Faculty / Institute / Laboratory name: Department of Human Pathology of adulthood and childhood
Street: Via Consolare Valeria 1
Postcode / Cedex: 98123
Town: Messina
Phone:+393400029733
Phone 2:

Education / training

Educational institution and location	Degree	Field of study	From year	To year
Univesiry of Messina	Specialization / Specializzazione	Pediatrics	2016	2021
University of Messina	Master's Degree / Laurea Magistrale	University Master II Level: endocrinologia della donna dell'infanzia e dell'adolescente	2015	2016
University of Messina	Single-cycle master's degree / Laurea magistrale a ciclo unico	Master degree Medicine and surgery	2009	2015

Personal Statement:

The Research Project brings together multidisciplinary competencies, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
Dr Laura Cannavò will contribute to ernoll poluatuion and to follow the babies with clinical and instrumental visits, according to the time line of the project. She has a particular expertise in Oxidative stress related diseases of newborn infant

Positions and honors

Positions

Institution	Division / Research group	Location	Position	From year	To year
University of Messina	Department of Biomedical Sciences and Dental and Functional Images	Messina	PhD student in ¿Translational molecular medicine and surgery¿	2021	2022

Other awards and honors

Prize 'Onore al merito', by University of Messina

Grant

Funded by Institution	Researcher inst. where grant is/was performed	Year	Title	Position in Projects	Fund (euro)	Source website grant listed
NA	NA	NA	NA	Collaborator	0,00	NA

2.17 Expertise Research Collaborators

Selected peer-reviewed publications of the Research Group / Collaborators

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
cannavò Laura	Potential benefits of melatonin to control pain in ventilated preterm newborns: An updated review	Review	NOT_FOUND	NOT_FOUND	2021	10.1111/papr.13069	NOT_FOUND	0	F
Pepe Giorgia	Minipuberty in born small for gestational age infants: A case control prospective pilot study	Article	NOT_FOUND	NOT_FOUND	2022	10.1007/s12020-022-03003-0	35142975	0	F
CORICA DOMENICO	Meal-Related Asprosin Serum Levels Are Affected by Insulin Resistance and Impaired Fasting Glucose in Children With Obesity	Article	NOT_FOUND	12	2022	10.3389/fendo.2021.805700	NOT_FOUND	1	F
CORICA DOMENICO	Prospective assessment of liver stiffness by shear wave elastography in childhood obesity: a pilot study	Article	59-69	75	2022	10.1007/s12020-021-02828-5	34302259	2	F
cannavò Laura	Oxidative stress and respiratory diseases in preterm newborns	Review	NOT_FOUND	22	2021	10.3390/ijms222212504	34830385	2	F
Pepe Giorgia	The metabolic syndrome in pediatrics: Do we have a reliable definition? A systematic review	Review	265-278	185	2021	10.1530/EJE-21-0238	34061767	1	O
Aversa Tommaso	Pubertal induction in girls with Turner Syndrome	Review	469-480	46	2021	10.23736/S2724-6507.20.03285-X	33435643	1	F
Pepe Giorgia	Bone Maturation as a Predictive Factor of Catch-Up Growth During the First Year of Life in Born Small for Gestational Age Infants: A Prospective Study	Article	NOT_FOUND	11	2020	10.3389/fendo.2020.00147	NOT_FOUND	2	F
cannavò Laura	Ventilation, oxidative stress and risk of brain injury in preterm newborn	Review	NOT_FOUND	46	2020	10.1186/s13052-020-00852-1	32703261	7	F
Pepe Giorgia	Prospective evaluation of autoimmune and non-autoimmune subclinical hypothyroidism in down syndrome children	Article	385-392	182	2020	10.1530/EJE-19-0823	31999620	7	F
cannavò Laura	In children with acquired hypothyroidism levothyroxine requirements may be significantly conditioned by the etiology of thyroid failure	Review	252-255	67	2020	10.1007/s12020-019-01965-2	31270749	3	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
STREET MARIA ELISABETH	Endocrine-disrupting chemicals in human fetal growth	Review	NOT_FOUND	21	2020	10.3390/ijms21041430	32093249	41	F
CORICA DOMENICO	Precocious Preclinical Cardiovascular Sonographic Markers in Metabolically Healthy and Unhealthy Childhood Obesity	Review	NOT_FOUND	11	2020	10.3389/fendo.2020.00056	NOT_FOUND	13	F
WASNIEWSKA MALGORZATA GABRIELA	Subclinical hypothyroidism in children: When a replacement hormonal treatment might be advisable	Article	NOT_FOUND	10	2019	10.3389/fendo.2019.00109	NOT_FOUND	28	L
DALL'ASTA ANDREA	Prediction of spontaneous vaginal delivery in nulliparous women with a prolonged second stage of labor: the value of intrapartum ultrasound	Article	642.e1-642.e13	221	2019	10.1016/j.ajog.2019.09.045	31589867	25	F
DI PASQUO ELVIRA	Outcome of non-visualization of fetal gallbladder on second-trimester ultrasound: cohort study and systematic review of literature	Review	582-588	54	2019	10.1002/uog.20252	30809885	12	F
Aversa Tommaso	Phenotypic expression of autoimmunity in children with autoimmune thyroid disorders	Article	NOT_FOUND	10	2019	10.3389/fendo.2019.00476	NOT_FOUND	17	F
CORICA DOMENICO	Could AGE/RAGE-related oxidative homeostasis dysregulation enhance susceptibility to pathogenesis of cardio-metabolic complications in childhood obesity?	Review	NOT_FOUND	10	2019	10.3389/fendo.2019.00426	NOT_FOUND	12	F
DALL'ASTA ANDREA	Cerebroplacental ratio assessment in early labor in uncomplicated term pregnancy and prediction of adverse perinatal outcome: prospective multicenter study	Article	481-487	53	2019	10.1002/uog.19113	29900608	34	F
STREET MARIA ELISABETH	Diagnosis, treatment and prevention of pediatric obesity: Consensus position statement of the Italian Society for Pediatric Endocrinology and Diabetology and the Italian Society of Pediatrics	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0525-6	30064525	70	O
CORICA DOMENICO	Does family history of obesity, cardiovascular, and metabolic diseases influence onset and severity of childhood obesity?	Review	NOT_FOUND	9	2018	10.3389/fendo.2018.00187	NOT_FOUND	24	F
Ghi Tullio	ISUOG Practice Guidelines: intrapartum ultrasound	Review	128-139	52	2018	10.1002/uog.19072	29974596	104	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
Pepe Giorgia	Peculiarities of precocious puberty in boys and girls with McCune-Albright syndrome	Review	NOT_FOUND	9	2018	10.3389/fendo.2018.00337	NOT_FOUND	7	O
Aversa Tommaso	Epidemiological and clinical aspects of autoimmune thyroid diseases in children with Down's syndrome	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0478-9	29562915	9	F
STREET MARIA ELISABETH	Current knowledge on endocrine disrupting chemicals (EDCs) from animal biology to humans, from pregnancy to adulthood: Highlights from a national italian meeting	Review	NOT_FOUND	19	2018	10.3390/ijms19061647	29865233	108	F
Aversa Tommaso	Atypical phenotypic aspects of autoimmune thyroid disorders in young patients with Turner syndrome	Review	NOT_FOUND	44	2018	10.1186/s13052-018-0447-3	29343299	7	F
DALL'ASTA ANDREA	Antiphospholipid antibody profile based obstetric outcomes of primary antiphospholipid syndrome: the PREGNANTS study	Article	525.e1-525.e12	216	2017	10.1016/j.ajog.2017.01.026	28153662	104	O
DALL'ASTA ANDREA	Qualitative evaluation of Crystal Vue rendering technology in assessment of fetal lip and palate	Article	549-552	49	2017	10.1002/uog.17346	27804201	15	F
WASNIEWSKA MALGORZATA GABRIELA	Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2016 Cincinnati International Turner Syndrome Meeting	Review	G1-G70	177	2017	10.1530/EJE-17-0430	28705803	461	O
WASNIEWSKA MALGORZATA GABRIELA	Autoimmune comorbidities in Hashimoto's thyroiditis: Different patterns of association in adulthood and childhood/adolescence	Article	133-141	176	2017	10.1530/EJE-16-0737	27913607	55	L
Ghi Tullio	Development of customized fetal growth charts in twins	Article	514.e1-514.e17	216	2017	10.1016/j.ajog.2016.12.176	28065816	32	F
DI PASQUO ELVIRA	Efficiency of prenatal diagnosis in Pierre Robin sequence	Review	1169-1175	37	2017	10.1002/pd.5162	28950416	13	F
WASNIEWSKA MALGORZATA GABRIELA	The Evolution of Thyroid Function after Presenting with Hashimoto Thyroiditis is Different between Initially Euthyroid Girls with and Those without Turner Syndrome	Article	403-409	86	2016	10.1159/000452722	27866202	10	F

Collaborato	Title	Type	Pag	Vol	Year	DOI	PMID	Cit.**	P.*
STREET MARIA ELISABETH	Di-(2-ethylhexyl) phthalate metabolites in urine show age-related changes and associations with adiposity and parameters of insulin sensitivity in childhood	Article	NOT_FOUND	10	2015	10.1371/journal.pone.0117831	25706863	41	C
STREET MARIA ELISABETH	Parma consensus statement on metabolic disruptors	Review	NOT_FOUND	14	2015	10.1186/s12940-015-0042-7	26092037	117	O
DI PASQUO ELVIRA	Is there any role for the hydroxychloroquine (HCQ) in refractory obstetrical antiphospholipid syndrome (APS) treatment?	Review	760-762	14	2015	10.1016/j.autrev.2015.04.010	25936295	26	O
WASNIEWSKA MALGORZATA GABRIELA	Five-year prospective evaluation of thyroid function in girls with subclinical mild hypothyroidism of different etiology	Article	801-808	173	2015	10.1530/EJE-15-0484	26374873	35	F
DI PASQUO ELVIRA	Fondaparinux in pregnancy: Could it be a safe option? A review of the literature	Review	1049-1051	135	2015	10.1016/j.thromres.2015.04.001	25912931	30	O
Ghi Tullio	ISUOG practice guidelines: Invasive procedures for prenatal diagnosis	Review	256-268	48	2016	10.1002/uog.15945	27485589	61	F
Ghi Tullio	Intrapartum transperineal ultrasound assessment of fetal head progression in active second stage of labor and mode of delivery	Article	430-435	41	2013	10.1002/uog.12379	23288706	59	F
Ghi Tullio	Fetal head-symphysis distance: A simple and reliable ultrasound index of fetal head station in labor	Article	419-424	41	2013	10.1002/uog.12335	23124698	77	L

* Position: F=First L=Last C=Correspondent O=Other N=Not applicable

** Autocertificated

3 - Ethics

1. HUMAN EMBRYOS/FOETUSES	
Does your research involve Human Embryonic Stem Cells (hESCs)?	No
Does your research involve the use of human embryos?	No
Does your research involve the use of human foetal tissues / cells?	No

2. HUMANS	
Does your research involve human participants?	Yes
Does your research involve physical interventions on the study participants?	No
3. HUMAN CELLS / TISSUES	
Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses?	No
4. PERSONAL DATA	
Does your research involve personal data collection and/or processing?	Yes
Does your research involve further processing of previously collected personal data (secondary use)?	No
5. ANIMALS	
Does your research involve animals?	No
6. ENVIRONMENT & HEALTH and SAFETY	
Does your research involve the use of elements that may cause harm to the environment, to animals or plants?	No
Does your research deal with endangered fauna and/or flora and/or protected areas?	No
Does your research involve the use of elements that may cause harm to humans, including research staff?	No
7. DUAL USE	
Does your research involve dual-use items in the sense of Regulation 428/2009, or other items for which an	No
8. EXCLUSIVE FOCUS ON CIVIL APPLICATIONS	
Could your research raise concerns regarding the exclusive focus on civil applications?	No
9. MISUSE	
Does your research have the potential for misuse of research results?	No
10. OTHER ETHICS ISSUES	
Are there any other ethics issues that should be taken into consideration? Please specify	Yes

I confirm that I have taken into account all ethics issues described above and that, if any ethics issues apply, I will complete the ethics self-assessment and attach the required documents. [X]

4 - Call-specific questions

Eligibility	
I acknowledge that I am aware of the eligibility requirements for applying as specified in the Call-PNRRXXXX_M6/C2, and certify that, to the best of my knowledge my application is in compliance with all these requirements. I understand that my proposal may be declared ineligible at any point during the evaluation or granting process if it is found not to be compliant with these eligibility criteria.	X
I confirm that the proposal that I am about to submit draws substantially don't repeat on an existing or recently finished GRANT funded.	X
Data-Related Questions and Data Protection (Consent to any question below is entirely voluntary. A positive or negative answer will not affect the evaluation of your project proposal in any form and will not be communicated to the evaluators of your project.)	
For communication purposes only, the MoH asks for your permission to publish,in whatever form and medium, your name, the proposal title, the proposal acronym, the panel, and host institution, should your proposal be retained for funding.	X
Some national and regional public research funding authorities run schemes to fund MoH applicants that score highly in the MoH's evaluation but which can not be funded by the MoH due to its limited budget. In case your proposal could not be selected for funding by the MoH do you consent to allow the MoH to disclose the results of your evaluation (score and ranking range) together with your name, non- confidential proposal title and abstract, proposal acronym, host institution and your contact details to such authorities?	X
The MoH is sometimes contacted for lists of MoH funded researchers by institutions that are awarding prizes to excellent researchers. Do you consent to allow the MoH to disclose your name, non-confidential proposal title and abstract, proposal acronym, host institution and your contact details to such institutions?	X
The Ministry of Health occasionally could contacts Principal Investigators of funded proposals for various purposes such as communication campaigns, pitching events, presentation of their project's evolution or outcomes to the public, invitations to represent the Ministry of Health in national and international forums, studies etc. Should your proposal be funded, do you consent to the Ministry of Health staff contacting you for such purposes?	X
For purposes related to monitoring, study and evaluating implementation of MoH actions, the MoH may need that submitted proposals and their respective evaluation data be processed by external parties. Any processing will be conducted in compliance with the requirements of Regulation 45/2001.	

5 – Description Project

Summary description

Any factors influencing peak bone mass, attained at skeletal maturity, are important in determining the individual¿s risk of developing osteoporosis in later life. Bone health begins with maternal health and nutrition, which influences skeletal mass and bone density already in utero.
The mechanisms underlying the effect of the intrauterine environment on bone health are currrently unknown but definitely include ``fetal programming¿¿ of oxidative stress and endocrine systems as these influence skeletal growth and development thereafter.

For the prevention of bone health, challenges rely 1) in the need for the new technology and software specific and applicable to the fetus and newborn; 2) in establishing the effect of environmental contaminants, and in particular of endocrine disruptors oxidative stress, and subsequent epigenetic changes in the mothers, and subsequently on the fetus, newborns and infant

Background / State of the art

Bone health begins with maternal health and nutrition, which influence skeletal mass and bone density in the fetus. Peak bone mass acquisition is also under a genetic influence from both parents. Evidence suggests that the risk of osteoporosis later in life may be determined by environmental influences during intrauterine or early postnatal life. The mechanisms underlying the long term effect of the intrauterine environment on bone health are currrently unknown but definitely include 'fetal programming' of oxidative stress and endocrine systems that influence skeletal growth and development. Osteopenia is recognized with increasing frequency in low-birth weight newborns. Intrauterine growth restriction also increases the risk of obesity and metabolic syndrome which dramatically affect bone quality. Micro RNAs have recently come into the spotlight due to their ability to control gene expression at the post-transcriptional level providing epigenetic modification and targeting the growth plate. Radiofrequency Echographic Multi Spectrometry (REMS) technology has proven to be useful in the assessment of bone mineral denisity (BMD) in pregnant women. Very few studies have reported that transmission ultrasound can also be used for the assessment of BMD in newborns. The attractiveness of REMS technology in fetus and newborns in its lack of ionizing radiation, ease of use and, above all, the possibility to perform longitudinal studies from intrauterine to extrauterine life

Description and distribution of activities of each operating unit

UO1 will perform: -assessment of the bone mineral density of the femur in low risk pregnant women at term gestation (>37 weeks) with REMS technology, -development of an ultrasound based software for the antenatal assessment of the bone mineral density of the femur in the fetus at term gestation (>37 weeks), -postnatal assessment of the bone mineral density of the femur in newborns and infants with REMS technology at birth and at 1 month and 3 months of life.
-postnatal assessment of biomarkers involved in bone mineral density (calcium phosforous metabolism, oxidative stress profile and lipid mediators involved in oxidative stress, endocrine disruptors)
- long term outcome of all enrolled babies (at 3-6-12 months clinical and auxological evaluation)

UO2 will perform a study to validate measurements and reproducibility of findings from UO-1. In particular, they will enrol 100 mothers and newborns.. Blood and urine will be drawn at time points as specified above. Specimens will be centralised for miRNA, for biomarkers of oxidative stress and for endocrine disruptors assays. Complete auxological measurements, and BMD evalution will be taken as in UO1

UO 1 and UO 2 will ensure that the subject¿s parents/legal representatives are given full and adequate oral and written information (subject¿s parents¿/legal representatives¿ information) about the nature, purpose, consequences and possible risk of the clinical study. Subjects¿ parents/legal representatives will be informed that they are free to withdraw the subject from the study at any time without any resulting disadvantages, how personal and health-related data of the subject and the parents will be collected and used during the study, and that the subject identity and medical information will not be disclosed. The subject¿s parents/legal representatives will be given the opportunity to ask questions and should be allowed sufficient time to consider the information provided. The subject¿s parents¿/legal representatives¿ signed and dated informed consent will be obtained before conducting any study specific procedure. A copy of the signed and dated informed consent form will be given to the subject¿s parent)/legal representatives, along with a copy of the insurance conditions.

5.4 Specific Aims and Experimental Design

Specific aim 1

To use antepartum the REMS technology to assess the BMD of the femur in a group of low risk pregnancies at term gestation
To develop an ultrasound based algorithm to assess in this population the bone mineral density of the fetal femur at term gestation.
To use after birth the REMS technology to evaluate the BMD of the femur in the same group of infants at serial follow up scans
To establish the reliability of the fetal evaluation performed with the new dedicated software in respect with the values obtained immediately after birth with the use of the previously validated REMS technology
REMS processes the raw, unfiltered ultrasound signals acquired during an echographic scan of the axial site (femur).
REMS will be used to measure BMD in fetus and neborns at 14 hours and 1 month of life.

Specific aim 2

To assess how mother's REMS patterns, and her anthropometric and gestational data influence BMD in the fetus, newborn and during the first year of life.
A specific questionnaires administered to the mothers will establish the possible exposure based nutrition, clothing and use of cosmetics and detergents, upholstery, etc in the houses.

Time points of sample collections:
At birth: Maternal urine and blood, Cord blood
48 hours of life: neonatal blood and urine
3th month of life: urine
6 months of life: urine and blood
12 months of life: urine

To assess bone biomarkers profile, the following parameters will be investigated:

MicroRNAs: In cord serum at birth (artery) total RNA will be extracted, and by TaqMan Advanced miRNA assays (Applied Biosystems) miRNAs will be quantified and normalized using hsa-miR-16-5p (Assay ID: 477860_mir) as endogenous control. Among a group of 8-10 candidate miRNAs, in particular miR-199a-5p, miR-335-5p, and miR-494-3p will be studied as it has benn recently shown that they vary in relationship to GH status, and are related to growth response. All three target genes in the growth plate
Endocrine disruptors (EDCs): A specific mix of endocrine disupting chemicals will be assayed. Thirteen different EDCs are assayed, namely: Di(2-ethylhexyl) phthalate and its oxidised metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP), Bisphenol (BP) A, BPS, BPF, polyciclic aromatic hydrocarbons, polychorodibenzophuranes and polichorodibenzo-p-dioxins, perfluoro-alchilic substances, gliphosate, and its main metabolite, parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid), piretroid insecticides,heavy metals (Pb, Cr)
Oxidative stress (OS) profile and lipid mediators involved in oxidative stress: will be evaluated both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA) . A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). To this end, highly specific and sensitive methods, such as high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed: HPLC to detect MDA, vitamin E, glutathione, GSH, and AA. The involvement of fatty acid and lipid metabolism will be also investigated by evaluating specialized pro-resolving lipid mediators (Resolvin D1, by ELISA test)
Standard biochemical tests: calcium, phosphorus, alkaline phosphatase, PTH, vitamin D (25 OH), and IGF-I.

Maternal and Cord blood: OS, EDCs markers, miRNA expression profiling (in cord blood).
48 hours of life: OS markers in blood. Urine EDCs markers
3 month of life: urine EDCs markers.
6 months of life: urine EDCs markers. Blood: OS and EDCs markers, standard biochemical tests for bone status evaluation. If changes will be present, these assays will be repeated at 12 months of age after adequate supplementation with vitamin D if necessary
12 months of life: urine EDCs markers

Specific aim 3

To unravel the relationships among early exposure to endocrine disruptors, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health

A long term outcome of all enrolled babies will be also performed: at 3-6-12 months of age, the infants will be placed under clinical and auxological evaluation (head circumference, length, weight, skinfolds, pubertal stages, and ano-genital distances, measurement of fontanels, arm span) in order to relate these measurements with those of BMD, assessed by ultrasound paramenters. The findings of BMD will be related to mothers height, weight gain in pregnancy, BMI at start of pregnancy. All measurements will be related with the miRNAs in cord serum, with the EDCs in mothers urine and in cord serum, and with the biomarkers of oxidative stress in serum. BMD during extrauterine life will be related with fetal measurements. Data in adeguate for gestational age infants (AGA), small for gestational age infants (SGA) and large for gestational age infants (LGA) will be compared

Experimental design aim 1

This is a multicentric longitudinal single group pilot study, whose primary aim is to confirm the feasibility of the use of REMS technology for the evaluation of the bone health status in mothers, fetuses, in newborns (14 hours after life) and in infants (until 1 year of life) and to assess the reliability and predictability of BMD serial measurements from the 37th gestational week to all subsequent timepoints until 1 year of life.
Asthe novel application of REMS technology in the fetal and neonatal population proposed in this project requires the preliminary construction of a reference database (from which the corresponding reference curves will be in turn extracted), population-based data will be gathered (i.e., without adopting exclusion criteria based on possible bone-related disorders), which is the approach adopted in the National Health and Nutrition Examination Survey (NHANES) III database (Looker et al., Osteoporos Int 1998, 8:468¿489), and is considered also as the best way to collect reference data in the field of bone densitometry (Engelke and Gluer 2006, Osteoporos Int 2006, 17: 1283¿1292).
The first 100 enrolled fetuses will be included in the reference database. . The same approach will be applied to the newborns, for which, obviously, the first 100 acquired cases will correspond to the first 100 enrolled fetuses.
The size of the sample to be included in the reference database (100 for the fetal database and 100 for the newborn one) was calculated taking into account the conclusions of the work by Hou et al. (Osteoporos Int 2008, 19:71¿78), according to whom, a suitable reference database can be obtained from a population of 458 women of the same ethnicity aged 6¿85 y , in which the most populated age interval includes 44 patients. We considered the fetuses as corresponding to an age interval and each considered newborn/infant age (14 h, 1 month, 3 months, 6 months, 12 months) as corresponding to a different age interval. Then, according to the methodology adopted in the construction of the reference database for REMS technology application in adults (Conversano et al., Ultrasound Med Biol 2015, 41:281-300), we rounded off this value (44) to 50 and multiplied it by a safety factor of 2.
The clinical personnel of the participating OUs will perform all the mentioned echographic acquisitions on fetuses and newborns at each established age by employing dedicated REMS devices provided in a customized research configuration and will take care toanonymize the corresponding datasets. These datasets will be transferred to the subcontractor, whose

researchers will adapt the REMS configuration already available for paediatric applications to recognize the target bone structures in fetuses and newborns and to provide the corresponding densitometric output. In this way, for each considered ¿age interval¿, a BMD value will be associated to each acquisition and from the first 100 values of each group mean value and standard deviation will be extracted, in order to obtain a 6-point reference curve of BMD as a function of age including fetuses (age ¿0¿) and newborns (age from 14 h to 12 months). The availability of such a curve will allow the expression of the densitometric result in terms of a statistically significant Z-score, which represents the most effective way to assess the bone growth. The whole process will be repeated separately for the male and female cases, in order to obtain a dedicated curve for each sex

Experimental design aim 2

As a natural extension of the primary aim of the study, we will also try to explore the association between mother's REMS patterns / anthropometric and gestational data and BMD values in the fetus and in the newborn during the first year of life.
A specific questionnaires wil be administered to the mothers to establish any possible exposure to endocrine disrupting chemicals (EDC) related with nutrition, clothing and use of cosmetics and detergents, upholstery, etc in their houses.
In the mothers, height, weight, and weight gain during pregnancy will be recorded. Body mass index (BMI) at the beginning of pregnancy will be calculated accordingly (Kg/m2).
To assess bone biomarker profiles, the following parameters will be investigated
-MicroRNAs: In cord serum at birth (artery) , miR-199a-5p, miR-335-5p, and miR-494-3p, mir-369-3p, mir-374-5p, mir-379-5p, and mir-503-5p, miR-140, and Lin28a (Let-7 family)
will be studied. Some vary in relationship to GH status, and are all related with longitudinal growth and gene regulation in the growth plate . All miRNAs will have target genes of importance in the growth plate
-Endocrine disruptors (EDCs): A specific mix of endocrine disupting chemicals will be assayed. Thirteen different EDCs will be assayed, namely: Di(2-ethylhexyl) phthalate and its oxidised metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP), Bisphenol (BP) A, BPS, BPF, polyciclic aromatic hydrocarbons, polychorodibenzophuranes and polichorodibenzo-p-dioxins, perfluoro-alchilic substances, gliphosate, and its main metabolite, parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid), piretroid insecticides,heavy metals (Pb, Cr)
-Oxidative stress (OS) profile and lipid mediators involved in oxidative stress: will be evaluated both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA) . A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). To this end, highly specific and sensitive methods, such as high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed: HPLC to detect MDA, vitamin E, glutathione, GSH, and AA. The involvement of fatty acid and lipid metabolism will be also investigated by evaluating specialized pro-resolving lipid mediators (Resolvin D1, by ELISA test)
-Standard biochemical tests: calcium, phosphorus, alkaline phosphatase, PTH, vitamin D (25 OH), ostecalcin IGF-I, glucose will be assayed to assess bone metabolim with LH, FSH, and Estradiol (E2) in females and Testosterone (T) in males to assess minipuberty that will have an effect on bone.

Time points of miRNAS, EDCs, OS and biochemical markers of bone metabolism and hormone measurements, auxological evaluation and pubertal staging
Mothers: EDCs markers.
Birth (cord blood): miRNAs, EDCs and OS markers, standard biochemical tests for bone status evaluation, standard anthropometric measurements of newborns
48 hours of life: OS markers in blood. Urine EDCs markers

3 month of life: urine EDCs markers. Complete auxological evaluations and pubertal staging
6 months of life: urine EDCs markers. Blood: miRNAs, OS and EDCs markers, standard biochemical tests for bone status evaluation, hormones for minipuberty assessment. If changes will be present, these assays will be repeated at 12 months of age after adequate supplementation with vitamin D if necessary. Complete auxological evaluations and pubertal staging
12 months of life: urine EDCs markers Complete auxological evaluations and pubertal staging

Experimental design aim 3

This is a nested longitudinal study with the aim to evaluate the long term outcome observed until 1 year of age of the newborns.
A long term outcome of all enrolled babies will be performed to unravel the relationships among early exposure to endocrine disruptors, miRNA expression, oxidative stress, and mother¿s nutrition as part of the in utero exposome, and subsequent body composition and bone health will be related with mothers height, weight gain in pregnancy, BMI at start of pregnancy, and biochemical data.
At 1, 3-6-12 months of age, length of newborns and infants will be taken on a horizontal harpenden stadiometer, and weight on an electronic scale. Body mass index (BMI) will be calculated accordingly (Kg/m2)and evaluated according to WHO standards (WHO website -https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). Head circumference, arm span, diameters of fontanels and pubertal stages will be recorded.
Skinfold thickness will be measured using a Holtain skinfold calliper at the triceps, biceps, subscapular and suprailiac sites. Specific validated algorithms for age will be used to describe subcutaneous body fat distribution.
Specific questionaires to mothers will be administered at the time of enrollment and the clinical evaluation of the newborn infants-at follow-up
Questionnaires 1 and 2 (mother life-style) and 3 (mother-to-child) are an adaptation of validated questionnaires (mother-child) within the previous project "Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases "(LIFE PERSUADED) LIFE13 ENV / IT / 000482, coordinated by the Istituto Superiore di Sanità. They have therefore been reworked on the basis of the recent report commissioned by the European Parliament (https://www.europarl.europa.eu/RegData/etudes/STUD/2019/608866/IPOL_STU (2019) 608866_EN.pdf) and current scientific literature, in order to identify possible sources of EDC release (foreseen in the project analyzes) in the usual environment of the mother-child couples recruited for the study (Martina et al. 2012; Wong et al. 2017; Mitro et al. 2016; Geens et al 2012; Serrano et al. 2014; Morgan et al. 2012; Tang et al. 2017; Phillips 1999; Borowska et al. 2015). When possible, an e-survey with partially assisted administration will be used for the administration of the Mother and Child questionnaires. The questionnaires will be built as a Google Form (Google Form): this structure allows you to build a questionnaire made available through the URL of the page, without the need to install it on a single server.
Any possible relationships among BMD established using the REMS technique, biochemical markers of bone metabolism measured in the mothers just before birth, and in the infants at 6 months of age, and anthropometric measurements will be studied
All measurements will be related with the miRNAs in cord serum, with the EDCs in mothers urine and in cord serum, and with the biomarkers of oxidative stress in serum. BMD during extrauterine life will be related with fetal measurements. Data in adeguate for gestational age infants (AGA), small for gestational age infants (SGA) and large for gestational age infants (LGA) will be compared

Picture to support preliminary data

Project- Picture.pptx

Hypothesis and significance

The Research Project brings together multidisciplinary competencies of excellence, aiming to meet important results that will reach over the medical field, and that may have relevant beneficial consequences on the health system and on the population.
A 2021 cross-sectional study of in-hospital births reported a prevalence rate increase by 23% (from 25.3 to 31.1 per 1000 hospital births). Scalp injuries composed 80% of all birth traumas and increased yearly from 19.87 to 26.46 per 1000 hospital births. Major birth trauma was associated with higher odds of hypoxic-ischemic encephalopathy, seizures, need for mechanical ventilation, meconium aspiration, and sepsis. Length of stay was increased by 56%, and total charges were almost doubled for major birth trauma.
The clinical diagnosis of osteoporosis relies heavily on bone mineral density (BMD) measured at the femoral neck, and although BMD has excellent predictive value for future fractures, the assessment of fracture risk has evolved over the years, resulting in the birth of fracture prediction tools. Fracture risk factors not currently present in these instruments are being studied for the inclusion of environmental factors that affect bone quality even before birth. The data from the knowledge of endocrine molecules and associated pathways triggered by oxidative stress are helping us to understand how to best manage patients from the earliest stages of life.
Understanding and improving the current data are critical to setting priorities for action and for tracking progress
An integrated, coordinated effort to address the unmet, significant research and development needs is required to identify causes and prevention strategies.
A prevailing theme is notable: more research and improved access to safe, timely health care are desperately needed if we are to achieve the goals of improving neonatal and child health outcomes.
Rather, bone mineral density comprises a set of interrelated factors of influence. Because of this complexity, a collaborative effort is imperative to both understand the relevant factors and design thoughtful, successful interventions.

5.5 Methodologies and statistical analyses

Methods of data collection

A traning course will be performed in Parma, to share and be familiar with the new REMS technology and to reach a common standard of bone assessment in pregnant women, fetuses, newborns and infants.
We will set up the research guidelines regarding both methodology of BMD scan and storage and shipment of urine, cord blood and peripheral blood. In addition, a common computerized data sheet will be kept for the description of clinical, biochemical, instrumental and auxological data.
Women will be enrolled andand gestational history, clinical maternal conditions, pharmacological therapy, demographic and anthropometric parameters will be recorded, and a specific questionnaire will be administered to establish any possible exposure to endocrine disrupting chemicals (EDC) related with nutrition, clothing and use of cosmetics and detergents.
The following data will be considered when available: measurement of cranial circumference and femur length of the fetus; measurement of the amniotic fluid index; active foetal movements; utero-placental hemodynamics; feto-placental hemodynamics; fetal hemodynamics (Doppler ultrasounds)
The BMD assessment by REMS technology will be scheduled as follows.
- Maternal and fetal BMD assessment: 37 weeks of gestation
- Neonatal assessment: 14 hours after birth and at 1-3-6-12 months of life

As depicted in Figure 1, samples (urine and blood) will be collected according to the following scheme:

- Maternal sample: at birth 3 mL of blood + urine
- Umbilical cord: l 4 ml of cord blood (0,5 ml + 1 ml +1 ml + 1,5 ml for measurement of OS, EDCs, standard biochemical tests, microRNAs, respectively)
- Neonate/infant:
0,5 ml of peripheral blood and 2 mL of urine at 48 hours of life (OS biomarkers)
4 ml of peripheral blood+ 2 mL of urine at 6 months (standard biochemical tests, EDCs, OS biomarkers
2 mL of urine at 12 months

Real-Time qRT-PCR will be used forthe specific candidate miRNAs: miR-199a-5p, miR-335-5p, and miR-494-3p, mir-369-3p, mir-374-5p, mir-379-5p, and mir-503-5p, miR-140, and Lin28a (Let-7 family)
Thirteen different EDCs will be assayed: 1) LC-MS for di(2-ethylhexyl) phthalate (DEHP) and its metabolites (MEHP, 6-OH-MEHP, 5-carboxy-MEPP, 5-oxo-MEHP, 5-OH-MEHP); bisphenol A and polycyclic aromatic hydrocarbons (PAHs); polychlorodibenzofurans (PCDFs) and polychlorodibenzo-p-dioxins (PCDDs), Glyphosate and its major metabolite aminomethylphosphonic acid; Parabens (methyl-, ethyl-, propyl-, butyl- esters of 4-Hydroxybenzoic acid); the pyrethroid insecticide. 2) ICP-MS for Heavy metals (i.e, Pb).
Oxidative stress profile will be analyzed both by biomarkers of oxidative protein damage (Advanced Oxidation Protein Products, AOPP) and lipid peroxidation (Isoprostanes, IsoPs, malondialdehyde, MDA). A further evaluation of oxidative stress profile will be performed by measuring non-enzymatic antioxidant molecules (vitamin E; glutathione, GSH, and ascorbic acid, AA) and enzymatic antioxidant molecules (superoxide dismutase, SOD, catalase, CAT, and glutathione peroxidase, GPx). For these assays high resolution liquid chromatography (HPLC), and gas chromatography interfaced mass spectrometry (GC-MS) will be employed.
Calcium, phosphorus, alkaline phosphatase and blood glucose will be measured on the Atellica CH Analyzer.
IGF-I, vitamin D (25 OH), PTH, osteocalcin, LH, FSH, E2, T levels will be measured using immunoassay on the LIAISON Analyzer Diasorin.

Data collection will be carried out using the REDCap platform (Research Electronic Data Capture, www.project-redcap.org) installed at the AOUPR and reachable at the URL: https://redcap.ao.pr.it:8443/ through which a specific computerized data collection form (eCRF, electronic Case Report Form) will be prepared. The system will be accessible only and exclusively to authorized personnel at each participating center

Statistic plan

According to primary objective we would evaluate the BMD density of the femur in the fetus at term gestation (>37 weeks)

with REMS technology to predict his change at 1 month of life.
Sample size was determined by performing a simulation using a one sided (alpha= 0.025) confidence intervals for Linear Regression Slope test, in which 300 newborns will allow to test if the regression coefficient, which represent the association degree between baseline and the 1 month BMD value, will be at least equal to 1.1 with a lower limit precision distance equal to 0.094. Higher thresholds of coefficient regression were evaluated showing a relative increase of the precision interval. This result was obtained by assuming a correlation value for the covariance matrix of the residual equal to 0.8. Alpha was set to 0.025 to allow a secondary key evaluation with an intermediate time point at 14 hours after birth.

Statistical analysis

Main descriptive statistics will be adopted to summarize the sample size characteristics in terms of mean and standard deviation for continuous variables and absolute and relative (percentage) frequencies for qualitative variable.
The main hypothesis will be firstly evaluated by means of linear regression model in which the dependent variable is the BMD value at 1 month and the independent regressor is the BMD value at baseline. More complex models comprehensive of mixed effects and repeated measures (MMRM) analysis will be implemented to evaluate the within and between variability components and the evolution of BMD values over time. Multivariable models will be applied to identify independent factors associated (MicroRNAs, Endocrine disruptors, Oxidative stress biomarkers and Standard biochemical tests, questionnaire items on nutrition, clothing and use of cosmetics and etc., detailed in previous section) with the outcome.
To take care of the multicollinearity issue generated in the multivariable model, a LASSO regression will be performed in order to shrink the regression coefficients toward zero by penalizing the regression model with a penalty term.
To further test the ability of significant regressors to predict an increase of BMD values over time, receiver operating characteristics (ROC) curve will be employed categorizing the outcome as a binary variable (BMD increased vs. BMD not increased).
Similar modeling will be implemented for long term outcomes detailed in aim 3 and Propensity score Matching will be adopted to enrobust the comparisons described in aim 2 section.
Due to the explorative nature of the study, we would not exclude at priori any additional hypothesis testing and unsupervised clustering analysis approach that could help to identify systematic patterns of patients with similar characteristics.
All the statistical analyses will be centralized to the unit of Clinical and Epidemiological Research Unit at U.O.1 performed using R-project and STATA statistical softwares.

Timing of analysis data

Study duration: 24 months
Protocol set up and Preparation of documents for the Ethical Committee submission: first 2 months:
1. Panel meeting of all project participants, elucidation of the critical points (recruitment of cases, sample collection, storage and shipping, common standards of care, and measurements) and related issues
2. Set-up of REMS evaluation of fetal and neonatal bone mineral density.
3. Training course for REMS evaluation of BMD in pregnant women and newborns for all the participants in the project during the 3rd month

Patient recruitment: from month 3 to 8.
1. Start recruiting patients.
2. Set up of REMS algorithm. Start bone health evaluation in mothers, fetuses and newborns.
3. Construction of REMS reference curve for fetuses and newborns. (At month 8 from project start, the available REMS

reference curve will include three ¿age points¿, i.e. ¿0¿ corresponding to the fetus, ¿14 h¿ and ¿1 month¿, then this curve will progressively extended up to the case of 12-month newborns during the clinical follow-up on the enrolled newbornsMeeting of all staff of researchers: verifying the correctness of procedures and resolve any issues arising
4. Meeting of all research staff to verify the correctness of procedures and resolve any issues arising

Follow up: from month 5 until month 20 (duration of follow up for each patient: 12 months)
Laboratory test and analysis of samples: from month 7 until month 21: two time-points for analyses (month 15 and month 21)

Data set revision: month 17 to 21

Statistical data analysis, interpretation and dissemination from month 21 to 24
1. Setting-up of the biophysical and biochemical profile of bone mineral density in fetus, newborn and child
2. Establishment of the role of the generated profile in predicting bone mineral density in childhood
3. Report of obtained data at scientific workshop and meetings.
4. Exploitation of the main results through press conferences.
5. Preparation of a full paper for ¿open access¿ submission to an international scientific journal.

5.6 Expected outcomes

When the project will be concluded, we expect to have achieved significant innovative tools for the early identification of bone health status in the fetuses and newborns. In this way, we will be able to identify which mother-fetus-newborn-infant will benefit from intervention (i.e. vit D supplementation and/or nutritional program), thereby reducing both birth fracture risk and long term adverse outcomes related to low bone density.

In particular, the following objectives will be reached:

1. Understanding of the bone mineral density values in fetus, newborn, infant and child, and of their temporal evolution;
2. Understanding the mother fetus cross-talk regarding bone mineral density;
3. Standardization of REMS technology as a tool for bone heath assessment starting from intrauterine life;
4.Recognition of microiRNAs pathway as biomarkers to assess bone health status and potential new targets for interventional therapy;
5. Verification of the oxidative stress following EDC exposome;
7. Enabling early assessment of bone mineral density in the neonatal population;
8. Developing marketable tools to bring these goals into clinical perinatal care practice;
9. Unifying standards of perinatal care.

The combined efforts of joint multidisciplinary expertise in this project will get insight on previously unexplored aspects of bone system allowing to follow bone health status from pregnancy to early childhood

5.7 Risk analysis, possible problems and solutions

Description of risk (level of likelihood: Low -L /Medium-M/ High-H)
Risk #1: Insufficient competence and effectiveness (L)
Solution #4: The project team is highly complementary and gathers the requested skills and responsibility for the main streams of research development.
Moreover, the engineering-technical skills will be acquired through appropriate sub-contracting.
Risk #2: Delays in the tasks (M)
Solution #2: All the involved staff members, and in particular the PI and the Co-PI, have significant experience both in the conduction of clinical studies involving pregnant women, fetuses and newborns and in the management of research projects. Therefore, they will adopt in advance all the typical experience-driven contingency measure to avoid possible delays. This will involve in particular some specific project activities which efficient development requires strong peculiar skills, such as protocol set up, preparation of the documentation for Ethical Committee, preparation of the statistical analysis plan, data set revision, scientific writing, etc.
Risk #3: No information sharing between members of the team (L)
Solution #3: A clear management structure with a defined meeting schedule and clear lines of authority/reporting will be established. Moreover, the staff members of the two participating UO already used to collaborate with each other and the 2-year pandemic period has further increased their ability of collaborating in the distance (Cannavò L, Perrone S, et al. Int J Mol Sci. 2021;22(22):12504; . Cannavò L, Perrone S, et al. Pain Pract. 2022;22:248-254)
Risk #4: Loss of research data due to technical problems (M)
Solution #4: A dedicated database for the storage of the data acquired during the present project will be specifically developed by an external supplier, and this will include all the most recent solutions to avoid data loss (e.g., automated backup on different hard-disks, advanced cybersecurity settings, etc.). The corresponding cost has been included in the project budget.
Risk #5: Not enough patients in clinical study (L).
Solution #5: This is actually unlikely to happen thanks to the reputation of the key opinion leaders involved as staff members, who will directly promote the project clinical study. However, specific local sensibilization campaigns will be set up, highlighting the importance of knowing in advance the bone health status of fetuses/newborns and the non-invasiveness of the proposed approaches.

5.8 Significance and Innovation

The main innovative aspect is to use REMs technology for bone health assessment, starting from fetuses. The project will provide the knowledge of mechanisms involved in perinatal bone growth and mineralization, using, for the fisrt time, a combined clinical and strumental strategy designed, on the one hand, to identify and evaluate bone status and possible etiopathogenetic factors of birth fracture in neonate and, on the other hand, to verify and confirm the role of such mechanisms in the instrumental evaluation of bone mineral density. Furthermore, we intend to ascertain the reliability and predictivity of these new markers in our population by clinical and auxological follow up.
Understanding the effects of changes in miRNAS, oxidative stress and endocrine disruptors
on the development of bone mineral densisty may lead to further research improving preventative and therapeutic measures that can fight osteoporosis, a main important contributor to morbidity and mortality worldwide

5.9 Bibliography

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5.10 Timeline / Deliverables / Payable Milestones

The Research team has been constructed in order to optimise enrolment of patients, appropriate timing of the research, and to have proper validation of the new technique emplyed for the bone study. All participants in the present project will join together with the aim of optimising the research to be conducted.
A traning course will be performed in Parma, to share and be familiar with the new REMS technology and to reach a common standard of bone assessment in pregnant women, fetuses, newborns and children.
This clinical study will be evaluated by the reference Ethics Committee before inclusion of the first subject.
Derivelables:
1)Enrolment of mathers and infants will be concluded at month 8
2)Bone status assessmet through REMS in mothers, fetus and neonate
3)Follow up (clinical and instrumental evaluations) concluded at month 20
4) Data analysiis interpration and data pubblication

Milestones 12 month

Enrollment of mothers and their children: concluded
First three months instrumental evaluation of BMD:
Preliminary data on pregnant women, fetus, newborns, and infants at 48 hours, 1 and three months of life
Preliminary results on short term perinatal outcome following birth

First and second questionnaire completed
Samples collection of enrolled mothers (urine and Blood)
Samples collection of all newbors and infants until three months of life (cord blood, peripheral blood and urine at 46 hours, 1 and 3 months of life)

Milestones 24 month

Instrumental, biochemical and clinical follow up concluded
Validation of REMS technology to assess bone mineral density from birth to infancy
Final statistical analysis of then relationships between, exposeme, oxidative stress and bone mineral density in the enrolled populaton enrolled
Knowledge on auxological data, endocrine parameters and bone mineral density in 1- years old children
Establishment of frequency of birth fractures
Report of obtained data at scientific workshops and meetings.
Exploitation of the main results through press conferences.
Submission of at least 1 full paper on the main results of the project to an international scientific journal focused on the relevant medical fields.

Gantt chart

Gantt-diagram.jpg

5.11 Equipment and resources available

Facilities Available

UO1 and UO2 have the facilities to perform patients enrolment and sample collection based on personnel with demonstrated capability, in strict observance of any relevant protocols at all times.
UO1 also provide the availability of use the infrastructure and technical equipment to measure:
- oxidative stress biomarkers: Trace GC and PolarisQ, Thermo/Finnigan; Waters 600 E System Controller HPLC equipped with a dual absorbance UV-visible detector); -80 ultra low temperature freezer
- microRNAs: Real time PCR machine; Real-Time Thermocycler 7900HT Fast PCR system (Applied Biosystems); PCR workstation; PCR hood and micro-centrifuge
-ECDs: ICP-MS and HP 1100 LC-MSD instruments (Agilent)
The suitability of the infrastructures is documented by the relevant funded projects and research activities conducted in recent years by the personnel involved in the project
Furthermore, UO1 has technical support, office space and maintenance, library, networking, high-speed computing, and administrative services. UO1 activities will be performed through integrated bioinformatics and molecular expertises.
UO2 will participate as recruiting center. The long lasting attention to studies and research activities is demonstrated by institutional repository IRIS. In addition, the PI has a long experience in endocrinology
Both, UO1 and UO2 will be equipped with 2 REMS devices with a convex probe operating at the nominal frequency of 3.5 MHz and operators will be trained to follow a standard procedure to acquire femur images and elaborate them by means of REMS algorithm.
The quality of the data will be guaranteed through the implementation of a series of automated controls in the phase of data entry in the eCRF (pre-calculated fields, branching logic, self-validations) and in the management of the data entered (deletion, display and filtering)

Subcontract

The novel application of REMS technology in the fetal and neonatal population requires the preliminary construction of a reference database (from which the corresponding reference curves will be in turn extracted).
The accomplishment of this task requires specific engineering-technical skills that are not available in the staff of the participant UOs and are essential in order to ensure the correct and rigorous application of the signal and image processing procedures detailed in the papers describing the principles of the technology that has later been identified as REMS (UMB 2015, 41:281; UMB 2016, 42:1337).

5.12 Desc. of the complementarity and sinergy of secondary collab. researchers

The consortium created for this project will integrate the expertises of each Research Units (UO) for successfully concluding all the programmed objectives.

Two Research Units are provided:
UO-1 AO-Parma
UO-2 AO-Messina

The role of each secondary collaborator researchers is complementary, according to an integrated vision of the project, in which the specific skills of each UO are highly coordinated. Gynecologists, Neonatologists and Pediatricians will ensure clinical and instrumental follow-up of the babies from birth until 1 year of life
The patient enrollment and the management of sample collection will be carried out by the UO-1 and UO-2.
UO-1 will prepare a detailed database to share with all the other collaborator researchers, including the general characteristics, the clinical data of pregnant women and their respective newborns, and laboratory results.

UO-1 collaborator researchers will perform:
- Patients enrolment and samples collection
- bone mineral density evaluation longitudinally from fetus to childhood (REMS technology)
- auxological outcome of newborn infant at 1, 3, 6 12 months of life
- OS, EDCs concentrations, miRNA in cord blood and plasma of newborn/infants
- EDCs concentrations in urine of newborns infants
-statistical analysis by experts bio-statisticians

UO-2 collaborator researchers will perform:
- patients enrolment and samples collection
- bone mineral density evaluation longitudinally from fetus to childhood (REMS technology)
- auxological outcome of newborn infant at 1, 3, 6 and 12 months of life

5.13 Translational relevance and impact for the national health system (SSN)

What is already know about this topic?

The amount of bone gained during growth and its consequent rate of loss is strictly related to the skeletal mass in adulthood (Heaney RP, 1995).
Bone health begins with maternal heath and nutrition (Godfrey K 2001).
The risk of osteoporosis later in life may be determined environmental influences during intrauterine or early postnatal life [Bocheva G, 2011; Holroyd C, 2012].
Oxidative stress in pregnancy impacts on fetal growth development and newborn infants are especially prone to oxidative

stress harmuful effects (Perrone S, 2016)
Exposure to EDCs at critical ages has been related with the development of obesity and metabolic syndrome, that are related with changes in bone composition (Street 2020; Predieri B 2021)
Radiofrequency Echographic Multi Spectrometry (REMS) technology is useful in the assessment of Bone mineral density in pregnant women (De Gennaro V, 2021)

Details on what is already know about this topic

REMS has been validated for BMD evaluation in a population of low-risk pregnant women at term of gestation. Change in bone mass density/composition involves mechanisms and pathways that aren¿t currently well defined and could be influenced by early exposure to EDCs. The action of endocrine disrupting chemicals during fetal and neonatal life is mainly exercised via epigenetic regulation of metabolic and endocrine pathways. Among these, oxidative stress and regulatory mechanisms of gene expression, the miRNA network, are of upmost importance (bocheva 2012). The molecular mechanisms by which miRNAs exert their regulatory role in longitudinal bone growth are involved with the regulation of cell growth, particularly of chondrocytes (Holroyd C 2012)
Studies performed by Basu S (2001) establish a biochemical link between increased oxidative stress and reduced bone density and provide a rational for this project investigating the role of pro- and antioxidants in bone mineral density

What this reasearch adds?

Understanding of the frequency of birth fractures at the centers participating in the study
Identification of REMs patterns characteristic of bone mineral density from prenatal to postnatal life
Recognition of changes in body composition, metabolism, changes in bone features and development in relationship with early exposure to EDCs and OS.
Validation of lipid peroxidation biomarkers as markers of perinatal oxidative stress involved in BMD
Standardization of the various endocrine disruptors and evaluation of their prognostic significance.
Unifying standards of BMD evaluation (biochemical and biophysical parameters) from early stage of life
Identification of targeted campaigns for osteopenia and osteoporosis prevention

Details on what this reasearch adds

This study project is pioneering in developing and standardize an ultrasound-based technique to assess the BMD from perinatal to post-natal life. The results from the project are expected to clarify important physio-pathological mechanism which may be implicated in the variation in individual bone mass or fracture risk.
As a first point, it is expected that this study will add important knowledge on the existing crosstalk between the maternal and the fetal bone and on how the exposure to EDCs and OS may interfere on this process since the intrauterine life.
Secondly, the post-natal longitudinal assessment is expected to clarify how the antenatal bone mineral status, the biochemical markers and the exposure to EDCs and to the OS correlate with the auxological evaluation and with the bone mineral status during the first year of life. The identification of a specific panel of biomarkers may anticipate the risk of future osteopenia or osteoporosis in the adulthood

What are the implications for public health, clinical practice, patient care?

This project may generate new knowledge on the nature-nurture interactions occurring in human infants - during a highly plastic period of development - and the focus on fetus may furthermore highlight how precocious exposures to OS and EDCs can be embedded into the biology of the human infant. The results will provide the information needed to organise specific and correct prevention campaigns to improve public health and in line with principle of the developmental origins of health and disease.
This project be beneficial to clinicians and to policy makers to further advance the quality of interventions based on scientific evidence. Studying the perinatal factors impacting bone health, setting up new technology, easy to use, for the assessment

of BMD will be effective in improvements in the quality of care that clinician deliver to infants and their parents.
The impact on economic cost reduction (prevention of birth fracture, osteopenia and osteoporosis) is equally relevant.

Details on what are the implications for public health, clinical practice, patient care

The understanding of the bone status before birth will allow a stratification of the specific risk of bone fractures at birth and during the early post-natal life
On one side this will represent a field of interest for the obstetricians which may tailor the type of obstetric interventions during delivery on the specific risk of fractures (eg. Type of operative delivery if needed, type of manouvres for the shoulder dystocia) and for the neonatologist/pediatrics which may develop specific programs on those neonates/infants with a suboptimal bone mineral status
At last, the increase in life expectancy more particularly in the developed countries, has made osteoporosis and associated fragility fractures of unusual economic interest. It has been estimated that, acresso 27 countries in the European Union, by 2025 the social costs of this disease will reach 120,000 million Euros

6 - Budget

Total proposed budget (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	110.047,00	110.047,00	not permitted	0,00
2 Researchers' Contracts	280.000,00	0,00	280.000,00	32,18
3a.1 Equipment (Leasing -	300.000,00	100.000,00	200.000,00	22,99
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	212.000,00	0,00	212.000,00	24,37
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts *	41.000,00	0,00	41.000,00	4,71
5 Patient Costs	30.000,00	0,00	30.000,00	3,45
6 IT Services and Data Bases	23.000,00	0,00	23.000,00	2,64
7 Travels	9.000,00	0,00	9.000,00	1,03
8 Publication Costs	9.000,00	0,00	9.000,00	1,03
9 Dissemination	9.000,00	0,00	9.000,00	1,03
10 Overheads *	57.000,00	0,00	57.000,00	6,55
11 Coordination Costs	0,00	0,00	0,00	0,00
Total	1.080.047,00	210.047,00	870.000,00	100,00

* percentage calculated as average value between all the Operating Units.

Report the Co-Funding Contributor:

Co-Funding will be granted by each UO, notably with an overall proportion of 19.4% (detailed: UO1 18.8%; UO2 20.3%)

Budget Justification

1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Researchers
2 Researchers' Contracts	2 Researchers for 2 years (80 kEuro each); 3 data scientists (2-year scholarships, 40 kEuro each)
3a.1 Equipment (Leasing - Rent)	Leasing of 4 echographic devices for REMS acquisitions provided in "open configuration" for research purposes 2 devices for each UO: in each UO, 1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborns).
3a.2 Equipment (buying)	NA

3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, paper, sterile needles, protection disposables, masks, gloves, disinfectant) Kits for biological sample tests (Kit elisa, kit for real time PCR, consumable for HPLC, GS-MS and ICP-MS, etc)
3c Model Costs	NA
4 Subcontracts	REMS data analysis, reference database construction and reference curve calculation for fetuses and newborns + statistical analyses of acquired REMS datasets
5 Patient Costs	Patient insurance
6 IT Services and Data Bases	NAS support at each center for networked data flow. A dedicated database for the storage of the data acquired during the present project will be specifically developed, and this will include all the most recent solutions to avoid data loss
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Communications at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Proposed total budget UO1 Institution: Azienda Ospedaliero Universitaria di Parma (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	71.170,00	71.170,00	not permitted	0,00
2 Researchers' Contracts	160.000,00	0,00	160.000,00	30,65
3a.1 Equipment (Leasing - Rent)	150.000,00	50.000,00	100.000,00	19,16
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	120.000,00	0,00	120.000,00	22,99
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts	41.000,00	0,00	41.000,00	7,85
5 Patient Costs	30.000,00	0,00	30.000,00	5,75
6 IT Services and Data Bases	23.000,00	0,00	23.000,00	4,41
7 Travels	5.000,00	0,00	5.000,00	0,96
8 Publication Costs	5.000,00	0,00	5.000,00	0,96
9 Dissemination	5.000,00	0,00	5.000,00	0,96
10 Overheads	33.000,00	0,00	33.000,00	6,32
11 Coordination Costs	0,00	0,00	0,00	0,00
Total	643.170,00	121.170,00	522.000,00	100,00

Budget Justification

1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Research
2 Researchers' Contracts	1 Researcher for 2 years (80 kEuro); 2 data scientists (2-year scholarships, 40 kEuro each)
3a.1 Equipment (Leasing - Rent)	Leasing of 2 echographic devices for REMS acquisitions provided in "open configuration" for research purposes (1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborn-infants).
3a.2 Equipment (buying)	NA
3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, paper, sterile needles, protection disposables, masks, gloves, disinfectant) Kits for biological sample tests (Kit elisa, kit for real time PCR, consumable for HPLC, GS-MS and ICP-MS, etc)
3c Model Costs	NA
4 Subcontracts	REMS data analysis, reference database construction and reference curve calculation for fetuses and newborns + statistical analyses of acquired REMS datasets
5 Patient Costs	Patient insurance
6 IT Services and Data Bases	NAS support at each center for networked data flow. A dedicated database for the storage of the data acquired during the present project will be specifically developed, and this will include all the most recent solutions to avoid data loss
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Communicatios at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Proposed total budget UO2 Institution: Sicily (Euro)

Costs	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the MOH	Percentage of total proposed to the MOH
1 Staff Salary	38.877,00	38.877,00	not permitted	0,00
2 Researchers' Contracts	120.000,00	0,00	120.000,00	34,48
3a.1 Equipment (Leasing - Rent)	150.000,00	50.000,00	100.000,00	28,74
3a.2 Equipment (buying)	0,00	0,00	0,00	0,00
3b Supplies	92.000,00	0,00	92.000,00	26,44
3c Model Costs	0,00	0,00	0,00	0,00
4 Subcontracts	0,00	0,00	0,00	0,00
5 Patient Costs	0,00	0,00	0,00	0,00
6 IT Services and Data Bases	0,00	0,00	0,00	0,00
7 Travels	4.000,00	0,00	4.000,00	1,15
8 Publication Costs	4.000,00	0,00	4.000,00	1,15
9 Dissemination	4.000,00	0,00	4.000,00	1,15
10 Overheads	24.000,00	0,00	24.000,00	6,90
11 Coordination Costs	not permitted	not permitted	not permitted	0,00
Total	436.877,00	88.877,00	348.000,00	100,00

Budget Justification	
1 Staff Salary	Staff salary has been calculated according to estimated time for management of project (including submission of the projects to each local Ethics Committee) and mentoring of Research
2 Researchers' Contracts	1 Researcher for 2 years (80 kEuro); 1 data scientist (2-year scholarships, 40 kEuro)
3a.1 Equipment (Leasing - Rent)	Leasing of 2 echographic devices for REMS acquisitions provided in "open configuration" for research purposes (1 device for acquisitions on pregnant women and fetuses and 1 device for acquisitions on newborn-infants
3a.2 Equipment (buying)	NA
3b Supplies	Consumable materials for clinical acquisition (es. coupling gel, sterile needles, protection disposables, disinfectant). Kit elisa, solvents, syringes, pipettes, sieroplast test tubes, urine tubes, reagents, chemistry and immunoassay tests.
3c Model Costs	NA
4 Subcontracts	NA
5 Patient Costs	NA
6 IT Services and Data Bases	NA
7 Travels	Travels will be planned for in-person group meetings
8 Publication Costs	Open access publication costs in scientific journals with high impact factor
9 Dissemination	Abstracts at national and international scientific congresses
10 Overheads	Costs derived from the project activation and conduction
11 Coordination Costs	NA

Principal Investigator Data

Cognome: Perrone
Nome: Serafina
Genere: F
Codice fiscale: PRRSFN68L63I119M
Documento: Carta d'identità, Numero: AS5134422
Data di nascita: 23/07/1968
Luogo di nascita: San Pietro Vernotico
Provincia di nascita: BR
Indirizzo lavorativo: Via Gramsci 14, Parma
Città: Parma
CAP: 43126
Provincia: PR
Email: saraspv@yahoo.it
Altra email: serafina.perrone@unipr.it
Telefono: +393388704211
Qualifica: Professore Universitario
Struttura: Unità Operativa Complessa di Neonatologia
Istituzione: Azienda Ospedaliero Universitaria di Parma
Datore/ente di lavoro? Yes
Datore/ente di lavoro SSN? No
Nome datore/ente di lavoro non SSN: Università
Nome istituzione SSN: Azienda Ospedaliera Universitaria di Parma
Tipo contratto: Lavoro Subordinato a Tempo Indeterminato

Con l'invio della presente proposta si dichiara che la stessa o parti significative di essa non sono oggetto di altri finanziamenti pubblici o privati e che di conseguenza vi è assenza del c.d. doppio finanziamento ai sensi dell'art. 9 del Regolamento (UE) 2021/241, ossia che non ci sia una duplicazione del finanziamento degli stessi costi da parte di altri programmi dell'Unione, nonché con risorse ordinarie da Bilancio statale.

By submitting this proposal, I declare that no significant part or parts of it are recipient of any other public or private funding and that consequently there isn't any so-called double financing pursuant to art. 9 of Regulation (EU) 2021/241, i.e. that there is no duplication in the financing of the same costs by other Euopean Union programs or any other ordinary resources from the State budget.

Project validation result

Prof.ssa Serafina Perrone
UO Neonatologia - AOU PARMA

Silvia Orzi - S.C.I. Esecuzione Contratti per Fornitura di Beni

Cristina Gazzola - S.C.I. Servizio Economico Finanziario e aspetti economici dell accesso alle prestazioni sanitarie

Michela Boschi - S.C.I. Logistica e Gestione Amministrativa Lavori Pubblici

Alessandra Zanardi - S.C. Farmacia e Governo Clinico del Farmaco

Giulia De Luca - S.C. Farmacia e Governo Clinico del Farmaco

Marco Brambilla - Servizio Interaziendale Tecnologie dell'Informazione

Matteo Berghenti - S.S.D.I. Ingegneria Clinica

Michela Guasti - S.C.I. Area Giuridica

Laura Oddi - S.C.I. Area Economica

Antonio Ventura - Direttore Amministrativo

Nunzia D'Abbiero - Direttore Sanitario

OGGETTO: Indicazioni per la gestione economico/amministrativa dello studio autorizzato con Delibera n .336/2023

Con la presente si comunica che, in seguito all'autorizzazione all'avvio del Progetto di Ricerca Bando PNRR Missione 6 - Componente 2 - Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Malattie croniche non trasmissibili (MCnT) ad alto impatto sui sistemi sanitari e socio-assistenziali - Codice progetto PNRR-MAD- , dal titolo 2022-12376819 "Getting bone health right from the start: innovative technology and new mechanims of mother-fetus cross talk for osteopenia and osteporosis

prevention - REMS-BONE (Promuovere la salute delle ossa fin dall'inizio della vita: tecnologia innovativa e nuovi meccanismi di dialogo madre-feto per la prevenzione dell'osteopenia e dell'osteoporosi)" – Principal Investigator Prof.ssa Serafina Perrone dell' U.O. di Neonatologia di questa Azienda, sono stati attribuiti i seguenti:

- **Commessa** (codice identificativo progetto): PNRR-MAD- 2022-12376819
- **ID Budget:** 1018977
- **Combinazione:** *-PRG-PROGETTI DI RICERCA-PNRR-MAD- 2022-12376819-2023/137 PNRR-MAD- 2022-12376819-2023/137 PNRR-MAD- 2022-12376819-_-_-_-_-_-_-_-

I sopracitati codici, dovranno essere indicati in tutte le richieste di acquisizione di beni, servizi e personale, da inoltrare ai competenti Servizi Aziendali.
Inoltre, per garantire la tracciabilità e la corretta rendicontazione delle prestazioni aggiuntive (esami strumentali o di laboratorio, procedure mediche o assistenziali), la commessa è registrata sul sistema AREAS (gestione degenze), dove alla pagina dedicata agli studi clinici occorre segnalare tutte le prestazioni aggiuntive erogate al paziente ai fini dello studio.
Si ricorda che, in conformità alla normativa vigente e al regolamento aziendale, costituisce uno specifico dovere del Responsabile scientifico comunicare all'Azienda la tipologia e il volume dei costi aggiuntivi effettivamente sostenuti, utili agli addebiti a carico dello Sponsor. E' inoltre sua responsabilità assicurarsi che venga trasmessa al Comitato Etico competente e all'Azienda un rapporto sullo stato di avanzamento dello studio al termine di ogni anno solare e al termine dello studio stesso, descrittivo dello stato di avanzamento (pazienti arruolati e costi sostenuti localmente per tipologia).

Ringraziando per la collaborazione, si inviano cordiali saluti

Firmato digitalmente da:
Teresa Coppola

Responsabile procedimento:
Rossella Zucchelli

Grant Office
Area Gestione Giuridica Amministrativi Studi
Tel. 0521/703686/3609

Azienda Ospedaliero - Universitaria di Parma
Via Gramsci, 14 - 43126 Parma
T. +39.0521.702111 - 703111
Partita Iva 01874240342
PEI: protocollo@cert.ao.pr.it