

Supplement S1. Steering committee member list

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Supplement S2. Case report form used for Development and Validation Cohorts

Demographic PMH and FH

Global ID in 6-digits. First 3 digits indicate a specific research center (please see below). Last 3 digits indicate subject ID within each center.

Continuous case number (assigned by coordination site)

Which of the following cohorts is it assigned to?

- Development cohort
 Validation cohort

Site ID may be looked up here

[Attachment: "Site ID file for redcap 2019.08.19.xlsx"]

Center ID (3 digits, assigned by coordinating site):

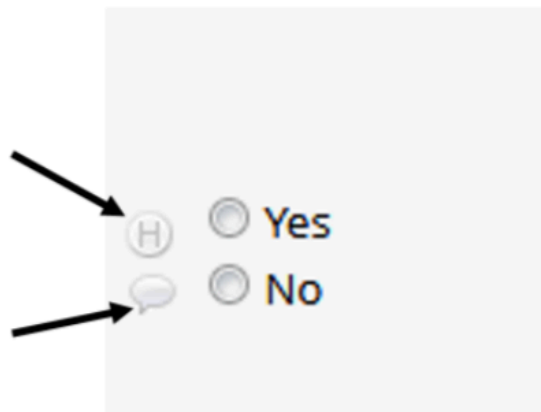
Subject ID within a center (3 digits, assigned by each center):

Please note that CNO/CRMO is used throughout this database to keep it consistent.

For each question, you may leave comments by clicking "bubble" button as shown in the illustration.

View data
entry history

Add
comments



Q1. Did this case meet all of the following criteria (MUST MEET ALL)?

- Yes
 No

1. Bone or joint pain
2. Imaging of symptomatic site prior to diagnosis, minimum but not limited to X-ray
3. Follow up for a minimum of 12 months since diagnosis of CNO/CRMO and/or CNO/CRMO mimicker disease and any secondary diagnosis (see next section) except when the diagnosis was confirmed by pathology or culture.

Q2. Case/control final diagnosis: (may select more than one, i.e. CNO/CRMO with accidental finding of bone cyst).

When there are two diagnoses, the date range of data collection is critical. There has to be AT LEAST 12 months after ANY diagnosis marked down for a subject.

For example, a patient is diagnosed with CNO/CRMO in 9/2008, PsA in 10/2009 then data need to be collected until 10/2010.

If CNO/CRMO case was diagnosed as unifocal and later became multifocal after diagnosis, please select "Unifocal".

- CNO/CRMO with unifocal lesion
- CNO/CRMO with multifocal lesions
- Leukemia
- Lymphoma
- Langerhans cell histiocytosis (LCH) or non LCH histiocytosis
- Primary malignant bone disease
- Benign bone tumor (osteoma, endochondroma)
- Infectious osteomyelitis
- Septic arthritis
- Avascular necrosis (AVN, osteonecrosis)
- Vitamin C deficiency (scurvy with bony changes)
- Enthesitis-related arthritis (ERA) or adult spondyloarthritis
- Psoriatic arthritis
- Other type of JIA or rheumatoid arthritis
- Amplified pain syndrome/Complex regional pain syndrome (CRPS)
- Other autoinflammatory diseases?
- Hypophosphatasia
- Fracture
- Other cancers (i.e. neuroblastoma, metastatic cancer)
- Other CRMO mimicker disease

Q2a. If a case has both joint effusion and bone abnormalities on imaging, is there any extra-articular bone involvement?

- Yes
 No

Other diseases

Q3a. Date of Diagnosis of CNO/CRMO with unifocal lesion

Q3b. Date of Diagnosis of CNO/CRMO with multifocal lesions

Q3c. Date of Diagnosis of Leukemia

Q3d. Date of Diagnosis of Lymphoma

Q3e. Date of Diagnosis of Langerhans cell histiocytosis (LCH) or non LCH histiocytosis

Q3f. Date of Diagnosis of Primary malignant bone disease	_____
Q3g. Date of Diagnosis of Benign bone tumor (osteoma, endochondroma)	_____
Q3h. Date of Diagnosis of Infectious osteomyelitis	_____
Q3i. Date of Diagnosis of Septic arthritis	_____
Q3j. Date of Diagnosis of Avascular necrosis (AVN, osteonecrosis)	_____
Q3k. Date of Diagnosis of Vitamin C deficiency (scurvy with bony changes)	_____
Q3L. Date of Diagnosis of Enthesitis-related arthritis (ERA) or adult spondyloarthritis	_____
Q3L1. Were there any abnormal bone imaging beyond known joints with arthritis including SI joints?	<input type="radio"/> Yes <input type="radio"/> No
Q3m. Date of Diagnosis of Psoriatic arthritis	_____
Q3m1. Were there any abnormal bone imaging beyond known joints with arthritis including SI joints?	<input type="radio"/> Yes <input type="radio"/> No
Q3n. Date of Diagnosis of Other type of JIA or rheumatoid arthritis	_____
Q3n1. Were there any abnormal bone imaging beyond known joints with arthritis including SI joints?	<input type="radio"/> Yes <input type="radio"/> No
Q3p. Date of Diagnosis of Amplified pain syndrome/Complex regional pain syndrome (CRPS)	_____
Q3q. Date of Diagnosis of Other autoinflammatory diseases?	_____
Q3r. Date of Diagnosis of hypophosphatasia	_____
Q3s. Date of Diagnosis if Fracture	_____
Q3t. Date of Diagnosis if other cancer	_____
Q3u. Date of Diagnosis if other CNO/CRMO mimicker	_____

Q4. Please assess your level of confidence that this case is CNO/CRMO by selecting one of the following +1 to +3 OR non-CNO/CRMO by selecting between -1 and -3.

For cases with both CNO and CNO mimicker diagnosis, make choice for CNO diagnosis.

If NOT highly confident, please also answer Q5.
MUST BE COMPLETED BY PRACTITIONER.

- +3 = highly confident this is CNO/CRMO
- +2 = moderately confident this is CNO/CRMO
- +1 = slightly confident this is CNO/CRMO
- 1 = slightly confident this is not CNO/CRMO
- 2 = moderately confident this is not CNO/CRMO
- 3 = highly confident this is not CNO/CRMO

Q4a. Keeping all other features the same, what would be your level of confidence that this case is CNO/CRMO if a bone biopsy had NOT been performed?

For cases with both CNO and CNO mimicker diagnosis, make choice for CNO diagnosis.

MUST BE COMPLETED BY PRACTITIONER.

- +3 = highly confident this is CNO/CRMO
- +2 = moderately confident this is CNO/CRMO
- +1 = slightly confident this is CNO/CRMO
- 1 = slightly confident this is not CNO/CRMO
- 2 = moderately confident this is not CNO/CRMO
- 3 = highly confident this is not CNO/CRMO
- Not applicable

Q5. If this is a case that you would NOT classify as CNO/CRMO (excluding cases with concurrent inflammatory disease e.g. CNO/CRMO/PsA or CNO/CRMO/ERA), please note the strongest features of the case which push you AWAY from CNO/CRMO:

OR this is a CNO/CRMO case that you are NOT highly confident, please answer.

MUST BE COMPLETED BY PRACTITIONER.

- High fevers
- Wasting (weight loss > 10%, extreme fatigue)
- Younger than 3 years of age
- Highly increased CRP (greater than 3X of upper limit of normal)
- Highly increased ESR (greater than 3X of upper limit of normal)
- Pathology consistent with CNO/CRMO mimicker disease
- Positive culture or other tests consistent with infection
- Other, please specify
- Lab tests consistent with CNO/CRMO mimicker diseases (i.e. vitamin C, alkaline phosphatase)
- High titers of rheumatoid factor
- Imaging features consistent with CNO/CRMO mimicker diseases
- Atypical location for CNO/CRMO based on imaging
- Quick response to antibiotics alone
- Findings of arthritis by physical exam and/or imaging
- Not applicable

If other, please specify _____

Q5a. If this is a case that you would NOT classify as CNO/CRMO (excluding cases with concurrent inflammatory disease e.g. CNO/CRMO/PsA or CNO/CRMO/ERA), has this patient been referred to pediatric rheumatology to work up for CNO/CRMO?

- Yes
- No

Q6. If this is a case that you would classify as CNO/CRMO (including combo cases of CNO/CRMO with any other condition), please note the STRONGEST features (there is branching logic) between onset and final diagnosis of the case which push you TOWARDS CNO/CRMO:

You may ONLY select one feature!

MUST BE COMPLETED BY PRACTITIONER.

- Imaging features
- Lab features
- Family history or comorbidities
- Clinical features
- Physical findings
- Bone biopsy
- treatment response
- Other
- Not applicable

Q6a. Detailed imaging features. Select ONLY one.	<input type="radio"/> Radiographic sclerotic lesions <input type="radio"/> Radiographic osteolytic lesions <input type="radio"/> Multifocal lesions on imaging <input type="radio"/> Symmetrical lesions on imaging <input type="radio"/> Typical location confirmed by imaging (clavicle, mandible, metaphyses of long bones, vertebra) <input type="radio"/> Abnormal signal in at least at least one bone on STIR or other fluid sensitive sequences (Fat sat, TIRM) on MRI
Q6b. Laboratory findings. Select ONLY one.	<input type="radio"/> Normal CBC <input type="radio"/> Normal CRP/ESR (within local reference range) <input type="radio"/> Mild to moderately increased CRP/ESR
Q6c. Family history or comorbidities. Select ONLY one.	<input type="radio"/> Comorbid associated disorders such as IBD, psoriasis, psoriatic arthritis, spondylitis/ERA <input type="radio"/> Family history of IBD, psoriasis, psoriatic arthritis, spondylitis/ERA
Q6d. Clinical features. Select ONLY one.	<input type="radio"/> Bone pain at typical location (clavicle, mandible, metaphyses of long bones, vertebra) <input type="radio"/> Absence of systemic features <input type="radio"/> Insidious onset of bone pain <input type="radio"/> Recurrence of bone pain <input type="radio"/> Waxing and waning of bone pain <input type="radio"/> Duration of the disease
Q6e. Physical findings. Select ONLY one.	<input type="radio"/> Presence of localized swelling unrelated to arthritis <input type="radio"/> Presence of bone tenderness <input type="radio"/> Presence of localized warmth overlying bone
Q6f. Bone biopsy. Select ONLY one.	<input type="radio"/> Ruling out malignancy and infection <input type="radio"/> Presence of fibrosis on pathology from bone biopsy <input type="radio"/> Presence of inflammation on pathology from bone biopsy
Q6g. Treatment response to antibiotics	<input type="radio"/> Yes <input type="radio"/> No
If other, please specify	_____
Q7. Birth gender:	<input type="radio"/> Male <input type="radio"/> Female
Q8. Date of birth (For day of birth please substitute the 1st day to protect identity).	_____
For example, enter "July 1, 2004" and if true birth day is 12th or 15th or 20th etc.	
Q9. Date of onset of bone pain (set all the days as 01 to protect identity)	_____

Q10. Race (choose all that apply):
If none describes a subject, please select other and free text with details.

- Asian
 Black, African American, African, or Afro-Caribbean
 Hispanic, Latino, or Spanish origin
 Middle Eastern/North African
 Native American, American Indian or Alaskan Native
 Native Hawaiian or Other Pacific Islander
 White
 Other

Q10a. Which subgroup of Asian is this case?

- Chinese (including mainland Chinese and Taiwan)
 Other East, and Southeast Asian (including Japan, Korea, Vietnam, Cambodia, Thailand, Malaysia, Indonesia)
 South Asian (including India, Pakistan and Bangladesh)

If other, please specify:

Q11. Geographic Location of patient's residence (country):

- Australia
 Canada
 Germany
 Israel
 Italy
 United Kingdom
 United States
 Turkey
 Russia
 Czech Republic
 Egypt
 Brazil
 Other country
 Unknown or do not wish to provide

Please specify which country (spell out full name).

Q12. Does patient have any of the following medical conditions concurrently or in the past? Choose all that apply.

- Psoriasis
 Inflammatory bowel disease
 Juvenile idiopathic arthritis/Rheumatoid arthritis
 Palmar plantar pustulosis (PPP)
 Acne fulminans
 Neutrophilic dermatosis
 Pyoderma gangrenosum
 Hidradenitis
 Involvement of others organs (Central Nervous system, lung etc.)
 None
 Other

If other, please specify:

Q13. Family history: Do patient's first degree relatives (biological parents, siblings, children) have any of the following medical conditions? Choose all that apply.

- Psoriasis
- Inflammatory bowel disease
- Psoriatic arthritis
- ERA/Adult Spondyloarthritis
- Other Juvenile idiopathic arthritis (Not jPsA or ERA)/Rheumatoid arthritis
- Chronic recurrent multifocal/nonbacterial osteomyelitis
- Majeed syndrome or DIRA
- None

Symptoms Ever Present

Symptoms ever present between onset and FINAL Diagnosis. Please do NOT include symptoms after treatment, i.e. psoriasis developed after a specific treatment.

Q14. Site of bone pain (only based on history without needing imaging or physical confirmation): Select all that apply as shown in illustration of entire skeleton.

- Head and face
- Neck and back (ONLY spine)
- Upper torso (clavicle, scapula, rib, sternum)
- Lower torso (sacrum, groin, buttock, hip)
- Upper extremity excluding shoulders or proximal humerus
- Lower extremity excluding hips or proximal femur

Illustration by Lauren Potts

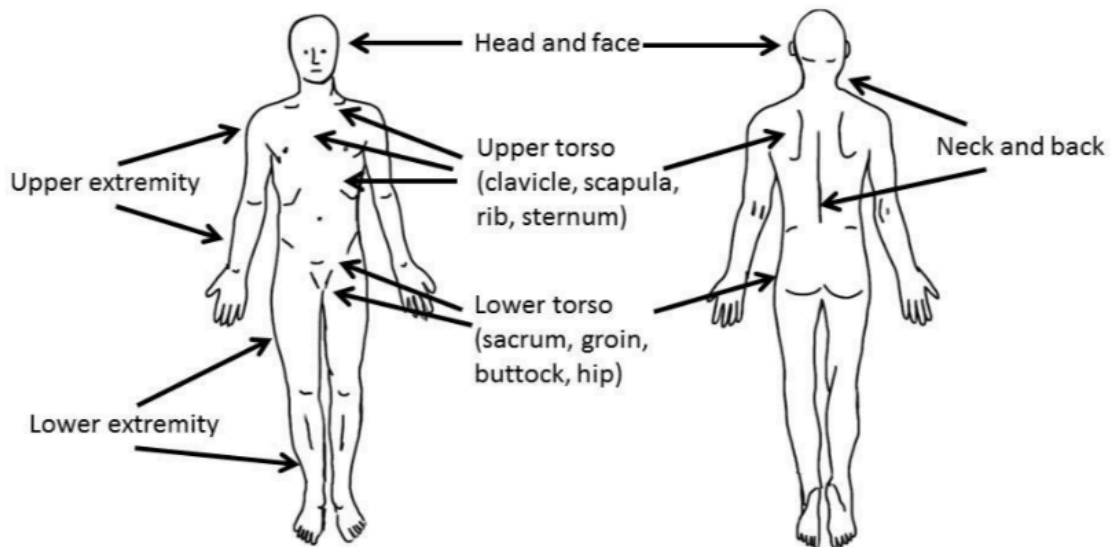


Illustration by Lauren Potts

Q15. Initial pain pattern (regardless of usage of the over the counter medicine):

- Constant at same intensity for at least a week?
- Constant but waxes and wanes for at least a week?
- Intermittent (pain free for at least 24 hour between two painful episodes)
- Unclear or unknown
- Other

If other, please specify

Q16. When did the patient have pain? Choose all that apply.

- Morning
- Daytime
- Nighttime
- During activity
- Resting
- Unknown
- Other

If other, please specify

Q17. Morning stiffness or stiffness after resting?

- Absent
- 1-30 minutes
- 31-60 minutes
- >60 minutes

Q18. Were there any constitutional features at the presentation? Choose all that apply.

- Fever (greater than 38 C)
- Night sweats
- Weight loss
- Fatigue
- Other
- None

Q18a. If there was weight loss, how significant?

- < 10%
- >=10%

Other, please describe:

Q18b. Other important symptoms pointing towards final CNO/CRMO or CNO/CRMO mimicker diagnosis not listed above:

Physical Exam

Practitioner-documented physical examination findings (Choose visit(s) that were most reflective of the disease that ever occurred between onset and when final diagnosis was made):

For example, if a patient had "finding A" at time T1 and "finding B" at time T2 that were both representative for the final diagnosis, please record both.

MUST BE COLLECTED BY PRACTITIONERS!

Q19. Were there any focal bone swelling at pain sites: Yes
 No
 Unknown

Q19a. If there is bone swelling, choose all that apply Head and face
 Neck and back (ONLY spine)
 Upper torso (clavicle, scapula, rib, sternum)
 Lower torso (sacrum, groin, buttock, hip)
 Upper extremity excluding shoulders or proximal humerus
 Lower extremity excluding hips or proximal femur

Q20. Were there any focal bone tenderness at pain sites: Yes
 No
 Unknown

Q20a. If there is bone tenderness, choose all that apply Head and face
 Neck and back (ONLY spine)
 Upper torso (clavicle, scapula, rib, sternum)
 Lower torso (sacrum, groin, buttock, hip)
 Upper extremity excluding shoulders or proximal humerus
 Lower extremity excluding hips or proximal femur

Q21. Was there active arthritis (swelling OR pain with motion and limitation of motion)? Yes
 No
 Unknown

Q21a. If there is arthritis, choose all that apply TMJ
 Intervertebral joints
 Shoulders, acromioclavicular joints
 Elbows
 Wrists
 MCPs, PIPs, DIPs
 Hips
 Knees
 Ankles, subtalar joints
 Tarsal joints
 MTPs, PIPs, DIPs
 Sacroiliac joints

Q22. Was rash present and consistent with any of following?

- Psoriasis
- Palmar plantar pustulosis (PPP)
- Acne fulminans
- Neutrophilic dermatosis
- Pyoderma gangrenosum
- Hidradenitis
- None
- Other

If other, please specify:

Q23. Did patient have any findings pertinent to the final diagnosis (CNO/CRMO or CNO/CRMO mimicker disease)?

- Diffuse lymphadenopathy
- Enlargement of liver and/or spleen
- Gingivitis and/or gingival hyperplasia
- Anorectal fistula/skin tag
- Other
- None

If other, please specify:

Lab Workup

Please record the value(s) most representative of any final CNO/CRMO or CNO/CRMO-mimicker diagnosis PRIOR to final diagnosis and/or corresponding treatment (OK if occasional NSAID was used).

For example, a patient has pneumonia during the period between onset and diagnosis, high CRP during pneumonia will NOT be recorded.

If a result is not available, please use comment function to add "NA"

Q24. White blood cell count, WBC
(x1,000/mm³=10E9/L):

_____ (x1000/mm³=10E9/L)

Q25. Hemoglobin, Hgb (g/dL, convert from g/L divided by 10):

_____ (g/dL, convert from g/L divided by 10)

Q26. Platelet, PLT (x1,000/mm³=10E9/L):

_____ (x1000/mm³=10E9/L)

Q27. Absolute neutrophil count, ANC (/mm³, convert from 10E9/L unit by x1000):

_____ (/mm³, convert from 10E9/L unit by x1000)

Do NOT report percentage

Q28. Absolute lymphocyte count, ALC (/mm³, convert from 10E9/L unit by x1000):

_____ (/mm³, convert from 10E9/L unit by x1000)

Do NOT report percentage

Q29. Absolute eosinophil count (/mm³, convert from 10E9/L unit by x1000):

_____ (/mm³, convert from 10E9/L unit by x1000)

Do NOT report percentage

Q30. Absolute monocyte count (/mm³, convert from 10E9/L unit by x1000):

_____ (/mm³, convert from 10E9/L unit by x1000)

Do NOT report percentage

Q31. Erythrocyte sedimentation rate, ESR (mm/hr):

If it is reported as < 1 etc, please record as so.

_____ (mm/hr)

Q32. C reactive protein, CRP (mg/L, please convert from mg/dL by x10):

_____ (mg/L, convert from mg/dL by x10)

If it is reported as < 8 etc, please record as so.

Q33. Lactate dehydrogenase, LDH (IU/L):

_____ (IU/L)

Q34. Uric acid (mg/dL, convert from umol/L by /0.0168):

_____ (mg/dL, convert from umol/L by /0.0168)

Q35. Alkaline phosphatase, ALP (IU/L):

_____ (IU/L)

Other important lab values with units (can include cytokine, vitamin C):

Q35a. If vitamin C level was done, please record actual values in the above answer, then choose the category below.

- Normal
 Lower than normal
 Undetectable
 Not available

Q36. Was a blood culture test done?

- Yes
 No
 Unknown

Q36a. Specify result:

- Negative
 Positive concerning for true infection
 Positive likely contamination
 Not available

Q37. Was tuberculosis/atypical mycobacteria considered in the diagnosis?

- No
 Unknown
 Confirmed positive by any of the following?
 Confirmed negative by any of the following?

Q37a. If applicable, tuberculosis or atypical mycobacteria was confirmed positive OR negative by which of the following?

If mixed, ONLY choose the option showing POSITIVE result.

- By PCR
 By geneXPRT
 By IFN gamma release assays (e.g. Quantiferon, Elispot)
 By purified protein derivative (PPD) test
 By Chest X-ray
 By any culture
 By family history

Q38. Was a bone biopsy done?

- Yes
 No

Q38a. Was this patient treated with antibiotics before bone biopsy was performed?

- Yes
 No

Q38b. What was the result of the culture from the bone biopsy?

- Negative
 Clinically-significant bacterial infection
 Clinically-significant mycobacterial infection
 Clinically-significant fungal infection
 Positive likely contamination
 Unknown
 Not done

Q38c. What bacteria?

Q38d. What was the result of PCR done for tuberculosis in the bone biopsy?

- Negative on fresh tissue
- Negative on fixed tissue
- Positive
- Not done
- Unknown

Q38e. What did the bone biopsy show? Check all that are applicable

- Not done
- Abundant presence of neutrophils
- Sparse presence of neutrophils
- Abundant presence of lymphocytes
- Sparse presence of lymphocytes
- Abundant presence of plasma cells
- Sparse presence of plasma cells
- Presence of bone necrosis
- Presence of bone fibrosis
- Presence of bone remodeling
- Presence of bone sclerosis
- Presence of reactive changes
- Chronic inflammation otherwise unspecified
- Benign bone tumor
- Normal bone
- Unknown
- Malignancy
- Infection
- Other

Other, please describe:

Q39. Was a bone marrow aspiration performed to consider malignancy?

- Yes, not consistent with malignancy
- Yes and consistent with malignancy
- No
- Unknown

Imaging

Imaging Results-Symptomatic and Asymptomatic. May INCLUDE images obtained after initiation of treatment if deemed representative for the final diagnosis of CNO/CRMO or CNO/CRMO mimickers.

Q40. Was there any whole body imaging performed?
Choose all that apply.

- None
- Unknown
- Radiographic skeletal survey
- Bone scintigraphy
- PET-CT
- Whole body MRI

Q41. Were there at least a pair of symmetrical lesions at any body site?

- Yes
- No

Q42. Among all imaging available, what sites/bones have been affected? Choose all that apply.

- Head and face
- Neck and back (i.e., spine)
- Upper torso (clavicle, scapula, rib, sternum)
- Lower torso (sacrum, groin)
- Upper extremity INCLUDING proximal humerus
- Lower extremity INCLUDING proximal femur
- None

Q42a. Head and face. Choose all that apply.

For example, in a subject with lesions in left mandible and multiple sites in skull, please choose #1 and #4.

- 1.Mandible: unilateral
- 2.Mandible: bilateral
- 3.Skull: unifocal
- 4.Skull: multifocal
- 5. Maxilla: unifocal
- 6. Maxilla: multifocal

Q42b. Neck and back (i.e., spine). Choose all that apply.

For example, in a subject with lesions in C4, T5, T6, please choose #1 and #4.

- 1.C spine: unifocal
- 2.C spine: multifocal
- 3.T spine: unifocal
- 4.T spine: multifocal
- 5.L spine: unifocal
- 6.L spine: multifocal

Q42c. Upper torso (clavicle, scapula, rib, sternum)

For example, in a subject with lesions in left clavicle and multiple sites in ribs, please choose #1 and #7.

- 1.Clavicle: unilateral
- 2.Clavicle: bilateral
- 3.Scapula: unilateral
- 4.Scapula: bilateral
- 5.Sternum/manubrium
- 6.Ribs: unifocal
- 7.Ribs: multifocal

Q42d. Lower torso (sacrum, groin). Choose all that apply.

For example, in a subject with a unifocal lesion in left ilium and bilateral sacrum please choose #1 and #6. Do NOT choose #4.

- 1.Ilium: unifocal
- 2.Ilium: multifocal but only on one side
- 3.Ilium: bilateral
- 4.Sacrum: unifocal
- 5.Sacrum: multifocal but only on one side
- 6.Sacrum: bilateral
- 7.Ischium: unifocal
- 8.Ischium: multifocal but only on one side
- 9.Ischium: bilateral
- 10.Periacetabulum: unifocal
- 11.Periacetabulum: multifocal but only on one side
- 12.Periacetabulum: bilateral
- 13.Sacroiliac region
- 14.Pubis: unifocal
- 15.Pubis: multifocal but only on one side
- 16.Pubis: bilateral

Q42e. Upper extremity INCLUDING proximal humerus. Choose all that apply.

Please select metaphysis, epiphysis or diaphysis that is affected if applicable.

For example, in a subject with a unifocal lesion in left proximal humerus (metaphysis) and bilateral radius (epiphysis and metaphysis) please choose #1, #6, #13 and #14.

- 1.Humerus: unifocal
- 2.Humerus: multifocal but only on one side
- 3.Humerus: bilateral
- 4.Radius: unifocal
- 5.Radius: multifocal but only on one side
- 6.Radius: bilateral
- 7.Ulna: unifocal
- 8.Ulna: multifocal but only on one side
- 9.Ulna: bilateral
- 10.Hand bones: carpals, metacarpals, phalanges: unifocal
- 11.Hand bones: carpals, metacarpals, phalanges: multifocal but only on one side
- 12.Hand bones: carpals, metacarpals, phalanges: bilateral
- 13.Metaphysis
- 14.Epiphysis
- 15.Diaphysis

Q42f. Lower extremity INCLUDING proximal femur. Choose all that apply.

Please select metaphysis, epiphysis or diaphysis that is affected if applicable.

For example, in a subject with a unifocal lesion in left distal femur (metaphysis) and bilateral tibia (epiphysis and diaphysis) please choose #1, #6, #13, #14 and #15.

- 1.Femur: unifocal
- 2.Femur: multifocal but only on one side
- 3.Femur: bilateral
- 4.Tibia: unifocal
- 5.Tibia: multifocal but only on one side
- 6.Tibia: bilateral
- 7.Fibula: unifocal
- 8.Fibula: multifocal but only on one side
- 9.Fibula: bilateral
- 10.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: unifocal
- 11.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: multifocal but only on one side
- 12.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: bilateral
- 13.Metaphysis
- 14.Epiphysis
- 15.Diaphysis
- 16.Patella:unifocal
- 17.Patella:bilateral

Q43. Which imaging modalities have been done? Choose all that apply.

- X-ray
 CT
 Bone scintigraphy
 MRI
 PET-CT

Q43a. What are abnormal findings from x-ray or CT of the bone sites? Choose all that apply.

- None
 Organized periosteal reaction (new bone formation)
 Sclerosis (increased density within the bone)
 Hyperostosis or bony expansion (excessive bone formation expanding from bone)
 Cortical thickening without bony expansion (beyond normal thickness)
 Cortical bone disruption
 Lytic lesion, osteolysis
 Fracture lines
 Soft tissue swelling
 Bone cyst with well-demarcated border
 Leukemia lines/Metaphyseal bands/Growth arrest lines (horizontal linear area of sclerosis on the diaphyseal side of the physis)
 Moth eaten (ill-defined lucency within marrow but intact cortex)
 Disorganized new bone formation such as "onion skinning", "sunburst" or "codman triangle"
 Peripherally enhanced fluid collection by contrast in CT (or "rim enhancement")
 Vertebral compression
 Lymphadenopathy
 Solid mass structure
 Focal demineralization
 Chronic draining sinus from bone
 Sequestrum within the bone
 Air within soft tissue
 Abscess
 Other features pointing TOWARDS final diagnosis of CNO/CRMO
 Other features pointing AWAY FROM final diagnosis of CNO/CRMO

Q43b. What tissue was occupied by solid mass structure? Choose all that apply.

- Osseous tissue
 Soft tissue
 Parenchymal tissue

If other, please specify:

If other, please specify:

Q43c. What are abnormal findings from bone scintigraphy or PET/CT of the bone sites? Choose all that apply.

- None
 Increased uptake at unifocal site
 Focal increased uptake at multifocal sites
 Decreased uptake at unifocal site
 Focal decreased uptake at multifocal sites
 Other features pointing TOWARDS final diagnosis of CNO/CRMO
 Other features pointing AWAY FROM final diagnosis of CNO/CRMO

If other, please specify:

If other, please specify:

Q43d. In MRI from fluid sensitive sequences (STIR or fat saturation or TIRM) and/or contrast, what are the abnormal findings of the bone sites? Choose all that apply

- None
- Hyperintensity in bone marrow
- Hyperintensity in surrounding soft tissue or periosteum
- Enhancement within bone marrow by contrast
- Enhancement within soft tissue by contrast
- Hypointensity within bone marrow
- Solid mass structure
- Excessive new bone formation
- Bone marrow infiltrate
- Lymphadenopathy
- Diffusion restriction within bone marrow
- Joint effusion and/or synovial enhancement
- Chronic draining sinus from bone
- Sequestrum within the bone
- Air within soft tissue
- Abscess
- Geographic appearance of abnormal marrow signal (bone infarction)
- Other features pointing TOWARDS final diagnosis of CNO/CRMO
- Other features pointing AWAY FROM final diagnosis of CNO/CRMO

Q43e. What tissue was occupied by solid mass structure? Choose all that apply.

- Osseous tissue
- Soft tissue
- Parenchymal tissue

If other, please specify:

If other, please specify:

Q43f. Which joints had ANY abnormality on imaging? Choose all that apply.

- TMJ
- Intervertebral joints
- Shoulders, acromioclavicular joints, sternoclavicular joints
- Elbows
- Wrists
- MCPs, PIPs, DIPs
- Hips
- Knees
- Ankles, subtalar joints
- Tarsal joints
- MTPs, PIPs, DIPs
- Sacroiliitis

Treatment

Q44. Did the patient receive antibiotic treatments TOWARDS bone disease before and/or during the first 3 months of final diagnosis of CRMO or CRMO mimickers?

- Antibiotics alone
- Antibiotics and NSAID
- None
- Unknown

Q45. Treatment response to the selected treatment

	No change	Partially improved	Completely resolved or normalized	Not available
Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Inflammation markers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Imaging	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q46. Did the patient have complete response WITHOUT recurrence of symptoms? Complete response is defined as resolution of pain and swelling and normalization of inflammation markers. Normalization of imaging is NOT required.

- Yes
- No
- Unknown

Supplement S3. An example of forced pair comparison within 1000minds

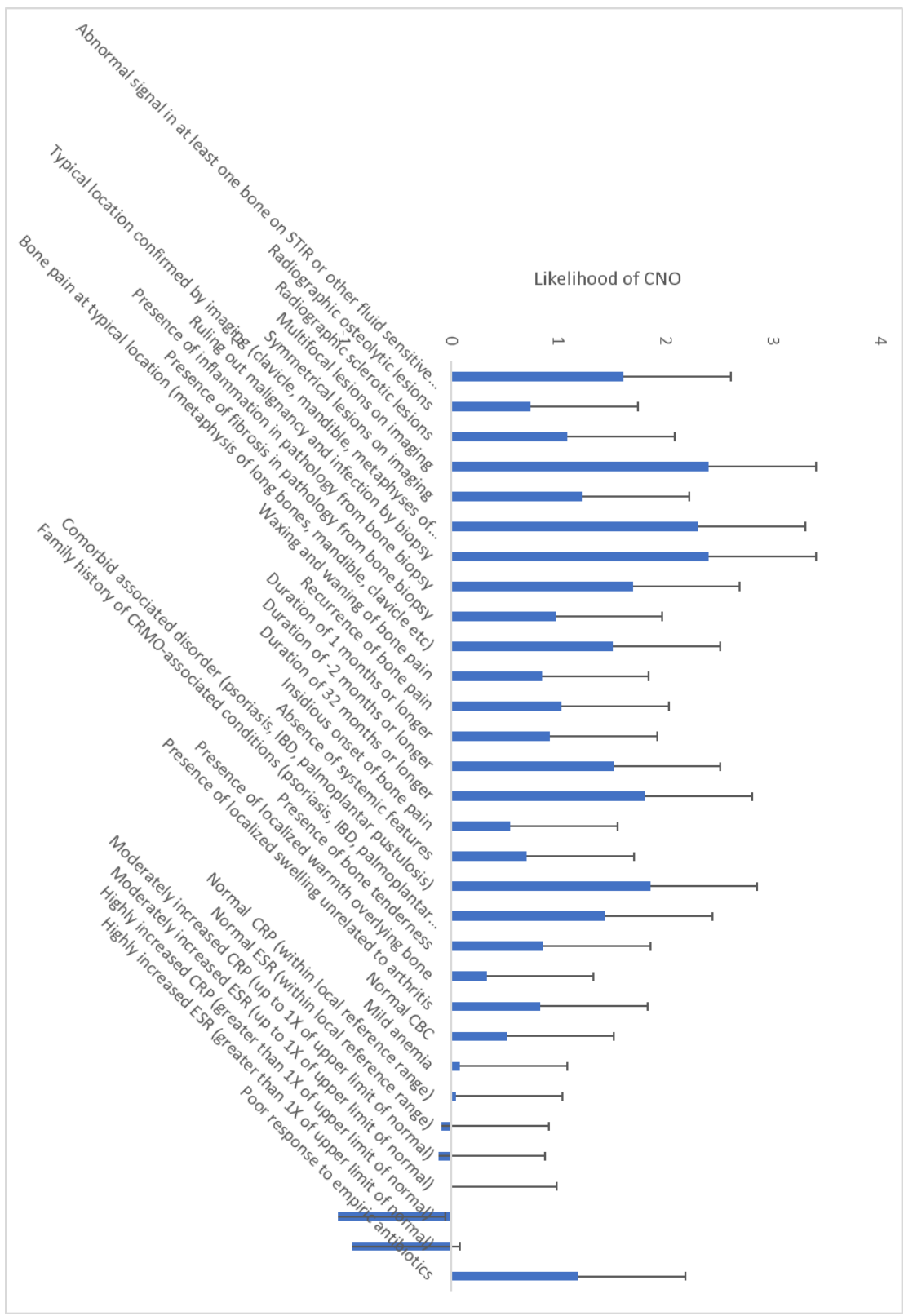
Patient A

Lesion site & Symmetry
Unilateral Tibia and Feet
Pain Frequency
Intermittent – Waxes & Wanes

Patient B

Lesion site & Symmetry
Symmetrical Clavicle
Pain Frequency
Continuous

Supplement S4. Aggregated discriminatory score of candidate items based on survey results



Supplement S5. Prevalence ratios and missing rates of items between CNO cohort and mimicker cohort in the development cohort

DEMOGRAPHICS AND COMORBIDITIES	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
'Sex at birth female'	161	60	61.2	40	1.53	2.37	0
Age at onset under 3	8	33	3	22	0.14	0.11	0
comorbidity: Psoriasis	11	1	4.2	0.7	6.27	6.5	0.0631
comorbidity: Inflammatory bowel disease	18	1	6.8	0.7	10.3	11	0.0027
comorbidity: Juvenile idiopathic arthritis/Rheumatoid arthritis	5	6	1.9	4	0.48	0.47	0.2175
comorbidity: Palmar plantar pustulosis (PPP)	2	0	0.8	0	Inf	Inf	0.5363
comorbidity: Acne fulminans	4	0	1.5	0	Inf	Inf	0.3014
comorbidity: Neutrophilic dermatosis	0	0	0	0	NA	NA	1
comorbidity: Pyoderma gangrenosum	0	0	0	0	NA	NA	1
comorbidity: Hidradenitis	0	1	0	0.7	0	0	0.3632
comorbidity: Involvement of others organs (Central Nervous system, lung etc.)	0	3	0	2	0	0	0.0473
comorbidity: None	208	124	79.1	82.7	0.96	0.79	0.4399
comorbidity: Other	25	14	9.5	9.3	1.02	1.02	1
Any comorbidity	37	12	14.1	8	1.76	1.88	0.0814
Any comorbidity except JIA/RA, involvement of other organs	33	3	12.5	2	6.27	7.03	0.0001
Rash: Psoriasis, Palmar plantar pustulosis (PPP), Acne fuminans, Neutrophilic dermatosis, Pyoderma gangrenosum, Hidradenitis	16	1	6.1	0.7	9.13	9.65	0.008
No arthritis	180	94	68.4	62.7	NA	NA	NA
Peripheral arthritis only	45	50	17.1	33.3	0.58	0.47	0.0022
Axial arthritis	38	6	14.4	4	2.91	3.31	0.0051
Sacroiliac region affected	36	5	13.7	3.3	4.11	4.6	0.0005
COMBINE - COMORBID and FAMILY HISTORY							
Any comorbidity	37	12	14.1	8	1.76	1.88	0.0814
comorbidity: psoriasis, IBD, PPP, axial arthritis	61	8	23.2	5.3	4.35	5.36	0
any family history	33	8	12.5	5.3	2.35	2.55	0.025
any family history except arthritis	26	3	9.9	2	4.94	5.38	0.0022

RESPONSE TO TREATMENT WITH ANTIBIOTICS	75% of CNO cases and 59% of mimic cases did not have antibiotic trial or the responses were unknown						
	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
Pain completely resolved with antibiotics alone	2	22	0.8	14.7	0.05	0.04	0.001
Inflammatory markers completely resolved with antibiotics alone	1	24	0.4	16	0.02	0.02	0.0014
Imaging completely resolved with antibiotics alone	0	3	0	2	0	0	0.5343
At least one outcome completely resolved with antibiotics alone	2	27	0.8	18	0.04	0.03	0.0001
Pain completely resolved with antibiotics + nsaid	15	13	5.7	8.7	0.66	0.64	0.0919
Inflammatory markers completely resolved with antibiotics + nsaid	15	18	5.7	12	0.48	0.44	0.0014
Imaging completely resolved with antibiotics + nsaid	5	5	1.9	3.3	0.57	0.56	0.1238
At least one outcome completely resolved with antibiotics + nsaid	27	20	10.3	13.3	0.77	0.74	0.0635
Pain completely resolved with antibiotics +/- nsaid	17	35	6.5	23.3	0.28	0.23	0.0002
Inflammatory markers completely resolved with antibiotics +/- nsaid	16	42	6.1	28	0.22	0.17	0
Imaging completely resolved with antibiotics +/- nsaid	5	8	1.9	5.3	0.36	0.34	0.1319
At least one outcome completely resolved with antibiotics +/- nsaid	29	47	11	31.3	0.35	0.27	0.0008
Bone site's location by report	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
Bone pain site: Head and face	22	7	8.4	4.7	1.79	1.86	0.2288
Bone pain site: Neck and back (ONLY spine)	46	13	17.5	8.7	2.01	2.23	0.0132
Bone pain site: Upper torso (clavicle, scapula, rib, sternum)	56	12	21.3	8	2.66	3.11	0.0003
Bone pain site: Lower torso (sacrum, groin, buttock, hip)	62	39	23.6	26	0.91	0.88	0.6343
Bone pain site: Upper extremity excluding shoulders or proximal humerus	37	24	14.1	16	0.88	0.86	0.6656
Bone pain site: Lower extremity excluding hips or proximal femur	171	100	65	66.7	0.97	0.93	0.7479
Bone site's location by exam	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
Swelling site: Head and face	15	7	5.7	4.7	1.21	1.23	0.8206
Swelling site: Neck and back (ONLY spine)	2	0	0.8	0	Inf	Inf	0.5363
Swelling site: Upper torso (clavicle, scapula, rib, sternum)	38	7	14.4	4.7	3.06	3.41	0.0017
Swelling site: Lower torso (sacrum, groin, buttock, hip)	3	1	1.1	0.7	1.57	1.58	1
Swelling site: Upper extremity excluding shoulders or proximal humerus	13	12	4.9	8	0.61	0.59	0.2828
Swelling site: Lower extremity excluding hips or proximal femur	66	42	25.1	28	0.9	0.86	0.5609
Tenderness site: Head and face	15	5	5.7	3.3	1.73	1.77	0.3459
Tenderness site: Neck and back (ONLY spine)	13	2	4.9	1.3	3.77	3.91	0.0972

Tenderness site: Upper torso (clavicle, scapula, rib, sternum)	35	5	13.3	3.3	4.03	4.5	0.0008
Tenderness site: Lower torso (sacrum, groin, buttock, hip)	18	19	6.8	12.7	0.54	0.5	0.0506
Tenderness site: Upper extremity excluding shoulders or proximal humerus	10	9	3.8	6	0.63	0.62	0.3338
Tenderness site: Lower extremity excluding hips or proximal femur	77	54	29.3	36	0.81	0.74	0.187
Bone site's location by imaging	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
Q41. Were there at least a pair of symmetrical lesions at any body site?	139	31	52.9	20.7	2.56	4.3	0
Imaging site: Head and face	26	11	9.9	7.3	1.36	1.4	0.4746
Imaging site: Neck and back (i.e., spine)	64	17	24.3	11.3	2.15	2.52	0.0012
Imaging site: Upper torso (clavicle, scapula, rib, sternum)	81	13	30.8	8.7	3.54	4.67	0
Imaging site: Lower torso (sacrum, groin)	102	38	38.8	25.3	1.53	1.87	0.0068
Imaging site: Upper extremity INCLUDING proximal humerus	67	28	25.5	18.7	1.36	1.49	0.1443
Imaging site: Lower extremity INCLUDING proximal femur	209	92	79.5	61.3	1.3	2.45	0.0001
Imaging site: None	0	8	0	5.3	0	0	0.0003
Detailed bone site's location by imaging	CNO	Mimic	CNO (%)	Mimic (%)	PR	OR	p-value
Detailed imaging site: 1.Mandible: unilateral	13	3	4.9	2	2.45	2.52	0.1864
Detailed imaging site: 2.Mandible: bilateral	7	0	2.7	0	Inf	Inf	0.0517
Detailed imaging site: 3.Skull: unifocal	5	4	1.9	2.7	0.7	0.7	0.7289
Detailed imaging site: 4.Skull: multifocal	1	4	0.4	2.7	0.15	0.14	0.0606
Detailed imaging site: 5. Maxilla: unifocal	1	1	0.4	0.7	0.57	0.57	1
Detailed imaging site: 6. Maxilla: multifocal	1	0	0.4	0	Inf	Inf	1
Detailed imaging site: 1.C spine: unifocal	7	3	2.7	2	1.35	1.36	0.7534
Detailed imaging site: 2.C spine: multifocal	5	3	1.9	2	0.95	0.95	1
Detailed imaging site: 3.T spine: unifocal	16	1	6.1	0.7	8.71	9.22	0.008
Detailed imaging site: 4.T spine: multifocal	29	7	11	4.7	2.34	2.51	0.0295
Detailed imaging site: 5.L spine: unifocal	18	4	6.8	2.7	2.52	2.63	0.073
Detailed imaging site: 6.L spine: multifocal	10	7	3.8	4.7	0.81	0.8	0.7975
Detailed imaging site: 1.Clavicle: unilateral	50	6	19	4	4.75	5.63	0
Detailed imaging site: 2.Clavicle: bilateral	10	1	3.8	0.7	5.43	5.6	0.0631
Detailed imaging site: 3.Scapula: unilateral	13	1	4.9	0.7	7	7.31	0.0221
Detailed imaging site: 4.Scapula: bilateral	3	1	1.1	0.7	1.57	1.58	1
Detailed imaging site: 5.Sternum/manubrium	19	1	7.2	0.7	10.3	11	0.0016
Detailed imaging site: 6.Ribs: unifocal	7	3	2.7	2	1.35	1.36	0.7534
Detailed imaging site: 7.Ribs: multifocal	7	3	2.7	2	1.35	1.36	0.7534

Detailed imaging site: 1.Ilium: unifocal	19	12	7.2	8	0.9	0.89	0.8465
Detailed imaging site: 2.Ilium: multifocal but only on one side	2	0	0.8	0	Inf	Inf	0.5363
Detailed imaging site: 3.Ilium: bilateral	9	7	3.4	4.7	0.72	0.71	0.5987
Detailed imaging site: 4.Sacrum: unifocal	31	4	11.8	2.7	4.37	4.82	0.0008
Detailed imaging site: 5.Sacrum: multifocal but only on one side	4	1	1.5	0.7	2.14	2.16	0.6572
Detailed imaging site: 6.Sacrum: bilateral	13	7	4.9	4.7	1.04	1.04	1
Detailed imaging site: 7.Ischium: unifocal	20	6	7.6	4	1.9	1.97	0.2056
Detailed imaging site: 8.Ischium: multifocal but only on one side	1	1	0.4	0.7	0.57	0.57	1
Detailed imaging site: 9.Ischium: bilateral	5	4	1.9	2.7	0.7	0.7	0.7289
Detailed imaging site: 10.Periacetabulum: unifocal	13	7	4.9	4.7	1.04	1.04	1
Detailed imaging site: 11.Periacetabulum: multifocal but only on one side	0	0	0	0	NA	NA	1
Detailed imaging site: 12.Periacetabulum: bilateral	19	4	7.2	2.7	2.67	2.8	0.0723
Detailed imaging site: 13.Sacroiliac region	36	5	13.7	3.3	4.15	4.65	0.0005
Detailed imaging site: 14.Pubis: unifocal	15	2	5.7	1.3	4.38	4.59	0.0378
Detailed imaging site: 15.Pubis: multifocal but only on one side	0	0	0	0	NA	NA	1
Detailed imaging site: 16.Pubis: bilateral	2	2	0.8	1.3	0.62	0.61	0.6237
Detailed imaging site: 1.Humerus: unifocal	19	9	7.2	6	1.2	1.22	0.6892
Detailed imaging site: 2.Humerus: multifocal but only on one side	1	1	0.4	0.7	0.57	0.57	1
Detailed imaging site: 3.Humerus: bilateral	15	6	5.7	4	1.43	1.45	0.4958
Detailed imaging site: 4.Radius: unifocal	15	4	5.7	2.7	2.11	2.18	0.2221
Detailed imaging site: 5.Radius: multifocal but only on one side	3	0	1.1	0	Inf	Inf	0.5566
Detailed imaging site: 6.Radius: bilateral	12	4	4.6	2.7	1.7	1.74	0.4322
Detailed imaging site: 7.Ulna: unifocal	8	4	3	2.7	1.11	1.11	1
Detailed imaging site: 8.Ulna: multifocal but only on one side	1	0	0.4	0	Inf	Inf	1
Detailed imaging site: 9.Ulna: bilateral	7	4	2.7	2.7	1	1	1
Detailed imaging site: 10.Hand bones: carpals, metacarpals, phalanges: unifocal	4	4	1.5	2.7	0.56	0.55	0.4689
Detailed imaging site: 11.Hand bones: carpals, metacarpals, phalanges: multifocal but only on one side	2	4	0.8	2.7	0.3	0.29	0.1959
Detailed imaging site: 12.Hand bones: carpals, metacarpals, phalanges: bilateral	3	1	1.1	0.7	1.57	1.58	1
Detailed imaging site: 13.Metaphysis, upper	47	15	17.9	10	1.79	1.96	0.0323
Detailed imaging site: 14.Epiphysis, upper	17	5	6.5	3.3	1.97	2.04	0.254
Detailed imaging site: 15.Diaphysis, upper	14	8	5.3	5.3	1	1	1
Detailed imaging site: 1.Femur: unifocal	48	40	18.3	26.7	0.69	0.61	0.0467
Detailed imaging site: 2.Femur: multifocal but only on one side	12	1	4.6	0.7	6.57	6.84	0.0372
Detailed imaging site: 3.Femur: bilateral	73	20	27.8	13.3	2.09	2.51	0.0006
Detailed imaging site: 4.Tibia: unifocal	58	22	22.1	14.7	1.5	1.65	0.0712

Detailed imaging site: 5.Tibia: multifocal but only on one side	13	2	4.9	1.3	3.77	3.91	0.0972
Detailed imaging site: 6.Tibia: bilateral	83	13	31.6	8.7	3.63	4.85	0
Detailed imaging site: 7.Fibula: unifocal	36	6	13.7	4	3.42	3.81	0.0012
Detailed imaging site: 8.Fibula: multifocal but only on one side	3	2	1.1	1.3	0.85	0.84	1
Detailed imaging site: 9.Fibula: bilateral	17	5	6.5	3.3	1.97	2.04	0.254
Detailed imaging site: 10.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: unifocal	21	2	8	1.3	6.15	6.6	0.0033
Detailed imaging site: 11.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: multifocal but only on one side	14	3	5.3	2	2.65	2.74	0.1256
Detailed imaging site: 12.Foot bones: calcaneus, talus, tarsals, metatarsals, phalanges: bilateral	30	4	11.4	2.7	4.22	4.64	0.0013
Detailed imaging site: 13.Metaphysis, lower	171	55	65	36.7	1.77	3.2	0
Detailed imaging site: 14.Epiphysis, lower	95	23	36.1	15.3	2.36	3.13	0
Detailed imaging site: 15.Diaphysis, lower	52	31	19.8	20.7	0.96	0.95	0.8985
Detailed imaging site: 16.Patella:unifocal	3	0	1.1	0	Inf	Inf	0.5566
Detailed imaging site: 17.Patella:bilateral	0	0	0	0	NA	NA	1
mandible	0	20	7.6	2	3.8	4.03	0.0234
clavicle	0	60	22.8	4.7	4.89	6.04	0
Tspine	0	45	17.1	5.3	3.21	3.66	0.0004
scapula	0	16	6.1	1.3	4.56	4.79	0.0237
sternum	0	19	7.2	0.7	10.8	11.6	0.0016
Sacrum	0	48	18.3	8	2.28	2.57	0.0054
sacroiliac	0	36	13.7	3.3	4.11	4.6	0.0005
pubis	0	17	6.5	2.7	2.42	2.52	0.1062
femur.unifocal	0	48	18.3	26.7	0.68	0.61	0.0467
femur.bi.multi	0	84	31.9	14	2.28	2.88	0.0001
tibia	0	153	58.2	24.7	2.36	4.25	0
fibula	0	56	21.3	8.7	2.46	2.85	0.0009
foot	0	65	24.7	6	4.12	5.14	0
skull	0	6	2.3	5.3	0.43	0.41	0.1544
maxilla	0	2	0.8	0.7	1.14	1.14	1
Cspine	0	12	4.6	4	1.14	1.15	1
Lspine	0	27	10.3	7.3	1.4	1.45	0.3785
ribs	0	14	5.3	4	1.33	1.35	0.639
ilium	0	30	11.4	12.7	0.9	0.89	0.7524
ischium	0	25	9.5	6.7	1.43	1.47	0.3627
Periacetabulum	0	32	12.2	7.3	1.66	1.75	0.1343
humerus	0	35	13.3	10.7	1.25	1.29	0.5342

radius	0	30	11.4	5.3	2.14	2.29	0.0505
ulna	0	16	6.1	5.3	1.14	1.15	0.8299
hand	0	9	3.4	6	0.57	0.56	0.2213
patella	0	3	1.1	0	Inf	Inf	0.5566
pelvis.exclude.sacrum	0	70	26.6	18.7	1.43	1.58	0.0722
OTHER CHARACTERISTICS OF LESIONS							
metaphysis	0	177	67.3	40.7	1.65	3	0
epiphysis	0	97	36.9	18	2.05	2.66	0.0001
diaphysis	0	59	22.4	24.7	0.91	0.88	0.6291
symmetrical	0	139	52.9	20.7	2.56	4.3	0
bonesites_bilateral	0	154	58.6	20.7	2.83	5.42	0
bilateral.or.symmetrical	0	160	60.8	22.7	2.68	5.3	0
bonesites_multifocal	0	77	29.3	18.7	1.57	1.8	0.0188
two.or.more.bone.sites	0	207	78.7	30	2.62	8.62	0
multifocal							
Imaging findings							
MRI: None	2	4	0.8	2.7	0.3	0.29	0.1852
MRI: Hyperintensity in bone marrow	217	79	82.5	52.7	1.57	4.23	0
MRI: Hyperintensity in surrounding soft tissue or periosteum	95	55	36.1	36.7	0.98	0.97	0.3745
MRI: Enhancement within bone marrow by contrast	84	55	31.9	36.7	0.87	0.81	0.0719
MRI: Enhancement within soft tissue by contrast	35	35	13.3	23.3	0.57	0.5	0.002
MRI: Hypointensity within bone marrow	13	4	4.9	2.7	1.81	1.86	0.4407
MRI: Solid mass structure	0	17	0	11.3	0	0	0
MRI: Excessive new bone formation	21	2	8	1.3	6.15	6.6	0.0105
MRI: Bone marrow infiltrate	6	12	2.3	8	0.29	0.27	0.004
MRI: Lymphadenopathy	8	8	3	5.3	0.57	0.55	0.1805
MRI: Diffusion restriction within bone marrow	2	5	0.8	3.3	0.24	0.24	0.0458
MRI: Joint effusion and/or synovial enhancement	19	31	7.2	20.7	0.35	0.3	0
MRI: Sequestrum within the bone	2	4	0.8	2.7	0.3	0.29	0.1852
MRI: Abscess	2	16	0.8	10.7	0.07	0.07	0
MRI: Geographic appearance of abnormal marrow signal (bone infarction)	0	4	0	2.7	0	0	0.0125
MRI: Other features pointing TOWARDS final diagnosis of CNO/CRMO	22	0	8.4	0	Inf	Inf	0.0001
MRI: Other features pointing AWAY FROM final diagnosis of CNO/CRMO	5	44	1.9	29.3	0.06	0.05	0
MRI: Osseous tissue occupied by solid mass structure	0	10	0	6.7	0	0	1.50E-05
MRI: Soft tissue occupied by solid mass structure	0	13	0	8.7	0	0	0
MRI: Parenchymal tissue occupied by solid mass structure	0	1	0	0.7	0	0	0.33684
MRI Favor CNO Excessive new bone formation	21	2	8	1.3	6.15	6.6	0.0105

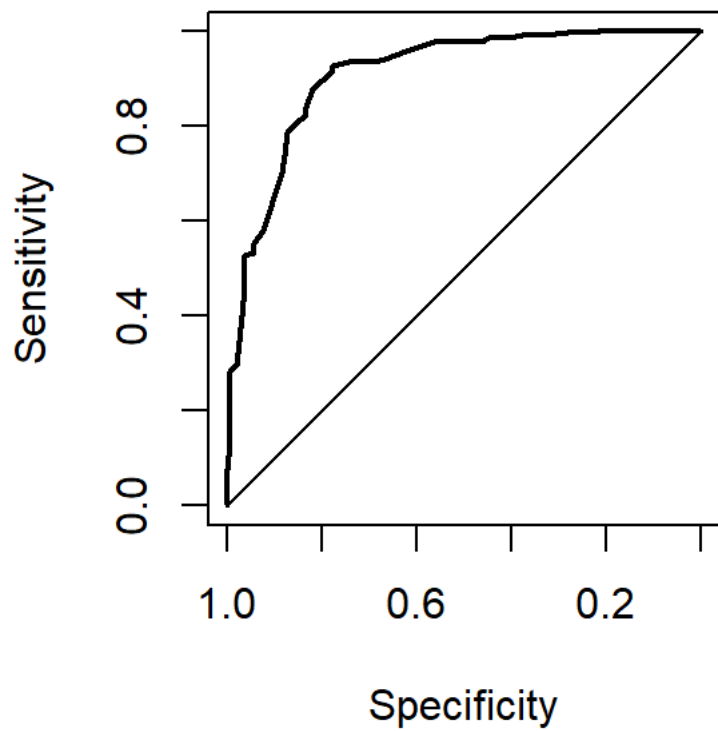
MRI Favor Mimic: mass structure OR enhancement by contrast OR marrow infiltrate OR lymphadenopathy OR abscess OR geographic appearance	16	48	6.1	32	0.19	0.14	0
MRI joints: TMJ	1	1	0.4	0.7	0.57	0.57	1
MRI joints: Intervertebral joints	0	1	0	0.7	0	0	0.3368
MRI joints: Shoulders, acromioclavicular joints, sternoclavicular joints	0	4	0	2.7	0	0	0.0125
MRI joints: Elbows	2	1	0.8	0.7	1.14	1.14	1
MRI joints: Wrists	1	1	0.4	0.7	0.57	0.57	1
MRI joints: Hips	5	7	1.9	4.7	0.4	0.39	0.1156
MRI joints: Knees	5	12	1.9	8	0.24	0.22	0.0024
MRI joints: Ankles, subtalar joints	6	2	2.3	1.3	1.77	1.79	0.7226
MRI joints: Tarsal joints	0	3	0	2	0	0	0.0376
MRI joints: MTPs, PIPs, DIPs	0	2	0	1.3	0	0	0.1129
MRI joints: Sacroiliitis	4	4	1.5	2.7	0.56	0.55	0.4506
MRI joints: Effusion in any joint	19	31	7.2	20.7	0.35	0.3	0
Xray/CT: None	25	35	9.5	23.3	0.41	0.35	0.0034
Xray/CT: Organized periosteal reaction (new bone formation)	50	16	19	10.7	1.78	1.96	0.0018
Xray/CT: Sclerosis (increased density within the bone)	90	20	34.2	13.3	2.57	3.39	0
Xray/CT: Hyperostosis or bony expansion (excessive bone formation expanding from bone)	22	9	8.4	6	1.4	1.44	0.1792
Xray/CT: Cortical thickening without bony expansion (beyond normal thickness)	15	5	5.7	3.3	1.73	1.77	0.1607
Xray/CT: Cortical bone disruption	10	23	3.8	15.3	0.25	0.22	0.0006
Xray/CT: Lytic lesion, osteolysis	75	47	28.5	31.3	0.91	0.87	0.4783
Xray/CT: Fracture lines	10	4	3.8	2.7	1.41	1.42	0.4113
Xray/CT: Soft tissue swelling	37	26	14.1	17.3	0.82	0.78	1
Xray/CT: Bone cyst with well-demarcated border	2	2	0.8	1.3	0.62	0.61	1
Xray/CT: Leukemia lines/Metaphyseal bands/Growth arrest lines	0	3	0	2	0	0	0.0691
Xray/CT: Moth eaten (ill-defined lucency within marrow but intact cortex)	6	5	2.3	3.3	0.7	0.69	0.7655
Xray/CT: Disorganized new bone formation such as onion skinning, sunburst or codman triangle	2	7	0.8	4.7	0.17	0.16	0.0358
Xray/CT: Peripherally enhanced fluid collection by contrast in CT (or rim enhancement)	0	1	0	0.7	0	0	0.4123
Xray/CT: Vertebral compression	9	2	3.4	1.3	2.62	2.67	0.1321
Xray/CT: Lymphadenopathy	3	7	1.1	4.7	0.23	0.23	0.0984
Xray/CT: Solid mass structure	0	5	0	3.3	0	0	0.0114
Xray/CT: Focal demineralization	2	5	0.8	3.3	0.24	0.24	0.1291
Xray/CT: Sequestrum within the bone	0	1	0	0.7	0	0	0.4123
Xray/CT: Abscess	2	3	0.8	2	0.4	0.4	0.4064

Xray/CT: Other features pointing TOWARDS final diagnosis of CNO/CRMO	6	0	2.3	0	Inf	Inf	0.0444
Xray/CT: Other features pointing AWAY FROM final diagnosis of CNO/CRMO	2	16	0.8	10.7	0.07	0.07	0
Xray/CT: solid mass in Osseous tissue	0	4	0	2.7	0	0	0.02811
Xray/CT: solid mass in Soft tissue	0	1	0	0.7	0	0	0.41234
Xray/CT favor CNO: new bone formation, increased density	111	33	42.2	22	1.92	2.59	0
Xray/CT favor Mimic: cortical bone disruption OR disorganized bone formation OR solid mass OR lymphadenopathy	14	35	5.3	23.3	0.23	0.18	0
Bonescan: None	7	4	2.7	2.7	1	1	0.4658
Bonescan: Increased uptake at unifocal site	41	18	15.6	12	1.3	1.36	0.1914
Bonescan: Focal increased uptake at multifocal sites	78	18	29.7	12	2.48	3.1	0.0688
Bonescan: Decreased uptake at unifocal site	0	2	0	1.3	0	0	0.0585
Bonescan: Focal decreased uptake at multifocal sites	0	1	0	0.7	0	0	0.244
Bonescan: Other features pointing TOWARDS final diagnosis of CNO/CRMO	1	0	0.4	0	Inf	Inf	1
Bonescan: Other features pointing AWAY FROM final diagnosis of CNO/CRMO	1	3	0.4	2	0.2	0.2	0.0454
Bonescan favor CNO: Focal increased uptake at multifocal sites	78	18	29.7	12	2.48	3.1	0.0688
Imaging pathology favoring CNO	179	47	68.1	31.3	2.18	4.69	0
Imaging pathology favoring Mimic	28	67	10.6	44.7	0.24	0.15	0
ESR	5% of CNO cases and 26% of mimic cases did not have ESR results						
CRP	5% of CNO cases and 21% of mimic cases did not have CRP results						
Hemoglobin (hgb)	1% of CNO cases and 8% of mimic cases did not have Hgb results						
esr >= 60	35	37	13.3	24.7	0.54	0.47	4.8E-05
crp >= 30	39	38	14.8	25.3	0.59	0.51	0.00031
ldh >= 800	0	7	0	4.7	0	0	0.00031
hgb < 10	11	31	4.2	20.7	0.2	0.17	0
plt < 250	25	36	9.5	24	0.4	0.33	3.4E-05
esr / plt ratio >= 0.2	12	26	4.6	17.3	0.26	0.23	0
At least one of: high CRP, low HGB, high ESR/PLT ratio, high LDH	51	66	19.4	44	0.44	0.31	0
ESR >= 10	201	89	76.4	59.3	1.29	2.22	1
ESR >= 20	141	76	53.6	50.7	1.06	1.13	0.02675
ESR >= 30	100	61	38	40.7	0.93	0.9	0.00817
ESR >= 40	75	50	28.5	33.3	0.86	0.8	0.00577
ESR >= 50	51	45	19.4	30	0.65	0.56	9.3E-05

ESR >= 60	35	37	13.3	24.7	0.54	0.47	4.8E-05
ESR >= 70	22	28	8.4	18.7	0.45	0.4	5.8E-05
ESR >= 80	17	23	6.5	15.3	0.42	0.38	0.0002
ESR >= 90	9	16	3.4	10.7	0.32	0.3	0.00044
CRP >= 10	89	63	33.8	42	0.81	0.71	0.00101
CRP >= 20	56	47	21.3	31.3	0.68	0.59	0.00047
CRP >= 30	39	38	14.8	25.3	0.59	0.51	0.00031
CRP >= 40	30	31	11.4	20.7	0.55	0.49	0.0008
CRP >= 50	23	23	8.7	15.3	0.57	0.53	0.00628
CRP >= 60	18	18	6.8	12	0.57	0.54	0.02219
ESR/PLT Ratio >= 0.10	81	54	30.8	36	0.86	0.79	0.00289
ESR/PLT Ratio >= 0.15	33	37	12.5	24.7	0.51	0.44	1.1E-05
ESR/PLT Ratio >= 0.20	12	26	4.6	17.3	0.26	0.23	0
ESR/PLT Ratio >= 0.25	8	15	3	10	0.3	0.28	0.00056
ESR/PLT Ratio >= 0.30	4	11	1.5	7.3	0.21	0.2	0.00059
Bone biopsy: Abundant presence of neutrophils	15	10	5.7	6.7	0.86	0.85	0.50436
Bone biopsy: Sparse presence of neutrophils	28	5	10.6	3.3	3.19	3.46	0.01844
Bone biopsy: Abundant presence of lymphocytes	27	2	10.3	1.3	7.7	8.47	0.00127
Bone biopsy: Sparse presence of lymphocytes	51	8	19.4	5.3	3.64	4.27	0.00026
Bone biopsy: Abundant presence of plasma cells	21	3	8	2	3.99	4.25	0.02392
Bone biopsy: Sparse presence of plasma cells	68	6	25.9	4	6.46	8.37	0
Bone biopsy: Presence of bone necrosis	12	7	4.6	4.7	0.98	0.98	0.80128
Bone biopsy: Presence of bone fibrosis	102	10	38.8	6.7	5.82	8.87	0
Bone biopsy: Presence of bone remodeling	50	5	19	3.3	5.7	6.81	9E-06
Bone biopsy: Presence of bone sclerosis	12	0	4.6	0	Inf	Inf	0.01009
Bone biopsy: Normal bone	11	1	4.2	0.7	6.27	6.5	0.11168
Bone biopsy: Unknown	5	0	1.9	0	Inf	Inf	0.17422
Bone biopsy: Malignancy	1	47	0.4	31.3	0.01	0.01	0
Bone biopsy: Infection	1	5	0.4	3.3	0.11	0.11	0.01619
Bone biopsy: Other	26	27	9.9	18	0.55	0.5	0.00314
Presence of adaptive immune cells and/or remodeling	143	20	54.4	13.3	4.08	7.75	0

Adjudicators disagreed with the diagnosis of 2 CNO cases and 2 mimicker cases.

Supplement S6. ROC plot of classification criteria using development cohort data*



*Score with inclusion requirement applied (AUC=.908)

Supplement S7. Typical imaging findings in CNO. A. lytic lesion on x ray; B. sclerosis on x ray; C. Hyperostosis; D. Hyperintensity signal within bone marrow.



